

Functional approach: we can't find it; treat it systemically

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CASE WESTERN RESERVE
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Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

Affiliation/Financial Relationship

- Grant/Research Support
- Consulting Fees/Honoraria
- Major Stock Shareholder/Equity
- Royalty Income
- Ownership/Founder

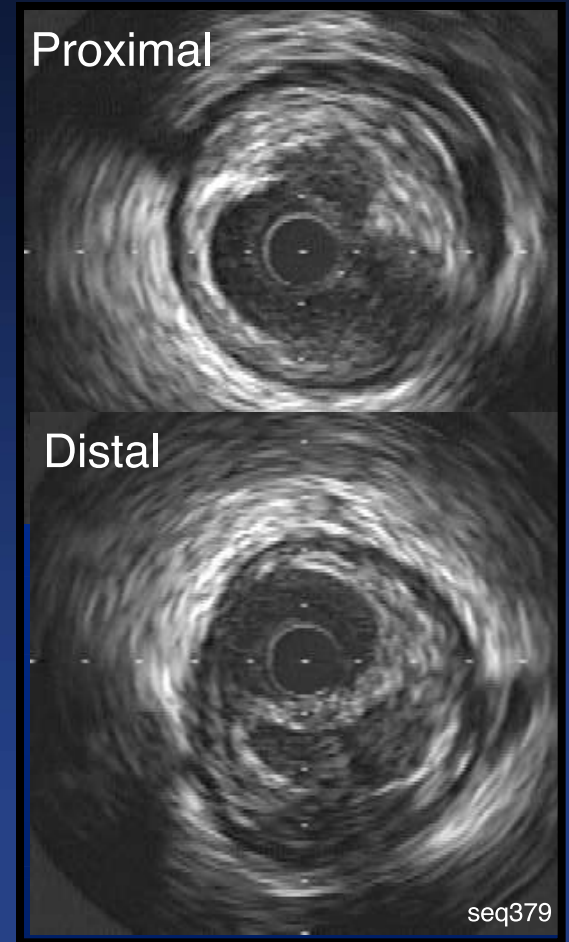
- Intellectual Property Rights
- Other Financial Benefit

Company

Volcano, Radi (St. Jude), BSC
Volcano
Technology Solutions Group
None
Technology Solutions Group,
BioInfo Accelerator Fund
None
None

Vulnerable patient; 1993

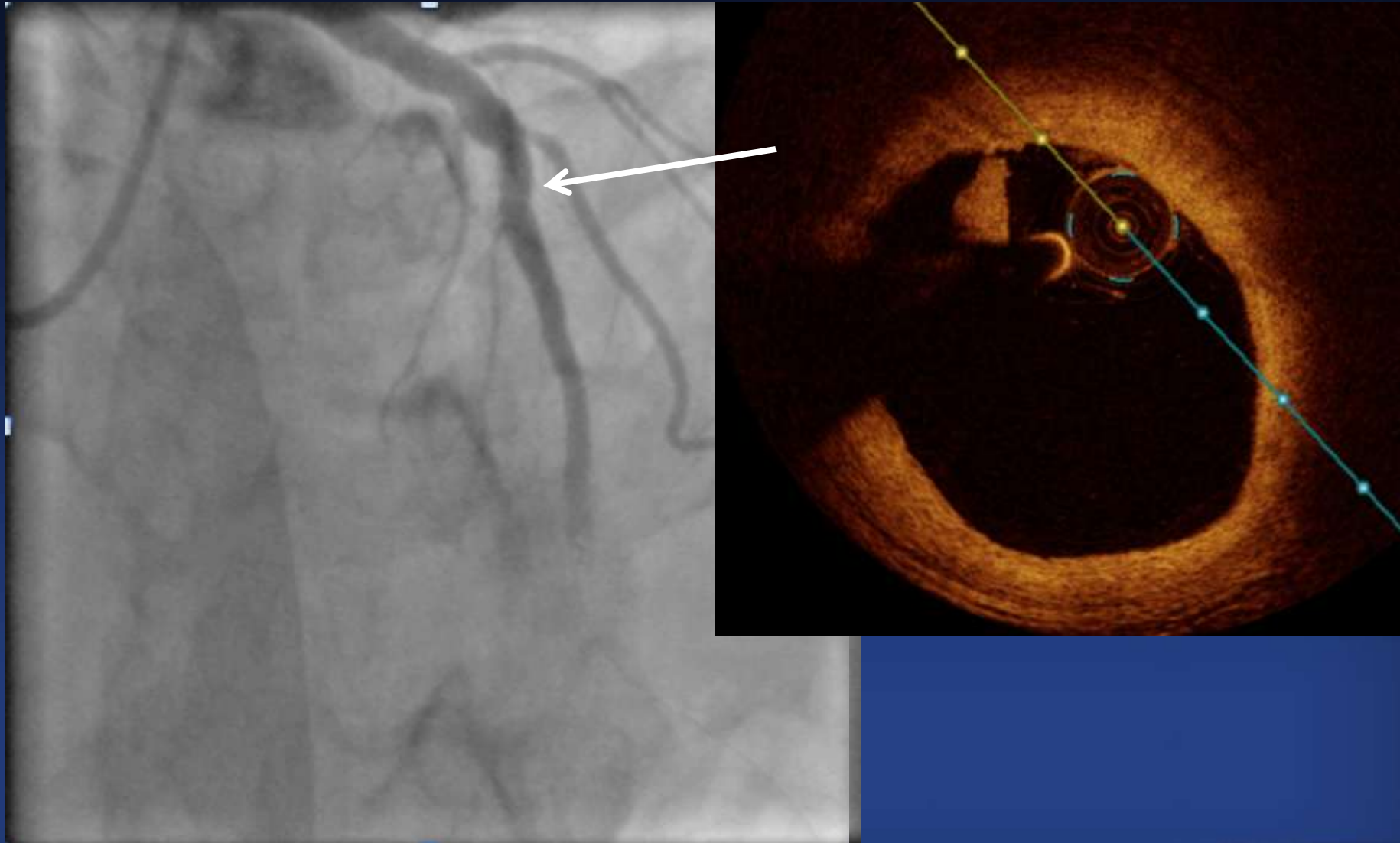
39 year old with Inferior MI. Non-culprit LAD imaged with multiple ruptured plaques



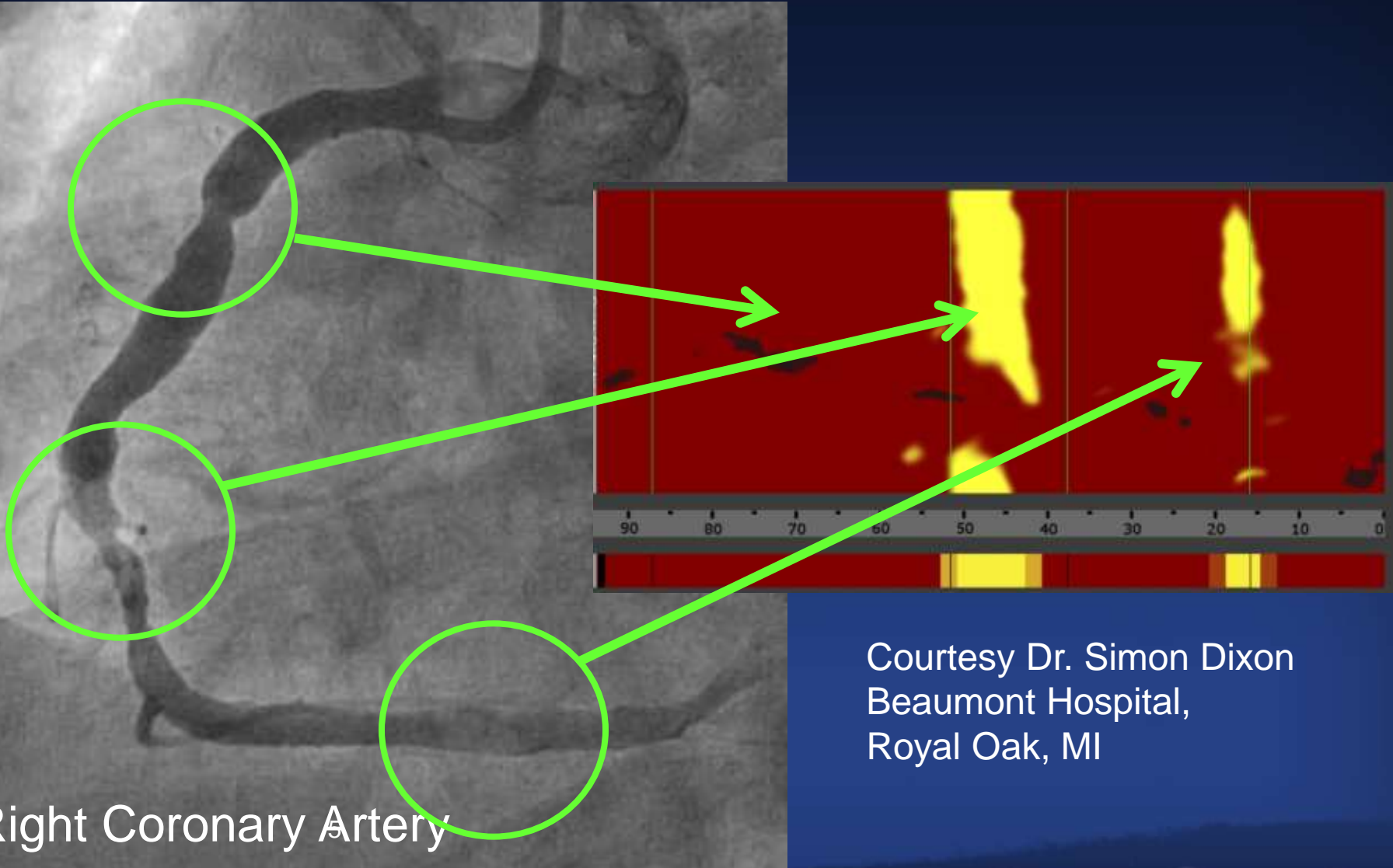
Can we predict this? Can we treat this?

Courtesy: Fitzgerald

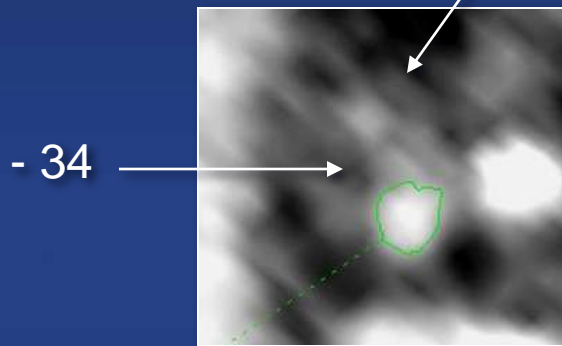
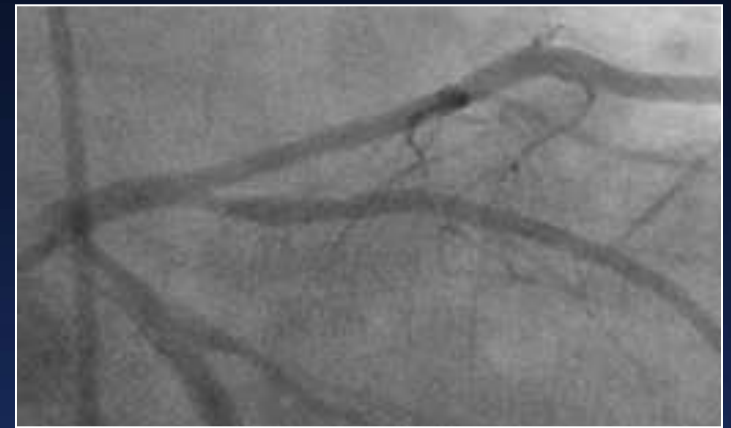
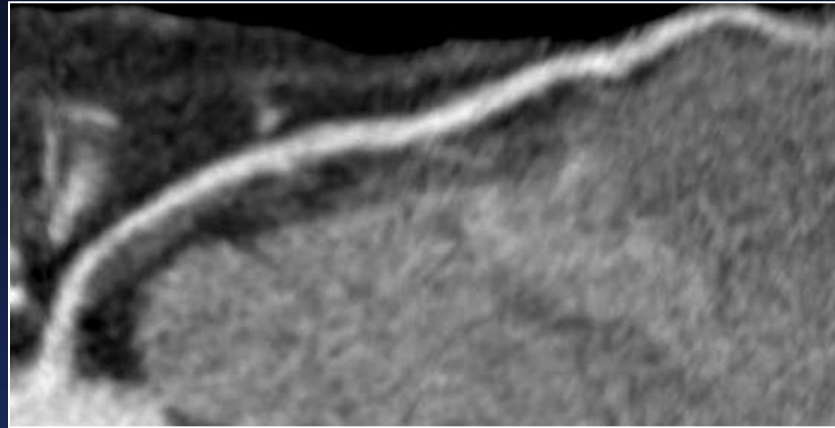
STEMI: Thrombus but no lesion?



Pre PCI imaging identifies lipid core plaque

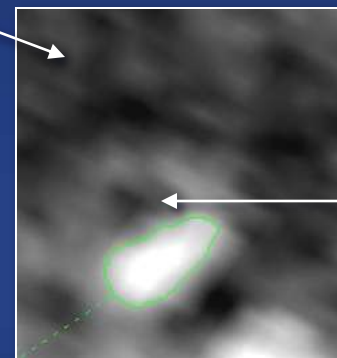


Cardiac CTA



- 34

MLA 2.8 mm²



- 105

5.2 mm²

TCFA ?

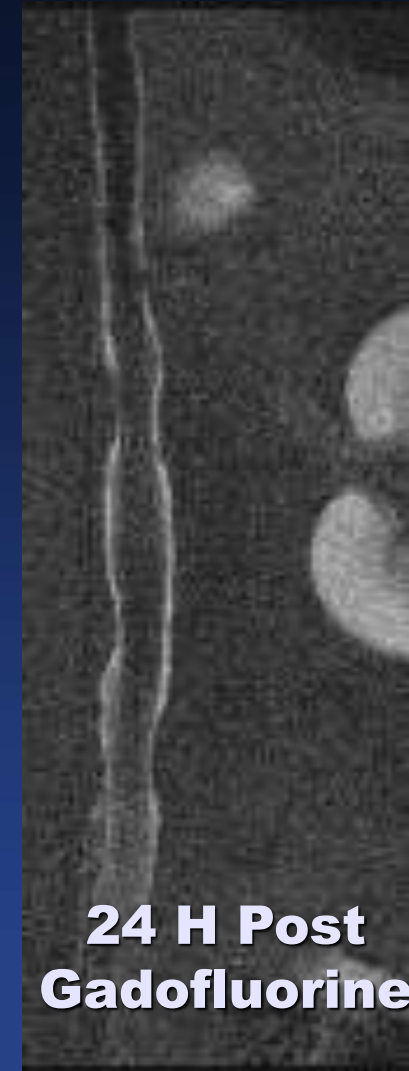
Courtesy: Harvey Hecht

Lipid Rich Atherosclerotic Rabbit 24h Post Gadofluorine



n=10 NZW
Atherosclerotic rabbits

No Enhancement in
Controls (n=6)



Sirol, M et. al. *Circulation* 2004; 109: 2890

Courtesy, V. Fuster

Facts about vulnerable plaque: USA 2010

- 620,000 first MI or SCD per year (acute events)
- No prior Sx in 50% of men and 68% of women
- Approximately 2.5 million catheterizations/year
- Approximately 1 million PCI/year
- US population > age 45: 121,757,000
 - 0.51%/year have an acute event

Sources:

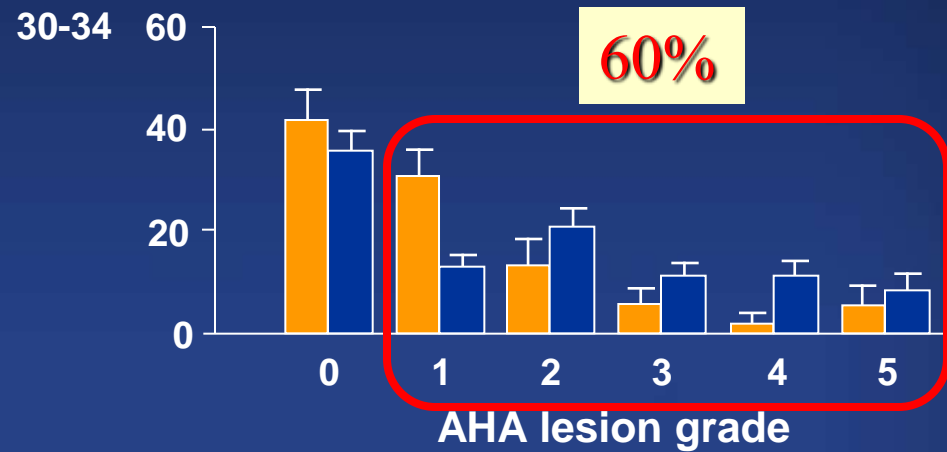
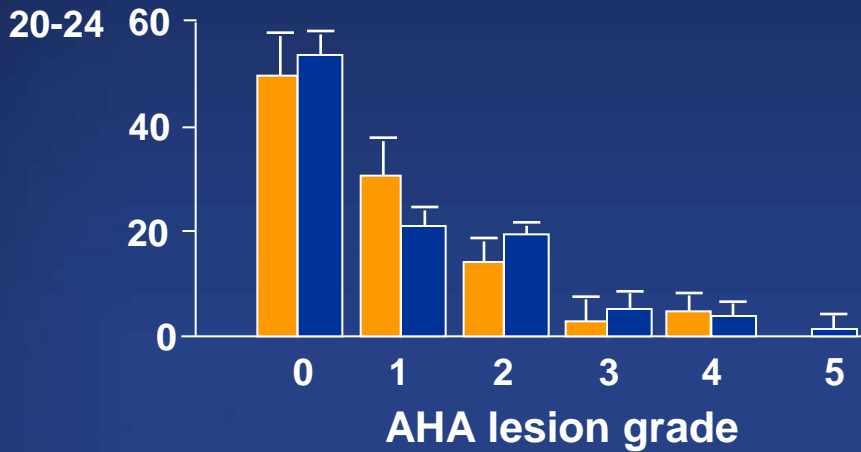
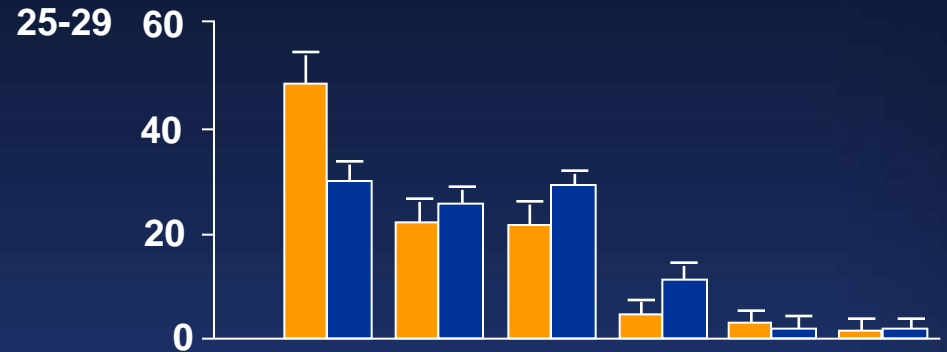
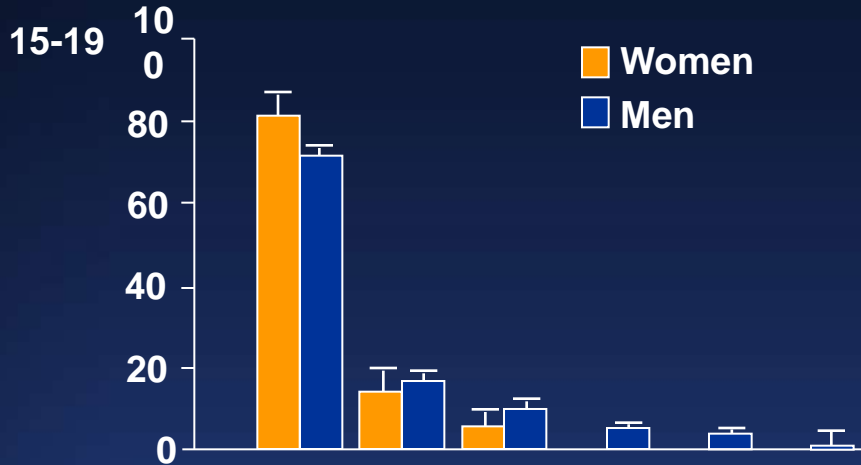
US Census, 2012

Circulation 2014;129:e28-e292

JACC 2012;60: S1-S49

PDAY: Prevalence of Lesions in LAD

Age (y) Prevalence (%)



Error bar=SE.

McGill HC Jr, et al. *Circulation*. 2000;102:374-379.

Prevalence of CAD in asymptomatic persons

- By CCS and CCTA: 22% (Korea, mean 50 yrs)¹
- By CCS >0: 68% (USA, mean 59 yrs)²
- By survey: 83 600 000 (35.3%) (>20 yrs)³

- Thus, of the population over 45 yrs between 22 and 82 million have phenotypic CAD
 - I will use 50 million for analysis

¹*J Am Coll Cardiol* 2008;52:357–65

²*J Am Coll Cardiol* 2005;46:158–65

³*Circulation* 2014;129:e28-e292

Prevalence of vulnerable plaque at cath

- VH IVUS (NC lesions in ACS): 22%-30%
- IB IVUS (ACS): 33%
- NIRS: 57%
- OCT: 19%
- Grey scale IVUS (AMI): 79%

- Thus, an optimistic evaluation of the chances for finding a VP at routine cath is 30%

Invasive approach

- If every cardiac cath (2.5M) employed a technique to find VP, only 5% of those with CAD would be studied.
- Of those, 30% would have a VP identified (830,000 persons)
- If a 100% safe, 100% effective treatment could be applied to these VP, we could remove them from the risk pool.
- This would leave 49,170,000 persons at risk, among an asymptomatic population of 121 million!

- Thus, best case invasive scenario: prevent all acute events in 1.7% of the at risk population, or 10,292 events. Since over 50% of acute events occur prior to Sx, a more realistic estimate is 5,146 events prevented.

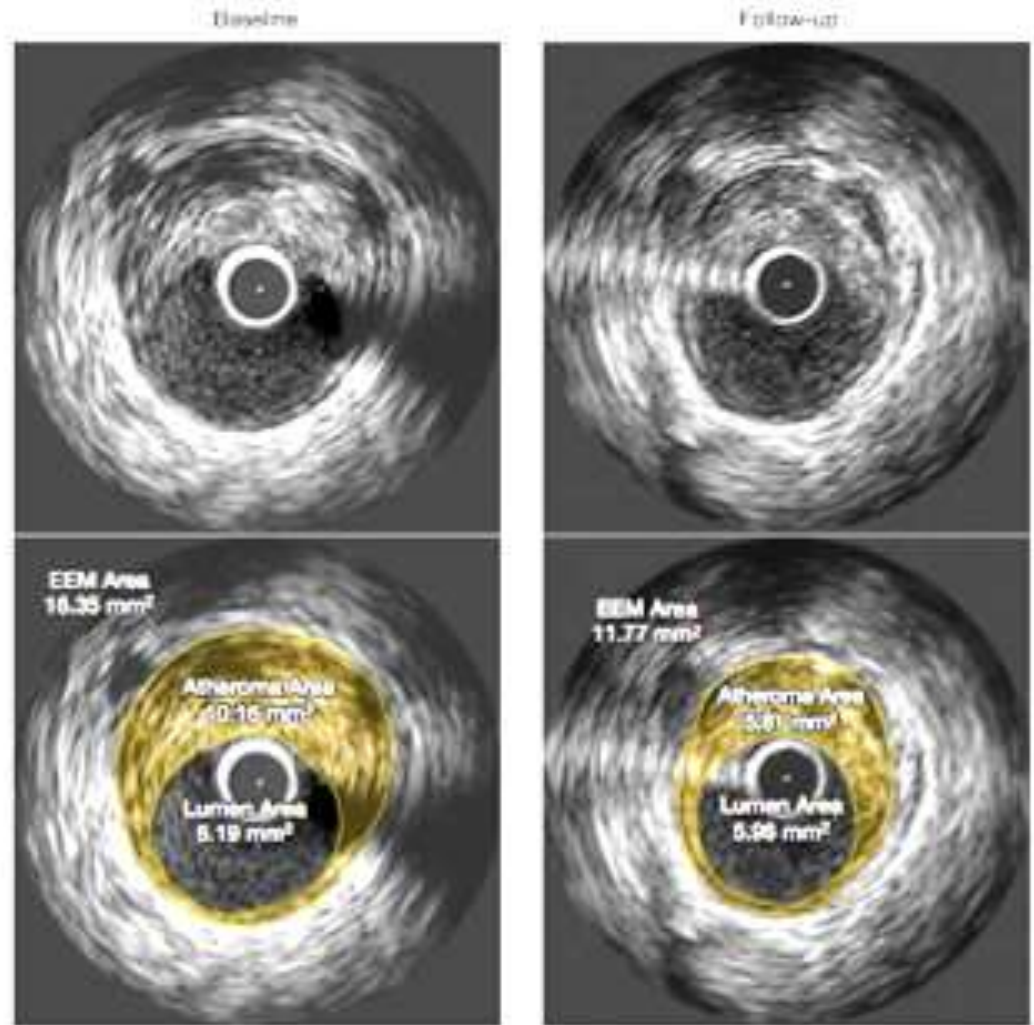
Systemic treatment

- Statins can slow atherosclerosis: Reversal, Asteroid
- Statins can modify plaque: GAIN (IVUS), Fluvastatin (VH-IVUS), YELLOW (NIRS)
- Atorvastatin 10mg: 36% reduction in AMI, SCD at 3.5 yrs (ASCOT LLA)
- Polypill: estimated 50-80% reduction at 2 years

Asteroid

Rosuvastatin 40 mg
24 months
LDL: 61 mg/dl
Volume down 6.8%

Figure 2. Example of Regression of Atherosclerosis in a Patient in the Trial

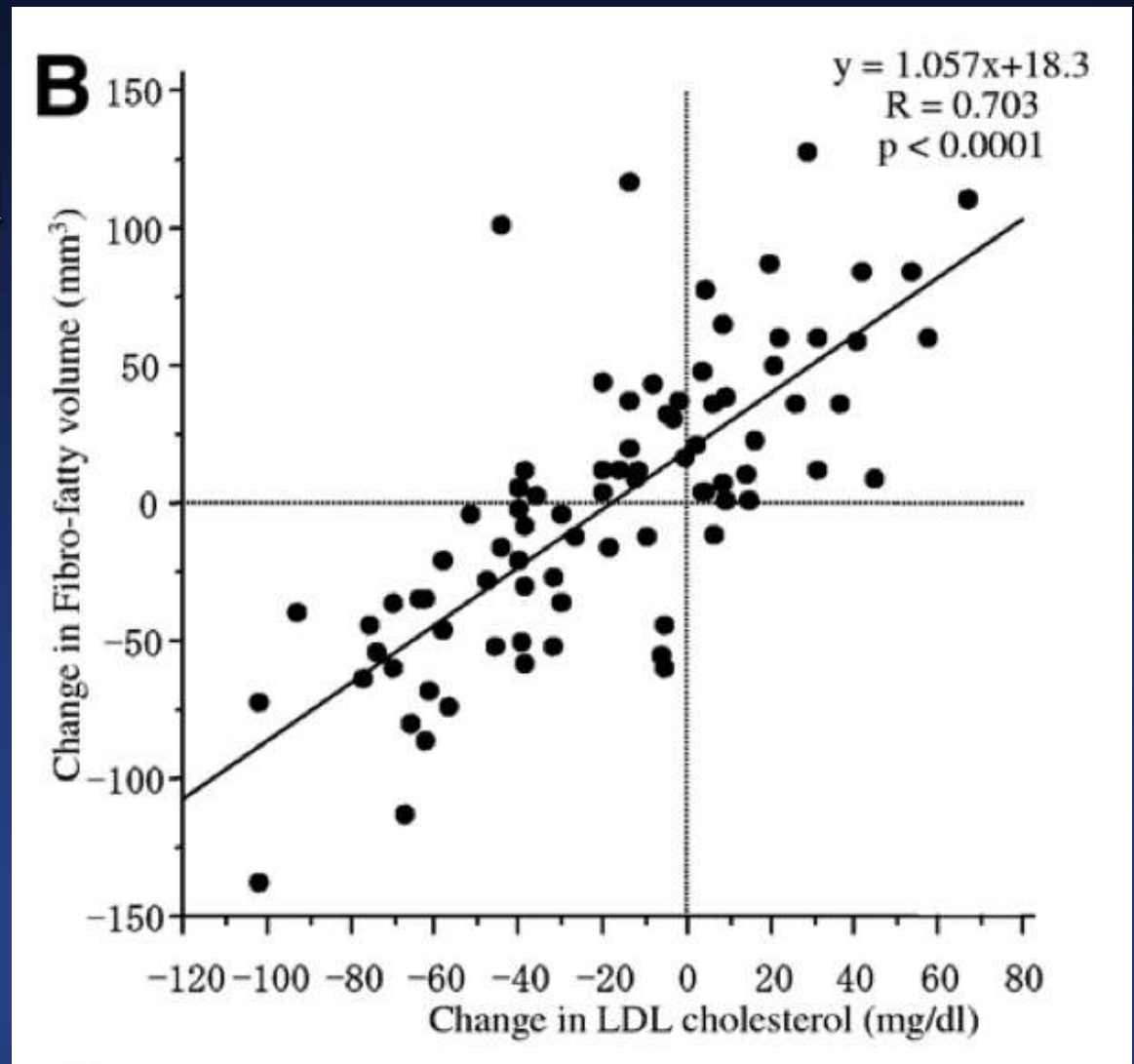


The top left panel illustrates the appearance of a single cross-section at baseline intravascular ultrasound examination, while the top right panel shows the same cross-section after 24 months of treatment. The bottom 2 panels illustrate the same cross sections, but with measurements superimposed. Atheroma area was reduced from 10.16 mm² to 5.01 mm². EEM indicates external elastic membrane.

JAMA 2006;295:epub

Effect of Statins on Fibroatheroma

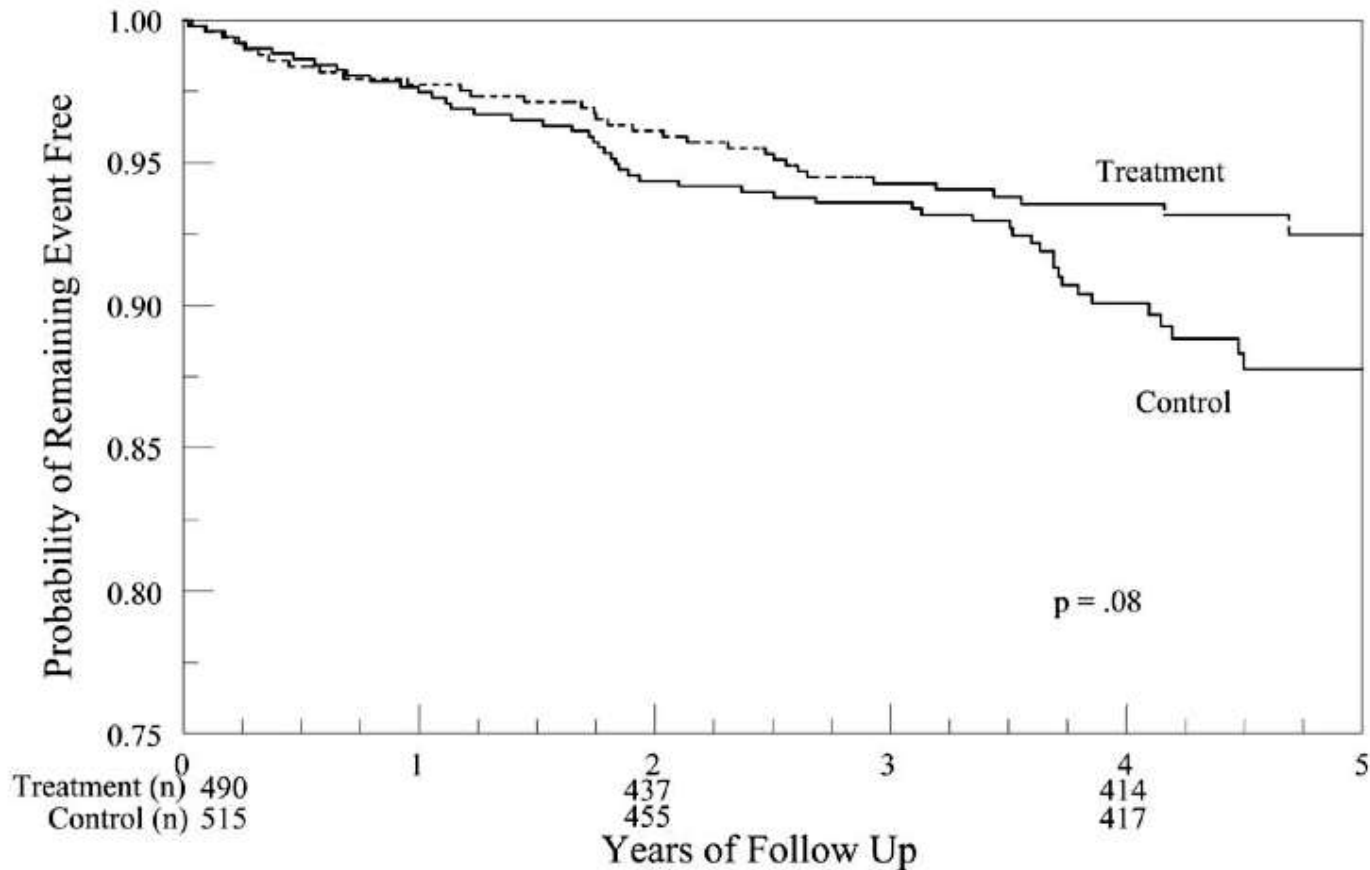
- Randomized Fluvastatin 60mg/d vs. control (n=80)
- Fibroatheromas detected by VH-IVUS
- Re-study at 12 months



St. Francis Heart Study

Randomized groups:

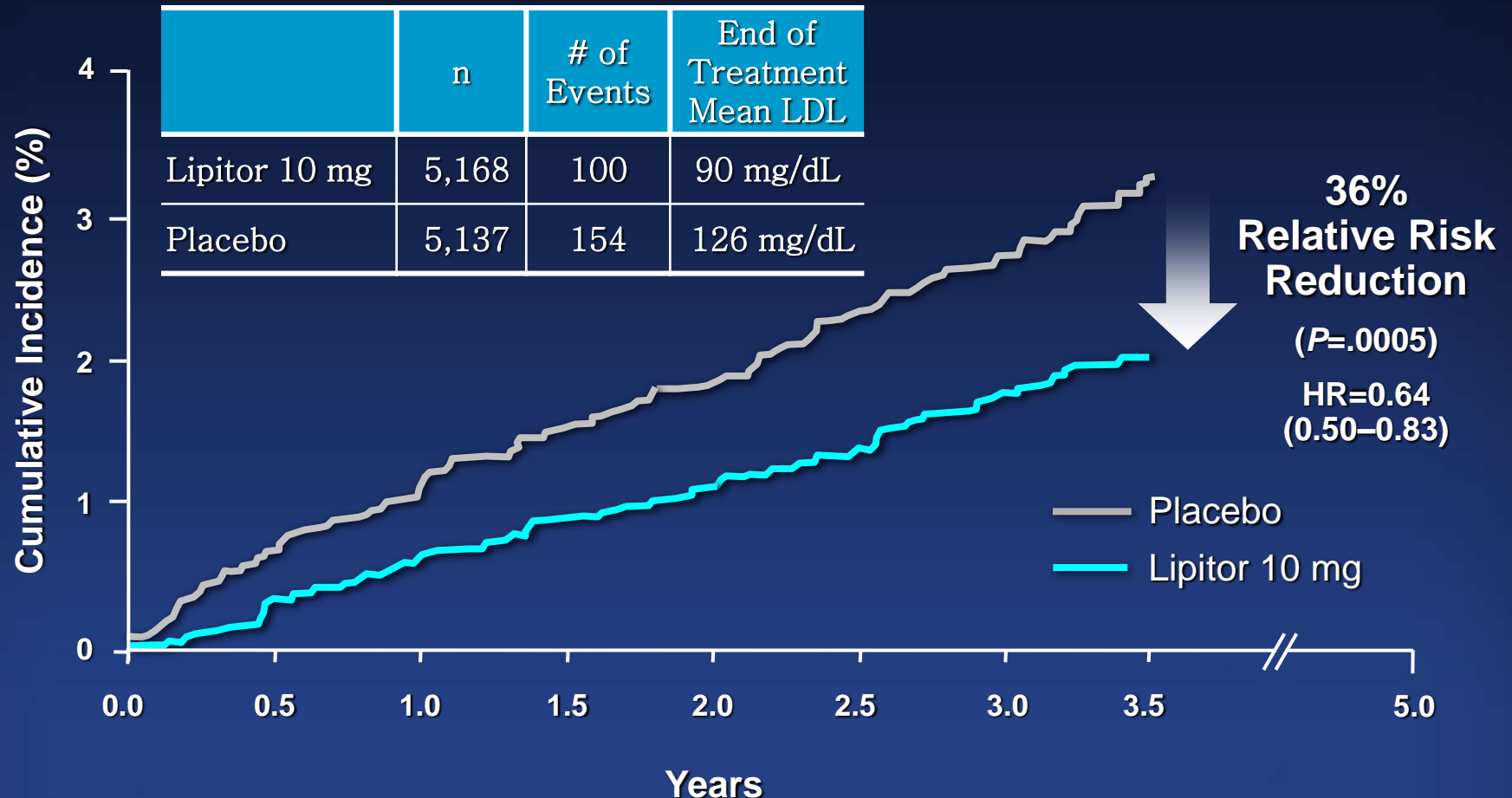
Atorvastatin 20mg, Vit E, Vit C vs. placebo



J Am Coll Cardiol 2005;46:158–65

JACC 2005;46:166

ASCOT-LLA Primary End Point: Nonfatal MI and Fatal CHD



In a post-hoc analysis, a significant difference at 90 days was observed between treatment groups

HR = hazard ratio

Sever PS, et al. *Lancet*. 2003;361:1149-1158.

Systemic approach

- Treatment of all persons with low dose atorvastatin: HR 0.64 for acute events (MI, SCD)
- If 50 million persons have CAD and these produce 620,000 acute events/year, treatment could prevent 223,000 events
- Thus, systemic approach prevents 36% of all events, while invasive approach prevents only 0.83% of all events

CV Devices in development: 2012

There are approximately 115 new cardiovascular devices currently under development

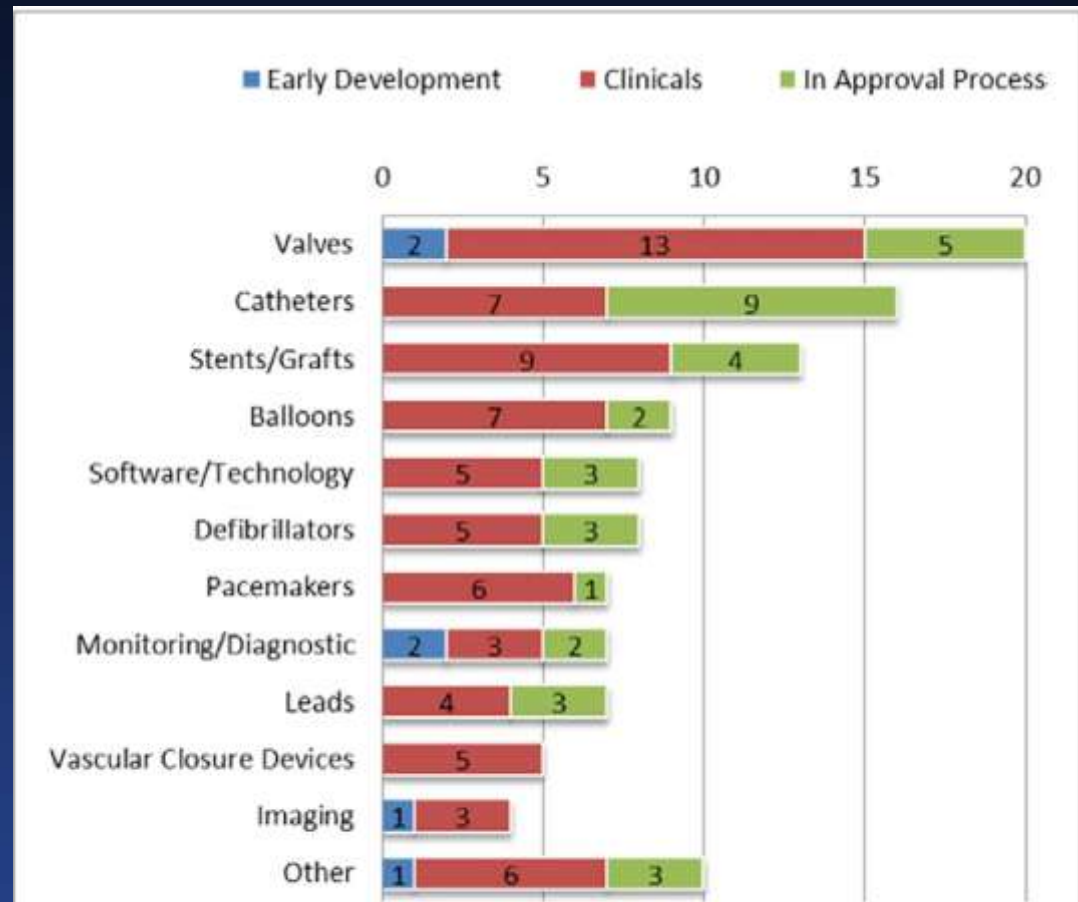


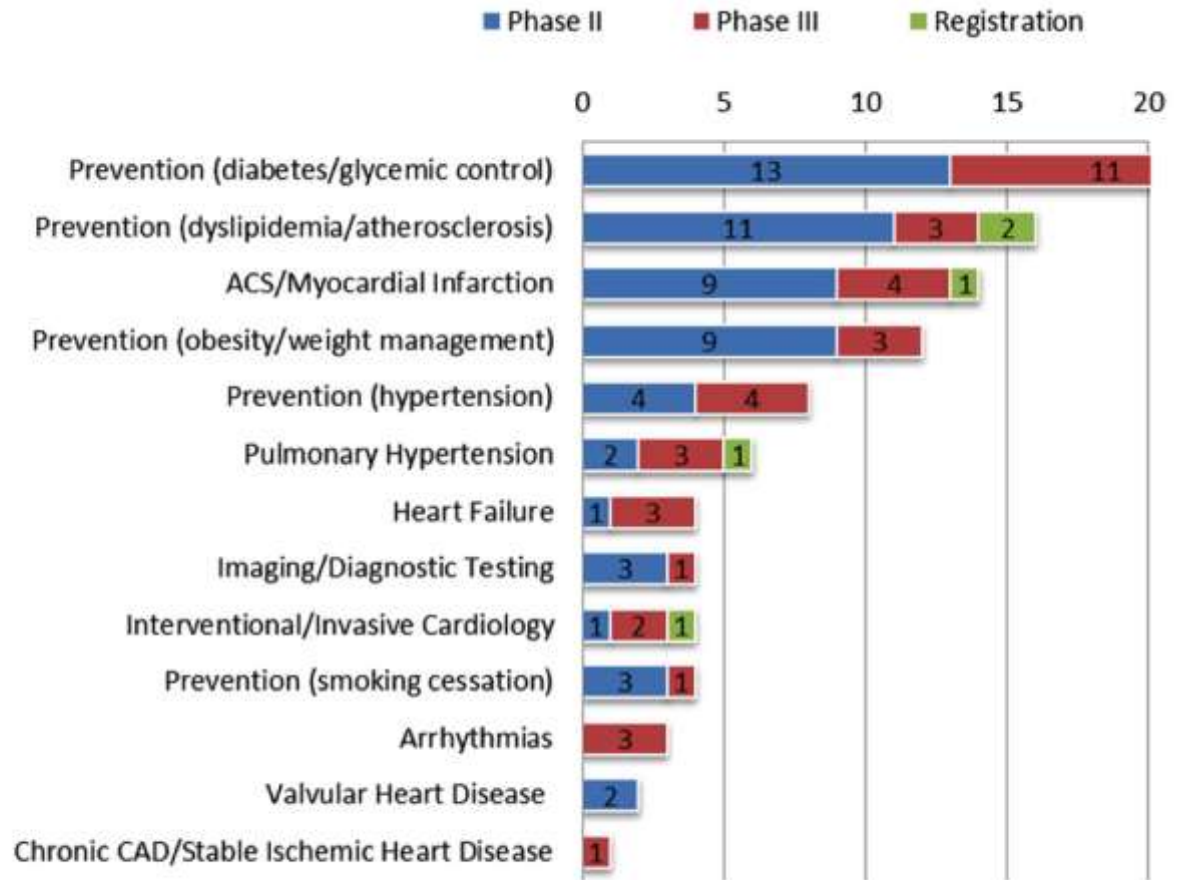
Figure 39

**CV Devices in Development
by Key Manufacturers by Category**

Access Communications. Cardiovascular Product and Disease Land- scape Analysis Playbook: Prepared for the American College of Cardiology. San Francisco, CA: Access Communications, 2012.

CV drugs in development: 2012

“There are only approximately 150 new cardiovascular drugs currently under development compared with some 700 new drugs in development for the treatment of cancer”



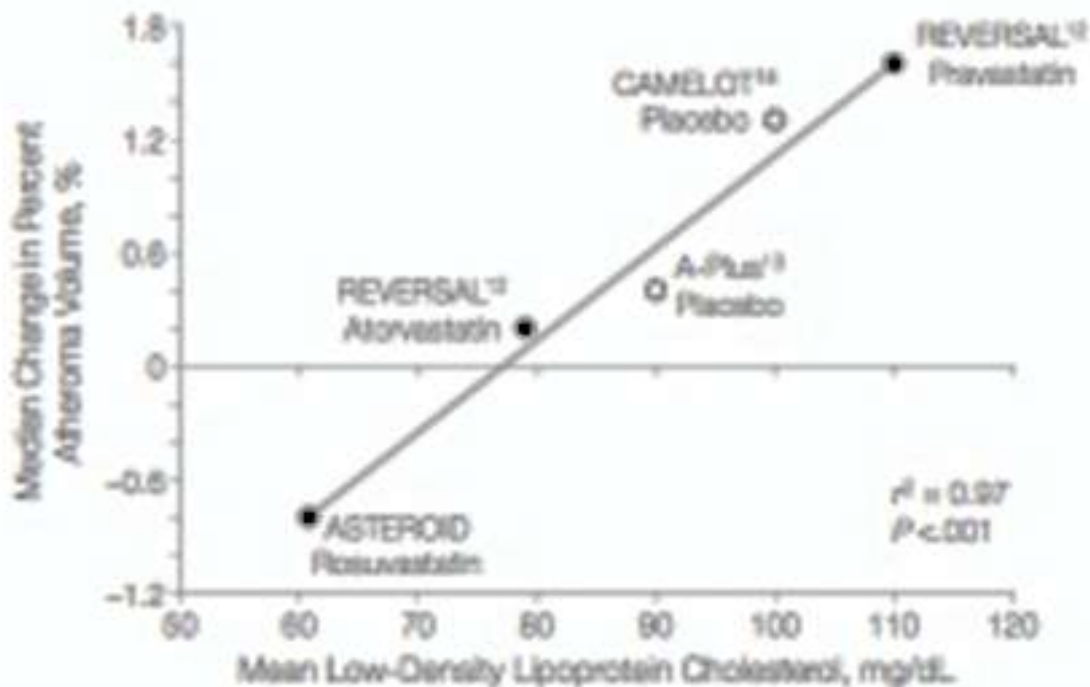
CV Pipeline Products by ACC-Defined Core Pathway and Phase of Development

Access Communications. Cardiovascular Product and Disease Landscape Analysis Playbook: Prepared for the American College of Cardiology. San Francisco, CA: Access Communications, 2012.

Cardio-oncologists

Statin “chemotherapy”

Figure 3. Relationship Between Mean Low-Density Lipoprotein Cholesterol Levels and Median Change in Percent Atheroma Volume for Several Intravascular Ultrasound Trials



JAMA 2006;295:epub

Cardiovascular Oncologists

■ Breast Cancer

- Tumor
 - Surgical excision
- Metastases
 - Chemotherapy
 - Radiation

■ Coronary disease

- Lesion
 - bypass/stent
- Atherosclerosis
 - Statins, et al
 - Antithrombotics

“The most important thing I do in the cath lab
is to start patients on a statin”