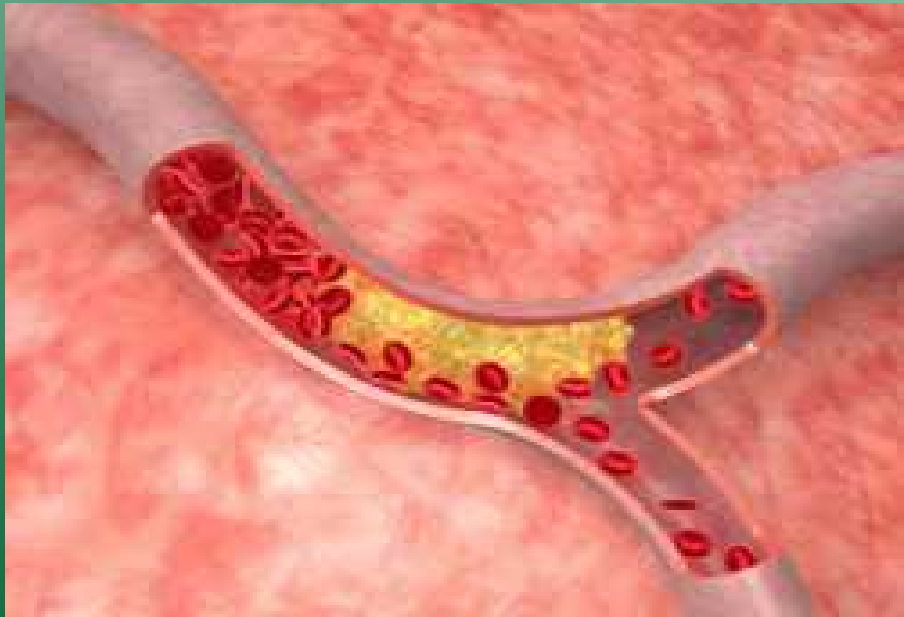# What's new in Lipid Management

ALL recommendations are intended to guide decision making but do not replace clinical judgment.

Guidelines advise that patients and clinicians engage in a "risk discussion."

Table. The 5 Ps

Variable	Question
Preference	What does the patient prefer based on his or her values and priority setting?
Precision	How precise is the patient's risk estimate, and is further testing warranted to refine it?
Participation	How motivated is the patient to participate in his or her ongoing care and improve lifestyle habits?
Potency	What treatment and dose are proposed?
Price	Can the patient afford the proposed treatment?

Dyslipidemia

➢ Disorder of Lipid & Lipoprotein Metabolism

➢ A common form of Dyslipidemia is characterized by three lipid abnormalities:

- Elevated triglycerides,

- Elevated LDL and

- Reduced HDL cholesterol.

➢ Important Modifiable Risk Factor for CAD

Dyslipidemia

Causes

Primary

Genetic Disorders

Secondary

Diabetes

Nephrotic Syndrome

Hypothyroidism

Drug – Induced

Hypertension

Secondary causes of Dyslipidemia

Selected Causes of Secondary Dyslipidemia

Increased LDL cholesterol level	Increased triglyceride level	Decreased HDL cholesterol level
Diabetes mellitus	Alcoholism	Cigarette smoking
Hypothyroidism	Diabetes mellitus	Diabetes mellitus
Nephrotic syndrome	Hypothyroidism	Hypertriglyceridemia
Obstructive liver disease	Obesity	Menopause
Drugs	Renal insufficiency	Obesity
Anabolic steroids	Drugs	Puberty (in males)
Progestins	Beta-adrenergic blockers (without	Uremia
Beta-adrenergic blockers (without	intrinsic sympathomimetic action)	Drugs
intrinsic sympathomimetic action)	Bile acid-binding resins	Anabolic steroids
Thiazides	Estrogens	Beta-adrenergic blockers (without
	Ticlopidine (	intrinsic sympathomimetic action)
		Progestins

LDL=low-density lipoprotein; HDL=high-density lipoprotein.
Adapted with permission from Schaefer EJ. Diagnosis and management of lipoprotein disorders. In: Rifkind BM, ed. Drug

Major ATP III Risk Factors

Coronary Heart Disease Risk Based on Risk Factors Other Than the LDL Level

Positive risk factors

- Male >=45 years
- Female >=55 years or postmenopausal without estrogen replacement therapy
- Family history of premature coronary heart disease (definite myocardial infarction or sudden death before age 55 in father or other male first-degree relative or before age 65 in mother or other female first-degree relative)
- Current cigarette smoking
- Hypertension (blood pressure >=140/90 mm Hg or patient is receiving antihypertensive drug therapy)
- HDL cholesterol level <35 ~~mg per dL (<0.90 mmol per L)~~ **< 40mg/dL (<1.03mmol/L)**
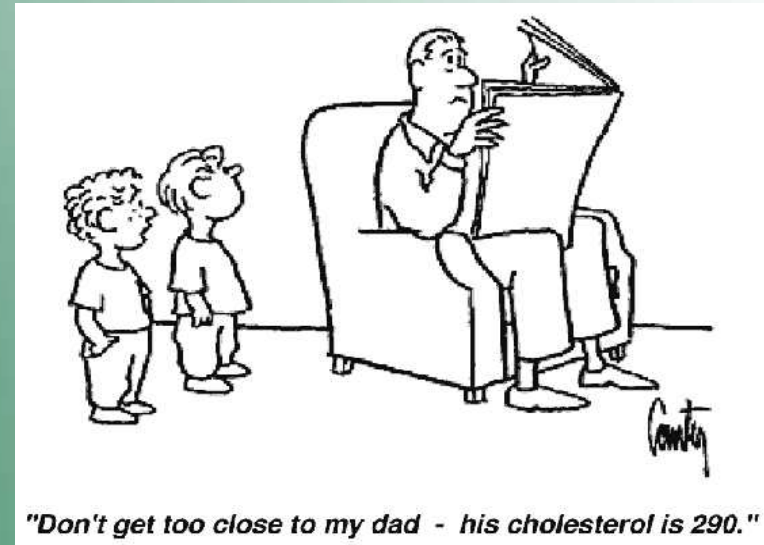- Diabetes mellitus

Negative risk factor*

- High HDL cholesterol level (>=60 mg per dL [>=1.60 mmol per L])

LDL=low-density lipoprotein; HDL=high-density lipoprotein.
*--Subtract one positive risk factor if negative risk factor is present.

CHD Equivalents

- **Diabetes Mellitus**

- **Carotid Artery Disease (>50% stenosis)**

- **Prior CVA or TIA**

- **Peripheral Arterial Disease**

- **Abdominal Aortic Aneurysm**

- Framingham Score >20% 10 yr Risk

- ?? Chronic Renal Insufficiency

- ?? Abnormal Coronary Calcium Scores

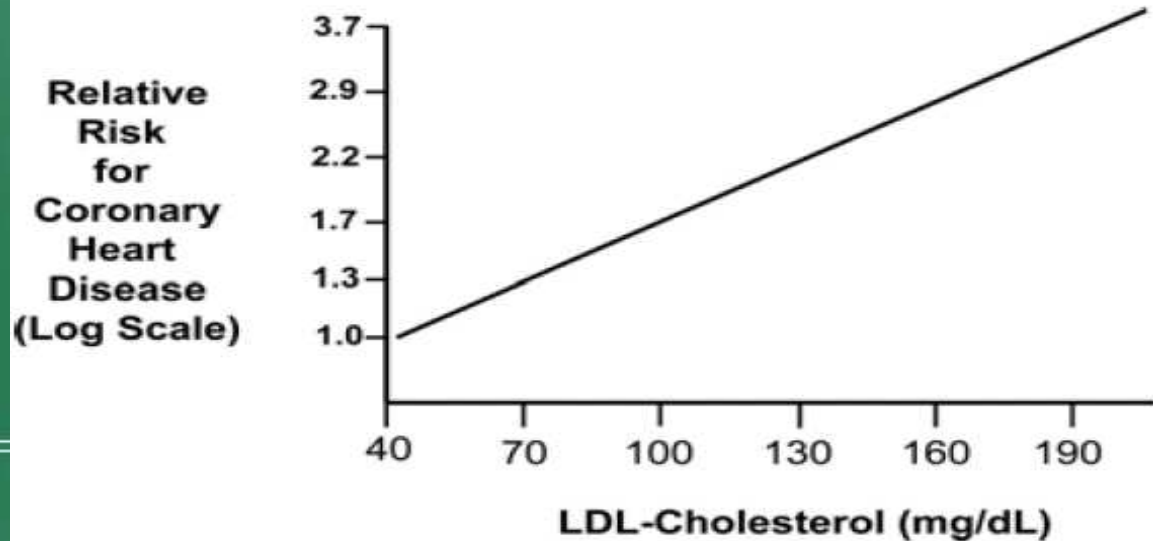"Don't get too close to my dad - his cholesterol is 290."

Relationship Between LDL-C and HDL-C Levels and CHD Risk

LDL-C
1-mg decrease
reduces CHD
risk by 1%

HDL-C
1-mg increase
reduces CHD
risk by 3%

Third Report of the NCEP Expert Panel. NIH Publication No. 01-3670. 2001.
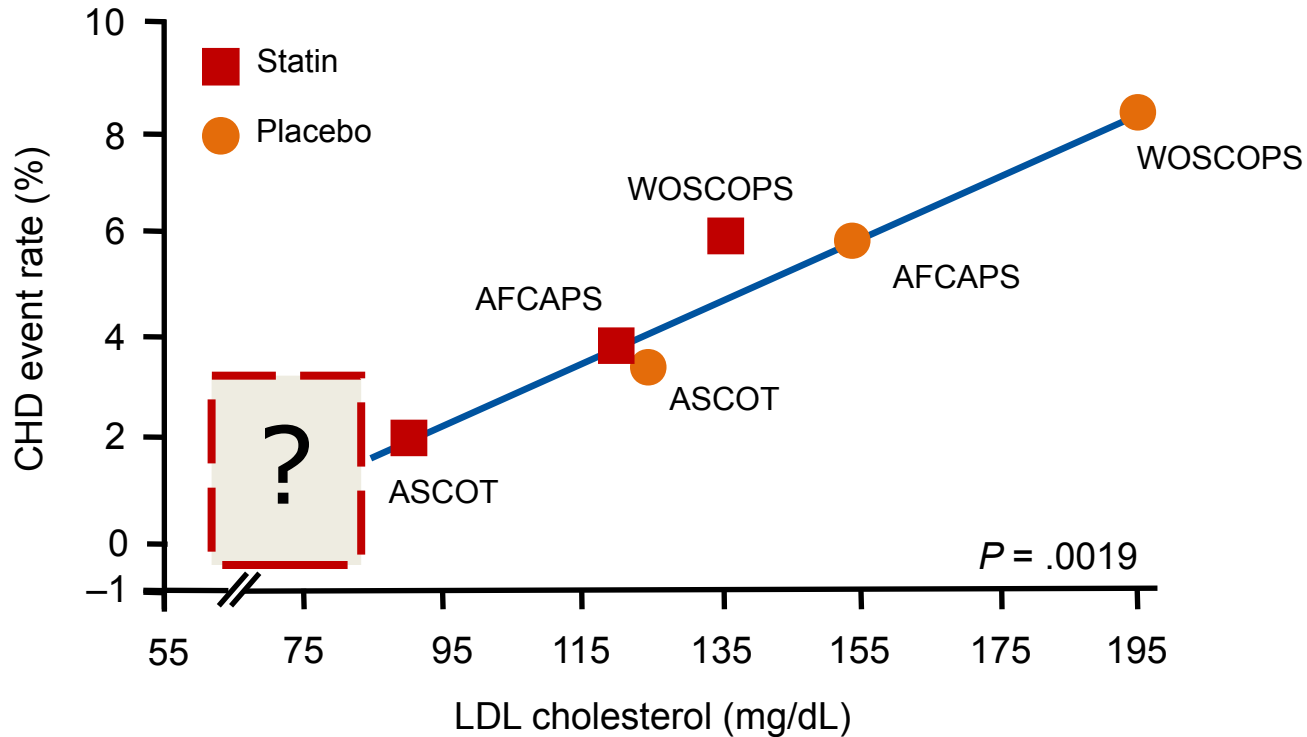
LDL-C and CV risk

Relative
Risk
for
Coronary
Heart
Disease
(Log Scale)

3.7
2.9
2.2
1.7
1.3
1.0

40   70   100   130   160   190

LDL-Cholesterol (mg/dL)

Circulation 2004; 110:227-239.

Primary Prevention—Statins

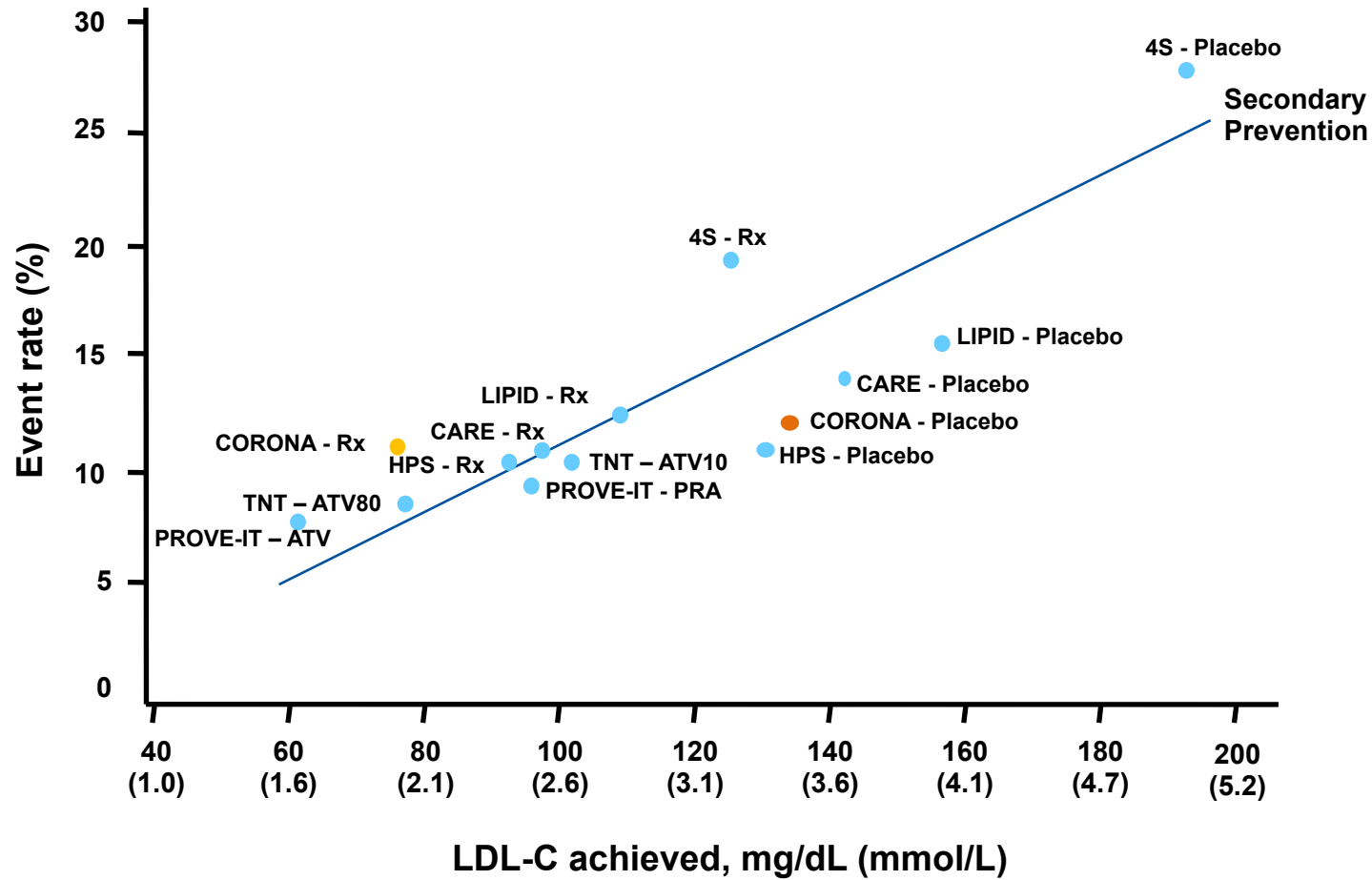## Relationship between LDL-C levels and event rates in primary prevention statin trials

AFCAPS, Air Force/Texas Coronary Atherosclerosis Prevention Study; ASCOT, Anglo-Scandinavian Cardiac Outcomes Trial—Lipid Lowering Arm, WOSCOPS, West of Scotland Coronary Prevention Study

- Click to edit the outline text format
  - Second Outline Level

Secondary Prevention and Target Values
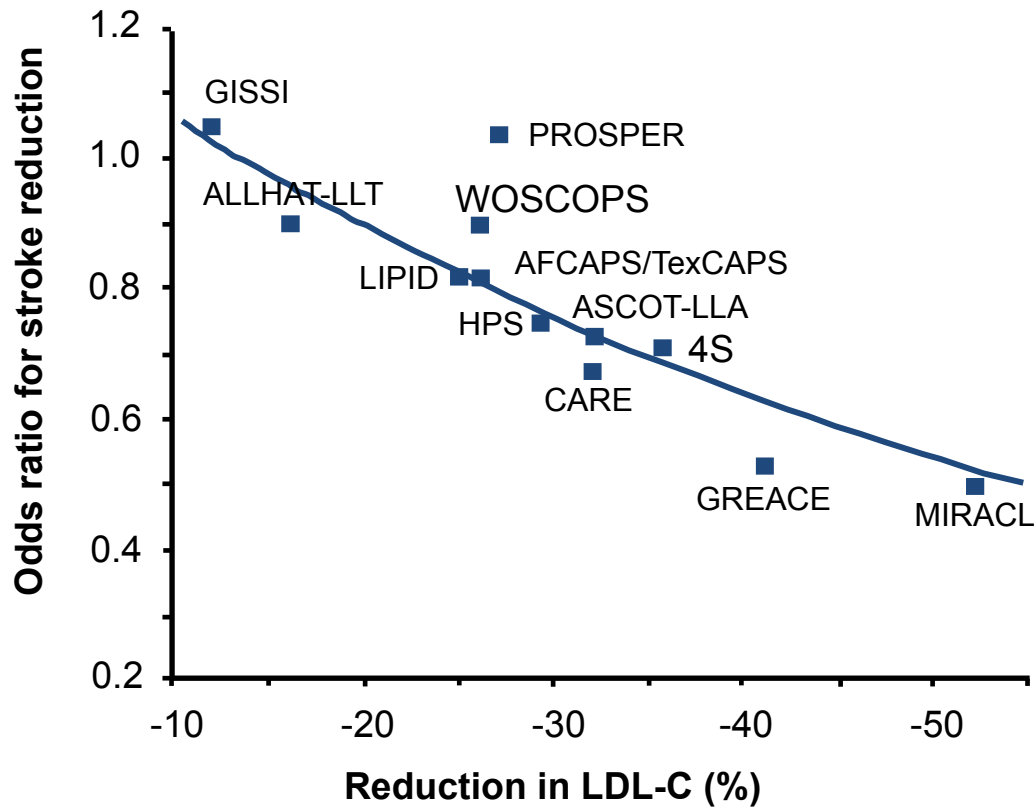
- Click to edit the outline text format
  - Second Outline Level

On-Treatment LDL-C Is Closely Related to Stroke Events in Statin Trials—Lower Is Better

Relationship between protection from stroke events and LDL-C reduction

- Click to edit the outline text format
  - Second Outline Level

Guidelines & management

"Don't come home till that bag is full of money."

ATP III: 2004 Update

Risk Category	LDL-C Goal (mg/dL)	Initiate TLC (mg/dL)	Consider Drug Rx (mg/dL)
High Risk CHD or equivalents (10 yr risk > 20%)	< 100 (Optional <70)[#]	≥100[*]	≥ 100[+] (<100: consider drug options)[**]
Moderately High Risk 2+ risk factors (10 yr risk 10 to 20%)	< 130 (Optional < 100)	≥ 130[*]	≥ 130 (100-129: consider drug options)[++]
Moderate Risk 2+ risk factors (10 yr risk < 10%)	< 130	≥ 130	≥ 160
Lower Risk 0 to 1 risk factors	< 160	≥ 160	≥ 190 (160-189: drug optional)

[#] Very high risk favors < 70 mg/dl, and patients with high TGs or non HDL >100 mg/dl

[*] High risk or moderately high with lifestyle related risk should be on TLC regardless of LDL

[+] LDL Tx based on clinical evidence; ↑TGs or↓ HDL consider combing with nicotinic acid or fibrate

[**] Achieve at least a 30 to 40% LDL reduction

[++] LDL Tx to achieve LDL < 100 mg/dl is an option based on clinical trials

Circulation 2004; 110:227-239.

Goals for Therapy: 2004 Addendum

NCEP ATP III guidelines for LDL Therapy

LDL-C <160 for 1 or less risk factors

LDL-C <130 for 2+ risk factors

> < 100 is a therapeutic option

LDL-C <100 for CAD and CAD equivalents

> <70 is option for very high risk patients

1. CAD + multiple risk factors, especially diabetes

2. CAD + severe or poorly controlled risk factor(s)

3. CAD + metabolic syndrome

4. Acute coronary syndrome

5. CAD event despite baseline LDL-C < 100

ATP III: 2004 Update
Standard Statin Doses to Attain 30 - 40% LDL- C Reductions

Drug	Dose (mg/d)	LDL-C reduction (%)
Atorvastatin	10	39
Lovastatin	40	31
Pravastatin	40	34
Simvastatin	20-40	35-41
Fluvastatin	40-80	25-35
Rosuvastatin	5-10	39-45

Lipid-Lowering Therapies

	LDL - C	HDL - C	TG
Statins (atorvastatin, fluvastatin, lovastatin, pravastatin, rosuvastatin, simvastatin)	↓ 18-63%	↑ 5-15%	↓ 7-30%
Bile Acid Sequestrants (colesevelam, cholestyramine, colestipol)	↓ 15-30%	↑ 3-5%	0 or ↑
Nicotinic Acid (ER or IR niacin)	↓ 5-25%	↑ 15-35%	↓ 20-50%
Fibric Acid Derivatives (benzafibrate, gemfibrozil, fenofibrate)	↓ 5-20 or ↑	↑ 10-20%	↓ 20-50%
Cholesterol Absorption Inhibitor (ezetimibe)	↓ 18%	↑ 1%	↓ 7%

Fragmingham Risk scoring

Risk Assessment Tool for Estimating Your 10-year Risk of Having a Heart Attack

The risk assessment tool below uses information from the Framingham Heart Study to predict a person's chance of having a heart attack in the next 10 years. This tool is designed for adults aged 20 and older who do not have heart disease or diabetes. To find your risk score, enter your information in the calculator below.

Age: `49` years

Gender: ○ Female ◉ Male

Total Cholesterol: `187` mg/dL

HDL Cholesterol: `40` mg/dL

Smoker: ○ No ◉ Yes

Systolic Blood Pressure: `136` mm/Hg

Are you currently on any medication to treat high blood pressure. ○ No ◉ Yes

[Calculate Your 10-Year Risk]

In the wake of the partnership struck between the American Heart Association (AHA), American College of Cardiology (ACC), and the original guidelines developer, the National Heart, Lung, and Blood Institute (NHLBI), the new guidelines and accompanying risk calculator were simultaneously published in the flagship journals of the two cardiology organizations.

2013 ACC/AHA Guideline on the Assessment of Cardiovascular Risk: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines

David C. Goff, Jr, Donald M. Lloyd-Jones, Glen Bennett, Sean Coady, Ralph B. D'Agostino, Sr, Raymond Gibbons, Philip Greenland, Daniel T. Lackland, Daniel Levy, Christopher J. O'Donnell, Jennifer Robinson, J. Sanford Schwartz, Susan T. Shero, Sidney C. Smith, Jr, Paul Sorlie, Neil J. Stone and Peter W.F. Wilson
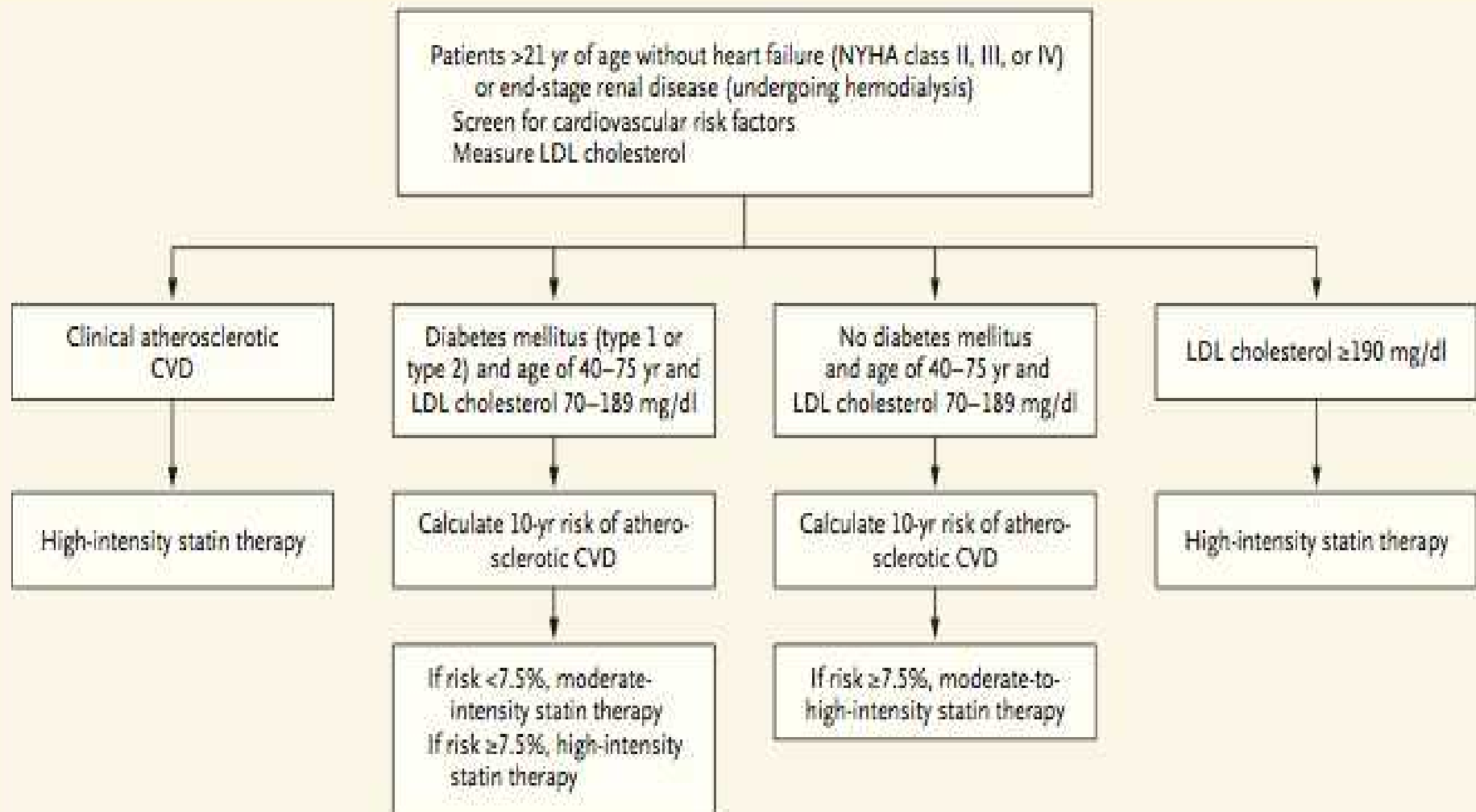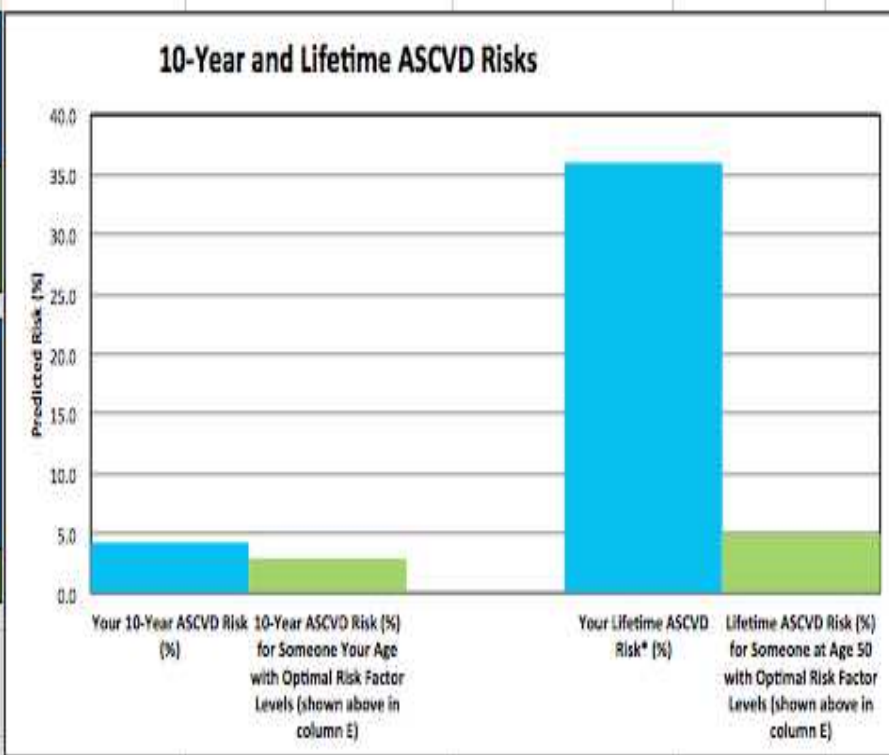
Figure 1. 2013 American College of Cardiology–American Heart Association Guidelines for Use of Statin Therapy in Patients at Increased Cardiovascular Risk.

	Risk Factor	Units	Enter patient values in this column Value	Acceptable range of values	Optimal values	
1						
2	Risk Factor	Units	Value	Acceptable range of values	Optimal values	
3	Sex	M (for males) or F (for females)	m	M or F		
4	Age	years	53	20-79		
5	Race	AA (for African Americans) or WH (for whites or others)	wh	AA or WH		
6	Total Cholesterol	mg/dL	192	130-320	170	
7	HDL-Cholesterol	mg/dL	45	20-100	50	
8	Systolic Blood Pressure	mm Hg	118	90-200	110	
9	Treatment for High Blood Pressure (if SBP >120)	Y (for yes) or N (for no)	n	Y or N	N	
10	Diabetes	Y (for yes) or N (for no)	n	Y or N	N	
11	Smoker	Y (for yes) or N (for no)	n	Y or N	N	
12						

13	Your 10-Year ASCVD Risk (%)	4.2	
14	10-Year ASCVD Risk (%) for Someone Your Age with Optimal Risk Factor Levels (shown above in column E)	2.9	
15			
16	Your Lifetime ASCVD Risk* (%)	36.0	
17	Lifetime ASCVD Risk (%) for Someone at Age 50 with Optimal Risk Factor Levels (shown above in column E)	5.0	

10-Year and Lifetime ASCVD Risks

*This is the lifetime ASCVD risk for an individual at age 50 years with your risk factor levels. In rare cases, 10-year risks may exceed lifetime risks given that the estimates come from different approaches.

Abbreviations: AA = African American; ASCVD = Atherosclerotic cardiovascular disease, defined as CHD death, nonfatal myocardial infarction, or fatal or nonfatal stroke; F = Female; M = Male; N = No; WH = White; Y = Yes.

The calculator uses nine pieces of information—sex, age, race, total cholesterol, HDL cholesterol, systolic blood pressure, current treatment for high blood pressure, diagnosis of diabetes, smoking habit—to do this.

The new guidelines recommend a statin for seemingly healthy people with a risk of 7.5% or higher.

Guidelines use specific risk factors to determine who should be prescribed statins, rather than a cholesterol number.

Persons with clinical atherosclerotic cardiovascular disease include those with an acute coronary syndrome and those with a history of myocardial infarction, stable or unstable angina, coronary or other arterial revascularization, or stroke, transient ischemic attack, or peripheral arterial disease that is presumed to be of atherosclerotic origin.

High-intensity statin therapy is recommended for most patients meeting these criteria. Patients predisposed to adverse statin effects (including those with impaired renal or hepatic function, other serious coexisting conditions, a history of statin intolerance, concomitant use of drugs affecting statin metabolism, an age of >75 years, or unexplained elevations in alanine aminotransferase levels >3 times the upper limit of the normal range) should use moderate-intensity statin therapy when high-intensity statin therapy would otherwise be recommended.

Table 1. High-Intensity and Moderate-Intensity Statin Therapy, According to 2013 American College of Cardiology–American Heart Association (ACC-AHA) Cholesterol Guidelines.

High-intensity statin therapy

Daily dose lowers LDL cholesterol level by approximately ≥50% on average

Recommended: atorvastatin, 40 to 80 mg; rosuvastatin, 20 to 40 mg

Moderate-intensity statin therapy

Daily dose lowers LDL cholesterol level by approximately 30 to <50% on average

Recommended: atorvastatin, 10 to 20 mg; rosuvastatin, 5 to 10 mg; simvastatin, 20 to 40 mg; pravastatin, 40 to 80 mg; lovastatin, 40 mg; extended-release fluvastatin, 80 mg; fluvastatin, 40 mg twice a day; pitavastatin, 2 to 4 mg

The guidelines say that the ones with the best evidence for preventing heart attack and stroke are simvastatin, atorvastatin, and rosuvastatin.

Using this new approach, the expert panel identified four subgroups of patients for whom the benefit of statins clearly outweighs the risk.   These groups are patients with

1. clinically evident atherosclerotic cardiovascular disease,

2. primary low-density lipoprotein (LDL) cholesterol levels of at least 190 mg per deciliter,

3. type 1 or type 2 diabetes and an LDL cholesterol level of 70 mg per deciliter or higher,

or 4. a 10-year risk of atherosclerotic cardiovascular disease of at least 7.5%, according to the new, publicly available, pooled cohort equations, and an LDL cholesterol level of at least 70 mg per deciliter.

1. Practicing clinicians will see considerable changes in practice patterns

2. elimination of routine assessments of LDL cholesterol levels in patients receiving statin therapy, because target levels are no longer emphasized;

3. avoidance of non-statin LDL cholesterol– lowering agents in statin-tolerant patients;

4. more conservative use of statins in patients older than 75 years of age who have no clinical atherosclerotic cardiovascular disease;

5. diminished use of surrogate markers such as C-reactive protein or calcium scores; and

6. the use of a new risk calculator that is certain to target larger numbers of patients for statin treatment.

Gone are the recommended LDL- and non-HDL–cholesterol targets, specifically those that ask physicians to treat patients with cardiovascular disease to less than 100 mg/dL or the optional goal of less than 70 mg/dL.

The new guidelines make no recommendations for specific LDL-cholesterol or non-HDL targets for the primary and secondary prevention of atherosclerotic cardiovascular disease.

Copyright 2003 by Randy Glasbergen.
www.glasbergen.com

"I found 1837 web sites about 'alternative medicine' but none of them recommend pizza or chocolate for lowering our cholesterol."

The New Calculator

Based on ATP 3, roughly about 15 million patients should be treated in the USA.

Based on present recommendations, it would be about 31 million, in the United States, there are roughly 100 million people between the age of 40 and 75.

Note that one out of three deaths are cardiac or stroke and 60% of people in their lifetime will have a heart attack or stroke.

Some things are made simple and some things more complicated.

Identify high-risk individuals.

These are people who had events; nobody would argue about that.

People who have diabetes and are 40-69 years of age are identified as high-risk.

People who have LDL levels more than 190 mg/dL -- we'd all agree that that is a high-risk group.

The controversy is people whose 10-year risk is more than 7.5%.

The controversy over the calculator doesn't affect anyone in categories 1, 2, or 3. For them, the benefits of taking a statin far outweigh the risks.

Category 4

For example, what if your is LDL high, say 150 mg/dL, and the calculator says you have an 8% risk of developing ASCVD in the next 10 years. The new guidelines say take a statin.

But guidelines are just information to guide a decision, not to mandate it. The best approach for such individuals is to have a discussion with a trusted physician.

To manage potential limitations of the risk calculator, a reasonable middle ground might be to expand the definition of intermediate risk from a range of 5.0% to 7.5% to a range of 5% to 15%. Patients falling in this range who desire greater certainty could then consider their family history or coronary artery calcium score to refine risk assessment.

Almost Everyone!!
The 7.5% risk threshold for primary prevention was selected based on analyses suggesting that benefit from treatment emerges at this threshold.

Once we get to be 70 years old, our 10-year risk is going to be high enough that we should be getting a statin, which is what is recommended.
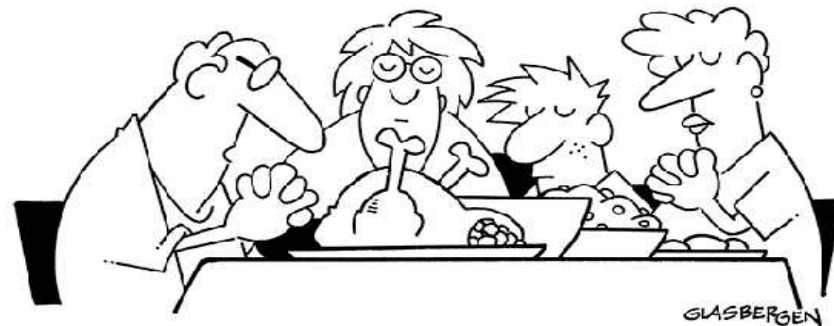
Does that strike you as being appropriate?

With few exceptions, use of lipid-modifying drugs other than statins is discouraged. The guidelines are easier because it's either moderate or high dose statins, and it knocks out other medications like fibrates, niacin, and ezetimibe unless patients are statin intolerant

Patients could have a completely normal lipid profile, with normal triglycerides, HDL cholesterol, and LDL cholesterol, but because of age or because blood pressure is 145 mm Hg, the guidelines will now recommend treatment.

This is going to be problematic for a lot of physicians and patients because just last week their LDL-cholesterol levels of 80 or 90 [mg/dL] is optimal
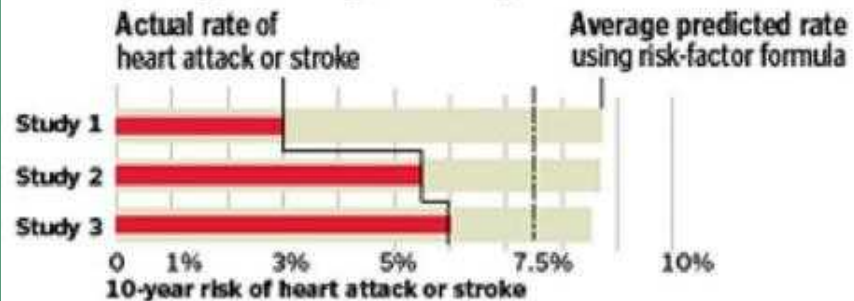

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glasbergen.com

"Lord, make us grateful for the cholesterol, diabetes, high blood pressure, weight gain and indigestion we are about to receive."

GLASBERGEN

The guidelines select 70 mg/dL as the threshold for treatment if their 10-year risk exceeds 7.5%.

There would likely be less resistance to change if the guideline writers selected 100 mg/dL as the lower threshold for treatment in this group

OVERESTIMATED RISK

Patients whose risk factors predicted between 7.5 and 10 percent chance of strokes or heart attacks had them far less frequently, according to an analysis of three studies.

Actual rate of heart attack or stroke

Average predicted rate using risk-factor formula

Study 1

Study 2

Study 3

0   1%   3%   5%   7.5%   10%
10-year risk of heart attack or stroke

SOURCE: Lancet

DAVID BUTLER/GLOBE STAFF

This guideline is designed explicitly to replace the widely used ATP3 guideline from the National Heart, Lung, and Blood Institutes, last updated in 2004.
The obvious major change is that clinicians now are directed to initiate either moderate-intensity or high-intensity statin therapy for patients who fall into the four aforementioned categories, without titration to a specific LDL cholesterol target.

Measuring lipids during follow-up of drug-treated patients is done to assess adherence to treatment and not to see whether a specific LDL cholesterol target has been achieved!

The new recommendations do not target fixed LDL-C and non–high-density lipoprotein cholesterol (HDL-C) goals. Rather, they recommend lipid measurement at baseline, 1 to 3 months after statin initiation, and yearly thereafter to check for the expected percentage decrease of LDL-C levels (30% to 45% with a moderate-intensity statin and ≥50% with a high-intensity statin).

Strict devotion to lipid targets might inadvertently lead to withholding treatment in high-risk patients with favorable baseline lipid levels or unnecessary addition of nonstatin drugs

NEW
CHOLESTEROL
RECOMMENDATIONS

SOURCE:
AMERICAN HEART
ASSOCIATION

HEART DISEASE

DIABETES (TYPE 1 OR 2)

TAKE STATIN

10 YEAR RISK OVER 7.5%

BAD CHOLESTEROL OVER 190

CNN

Cholesterol Guidelines Under Attack

By THE EDITORIAL BOARD

Published: November 18, 2013

Patients in good cardiovascular health would be well advised to stay away for now from following the cholesterol guidelines issued last week by the nation's two leading heart organizations.
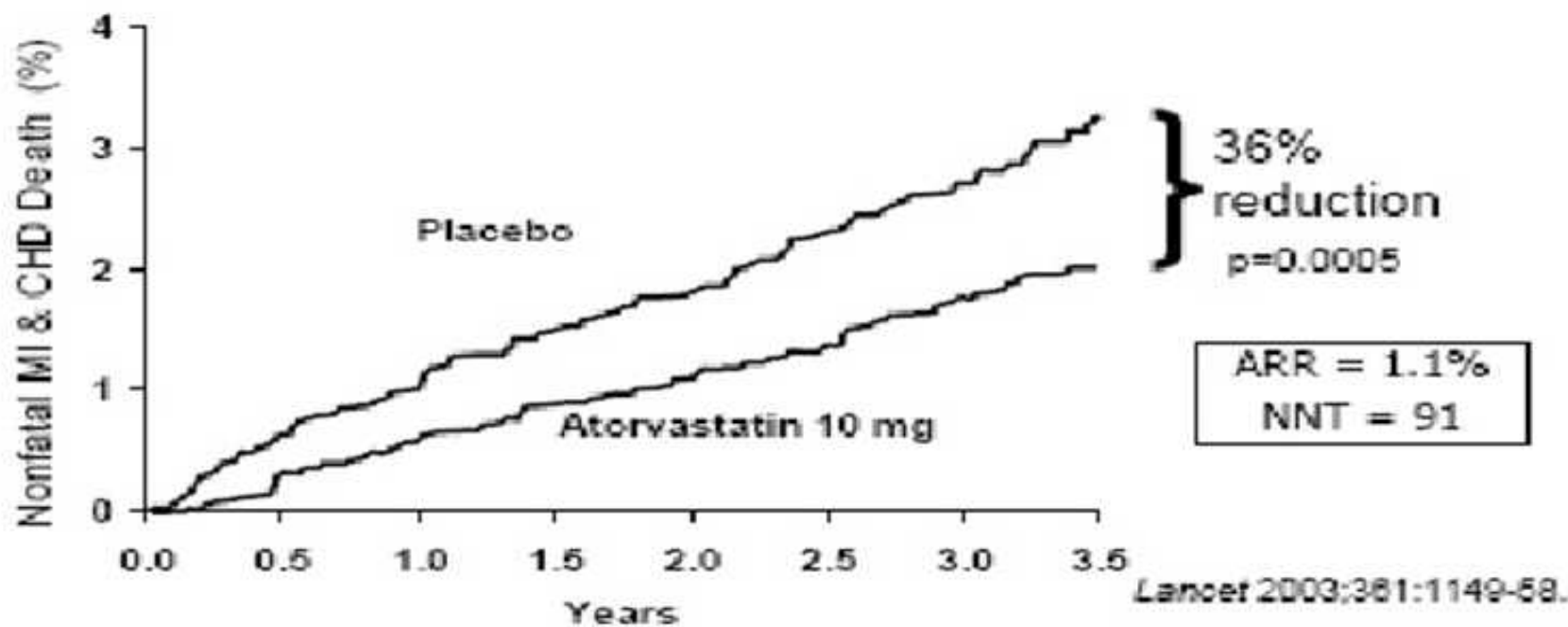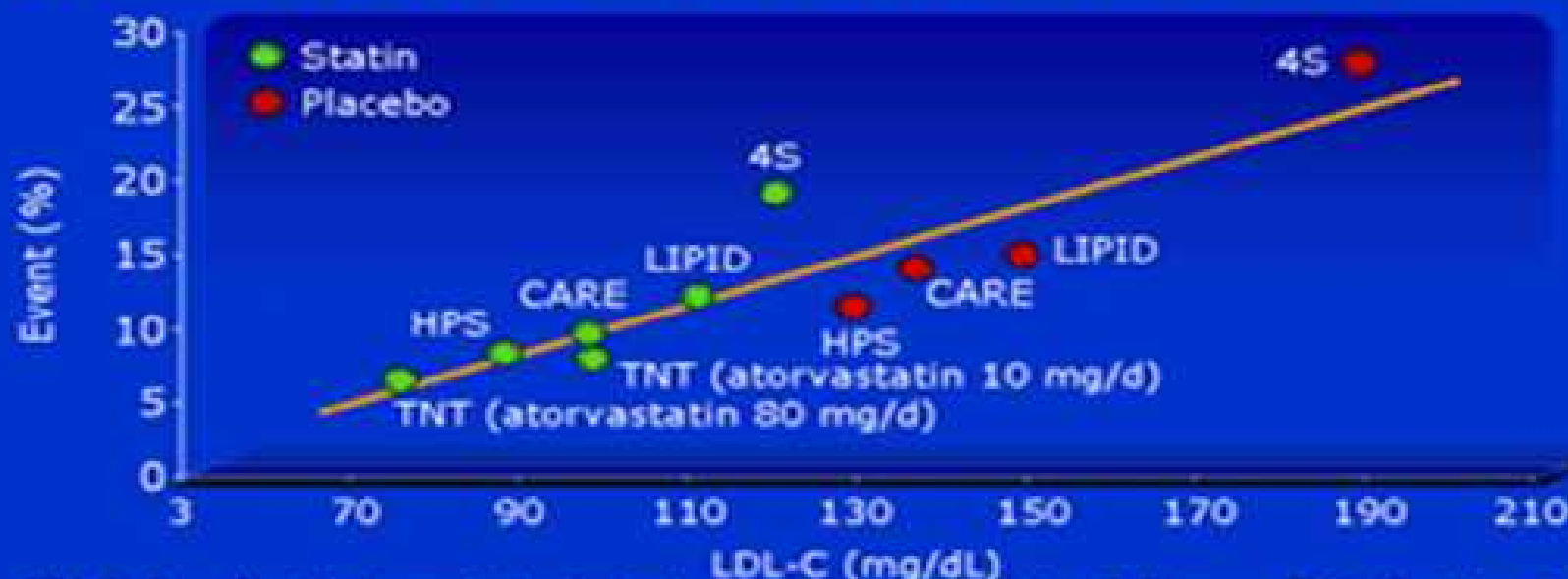
ASCOT-Lipid Lowering Arm

▸ 10,305 primary prevention patients, multiple CV risk factors randomized to placebo or atorvastatin 10 mg daily for 3.3 yrs

▸ Mean baseline LDL 133 mg/dL decreased to 90 mg/dL

Lancet 2003;361:1149-58.

Statin-Based Outcomes Trials

There is no question that statin trials have been dramatically effective at reducing the rate of heart disease. No question at all.

From mortality or event statistics, heart attacks used to be 5:1 compared with strokes. Now it's about 1.5:1. Note major work in stroke prevention with our antihypertensives.

We didn't have anything like statins that were safe and tolerated well by most people until statins came along.

Obesity

- Goal: to help PCPs manage obesity and weight management for their patients
- Attempted to address misinformation in the society at large
- Questions addressed (limited scope
  - Health risks associated with obesity related problems? => use BMI and waist circumference
  - What are the benefits of weight loss? - even modest weight loss can improve outcomes (even 3%-5% weight loss can be beneficial)
  - What are the best diets? There is no superiority for weight loss of 17 diets examined => recommend reduced calories
  - Lifestyle Intervention? Comprehensive approach recommend diet AND exercise. Recommend 6 -12 months counseling and recommended trained interventionist for counseling as best options. Web- or commercial-based programs are a second alternative.
  - If BMI > 30 with comorbidity or if BMI > 40, consider bariatric surgery
- Did not cover pharmaceutical therapies for obesity or drugs that contribute to weight gain

Summary: Ask 4 Questions

Cholesterol Treatment to Reduce Atherosclerotic Risk
Attempt to Identify 4 Statin Groups

1. Does the patient have a history of heart disease or stroke? Are they using secondary prevention? (Use 2011 AHA/ACC secondary prevention guidelines)

2. Is LDL > 190 mg/dL? They have FH.

3. Does patient have diabetes, 40-75 years old, with LDL of 70-189 mg/dL?

4. Does patient have global 10-year risk score $\geq$ 7.5% for primary prevention of risk assessment?

High-, Moderate-, and Low-Intensity Statin Therapy

High-Intensity Statin Therapy
Lowers LDL-C, on average, by approximately ≥ 50%

- **Atorvastatin (40)-80 mg**
- **Rosuvastatin 20** *(40)* **mg**

Moderate-Intensity Statin Therapy
Lowers LDL-C, on average, by approximately 30% to < 50%

- **Atorvastatin 10** *(20)* **mg**
- **Rosuvastatin** *(5)* **10 mg**
- **Simvastatin 20-40 mg‡**
- **Pravastatin 40** *(80)* **mg**
- **Lovastatin 40 mg**
- *Fluvastatin XL 80 mg*
- **Fluvastatin 40 mg bid**
- *Pitavastatin 2-4 mg*

Thank You