On The Cusp of a New Lipid Treatment Guideline

How the ATP IV Recommendations Could Change Cardiovascular Risk Reduction in Practice

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Disclosures

Consulting-National Lipid Association

Evolution of the Lipid Treatment Guidelines

Framingham Study, MRFIT Study | **ARIC Study, AMORIS Study** | **Framingham Offspring Study, MESA Study**

Pre-Statin Trials	Angiographic Trials	Major Statin Trials	Statin Trials in Lower Risk Subjects, *or* for Intensive Lipid Lowering, *or* for Residual Dyslipidemia	
CDP	CLAS	4S	HPS	TNT
LRC-CPPT	FATS	CARE	PROSPER	IDEAL
HHS	STARS	LIPID	ASCOT-LLA	SEARCH
	MARS	WOSCOPS	ALLHAT-LLT	JUPITER
	SCOR	AF/TexCAPS	REVERSAL	ACCORD
	Ornish	Fibrate Trials	PROVE-IT	AIM-HIGH
	REGRESS	VAHIT	A to Z	HPS2-THRIVE
	HARP	DIAS		
	POSCH	FIELD		

NCEP ATP I 1988	NCEP ATP II 1993	NCEP ATP III 2001	ATP III Update 2004	ACC/AHA ATP IV (PENDING)

More Intensive Treatment Recommendations

Classification of Lipid Levels Per ATP III

ATP III Classification of LDL, Total, and HDL Cholesterol (mg/dL)

LDL Cholesterol – Primary Target of Therapy	
<100	Optimal
100-129	Near optimal/above optimal
130-159	Borderline high
160-189	High
≥190	Very high
Total Cholesterol	
<200	Desirable
200-239	Borderline high
≥240	High
HDL Cholesterol	
<40	Low
≥60	High

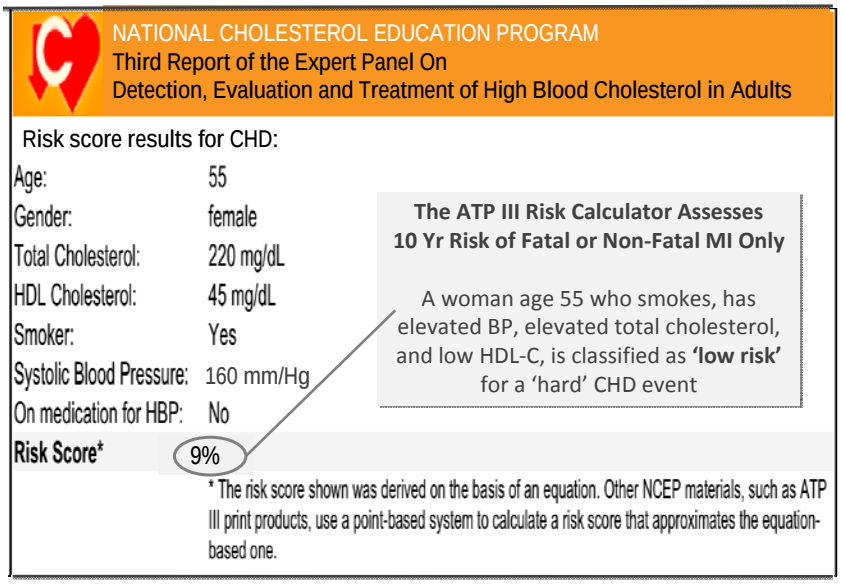
JAMA 2001;285:2486-97.

Anticipated Lipid Classification Changes
In ATP IV

- Reduction in the number of sub-categories
- Removal of misleading descriptions
- ? New cutoffs for "Optimal" LDL
  - ? <100 mg/dl for primary prevention
  - ? <70 mg/dl for secondary prevention

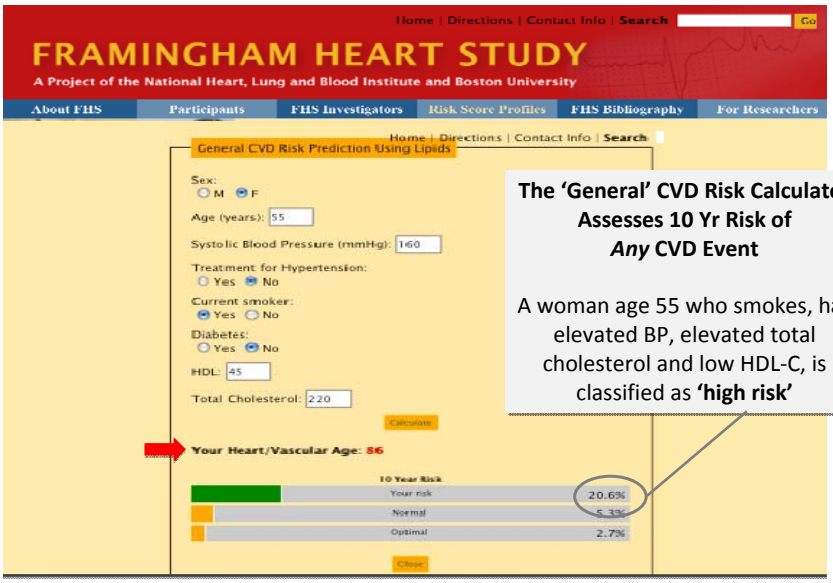
Martin, Seth et al. Amer Jour Cardiol 2012;110:307-13.

Risk Assessment Per ATP III



JAMA 2001;285:2486-97.

Risk Assessment Using a Global CVD Score



The 'General' CVD Risk Calculator Assesses 10 Yr Risk of *Any* CVD Event

A woman age 55 who smokes, has elevated BP, elevated total cholesterol and low HDL-C, is classified as **'high risk'**

www.framinghamheartstudy.org

Anticipated Risk Assessment Changes

In ATP IV

- **Consideration of *lifetime* cardiovascular risk**
- **Consideration of *imaging studies***
  - **Coronary Calcium Score (CAC)**
  - **Carotid Intima Media Thickness (CIMT)**
- **? Communication of *vascular age* to patients**

*Adds parental history and hsCRP

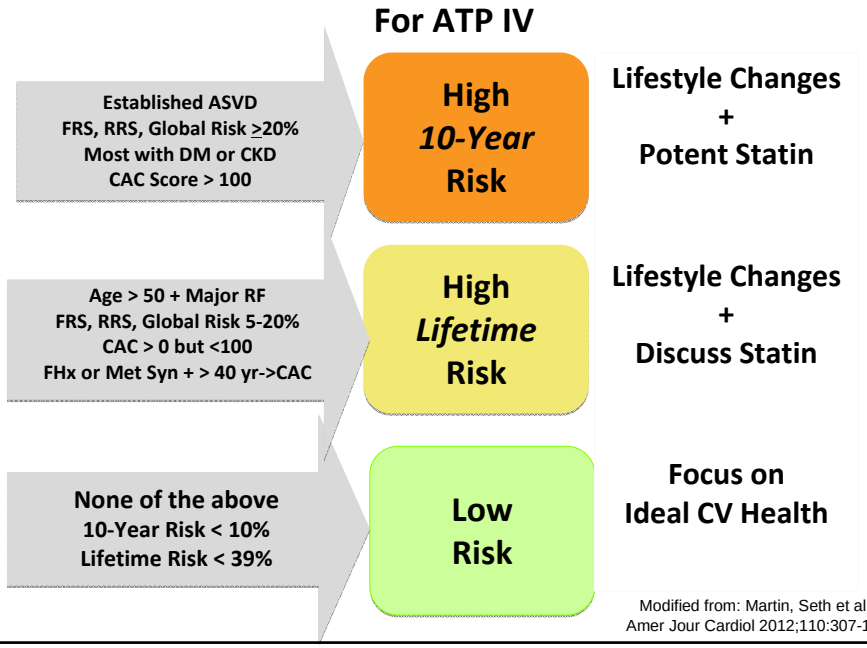
Lipid Treatment Algorithm Per ATP III

LDL Cholesterol Goals and Cut-Points for Therapeutic Life Style Changes and Drug Therapy in Different Risk Categories

Risk Category	LDL Goals	LDL Level at Which To Initiate Therapeutic Lifestyle Changes	LDL Level at Which To Consider Drug Therapy
CHD or CHD Risk Equivalents (10-year risk >20%)	<100 mg/dL < 70 Optional**	≥100 mg/dL	≥130 mg/dL (100-129 mg/dL: drug optional)*
2+ Risk Factors (10-year risk ≤20%)	<130 mg/dL < 100 Optional**	≥130 mg/dL	10-year risk 10-20%: ≥130 mg/dL 100-129 mg/dl: drug optional ** 10-year risk <10%: ≥160 mg/dL
0-1 Risk Factor†	<160 mg/dL	≥160 mg/dL	≥190 mg/dL (160-189 mg/dL: LDL-lowering drug optional)

JAMA 2001;285:2486-97. ** Changes made in the ATP III 2004 Update: Circulation 2004; 110:227-239.

Proposed Lipid Treatment Algorithm Changes



Modified from: Martin, Seth et al. Amer Jour Cardiol 2012;110:307-13.

Lipid Targets per ATP III

Comparison of LDL Cholesterol and Non-HDL Cholesterol Goals for Three Risk Categories

Risk Category	Primary Target LDL-C Goal (mg/dl)	Secondary Target Non-HDL-C Goal (mg/dl)
CHD and CHD Risk Equivalent (10-year risk for CHD >20%)	<100 < 70 Optional**	<130 < 100 Optional**
Multiple (2+) Risk Factors and 10-year risk ≤20%	<130 < 100 Optional**	<160
0-1 Risk Factor	<160	<190

** Per the ATP III 2004 Update: Circulation 2004; 110:227-239.

JAMA 2001;285:2486-97.

Distinction Between LDL-C, Non-HDL-C and Apo-B

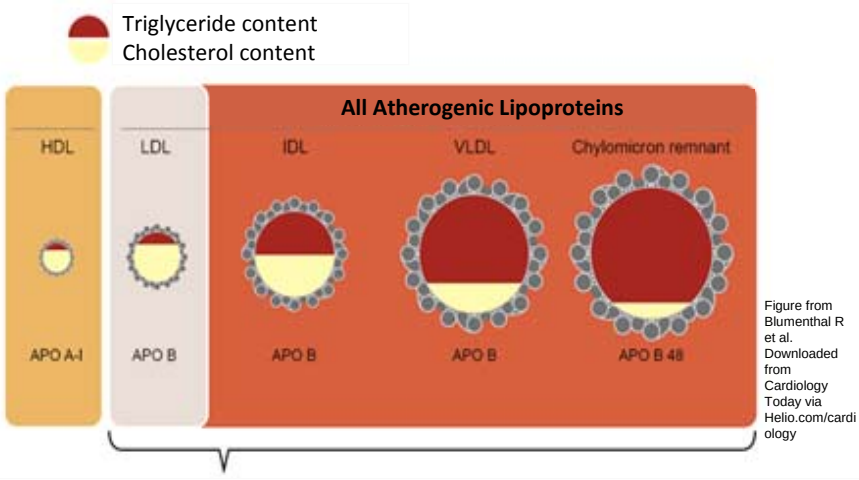


Figure from Blumenthal R et al. Downloaded from Cardiology Today via Helio.com/cardiology

Non-HDL-C = Total-C minus HDL-C = Better marker of risk than LDL, esp. if high TG present

Apo-B = a reflection of the total *number* of atherogenic particles and may be best predictor

Proposed Lipid Target Changes
In ATP IV

- LDL-C
  - Consider a single LDL target if drug treated
  - Consider one LDL target for primary prevention and one for secondary prevention
  - Abolish LDL targets
- Non-HDL-C
  - Consider as a primary target in all with high TG
  - Consider as an alternative primary target in all
- Apo-B
  - Consider as a target in all with CHD, DM or high TG

Martin, Seth et al. Amer Jour Cardiol 2012;110:30.
Haymard, R and Krumholz, H Circulation Cardiovas Qual Outcomes 2012;5:2-5.

Drug Treatment Per ATP III

Drugs Affecting Lipoprotein Metabolism

Drug Class	Agents and Daily Doses	Lipid/Lipoprotein Effects		Side Effects	Contraindications
HMG CoA Reductase Inhibitors (Statins)	Lovastatin (20-80 mg) Pravastatin (20-40 mg) Simvastatin (20 Fluvastatin (20 Atorvastatin (1 Cerivastatin (0.	LDL HDL	↓18-55% ↑5-15%	Myopathy Increased liver	Absolute: • Active or chronic liver disease Relative: • Concomitant use of certain drugs*
Bile Acid Sequestrants	Cholestyramine (4-16 g) Colestipol (5-20 g) Colesevelam (2.6-3.8 g)	LDL HDL TG	↓15-30% ↑3-5% No change or increase	Gastrointestinal distress Constipation Decreased absorption of other drugs	Absolute: • dysbeta-lipoproteinemia • TG >400 mg/dL Relative: • TG >200 mg/dL
Nicotinic Acid	Immediate release (crystalline) nicotinic acid (1.5-3 gm), extended release nicotinic acid (Niaspan®) (1-2 g), sustained release nicotinic acid (1-2 g)	LDL HDL TG	↓5-25% ↑15-35% ↓20-50%	Flushing Hyperglycemia Hyperuricemia (or gout) Upper GI distress Hepatotoxicity	Absolute: • Chronic liver disease • Severe gout Relative: • Diabetes • Hyperuricemia • Peptic ulcer disease
Fibric Acids	Gemfibrozil (600 mg BID) Fenofibrate (200 mg) Clofibrate (1000 mg BID)	LDL *(may be increased in patients with high TG)* HDL TG	↓5-20% ↑10-20% ↓20-50%	Dyspepsia Gallstones Myopathy	Absolute: • Severe renal disease • Severe hepatic disease

" Start Statin or Bile Acid Sequestrant or Niacin."

JAMA 2001; 285: 2486-97.

Simvastatin 80mg no longer recommended

Anticipated Drug Treatment Changes

In ATP IV

- Prioritize statins over all other drugs
- Use potent statins at tailored doses
- For statin intolerant patients
  - Change to different statin
  - Reduce daily statin dose
  - Use alternate day dosing
- For LDL > desired on maximum statin
  - Add on Ezetimibe or BAS
- For High TG
  - Titrate statin OR add on other agents
- Individualize follow-up lab testing

Diet Recommendations Per ATP III

Initiate therapeutic lifestyle changes (TLC) if LDL is above goal

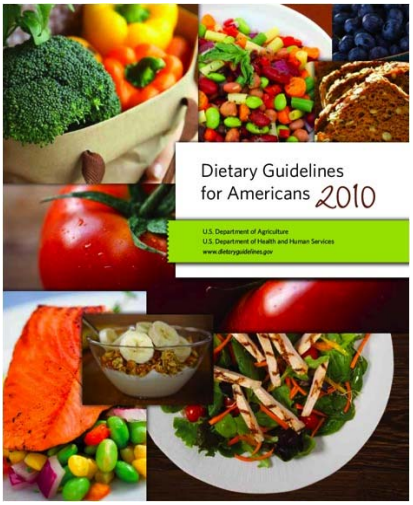
TLC Diet Features

Nutrient	Recommended Intake
Saturated fat	< 7% of total calories
Polyunsaturated fat	Up to 10% of total calories
Monounsaturated fat	Up to 20% of total calories
Total fat	25-35% of total calories
Carbohydrate	50-60% of total calories
Fiber	20-30 g/day
Protein	Approximately 15% of total calories
Cholesterol	<200mg/day
Total calories	Balance energy intake and expenditure

JAMA 2001;285:2486-97.

Anticipated Diet Recommendation Changes
In ATP IV

- Remove recommendations for nutrient intake as "% of calories"
- Promote specific diet patterns
  - Mediterranean
  - DASH
- Promote specific nutrient-rich foods
  - Dark fruits and vegetables
  - Fatty fish
  - Nuts and seeds



Summary

- The ATP III guideline has been viewed as complex, and may misclassify risk and under treat some groups
- The following have been suggested for ATP IV
  - Reclassify lipoprotein levels and targets
  - Assess risk based on global and lifetime CVD risk
  - Simplify the treatment algorithm (risk→treatment)
  - Consider primary therapeutic targets other than LDL
  - Prioritize statins for all
  - Provide more food-specific diet messages
  - Allow more Individualized laboratory F/U
- Actual recommendations await the ATP IV guideline