האיגוד הישראלי לכירורגית לב וחזה
THE ISRAEL SOCIETY OF CARDIOTHORACIC SURGERY
האיגוד הקרדיולוגי בישראל
ISRAEL HEART SOCIETY
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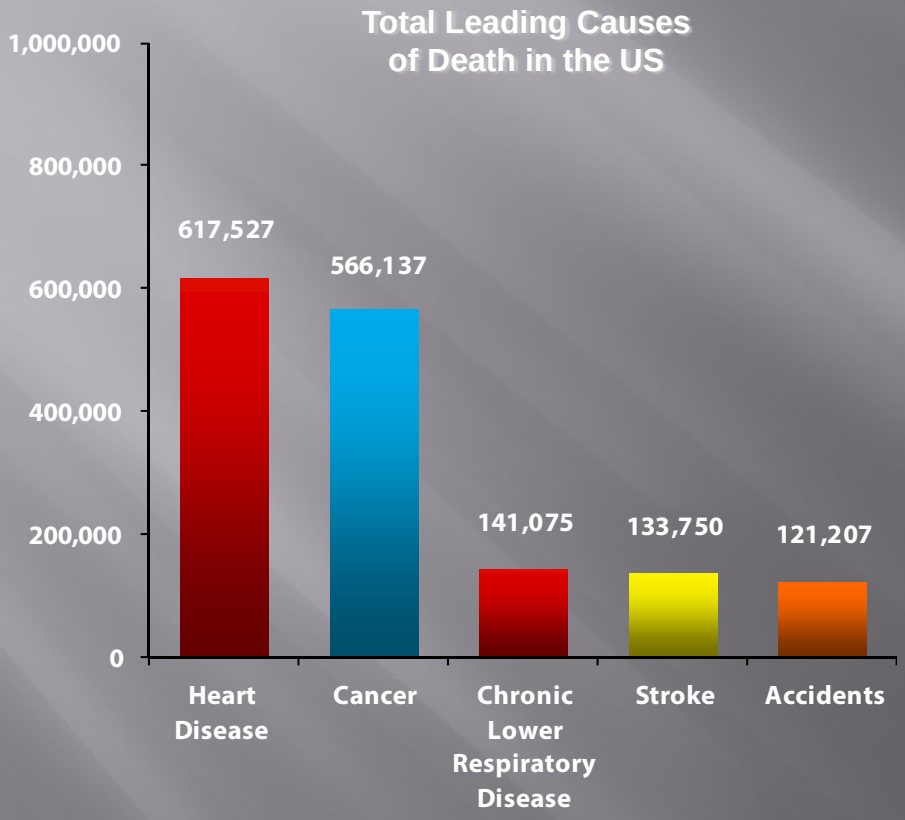
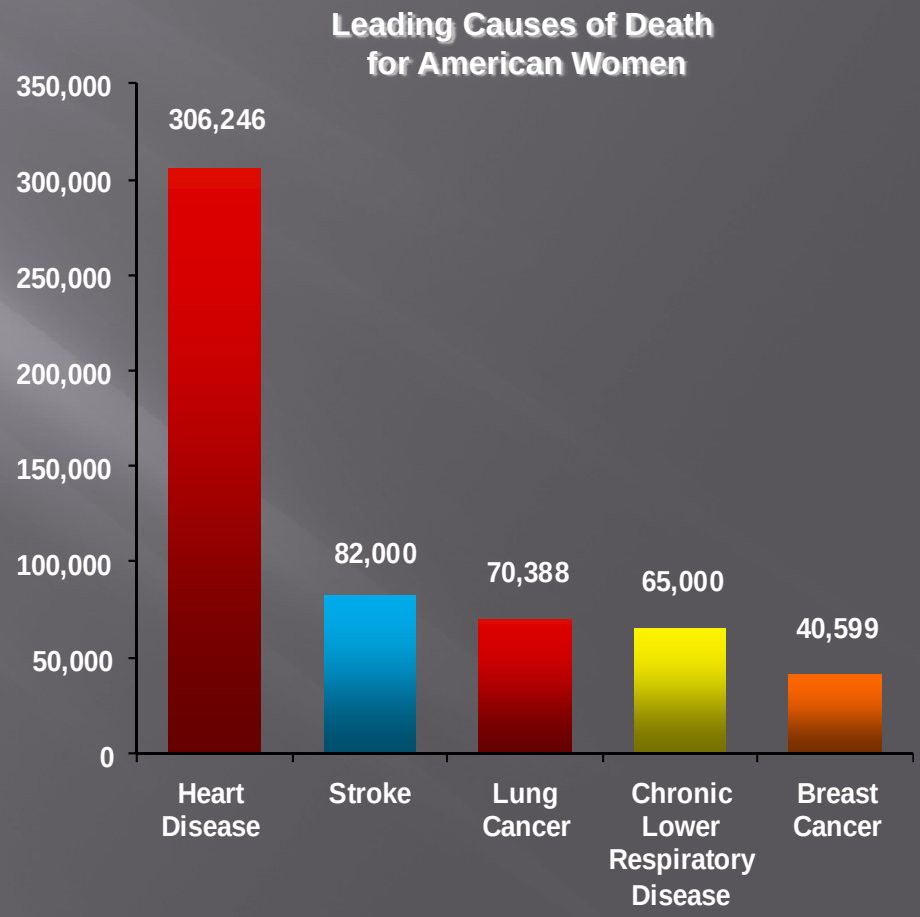
The 60th International Conference of the Israel Heart Society
in association with the Israel Society of Cardiothoracic Surgery
22-23 April 2013, ICC International Convention Center, Jerusalem

The Diagnosis Often Comes Too Late

Basil S. Lewis, MD, FRCP, FACC, FESC
Louis Edelstein Professor of Medicine and Medical Research
Ruth and Bruce Rappaport School of Medicine, Technion-IIT
Director, Cardiovascular Clinical Research Institute
Lady Davis Carmel Medical Center

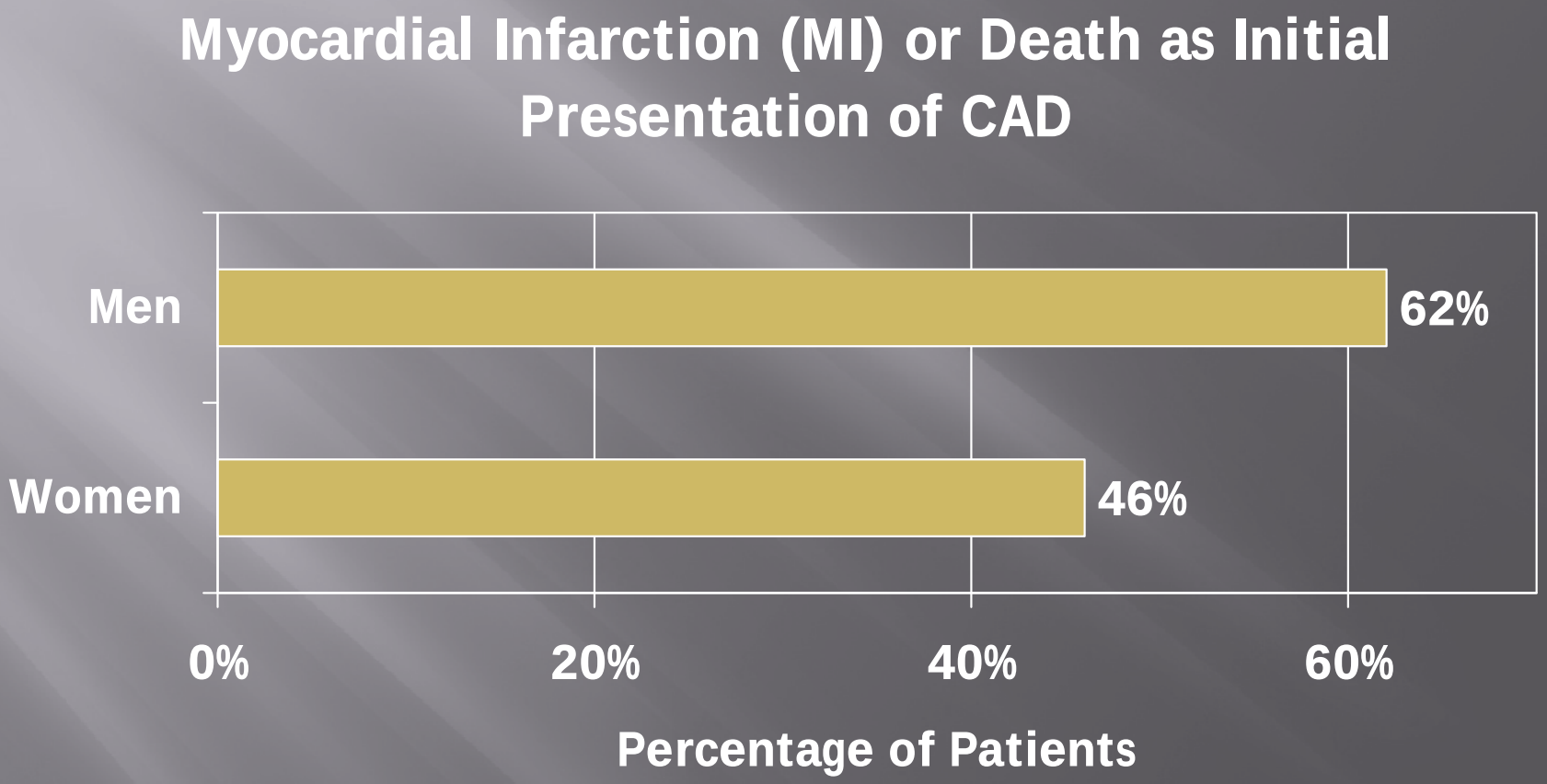
Heart Disease is the Leading Cause of Death in the United States, Stroke is Fourth / Second for Women





National Vital Statistics Report, December 9, 2010. (Includes final data for 2007)

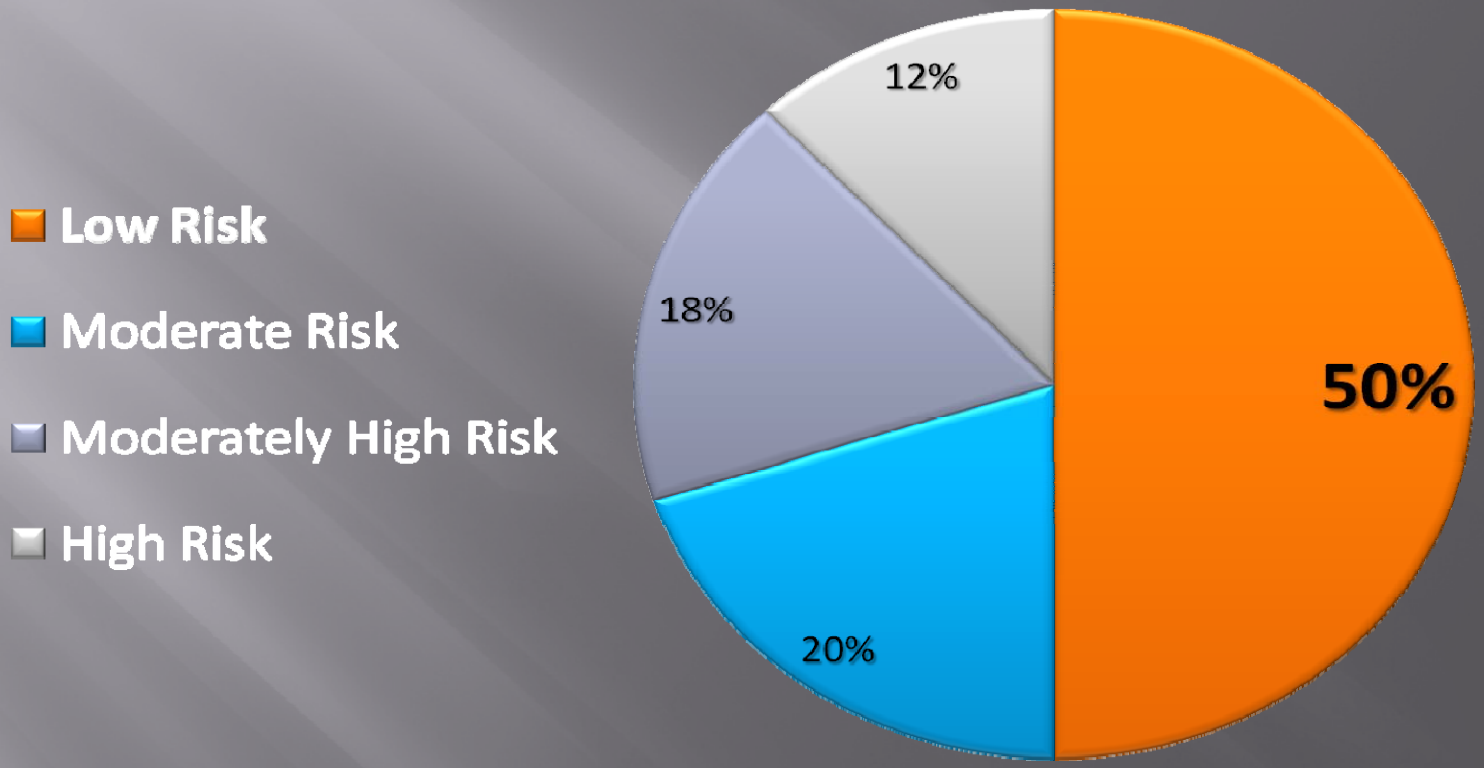
Coronary Artery Disease (CAD): The Diagnosis Often Comes Too Late



Adapted from Levy et al in *Textbook of Cardiovascular Medicine*, 1998

How Good Is NCEP ATP III At Predicting MI in Young People?

222 patients with 1st acute MI, no prior CAD, no DM men <55, women <65



~75% did not qualify for statins

JACC 2003;41:1475

Framingham Risk Score: Men

Age

Years	Pts
20-34	-9
35-39	-4
40-44	0
45-49	3
50-54	6
55-59	8
60-64	10
65-69	11
70-74	12
75-79	13

HDL-C

(mg/dL)	Pts
> 60	-1
50-59	0
40-49	1
< 40	2

Systolic Blood Pressure

	Untreated	Treated
<120	0	0
120-129	0	1
130-139	1	2
140-159	1	2
≥ 160	2	3

Total Cholesterol

(mg/dL)	20-39	40-49	50-59	60-69	70-79
<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

Cigarette Smoking

Nonsmoker	0	0	0	0	0
Smoker	8	5	3	1	1

45 yo male
BP 135/85
TC 220
HDL-C 40
LDL-C 130
Non-smoker
No DM
Family Hx ??

JAMA 2001; 285: 2486-2497

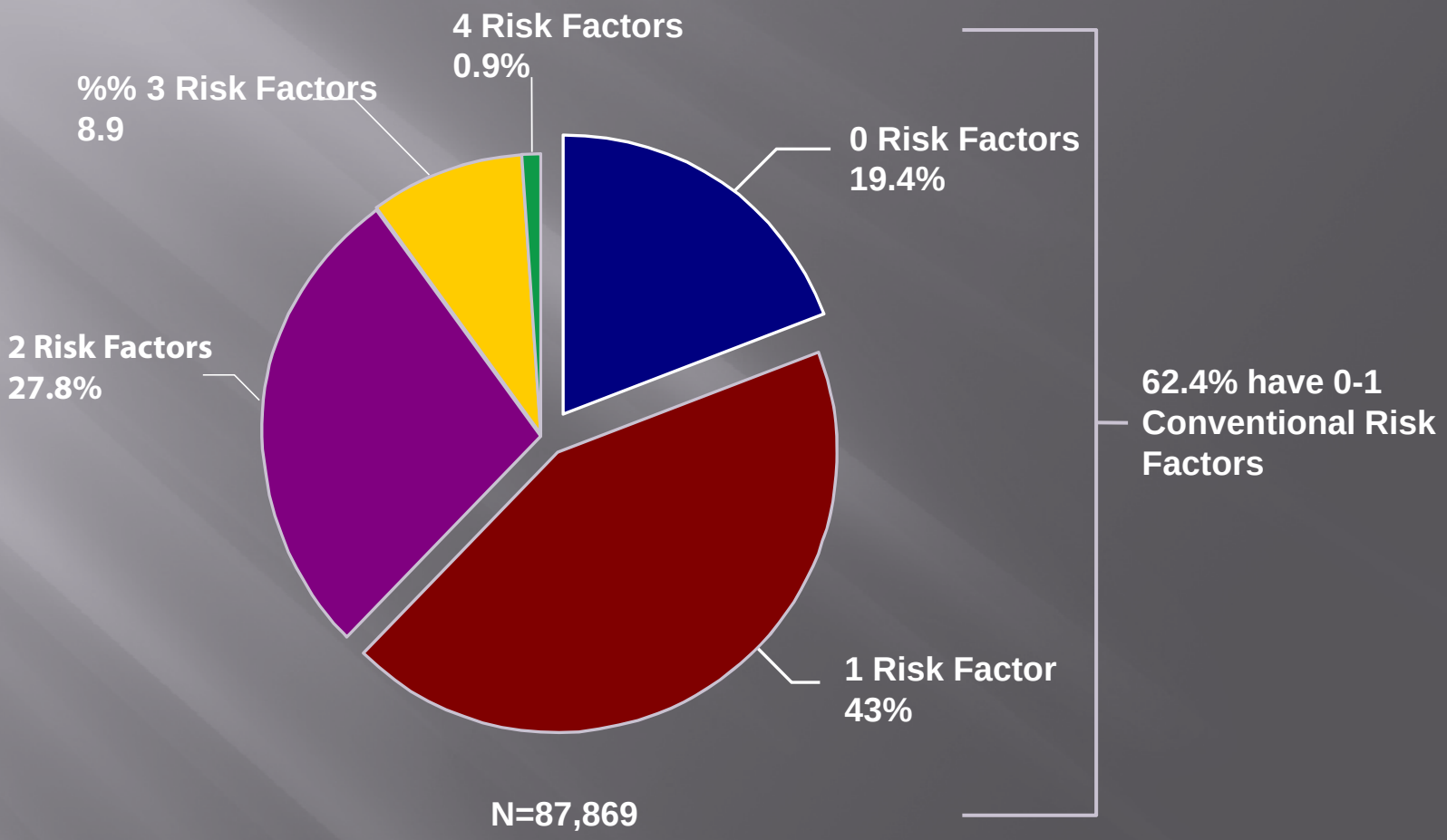
Limitations of Total Cholesterol and LDL Alone in Predicting Coronary Heart Disease

Framingham Heart Study - 26 year follow-up data

1. 35% of persons who develop CHD have total cholesterol < 200 mg/dL[1]
2. 80% of the MI patient population had similar cholesterol levels as those who did not have an MI[1]
3. The median LDL level in CHD is 150 mg/dL[1]
4. As little as 25% of premature CHD is attributable to elevated LDL-C values[2]

[1]Castelli W, *Atherosclerosis* 1996
[2]Genest J Jr, et al. *J Am Coll Cardiol* 1992

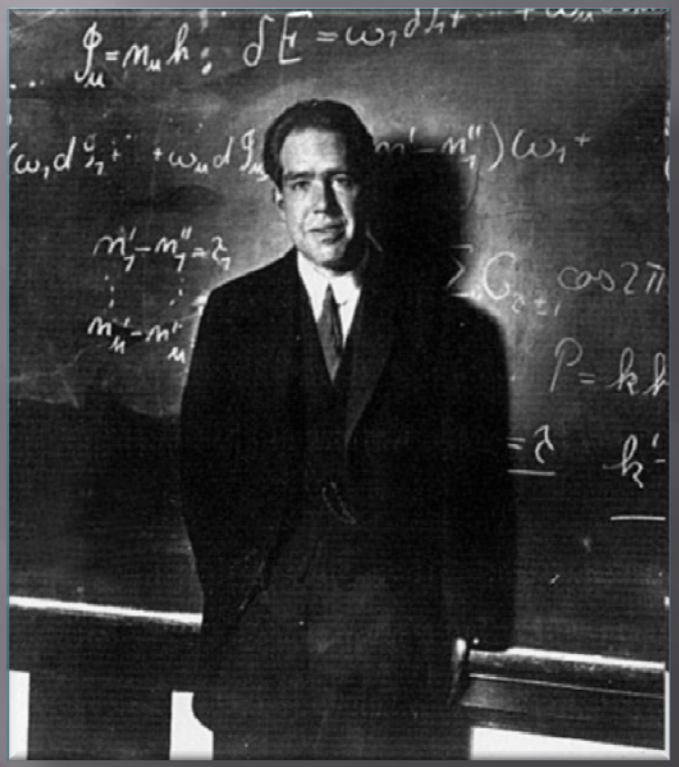
Prevalence of Conventional Risk Factors in 87,869 Patients with Established CHD



4 Conventional Risk Factors:
Hypertension, Smoking, Hypercholesterolemia, Diabetes

Khot UM, et al. *JAMA* 2003

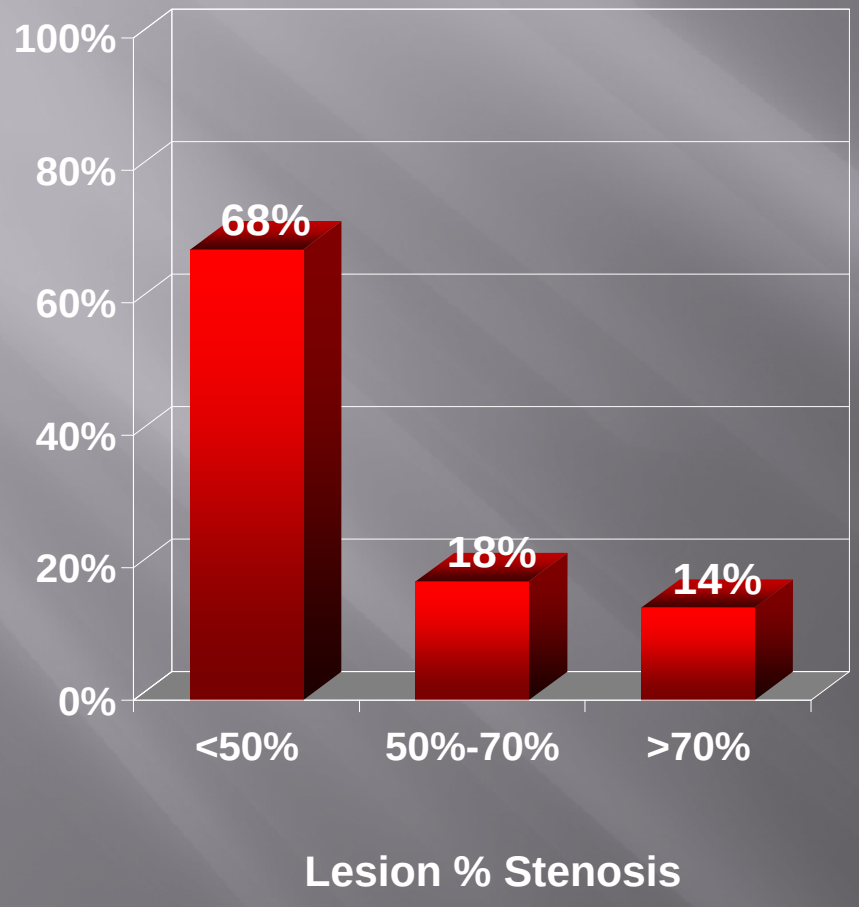
“Prediction Is Very Difficult, Especially If It’s About The Future”



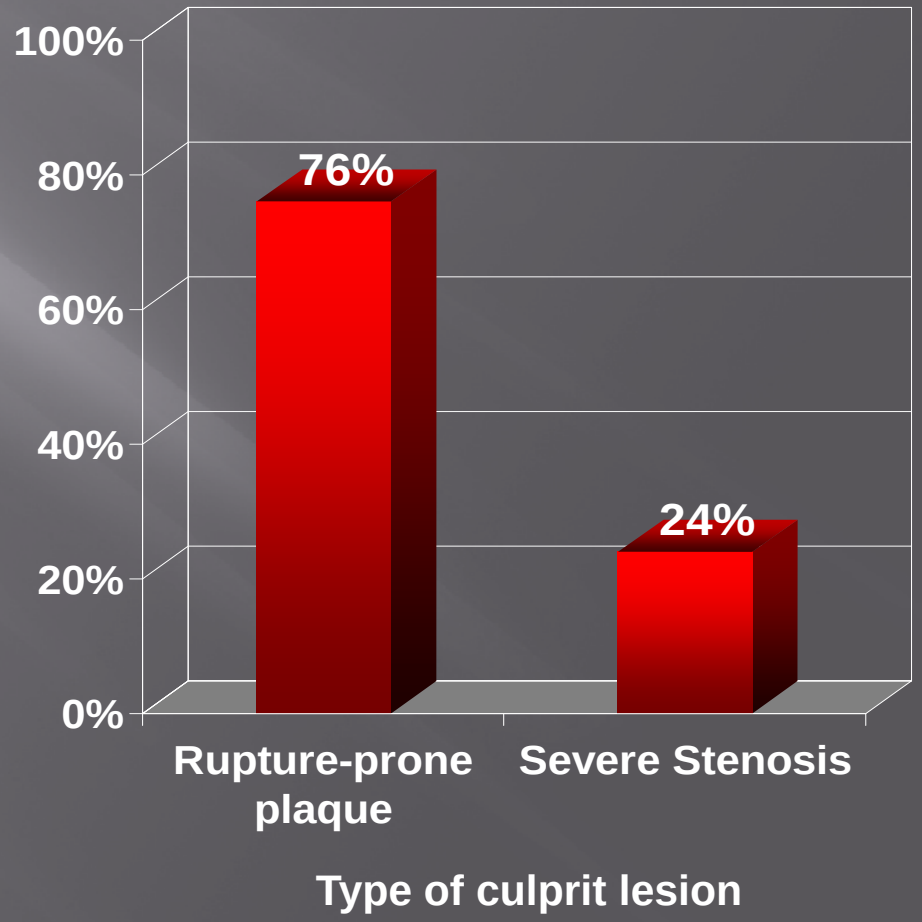
Nils Böhr

More than 2/3 of all events, Heart Attack and Stroke, Fatal or Non-Fatal are from plaque rupture

Acute Myocardial Infarction

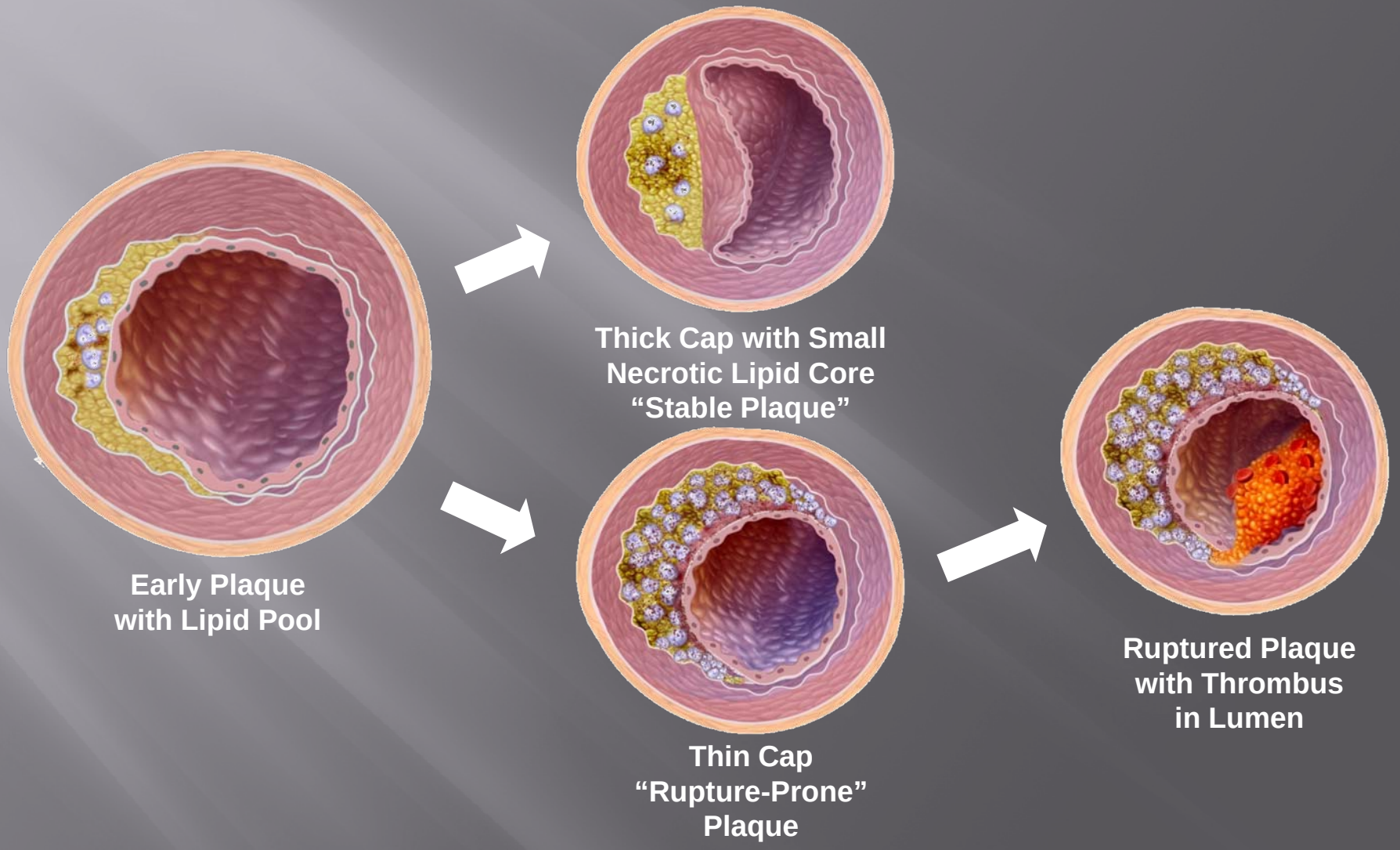


Sudden Cardiac Death



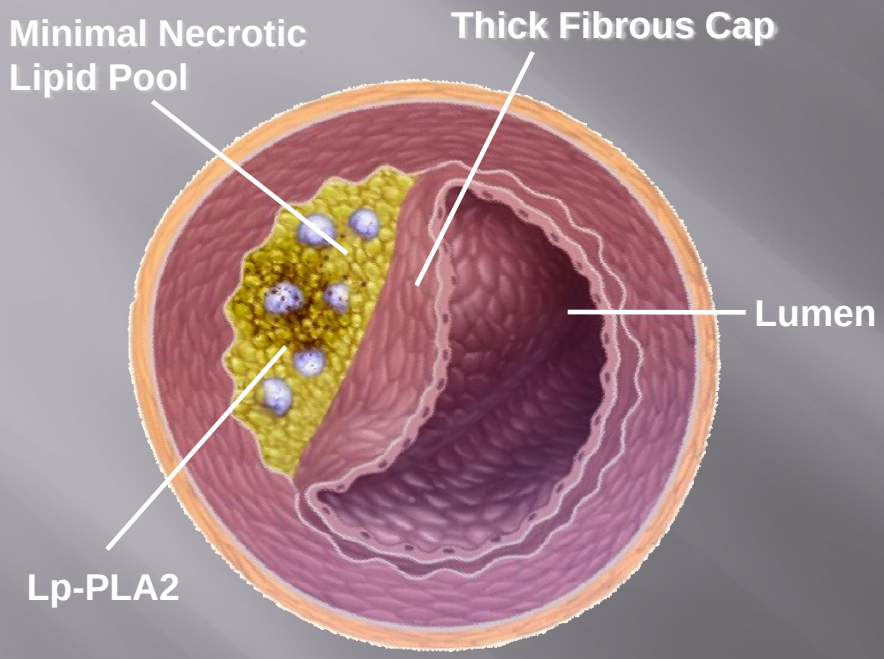
Kolodgie F, et al. *ATVB* 2006

Rupture-Prone Plaques may not be Severely Stenosed but are Inflamed with Thin Fibrous Caps



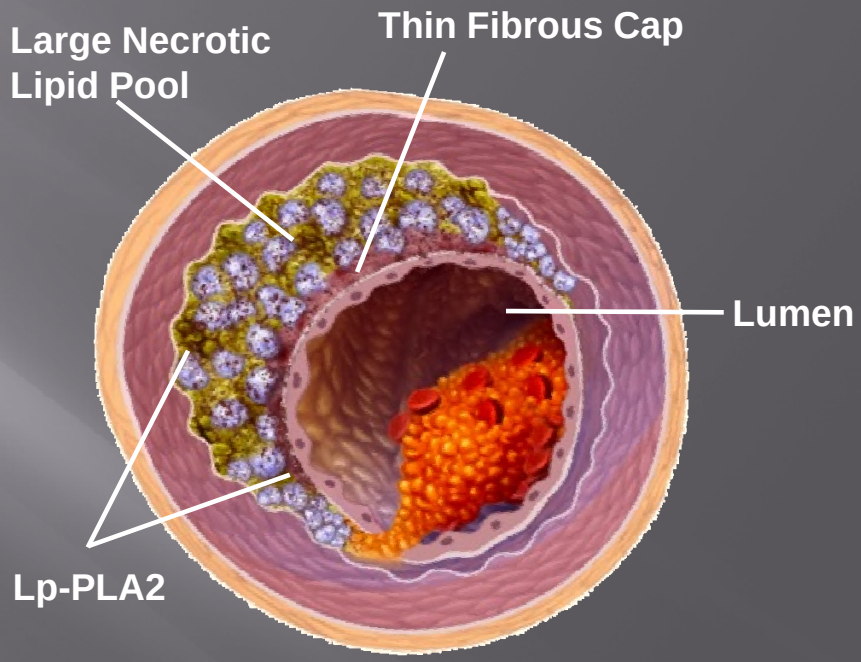
Adapted from Kolodgie F, et al. *Arterioscler Thromb Vasc Biol* 2006.

Contrasting Histopathological Characteristics of a Stable versus Ruptured Plaque



Stable Plaque

- Low Lp-PLA_2 content (dark staining)
- May have significant stenosis
- Thick fibrous cap / high collagen content
- Minimal necrotic lipid pool
- Few inflammatory cells

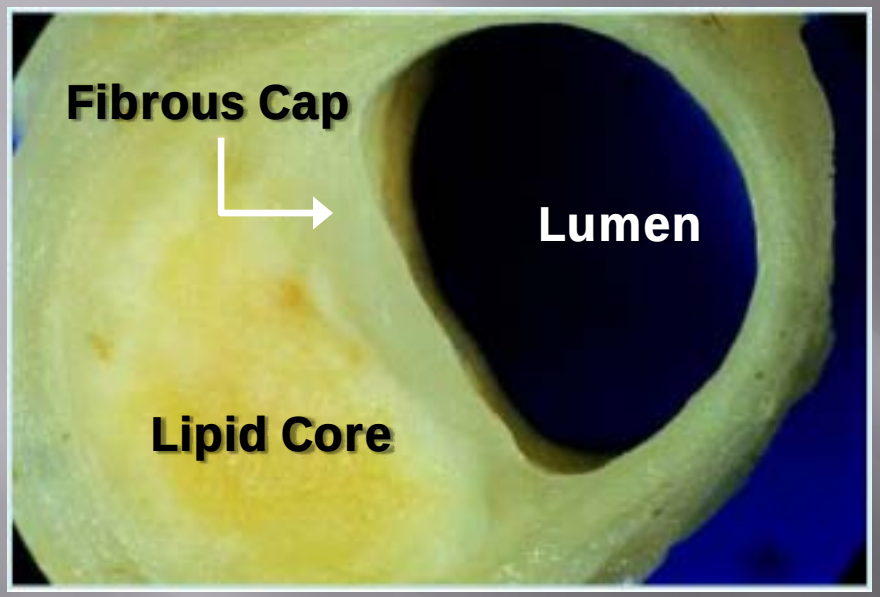


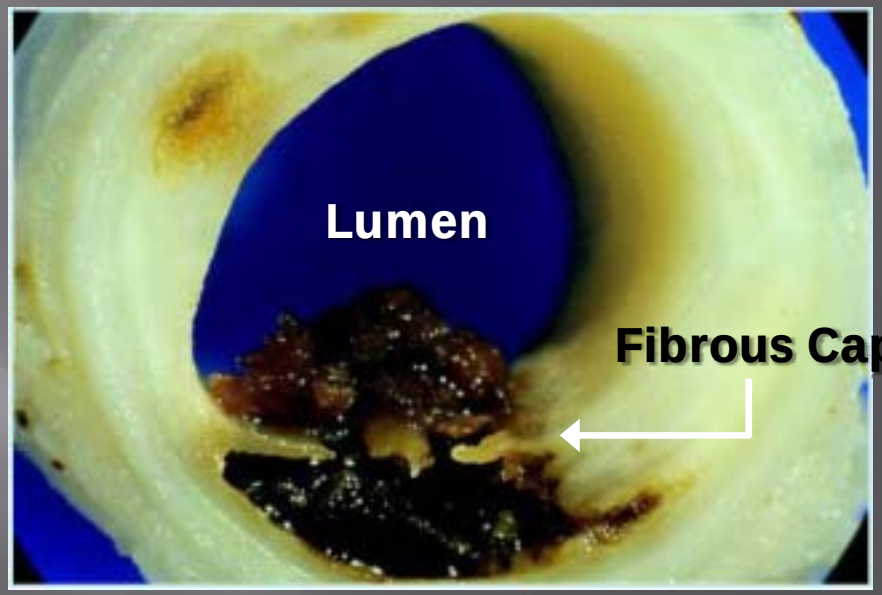
Ruptured Plaque

- High Lp-PLA_2 content (dark staining)
- May have minimal stenosis
- Thin fibrous cap / low collagen content
- Large necrotic lipid pool
- Many inflammatory cells

Davidson MH, Jones PH. *Am J Card Suppl* 2008.

Contrasting Histopathological Characteristics of a Stable versus Ruptured Plaque





Stable Plaque

- Lumen stenotic but plaque stable
- Thick fibrous cap

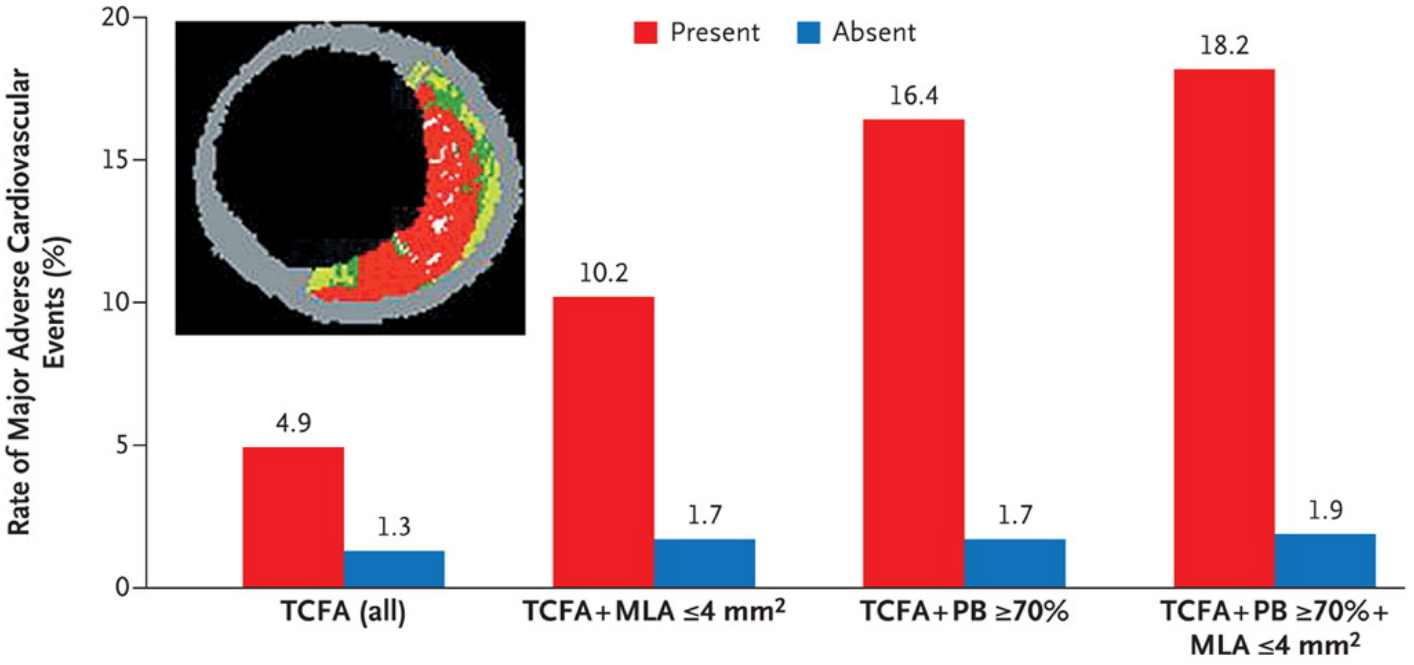
Ruptured Plaque

- Lumen not stenotic but inflamed
- Thin fibrous cap ruptured, leading to thrombus formation

Inflammation Leads to Plaque Rupture

PROSPECT: Event Rates in Relation to Presence or Absence of Thin-Cap Fibroatheroma

Median Follow-up 3.4 Yrs



Lesion hazard ratio (95% CI)	3.90 (2.25–6.76)	6.55 (3.43–12.51)	10.83 (5.55–21.10)	11.05 (4.39–27.82)
P value	<0.001	<0.001	<0.001	<0.001
Prevalence (%)	46.7	15.9	10.1	4.2

Stone GW et al, N Engl J Med 2011;364:226-235

The NEW ENGLAND JOURNAL of MEDICINE

Lp-PLA2 at the "Scene of the Crime": As Lesions Progress so Does Staining Intensity

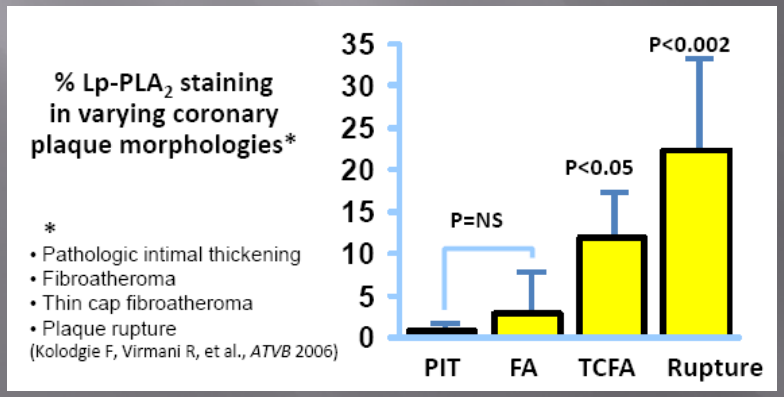
Early plaque with lipid pool

Thinning cap with small necrotic lipid core "stable plaque"

Reddish-brown staining depicts presence of Lp-PLA$_2$

Thin cap "rupture prone" plaque

Ruptured plaque with thrombus in lumen



Kolodgie F, et al. *Arterioscler Thromb Vasc Biol* 2006

Thank you