2017 MID-ATLANTIC
CONFERENCE

7th ANNUAL CURRENT CONCEPTS IN
VASCULAR THERAPIES

2017

John E. Brush, Jr.,
MD, FACC
Professor, EVMS
Sentara Cardiology

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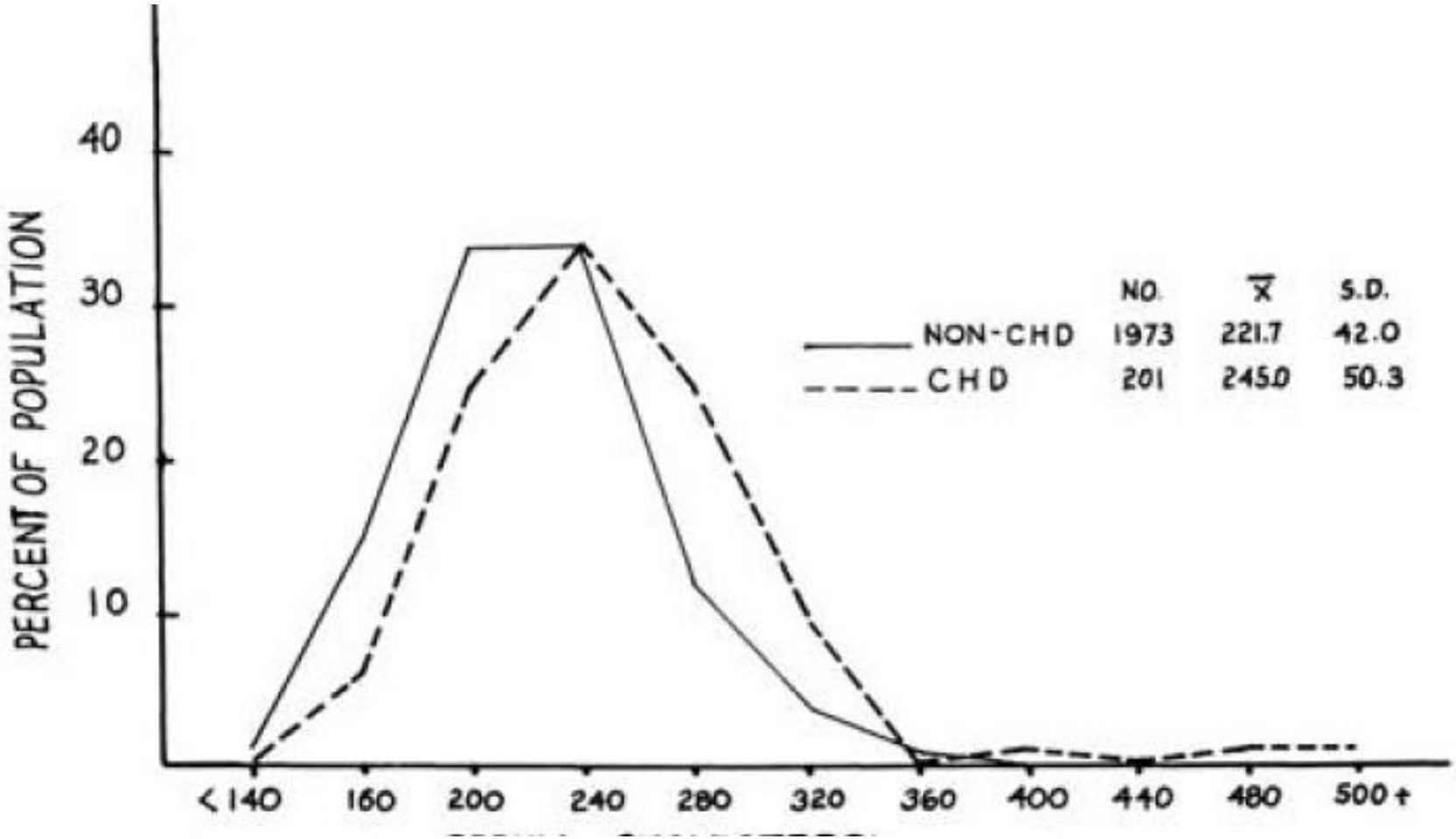
All Vascular Patients Should Be on High Dose Statin Therapy

Disclosures

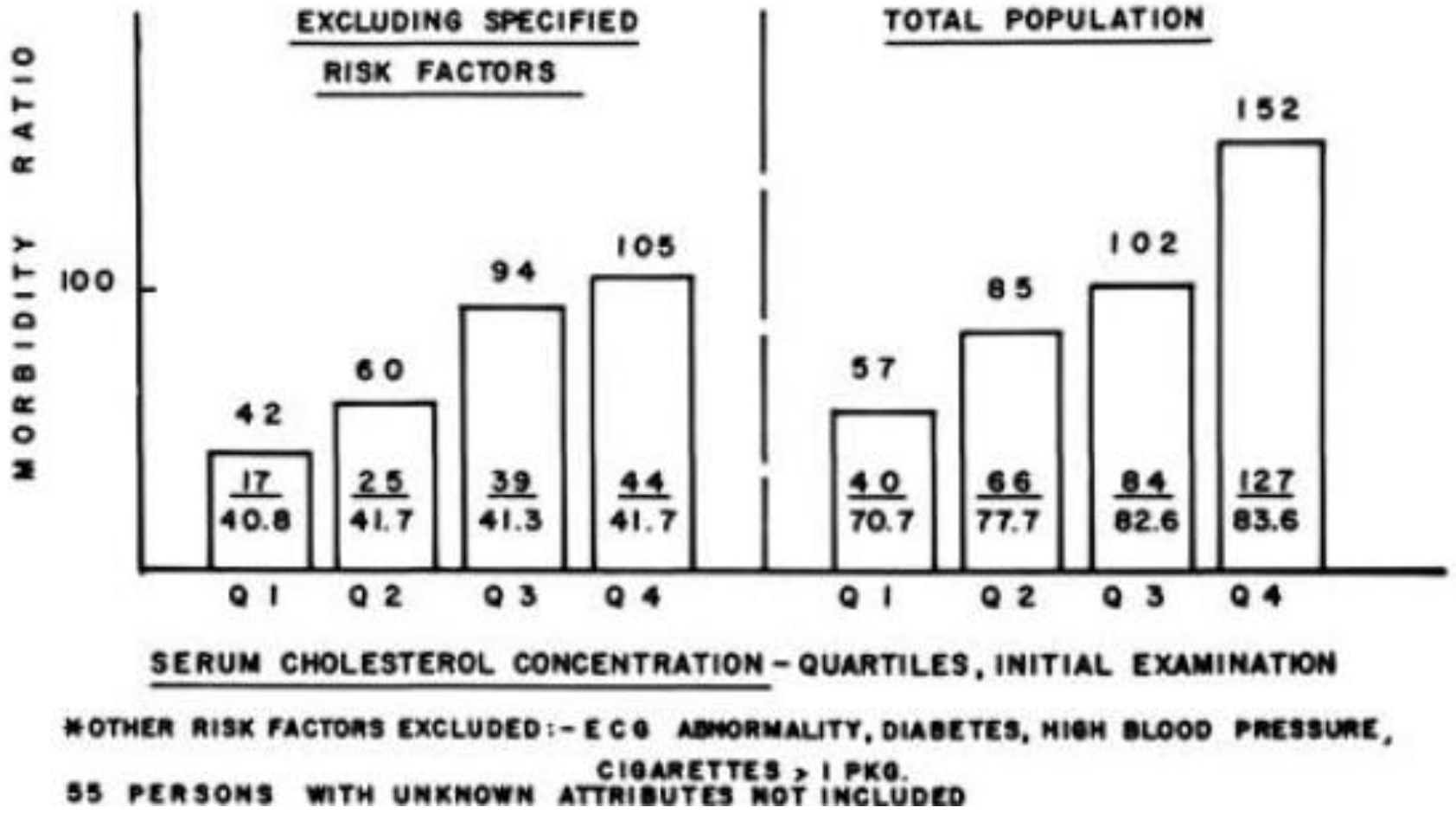
- None

Cholesterol and Coronary Artery Disease Framingham Study



Kannel, et al Ann Intern Med 1964; 61:888-899

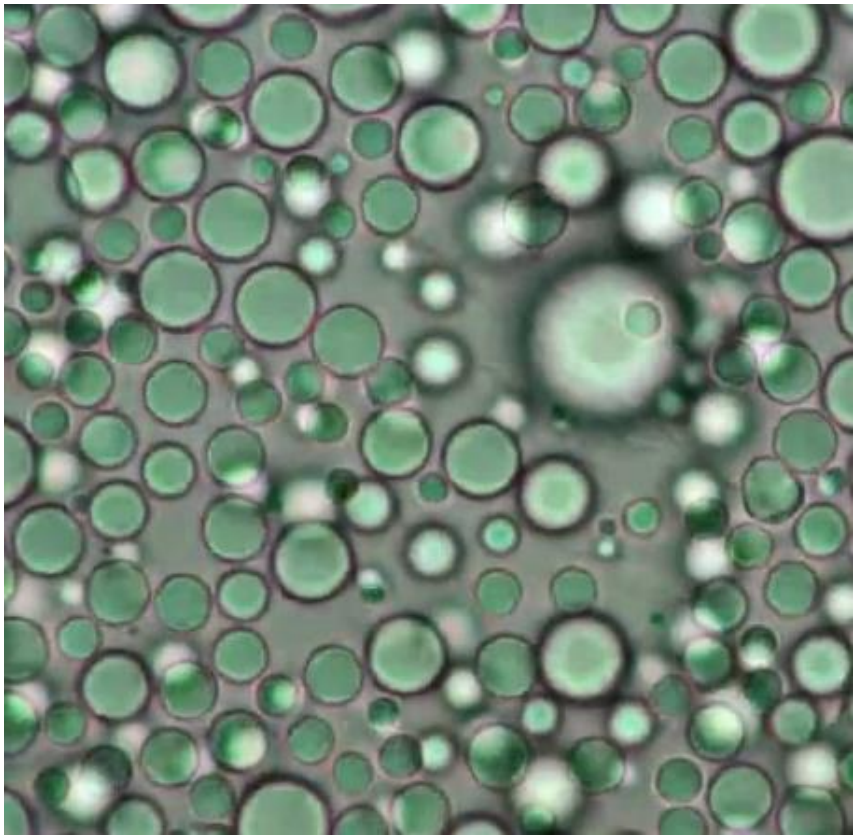
Risk of CAD, Framingham



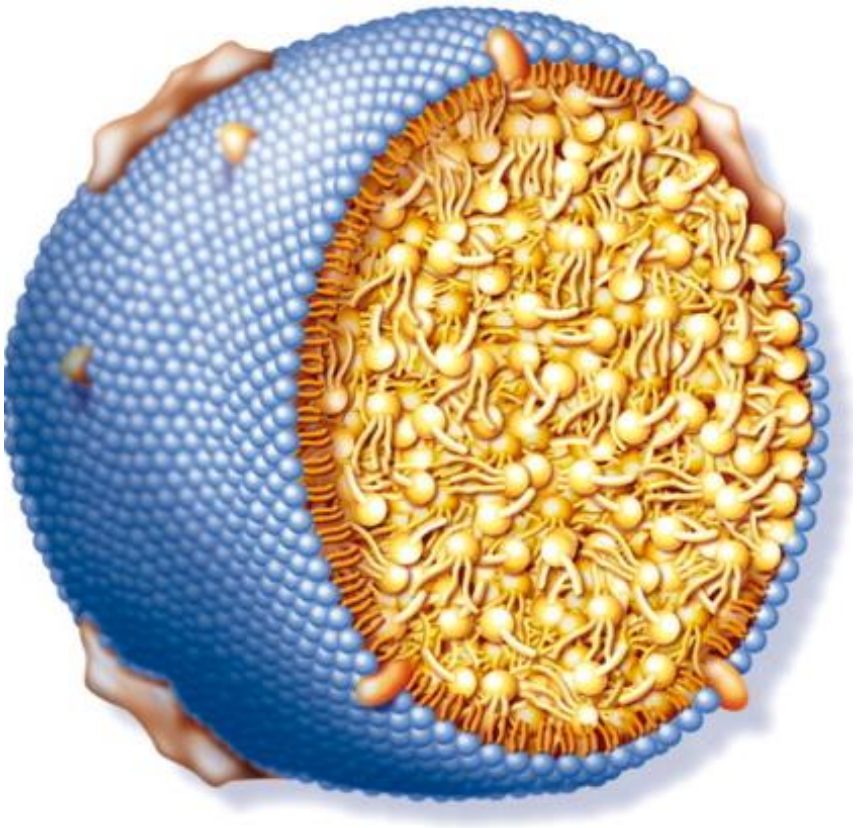
Kannel, et al. Ann Internal Med 1971:74:1-12

Cholesterol

Fat Globules

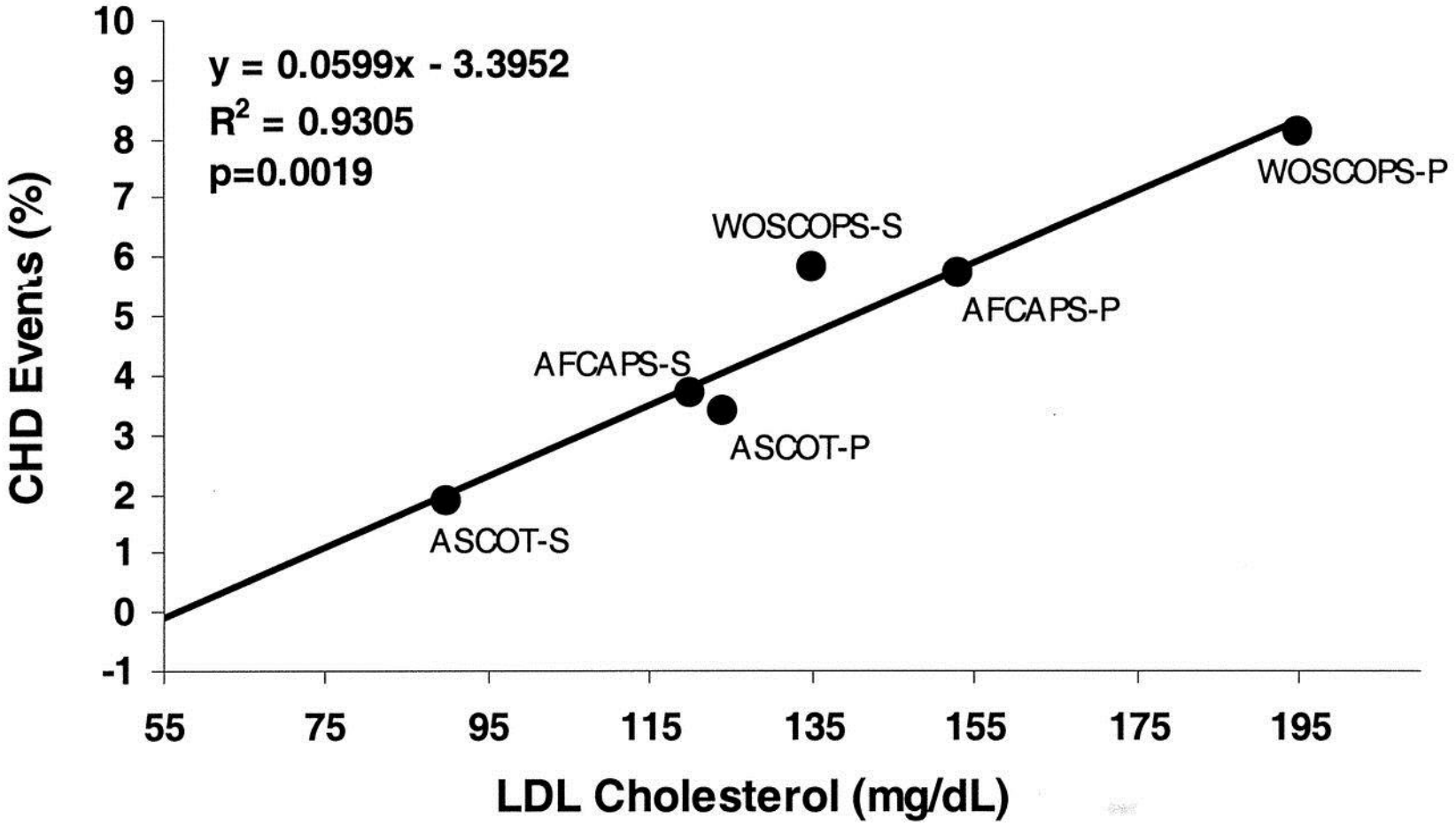


LDL



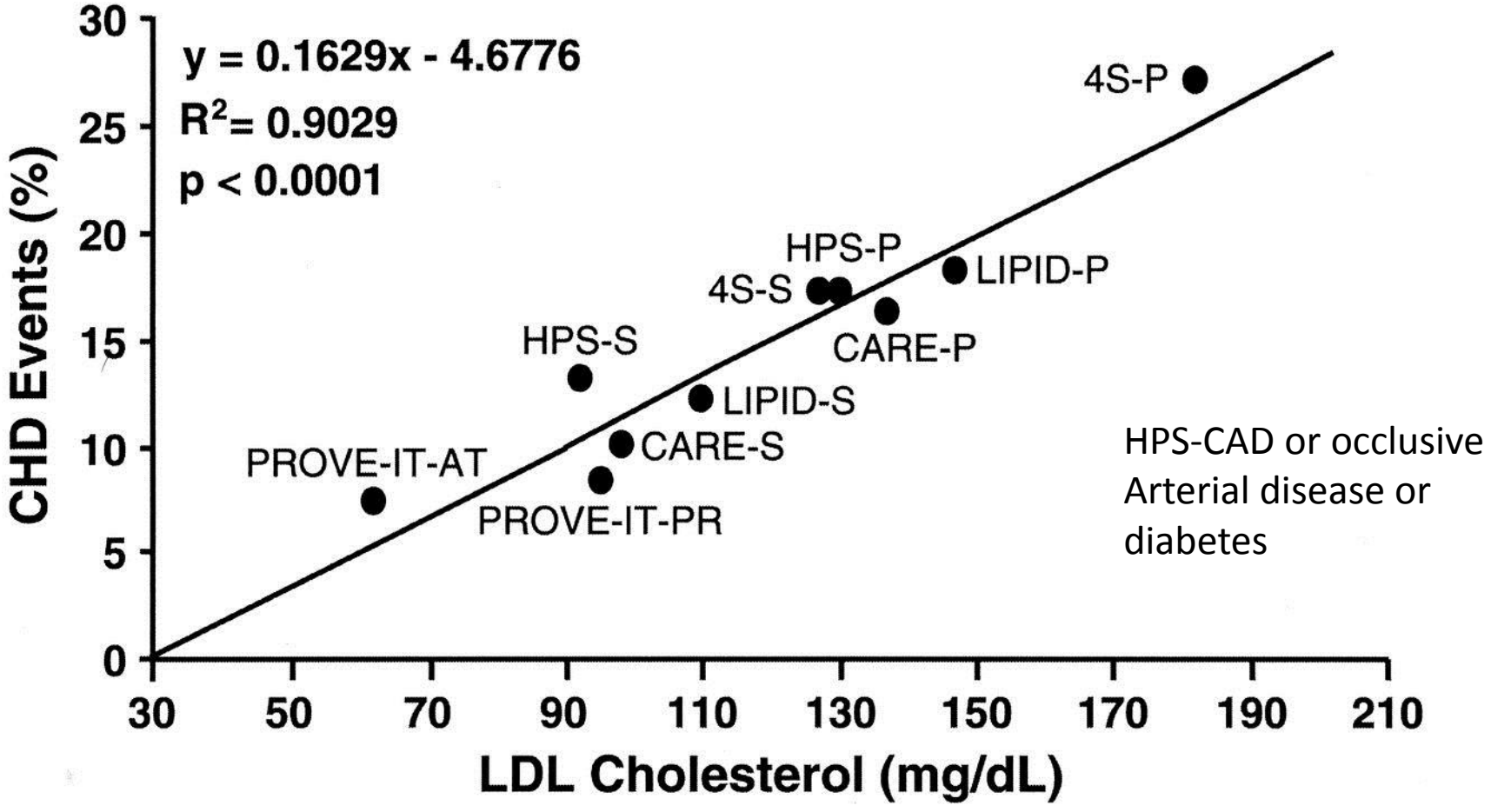
Phospholipid membrane (blue), cholesterol (yellow), apolipoproteins (beige).

Primary Prevention Trials



James H O'Keefe, Jr et al. JACC 2004;43:2142-2146

Secondary Prevention Trials

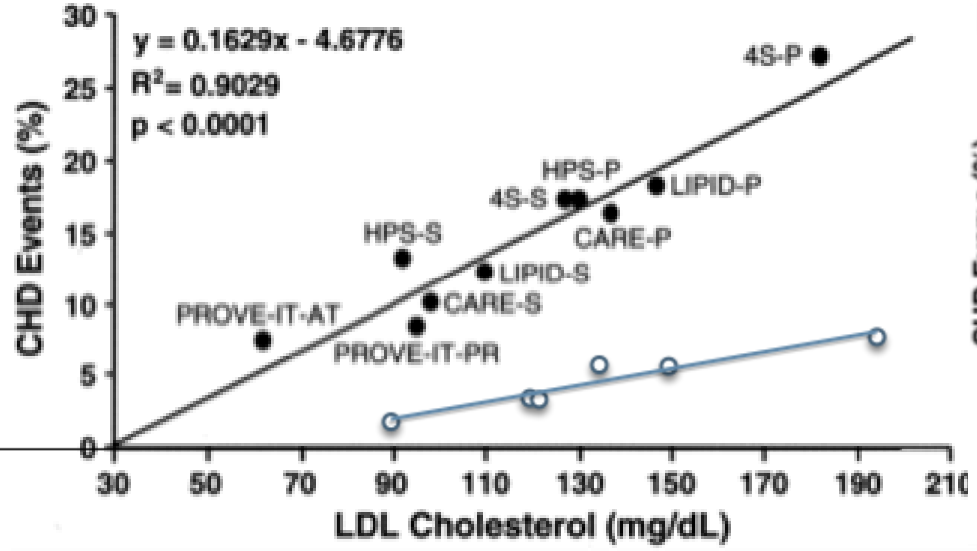


HPS-CAD or occlusive Arterial disease or diabetes

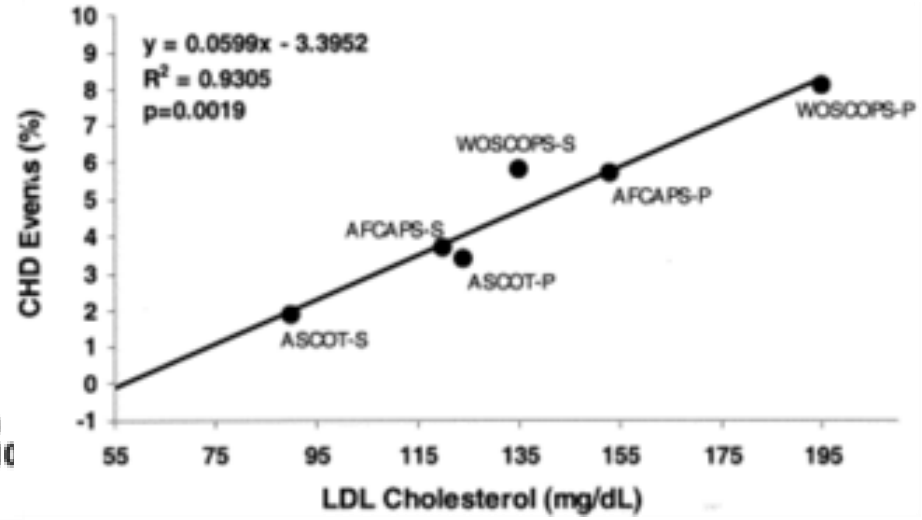
James H O'Keefe, Jr et al. JACC 2004;43:2142-2146

LDL and CHD Events

Secondary Prevention Trials

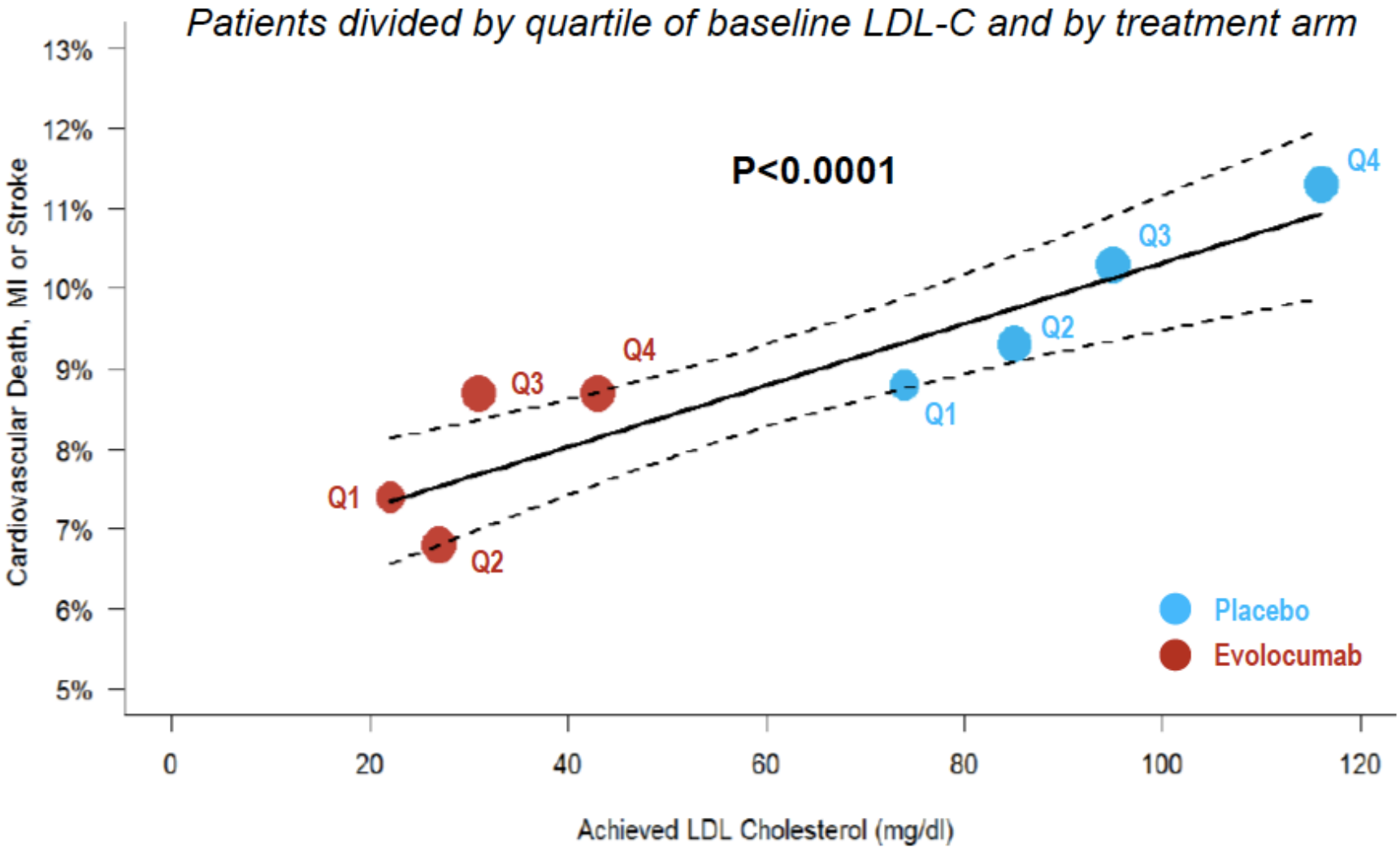


Primary Prevention Trials

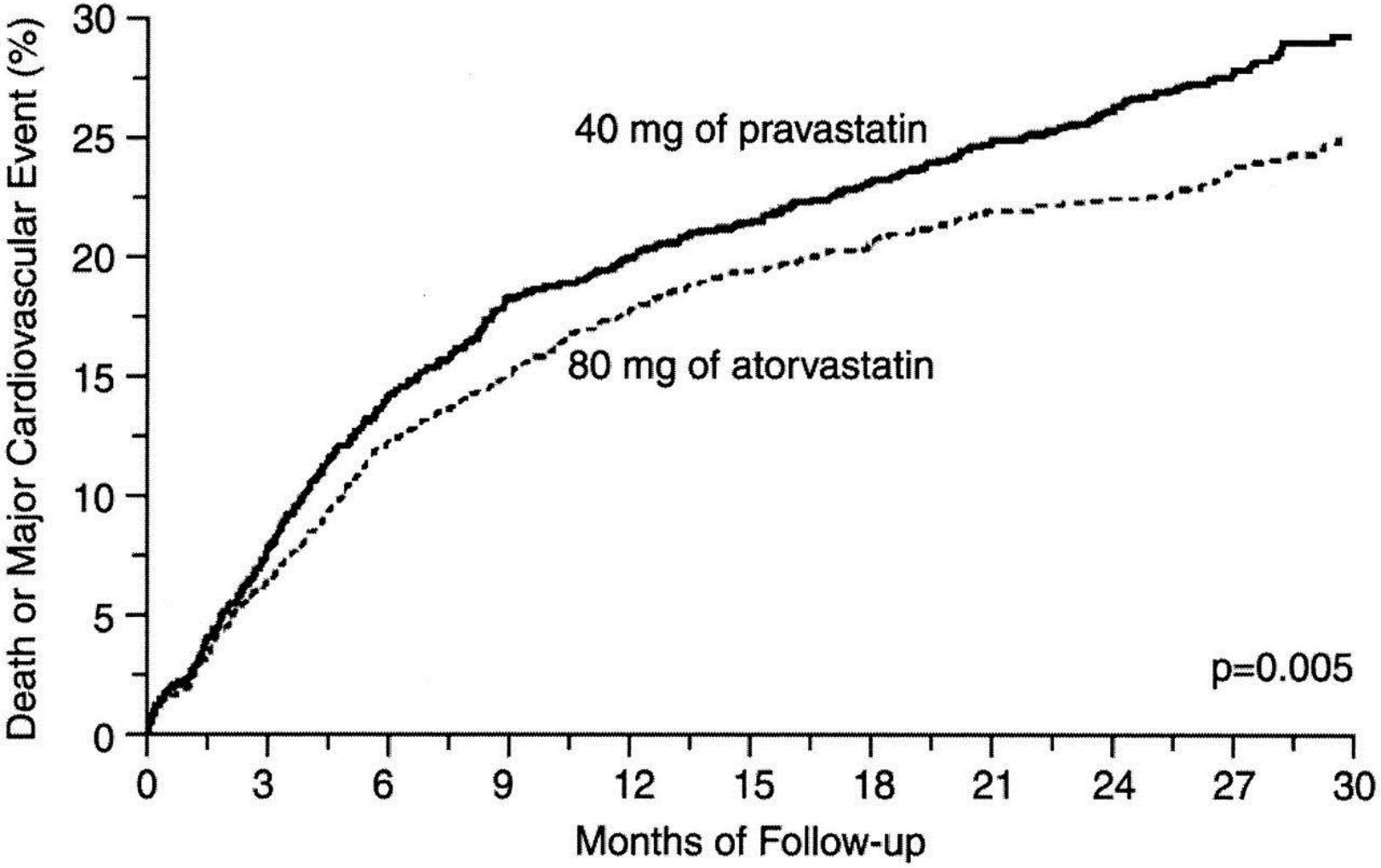


O'Keefe JACC 2004;43:2142

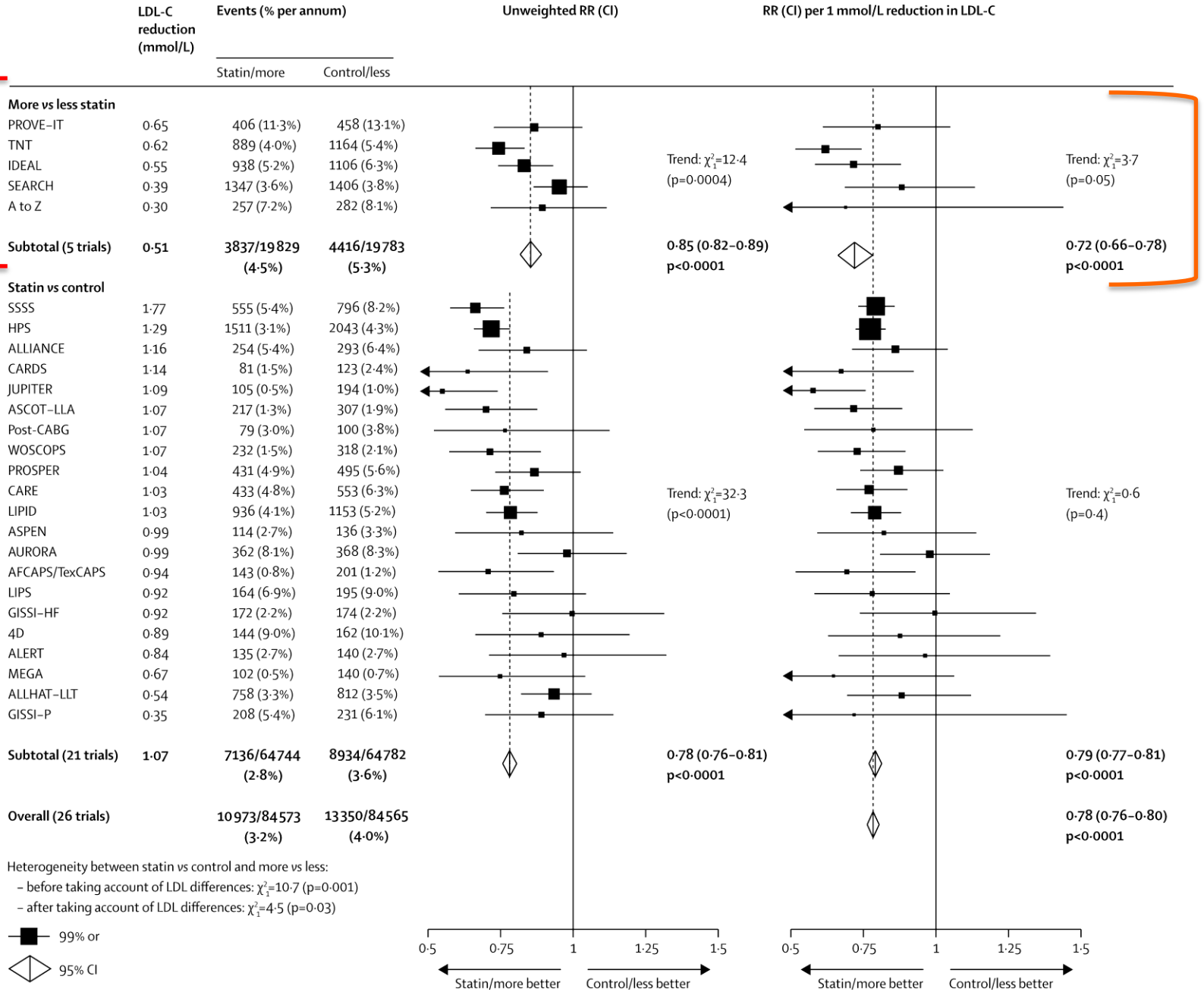
Lower LDL-C Is Better



PROVE-IT Trial



Cannon, et al. NEJM 2004: 350:1495-1505



Cholesterol Treatment Trialist Collaboration
The Lancet 2010 376, 1670-1681DOI: (10.1016/S0140-6736(10)61350-5)

Historical Perspective on Prevention Guidelines

- 1977- First NIH Guidelines
  - National High Blood Pressure Education Program
    - Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC-7), published in 2003.
  - National Cholesterol Education Program
    - Expert Panel on Prevention, Detection, Evaluation and Treatment of High Blood Cholesterol in Adults, (Adult Treatment Panel III), published in 2002, updated in 2004
- 2008 - NHLBI commissioned 5 guideline writing committees to rewrite prevention guidelines.
- 2011- IOM report on Guidelines
- 2013 - NHLBI announced that they will produce evidentiary reviews, but will rely on partnering organizations to produce guidelines.
- April, 2013 - NHLBI approached ACC/AHA (as well as ACP and AAFP)
- November, 2013 - ACC/AHA released 4 of 5 prevention guidelines

Revised ATP-III Goals, 2004

Risk category	LDL cholesterol goal	Initiate therapeutic lifestyle changes	Consider drug therapy
High risk: CHD or CHD risk equivalents (10-year risk >20%)	<100 mg/dL (with an optional goal of <70 mg/dL)	>100 mg/dL	>100 mg/dL (consider drug options if LDL-C <100 mg/dL)
Moderately high risk: two or more risk factors (10-year risk 10%-20%)	<130 mg/dL (with an optional goal of <100 mg/dL)	>130 mg/dL	>130 mg/dL (consider drug options if LDL-C 100-129 mg/dL)
Moderate risk: two or more risk factors (10-year risk <10%)	<130 mg/dL	>130 mg/dL	>160 mg/dL
Low risk: <1 risk factor	<160 mg/dL	>160 mg/dL	>190 mg/dL (consider drug options if LDL-C 160-189 mg/dL)

Cholesterol Guidelines Critical Questions

1. What is the evidence for LDL and non-HDL goals for secondary prevention?
2. What is the evidence for LDL and non-HDL goals for primary prevention?
3. What is the role for drugs in general and in specific sub-groups?

Cholesterol Guidelines

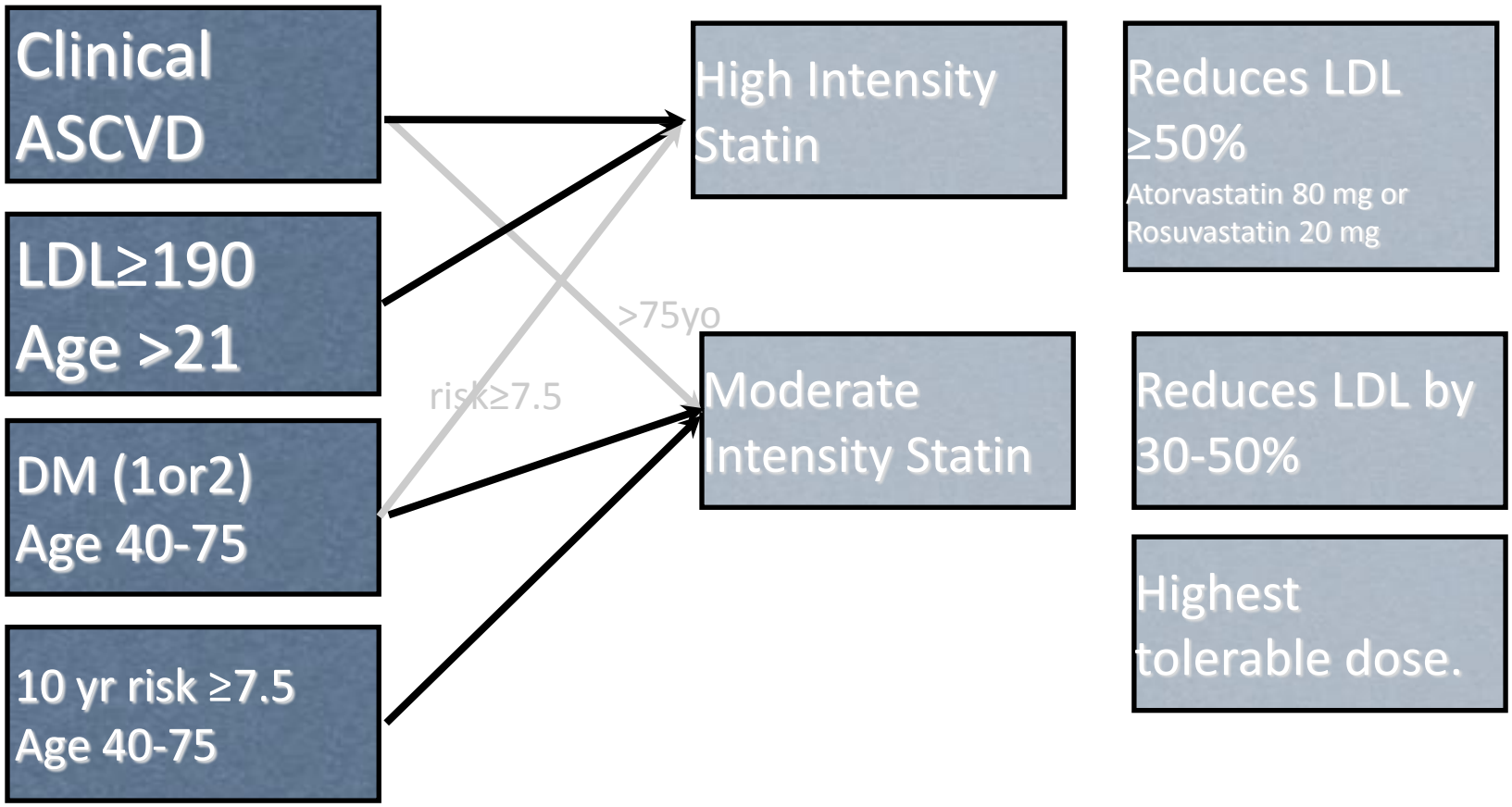
- No evidence for specific cholesterol targets. No recommendation for or against.
- Cholesterol is like an environmental exposure where there is a linear relationship between level and risk.
- Non-statin drugs have no proven benefit for ASCVD risk reduction.
- Statins are recommended based on overall ASCVD risk.

Cholesterol Guidelines
Treatment Groups

1. Secondary prevention for patients with clinical ASCVD*
2. Patients with Diabetes
3. Patients with LDL≥190
4. Patients with a calculated 10 risk of MI, CVA, or CV death of ≥7.5%

***Clinical ASCVD includes acute coronary syndromes, history of MI, stable or unstable angina, coronary or other arterial revascularization, stroke, TIA, or peripheral arterial disease presumed to be of atherosclerotic origin.**

Treatment Groups and Statin Dosing



Non-statins?

- Ezetimide
  - Enhance Trial - reduced LDL by 17%, yet no effect on CIMT in FH patients
  - ARBITER 6-HALTS Trial - Niacin versus ezetimide on CIMT, no effect.
  - CIMT is surrogate endpoint, ?lack of power?
  - IMPROVE-IT Trial - ezetimibe/simvastatin 10/40 mg compared with simvastatin 40 mg in 18,144 patients with ACS, over 7 years: 34.7% vs. 32.7% (CV death, MI, CVA, UA hosp, revas.)

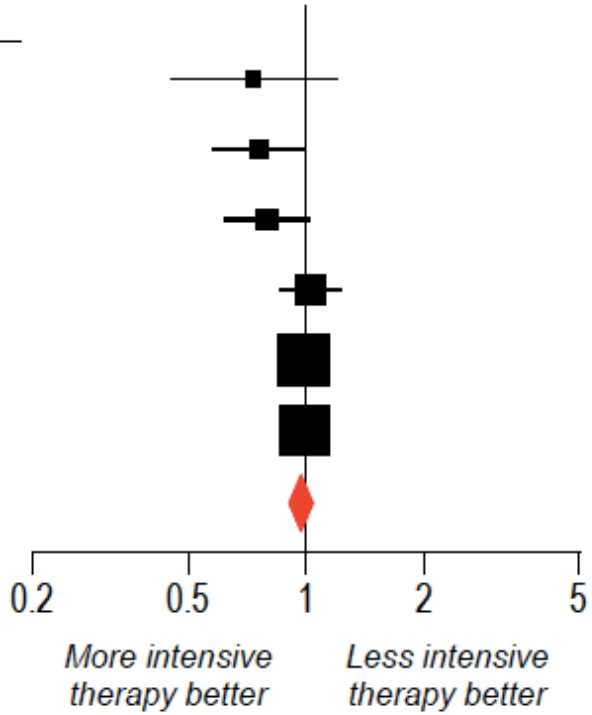
Non-statins?

- Niacin - avoid if elevated transaminases, or cutaneous side-effects, or new-onset Afib or weight loss occurs. (AIM-HIGH Trial showed no benefit when added to statin in CAD pts)
- Fibrates - contraindicated if taking statins. Can be considered if severely elevated TG
- Omega - 3-fatty acids (several meta-analyses show no benefit for secondary prevention)
- Bile-acid Sequestrants - avoid if fasting TG ≥300mg/dl
- PCSK9 Inhibitors-very effective, very expensive.

More Intensive LDL-C Lowering & CV Death

No clear benefit on CV mortality

Trial	Year	# of CV Deaths: More Intensive Rx Arm	# of CV Deaths: Less Intensive Rx Arm	HR (95% CI)
PROVE-IT TIMI 22	2004	27	36	0.74 (0.45-1.22)
A2Z	2004	86	111	0.76 (0.57-1.01)
TNT	2005	101	127	0.80 (0.61-1.03)
IDEAL	2005	223	218	1.03 (0.85-1.24)
SEARCH	2010	565	572	0.99 (0.88-1.11)
IMPROVE-IT	2015	538	537	1.00 (0.89-1.13)
Summary		**1540**	**1601**	**0.96 (0.90-1.03)**



NEJM 2004;350:1495-504
JAMA 2004;292:1307-16
NEJM 2005;352:1425-35
JAMA 2005;294:2437-45
Lancet 2010;376:1658-69
NEJM 2015;372:2387-97

All Vascular Patients Should Be on High Dose Statin Therapy

- It’s supported by 5 clinical trials.
- It’s supported by the guidelines.
- It’s well tolerated.
- It’s affordable.
- It seems to make sense.

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