

**Using VAP Expanded Lipid Testing
from Atherotech to Develop
Optimal Patient Treatment Plans
(Fourth Edition)**

**Incorporating NCEP ATP-III and the
2004 Updated Guidelines**

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Introduction

Traditional lipid risk factors for atherosclerosis account for only 40% of premature cardiovascular disease⁽¹⁾. Seventy five percent of patients with myocardial infarctions have "normal" levels of LDL and HDL cholesterol⁽²⁾. Eighty percent of the patients who had an event in the landmark Framingham Study had lipid levels identical to the population that was event free⁽³⁾. It is clear that in order to stratify patient risk optimally (and to intervene to reduce that risk) information beyond the traditional lipid panel is required.

Atherotech's VAP (Vertical Auto-Profile) provides much of that missing information. Using a patented vertical ultra centrifugation technique^(4,5), the VAP test results provide all the information found in a traditional lipid panel (total cholesterol, direct measured LDL-C, HDL-C and triglycerides) along with LDL density (i.e. pattern A versus pattern B), IDL, HDL sub types, VLDL density and Lp(a). Based on the prevalence of expanded lipid abnormalities in CAD patients, the additional information provided by the VAP test can improve your ability to predict the risk of your patients developing cardiovascular disease from about 40% to more than 90%⁽⁶⁾. Atherotech also provides a number of non-lipid cardiovascular risk assessment tools, including high sensitivity C-reactive protein, homocysteine, Lp-PLA2, apo-E genotype, vitamin D, cystatin and NT-proBNP.

Traditional Lipid Risk Factors

LDL cholesterol has been and will continue to be the focus of risk reduction intervention strategies. More than 80,000 patients followed in aggregate for over 40 years in the mega-outcome studies (4S⁽⁷⁾, WOSCOPS⁽⁸⁾, CARE⁽⁹⁾, LIPID⁽¹⁰⁾, AFCAPS⁽¹¹⁾, HPS⁽¹²⁾, ASCOT⁽¹³⁾, PROVE-IT⁽¹⁴⁾, ALLIANCE⁽¹⁵⁾ and JUPITER⁽¹⁶⁾) have proven beyond a shadow of a doubt that lowering LDL levels in patients at risk for cardiovascular disease decreases the incidence of MIs and strokes and decreases all-cause mortality in both primary and secondary prevention models.

Limited fat and low cholesterol diets like the NCEP Therapeutic Lifestyle Change diet⁽¹⁷⁾ are the cornerstone for treating elevated LDL cholesterol. On a population basis these diets can be expected to reduce LDL levels about 7 to 8%⁽¹⁸⁾ but individual responses can vary widely.

The drugs of choice for lowering total LDL cholesterol are the HMG-CoA-reductase inhibitors: generic [lovastatin, simvastatin, and pravastatin], Lipitor (atorvastatin), Lescol (fluvastatin), Crestor (rosuvastatin) and Livalo (pitavastatin). These drugs, collectively referred to as "statins"⁽¹⁹⁾, can lower LDL cholesterol by as much as 50 to 60% with monotherapy⁽²⁰⁾. Niacin⁽²¹⁾, the bile acid binding resins [cholestyramine, colestipol and Welchol (colsevelam)], the fenofibrates (generic, Tricor, Lipofen, Fenofibrate and Antara), fenofibric acid (Trilipix and Fibracor) and Zetia (ezetimibe)^(22,23) also significantly lower LDL cholesterol.

HDL cholesterol has a strong inverse relationship with cardiovascular risk in

epidemiological studies. Low levels of HDL were first identified as a coronary disease risk factor in 1951⁽²⁴⁾. Data extrapolated from observational studies suggest that for each 1 milligram per deciliter increase in HDL cholesterol there is a corresponding 3 to 4% reduction in coronary heart disease risk⁽²⁵⁾. Lifestyle interventions can have a modest effect on HDL cholesterol levels: smoking cessation can raise HDL 4 to 5%⁽²⁶⁾ in patients who smoke more than one pack per day; aerobic activity can raise HDL levels⁽²⁷⁾, as can moderate alcohol intake⁽²⁸⁾. There is a strong inverse relationship between triglyceride levels and HDL levels⁽²⁹⁾. If the triglycerides are elevated (i.e. over 100 to 150 mg/dl), treatment with a fibric acid derivative [gemfibrozil, fenofibrate or fenofibric acid]⁽³⁰⁾ or niacin can result in both a reduction in triglycerides and a marked increase in HDL⁽³¹⁾. In the absence of elevated triglycerides the drugs that have shown an ability to increase HDL significantly include niacin⁽³¹⁾ (niacin up to 2 grams daily), Crestor (rosuvastatin)⁽³²⁾ at 10 mg per day, simvastatin⁽³³⁾ at 40 to 80 mg per day, fenofibric acid (Trilipix and Fibracor) and any of the fenofibrates (Tricor, Lipofen, Triglide, Antara and generic)

Elevated triglycerides have been associated with increased cardiovascular risk since 1959⁽³⁴⁾ and multiple studies have shown a near linear relationship between triglyceride concentration and coronary heart disease event rates^(35,36,37). Special populations such as diabetics⁽³⁸⁾ and post-menopausal women⁽³⁹⁾ are especially affected. Diet intervention, using a restricted fat and modest carbohydrate intake can lower triglyceride levels dramatically, as can alcohol restriction⁽⁴⁰⁾. The drugs of choice for lowering triglycerides are the fibrates [gemfibrozil, fenofibrate and fenofibric acid], niacin and omega-3-fatty acids (frequently referred to as "fish oils" available both over the counter and by prescription as Lovaza)⁽⁴¹⁾.

Additional VAP Lipid Risk Factors

LDL cholesterol is not present in the circulation as one well defined structure but rather as particles in a continuum of size and density⁽⁴²⁾. The presence of small, dense LDL quadruples the risk of heart disease compared to the same total LDL concentration present in a large, buoyant form⁽⁴³⁾. LDL size is partially genetically determined⁽⁴⁴⁾ but significant size and density shifts can occur as a result of non-genetic causes. Hypertriglyceridemia (triglyceride concentrations over 100 to 150 mg/dl)⁽⁴⁵⁾ cause a shift in LDL to a smaller, denser, more atherogenic form. Certain drugs such as non-selective beta-blockers, thiazide and loop diuretics⁽⁴⁶⁾ and insulin⁽⁴⁷⁾ cause a shift in LDL to a smaller, denser form. Other drugs, such as estrogen⁽⁴⁸⁾, have the opposite effect, shifting LDL density to a larger, more buoyant, less atherogenic form. Niacin⁽⁴⁹⁾ is the most potent drug to shift LDL to a larger more buoyant form but some of the "statins"^(50,51,52,53), especially Crestor^(54,55) (rosuvastatin) and Livalo⁽⁵⁶⁾ (pitavastatin). Zetia⁽⁵⁷⁾ (ezetimibe) and fenofibrate and fenofibric acid⁽⁵⁸⁾ are also associated with beneficial shifts in particle size.

Lp(a) is a small, dense LDL-like particle which is covalently linked to a protein resembling plasminogen⁽⁵⁹⁾. In most populations the cholesterol content of Lp(a) is estimated to be 10 times as atherogenic as LDL-C on a mg per deciliter basis⁽⁶⁰⁾, but in some ethnic groups like African Americans it does not appear to be correlated with increased CHD risk. Lp(a) levels are under strong genetic control with minimal

environmental influences⁽⁶¹⁾. There are different ways to measure Lp(a) levels. The VAP technique directly measures the actual cholesterol content of Lp(a) and acceptable levels are less than 10 mg/dl⁽⁶²⁾. Other lab procedures, which measure total particle mass (including protein), have an upper limit of normal of 30 mg/dl. Exercise, and smoking cessation have no effect on Lp(a) levels⁽⁶³⁾. Likewise, the "statins"⁽⁶⁴⁾, gemfibrozil, Zetia (ezetimibe) and bile acid binding resins⁽⁶⁵⁾ do not lower Lp(a) levels. Niacin⁽⁶⁶⁾, fenofibrate and fenofibric acid⁽⁶⁷⁾ and estrogen⁽⁶⁸⁾ can lower Lp(a). Some data suggests that aspirin⁽⁶⁹⁾ at 81 mg per day and omega-3 fatty acids⁽⁷⁰⁾ at 9 grams per day also lower Lp(a) levels. An analysis of recent studies suggests the treatment of choice for elevated Lp(a) may be to lower the LDL more aggressively^(71,72). Lp(a) appears to lose most of its predictive value of premature atherosclerosis if the total LDL concentration is below 70 mg/dl. The only drugs that can reach this LDL goal effectively with monotherapy are the high potency statins, specifically Crestor (rosuvastatin), simvastatin, Livalo (pitavastatin) and Lipitor (atorvastatin).

IDL, or intermediate density lipoprotein, represents a lipoprotein transition between VLDL and LDL particles⁽⁷³⁾. Data from a number of angiographic trials^(74,75,76), show IDL is significantly more atherogenic than LDL alone. IDL concentration is under strong genetic control⁽⁷⁷⁾ and diet and exercise have little effect on IDL levels⁽⁷⁸⁾. The combination of low dose niacin plus a low dose statin is especially effective at lowering IDL⁽⁷⁹⁾ although both drugs individually also have an effect.

It is important to note in the traditional lipid profile "LDL cholesterol concentration"⁽⁸⁰⁾ actually represents the sum of the real LDL-C, IDL-C and Lp(a)-C concentrations.

VLDL, the main lipoprotein transporting triglycerides in the fasting state in the circulation, is like LDL in that it is also present in a gradient of particle size and density⁽⁸¹⁾. Large buoyant VLDL is atherogenic by shifting LDL particle size to smaller denser forms⁽⁸²⁾ and may be prothrombotic^(83,84) but large buoyant VLDL does not directly cause atherosclerosis via foam cell transformation. The VAP test measures VLDL density and separates out VLDL3, the small dense form of VLDL. VLDL3 is directly atherogenic⁽⁸⁵⁾ and can lead to foam cell transformation and subsequent raised plaque formation⁽⁸⁶⁾. As with other types of triglyceride disorders, elevated VLDL3 levels are sensitive to diet⁽⁸⁷⁾. If diet fails to lower VLDL3 it can be treated with fibric acid derivatives⁽⁸⁸⁾ [gemfibrozil, fenofibrate and fenofibric acid], niacin⁽⁸⁹⁾ or omega-3 fatty acids.

HDL is present as five distinct sub-types in circulation: HDL2a, HDL2b, HDL2c, HDL3a and HDL3b⁽⁹⁰⁾. The cardio-protection from HDL is attributable mainly to the HDL2b subfraction⁽⁹¹⁾ and, in fact, elevated HDL3b may actually be associated with an increased risk of coronary heart disease⁽⁹²⁾. If the concentration of HDL2b is depressed there are several interventions that can raise it. Niacin at 1 to 2 gms/day will raise HDL2b by as much as 40%⁽⁹³⁾. Fibrates raise total HDL but it is exclusively the HDL3 subfraction that is increased⁽⁹⁴⁾. Crestor (rosuvastatin) is associated with a 7-10% increase in total HDL and a 15-25% increase in HDL2 at 10 mg per day⁽⁹⁵⁾. An alternative approach to low HDL2b levels is to be more aggressive in lowering LDL. (Some studies suggest that when the LDL concentration is below 60 to 70 mg/dl HDL2b

is no longer an independent risk factor for premature heart disease.) Similarly, a high total HDL secondary to HDL3b elevation is NOT cardioprotective and may likewise warrant more aggressive LDL lowering.

Additional Atherotech Non-Lipid Risk Factors

The presence of any one or more of the following non-lipid risk factors should make you seriously consider setting the NCEP LDL goal AT LEAST 30 mg% lower than the guidelines recommend.

High sensitivity C-reactive protein (hs-CRP):

Hs-CRP is a non-specific acute phase reactant produced by the liver in response to inflammatory cytokines such as Tumor Necrosis Factor-Alpha and Interleukons 1 and 6^(96,97,98). While some evidence suggests that hs-CRP may be directly involved in causing atherosclerosis⁽⁹⁹⁾, it is most useful as a marker of active vascular inflammation. Hs-CRP levels are divided into low risk (<1 mg/L), intermediate risk (between 1 and 3 mg/L) and high risk (>3 mg/L). Multiple population studies have shown that an elevated hs-CRP is a strong and independent risk factor for primary and secondary CHD events, sudden death, stroke and peripheral vascular disease^(97,99,100). The JUPITOR study showed that patients with relatively normal lipid levels but elevated hs-CRP had a significant reduction in CHD risk when treated with Crestor (rosuvastatin)⁽¹⁶⁾. Weight loss, increased physical activity and smoking cessation have been shown to reduce hs-CRP, as does any pharmacologic treatment that improves insulin sensitivity (i.e. metformin and the thiazolidinediones)⁽⁹⁹⁾. Niacin, fenofibrate and fenofibric acid, colesevalam and the statins (but not ezetimibe) have all been shown to lower hs-CRP⁽⁹⁹⁾.

Lipoprotein-associated phospholipase A2 (Lp-PLA2):

Lp-PLA2 is an enzyme responsible for the hydrolysis of oxidized phospholipids on LDL and it is a very specific marker for vascular inflammation⁽¹⁰¹⁾. It is essentially produced only in unstable atherosclerotic plaques and serum levels of Lp-PLA2 accurately reflect the total burden of active atherosclerosis⁽¹⁰²⁾. A panel of experts have defined an elevated Lp-PLA2 as a level greater than 200 ng/ml and have recommended that in the setting of an elevated Lp-PLA2 the NCEP target LDL should be reduced by an additional 30 mg%⁽¹⁰⁵⁾. Multiple studies consistently show that an Lp-PLA2 > 200 ng/ml is associated with a doubling of the risk for CHD events and strokes^(100,104). Risk for a premature event is increased 11 times if both hs-CRP and Lp-PLA2 are increased⁽¹¹⁰⁾. Any agent that beneficially effects the lipid profile will lower Lp-PLA2, including ezetimibe, statins, fenofibrate and fenofibric acid, niacin and the omega-3 fatty acids⁽¹⁰⁶⁻¹⁰⁹⁾.

Homocysteine (Hcy):

Hcy is an amino acid produced during methionine metabolism. An elevated level of Hcy was first associated with an increased risk for CAD by Wilcken in 1976⁽¹¹¹⁾.

Hyperhomocysteinemia is defined as a fasting level of Hcy greater than 15 $\mu\text{mol} / \text{L}$. Secondary causes of elevated Hcy include several genetic disorders of methionine metabolism, chronic renal failure and vitamin B deficiencies^(112,113). Lipid therapy with fibrates, niacin and resins is associated with a 20 to 55% increase in Hcy levels, while statin therapy has no effect on Hcy^(114 - 119). Hcy is a unique CHD risk factor in that a baseline elevation can predict premature CVD events, but specifically lowering the Hcy concentration does not alter baseline risk prediction. Overwhelming epidemiologic data support hyperhomocysteinemia as an independent risk factor for primary and secondary CHD events, CHD death, stroke and all cause mortality^(120 - 130). However, an even more impressive collection of studies show that lowering Hcy levels, usually with B vitamin supplements, has no effect on these risks^(131 - 137).

Elevated baseline fasting Hcy levels are useful in predicting an increased risk for premature CHD and in identifying those patients who might benefit from more aggressive management of traditional atherosclerosis risk factors such as LDL, HDL and triglycerides.

Apo-E genotype:

Apo E is a 299 amino acid polymorphic glycoprotein found on chylomicrons, VLDL, IDL and HDL^(138,139). There are 3 isoforms of the apoE gene designated $\epsilon 2$, $\epsilon 3$ and $\epsilon 4$, so there are 6 possible phenotypes – the most common being $\epsilon 3\epsilon 3$, which is considered the wild or normal variety. Because each isoform has slightly different receptor binding characteristics and enzyme modulating effects, they can influence lipoprotein metabolism and CHD risk differently^(140, 141).

Apo $\epsilon 2$ carriers have lower LDL levels and higher triglycerides compared to $\epsilon 3\epsilon 3$ ^(141 - 143). Apo $\epsilon 2$ carriers also tend to be less responsive to dietary interventions and hyper-responsive to medications that interfere with cholesterol production such as the statins, fibrates and niacin^(144,145). Apo $\epsilon 2$ carriers are also the patients who get the most cardioprotection from moderate alcohol intake^(146,147).

Apo $\epsilon 4$ carriers have higher LDL than $\epsilon 3\epsilon 3$ and it tends to be localized in the small, dense LDL Pattern B component^(139,148). Perhaps because of this apo $\epsilon 4$ carriers have a 40% greater risk CHD than $\epsilon 3\epsilon 3$ ^(149,150). Apo $\epsilon 4$ carriers have the best response to diet and drugs that effect cholesterol absorption (such as ezetimibe and plant sterols)^(151 - 153) and are poor responders to statins and fibrates^(139,154 - 156). Alcohol is not cardioprotective in apo $\epsilon 4$ carriers^(146,157 - 160). Additionally apo $\epsilon 4$ carriers have a significantly increased risk for developing Alzheimer Disease, which tends to be more severe and earlier onset than non- $\epsilon 4$ carriers^(161 - 163).

Knowledge of a patient's apo E genotype can be very helpful developing a customized treatment plan. While everyone with dyslipidemia needs dietary counseling, apo $\epsilon 4$ carriers should spend the most time with the dietitian. The initial drug of choice for lowering LDL in apo $\epsilon 2$ carriers should be a statin, but for apo $\epsilon 4$ carriers a cholesterol absorption inhibitor might be a better choice.

Vitamin D:

Vitamin D is a fat soluble vitamin made by humans through ultraviolet light activity on exposed skin. It then undergoes a series of chemical modifications until the active form, 1,25 dihydroxy-vitamin D (1,25(OH)₂D₃) is produced. Because 1,25(OH)₂D₃ has a very short half life and is present in very low concentrations, the preferred form to measure is its immediate precursor 25hydroxy-vitamin D₃ (25(OH)D₃)^(164 - 166). While there is some controversy regarding what constitutes a “normal” level, from a cardiovascular risk standpoint normal values for 25(OH)D₃ are between 30 and 50 ng/ml^(167 - 170). 25(OH)D₃ deficiency is associated with a significant, graded increased risk for primary^(171 - 173) and secondary⁽¹⁶⁷⁾ CAD events, peripheral arterial disease⁽¹⁷²⁾, stroke⁽¹⁷²⁾ and all cause mortality^(170,174).

Besides being useful in risk stratification, 25(OH)D₃ deficiency has been shown to predispose patients to statin-induced myalgias, and that once the levels were replaced 92% of the previously intolerant patients could take their statin without recurrent myalgia⁽¹⁷⁵⁾.

A typical vitamin D replacement protocol for a patient with a deficiency is 50,000 IU of vitamin D₂ po once weekly for 8 weeks. Then recheck a level – if it’s over 30 ng/ml switch to 1000 – 2000 IU vitamin D₃ po qD; if it’s still less than 30 ng/ml repeat the 50,000 units for another 8 weeks and then recheck again.

N-Terminal Fragment of B-Type of the Prohormone Natriuretic Peptide (NT-proBNP)

NT-proBNP is a neurohormone secreted mainly from cardiac monocytes in response to cardiac stress. Historically NT-proBNP has been used to stage and follow congestive heart failure^(176 - 181), but more recent information confirms that elevated levels also help stratify coronary artery disease risk^(182 - 186). A NT-proBNP less than 125 pg/ml virtually rules out the possibility of subclinical CAD or CHF^(187 - 189).

Cystatin C:

Cystatins are a super-family of cysteine peptidase inhibitors⁽¹⁹⁰⁾. Cystatin C is a low molecular weight peptidase inhibitor made by humans that has been extensively studied as a marker of renal function⁽¹⁹¹⁾ since it is cleared from circulation exclusively by glomerular filtration and tubular resorption⁽¹⁹²⁾. It is a more reliable indicator of renal function than creatinine since cystatin C concentration is not dependent on diet, age, gender or muscle mass⁽¹⁹³⁾. Cystatin C may detect mild to moderate decreases in glomerular filtration that are not evident with serum creatinine.

Increases in cystatin C levels have been associated with increased risk of CAD even in the absence of established renal disease^(194,195). Levels greater than 1 mg/L are associated with a 1.43 increase in CVD mortality⁽¹⁹⁴⁾. The mechanism by which increased cystatin C is associated with increased CHD risk is uncertain but may reflect the presence of early kidney disease⁽¹⁹⁶⁾.

USE OF THIS MONOGRAPH

This monograph will present some interventions known to reduce the traditional and advanced lipid risk factors and help you develop a customized treatment plan to minimize your patients' chances of developing or accelerating atherosclerosis. The LDL thresholds to initiate lifestyle and drug therapy used in these treatment algorithms are based on the 2001 National Cholesterol Education Program Adult Treatment Panel - III Report⁽¹⁹⁷⁾ and the 2004 ATP-III update⁽¹⁹⁸⁾. While many healthcare providers feel these guidelines are not aggressive enough, they do represent the *minimum* levels of treatment for dyslipidemia. To use this resource you must first determine your patient's NCEP defined risk category and LDL treatment threshold level. Once this is obtained go to page 14 of this monograph and combine the information from the traditional lipid panel data (provided by the VAP) with the Lp(a) level to determine which treatment guideline applies to your patient's VAP profile. Then go to that treatment guideline to fine tune your treatment plan based on LDL density, IDL level, VLDL3 level and HDL sub type.

Very High Risk Patients:

The ATP-III update in 2004 created the new category of “very high risk” – these are patients with a history of a known cardiovascular event AND one or more of the following conditions: an acute coronary syndrome, diabetes, the metabolic syndrome or multiple other risk factors. In these cases the LDL treatment goal is 70 to 100 mg%. The level of 70 mg% is considered a “therapeutic option”, with an absolute goal of less than 100 mg%.

High Risk Patients:

To establish your patient's LDL treatment threshold you must first determine if they have coronary heart disease (i.e. history of an MI, PTCA, angina), other forms of atherosclerosis (e.g. peripheral vascular disease, carotid disease, abdominal aortic aneurism) or diabetes. If any of these conditions are present your patient is considered to be at *high risk* and their LDL treatment goal is less than 100 mg%.

If your patient does not have known cardiovascular disease or diabetes you must add the number of NCEP-defined major risk factors (RFs):

Smoking

Hypertension (BP>140/90 or on treatment)

HDL < 40 mg%

Family history of premature vascular disease

Age (male over 45 or female over 55 years old)

Multiple Risk Factor Patients:

If your patient has 2 or more major risk factors (but no known cardiovascular disease or diabetes) you must calculate their estimated 10 year risk based on their Framingham Point Score (see the tables I and II that follow – **Note** that female and male patients use different risk factor tables).

If their 10 year risk is:

>20%	their LDL treatment goal is less than 100 mg% (<i>high risk, also called a CHD equivalent</i>)
10 – 20%	their LDL treatment goal is less than 100 to 130 mg% (<i>high intermediate risk</i>) less than 100 mg% is considered a therapeutic option with an absolute goal of less than 130 mg%.
<10%	their LDL treatment goal is less than 130 mg% (<i>intermediate risk</i>)

Low Risk Patients:

If your patient has 0 or 1 major risk factor, they are considered *low risk* and their LDL treatment goal is less than 160 mg%.

NOTE: This monograph contains treatment suggestions based on the most recent clinical trial and epidemiological data. These are suggestions only and each individual clinician ultimately must use their best judgement in designing a treatment plan for their individual patients. This monograph contains many references to non-FDA approved uses of medications. This monograph also contains many references to combination therapy. Please read Appendix I on page 75 for a discussion on combination therapy for dyslipidemia.

Table I

Calculating Estimated 10-Year Risk for MEN

<u>Age:</u>	<u>Points:</u>	<u>HDL (mg%):</u>	<u>Points:</u>
20 – 34	-9	>=60	-1
35 – 39	-4	50 – 59	0
40 – 44	0	40 – 49	1
45 – 49	3	<40	2
50 – 54	6		
55 – 59	8		
60 – 64	10		
65 – 69	11		
70 – 74	12		
74 – 79	13		

Total Cholesterol (mg%)	POINTS:				
	Age 20 - 39 y	Age 40 – 49 y	Age 50 – 59 y	Age 60 – 69 y	Age 70 – 79 y
<160	0	0	0	0	0
160 – 199	4	3	2	1	0
200 – 239	7	5	3	1	0
240 – 279	9	6	4	2	1
>=280	11	8	5	3	1

	POINTS:				
	Age 20 - 39 y	Age 40 – 49 y	Age 50 – 59 y	Age 60 – 69 y	Age 70 – 79 y
Nonsmoker	0	0	0	0	0
Smoker	8	5	3	1	1

Systolic BP (mm Hg)	If Untreated	If Treated
<120	0	0
120-129	0	1
130-139	1	2
140-159	1	2
>=160	2	3

Now add up the total point score and determine your male patient's 10 year percent risk for having a cardiovascular event:

Point Total	10 Year Risk (%)
<0	<1
0	1
1	1
2	1
3	1
4	1
5	2
6	2
7	3
8	4
9	5
10	6
11	8
12	10
13	12
14	16
15	20
16	25
>=17	>30

Table II
Calculating Estimated 10-Year Risk for WOMEN

<u>Age:</u>	<u>Points:</u>		
20 – 34	-7		
35 – 39	-3		
40 – 44	0	<u>HDL (mg%):</u>	<u>Points:</u>
45 – 49	3	>=60	-1
50 – 54	6	50 – 59	0
55 – 59	8	40 – 49	1
60 – 64	10	<40	2
65 – 69	12		
70 – 74	14		
74 – 79	16		

Total	POINTS:				
Cholesterol	Age	Age	Age	Age	Age
(mg%)	20 - 39 y	40 – 49 y	50 – 59 y	60 – 69 y	70 – 79 y
<160	0	0	0	0	0
160 – 199	4	3	2	1	1
200 – 239	8	6	4	2	1
240 – 279	11	8	5	3	2
>=280	13	10	7	4	2

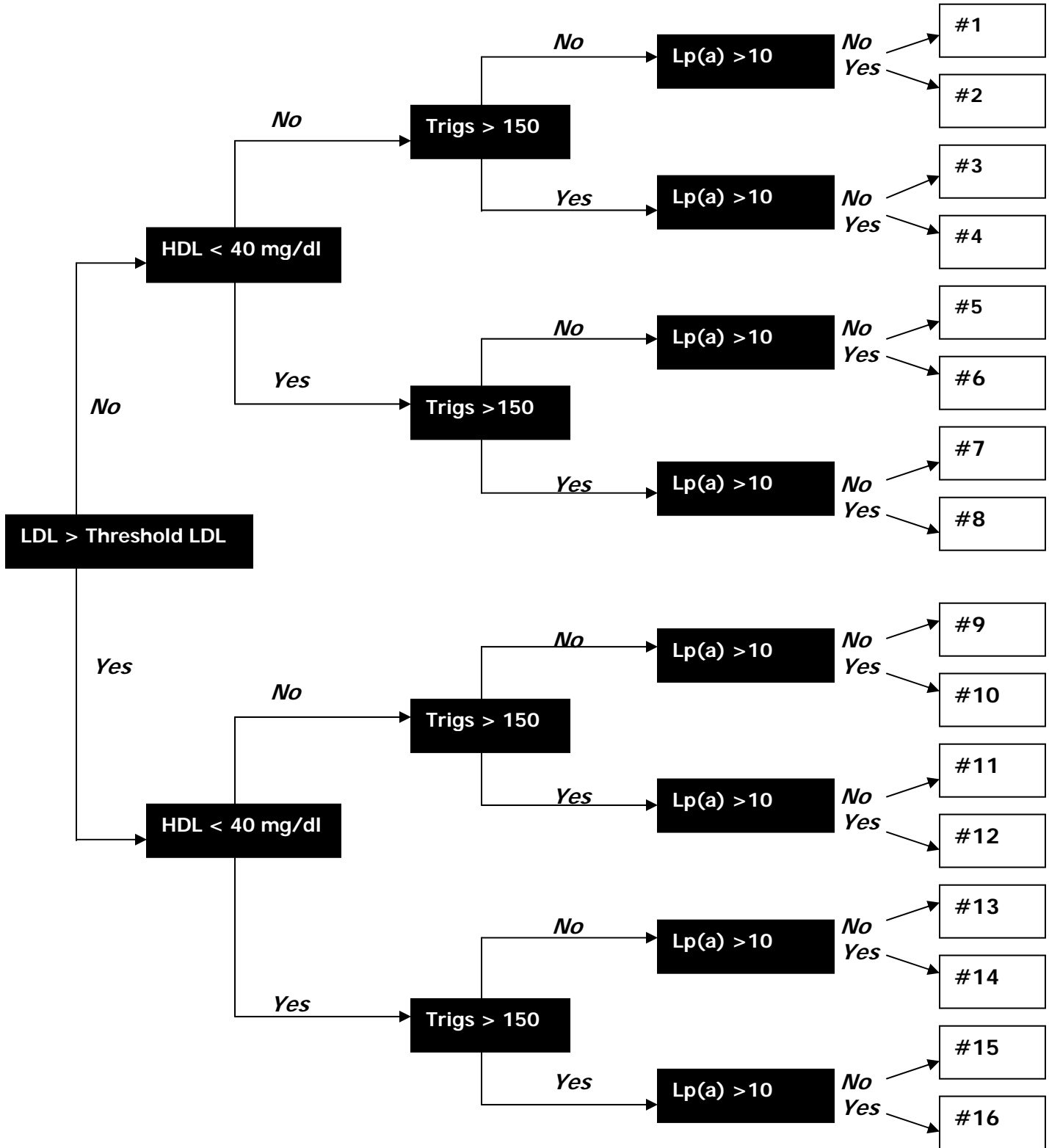
	POINTS:				
	Age	Age	Age	Age	Age
	20 - 39 y	40 – 49 y	50 – 59 y	60 – 69 y	70 – 79 y
Nonsmoker	0	0	0	0	0
Smoker	9	7	4	2	1

Systolic BP (mm Hg)	If Untreated	If Treated
<120	0	0
120-129	1	3
130-139	2	4
140-159	3	5
>=160	4	6

Now add up the total point score and determine your female patient's 10 year percent risk for having a cardiovascular event:

Point Total	10 Year Risk (%)
<9	<1
9	1
10	1
11	1
12	1
13	2
14	2
15	3
16	4
17	5
18	6
19	8
20	11
21	14
22	17
23	22
24	27
>=25	>30

Treatment Guideline



Module #1

Normal Traditional Lipid Panel

VAP PROFILE ABNORMALITIES

LDL Pattern B:

General / Low Risk

- Rule out and treat secondary causes if possible:
 1. iatrogenic: non-selective beta blockers, HCTZ, loop diuretics, steroids
 2. metabolic: diabetes / insulin resistance / metabolic syndrome
- Aggressive dietary counseling to ensure compliance with the NCEP TLC diet (i.e. dietitian referral)
- If not contraindicated use a drug that improves insulin sensitivity in diabetics (i.e. agent in the metformin or "glitazone" class)

Moderate Risk

- Same as General / Low Risk PLUS:
- Target [triglycerides] < 150 mg%
 1. with aggressive diet
 2. if diet unsuccessful consider fenofibrate or fenofibric acid and/or niacin (up to 2 grams daily) and/or omega-3 fatty acids
- If unable to shift LDL density consider lowering target [LDL] to less than 100 mg%

High Risk

- Same as General / Low Risk PLUS:
- Target [triglycerides] < 100mg%
 1. with aggressive diet
 2. if diet unsuccessful consider fenofibrate or fenofibric acid and/or niacin (up to 2 grams daily) and/or omega-3 fatty acids
- Consider specific drug therapy to shift LDL density
 1. niacin 1-2 grams per day
 2. fenofibrate or fenofibric acid
- If unable to shift LDL density consider lowering target [LDL] to < 70 mg%

Increased IDL:

General / Low Risk

- Rule out and treat secondary causes:
 1. diabetes / insulin resistance / metabolic syndrome
 2. very low fat, high carbohydrate diet

Moderate Risk

- Same as General / Low Risk PLUS:
- Drug treatment with fenofibrate or fenofibric acid if [triglycerides]>150 mg%

High Risk

- Same as General / Low Risk PLUS:
- Drug treatment with combined low dose statin and low dose niacin

Decreased HDL2:

General / Low Risk

- Rule out and treat secondary causes:
 1. metabolic: hypothyroidism, diabetes / insulin resistance / metabolic syndrome
 2. iatrogenic: androgens, HCTZ, loop diuretics, non-selective beta blockers
- Smoking cessation and aerobic activity
- Moderate alcohol consumption (equivalent of ~2 ounces pure EtOH/day) if not contraindicated

Moderate Risk

- Same as General / Low Risk

High Risk

- Same as General / Low Risk PLUS:
- Drug therapy to lower triglycerides if [triglycerides]> 150 mg%
 1. using fenofibrate or fenofibric acid and/or niacin 1-2 grams per day
- Drug therapy to raise HDL2
 1. Drug of choice: niacin 1-2 grams per day
 2. alternative: rosuvastatin (Crestor) 10 mg qD or simvastatin 40 or 80 mg qD
- If unable to raise [HDL2] consider lowering target [LDL] to less than 70 mg% preferably using rosuvastatin (Crestor) or simvastatin or a preferred statin – ezetimibe combination

Increased VLDL3:

General / Low Risk

- Rule out and correct secondary causes:
 1. metabolic: diabetes / insulin resistance / metabolic syndrome, hypothyroidism
 2. iatrogenic: oral estrogen, non-selective beta blockers, steroids, diuretics, resins, protease inhibitors
- Dietary therapy with NCEP TLC diet with additional carbohydrate restriction
- If overweight target 5-10% reduction in body weight

Moderate Risk

- Same as General / Low Risk

High Risk

- Same as General / Low Risk PLUS
- Target [triglycerides]<150 mg%
consider use of:
 1. fenofibrate or fenofibric acid &/or
 2. niacin (up to 2 grams daily) &/or
 3. omega-3-fatty acids (EPA+DHA to total 4grams) per day

Module #2

Increased Lp(a)

First Priority: Lower Lp(a)

If patient is an Afro-American without premature family history no treatment needed

Rule out and treat secondary causes if possible:

- factitious: acute phase response
- metabolic: hypothyroidism, microalbuminuria / proteinuria in diabetes
 1. thyroid hormone replacement to normalize TSH if hypothyroid
 2. ACE / ARB therapy in diabetics with microalbuminuria / proteinuria

Lifestyle / non-pharmacological intervention:

- moderate alcohol consumption (equivalent of ~2 ounces pure EtOH per day) if not contraindicated
- aspirin 81 mg qD if not contraindicated
- restriction of dietary trans-fatty acids

Drug therapy:

- niacin (up to 2 grams daily) *&/or*
- omega-3-fatty acids (EPA+DHA to total 4grams) per day *&/or*
- fenofibrate or fenofibric acid
- Alternative approach to lowering [Lp(a)] is to lower the [LDL] below current NCEP guidelines *{Lp(a) loses predictive value if [LDL]<70 mg%}*

If the patient is on a statin consider the use of rosuvastatin (Crestor), pitavastatin (Livalo), simvastatin or pravastatin which do not raise [Lp(a)]

VAP PROFILE ABNORMALITIES

LDL Pattern B:

General / Low Risk

- Rule out and treat secondary causes if possible:
 1. iatrogenic: non-selective beta blockers, HCTZ, loop diuretics, steroids
 2. metabolic: diabetes / insulin resistance / metabolic syndrome
- Aggressive dietary counseling to ensure compliance with the NCEP TLC diet (i.e. dietitian referral)
- If not contraindicated use a drug that improves insulin sensitivity in diabetics (i.e. agent in the metformin or “glitizone” class)

Moderate Risk

- Same as General / Low Risk PLUS:
 1. Target [triglycerides]<150 mg%
 - with aggressive diet
 - if diet unsuccessful consider fenofibrate or fenofibric acid and/or niacin (up to 2 grams daily) and/or Omega-3 fatty acids *{all of which can also lower Lp(a)}*
 2. If unable to shift LDL density consider lowering target [LDL] to less than 100 mg%

When selecting a statin consider that rosuvastatin (Crestor), pitavastatin (Livalo), simvastatin and pravastatin are the only ones that do not cause a secondary increase in Lp(a)

High Risk

- Same as General / Low Risk PLUS
- Consider specific drug therapy to shift LDL density
 1. niacin 1-2 grams per day *{can also lower Lp(a)}*
 2. fenofibrate or fenofibric acid *{can also lower Lp(a)}*

Increased IDL:

General / Low Risk

- Rule out and treat secondary causes:
 1. diabetes / insulin resistance / metabolic syndrome
 2. a very low fat, high carbohydrate diet

Moderate Risk

- Same as General / Low Risk PLUS:
- Drug treatment with fenofibrate or fenofibric acid if [triglycerides]>150 mg% *{can also lower Lp(a)}*

High Risk

- Same as General / Low Risk PLUS:
- Drug treatment with combined low dose statin and low dose niacin *{can also lower Lp(a)}*
 - When selecting a statin be aware that the only ones that do not raise Lp(a) are rosuvastatin (Crestor), pitavastatin (Livalo), simvastatin and pravastatin

Decreased HDL2:

General / Low Risk

- Rule out and treat secondary causes:
 1. metabolic: hypothyroidism, diabetes / insulin resistance / metabolic syndrome
 2. iatrogenic: androgens, HCTZ, non-selective beta blockers
- Smoking cessation and increased aerobic activity
- Especially strong reason to consider moderate alcohol consumption (equivalent of ~2 ounces pure EtOH/day) if not contraindicated *{can also lower Lp(a)}*

Moderate Risk

- Same as General / Low Risk

High Risk

- Same as General / Low Risk PLUS:
- Drug therapy to lower triglycerides if [triglycerides] > 150 mg%
 1. Using fenofibrate or fenofibric acid and/or niacin 1-2 grams per day *{both can also lower Lp(a)}*
- Drug therapy to specifically raise HDL2
 1. Drug of choice: niacin 1-2 grams per day *{can also lower Lp(a)}*
 2. Alternative: rosuvastatin (Crestor) 10 mg qD or simvastatin 40 or 80 mg qD
- If unable to raise [HDL2] consider lowering target [LDL] less than 70 mg%
 1. use statins {preferably rosuvastatin (Crestor), pitavastatin (Livalo), simvastatin or pravastatin which are Lp(a) neutral} or a preferred statin / ezetimibe (Zetia) combination

Increased VLDL3:

General / Low Risk

- Rule out and correct secondary causes:
 1. metabolic: diabetes / insulin resistance / metabolic syndrome, hypothyroidism
 2. iatrogenic: oral estrogen, non-selective beta blockers, steroids, diuretics, resins
- Dietary therapy with NCEP TLC diet with additional carbohydrate
- If overweight target 5-10% reduction in body weight

Moderate Risk

- Same as General / Low Risk

High Risk

- Same as General / Low Risk PLUS
 - Target [triglycerides]<150 mg% {*all these agents can also lower Lp(a)*}
- consider use of:
1. fenofibrate or fenofibric acid
 2. niacin (up to 2 grams daily) &/or
 3. omega-3-fatty acids (EPA+DHA to total 4grams) per day

Module #3

Increased Triglycerides

First Priority: Lower Triglycerides

Rule out and treat secondary causes if possible:

- factitious: non-fasting specimen
- metabolic: hypothyroidism, diabetes / insulin resistance / metabolic syndrome, proteinuria / nephrotic syndrome
- iatrogenic: estrogen (oral), non-selective beta blockers, diuretics, resins, steroids, protease inhibitors, alcohol

Dietary therapy: NCEP TLC diet with additional carbohydrate restriction & alcohol avoidance

-if overweight target 5 to 10% reduction in body weight

If drug therapy needed:

- Drug of choice - fibrates
 1. fenofibrate or fenofibric acid
 2. gemfibrozil
- Alternative agents:
 1. niacin (up to 2 grams daily) &/or
 2. omega-3-fatty acids (EPA+DHA to total 4grams) per day&/or
 3. statins {especially rosuvastatin (Crestor) , atorvastatin (Lipitor) or pitavastatin (Livalo)}

VAP PROFILE ABNORMALITIES

LDL Pattern B:

General / Low Risk

- Rule out and treat secondary causes if possible:
 1. iatrogenic: non-selective beta blockers, HCTZ, loop diuretics, steroids
 2. metabolic: diabetes / insulin resistance / metabolic syndrome
- Aggressive dietary counseling to ensure compliance with the NCEP TLC diet (i.e. dietitian referral)
- If not contraindicated use a drug that improves insulin sensitivity in diabetics (i.e. agent in the metformin or "glitazone" class)

Moderate Risk

Same as General / Low Risk PLUS-

- Target triglycerides < 150 mg%
- If unable to shift LDL density consider lowering target LDL to less than 100 mg%

High Risk

Same as General / Low Risk PLUS

- Target triglycerides < 100mg%

Consider specific drug therapy to shift LDL density

- niacin 1-2 grams per day *{will also lower triglycerides}*
- fenofibrate or fenofibric acid *{will also lower triglycerides}*

Increased IDL:

General / Low Risk

- Rule out and treat secondary causes:
 1. diabetes / insulin resistance / metabolic syndrome
 2. a very low fat, high carbohydrate diet

Moderate Risk

- Same as General / Low Risk PLUS:
Drug treatment with fenofibrate or fenofibric acid to get triglycerides < 150 mg%
{will also lower triglycerides}

High Risk

- Same as General / Low Risk PLUS:
Drug treatment with combined low dose statin and low dose niacin *{will also lower triglycerides}*

Decreased HDL2:

General / Low Risk

- Rule out and treat secondary causes:
 1. metabolic: hypothyroidism, diabetes / insulin resistance / metabolic syndrome
 2. iatrogenic: androgens, HCTZ, loop diuretics, non-selective beta blockers
- If possible correct triglyceride disorder before using drug therapy to specifically raise HDL2
- Smoking cessation
- Aerobic activity
- AVOID alcohol consumption in setting of increased triglycerides

Moderate Risk

- Same as General / Low Risk

High Risk

- Same as General / Low Risk PLUS:
- Drug therapy to raise HDL2
 1. Drug of choice: niacin 1-2 grams per day *{will also lower triglycerides}*
 2. alternative: rosuvastatin (Crestor) 10 mg qD or simvastatin 40 or 80 mg qD *{will also lower triglycerides}*
- If unable to raise [HDL2] consider lowering target [LDL] less than 70 mg%

Increased VLDL3:

General / Low Risk

See treatment for lowering total triglycerides (see "First Priority" - this Module)

- Target [triglycerides] <150 mg%

Moderate Risk

- Same as General / Low Risk

High Risk

- Same as General / Low Risk PLUS
Target [triglycerides] <100 mg%

Module #4

Increased Triglycerides & Lp(a)

First Priority: Lower Triglycerides

- Rule out and treat secondary causes if possible:
 1. factitious: non-fasting specimen
 2. metabolic: hypothyroidism, diabetes / insulin resistance / metabolic syndrome, proteinuria / nephrotic syndrome
 3. iatrogenic: estrogen (oral), non-selective beta blockers, diuretics, resins, steroids, protease inhibitors, alcohol
- Dietary therapy: NCEP TLC diet with additional carbohydrate restriction & alcohol avoidance if overweight target 5 to 10% reduction in body weight
- If drug therapy needed:
 1. Drug of choice-fibrates
 - fenofibrate or fenofibric acid *{also lowers Lp(a)}*
 - gemfibrozil
 2. Alternative agents:
 - niacin (up to 2 grams daily) *{also lowers Lp(a)}*
 - omega-3-fatty acids (EPA+DHA to total 4grams) per day *{also lowers Lp(a)}*
 - statins
 - when selecting statins consider that only rosuvastatin (Crestor), pitavastatin (Livalo), simvastatin and pravastatin are Lp(a) neutral – all other statins raise Lp(a) by 10 to 33%

Second Priority: Lower Lp(a)

- If patient is an Afro-American without premature family history no treatment needed
- Rule out and treat secondary causes if possible:
 1. factitious: acute phase response
 2. metabolic: hypothyroidism, microalbuminuria / proteinuria in diabetes
 - thyroid hormone replacement to normalize TSH if hypothyroid
 - ACE / ARB therapy in diabetics with microalbuminuria / proteinuria
- Lifestyle / non-pharmacological intervention:
 1. aspirin 81 mg qD if not contraindicated
 2. restriction of dietary trans-fatty acids
- AVOID alcohol in setting of elevated triglycerides

- Drug therapy:
 1. niacin (up to 2 grams daily) *{also lowers triglycerides}*
 2. omega-3-fatty acids (EPA+DHA to total 4grams) per day *{also lowers triglycerides}*
 3. fenofibrate or fenofibric acid *{also lowers triglycerides}*
- Alternative approach to specifically lowering [Lp(a)] is to lower the [LDL] below current NCEP guidelines *{Lp(a) loses predictive value if [LDL]<70 mg%}*
 - When selecting a statin consider that rosuvastatin (Crestor), pitavastatin (Livalo), simvastatin and pravastatin are the only ones that do not cause a secondary increase in Lp(a)

VAP PROFILE ABNORMALITIES

LDL Pattern B:

General / Low Risk

- Rule out and treat secondary causes if possible:
 1. iatrogenic: non-selective beta blockers, HCTZ, loop diuretics, steroids
 2. metabolic: diabetes / insulin resistance / metabolic syndrome
- Aggressive dietary counseling to ensure compliance with the NCEP TLC diet (i.e. dietitian referral)
- If not contraindicated use a drug that improves insulin sensitivity in diabetics (i.e. agent in the metformin or "glitazone" class)

Moderate Risk

- Same as General / Low Risk PLUS-
- Target [triglycerides]<150 mg%
- If unable to shift LDL density consider lowering target [LDL] to less than 100 mg%

High Risk

- Same as General / Low Risk PLUS
- Target triglycerides< 100mg%
- Consider specific drug therapy to shift LDL density
 - niacin 1-2 grams per day *{will also lower triglycerides and Lp(a)}*
 - fenofibrate or fenofibric acid *{will also lower triglycerides and Lp(a)}*

Increased IDL:

General / Low Risk

- Rule out and treat secondary causes:
 1. diabetes / insulin resistance / metabolic syndrome
 2. a very low fat, high carbohydrate diet

Moderate Risk

- Same as General / Low Risk

High Risk

- Same as General / Low Risk PLUS:

Drug treatment with combined low dose statin and low dose niacin *{will also lower triglycerides and Lp(a)}*

 - when selecting a statin consider that only rosuvastatin (Crestor), pitavastatin (Livalo), simvastatin and pravastatin do not cause a secondary increase in Lp(a)

Decreased HDL2:

General / Low Risk

- Rule out and treat secondary causes:
 1. metabolic: hypothyroidism, diabetes / insulin resistance / metabolic syndrome
 2. iatrogenic: androgens, HCTZ, loop diuretics, non-selective beta blockers
- Smoking cessation
- Aerobic activity

Moderate Risk

- Same as General / Low Risk PLUS:
- Drug therapy to lower triglycerides if [triglycerides]>150 mg%

High Risk

- Same as General / Low Risk PLUS:
- Target [triglycerides]< 100 mg%
- Drug therapy to specifically raise HDL2
 1. Drug of choice: niacin 1-2 grams per day *{will also lower Lp(a) and triglycerides}*
 2. alternative: rosuvastatin (Crestor) 10 mg qD or simvastatin 40 or 80 mg qD *{will also lower triglycerides}*
- If unable to raise [HDL2] consider lowering target [LDL] to below 70 mg%

Increased VLDL3:

General / Low Risk

- Treat elevated triglycerides as outlined in "First Priority" - this module
Target [triglyceride]< 150mg%

Moderate Risk

- Same as General / Low Risk

High Risk

- Same as General / Low Risk PLUS
Target [triglycerides]<100 mg%

Module #5

Decreased HDL

First Priority: Raise HDL

Rule out and treat secondary causes if possible

- metabolic: diabetes / insulin resistance / metabolic syndrome, hypothyroidism
- iatrogenic: androgens, HCTZ, non-selective beta blockers

Target [total HDL] > 40 mg% in men / >50 mg% in women

Lifestyle interventions:

- smoking cessation
- aerobic exercise
- modest alcohol intake (equivalent of ~2 ounces pure EtOH per day) if not contraindicated

Drug therapy to raise HDL:

- drug of choice: niacin 1 to 2 grams per day
- alternative: rosuvastatin (Crestor) 10 mg qD, simvastatin 40 or 80 mg qD and/or fenofibrate or fenofibric acid

In high risk patients unresponsive to efforts to raise HDL consider lowering [LDL] to below NCEP target

VAP PROFILE ABNORMALITIES

LDL Pattern B:

General / Low Risk

- Rule out and treat secondary causes if possible:
 1. iatrogenic: non-selective beta blockers, HCTZ, loop diuretics, steroids
 2. metabolic: diabetes / insulin resistance / metabolic syndrome
- Aggressive dietary counseling to ensure compliance with the NCEP TLC diet (i.e. dietitian referral)
- If not contraindicated use a drug that improves insulin sensitivity in diabetics (i.e. agent in the metformin or "glitazone" class)

Moderate Risk

- Same as General / Low Risk PLUS:
- Target [triglycerides] <150 mg% with aggressive diet
 1. If diet unsuccessful consider fenofibrate or fenofibric acid and/or niacin (up to 2 grams daily) *{will also raise HDL}*

If unable to shift LDL density consider lowering target [LDL] to less than 100 mg%

High Risk

- Same as General / Low Risk PLUS:
- Target [triglycerides] < 100mg%
- Consider specific drug therapy to shift LDL density
 1. niacin 1-2 grams per day *{will also raise HDL}*
 2. fenofibrate or fenofibric acid *{will also raise HDL}*

Increased IDL:**General / Low Risk**

- Rule out and treat secondary causes:
 - diabetes / insulin resistance / metabolic syndrome
 - a very low fat, high carbohydrate diet

Moderate Risk

- Same as General / Low Risk PLUS:
Drug treatment with fenofibrate or fenofibric acid if [triglycerides] >150 mg% *{will also raise HDL}*

High Risk

- Same as General / Low Risk PLUS: Drug treatment with combined low dose statin and low dose niacin *{will also raise HDL}*

Decreased HDL2:**General / Low Risk**

- Same approach as for decreased total HDL as outlined in "First Priority" - this module

Moderate Risk

- Same as General / Low Risk PLUS:
- Drug therapy to lower triglycerides if [triglycerides] >150 mg%

High Risk

- Same as General / Low Risk PLUS:
- Drug therapy to lower triglycerides if [triglycerides]> 100 mg%
- If unable to raise [HDL2] consider lowering target [LDL] to less than 70 mg%

Increased VLDL3:

General / Low Risk

- Rule out and correct secondary causes:
 1. metabolic: diabetes / insulin resistance / metabolic syndrome, hypothyroidism
 2. iatrogenic: oral estrogen, non-selective beta blockers, steroids, diuretics, resins, protease inhibitors
- Dietary therapy with NCEP TLC diet with additional carbohydrate restriction
- If overweight target 5-10% reduction in body weight

Moderate Risk

- Same as General / Low Risk

High Risk

- Same as General / Low Risk PLUS:
- Target [triglycerides]<100 mg%
consider use of:
 1. fenofibrate or fenofibric acid *{will also raise HDL}* &/or
 2. niacin (up to 2 grams daily) *{will also raise HDL}* &/or
 3. omega-3-fatty acids (EPA+DHA to total 4grams) per day

Module #6

Decreased HDL & Increased Lp(a)

First Priority: Raise HDL

Rule out and treat secondary causes if possible

- metabolic: diabetes / insulin resistance / metabolic syndrome, hypothyroidism
- iatrogenic: androgens, HCTZ, loop diuretics, non-selective beta blockers

Target [total HDL] > 45 mg% in men / >55mg% in women

Lifestyle interventions:

- smoking cessation
- aerobic exercise
- strong reason to consider modest alcohol intake (equivalent of ~2 ounces pure EtOH per day) if not contraindicated *{can also lower Lp(a)}*

Drug therapy to raise HDL:

- drug of choice: niacin 1 to 2 grams per day *{can also lower Lp(a)}*
- alternative: rosuvastatin (Crestor) 10 mg qD or simvastatin 40 or 80 mg qD and/or fenofibrate or fenofibric acid *{can also lower Lp(a)}*

In high risk patients unresponsive to efforts to raise HDL consider lowering [LDL] to below NCEP target

Second Priority: Lower Lp(a)

If patient is an Afro-American without premature family history no treatment needed

Rule out and treat secondary causes if possible:

- factitious: acute phase response
- metabolic: hypothyroidism, microalbuminuria / proteinuria in diabetes
 1. thyroid hormone replacement to normalize TSH if hypothyroid
 2. ACE / ARB therapy in diabetics with microalbuminuria / proteinuria

Lifestyle / non-pharmacological intervention:

- aspirin 81 mg qD if not contraindicated
- moderate alcohol consumption (equivalent of 2 oz. EtOH per day) if not contra-indicated
- restriction of dietary trans-fatty acids

Drug therapy:

- niacin (up to 2 grams daily) *{will also raise HDL}*
- omega-3-fatty acids (EPA+DHA to total 4grams) per day
- fenofibrate or fenofibric acid *{will also raise HDL}*

Alternative approach to specifically lowering [Lp(a)] is to lower the [LDL] below current NCEP guidelines *{Lp(a) loses predictive value if [LDL] < 70 mg%}*

- when selecting a statin consider that only rosuvastatin (Crestor), pitavastatin (Livalo), simvastatin and pravastatin do not cause a secondary increase in Lp(a)

VAP PROFILE ABNORMALITIES

LDL Pattern B:

General / Low Risk

- Rule out and treat secondary causes if possible:
 1. iatrogenic: non-selective beta blockers, HCTZ, loop diuretics, steroids
 2. metabolic: diabetes / insulin resistance / metabolic syndrome
- Aggressive dietary counseling to ensure compliance with the NCEP TLC diet (i.e. dietitian referral)
- If not contraindicated use a drug that improves insulin sensitivity in diabetics (i.e. agent in the metformin or "glitazone" class)

Moderate Risk

- Same as General / Low Risk PLUS-
Target [triglycerides] < 150 mg%
 1. with aggressive diet
 2. if diet unsuccessful consider fenofibrate or fenofibric acid and/or niacin (up to 2 grams daily) *{both will also raise HDL and lower Lp(a)}*
- If unable to shift LDL density consider lowering target [LDL] to less than 100 mg%

High Risk

- Same as General / Low Risk PLUS
Target [triglycerides] < 100mg%
 1. with aggressive diet
 2. if diet unsuccessful consider fenofibrate or fenofibric acid and/or niacin (up to 2 grams daily) *{both will also raise HDL and lower Lp(a)}*
- Consider specific drug therapy to shift LDL density
 1. niacin 1-2 grams per day *{will also raise HDL and lower Lp(a)}*
 2. fenofibrate or fenofibric acid *{will also raise HDL and lower Lp(a)}*

Increased IDL:

General / Low Risk

- Rule out and treat secondary causes:
 1. diabetes / insulin resistance / metabolic syndrome
 2. a very low fat, high carbohydrate diet

Moderate Risk

- Same as General / Low Risk PLUS:
- Drug treatment with fenofibrate or fenofibric acid if [triglycerides]>150 mg% *{will also raise HDL and lower Lp(a)}*

High Risk

- Same as General / Low Risk PLUS:
- Drug treatment with combined low dose statin and low dose niacin *{will also raise HDL and will usually lower Lp(a)}*
 - When choosing a statin consider that only rosuvastatin (Crestor), pitavastatin (Livalo), simvastatin and pravastatin do not cause a secondary increase in Lp(a)

Decreased HDL2:

General / Low Risk

- Same approach as for decreased total HDL as discussed in "First Priority" - this module

Moderate Risk

- Same as General / Low Risk

High Risk

- Same as General / Low Risk PLUS:
Drug therapy to lower triglycerides if [triglycerides]> 100 mg%

Increased VLDL3:

General / Low Risk

- Rule out and correct secondary causes:
 1. metabolic: diabetes / insulin resistance / metabolic syndrome, hypothyroidism
 2. iatrogenic: oral estrogen, non-selective beta blockers, steroids, diuretics, resins, protease inhibitors
- Dietary therapy with NCEP TLC diet with additional carbohydrate restriction
- If overweight target 5-10% reduction in body weight

Moderate Risk

- Same as General / Low Risk PLUS
Target [triglycerides] < 150 mg%

High Risk

- Same as General / Low Risk PLUS target [triglycerides] < 100 mg%

consider the use of:

1. fenofibrate or fenofibric acid *{will also raise HDL and lower Lp(a)}*
2. niacin (up to 2 grams daily) *{will also raise HDL and lower Lp(a)}*
3. omega-3-fatty acids (EPA+DHA to total 4grams) per day *{can also lower Lp(a)}*

Module #7

Decreased HDL & Increased Triglycerides

First Priority: Lower Triglycerides

Rule out and treat secondary causes if possible:

- factitious: non-fasting specimen
- metabolic: hypothyroidism, insulin resistance / metabolic syndrome / diabetes, proteinuria / nephrotic syndrome
- iatrogenic: estrogen (oral), non-selective beta blockers, diuretics, resins, steroids, protease inhibitors, alcohol

Dietary therapy: NCEP TLC diet with additional carbohydrate restriction & alcohol avoidance

- if overweight target 5 to 10% reduction in body weight

If drug therapy needed:

- Drug of choice-fibrates *{will also raise HDL}*
 1. fenofibrate or fenofibric acid
 2. gemfibrozil
- Alternative agents:
 1. niacin (up to 2 grams daily) *{will also raise HDL}*
 2. omega-3-fatty acids (EPA+DHA to total 4grams) per day
 3. statins (especially rosuvastatin (Crestor) and simvastatin) *{will also raise HDL}*

Second Priority: Raise HDL

Rule out and treat secondary causes if possible

- metabolic: diabetes / insulin resistance / metabolic syndrome, hypothyroidism
- iatrogenic: androgens, HCTZ, non-selective beta blockers
- Target [total HDL] > 40 mg% in men / >50 mg% in women

Lifestyle interventions:

- smoking cessation
- aerobic exercise

If possible defer drug treatment to specifically raise HDL until triglyceride disorder corrected

AVOID alcohol use in the setting of elevated triglycerides

Drug therapy to raise HDL:

- drug of choice: niacin 1 to 2 grams per day *{will also lower triglycerides}*
- alternative:
 - rosuvastatin (Crestor) 10 mg qD *{also lowers triglycerides}*
 - simvastatin 40 or 80 mg qD *{also lowers triglycerides}*
 - fenofibrate or fenofibric acid *{also lowers triglycerides}*

In high risk patients unresponsive to efforts to raise HDL consider lowering [LDL] to below NCEP target

VAP PROFILE ABNORMALITIES

LDL Pattern B:

General / Low Risk

- Rule out and treat secondary causes if possible:
 1. iatrogenic: non-selective beta blockers, HCTZ, loop diuretics, steroids
 2. metabolic: diabetes / insulin resistance / metabolic syndrome
- Aggressive dietary counseling to ensure compliance with the NCEP TLC diet (i.e. dietitian referral)
- If not contraindicated use a drug that improves insulin sensitivity in diabetics (i.e. agent in the metformin or "glitazone" class)

Moderate Risk

- Same as General / Low Risk PLUS-
Target [triglycerides]<150 mg%
 1. with aggressive diet
 2. if diet unsuccessful consider fenofibrate or fenofibric acid and/or niacin (up to 2 grams daily) *{both will also lower triglycerides and raise HDL}*
 3. if unable to shift LDL density consider lowering target [LDL] to below 100 mg%

High Risk

- Same as General / Low Risk PLUS
Target [triglycerides]< 100mg%
 1. with aggressive diet
 2. if diet unsuccessful consider fenofibrate or fenofibric acid and/or niacin (up to 2 grams daily) *{both will also lower triglycerides and raise HDL}*
- Consider specific drug therapy to shift LDL density
 1. niacin 1-2 grams per day *{will also raise HDL and lower triglycerides}*
 2. fenofibrate or fenofibric acid *{will also raise HDL and lower triglycerides}*

Increased IDL:

General / Low Risk

- Rule out and treat secondary causes:
 1. Diabetes / insulin resistance / metabolic syndrome
 2. A very low fat, high carbohydrate diet

Moderate Risk

- Same as General / Low Risk PLUS:
- Drug treatment with fenofibrate or fenofibric acid if [triglycerides]> 150 mg% *{will also lower triglycerides and raise HDL}*

High Risk

- Same as General / Low Risk PLUS:
- Drug treatment with combined low dose statin and low dose niacin *{will also lower triglycerides and raise HDL}*

Decreased HDL2:

General / Low Risk

- Same approach as for decreased total HDL as outlined under "Second Priority" - this module

Moderate Risk

- Same as General / Low Risk PLUS:
- Drug therapy to lower triglycerides if [triglycerides]>150 mg%

High Risk

- Same as General / Low Risk PLUS:
- Drug therapy to lower triglycerides if [triglycerides]> 100 mg%

Increased VLDL3:

General / Low Risk

- Same approach as for lowering total triglycerides as outlined under "First Priority" - this module

Moderate Risk

- Same as General / Low Risk PLUS:
- Target [triglycerides]< 150 mg%

High Risk

- Same as General / Low Risk PLUS:
- Target [triglycerides]<100 mg%

Module #8

Decreased HDL & Increased Triglycerides & Lp(a)

First Priority: Lower Triglycerides

Rule out and treat secondary causes if possible:

- factitious: non-fasting specimen
- metabolic: hypothyroidism, diabetes / insulin resistance / metabolic syndrome, proteinuria / nephrotic syndrome
- iatrogenic: estrogen (oral), non-selective beta blockers, diuretics, resins, steroids, protease inhibitors, alcohol

Dietary therapy: NCEP TLC diet with additional carbohydrate restriction & alcohol avoidance

- if overweight target 5 to 10% reduction in body weight

If drug therapy needed: drugs of choice-fibrates

- fenofibrate or fenofibric acid *{will also raise HDL and lower Lp(a)}*
- gemfibrozil *{will also raise HDL}*

Alternative agents:

- niacin (up to 2 grams daily) *{will also raise HDL and lower Lp(a)}*
- omega-3-fatty acids (EPA+DHA to total 4grams) per day *{can also lower Lp(a)}*
- statins *{with simvastatin and rosuvastatin will also raise HDL}*
 - When selecting a statin consider that rosuvastatin (Crestor), pitavastatin (Livalo), simvastatin and pravastatin are the only ones that do not cause a secondary increase in Lp(a)

Second Priority: Raise HDL

Rule out and treat secondary causes if possible

- metabolic: diabetes / insulin resistance / metabolic syndrome, hypothyroidism
- iatrogenic: androgens, HCTZ, non-selective beta blockers
- Target [total HDL] > 45 mg% in men / >55mg% in women

Lifestyle interventions:

- smoking cessation
- aerobic exercise
- AVOID alcohol use in setting of high triglycerides

If possible defer specific drug therapy to raise HDL until triglyceride disorder corrected

Drug therapy to raise HDL:

- drug of choice: niacin 1 to 2 grams per day *{will also lower triglycerides and Lp(a)}*
- alternative:
 1. rosuvastatin (Crestor) 10 mg qD *{will also lower triglycerides}*
 2. simvastatin 40 or 80 mg qD *{will also lower triglycerides}*
 3. fenofibrate or fenofibric acid *{will also lower triglycerides and Lp(a)}*

In high risk patients unresponsive to efforts to raise HDL consider lowering [LDL] to below NCEP target

- when selecting a statin consider that rosuvastatin (Crestor), pitavastatin (Livalo), simvastatin and pravastatin are the only ones that do not cause a secondary increase in Lp(a)

Third Priority: Lower Lp(a)

If patient is an Afro-American without premature family history no treatment needed

Rule out and treat secondary causes if possible:

- factitious: acute phase response
- metabolic: hypothyroidism, microalbuminuria / proteinuria in diabetes
 - thyroid hormone replacement to normalize TSH if hypothyroid
 - ACE / ARB therapy in diabetics with microalbuminuria / proteinuria

Lifestyle / non-pharmacological intervention:

- aspirin 81 mg qD if not contraindicated
- restriction of dietary trans-fatty acids
- Avoid alcohol use in the setting of elevated triglycerides

Drug therapy:

- niacin (up to 2 grams daily) *{will also raise HDL and lower triglycerides}*
- omega-3-fatty acids (EPA+DHA to total 4grams) per day *{also lowers triglycerides}*
- fenofibrate or fenofibric acid *{will also raise HDL and lowers triglycerides}*

Alternative approach to specifically lowering [Lp(a)] is to lower the [LDL] below current NCEP guidelines *{Lp(a) loses predictive value if [LDL] < 70 mg%}*

- when selecting a statin consider that rosuvastatin (Crestor), pitavastatin (Livalo), simvastatin and pravastatin are the only ones that do not cause a secondary increase in Lp(a)

VAP PROFILE ABNORMALITIES

LDL Pattern B:

General / Low Risk

- Rule out and treat secondary causes if possible:
 1. iatrogenic: non-selective beta blockers, HCTZ, loop diuretics, steroids
 2. metabolic: diabetes / insulin resistance / metabolic syndrome
- Aggressive dietary counseling to ensure compliance with the NCEP TLC diet (i.e. dietitian referral)
- If not contraindicated use a drug that improves insulin sensitivity in diabetics (i.e. agent in the metformin or "glitazone" class)

Moderate Risk

- Same as General / Low Risk PLUS-
Target [triglycerides]<150 mg%
- If unable to shift LDL density consider lowering target [LDL] to less than 100 mg%
 1. when selecting a statin consider that rosuvastatin (Crestor), pitavastatin (Livalo), simvastatin and pravastatin are the only ones that do not cause a secondary increase in Lp(a)

High Risk

- Same as General / Low Risk PLUS
Target [triglycerides]< 100mg%
- Consider specific drug therapy to shift LDL density:
 1. niacin 1-2 grams per day *{will also raise HDL and lower triglycerides and Lp(a)}*
 2. fenofibrate or fenofibric acid *{will also raise HDL and lower triglycerides and Lp(a)}*

Increased IDL:

General / Low Risk

- Rule out and treat secondary causes:
 1. diabetes / insulin resistance / metabolic syndrome
 2. a very low fat, high carbohydrate diet

Moderate Risk

- Same as General / Low Risk PLUS:
- Drug treatment with fenofibrate or fenofibric acid if [triglycerides]>150 mg% *{will also raise HDL and lower triglycerides and Lp(a)}*

High Risk

- Same as General / Low Risk PLUS:
- Drug treatment with combined low dose statin and low dose niacin *{will also raise HDL and lower triglycerides and Lp(a)}*
 - when selecting a statin consider that rosuvastatin (Crestor), pitavastatin (Livalo), simvastatin and pravastatin are the only ones that do not cause a secondary increase in Lp(a)

Decreased HDL2:**General / Low Risk**

- Same approach as outlined for low total HDL under "Second Priority" - this module

Moderate Risk

- Same as General / Low Risk

High Risk

- Same as General / Low Risk PLUS:
Drug therapy to lower triglycerides if [triglycerides] >100 mg%

Increased VLDL3:**General / Low Risk**

- Same approach as used for elevated triglycerides as outlined under "First Priority" - this module

Moderate Risk

- Same as General / Low Risk PLUS
Target [triglycerides] <150 mg%

High Risk

- Same as General / Low Risk PLUS
Target [triglycerides] <100 mg%

Module #9

Increased LDL

First Priority: Lower LDL

Rule out and treat secondary causes if possible:

- metabolic: hypothyroidism, diabetes / insulin resistance / metabolic syndrome

Dietary therapy: NCEP TLC diet

-if overweight target 5 to 10% reduction in body weight

If LDL exceeds NCEP drug initiation level or if patient extremely high risk start drug therapy

Drugs of choice: statins

- select agent and initial dose based on %LDL reduction needed to get to goal

Alternative drugs:

- ezetimibe (Zetia) 10 mg qD
- niacin (up to 2 grams daily)
- resins
- fenofibrate or fenofibric acid

If unable to get to goal on monotherapy consider combination therapy:

- statin plus ezetimibe
- statin plus resin
- statin plus niacin
- statin plus fenofibric acid
- triple therapy

VAP PROFILE ABNORMALITIES

LDL Pattern B:

General / Low Risk

- Rule out and treat secondary causes if possible:
 1. iatrogenic: non-selective beta blockers, HCTZ, loop diuretics, steroids
 2. metabolic: diabetes / insulin resistance / metabolic syndrome
- Aggressive dietary counseling to ensure compliance with the NCEP TLC diet (i.e. dietitian referral)
- If not contraindicated use a drug that improves insulin sensitivity in diabetics (i.e. agent in the metformin or "glitazone" class)

Moderate Risk

- Same as General / Low Risk PLUS-
Target [triglycerides]<150 mg%
 1. with aggressive diet
 2. if diet unsuccessful consider fenofibrate or fenofibric acid and/or niacin (up to 2 grams daily) *{both will also lower LDL}*
 3. if unable to shift LDL density consider lowering target [LDL] to less than 100 mg%

High Risk

- Same as General / Low Risk PLUS
Target [triglycerides]< 100mg%
 1. with aggressive diet
 2. if diet unsuccessful consider fenofibrate or fenofibric acid and/or niacin (up to 2 grams daily) *{both will also lower LDL}*
 3. consider specific drug therapy to shift LDL density
 - niacin 1-2 grams per day *{will also lower LDL}*
 - fenofibrate or fenofibric acid *{will also lower LDL}*

Increased IDL:

General / Low Risk

- Rule out and treat secondary causes:
 1. diabetes / insulin resistance / metabolic syndrome
 2. a very low fat, high carbohydrate diet

Moderate Risk

- Same as General / Low Risk PLUS:
- Drug treatment with fenofibrate or fenofibric acid if [triglycerides]>150 mg% *{will also lower LDL}*

High Risk

- Same as General / Low Risk PLUS:
- Drug treatment with combined low dose statin and low dose niacin *{will also lower LDL}*

Decreased HDL2:

General / Low Risk

- Rule out and treat secondary causes:
 1. metabolic: hypothyroidism, diabetes / insulin resistance / metabolic syndrome
 2. iatrogenic: androgens, HCTZ, loop diuretics, non-selective beta blockers
- smoking cessation
- aerobic activity
- moderate alcohol consumption (equivalent of ~2 ounces pure EtOH/day) if not contraindicated

Moderate Risk

- Same as General / Low Risk

High Risk

- Same as General / Low Risk PLUS:

Drug therapy to lower triglycerides if [triglycerides] > 100 mg%

 1. using fenofibrate or fenofibric acid and/or niacin 1-2 grams per day *{both will also lower LDL}*

Drug therapy to raise HDL2

 1. Drug of choice: niacin 1-2 grams per day *{will also lower LDL}*
 2. alternative:
 - rosuvastatin (Crestor) 10 mg qD *{will also lower LDL}*
 - simvastatin 40 or 80 mg qD *{will also lower LDL}*
- If unable to raise [HDL2] consider lowering target [LDL] to less than 70 mg%
-use preferred statins as needed

Increased VLDL3:

General / Low Risk

- Rule out and correct secondary causes:
 1. metabolic: diabetes / insulin resistance / metabolic syndrome, hypothyroidism
 2. iatrogenic: oral estrogen, non-selective beta blockers, steroids, diuretics, resins, protease inhibitors
- Dietary therapy with NCEP TLC diet with additional carbohydrate restriction
- If overweight target 5-10% reduction in body weight

Moderate Risk

- Same as General / Low Risk PLUS
Target [triglycerides] < 150 mg%

High Risk

- Same as General / Low Risk PLUS

Target [triglycerides]<100 mg% - consider use of:

1. fenofibrate or fenofibric acid *{will also lower LDL}*
2. niacin (up to 2 grams daily) *{will also lower LDL}*
3. omega-3-fatty acids (EPA+DHA to total 4grams) per day

Module #10

Increased LDL & Lp(a)

First Priority: Lower LDL

Rule out and treat secondary causes if possible:

- metabolic: hypothyroidism, diabetes / insulin resistance / metabolic syndrome

Dietary therapy: NCEP TLC diet

- if overweight target 5 to 10% reduction in body weight

If LDL exceeds NCEP drug initiation level or if patient extremely high risk start drug therapy

- Drugs of choice: statins
 - select agent and initial dose based on %LDL reduction needed to get to goal
 - when selecting a statin consider that rosuvastatin (Crestor), pitavastatin (Livalo), simvastatin and pravastatin are the only ones that do not cause a secondary increase in Lp(a)
- Alternative drugs:
 1. ezetimibe (Zetia) 10 mg qD
 2. niacin (up to 2 grams daily) *{can also lower Lp(a)}*
 3. resins
 4. fenofibrate or fenofibric acid *{can also lower Lp(a)}*
- If unable to get to goal on monotherapy consider combination therapy:
 1. statin plus ezetimibe (Zetia)
 2. statin plus resin
 3. statin plus niacin *{especially good combination with increased LDL and Lp(a)}*
 4. statin plus fenofibric acid *{can also lower Lp(a)}*
 5. triple therapy

Second Priority: Lower Lp(a)

If patient is an Afro-American without premature family history no treatment needed

Rule out and treat secondary causes if possible:

- factitious: acute phase response
- metabolic: hypothyroidism, microalbuminuria / proteinuria in diabetes
 1. thyroid hormone replacement to normalize TSH if hypothyroid
 2. ACE / ARB therapy in diabetics with microalbuminuria / proteinuria

Lifestyle / non-pharmacological intervention:

- moderate alcohol consumption (equivalent of ~2 ounces pure EtOH per day) if not contraindicated
- aspirin 81 mg qD if not contraindicated
- restriction of dietary trans-fatty acids

Drug therapy:

- niacin (up to 2 grams daily) *{can also lower LDL}*
- omega-3-fatty acids (EPA+DHA to total 4grams) per day
- fenofibrate or fenofibric acid *{will also lower LDL}*

Alternative approach to specifically lowering [Lp(a)] is to lower the [LDL] below current NCEP guidelines *{Lp(a) loses predictive value if [LDL] < 70 mg%}*

- when selecting a statin consider that rosuvastatin (Crestor), pitavastatin (Livalo), simvastatin and pravastatin are the only ones that do not cause a secondary increase in Lp(a)

VAP PROFILE ABNORMALITIES

LDL Pattern B:

General / Low Risk

- Rule out and treat secondary causes if possible:
 1. iatrogenic: non-selective beta blockers, HCTZ, loop diuretics, steroids
 2. metabolic: diabetes/ insulin resistance / metabolic syndrome
- Aggressive dietary counseling to ensure compliance with the NCEP TLC diet (i.e. dietitian referral)
- If not contraindicated use a drug that improves insulin sensitivity in diabetics (i.e. agent in the metformin or "glitazone" class)

Moderate Risk

- Same as General / Low Risk PLUS-
Target [triglycerides] < 150 mg%
 1. with aggressive diet
 2. if diet unsuccessful consider fenofibrate or fenofibric acid and/or niacin (up to 2 grams daily) *{both would also lower LDL and Lp(a)}*
 3. if unable to shift LDL density consider lowering target [LDL] to less than 100 mg%
 - when selecting a statin consider that rosuvastatin (Crestor), pitavastatin (Livalo), simvastatin and pravastatin are the only ones that do not cause a secondary increase in Lp(a)

High Risk

- Same as General / Low Risk PLUS

Target [triglycerides] < 100mg%

1. with aggressive diet
2. if diet unsuccessful consider fenofibrate or fenofibric acid and/or niacin (up to 2 grams daily) *{both would also lower LDL and Lp(a)}*

Consider specific drug therapy to shift LDL density

1. niacin 1-2 grams per day *{will also lower LDL and Lp(a)}*
2. fenofibrate or fenofibric acid *{will also lower LDL and Lp(a)}*

Increased IDL:

General / Low Risk

- Rule out and treat secondary causes:
 1. diabetes / insulin resistance / metabolic syndrome
 2. a very low fat, high carbohydrate diet

Moderate Risk

- Same as General / Low Risk PLUS:

Drug treatment with fenofibrate or fenofibric acid if [triglycerides] > 150 mg% *{would also lower LDL and Lp(a)}*

High Risk

- Same as General / Low Risk PLUS:

Drug treatment with combined low dose statin and low dose niacin *{would also lower LDL and Lp(a)}*

- when selecting a statin consider that rosuvastatin (Crestor), pitavastatin (Livalo), simvastatin and pravastatin are the only ones that do not cause a secondary increase in Lp(a)

Decreased HDL2:

General / Low Risk

- Rule out and treat secondary causes:
 1. metabolic: hypothyroidism, diabetes / insulin resistance / metabolic syndrome
 2. iatrogenic: androgens, HCTZ, loop diuretics, non-selective beta blockers
- smoking cessation
- aerobic activity
- especially strong reason to consider moderate alcohol consumption (~2 ounces pure EtOH/day) if not contraindicated *{would also lower Lp(a)}*

Moderate Risk

- Same as General / Low Risk PLUS:
Drug therapy to lower triglycerides if [triglycerides]>150 mg%
fenofibrate or fenofibric acid and/or niacin 1-2 grams per day *{both would also lower LDL and Lp(a)}*

High Risk

- Same as General / Low Risk PLUS:
Drug therapy to lower triglycerides if [triglycerides]> 100 mg%
using fenofibrate or fenofibric acid and/or niacin 1-2 grams per day *{both would also lower LDL and Lp(a)}*
Drug therapy to raise HDL2
 1. Drug of choice: niacin 1-2 grams per day *{will also lower LDL and Lp(a)}*
 2. Alternative:
 - rosuvastatin (Crestor) 10 mg qD *{will also lower LDL}*
 - simvastatin 40 or 80 mg qD *{will also lower LDL}*
- If unable to raise [HDL2] consider lowering target [LDL] to less than 70 mg%
use statins as needed
 - when selecting a statin consider that rosuvastatin (Crestor), pitavastatin (Livalo), simvastatin and pravastatin are the only ones that do not cause a secondary increase in Lp(a)

Increased VLDL3:

General / Low Risk

- Rule out and correct secondary causes:
 1. metabolic: diabetes / insulin resistance / metabolic syndrome, hypothyroidism
 2. iatrogenic: estrogen, non-selective beta blockers, steroids, diuretics, resins, protease inhibitors
- Dietary therapy with NCEP TLC diet with additional carbohydrate
- If overweight target 5-10% reduction in body weight

Moderate Risk

- Same as General / Low Risk PLUS
Target [triglycerides]< 150 mg%

High Risk

- Same as General / Low Risk PLUS

Target [triglycerides]<100 mg%

Consider use of:

1. fenofibrate or fenofibric acid *{will also lower LDL and Lp(a)}*
2. niacin (up to 2 grams daily) *{will also lower LDL and Lp(a)}*
3. omega-3-fatty acids (EPA+DHA to total 4grams) per day *{can also lower Lp(a)}*

Module #11

Increased LDL & Triglycerides

First Priority: Lower LDL

Rule out and treat secondary causes if possible:

- metabolic: hypothyroidism, diabetes / insulin resistance / metabolic syndrome

Dietary therapy: NCEP TLC diet

if overweight target 5 to 10% reduction in body weight

If LDL exceeds NCEP drug initiation level or if patient extremely high risk start drug therapy

- Drugs of choice: statins *{will also lower triglycerides}*
select agent and initial dose based on %LDL reduction needed to get to goal
- Alternative drugs:
 - ezetimibe (Zetia) 10 mg qD
 - niacin (up to 2 grams daily) *{will also lower triglycerides}*
 - fenofibrate or fenofibric acid *{will also lower triglycerides}*
- If unable to get to goal on monotherapy consider combination therapy:
 - statin plus niacin or statin plus fenofibric acid *{both will also lower triglycerides}* or
 - statin plus ezetimibe or triple therapy
 - avoid the use of resins in the setting of elevated triglycerides

Second Priority: Lower Triglycerides

Rule out and treat secondary causes if possible:

- factitious: non-fasting specimen
- metabolic: hypothyroidism, diabetes / insulin resistance / metabolic syndrome, proteinuria / nephrotic syndrome
- iatrogenic: estrogen (oral), non-selective beta blockers, diuretics, resins, steroids, protease inhibitors, alcohol

Dietary therapy: NCEP TLC diet with additional carbohydrate restriction & alcohol avoidance

if overweight target 5 to 10% reduction in body weight

If drug therapy needed:

Drug of choice-fibrates *{will also lower LDL}*

- fenofibrate or fenofibric acid with food

Alternative agents:

- niacin (up to 2 grams daily) *{will also lower LDL}*
- omega-3-fatty acids (EPA+DHA to total 4grams) per day
- statins *{will also lower LDL}*

VAP PROFILE ABNORMALITIES

LDL Pattern B:

General / Low Risk

- Rule out and treat secondary causes if possible:
 1. iatrogenic: non-selective beta blockers, HCTZ, loop diuretics, steroids
 2. metabolic: diabetes / insulin resistance / metabolic syndrome
- Aggressive dietary counseling to ensure compliance with the NCEP TLC diet (i.e. dietitian referral)
- If not contraindicated a drug that improves insulin sensitivity in diabetics (i.e. agent in the metformin or "glitazone" class)

Moderate Risk

- Same as General / Low Risk PLUS-
Target [triglycerides]<150 mg%
 1. with aggressive diet
 2. if diet unsuccessful consider fenofibrate or fenofibric acid and/or niacin (up to 2 grams daily) *{both will also lower LDL and triglycerides}*
 3. if unable to shift LDL density consider lowering target [LDL] to less than 100 mg%

High Risk

- Same as General / Low Risk PLUS
Target [triglycerides]< 100mg%
 1. with aggressive diet
 2. if diet unsuccessful, consider fenofibrate or fenofibric acid and/or niacin (up to 2 grams daily) *{both will also lower LDL and triglycerides}*
 3. consider specific drug therapy to shift LDL density
 - a. niacin 1-2 grams per day *{will also lower LDL and triglycerides}*
 - b. fenofibrate or fenofibric acid *{will also lower LDL and triglycerides}*

Increased IDL:

General / Low Risk

- Rule out and treat secondary causes:
 1. diabetes / insulin resistance / metabolic syndrome
 2. a very low fat, high carbohydrate diet

Moderate Risk

- Same as General / Low Risk PLUS:
Drug treatment with fenofibrate or fenofibric acid if [triglycerides]>150 mg% *{will also lower LDL and triglycerides}*

High Risk

- Same as General / Low Risk PLUS:
Drug treatment with combined low dose statin and low dose niacin *{will also lower LDL and triglycerides}*

Decreased HDL2:

General / Low Risk

- Rule out and treat secondary causes:
 1. metabolic: hypothyroidism, diabetes / insulin resistance / metabolic syndrome
 2. iatrogenic: androgens, HCTZ, loop diuretics, non-selective beta blockers
- Smoking cessation
- Aerobic activity
- AVOID alcohol in the setting of elevated triglycerides

Moderate Risk

- Same as General / Low Risk

High Risk

- Same as General / Low Risk PLUS:
Drug therapy to lower triglycerides if [triglycerides]> 100 mg%
 - using fenofibrate or fenofibric acid and/or niacin 1-2 grams per day *{both will also lower LDL and triglycerides}*
Drug therapy to raise HDL2
Drug of choice: niacin 1-2 grams per day *{will also lower LDL and triglycerides}*
 1. alternative: rosuvastatin (Crestor) 10 mg qD or simvastatin 40 or 80 mg qD *{will also lower LDL and triglycerides}*
 2. if unable to raise [HDL2] consider lowering target [LDL] to less than 70 mg%

Increased VLDL3:

General / Low Risk

- Same approach as for treating elevated total triglycerides under "Second Priority" - this module

Moderate Risk

- Same as General / Low Risk
Target [triglycerides]<150mg%

High Risk

- Same as General / Low Risk PLUS
Target [triglycerides]<100 mg%

Module #12

Increased LDL, Triglycerides & Lp(a)

First Priority: Lower LDL

Rule out and treat secondary causes if possible:

- metabolic: hypothyroidism, diabetes / insulin resistance / metabolic syndrome

Dietary therapy: NCEP TLC diet

if overweight target 5 to 10% reduction in body weight

If LDL exceeds NCEP drug initiation level or if patient extremely high risk start drug therapy

- Drugs of choice: statins *{will also lower triglycerides}*
 - select agent and initial dose based on %LDL reduction needed to get to goal
 - when selecting a statin consider that rosuvastatin (Crestor), pitavastatin (Livalo), simvastatin and pravastatin are the only ones that do not cause a secondary increase in Lp(a)

Alternative drugs:

- ezetimibe (Zetia) 10 mg qD
- niacin (up to 2 grams daily) *{will also lower triglycerides and Lp(a)}*
- fenofibrate or fenofibric acid *{will also lower triglycerides and Lp(a)}*

If unable to get to goal on monotherapy consider combination therapy:

- statin plus ezetimibe
- statin plus niacin *{will also lower triglycerides and Lp(a)}*
- statin plus fenofibric acid *{will also lower triglycerides and Lp(a)}*
- triple therapy

Avoid the use of resins in the setting of elevated triglycerides

Second Priority: Lower Triglycerides

Rule out and treat secondary causes if possible:

- factitious: non-fasting specimen
- metabolic: hypothyroidism, diabetes / insulin resistance / metabolic syndrome, proteinuria / nephrotic syndrome
- iatrogenic: estrogen (oral), non-selective beta blockers, diuretics, resins, steroids, protease inhibitors, alcohol

Dietary therapy: NCEP TLC diet with additional carbohydrate restriction & alcohol avoidance

- if overweight target 5 to 10% reduction in body weight

If drug therapy needed:

- Drug of choice-fibrates
 1. fenofibrate or fenofibric acid *{will also lower LDL and Lp(a)}*

- Alternative agents:
 1. niacin (up to 2 grams daily) *{will also lower LDL and Lp(a)}*
 2. omega-3-fatty acids (EPA+DHA to total 4grams) per day *{can also lower Lp(a)}*
 3. statins *{will also lower LDL}*
 - when selecting a statin consider that rosuvastatin (Crestor), pitavastatin (Livalo), simvastatin and pravastatin are the only ones that do not cause a secondary increase in Lp(a)

Third Priority: Lower Lp(a)

If patient is an Afro-American without premature family history no treatment needed

Rule out and treat secondary causes if possible:

- factitious: acute phase response
- metabolic: hypothyroidism, microalbuminuria / proteinuria in diabetes
 - thyroid hormone replacement to normalize TSH if hypothyroid
 - ACE / ARB therapy in diabetics with microalbuminuria / proteinuria

Lifestyle / non-pharmacological intervention:

- dietary restriction of trans-fatty acids
- AVOID alcohol in the setting of elevated triglycerides
- aspirin 81 mg qD if not contraindicated

Drug therapy:

- niacin (up to 2 grams daily) *{will also lower LDL and triglycerides}*
- omega-3-fatty acids (EPA+DHA to total 4grams) per day *{will also lower triglycerides}*
- fenofibrate or fenofibric acid *{will also lower triglycerides and LDL}*

Alternative approach to specifically lowering [Lp(a)] is to lower the [LDL] below current NCEP guidelines *{Lp(a) loses predictive value if [LDL] < 70 mg%}*

- when selecting a statin consider that rosuvastatin (Crestor), pitavastatin (Livalo), simvastatin and pravastatin are the only ones that do not cause a secondary increase in Lp(a)

VAP PROFILE ABNORMALITIES

LDL Pattern B:

General / Low Risk

- Rule out and treat secondary causes if possible:
 - iatrogenic: non-selective beta blockers, HCTZ, loop diuretics, steroids
 - metabolic: diabetes / insulin resistance / metabolic syndrome
- Aggressive dietary counseling to ensure compliance with the NCEP TLC diet (i.e. dietitian referral)
- If not contraindicated use a drug that improves insulin sensitivity in diabetics (i.e. agent in the metformin or "glitazone" class)

Moderate Risk

- Same as General / Low Risk PLUS-
Target [triglycerides]<150 mg%
 1. with aggressive diet
 2. if diet unsuccessful consider fenofibrate or fenofibric acid and/or niacin (up to 2 grams daily) *{both will also lower LDL, triglycerides, and Lp(a)}*
 3. if unable to shift LDL density consider lowering target [LDL] to less than 100 mg%
 - when selecting a statin consider that rosuvastatin (Crestor), pitavastatin (Livalo), simvastatin and pravastatin are the only ones that do not cause a secondary increase in Lp(a)

High Risk

- Same as General / Low Risk PLUS
Target [triglycerides]< 100mg%
 1. with aggressive diet
 2. if diet unsuccessful, consider fenofibrate or fenofibric acid and/or niacin (up to 2 grams daily) *{both will also lower LDL, triglycerides, and Lp(a)}*

Consider specific drug therapy to shift LDL density

 1. niacin 1-2 grams per day *{will also lower LDL, triglycerides, and Lp(a)}*
 2. fenofibrate or fenofibric acid *{will also lower LDL, triglycerides, and Lp(a)}*

Increased IDL:

General / Low Risk

- Rule out and treat secondary causes:
 - diabetes / insulin resistance / metabolic syndrome
 - a very low fat, high carbohydrate diet

Moderate Risk

- Same as General / Low Risk PLUS:
Drug treatment with fenofibrate or fenofibric acid if [triglycerides]>150 mg% *{will also lower LDL, triglycerides, and Lp(a)}*

High Risk

- Same as General / Low Risk PLUS:
Drug treatment with combined low dose statin and low dose niacin *{will also lower LDL, triglycerides, and Lp(a)}*
 - when selecting a statin consider that rosuvastatin (Crestor), pitavastatin (Livalo), simvastatin and pravastatin are the only ones that do not cause a secondary increase in Lp(a)

Decreased HDL2:

General / Low Risk

- Rule out and treat secondary causes:
 1. metabolic: hypothyroidism, diabetes / insulin resistance / metabolic syndrome
 2. iatrogenic: androgens, HCTZ, loop diuretics, non-selective beta blockers
- Smoking cessation
- Aerobic activity
- AVOID alcohol in the setting of elevated triglycerides

Moderate Risk

- Same as General / Low Risk PLUS:
Drug therapy to lower triglycerides if [triglycerides]>150 mg%

High Risk

- Same as General / Low Risk PLUS:
Drug therapy to lower triglycerides if [triglycerides]> 100 mg%
Drug therapy to raise HDL2
 1. Drug of choice: niacin 1-2 grams per day *{will also lower LDL, triglycerides, and Lp(a)}*
 2. Alternative:
 - a. rosuvastatin (Crestor) 10 mg qD *{will also lower total LDL and triglycerides}*
 - b. simvastatin 40 or 80 mg qD *{will also lower total LDL and triglycerides}*

If unable to raise [HDL2] consider lowering target [LDL] to less than 70 mg% using statins as needed

 - when selecting a statin consider that rosuvastatin (Crestor), pitavastatin (Livalo), simvastatin and pravastatin are the only ones that do not cause a secondary increase in Lp(a)

Increased VLDL3:

General / Low Risk

- Same approach as used to lower total triglycerides: see "Second Priority" - this module

Moderate Risk

- Same as General / Low Risk PLUS
Target [triglycerides]< 150mg%

High Risk

- Same as General / Low Risk PLUS
Target [triglycerides]<100 mg%

Module #13

Increased LDL and Decreased HDL

First Priority: Lower LDL

Rule out and treat secondary causes if possible:

- metabolic: hypothyroidism, diabetes / insulin resistance / metabolic syndrome

Dietary therapy: NCEP TLC diet

- if overweight target 5 to 10% reduction in body weight

If LDL exceeds NCEP drug initiation level or if patient extremely high risk start drug therapy

- Drugs of choice: statins *{selected agents (i.e. Crestor and simvastatin) more effective at raising HDL}*

select agent and initial dose based on %LDL reduction needed to get to goal

- Alternative drugs:

ezetimibe (Zetia) 10 mg qD

niacin (up to 2 grams daily) *{will also raise HDL}*

resins

fenofibrate or fenofibric acid *{will also raise HDL}*

- If unable to get to goal on monotherapy consider combination therapy:

statin plus ezetimibe

statin plus resin

statin plus niacin *{will also raise HDL}*

statin plus fenofibric acid *{will also raise HDL}*

triple therapy

Second Priority: Raise HDL

- Rule out and treat secondary causes if possible

1. metabolic: diabetes / insulin resistance / metabolic syndrome, hypothyroidism

2. iatrogenic: androgens, HCTZ, loop diuretics, non-selective beta blockers

- Target [total HDL] > 45 mg% in men / >55mg% in women

- Lifestyle interventions:

1. smoking cessation and aerobic exercise

2. modest alcohol intake (equivalent of ~2 ounces pure EtOH per day) if not contraindicated

- Drug therapy to raise HDL:
 1. drug of choice: niacin 1 to 2 grams per day *{will also lower LDL}*
 2. alternative:
 - rosuvastatin (Crestor) 10 mg qD *{will also lower LDL}*
 - simvastatin 40 or 80 mg qD *{will also lower LDL}*
 - fenofibrate or fenofibric acid *{will also lower LDL}*
- In high risk patients unresponsive to efforts to raise HDL consider lowering [LDL] to below NCEP target

VAP PROFILE ABNORMALITIES

LDL Pattern B:

General / Low Risk

- Rule out and treat secondary causes if possible:
 1. iatrogenic: non-selective beta blockers, HCTZ, loop diuretics, steroids
 2. metabolic: diabetes / insulin resistance / metabolic syndrome
- Aggressive dietary counseling to ensure compliance with the NCEP TLC diet (i.e. dietitian referral)
- If not contraindicated use a drug that improves insulin sensitivity in diabetics (i.e. agent in the metformin or "glitazone" class)

Moderate Risk

- Same as General / Low Risk PLUS-
Target [triglycerides]<150 mg%
 1. with aggressive diet
 2. if diet unsuccessful consider fenofibrate or fenofibric acid and/or niacin (up to 2 grams daily) *{both will also lower LDL and raise HDL}*
 3. if unable to shift LDL density consider lowering target [LDL] to less than 100 mg%

High Risk

- Same as General / Low Risk PLUS
Target [triglycerides]< 100 mg%
 1. with aggressive diet
 2. if diet unsuccessful consider fenofibrate or fenofibric acid and/or niacin (up to 2 grams daily) *{both will also lower LDL and raise HDL}*

Consider specific drug therapy to shift LDL density

1. niacin 1-2 grams per day *{will also lower LDL and raise HDL}*
2. fenofibrate or fenofibric acid *{will also lower LDL and raise HDL}*

Increased IDL:

General / Low Risk

- Rule out and treat secondary causes:
 1. diabetes, insulin resistance / metabolic syndrome
 2. a very low fat, high carbohydrate diet

Moderate Risk

Same as General / Low Risk PLUS:

Drug treatment with fenofibrate or fenofibric acid if [triglycerides]>150 mg% *{will also lower LDL and raise HDL}*

High Risk

- Same as General / Low Risk PLUS:
Drug treatment with combined low dose statin and low dose niacin *{will also lower LDL and raise HDL}*

Decreased HDL2:

General / Low Risk

- Same approach as used to raise HDL - see "Second Priority" - this module

Moderate Risk

- Same as General / Low Risk PLUS:
Drug therapy to lower triglycerides if [triglycerides]>150 mg% using fenofibrate or fenofibric acid and/or niacin 1-2 grams per day *{both will also lower LDL and raise HDL}*

High Risk

- Same as General / Low Risk PLUS:
Drug therapy to lower triglycerides if [triglycerides]> 100 mg%
 1. fenofibrate or fenofibric acid and/or niacin 1-2 grams per day *{both will also lower LDL and raise HDL}*
Drug therapy to raise HDL2
 2. Drug of choice: niacin 1-2 grams per day *{will also lower LDL and raise HDL}*
 3. Alternative:
 - rosuvastatin (Crestor) 10 mg qD *{will also lower LDL and raise HDL}*
 - simvastatin 40 or 80 mg qD *{will also lower LDL and raise HDL}*

If unable to raise [HDL2] consider lowering target [LDL] to less than 70 mg%

Increased VLDL3:

General / Low Risk

- Rule out and correct secondary causes:
 1. metabolic: diabetes / insulin resistance / metabolic syndrome, hypothyroidism
 2. iatrogenic: non-selective beta blockers, steroids, diuretics
- Dietary therapy with the NCEP TLC diet with additional carbohydrate restriction
- If overweight target 5-10% reduction in body weight

Moderate Risk

- Same as General / Low Risk PLUS
Target [triglycerides] < 150mg%

High Risk

- Same as General / Low Risk PLUS
Target [triglycerides] < 100 mg%
Consider use of:
 1. fenofibrate or fenofibric acid *{will also lower LDL and raise HDL}*
 2. niacin (up to 2 grams daily) *{will also lower total LDL and raise HDL}*
 3. omega-3-fatty acids (EPA+DHA to total 4grams) per day

Module #14

Increased LDL & Lp(a) and Decreased HDL

First Priority: Lower LDL

Rule out and treat secondary causes if possible:

- metabolic: hypothyroidism, diabetes / insulin resistance / metabolic syndrome

Dietary therapy: NCEP TLC diet

if overweight target 5 to 10% reduction in body weight

If LDL exceeds NCEP drug initiation level or if patient extremely high risk start drug therapy

- Drugs of choice: statins
 - select agent and initial dose based on %LDL reduction needed to get to goal
 - when selecting a statin consider that rosuvastatin (Crestor), pitavastatin (Livalo), simvastatin and pravastatin are the only ones that do not cause a secondary increase in Lp(a)
- Alternative drugs:
 - ezetimibe (Zetia) 10 mg qD
 - niacin (up to 2 grams daily) *{will also lower Lp(a) and raise HDL}*
 - resins
 - fenofibrate or fenofibric acid *{will also lower Lp(a) and raise HDL}*
- If unable to get to goal on monotherapy consider combination therapy:
 - statin plus ezetimibe
 - statin plus resin
 - statin plus niacin *{will also lower Lp(a) and raise HDL}*
 - statin plus fenofibric acid *{will also lower Lp(a) and raise HDL}*
 - triple therapy

Second Priority: Raise HDL

Rule out and treat secondary causes if possible

- metabolic: diabetes / insulin resistance / metabolic syndrome, hypothyroidism
- iatrogenic: androgens, HCTZ, loop diuretics, non-selective beta blockers

Target [total HDL] > 45 mg% in men / >55mg% in women

Lifestyle interventions:

- smoking cessation
- aerobic exercise
- especially strong reason to consider modest alcohol intake (equivalent of ~2 ounces pure EtOH per day) if not contraindicated *{can also lower Lp(a)}*

Drug therapy to raise HDL:

- drug of choice: niacin 1 to 2 grams per day *{will also lower LDL and Lp(a)}*
- alternative:
 1. rosuvastatin (Crestor) 10 mg qD *{will also lower LDL}*
 2. simvastatin 40 or 80 mg qD *{will also lower LDL}*
 3. fenofibrate or fenofibric acid *{will also lower LDL and Lp(a)}*

In high risk patients unresponsive to efforts to raise HDL consider lowering [LDL] to below NCEP target

- when selecting a statin consider that rosuvastatin (Crestor), pitavastatin (Livalo), simvastatin and pravastatin are the only ones that do not cause a secondary increase in Lp(a)

Third Priority: Lower Lp(a)

If patient is an Afro-American without premature family history no treatment needed Rule out and treat secondary causes if possible:

- factitious: acute phase response
- metabolic: hypothyroidism, microalbuminuria / proteinuria in diabetes
 - thyroid hormone replacement to normalize TSH if hypothyroid
 - ACE / ARB therapy in diabetics with microalbuminuria / proteinuria

Lifestyle / non-pharmacological intervention:

- aspirin 81 mg qD if not contraindicated
- moderate alcohol consumption (equivalent of 2 oz. EtOH per day) if not contra-indicated
- dietary restriction of trans-fatty acids

Drug therapy:

- niacin (up to 2 grams daily) *{will also lower LDL and raise HDL}*
- omega-3-fatty acids (EPA+DHA to total 4grams) per day *{can also lower Lp(a)}*
- fenofibrate or fenofibric acid *{will also lower LDL and Lp(a)}*

Alternative approach to specifically lowering [Lp(a)] is to lower the [LDL] below current NCEP guidelines *{Lp(a) loses predictive value if [LDL] < 70 mg%}*

- when selecting a statin consider that rosuvastatin (Crestor), pitavastatin (Livalo), simvastatin and pravastatin are the only ones that do not cause a secondary increase in Lp(a)

VAP PROFILE ABNORMALITIES

LDL Pattern B:

General / Low Risk

- Rule out and treat secondary causes if possible:
 1. iatrogenic: non-selective beta blockers, HCTZ, loop diuretics, steroids
 2. metabolic: diabetes / insulin resistance / metabolic syndrome
- aggressive dietary counseling to ensure compliance with the NCEP TLC diet
- if not contraindicated use a drug that improves insulin sensitivity in diabetics (i.e. agent in the metformin or "glitazone" class)

Moderate Risk

- Same as General / Low Risk PLUS-
Target [triglycerides]<150 mg%
 1. with aggressive diet
 2. if diet unsuccessful consider fenofibrate or fenofibric acid and/or niacin (up to 2 grams daily) *{both will also lower Lp(a) and raise HDL}*
 3. if unable to shift LDL density consider lowering target [LDL] to less than 100 mg%
 - when selecting a statin consider that rosuvastatin (Crestor), pitavastatin (Livalo), simvastatin and pravastatin are the only ones that do not cause a secondary increase in Lp(a)

High Risk

- Same as General / Low Risk PLUS
Target [triglycerides]< 100mg%
 1. with aggressive diet
 2. if diet unsuccessful consider fenofibrate or fenofibric acid and/or niacin (up to 2 grams daily) *{both will also lower LDL and Lp(a) and raise HDL}*
 3. consider specific drug therapy to shift LDL density
 - a. niacin 1-2 grams per day *{will also lower LDL and Lp(a), and raise HDL}*
 - b. fenofibrate or fenofibric acid *{will also lower LDL and Lp(a) and raise HDL}*

Increased IDL:

General / Low Risk

- Rule out and treat secondary causes:
 - diabetes / insulin resistance / metabolic syndrome
 - a very low fat, high carbohydrate diet

Moderate Risk

- Same as General / Low Risk PLUS:
 - Drug treatment with fenofibrate or fenofibric acid if [triglycerides]>100 mg% *{will also lower LDL and Lp(a), and raise HDL}*

High Risk

- Same as General / Low Risk PLUS:
- Drug treatment with combined low dose statin and low dose niacin *{will also lower LDL and Lp(a), and raise HDL}*
 - when selecting a statin consider that rosuvastatin (Crestor), pitavastatin (Livalo), simvastatin and pravastatin are the only ones that do not cause a secondary increase in Lp(a)

Decreased HDL2:

General / Low Risk

- Same approach as used to raise HDL - see "Second Priority" - this module

Moderate Risk

- Same as General / Low Risk PLUS:
- Drug therapy to lower triglycerides if [triglycerides]>150 mg%

High Risk

- Same as General / Low Risk PLUS:
 - Drug therapy to lower triglycerides if [triglycerides]> 100 mg%
- If unable to raise [HDL2] consider lowering target [LDL] to less than 70 mg%
 - when selecting a statin consider that rosuvastatin (Crestor), pitavastatin (Livalo), simvastatin and pravastatin are the only ones that do not cause a secondary increase in Lp(a)

Increased VLDL3:

General / Low Risk

- Rule out and correct secondary causes:
 1. metabolic: diabetes / insulin resistance / metabolic syndrome , hypothyroidism
 2. iatrogenic: non-selective beta blockers, steroids, diuretics, resins, protease inhibitors
- Dietary therapy with NCEP TLC diet with additional carbohydrate restriction
- If overweight target 5-10% reduction in body weight

Moderate Risk

- Same as General / Low Risk PLUS
Target [triglycerides] < 150 mg%

High Risk

- Same as General / Low Risk PLUS
 - Target [triglycerides] < 100 mg%
Consider use of:
 1. fenofibrate or fenofibric acid *{will also lower LDL and Lp(a) and raise HDL}*
 2. niacin (up to 2 grams daily) *{will also lower LDL, Lp(a), and raise HDL}*
 3. omega-3-fatty acids (EPA+DHA to total 4grams) per day *{will also lower Lp(a)}*

Module #15

Increased LDL & Triglycerides and Decreased HDL

First Priority: Lower LDL

Rule out and treat secondary causes if possible:

- metabolic: hypothyroidism, diabetes / insulin resistance / metabolic syndrome

Dietary therapy: NCEP TLC diet

- if overweight target 5 to 10% reduction in body weight

If LDL exceeds NCEP drug initiation level or if patient extremely high risk start drug therapy

- Drugs of choice: statins *{will also lower triglycerides, and selected agents (i.e. Crestor and simvastatin) will raise HDL}*

-select agent and initial dose based on %LDL reduction needed to get to goal

- Alternative drugs:

ezetimibe (Zetia) 10 mg qD

niacin (up to 2 grams daily) *{will also lower triglycerides and raise HDL}*

fenofibrate or fenofibric acid *{will also lower triglycerides and raise HDL}*

- If unable to get to goal on monotherapy consider combination therapy:

statin plus ezetimibe

statin plus niacin

statin plus fenofibric acid

triple therapy

Avoid resin use in the setting of elevated triglycerides

Second Priority: Lower Triglycerides

Rule out and treat secondary causes if possible:

- factitious: non-fasting specimen
- metabolic: hypothyroidism, diabetes / insulin resistance / metabolic syndrome, proteinuria / nephrotic syndrome
- iatrogenic: estrogen (oral), non-selective beta blockers, diuretics, resins, steroids, protease inhibitors, alcohol

Dietary therapy: NCEP TLC diet with additional carbohydrate restriction & alcohol avoidance

- if overweight target 5 to 10% reduction in body weight

If drug therapy needed:

Drug of choice-fibrates *{will also lower LDL and raise HDL}*

- fenofibrate or fenofibric acid

Alternative agents:

- niacin (up to 2 grams daily) *{will also lower LDL and raise HDL}*
- omega-3-fatty acids (EPA+DHA to total 4grams) per day
- statins *{will also lower LDL and selected agents (i.e.Crestor and simvastatin) will raise HDL}*

Third Priority: Raise HDL

Rule out and treat secondary causes if possible

- metabolic: diabetes / insulin resistance / metabolic syndrome, hypothyroidism
- iatrogenic: androgens, HCTZ, non-selective beta blockers

Target [total HDL] > 45 mg% in men / >55mg% in women

Lifestyle interventions:

- smoking cessation
- aerobic exercise

If possible defer drug treatment to specifically increase HDL until the triglyceride disorder is corrected

Drug therapy to raise HDL:

- drug of choice: niacin (up to 2 grams daily) *{will also lower LDL and triglycerides}*
- alternative:
 1. rosuvastatin (Crestor) 10 mg qD *{will also lower LDL and triglycerides}*
 2. simvastatin 40 or 80 mg qD *{will also lower LDL and triglycerides}*
 3. fenofibrate or fenofibric acid *{will also lower LDL and triglycerides}*

In high risk patients unresponsive to efforts to raise HDL consider lowering [LDL] to below NCEP target

VAP PROFILE ABNORMALITIES

LDL Pattern B:

General / Low Risk

- Rule out and treat secondary causes if possible:
 1. iatrogenic: non-selective beta blockers, HCTZ, loop diuretics, steroids
 2. metabolic: diabetes / insulin resistance / metabolic syndrome
- aggressive dietary counseling to ensure compliance with the NCEP TLC diet (i.e. dietitian referral)
- if not contraindicated use a drug that improves insulin sensitivity in diabetics (i.e. agent in the metformin or "glitazone" class)

Moderate Risk

- Same as General / Low Risk PLUS-
 - Target [triglycerides]<150 mg%
 - If unable to shift LDL density consider lowering target [LDL] to less than 100 mg%

High Risk

- Same as General / Low Risk PLUS
 - Target [triglycerides]< 100mg%
 - Consider specific drug therapy to shift LDL density1.
 1. niacin 1-2 grams per day *{will also lower LDL, triglycerides and raise HDL}*
 2. fenofibrate or fenofibric acid *{will also lower LDL, triglycerides and raise HDL}*

Increased IDL:

General / Low Risk

- Rule out and treat secondary causes:
 1. diabetes / insulin resistance / metabolic syndrome
 2. a very low fat, high carbohydrate diet

Moderate Risk

- Same as General / Low Risk PLUS:
 1. Drug treatment with fenofibrate or fenofibric acid if [triglycerides]>150 mg% *{will also lower LDL, triglyceride, and raise HDL}*

High Risk

- Same as General / Low Risk PLUS:
 1. Drug treatment with combined low dose statin and low dose niacin *{will also lower LDL, triglycerides and raise HDL}*

Decreased HDL2:

General / Low Risk

- Same approach as used to raise total HDL - see "Third Priority" - this module

Moderate Risk

- Same as General / Low Risk PLUS:
 - Drug therapy to lower triglycerides if [triglycerides]> 150 mg%

High Risk

- Same as General / Low Risk PLUS:
Drug therapy to lower triglycerides if [triglycerides] > 100 mg%

Increased VLDL3:**General / Low Risk**

- Same approach as used to lower triglycerides - see "Second Priority" - this module

Moderate Risk

- Same as General / Low Risk PLUS
Target [triglycerides] < 150 mg%

High Risk

- Same as General / Low Risk PLUS
Target [triglycerides] < 100 mg%

Module #16

Increased LDL, Triglycerides & Lp(a) and Decreased HDL

First Priority: Lower LDL

Rule out and treat secondary causes if possible:

- metabolic: hypothyroidism, diabetes / insulin resistance / metabolic syndrome

Dietary therapy: NCEP TLC diet

- if overweight target 5 to 10% reduction in body weight

If LDL exceeds NCEP drug initiation level or if patient extremely high risk start drug therapy

- Drugs of choice: statins *{will also lower triglycerides, and selected agents (i.e. rosuvastatin (Crestor) and simvastatin) will raise HDL}*
 - select agent and initial dose based on %LDL reduction needed to get to goal
 - when selecting a statin consider that rosuvastatin (Crestor), pitavastatin (Livalo), simvastatin and pravastatin are the only ones that do not cause a secondary increase in Lp(a)
- Alternative drugs:
 - ezetimibe (Zetia) 10 mg qD
 - niacin (up to 2 grams daily) *{will also lower triglycerides and Lp(a), and raise HDL}*
 - fenofibrate or fenofibric acid *{will also lower triglycerides and Lp(a) and raise HDL}*
- AVOID use of resins in setting of elevated triglycerides
- If unable to get to goal on monotherapy consider combination therapy:
 - statin plus ezetimibe
 - statin plus niacin
 - statin plus fenofibric acid
 - triple therapy

Second Priority: Lower Triglycerides

Rule out and treat secondary causes if possible:

- factitious: non-fasting specimen
- metabolic: hypothyroidism, diabetes / insulin resistance / metabolic syndrome, proteinuria / nephrotic syndrome
- iatrogenic: estrogen (oral), non-selective beta blockers, diuretics, resins, steroids, protease inhibitor, alcohol

Dietary therapy: NCEP TLC diet with additional carbohydrate restriction & alcohol avoidance

- if overweight target 5 to 10% reduction in body weight

If drug therapy needed

Drug of choice-fibrates

1. fenofibrate or fenofibric acid *{will also lower LDL and Lp(a) and raise HDL}*

Alternative agents:

1. niacin (up to 2 grams daily) *{will also lower LDL, Lp(a), and raise HDL}*
2. omega-3-fatty acids (EPA+DHA to total 4grams) per day *{will also lower Lp(a)}*

Third Priority: Raise HDL

Rule out and treat secondary causes if possible

- metabolic: diabetes / insulin resistance / metabolic syndrome, hypothyroidism
- iatrogenic: androgens, HCTZ, non-selective beta blockers

Target [total HDL] > 45 mg% in men / >55mg% in women

AVOID alcohol therapy in the setting of elevated triglycerides

Lifestyle interventions:

- smoking cessation
- aerobic exercise

If possible defer drug therapy to specifically raise HDL until triglyceride disorder corrected

Drug therapy to raise HDL:

- drug of choice: niacin 1 to 2 grams per day *{will also lower LDL, triglycerides, and Lp(a)}*
- alternative:
 1. rosuvastatin (Crestor) 10 mg qD *{will also lower LDL and triglycerides}*
 2. simvastatin 40 or 80 mg qD *{will also lower LDL and triglycerides}*
 3. fenofibrate or fenofibric acid *{will also lower LDL, Lp(a), and triglycerides}*

In high risk patients unresponsive to efforts to raise HDL consider lowering [LDL] to below NCEP target

- when selecting a statin consider that rosuvastatin (Crestor), pitavastatin (Livalo), simvastatin and pravastatin are the only ones that do not cause a secondary increase in Lp(a)

Fourth Priority: Lower Lp(a)

If patient is an Afro-American without premature family history no treatment needed.

Rule out and treat secondary causes if possible:

- factitious: acute phase response
- metabolic: hypothyroidism, microalbuminuria / proteinuria in diabetes
 - thyroid hormone replacement to normalize TSH if hypothyroid
 - ACE / ARB therapy in diabetics with microalbuminuria / proteinuria

Lifestyle / non-pharmacological intervention:

- aspirin 81 mg qD if not contraindicated
- restriction of dietary trans-fatty acids
- avoid alcohol in the setting of elevated triglycerides

Drug therapy:

- niacin (up to 2 grams daily) *{will also lower LDL and triglycerides, and raise HDL}*
- omega-3-fatty acids (EPA+DHA to total 4grams) per day *{will also lower triglycerides}*
- fenofibrate or fenofibric acid *{will also lower LDL and triglycerides and raise HDL}*

Alternative approach to specifically lowering [Lp(a)] is to lower the [LDL] below current NCEP guidelines *{Lp(a) loses predictive value if [LDL]< 70 mg%}*

- when selecting a statin consider that rosuvastatin (Crestor), pitavastatin (Livalo), simvastatin and pravastatin are the only ones that do not cause a secondary increase in Lp(a)

VAP PROFILE ABNORMALITIES

LDL Pattern B:

General / Low Risk

- Rule out and treat secondary causes if possible:
 1. iatrogenic: non-selective beta blockers, HCTZ, loop diuretics, steroids
 2. metabolic: diabetes / insulin resistance / metabolic syndrome
- Aggressive dietary counseling to ensure compliance with the NCEP TLC diet (i.e. dietitian referral)
- If not contraindicated use a drug that improves insulin sensitivity in diabetics (i.e. agent in the metformin or "glitazone" class)

Moderate Risk

- Same as General / Low Risk PLUS-
Target [triglycerides]<150 mg%

If unable to shift LDL density consider lowering target [LDL] to less than 100 mg%

- when selecting a statin consider that rosuvastatin (Crestor), pitavastatin (Livalo), simvastatin and pravastatin are the only ones that do not cause a secondary increase in Lp(a)

High Risk

- Same as General / Low Risk PLUS
Target [triglycerides]< 100mg%
- Consider specific drug therapy to shift LDL density
 1. niacin 1-2 grams per day *{will also lower LDL, triglycerides, Lp(a) and raise HDL}*
 2. fenofibrate or fenofibric acid *{will also lower LDL, triglycerides and Lp(a) and raise HDL}*

Increased IDL:

General / Low Risk

- Rule out and treat secondary causes:
- diabetes / insulin resistance / metabolic syndrome
- a very low fat, high carbohydrate diet

Moderate Risk

- Same as General / Low Risk PLUS:
Drug treatment with fenofibrate or fenofibric acid if [triglycerides]>150 mg% *{will also lower LDL, triglycerides, Lp(a) and raise HDL}*

High Risk

- Same as General / Low Risk PLUS:
Drug treatment with combined low dose statin and low dose niacin *{will also lower LDL, triglycerides, Lp(a) and raise HDL}*
 - when selecting a statin consider that rosuvastatin (Crestor), pitavastatin (Livalo), simvastatin and pravastatin are the only ones that do not cause a secondary increase in Lp(a)

Decreased HDL2:

General / Low Risk

- Same approach as used to raise total HDL - see "Third Priority" - this module

Moderate Risk

- Same as General / Low Risk PLUS:
Drug therapy to lower triglycerides if [triglycerides]> 150 mg%

High Risk

- Same as General / Low Risk PLUS:
Drug therapy to lower triglycerides if [triglycerides]> 100 mg%

Increased VLDL3:

General / Low Risk

- Same approach as used to lower triglycerides - see "Second Priority" - this module

Moderate Risk

- Same as General / Low Risk PLUS
Target [triglycerides] < 150 mg%

High Risk

- Same as General / Low Risk PLUS
Target [triglycerides] < 100 mg%

APPENDIX I

CONSIDERATIONS IN COMBINATION THERAPY

Combination pharmacotherapy for dyslipidemia offers the potential for significant improvement in beneficial lipoprotein modification compared to monotherapy and preliminary data suggests the resultant changes in lipid sub-fractions translate into dramatic improvements in angiographic atherosclerotic disease and clinical outcomes^(199,200). However, some drug combinations may increase the potential for adverse effects and should be used with caution and only in those patients for whom the potential benefit outweighs the risks.

STATINS AND FIBRATES:

The combined use of statins and early fibrates (clofibrate and gemfibrozil) has clearly been associated with an increased risk of rhabdomyolysis. However, with fenofibrate and fenofibric acid, this combination may be used if certain precautions are observed^(201,202).

When combining a statin and a fibrate it is always advisable to use a water soluble statin (i.e. rosuvastatin [Crestor], pravastatin or fluvastatin [Lescol]) dosed approximately 12 hours apart from the fibrate dose. Never combine ANY statin with gemfibrozil. One of the more common dosing regimens is fenofibrate or fenofibric acid given with breakfast and either rosuvastatin [Crestor] or pravastatin dosed at bedtime. This dosing split allows the maximum concentrations of both drugs to be separated in time and minimizes combined tissue exposure to both drugs. When adding a fibrate to ongoing statin therapy it is usually advisable to reduce the dose of the statin by one or two dose titration levels.

In 2009 the FDA approved the combination of simvastatin, rosuvastatin (Crestor) and atorvastatin (Lipitor) with TriLipix, one of the branded fenofibric acid preparations. From the medical-legal standpoint, this combination has become the preferred choice for treating combined dyslipidemia. It is anticipated that a fixed dose combination pill with rosuvastatin (Crestor) and fenofibric acid (TriLipix) will be approved.

Combination therapy with fibrates and statins should be avoided in patients with significant hepatic or renal disease, advanced age, hypothyroidism or pre-existing muscle disorders.

STATINS AND NIACIN:

The combined use of statins and niacin initially was thought to be associated with an increased risk of rhabdomyolysis but more recent data confirms that this is not the case⁽²⁰³⁾.

The combination is especially useful in mixed dyslipidemias or in settings of elevated LDL with increased Lp(a), low HDL2 and/or LDL pattern B. There are no special concerns regarding the combination of any statin with niacin and there is a fixed-dose combination pill of Niaspan –simvastatin available [Simcor]. A previous fixed dose

combination of Niaspan – lovastatin is no longer available.

Combined niacin / statin therapy should not be used in patients with significant renal or hepatic disease.

STATINS AND OMEGA-3-FATTY ACIDS:

The combination of statins and omega-3-fatty acids (i.e. “fish oils”) is very effective for the treatment of mixed cholesterol and triglyceride disorders, and is especially useful when a statin / fibrate or statin / niacin combination is contra-indicated or not tolerated . There are no known adverse interactions between any statin and any brand of omega-3-fatty acids.

STATINS AND EZETIMIBE (ZETIA):

The combination of a statin and ezetimibe is exceptionally potent for LDL reduction. The addition of ezetimibe [Zetia] 10 mg to any statin is equivalent to three dose titrations of that statin (or an addition ~25% LDL reduction)⁽²⁰⁴⁾, effectively making simvastatin 10 plus Zetia 10 equivalent to simvastatin 80 in term of LDL reduction.

Although ezetimibe (Zetia) received some bad press in 2009 and 2010, the FDA has reiterated its position that there are no special concerns with the combination of any statin with ezetimibe and specifically with a fixed dose combination pill with simvastatin plus ezetimibe [Vytorin].

STATINS AND RESINS:

Statin / resin combinations are very effective in treating isolated LDL elevations. Water soluble statins (rosuvastatin [Crestor], pravastatin and fluvastatin [Lescol]) can be bound by the older resins (questran and colestid), preventing their absorption. If these drugs are used in combination the statin should be given 1 hour before or 4 hours after the resin dose.

None of the currently available statins have any interaction with the newer resin colsevelam [Welchol].

OTHER COMBINATIONS:

Combinations of fibrates +/- niacin +/- omega-3-fatty acids are very effective in treating recalcitrant triglyceride disorders, elevated Lp(a), low HDL, and LDL pattern B dyslipidemias. There are no known interactions between fibrates, niacin, and omega-3-fatty acids.

The combination of a resin with niacin and / or a fibrate is effective therapy for mixed dyslipidemias, especially when the patient is not a candidate for combination therapy with a statin. The older resins (questran and colestid) do have the potential to bind fibrates and some forms of niacin, and appropriate adjustments to the times of the doses should be made if these agents are used. The resin (colsevelam [Welchol]) does not have an interaction with fibrates or any niacin product. Another potential therapy for mixed

dyslipidemia is ezetimibe [Zetia] with either a fibrate or niacin.

APPENDIX II
EFFECTS OF LIPID-ACTIVE AGENTS ON SELECTED
ADVANCED LIPID PARAMETERS

	LDL-size	Lp(a)	HDL2
STATINS			
Lovastatin	↑	↑	↑
Pravastatin	↔/↓	↔	↑
Simvastatin	↑	↔	↑↑
Fluvastatin [Lescol]	?	↔	↑
Atorvastatin [Lipitor]	↑	↑↑	↓
Rosuvastatin [Crestor]	↑↑	↔	↑↑↑
Pitavastatin [Livalo]	↑↑	↔	↔
FIBRATES			
Gemfibrozil [Lopid]	↔/↑	↔	↔
Fenofibrate	↑↑	↓	↔
Fenofibric acid	↑↑	↓	↔
Ezetimibe [Zetia]	↑	↔	↔
RESINS			
Colesevelam [Welchol]	↑	↔	↔
Colestyramine	↑	↔	↔
Colestipol	↑	↔	↔
Niacin	↑↑↑	↓↓	↑↑↑
Omega-3 Fatty Acids	↔	↓	↔

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