"Why carry malpractice insurance if you don't malpractice once in a while?"

Coronary Calcium Scoring

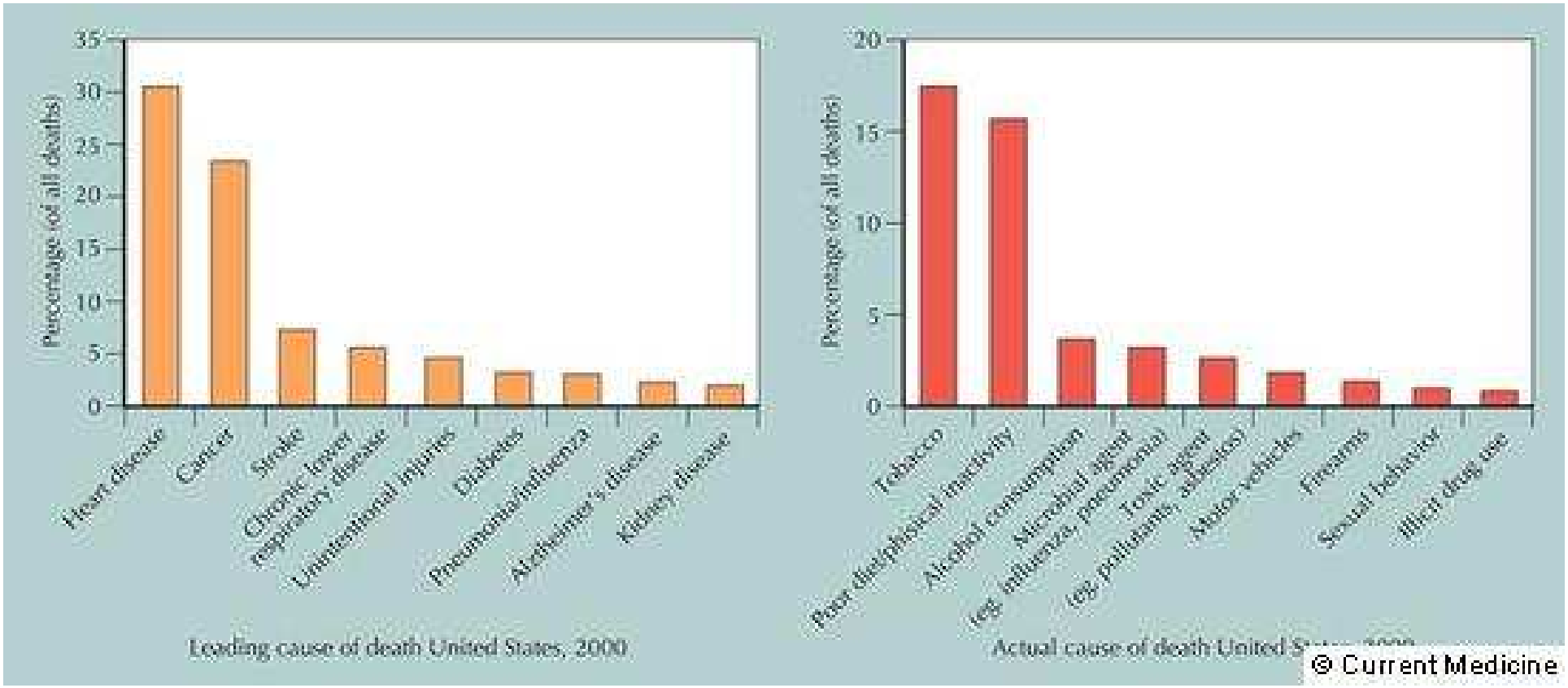
Myth or Reality?

David Stultz, MD

May 17, 2006

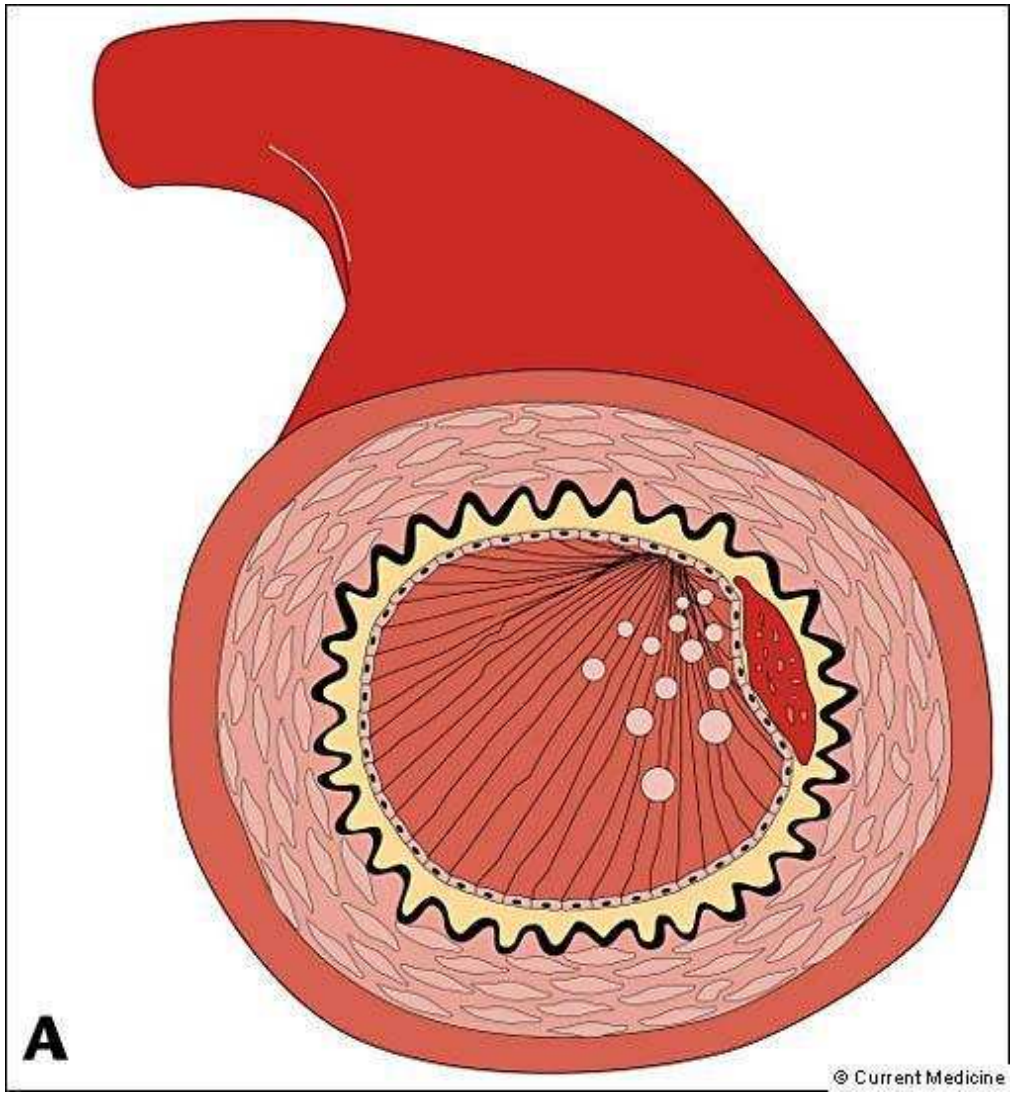
Cardiology Fellow, PGY-6

Leading causes and contributions of death in the USA (2000)



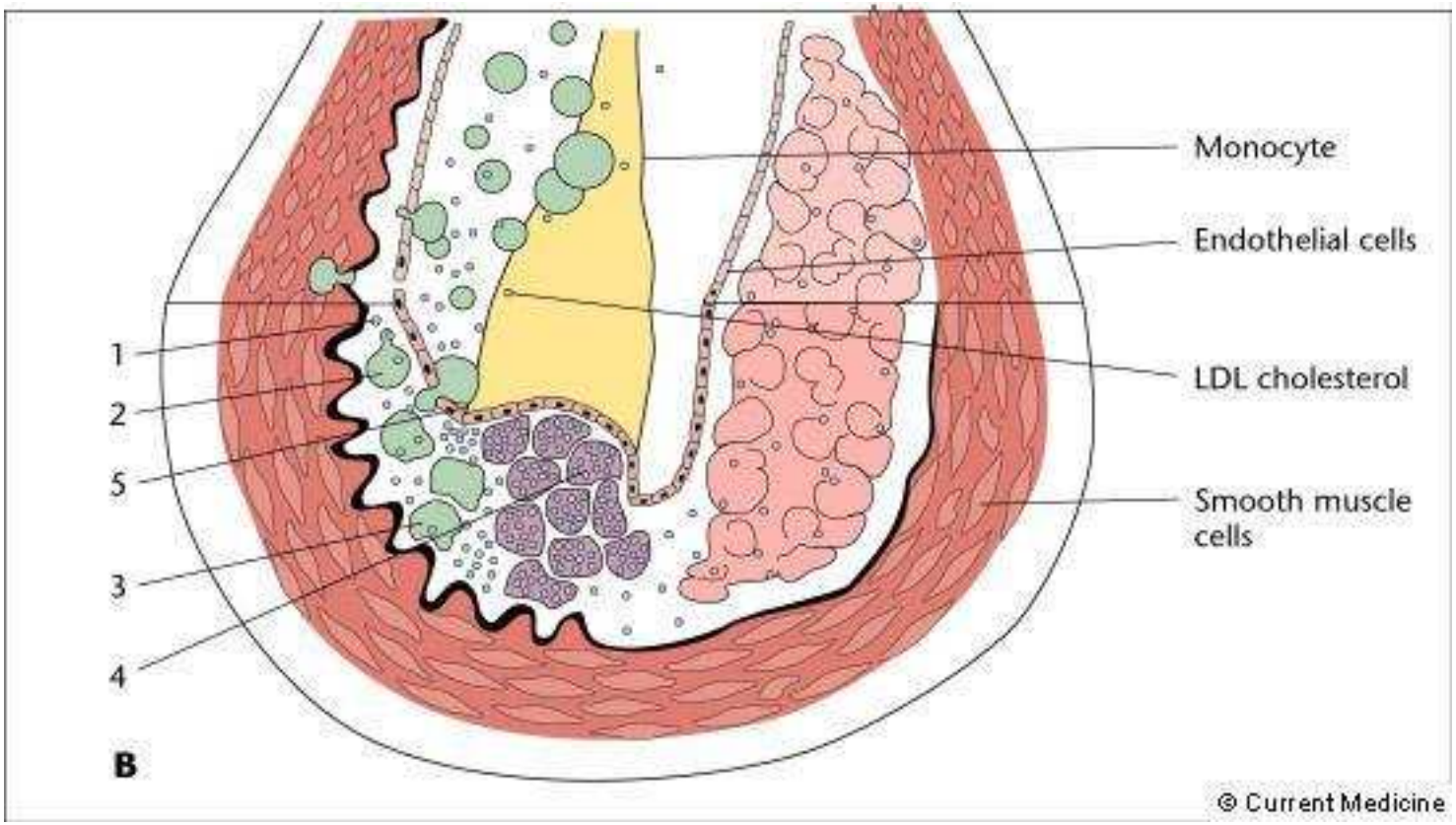
Braunwald Atlas of Internal Medicine

The atherosclerotic process (A)



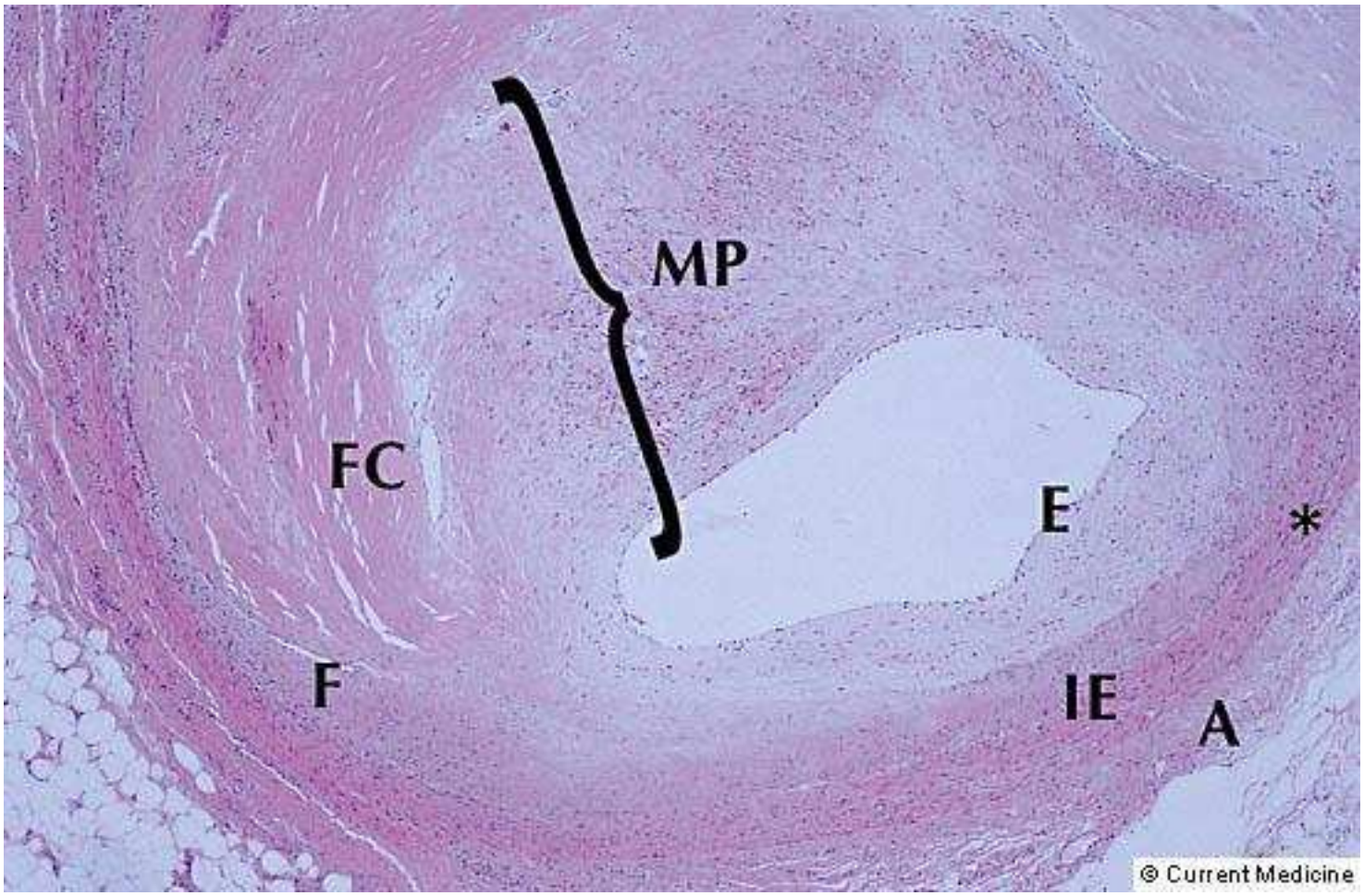
Braunwald Atlas of Internal Medicine

The atherosclerotic process (B)



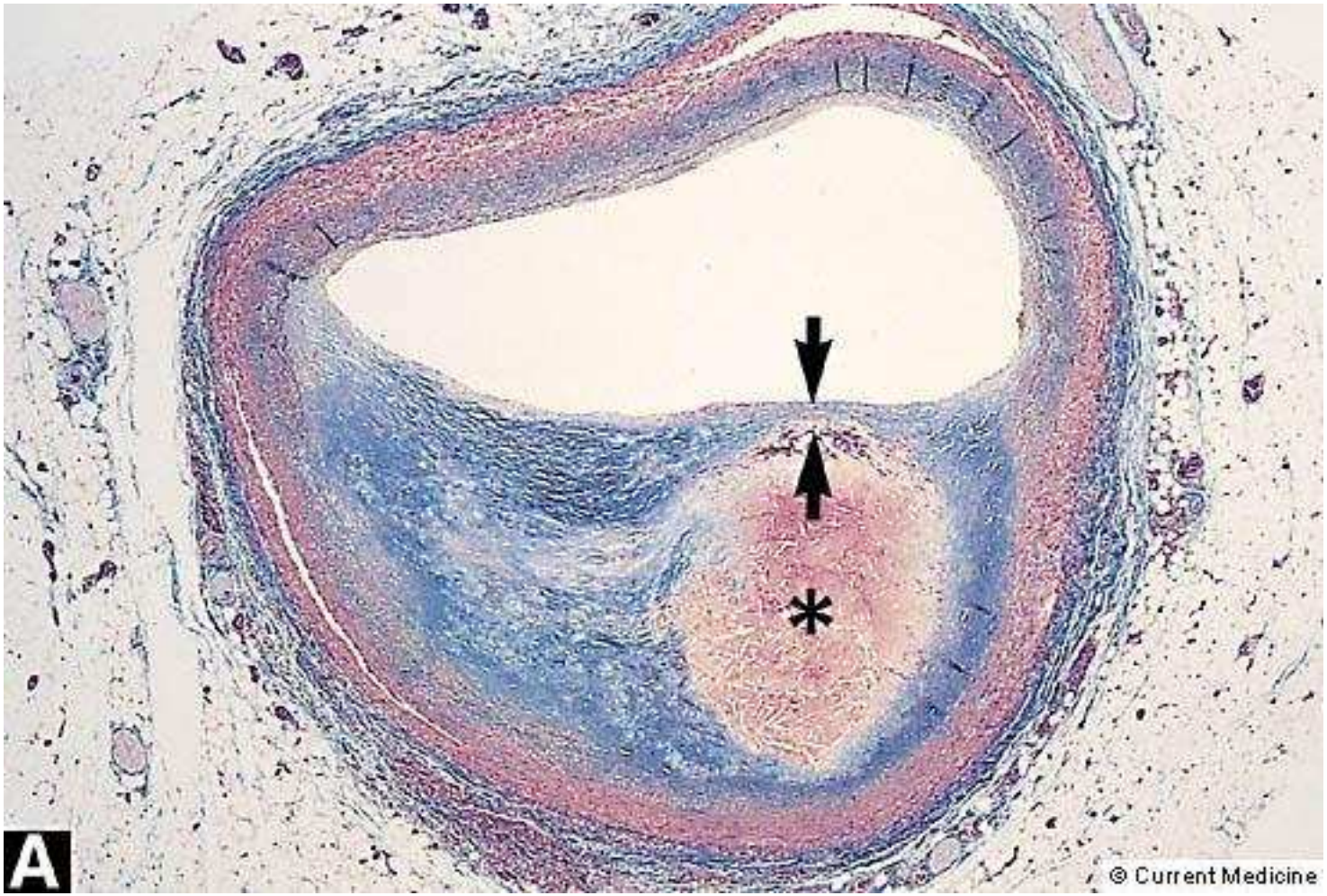
Braunwald Atlas of Internal Medicine

Plaque development and localization



Braunwald Atlas of Internal Medicine

Differences in consistency and rupture vulnerability of coronary plaques (A)



Braunwald Atlas of Internal Medicine

Framingham Risk Score

- Estimates of total CHD risk (risk of developing one of the following) over the course of 10 years
  - angina pectoris
  - myocardial infarction
  - coronary disease death
- Separate score sheets are used for men and women
- Factors used to estimate risk
  - Age
  - blood cholesterol (or LDL cholesterol)
  - HDL cholesterol
  - blood pressure
  - cigarette smoking
  - diabetes mellitus
- Relative risk for CHD is estimated by comparison to low risk Framingham participants

Wilson PWF, D'Agostino RB, Levy D, Belanger AM, Silbershatz H, Kannel WB. Prediction of coronary heart disease using risk factor categories. Circulation 1998;97:1837-1847.

Users of this risk algorithm should be aware of several caveats:

1. … only for persons without known heart disease.
2. … only coronary heart disease, not other heart and vascular diseases.
3. … almost all Caucasian. The Framingham risk algorithm may not fit other populations quite as well.
4. For some of the sex-age groups … events are quite small. Therefore, the estimates of risk for those groups may lack precision.
5. Other organizations are considering how the information from the Framingham risk algorithm, as well as other assessments of risk, might best be incorporated into clinical practice.
6. … estimates the risk of developing CHD within a 10-year time period. This risk score may not adequately reflect the long-term or lifetime CHD risk of young adults, which is: one in two for men and one in three for women.
7. The presence of any CHD risk factor requires appropriate attention because a single risk factor may confer a high risk for CHD in the long run, even if the 10-year risk does not appear to be high.
8. Since age is a prominent determinant of the CHD risk score, the 10-year hazards of CHD are, on average, high in older persons. This may over-identify candidates for aggressive interventions.
9. The score derived from this algorithm ***should not*** *be used in place of a medical examination*.

http://www.nhlbi.nih.gov/about/framingham/riskabs.htm

Coronary Disease Risk Prediction Score Sheet for Men Based on LDL Cholesterol Level

Step 1

Age	
Years	Points
30-34	-1
35-39	0
40-44	1
45-49	2
50-54	3
55-59	4
60-64	5
65-69	6
70-74	7

Step 2

LDL - Cholesterol		
(mg/dl)	(mmol/L)	Points
<100	≤2.59	-3
100-129	2.60-3.36	0
130-159	3.37-4.14	0
160-189	4.15-4.91	1
≥190	≥4.92	2

Key	
Color	Risk
green	Very low
white	Low
yellow	Moderate
rose	High
red	Very high

Step 3

HDL - Cholesterol		
(mg/dl)	(mmol/L)	Points
<35	≤0.90	2
35-44	0.91-1.16	1
45-49	1.17-1.29	0
50-59	1.30-1.55	0
≥60	≥1.56	-1

Step 4

Blood Pressure				
Systolic (mmHg)	Diastolic (mmHg)			
<80	80-84	85-89	90-99	≥100

Step 7 (sum from steps 1-6)

Adding up the points	
Age	_____
LDL Cholesterol	_____
HDL Cholesterol	_____
Blood Pressure	_____
Diabetes	_____
Smoker	_____
Point Total	_____

Step 8 (determine CHD risk from point total)

CHD Risk	
Point Total	10 Yr CHD Risk
≤-3	1%
-2	2%
-1	2%
0	3%
1	4%
2	4%
3	6%
4	7%
5	9%
6	11%
7	14%
8	18%
9	22%
10	27%
11	33%
12	40%

Updated ATP III LDL-C Goals and Cutpoints for Therapy

Risk Category	LDL-C (mg/dL)		
	Goal	Initiation Level for TLC	Consideration Level for Drug Therapy
High risk: CHD or CHD risk equivalents (10-yr risk >20%)	<100 (optional: <70)	≥100	≥100 (<100: consider drug options)
Moderately high risk: 2+ risk factors (10-yr risk 10−20%)	<130 (optional: <100)	≥130	≥130 (100−129: consider drug options)
Moderate risk: 2+ risk factors (10-yr risk <10%)	<130	≥130	≥160
Lower risk: 0−1 risk factor	<160	≥160	≥190 (160−189: LDL-C−lowering drug optional)

Grundy SM et al. *Circulation* 2004;110:227-239.

Cholesterol as a risk for CAD

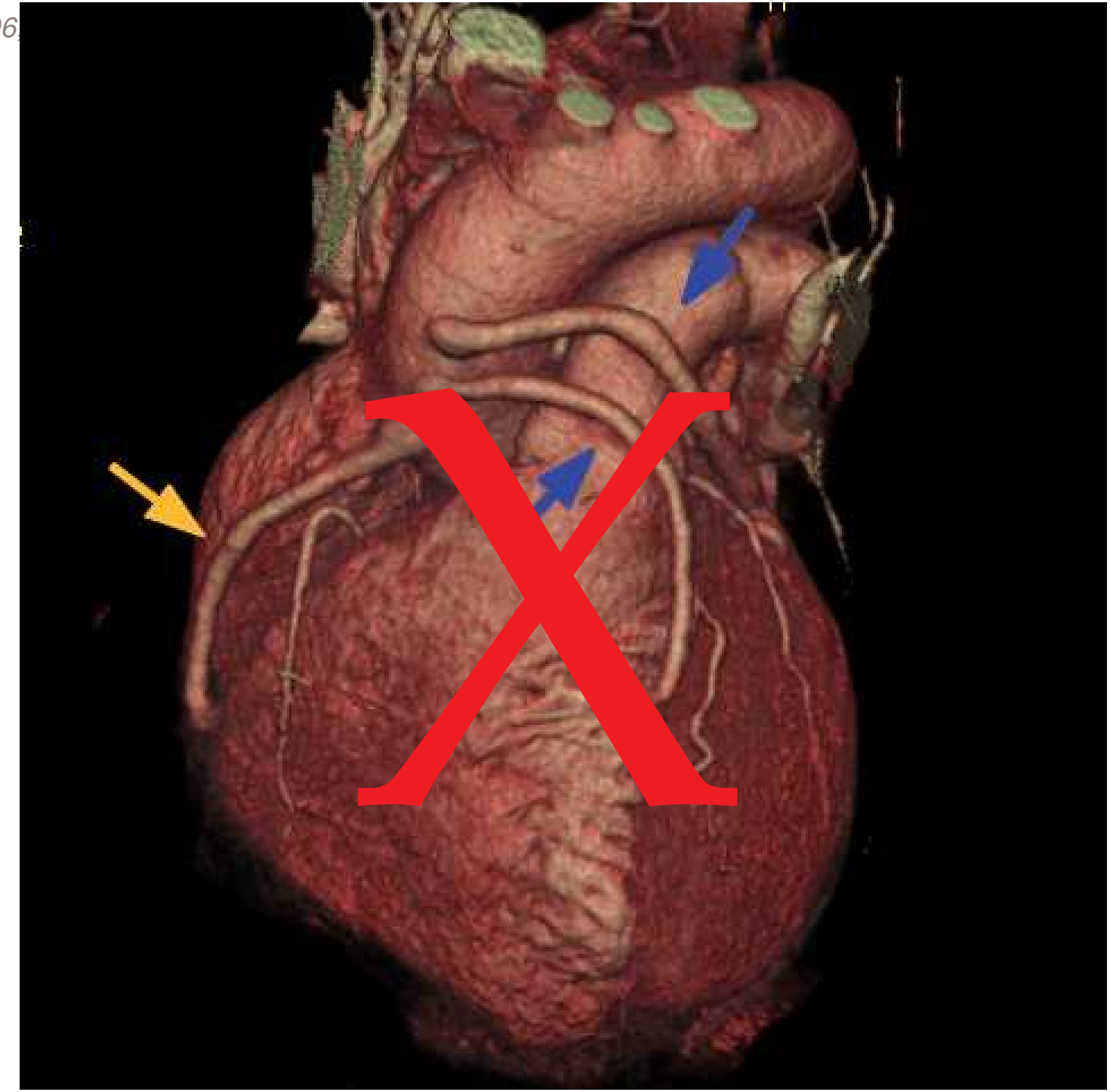
- Up to 50% of patients with atherosclerotic disease present with either ischemic heart disease or sudden death
- 150,000 patients have a fatal heart attack as the first symptom of heart disease
  - 50% of these myocardial infarctions (MIs) occur in patients with no prior history of disease
  - 68% of these are due to lesions representing a stenosis diameter <50%
- About 35% of patients with established heart disease have total cholesterol levels <250 mg/dL
- Cholesterol has failed to predict up to one third of future deaths resulting from coronary artery disease.

Clouse ME. How useful is computed tomography for screening for coronary artery disease? Noninvasive screening for coronary artery disease with computed tomography is useful. Circulation. 2006 Jan 3;113(1):125-46.

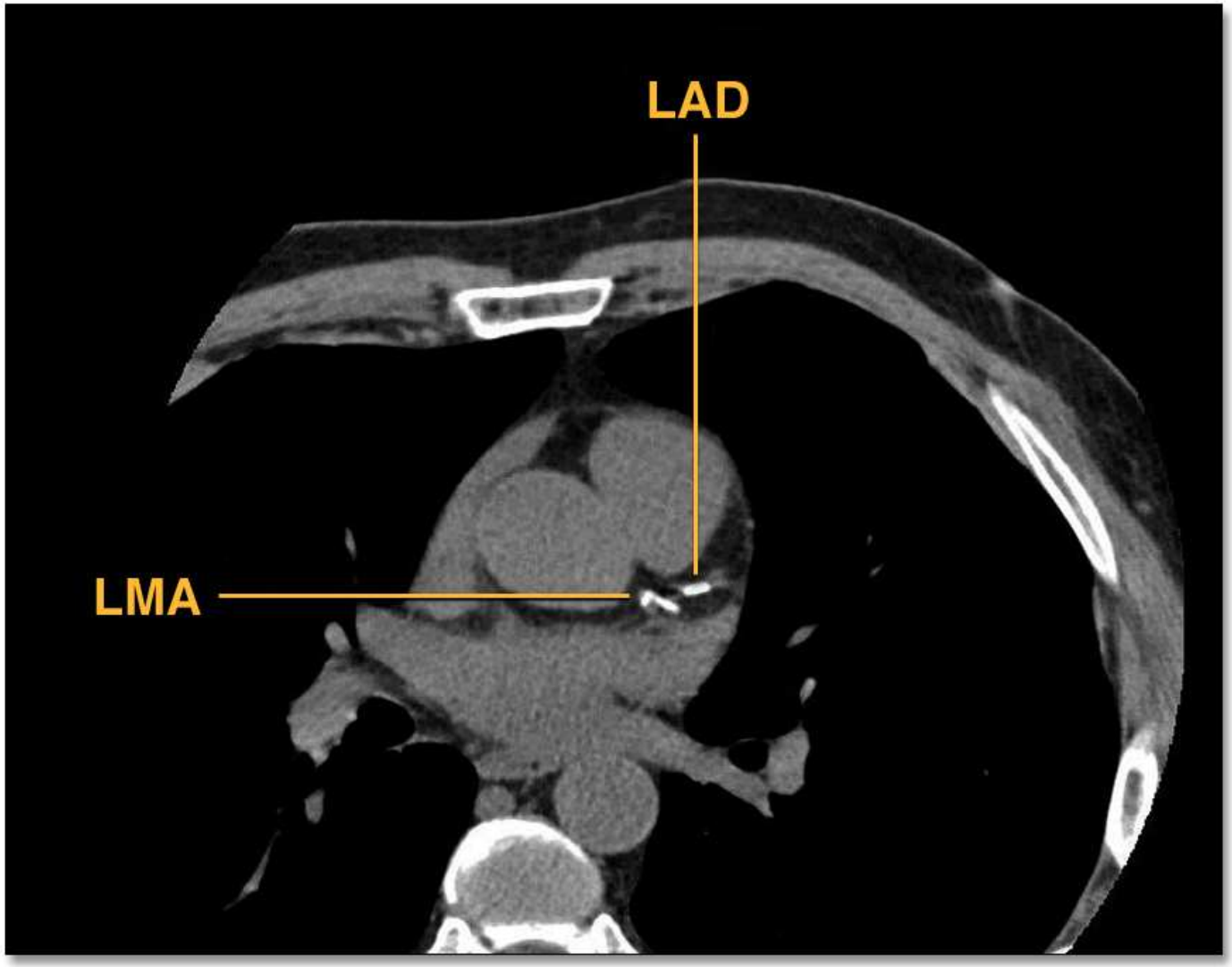
Relationship of Coronary Calcium to Atherosclerosis

- Calcification represents a healed plaque
- Autopsy studies showed link between extent of atherosclerosis and coronary calcification[1]
- Patients dying from coronary atherosclerosis found to have 2-5x more coronary calcium than age matched controls dying from other causes[2]

1 Rifkin RD, Parisi AF, Folland E. Coronary calcification in the diagnosis of coronary artery disease. Am J Cardiol 1979;44:141-7.
2 Eggen DA, Strong JP, McGill HC Jr. Coronary calcification. Relationship to clinically significant coronary lesions and race, sex, and topographic distribution. Circulation 1965;32:948-55

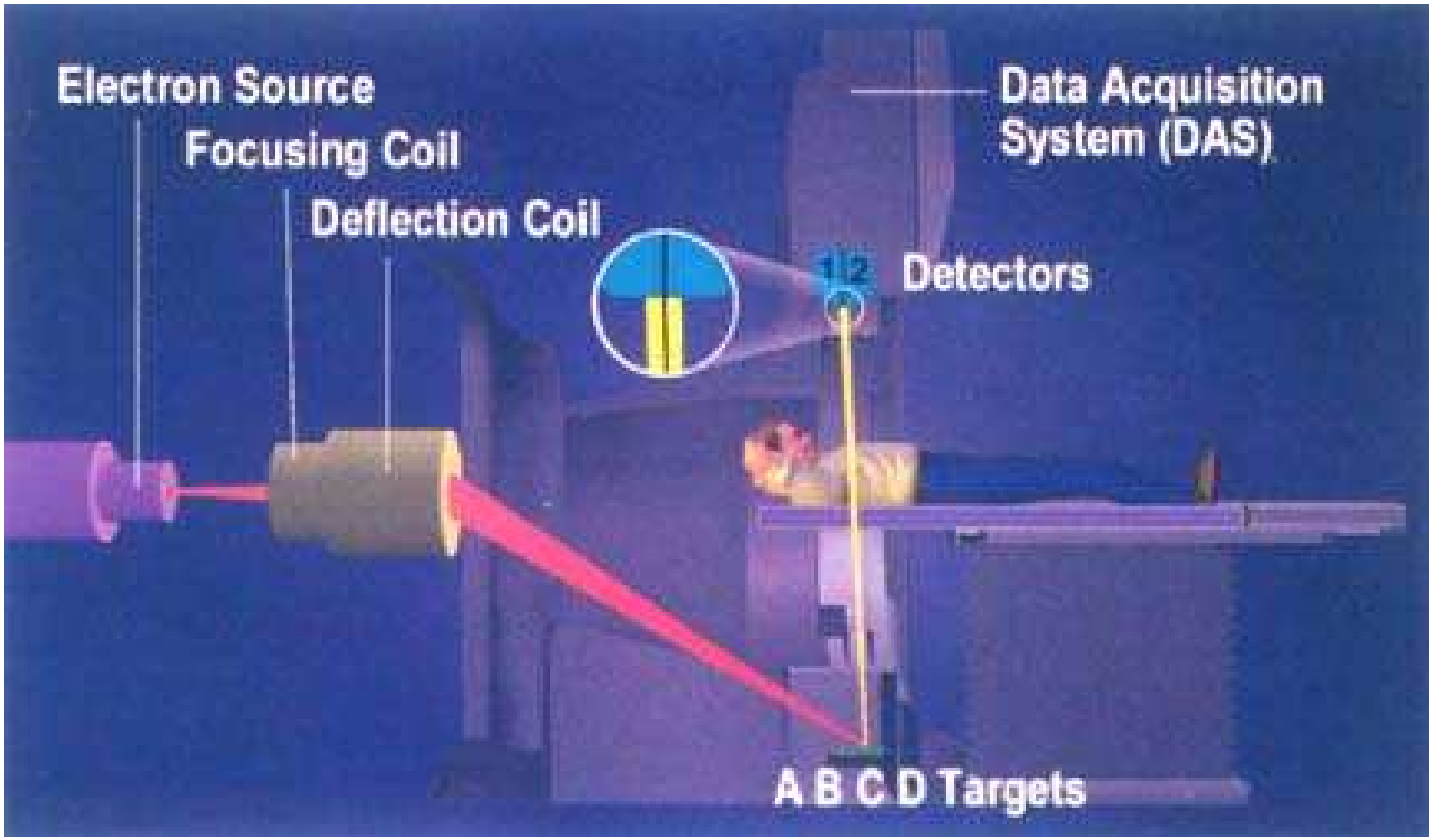


Left Main and LAD Calcium



Technical Aspects

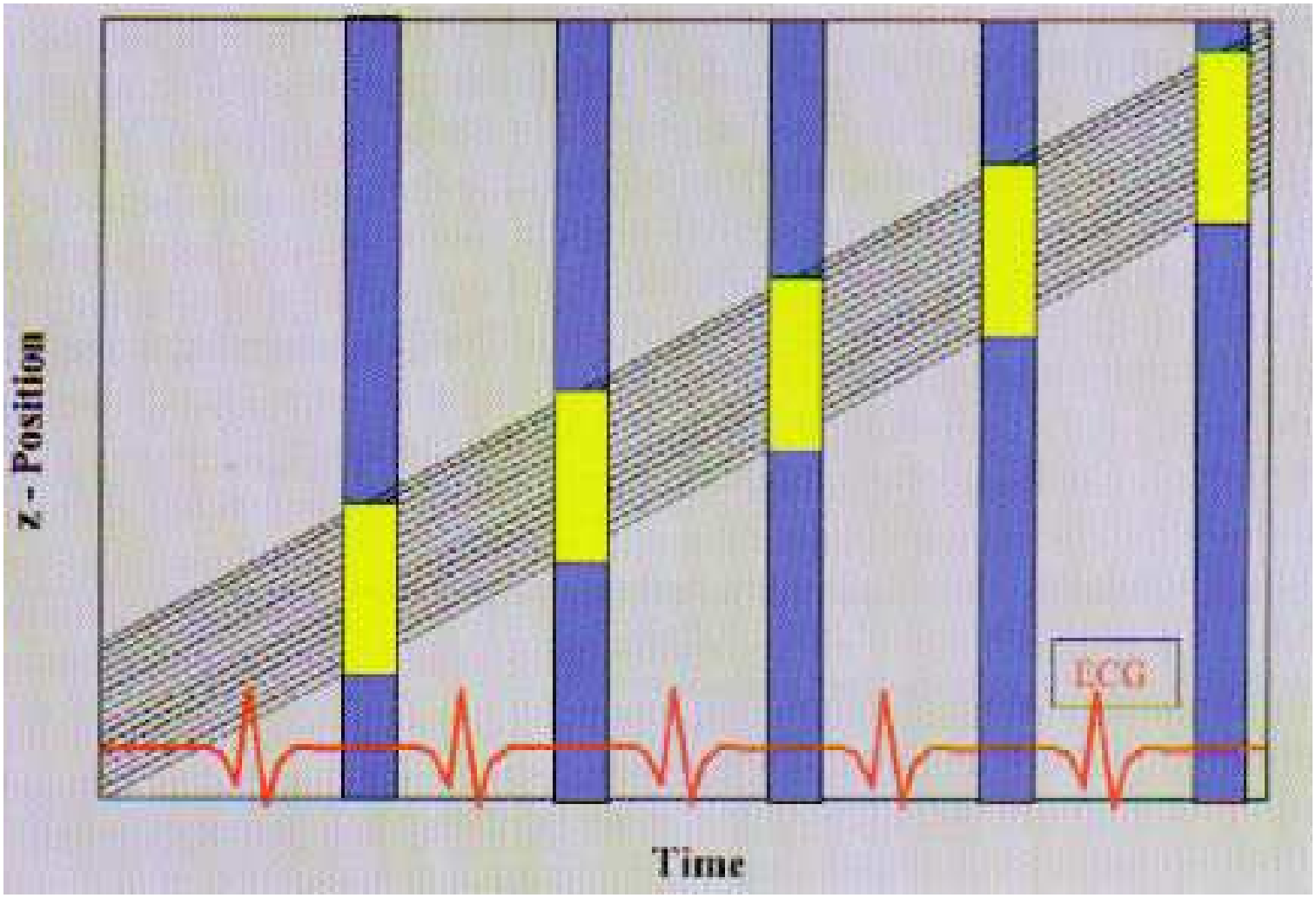
- Computed tomography
  - Electron Beam CT
  - Multidetector CT (at least 4)
- 3mm thick slices
- Acquired at 80% of R-R interval
  - Prospective gating
- Radiation dose 1-2 mSv
- Single breath hold (10 s)
- Calcium detected as >130 Hounsfield units



- Beam focused by electromagnetic coil
- Very rapid imaging (50-100ms)

Braunwald, 7th ed

EKG gating



Schoenhagen P. Atlas and Manual of Cardiovascular Multidetector Computed Tomography. Taylor & Francis: 2005.

The initial studies

- South Bay Heart Watch
- Arad
- Wong
- Kondos
- Shaw

South Bay Heart Watch Study

- Prospective evaluation of calcium scoring
- Asymptomatic patients over age 45 with at least one risk factor
- Started 1990 with Fluorsocopy
- 1992 EBCT performed on 1,289 patients
  - mean age 66 ± 8 years
- 3 year analysis showed no advantage of EBCT scan[1]
  - "Neither risk-factor assessment nor EBCT calcium is an accurate event predictor in high-risk asymptomatic adults"
- Median 7 year followup showed incremental predictive power beyond standard CAD risks and CRP
  - Excluded diabetics in analysis
- CAC score >300 was independently predictive of fatal or nonfatal MI when compared to those with scores of 0 (HR 3.9, $p<0.001$)

1 Detrano RC, Wong ND, Doherty TM, et al. Coronary calcium does not accurately predict near-term coronary events in high-risk adults. Circulation 1999;99:2633-8.

2 Greenland P, LaBree L, Azen SP,Doherty TM, Detrano RC. Coronary artery calcium score combined with Framingham score for risk prediction in asymptomatic individuals. JAMA 2004;291:210-5.

Raggi et al, 2000

- Cohort of 623 asymptomatic subjects
- mean age 52 ± 9 years, mean follow-up 2.7 years
- Majority of events occurred in patients >75th percentile

Annualized Acute MI/Cardiac Death Rate by Calcium Score	
0	0.11%
1-99	2.1%
100-400	4.1%
>400	4.8%

Raggi P, Callister TQ, Cooil B, et al. Identification of patients at increased risk of first unheralded acute myocardial infarction by electron-beam computed tomography. Circulation 2000;101:850-5.

TABLE 3. Distribution of Absolute CS Values and CS Percentiles

		Group A (n=172)	Group B, Hard Event (n=27)	Group B, No Hard Event (n=605)
Absolute CS				
0	1/292 = 0.3%	7 (4)	1 (4)	291 (48)
1–99	12/219 = 5.5%	58 (34)	12 (44)	207 (34)
100–400	8/74 = 11%	60 (35)	8 (30)	66 (11)
>400	6/47 = 12.7%	47 (27)	6 (22)	41 (6)
CS percentiles				
>50th percentile		150 (87)	23 (85)	258 (43)
>75th percentile		121 (70)	19 (70)	162 (27)
>90th percentile		72 (42)	11 (41)	82 (14)

Values are n (%).

Raggi P, Callister TQ, Cooil B, et al. Identification of patients at increased risk of first unheralded acute myocardial infarction by electron-beam computed tomography. Circulation 2000;101:850-5.

Arad et al, 2000

- 1172 patients
- age 53 +/- 11 years, 71% men
- Average 3.6 year followup
- 39 (3.3%) patients with event (mean calcium score 764 +/- 935)
  - 3 coronary deaths
  - 15 nonfatal MI
  - 21 coronary revascularization
- Patients without event had mean calcium score 135 +/- 432
- Calcium Score >=160, odds ratio 15.8 for prediction of all coronary events

Arad Y, Spadaro LA, Goodman K, Newstein D, Guerci AD. Prediction of coronary events with electron beam computed tomography. J Am Coll Cardiol 2000;36:1253-60

Wong et al, 2000

- 926 asymptomatic persons
  - 735 men and 191 women
  - mean age 54 years
  - Mean 3.3 year followup
- 28 (3.8%) events (MI, stroke, revascularization)

Wong ND, Hsu JC, Detrano RC, et al. Coronary artery calcium evaluation by electron beam computed tomography and its relation to new cardiovascular events. Am J Cardiol 2000;86:495-8

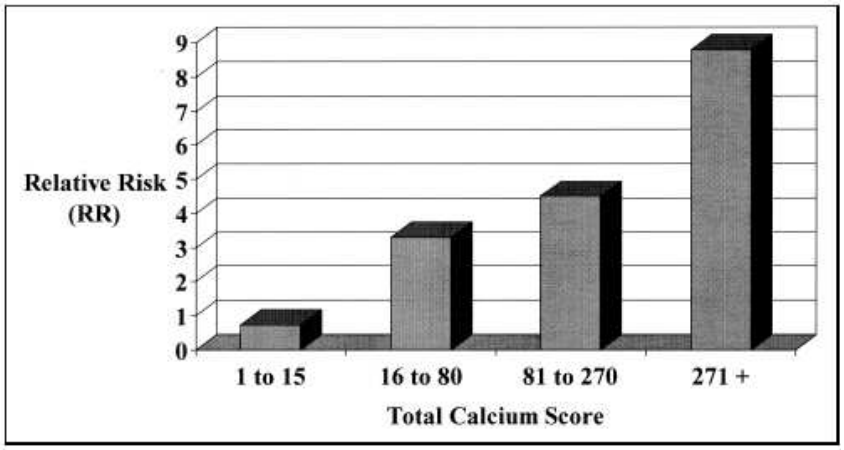
TABLE I Prevalence of Coronary Risk Factors at Baseline by

TABLE II Bivariate Analysis of Coronary Calcium and Cardiovascular Events

	Myocardial Infarction		Revascularization		Total Cardiovascular Events*	
	Yes (n = 6)	No (n = 897)	Yes (n = 23)	No (n = 900)	Yes (n = 28)	No (n = 898)
Calcium absent						
Calcium score = 0	0 (0%)	392 (43.7%)	4 (17.4%)	394 (43.8%)	4 (14.3%)	394 (43.9%)
Calcium present	6 (100%)§	505 (56.3%)	19 (56.2%)‖	506 (82.6%)	24 (85.7%)‖	504 (56.1%)
Calcium score 1–15	0 (0%)	131 (14.6%)	0 (0%)	132 (14.7%)	1 (3.6%)	132 (14.6%)
Calcium score 16–80	2 (33.3%)	129 (14.4%)	4 (17.4%)	129 (14.3%)	5 (17.9%)	129 (14.3%)
Calcium score 81–270	3 (50.0%)	124 (13.8%)	5 (21.7%)	124 (13.8%)	7 (25.0%)	124 (13.8%)
Calcium score 271+	1 (16.7%)	121 (13.5%)	10 (43.5%)	121 (13.4%)	11 (39.3%)	121 (13.5%)
Test of trend	p <0.05		p <0.001		p <0.001	

*Includes 2 reported strokes.
†p <0.01, ‡p <0.001 compared to those with and without events, or across calcium score categories.
§p <0.05; ‖p <0.001 from Fisher's exact test compared to those with or without calcium.

n = 908 to 926 because of missing data from some risk factors.



- **Rates of Total CV Events over 3.3 years**
  - **0 (4/398) = 1.0% [0.3%]**
  - **1-15 (1/133) = 0.8% [0.2%]**
  - **16-80 (5/134) = 3.7% [1.1%]**
  - **81-270 (7/131) = 5.3% [1.6%]**
  - **271+ (11/132) = 8.3% [2.5%]**

Kondos et al, 2003

- 8855 initially asymptomatic adults 30 to 76 years old (26% women) who self-referred for EBT CAC screening
- CAD risks assessed by questionnaire
- Mean followup 37 months
- "In men, events (n=192) were associated with the presence of CAC (RR=10.5, P<0.001), diabetes (RR=1.98, P=0.008), and smoking (RR=1.4, P=0.025), whereas in women, events (n=32) were linked to the presence of CAC (RR=2.6, P=0.037) and not risk factors"

- Followup only in 64% of patients

TABLE 1. Event Rates for Men and Women With Detectable CAC Compared to No Detectable CAC

	CAC Present	No CAC	*P*
Men			
Total No.	3065	1086	
Hard events, %	1.6	0.3	0.001
Soft events, %	4.5	0.1	<0.001
All events, %	6.1	0.4	<0.001
Women			
Total No.	754	730	
Hard events, %	0.5	0.3	0.4
Soft events, %	2.8	0.7	0.002
All events, %	3.3	1	0.002

Kondos GT, Hoff JA, Sevrukov A, et al. Electron-beam tomography coronary artery calcium and cardiac events: a 37-month follow-up of 5635 initially asymptomatic low- to intermediate-risk adults. Circulation 2003;107:2571-6.

Shaw et al, 2003

- Retrospective cohort of 10,377 asymptomatic people
- Mean followup 5.0 years
- All cause mortality assessed
- CAC score adds incremental prediction to standard risk factors

Shaw LJ, Raggi P, Schisterman E, Berman DS, Callister TQ. Prognostic value of cardiac risk factors and coronary artery calcium screening for all-cause mortality. Radiology 2003;228:826-33

TABLE 1
Clinical and Electron-Beam CT Characteristics of the Study Population

Characteristic	Study Cohort (n = 10,377)*
Age (y)†	
30–39	7.9 (820)
40–49	30.0 (3,113)
50–59	35.3 (3,663)
60–69	19.2 (1,992)
70–79	6.9 (716)
80 or older	0.7 (73)
Sex	
M	59.6 (6,186)
F	40.4 (4,191)

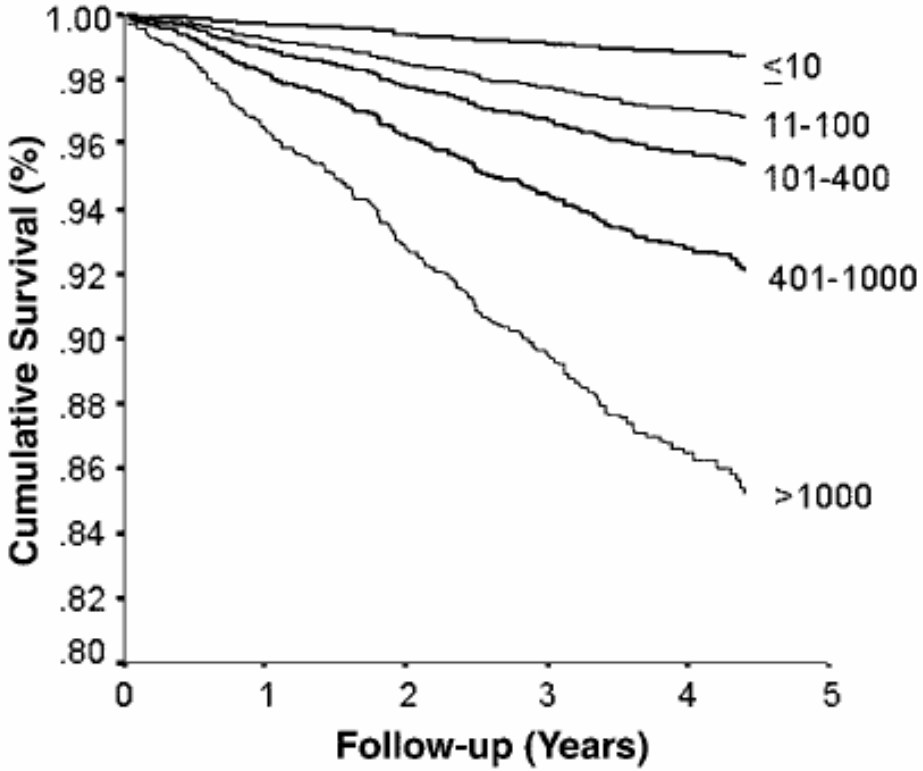


Figure 1. Graph shows unadjusted all-cause survival according to calcium score subsets. Survival rate is proportionally worse as the baseline calcium score increases.

TABLE 3
Overall Rates of All-Cause Mortality according to Clinical and Electron-Beam CT Characteristics of Study Population

Characteristic	Study Population (n = 10,377): All-Cause Death (n = 249, 2.4%)	Study Population (n = 10,377): No Death (n = 10,128, 97.6%)	P Value
Age			<.001
30–39 y (n = 820)	1.3 (11)	98.7 (809)	
40–49 y (n = 3,113)	0.7 (22)	99.3 (3,091)	
50–59 y (n = 3,663)	1.7 (64)	98.3 (3,599)	
60–69 y (n = 1,992)	4.1 (82)	95.9 (1,910)	
70–79 y (n = 716)	8.4 (60)	91.6 (656)	
80 y or older (n = 73)	14.5 (10)	85.5 (63)	
			.5
	2.3 (144)	97.7 (6,042)	
	2.5 (105)	97.5 (4,086)	
			.01
	2.9 (115)	97.1 (3,880)	
	2.1 (133)	97.9 (6,249)	
Calcium score			
≤10 (n = 5,946)			1.0
11–100 (n = 2,044)			2.6
101–400 (n = 1,432)			3.8
401–1,000 (n = 623)			6.3
>1,000 (n = 332)			12.3
	2.1 (151)	97.9 (6,988)	
			<.001
	1.0 (62)	99.0 (5,884)	
	2.6 (53)	97.4 (1,991)	
	3.8 (54)	96.2 (1,378)	
	6.3 (39)	93.7 (584)	
	12.3 (41)	87.7 (293)	

tages. Data in parentheses are numbers of patients.
tery disease.

Mortality Rate at 5 years

Newer Prospective Studies

- St. Francis Heart Study
- Rotterdam Study
- Prospective Army Coronary Calcium (PACC) Project
- Munich Study
- Cooper Clinic

St Francis Heart Study, 2005

- Prospective
- 4,903 patients aged 50-70, asymptomatic
- Mean followup 4.3 years (94%)
- 119 (2.4%) Atherosclerotic events
- "The electron beam CT coronary calcium score predicts CAD events independent of standard risk factors, more accurately than standard risk factors and CRP, and refines Framingham risk stratification."

Arad Y, Goodman KJ, Roth M, Newstein D, Guerci AD. Coronary calcification, coronary disease risk factors, C-reactive protein, and atherosclerotic cardiovascular disease events: the St. Francis Heart Study. J Am Coll Cardiol. 2005;46:158-65.

Table 1. Baseline Characteristics of Study Population

Age (yrs)*	59 ± 6
Women (%)*	35
Total cholestrol (mg/dl)	224 ± 33
LDL cholestrol (mg/dl)	143 ± 33
HDL cholestrol (mg/dl)	52 ± 15
Triglycerides (mg/dl)	141 ± 10
Hypertension (%)	34
Diabetes (%)	6
Current smokers (%)	10
Family history of premature CAD (%)	21
Body mass index	28 ± 5
C-reactive protein (mg/l)	1.84 (0.89,
Calcium score*	
All	10 (0, 105)
Men	30 (1, 174)
Women	0.5 (0, 20)

Table 2. Coronary Calcium Score and All Coronary Disease Events*

Score	n (Weighted)	Event Rate (%)	Relative Risk (95% CI)
0	1,504	0.54	1.0
1–99	1,973	1.00	1.9 (0.8–4.2)
100–399	686	5.5	10.2 (4.8–21.6)
≥400	450	14.0	26.2 (12.6–53.7)

*Includes coronary death, nonfatal myocardial infarction, coronary bypass surgery, and percutaneous coronary angioplasty (n = 4,613). Relative risk is based on comparison to subjects with calcium scores of zero. Analysis of unweighted sample yielded similar results, with relative risks of 1.0, 1.9, 10.3, and 26.9, respectively, for the different strata of calcium scores.

CI = confidence interval.

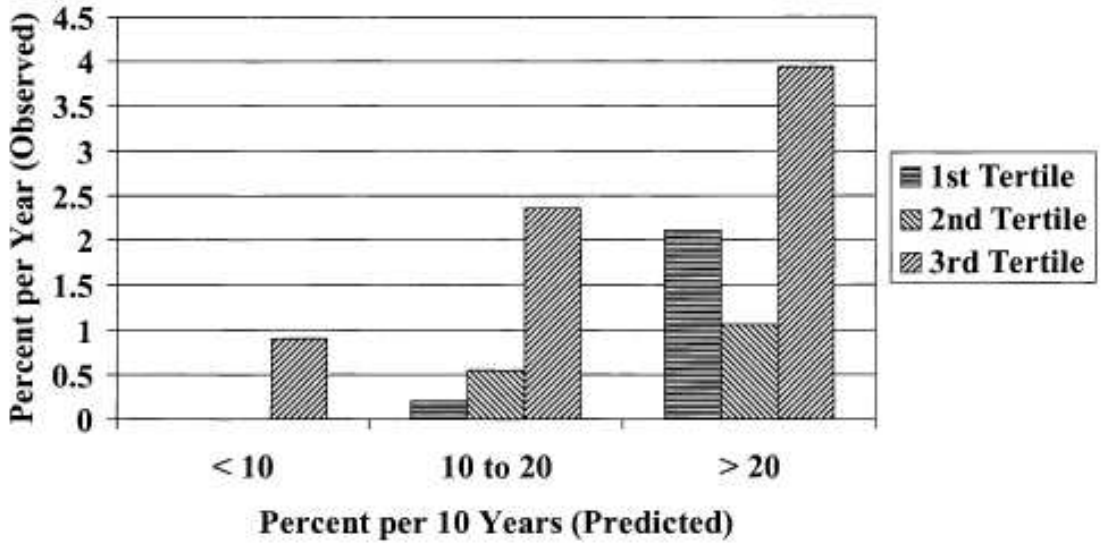


Figure 3. Coronary event rates as a function of calcium score within the Framingham risk groups (low: <10% per 10 years; intermediate: 10% to 20% per 10 years; and high: >20% per year). There were no coronary events in the first and second tertile of calcium scores in the Framingham low-risk group (n = 1,293).

Arad Y, Goodman KJ, Roth M, Newstein D, Guerci AD. Coronary calcification, coronary disease risk factors, C-reactive protein, and atherosclerotic cardiovascular disease events: the St. Francis Heart Study. J Am Coll Cardiol 2005;46:158-65.

Rotterdam Study, 2005

- Prospective
- 1795 asymptomatic participants
  - mean age 71 years (62-85)
- Mean 3.3 year followup
- 88 cardiovascular events (4.9%)
- “Coronary calcification is a strong and independent predictor of coronary heart disease, also in the elderly”

Vliegenthart R, Oudkerk M, Hofman A, et al. Coronary calcification improves cardiovascular risk prediction in the elderly. Circulation 2005;112:572-7.

Baseline Characteristics of the Study Population (n=1795)

Variable	Mean or Percentage'
Age, y	71.1±5.7
Male	42.5
Body mass index, kg/m2	27.0±4.0
Hypertension	59.8
Total cholesterol, mmol/L	5.9±0.9
HDL cholesterol, mmol/L	1.4±0.4
Smokers	
Current	16.4
Past	52.3
Diabetes mellitus	12.3
History of stroke	2.8
Family history of myocardial infarction	18.7
Calcium score^	98 (10. 430)
Time between risk factor assessment and EBT scanning, dt	49 130, 112)

'Categorical variables are expressed as percentage.
Values of continuous variables are expressed as mean (SD).

^Median (25th. 75th percentiles) are reported because of skewed distribution.

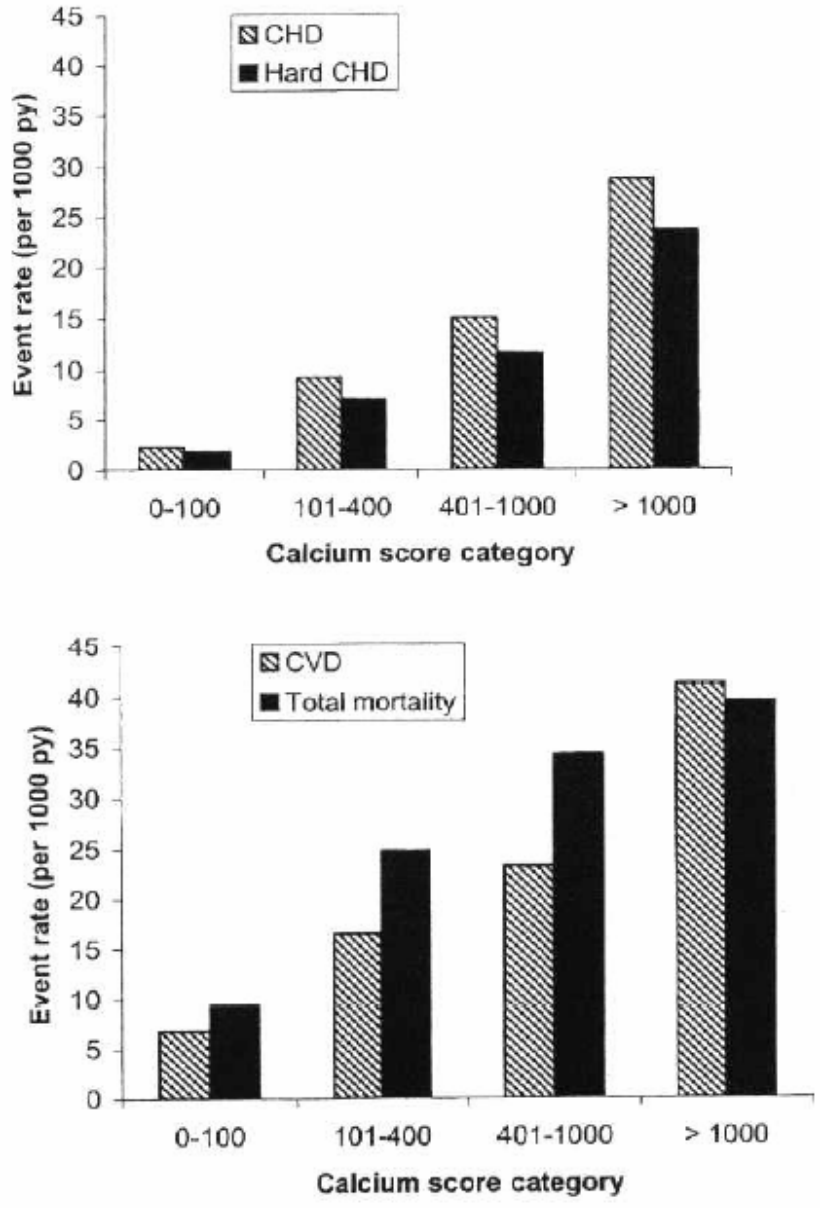


Figure 2. Event rates according to calcium score category.

Vliegenthart R, Oudkerk M, Hofman A, et al. Coronary calcification improves cardiovascular risk prediction in the elderly. Circulation 2005;112:572-7.

Relative Risks of Events According to Calcium Score Category					
		Relative Risk (95% CI)			
Calcium Score	Total/Events,	Age and	Multivariate		
	n	Sex Adjusted	Adjusfed*	Event rate	Annual rate
CHD					
0-100	905/7	1.0 (Reference)	1.0 (Reference)	0.8%	0.2%
101-400	425/13	3.2 (1.3-8.2)	3.1 (1.2-7.9)	3.1%	0.9%
401-1000	269/13	4.7 (1.8-12.0)	4.6 (1.8-11.8)	4.8%	1.5%
>1000	196/17	8.2 (3.3-20.5)	8.3(3.3-21.1)	8.7%	2.6%
Hard CHD					
0-100	905/6	1.0 (Reference)	1.0 (Reference)	0.7%	0.2%
101-400	425/10	2.8 (1.0-7.8)	2.7 (1.0-7.7)	2.4%	0.7%
401-1000	269/10	3.9(1.4-11.1)	4.1 (1.4-11.6)	3.7%	1.1%
>1000	196/14	7.5 (2.8-20.2)	8.1 (2.9-22.3)	7.1%	2.2%
CVD					
0-100	905/21	1.0 (Reference)	1.0 (Reference)	2.3%	0.7%
101-400	425/23	2.0 (1.1-3.6)	1.9 (1.0-3.4)	5.4%	1.6%
401-1000	269/20	2.5 (1.4-4.81	2.4 (1.3-4.5)	7.4%	2.3%
>1000	196/24	4.3 (2.3-7.9)	3.9 (2.1-7.3)	12.2%	3.7%
Total mortality					
0-100	905/29	1.0 (Reference)	1.0 (Reference)	3.2%	1.0%
101-400	425/35	1.9 (1.2-3.2)	2.0 (1.2-3.3)	8.2%	2.5%
401-1000	269/30	2.4 (1.4-4.2)	2.4 (1.4-4.2)	11.2%	3.4%
>1000	196/24	2.7 (1.5-4.7)	2.7 (1.5-4.9)	12.2%	3.7%
*Additionally adjusted for body mass index, hypertension, total cholesterol,					
HDL cholesterol, smoking, diabetes mellitus, and family history of MI					

Vliegenthart R, Oudkerk M, Hofman A, et al. Coronary calcification improves cardiovascular risk prediction in the elderly. Circulation 2005;112:572-7.

Prospective Army Coronary Calcium (PACC) Project

- Prospective
- Non-referred healthy Men and Women, age 40-50 (mean 43)
- 2000 subjects
- Calcium in 22.4% of men, 7.9% of women
- mean 3 year followup (99.2%)
- 9 (0.5%) events, all in men

Taylor AJ, Bindeman J, Feuerstein I, Cao F, Brazaitis M, O'Malley PG. Coronary calcium independently predicts incident premature coronary heart disease over measured cardiovascular risk factors: mean three-year outcomes in the Prospective Army Coronary Calcium (PACC) project. J Am Coll Cardiol 2005;46:807-14

Table 2. The Distribution of CHD Events by Coronary Calcium, Framingham Risk Score Categories, and Family History of CHD

Variable	CHD Events		n
	Yes	No	
Coronary calcium			
Present	7	357	364
Absent	2	1,261	1,263
Coronary calcium score tertiles			
CAC score = 1–9	0	120	120
CAC score = 10–44	2	118	120
CAC score ≥45	5	119	124
Framingham risk score			
<6%	4	1,233	1,237
6%–10%	5	311	316
>10%	0	72	72
Family history of CHD			
No family history	4	1,093	1,097
With either 1st- or 2nd-degree family history	2	411	413
With both 1st- and 2nd-degree family history	3	94	97

2/1263 = 0.1%

5/124 = 4%

4/1237 = 0.3%

5/316 = 1.6%

Sudden cardiac death, Myocardial infarction, Unstable Angina

* Revascularization/Stable Angina excluded

Taylor AJ, Bindeman J, Feuerstein I, Cao F, Brazaitis M, O'Malley PG. Coronary calcium independently predicts incident premature coronary heart disease over measured cardiovascular risk factors: mean three-year outcomes in the Prospective Army Coronary Calcium (PACC) project. J Am Coll Cardiol 2005;46:807-14

Munich Study

- Prospective
- 924 patients
  - 443 men, 481 women
  - age 59.4 +/- 18.7 years
  - Had CAC score after cath showed no atherosclerosis
- 36 month followup
- Patients above 75th percentile vs total group
  - Revascularization rate
    - 5.4%/year vs 2.9%year
  - Myocardial infarction
    - 3.8%/year vs 1.8%/year
- Calcium scores in patients with revascularization (397 +/- 187), myocardial infarction (412 +/- 176), and cardiac death (422 +/- 184) were significantly higher compared to patients without cardiovascular events (218 +/- 167).
- Calcium score of 0 = no events

Becker A, Knez A, Becker C, et al. Prediction of serious cardiovascular events by determining coronary artery calcification measured by multi-slice computed tomography. Dtsch Med Wochenschr 2005;130:2433-8

Cooper Clinic Study

- 10,746 subjects
  - 22-96 years of age
  - free of known CHD
- Mean followup 3.5 years
- 81 hard events (CHD death, nonfatal myocardial infarction) and 287 total events (hard events plus coronary revascularization)
- “CAC is associated with an increased risk of CHD events in asymptomatic women and men”

LaMonte MJ, FitzGerald SJ, Church TS, et al. Coronary artery calcium score and coronary heart disease events in a large cohort of asymptomatic men and women. Am J Epidemiol 2005;162:421-9.

TABLE 1. Baseline characteristics of study participants by sex and coronary heart disease event status, Aerobics Center Longitudinal Study (Dallas, Texas), 1995–2000

	Men		Women	
	Event free ($n = 6,597$)	CHD† event ($n = 238$)	Event free ($n = 3,862$)	CHD event ($n = 49$)
Age (years)‡	53.3 (10.0)	60.1 (9.7)*	54.1 (9.7)	64.1 (9.1)*
Coronary artery calcium score‡	222.4 (668.4)	1,017.7 (1,133.8)	51.3 (229.1)	619.3 (1,085.2)
Median (IQR†)	7 (138)	634.5 (1,259)*	0 (2)	111 (833)*
High cholesterol (%)	27.6	39.9*	30.5	59.2*
High blood pressure (%)	17.8	27.7*	15.9	46.9*
Diabetes (%)	2.9	10.1*	2.9	24.5*
Current smoker (%)	10.3	13.0	6.7	8.2
CHD death or nonfatal MI† (%)		26.1		38.8

* $p \leq 0.01$ with same-sex, event-free individuals.
† CHD, coronary heart disease; IQR, interquartile range; MI, myocardial infarction.
‡ Data are expressed as mean (standard deviation).

LaMonte MJ, FitzGerald SJ, Church TS, et al. Coronary artery calcium score and coronary heart disease events in a large cohort of asymptomatic men and women. Am J Epidemiol 2005;162:421-9.

TABLE 3. Risk of coronary heart disease events according to categories of no detectable calcium and sex-specific thirds of coronary artery calcium, Aerobics Center Longitudinal Study (Dallas, Texas), 1995–2000

Coronary artery calcium score	No.	Person-years	Hard events*					All events†				
			No.	HR‡,§	95% CI‡	HR¶	95% CI	No.	HR§	95% CI	HR¶	95% CI
Men												
0	2,692	8,922	3					5	1.0		1.0	
1–38	1,381	4,968	6				0.8, 13.4	14	5.1	1.9, 14.3	5.0	1.8, 13.8
39–249	1,382	4,856	19				3.0, 35.4	52	19.5	7.7, 49.3	18.5	7.3, 46.6
≥250	1,380	4,544	34				5.1, 61.8	167	67.0	26.9, 166.7	61.7	24.7, 153.7
p linear trend				<0.0001		<0.0001			<0.0001		<0.0001	
Women												
0	2,780	9,910	4	1.0		1.0		10	1.0		1.0	
1–16	379	1,414	3	3.3	0.7, 15.3	2.2	0.5, 10.1	5	2.6	0.9, 7.8	1.8	0.6, 5.5
17–112	376	1,384	5	4.6	1.2, 18.4	3.9	1.0, 15.2	10	4.7	1.9, 11.8	3.7	1.5, 9.2
≥113	376	1,328	7	9.3	1.2, 18.9	7.2	0.8, 12.5	24	9.3	4.1, 21.6	6.2	2.7, 14.4
p linear trend				<0.0001		<0.0001			<0.0001		<0.0001	

3/2692 = 0.1%
6/1381 = 0.4%
19/1382 = 1.4%
34/1380 = 2.5%

* Coronary heart disease death, nonfatal myocardial infarction.
† Hard events plus coronary revascularization.
‡ HR, hazard ratio; CI, confidence interval.
§ Adjusted for age.
¶ Adjusted for age, smoking, high cholesterol, high blood pressure, and diabetes.

LaMonte MJ, FitzGerald SJ, Church TS, et al. Coronary artery calcium score and coronary heart disease events in a large cohort of asymptomatic men and women. Am J Epidemiol 2005;162:421-9.

2004 Meta-Analysis

Table 1. Articles Presenting Data on Coronary Heart Disease Outcomes and CAC Scores

Source	Inclusion Criteria					
	Is This the Definitive Data Presentation?*	Patients Asymptomatic?†	Patients Followed up Prospectively After EBCT Scan?	Multivariate Adjustment Attempted?	CAC Score–Specific Risk Extractable?‡	Included in Meta-analysis?
Arad et al,[15] 1996	No (Arad et al,[10] 2000)	Yes	Yes	No	Yes	No
Secci et al,[16] 1997	No (Yang et al,[11] 1999)	Yes	Yes	Yes	Yes	No
Detrano et al,[17] 1999	No (Yang et al,[11] 1999)	Yes	Yes	Yes	Yes	No
Doherty et al,[5] 1999	No (Yang et al,[11] 1999)	Yes	Yes	No	Yes	No
Yang et al,[11] 1999	Yes	Yes	Yes	Yes	Yes	Yes
Arad et al,[10] 2000	Yes	Yes	Yes	Yes	Yes	Yes
Raggi et al,[9] 2000	No (Raggi et al,[12] 2001)	Yes	Yes	Crude	Yes	No
Wong et al,[7] 2000	Yes	Yes	Yes	Yes	Yes	Yes
Raggi et al,[12] 2001	Yes	Yes	Yes	Yes	Yes	Yes
Wayhs et al,[18] 2002	No (Raggi et al,[12] 2001)	Yes	Yes	No	No	No
Wong et al,[19] 2002	No (Wong et al,[7] 2000)	Yes	Yes	Yes	Yes	No
Park et al,[20] 2002	No (Yang et al,[11] 1999)	Yes	Yes	Yes	Yes	No
Vliegenthart et al,[21] 2002	Yes	Yes	No§	Yes	Yes	No

Abbrevations: CAC, coronary artery calcium; EBCT, electron beam computed tomography.

*If data from the same subjects were presented in a subsequent article in a more complete form, the article was not considered the definitive data presentation. The article thought to contain the definitive data presentation is listed in parentheses.

†If patients were noted to be symptomatic or also received a coronary angiogram or stress test (and were not specifically noted to be asymptomatic), the patients in the article were determined to be symptomatic and the article was not included in the meta-analysis.

‡If the distributions of events and total persons were reported for specific CAC scores or CAC score–specific risk estimates were reported in any way, the article was determined to have an "extractable" score-specific risk.

§This is a cross-sectional study. Persons in the sample who had had a heart attack in the past (before their EBCT scan) were compared with persons who had not had an attack. There was no follow-up after EBCT scanning presented, so this study was found to be ineligible.

Pletcher MJ, Tice JA, Pignone M, Browner WS. Using the coronary artery calcium score to predict coronary heart disease events: a systematic review and meta-analysis. Arch Intern Med 2004;164:1285-92.

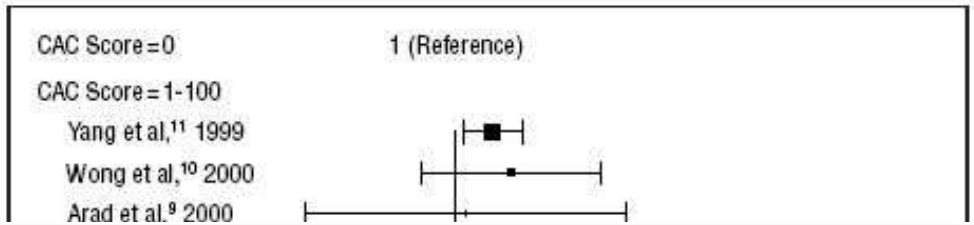


Table 4. Sensitivity Analysis: Summary Adjusted Odds Ratios for Each CAC Score Category Under Different Assumptions

Assumption	Summary Adjusted Odds Ratio (95% CI) in Given CAC Score Category*		
	1-100	101-400	>400
CAC distribution used for calculation of median scores in each category			
40-year-old man	2.2 (1.2-4.0)	6.1 (2.1-17)	11 (3.1-36)
50-year-old man†	2.1 (1.6-2.9)	5.4 (2.2-13)	10 (3.1-34)
60-year-old man	1.8 (1.4-2.3)	4.1 (2.3-7.3)	9.4 (3.1-29)
40-year-old woman	2.2 (1.0-4.7)	6.4 (2.3-18)	11 (3.1-36)
50-year-old woman	2.2 (1.2-4.0)	6.0 (2.1-17)	11 (3.1-36)
60-year-old woman	2.0 (1.5-2.7)	5.3 (2.3-13)	10 (3.1-34)
Maximum CAC score used for extrapolation in highest CAC score category			
600	2.1 (1.6-2.9)	5.5 (2.3-14)	10 (2.9-36)
1000†	2.1 (1.6-2.9)	5.4 (2.2-13)	10 (3.1-34)
2000	2.1 (1.6-2.9)	5.4 (2.2-13)	11 (3.3-33)
4000	2.1 (1.6-2.9)	5.3 (2.2-13)	11 (3.6-32)
Meta-analytic model			
Fixed effects	2.1 (1.6-2.9)	4.2 (2.5-7.2)	7.2 (3.9-13)
Random effects†	2.1 (1.6-2.9)	5.4 (2.2-13)	10 (3.1-34)

Abbreviations: CAC, coronary artery calcium; CI, confidence interval.
*Compared with a CAC score of 0.
†Assumption used in primary analysis.

disease event in persons with low (1-100), medium (101-400), and high (>400) coronary artery calcium (CAC) scores to persons without calcification. Error bars indicate 95% confidence interval (CI).

Pletcher MJ, Tice JA, Pignone M, Browner WS. Using the coronary artery calcium score to predict coronary heart disease events: a systematic review and meta-analysis. Arch Intern Med 2004;164:1285-92.

Negative Trials and Opinions

- Calcium score does not add to Framingham risk
- Calcium is a surrogate marker
- Vulnerable plaques not identified
- Calcium does not correlate with stenosis
- Trial criticisms
- Calcium score does not change treatment
- Outcomes cannot be changed

Detrano et al, 1999

- 1196 Asymptomatic, high risk patients
- 41 month followup (99%)
- mean age 66 years
- mean 3-year Framingham risk was 3.3 +/- 3.6%
- 818 (68%) had coronary calcium
- 17 coronary deaths (1.4%)
- 29 nonfatal infarctions (2.4%)

- ROC curve areas of Framingham model, data-derived model, and caclium score were similar (0.65-0.69, p = NS)
- “Neither risk-factor assessment nor EBCT calcium is an accurate event predictor in high-risk asymptomatic adults. EBCT calcium score does not add significant incremental information to risk factors, and its use in clinical screening is not justified at this time.”

Detrano RC, Wong ND, Doherty TM, Shavelle RM, Tang W, Ginzton LE, Budoff MJ, Narahara KA. Coronary calcium does not accurately predict near-term future coronary events in high-risk adults. Circulation 1999;99:2633-2638.

Calcium is a surrogate marker

- Value of a marker is to predict an event that could be prevented
  - Hormone replacement therapy showed benefit using surrogate markers (LDL, HDL, fibrinogen, coronary calcium)
- Coronary artery calcification is present in 10-100 times more people than those who have clinical heart disease[1]

1 Wexler L, Brundage B, Crouse J, Detrano R, Fuster V, Maddahi J, Rumberger J, Stanford W, White R, Taubert K. Coronary artery calcification: pathophysiology, epidemiology, imaging methods, and clinical implications. A statement for health professionals from the American Heart Association Writing Group. Circulation. 1996 Sep 1;94(5):1175-92.

Calcium score does not predict stenosis

- Meta-analysis of 16 studies totaling 3683 patients
  - no known CAD
  - cardiac catheterization performed
- Sensitivity 90.5% and specificity 49.2% for angiographic lesions
- Definition of “clinically significant” CAD varied across studies
  - Luminal irregularities in 2 studies
  - 50% stenosis in 11 studies
  - 70% or 75% stenosis in 3 studies
- Definition of an abnormal EBCT also varied
  - 8 studies using a calcium score 0
  - 7 studies using a score from 0 to 5
  - 1 study using a score 100.

O’Rourke RA, Brundage BH, Froelicher VF, Greenland P, Grundy SM, Hachamovitch R, Pohost GM, Shaw LJ, Weintraub WS, Winters WL Jr, Forrester JS, Douglas PS, Faxon DP, Fisher JD, Gregoratos G, Hochman JS, Hutter AM Jr, Kaul S, Wolk MJ. American College of Cardiology/American Heart Association Expert Consensus document on electron-beam computed tomography for the diagnosis and prognosis of coronary artery disease. Circulation. 2000;102:126 –140.

TABLE 1. Sensitivity and Specificity of Stress Testing and EBCT for Angiographic CAD

Type of Stress Testing	Studies, n	Patients, n	Sensitivity, %	Specificity, %
Meta-analysis of standard stress ECG testing	147	24 047	68	77
Excluding MI patients	41	11 691	67	74
Perfusion scintigraphy	2	28 751	89	80
Exercise echocardiography	58	5000	85	79
Nonexercise stress tests				
Pharmacological stress scintigraphy	11	<1000	85	91
Dobutamine echocardiography	5	<1000	88	84
EBCT (from O'Rourke et al[23])	16	3683	91	49
EBCT (from Nallamothu et al[24])	9	1662	92	51

Adapted from O'Rourke et al.[23]

Chen J, Krumholz HM. How useful is computed tomography for screening for coronary artery disease? Screening for coronary artery disease with electron-beam computed tomography is not useful. Circulation. 2006 Jan 3;113(1):125-46

Criticisms of trials

TABLE 2. Studies of EBCT and CAD Events in Asymptomatic Patients

Study	Subjects, n	Mean+SD Age, y	Male, %	Nonwhite, %	Follow-Up, mo (%)*	Events	Annual Event Rate† (Nonfatal MI and CAD Death), %	Coronary Artery Calcium		Risk Factors
								Definition	Prevalence	
Arad et al[33] (follow-up of Arad et al[37])	1172	53+11	71	5	43 (99.6)	CAD death, 3; MI, 15; Revasc, 21	0.4	>0	~50% from Arad et al[37]	Pt reported
Detrano et al[36]	1196	66+8	89	12	41 (99)	CAD death, 17; MI, 29; Revasc, 42	1.1	>0	~67	Measured
Wong et al[34]	926	54+10	79	NR	(61)	Death, 0; MI, 6; CVA, 2; Revasc, 20	0.2	>0	57	Pt reported
Raggi et al[41] (follow-up of Raggi et al[35])	676	52+10	51	NR	32(NR)	CAD death, 9; MI, 21	1.7	>0	53	Pt reported
Kondros et al[38]	5635	50+9	74	5	37 (64)	CAD death, 21; MI, 37; Revasc, 66	0.3	>0	74 men, 51 women	Pt reported
Shaw et al[39]	10 377	53+0.10	60	NR	60 (100)	All-cause death, 249	0.5 (All-cause death)	≥11	43	Pt reported
Greenland et al[40] (subset of Detrano et al[36])	1029	66+8	90	15	76 (87.5)	CAD death, 16; MI, 68	0.7	>100	50	Measured
Vliegenhart et al[69]	1795	71+6	43	NR	40 (99)	CAD death or MI, 40; Revasc, 11; CVA, 38	0.2	>0	63	Pt report and measured
Arad et al[89]	4903	59+6	65	12%	52 (94)	CAD death or MI, 40; Revasc, 59; CVA, 7	0.2	>0	49	Pt reported
LaMonte et al[90]	10 746	54+10	64	<3%	42 (67)	CAD death, 19; MI, 62; Revasc, 206	0.7	>100	50	Measured

Adapted from Pletcher et al.[37]

*Average follow-up: duration (rate).

†Annual event rate: events/person-year.

NR indicates not reported; Revasc, revascularization; Pt, patient; and CVA, cerebral vascular accident.

Chen J, Krumholz HM. How useful is computed tomography for screening for coronary artery disease? Screening for coronary artery disease with electron-beam computed tomography is not useful. Circulation. 2006 Jan 3;113(1):125-46

Would Calcium score change risk?

- High Framingham risk score with Calcium score of 0[1]
  - 7-year event rate of 9.3% (7 events in 75 patients)
- 4 of 23 patients (17.4%) who underwent revascularization had calcium scores of 0[2]
- Theoretical Bayesian argument – a low pre-test probability with a positive test results in a low post-test probability[3]

1 Greenland P, LaBree L, Azen SP, Doherty TM, Detrano RC. Coronary artery calcium score combined with Framingham score for risk prediction in asymptomatic individuals. JAMA. 2004;291:210 –215.
2 Wong ND, Hsu JC, Detrano RC, Diamond G, Eisenberg H, Gardin JM. Coronary artery calcium evaluation by electron beam computed tomography and its relation to new cardiovascular events. Am J Cardiol. 2000;86:495– 498.
3 Greenland P, Gaziano JM. Clinical practice: selecting asymptomatic patients for coronary computed tomography or electrocardiographic exercise testing. N Engl J Med. 2003;349:465– 473.

Do Statins Affect Coronary Calcium?

- Intensive (80mg) vs conventional (10mg) atorvastatin daily x 12 months
- 471 patients (age 61+/-8 years)
  - no history of coronary artery disease
  - no evidence of high-grade coronary stenoses (>50% diameter reduction)
  - >=2 cardiovascular risk factors
  - CAC score >=30
- Progression evaluated in 366 patients (78%)
- 80mg statin lowered LDL: 106+/-22 to 87+/-33 mg/dL
- 10mg statin did not lower LDL: 108+/-23 to 109+/-28
- Mean CAC volume progression 27% (80mg) and 25% (10mg)

Schmermund A, Achenbach S, Budde T, Buziashvili Y, Forster A, Friedrich G, Henein M, Kerkhoff G, Knollmann F, Kukharchuk V, Lahiri A, Leischik R, Moshage W, Schartl M, Siffert W, Steinhagen-Thiessen E, Sinitsyn V, Vogt A, Wiedeking B, Erbel R. Effect of intensive versus standard lipid-lowering treatment with atorvastatin on the progression of calcified coronary atherosclerosis over 12 months: a multicenter, randomized, double-blind trial. Circulation. 2006 Jan 24;113(3):427-37. Epub 2006 Jan 16.

BELLES trial

- 615 postmenopausal hyperlipidemic women
- Atorvastatin 80 qd vs pravastatin 40 qd
- 475 completed study (77%)
- Calcium score at start and at mean 344 +/- 55 days
- Results
  - LDL reduced 46.6%+/-19.9% and 24.5%+/-18.5 (P<0.0001)
  - ATP III LDL goal reached in 85.3% and 58.8% (P<0.0001)
  - Calcium Volume Score (CVS)% change was similar in the 2 treatment groups (median 15.1% and 14.3%; P=NS)
  - Single-artery CVS% changes and absolute changes were also similar (P=NS)

Raggi P, Davidson M, Callister TQ, Welty FK, Bachmann GA, Hecht H, Rumberger JA. Aggressive versus moderate lipid-lowering therapy in hypercholesterolemic postmenopausal women: Beyond Endorsed Lipid Lowering with EBT Scanning (BELLES). Circulation. 2005 Jul 26;112(4):563-71.

Do Statins Affect Outcomes?
St. Francis Treatment Arm

- Double-blind, placebo-controlled randomized clinical trial
- 1,005 asymptomatic, apparently healthy men and women age 50 to 70 years with CCSs >= 80th percentile for age and gender
  - Atorvastatin 20 mg daily, vitamin C 1 g daily, and vitamin E (alpha-tocopherol) 1,000 U daily versus matching placebos
  - All subjects received aspirin 81 mg daily
- Mean duration of treatment was 4.3 years.
- Randomization was stratified by gender, age, ratio of low-density lipoprotein/high-density lipoprotein cholesterol (LDL/HDL-C), and the number of nonlipid risk factors.

Arad Y, Spadaro LA, Roth M, Newstein D, Guerci AD. Treatment of Asymptomatic Adults With Elevated Coronary Calcium Scores With Atorvastatin, Vitamin C, and Vitamin E: The St. Francis Heart Study Randomized Clinical Trial . *J Am Coll Cardiol.* 2005;46:166-172.

St. Francis Treatment Arm

- No differences in trial groups
  - Mean age 59 ± 6 years
  - 74% male
  - LDL-C 146 mg/dl
  - HDL-C 51 mg/dl
  - 12% smokers
  - 9% diabetics
  - mean CCS of about 530, median 375, and 25th, 75th percentile CCS 150, 671.
- Treatment
  - Reduced LDL-C by 39.1% to 43.4% ($p<0.0001$)
  - Reduced Triglycerides by 11.2% to 17.0% ($p\leq0.02$),
  - No effect ($p=0.80$) on progression of CCS
  - Mean increase in CCS at four years was about 330 ± 420 in each group
- No change in primary endpoint, a composite of all atherosclerotic cardiovascular disease (ASCVD) events (6.9% vs. 9.9%, $p=0.08$).
- Event rates were related to baseline calcium score
- May have reduced events in a subgroup with baseline calcium score >400 (8.7% vs. 15.0%, $p=0.046$ [not a prespecified analysis]).
- The CCS increased more from baseline in those who experienced ASCVD events.

Arad Y, Spadaro LA, Roth M, Newstein D, Guerci AD. Treatment of Asymptomatic Adults With Elevated Coronary Calcium Scores With Atorvastatin, Vitamin C, and Vitamin E: The St. Francis Heart Study Randomized Clinical Trial . *J Am Coll Cardiol.* 2005;46:166-172.

How to sum it all up?

- Large cohort population studies showing increased event rates with increasing coronary calcium
- Excellent negative predictive value
- Not likely to elevate risk of low-risk patients
- Not likely to lower risk of high-risk patients
- Most useful for intermediate risk, asymptomatic patients
- CAC score >400 should have a stress/perfusion test

What do the guidelines say? (ACC 2000)

- Guideline states the following:
  - A negative EBCT test makes the presence of atherosclerotic plaque, including unstable plaque, very unlikely.
  - A negative test is highly unlikely in the presence of significant luminal obstructive disease.
  - Negative tests occur in the majority of patients who have angiographically normal coronary arteries.
  - A negative test may be consistent with a low risk of a cardiovascular event in the next 2 to 5 years.
  - A positive EBCT confirms the presence of a coronary atherosclerotic plaque.
  - The greater the amount of calcium, the greater the likelihood of occlusive CAD, but there is not a 1-to-1 relationship, and findings may not be site specific.
  - The total amount of calcium correlates best with the total amount of atherosclerotic plaque, although the true "plaque burden" is underestimated.
  - A high calcium score may be consistent with moderate to high risk of a cardiovascular event within the next 2 to 5 years.

- But EBCT is not recommended due to lack of specificity (high false +) and lack of benefit over Framingham risk

O'Rourke RA, Brundage BH, Froelicher VF, Greenland P, Grundy SM, Hachamovitch R, Pohost GM, Shaw LJ, Weintraub WS, Winters WL Jr. American College of Cardiology/American Heart Association Expert Consensus Document on electron-beam computed tomography for the diagnosis and prognosis of coronary artery disease. J Am Coll Cardiol. 2000 Jul;36(1):326-40.

U.S. Preventive Services Task Force (2004)

- Recommends against routine screening with resting ECG, ETT, or EBCT for either the presence of severe coronary artery stenosis (CAS) or the prediction of coronary heart disease (CHD) events in adults at low risk for CHD events.
  - The USPSTF found at least fair evidence that ECG or ETT can detect some asymptomatic adults at increased risk for CHD events independent of conventional CHD risk factors, and that ETT can detect severe CAS in a small number of asymptomatic adults. Similar evidence for EBCT is limited. In the absence of evidence that such detection by ECG, ETT, or EBCT among adults at low risk for CHD events ultimately results in improved health outcomes, and because false-positive tests are likely to cause harm, including unnecessary invasive procedures, over-treatment, and labeling, the USPSTF concluded that the potential harms of routine screening for CHD in this population exceed the potential benefits.
- Insufficient evidence to recommend for or against routine screening with ECG, ETT, or EBCT scanning for coronary calcium for either the presence of severe CAS or the prediction of CHD events in adults at increased risk for CHD events.
  - The USPSTF found inadequate evidence to determine the extent to which the added detection offered by ECG, ETT, or EBCT (beyond that obtained by ascertainment of conventional CHD risk factors) would result in interventions that lead to improved CHD-related health outcomes among adults at increased risk for CHD events. Although there is limited evidence to determine the magnitude of harms from screening this population, harms from false-positive tests (i.e., unnecessary invasive procedures, over-treatment, and labeling) are likely to occur. As a result, the USPSTF could not determine the balance between benefits and harms of screening this population for CHD.

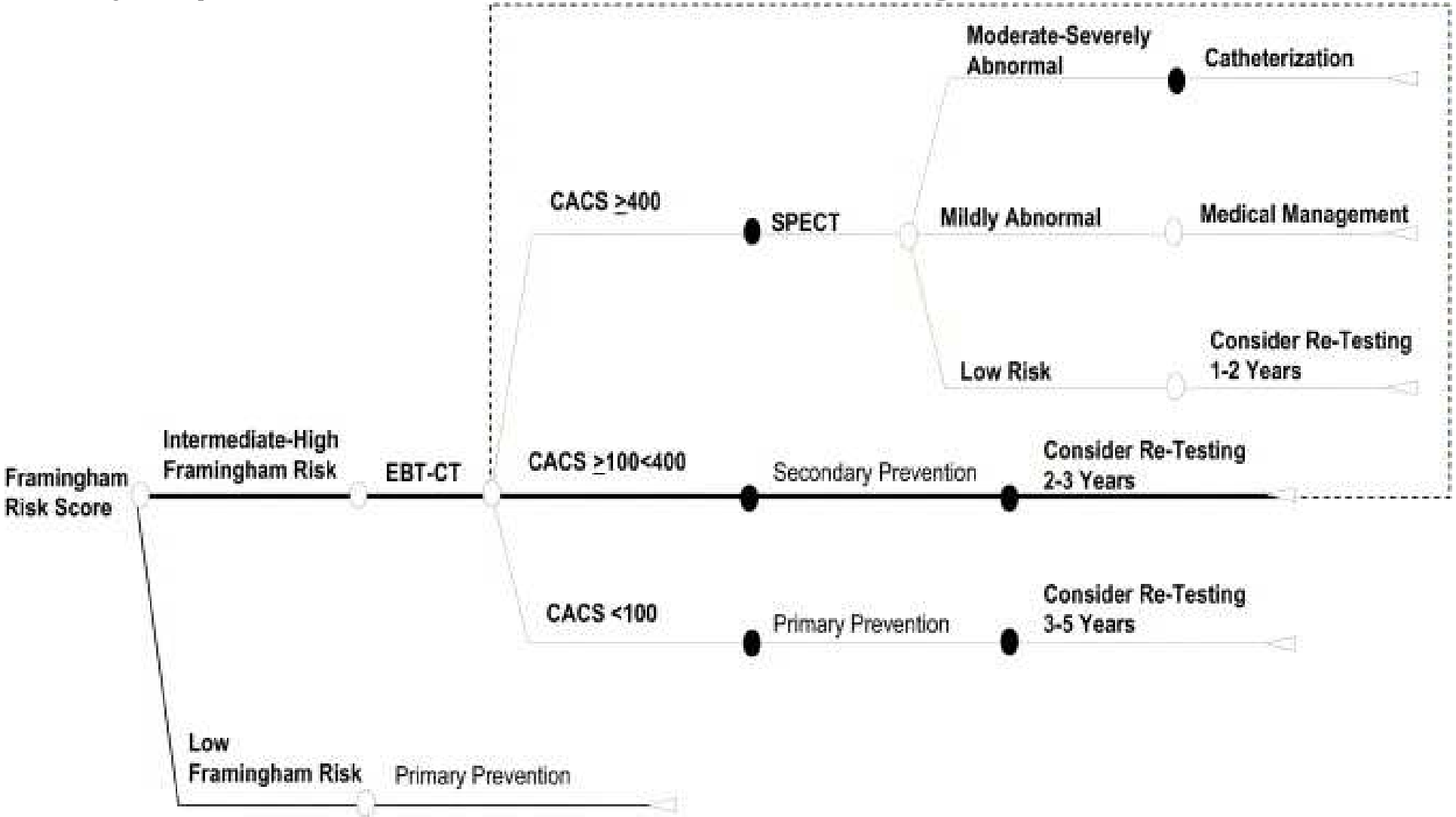
U.S. Preventive Services Task Force. Screening for coronary heart disease: recommendation statement.. Ann Intern Med. 2004 Apr 6;140(7):569-72.

Interpreting Calcium Score in Asymptomatic Patients

	Calcium Score	Annual coronary event rate
Low risk	0	0.12%
Mild risk	1-100	0.37%
Moderate risk	101-299 or 399	0.71%
High risk	>=300 or 400	1.56%

Shaw LJ, Taylor A, Raggi P, Berman DS. Role of noninvasive imaging in asymptomatic high-risk patients. J Nucl Cardiol. 2006 Mar-Apr;13(2):156-62.

Proposed Scheme for Evaluation of Asymptomatic **Intermediate-High Risk Patients**



Shaw LJ, Taylor A, Raggi P, Berman DS. Role of noninvasive imaging in asymptomatic high-risk patients. J Nucl Cardiol. 2006 Mar-Apr;13(2):156-62.

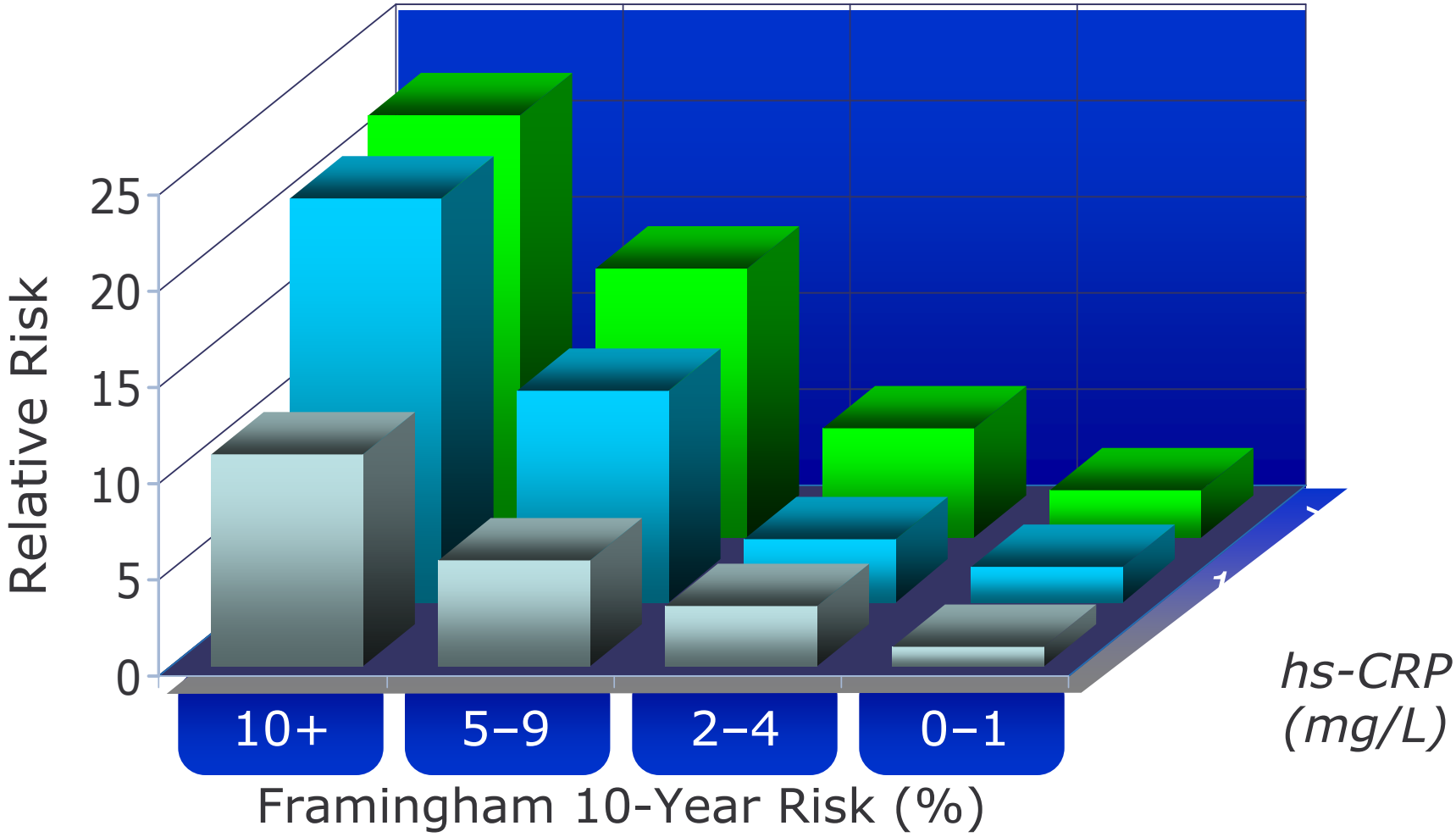
Dyslipidemias in Adults with Diabetes

Framingham Heart Study

	MEN		WOMEN	
	Normal	DM	Normal	DM
Increased cholesterol	14%	13%	21%	24%
Increased LDL	11%	9%	16%	15%
Decreased HDL	12%	21%	10%	25%
Increased triglycerides	9%	19%	8%	17%

Garg A et al. *Diabetes Care* 1990;13:153-169.

CRP Adds Prognostic Information at All Levels of Risk as Defined by the Framingham Risk Score



Ridker PM et al. *N Engl J Med* 2002;347:1557-1565.

All-Cause Mortality by Coronary Calcium Scores Determined with Electron-Beam Computed Tomography (CT)

	All-Cause Death (n = 249, 2.4%)	No Death (n= 10,128, 97.6%)	p
Calcium score			**<0.001**
≤10 (n = 5,946)	1.0% (62)	99.0% (5,884)	
11-100 (n = 2,044)	2.6% (53)	97.4% (1,991)	
101-400 (n = 1,432)	3.8% (54)	96.2% (1,378)	
401-1000 (n = 623)	6.3% (39)	93.7% (584)	
>1,000 (n = 332)	12.3% (41)	87.7% (293)	

Shaw LJ, Raggi P, Schisterman E, Berman DS, Callister TQ. Prognostic value of cardiac risk factors and coronary artery calcium screening for all-cause mortality. Radiology 2003;228:826-33.

Statistical Correlates of EBCT at Various Coronary Artery Calcium (CAC) Thresholds

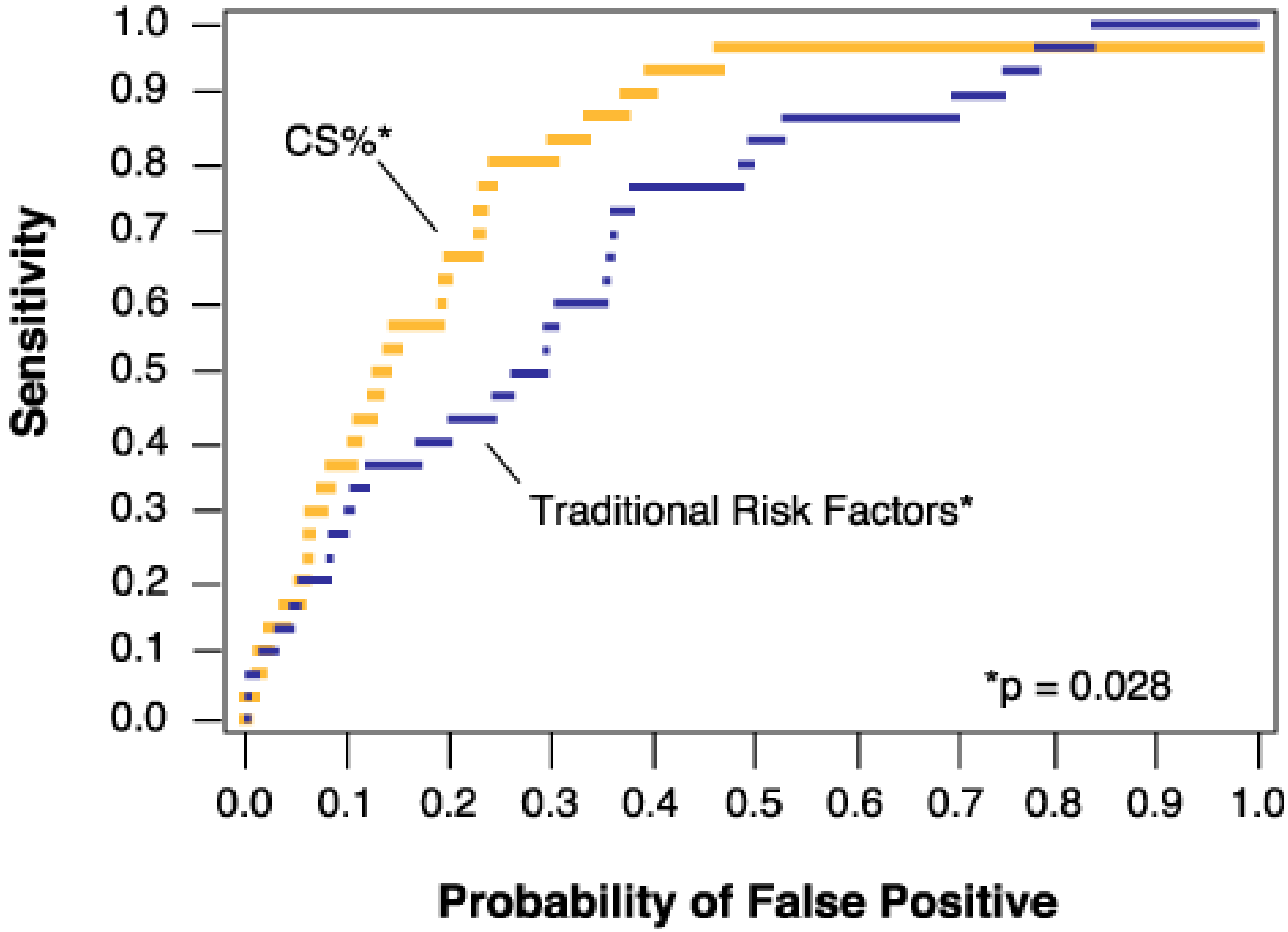
CAC Score Threshold	Sensitivity	Specificity	PPV	NPV	OR	95% CI	p
≥100	0.89	0.77	0.055	0.998	25.8	5.9-113	<0.00001
≥160	0.89	0.82	0.071	0.998	35.4	8.1-155	<0.00001
≥680	0.50	0.95	0.140	0.992	20.0	7.6-52	<0.00001

EBCT = Electron Beam Computed Tomography; PPV = Positive Predictive Value; NPV = Negative Predictive Value; OR = Odds Ratio; CI = Confidence Index

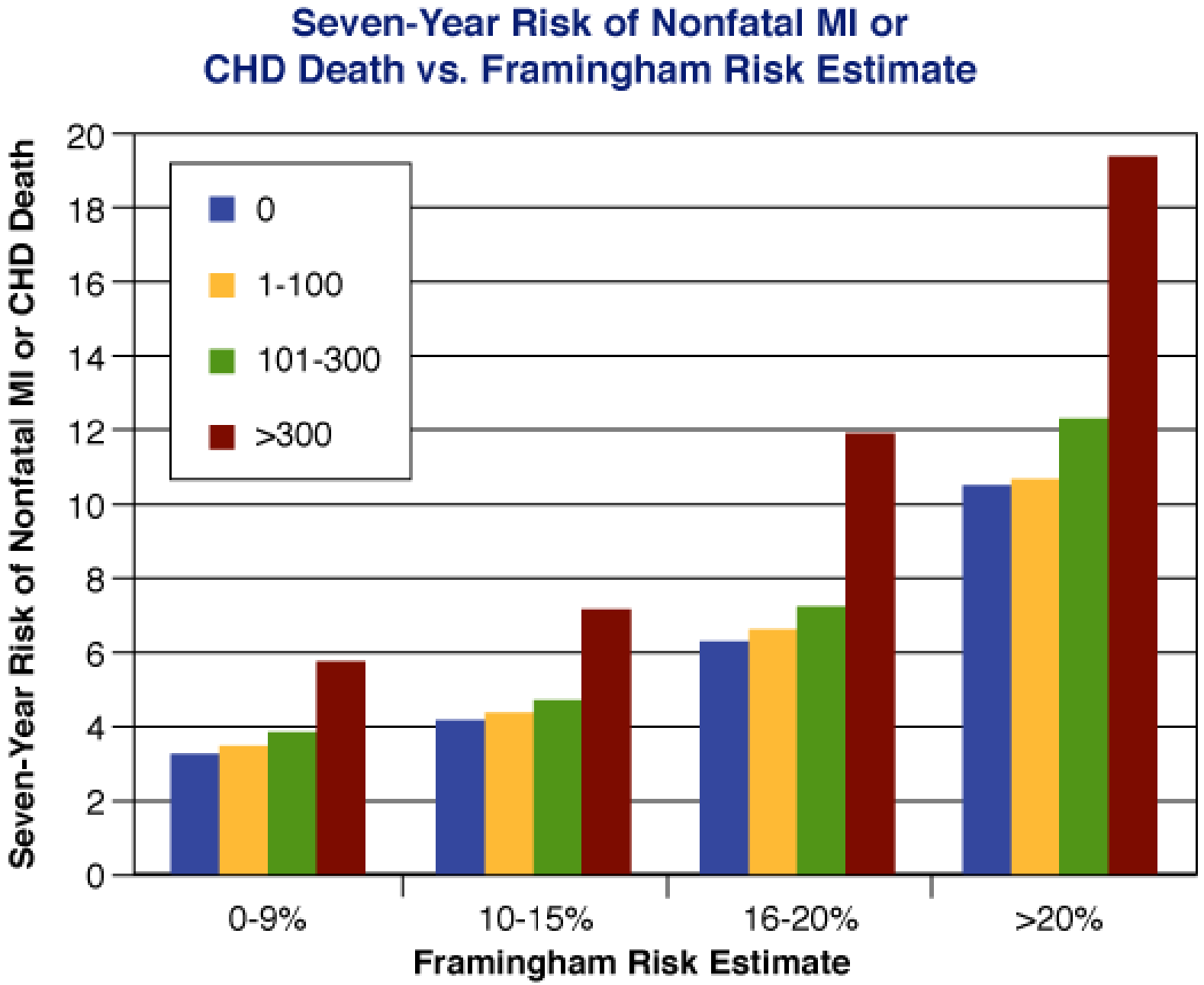
CAC Thresholds of 100 and 680 were previously found to correlate with worst stenosis of 20% and 50%, respectively, on quantitative coronary angiography. CAC of 160 represents the maximum of sensitivity plus specificity.

Arad Y, Spadaro LA, Goodman K. Predictive value of electron beam computed tomography of the coronary arteries. 19-month follow-up of 1173 asymptomatic subjects. Circulation 1996;93:1951-3.

Predictive Ability for Hard Events of Coronary Calcification and Risk Factors

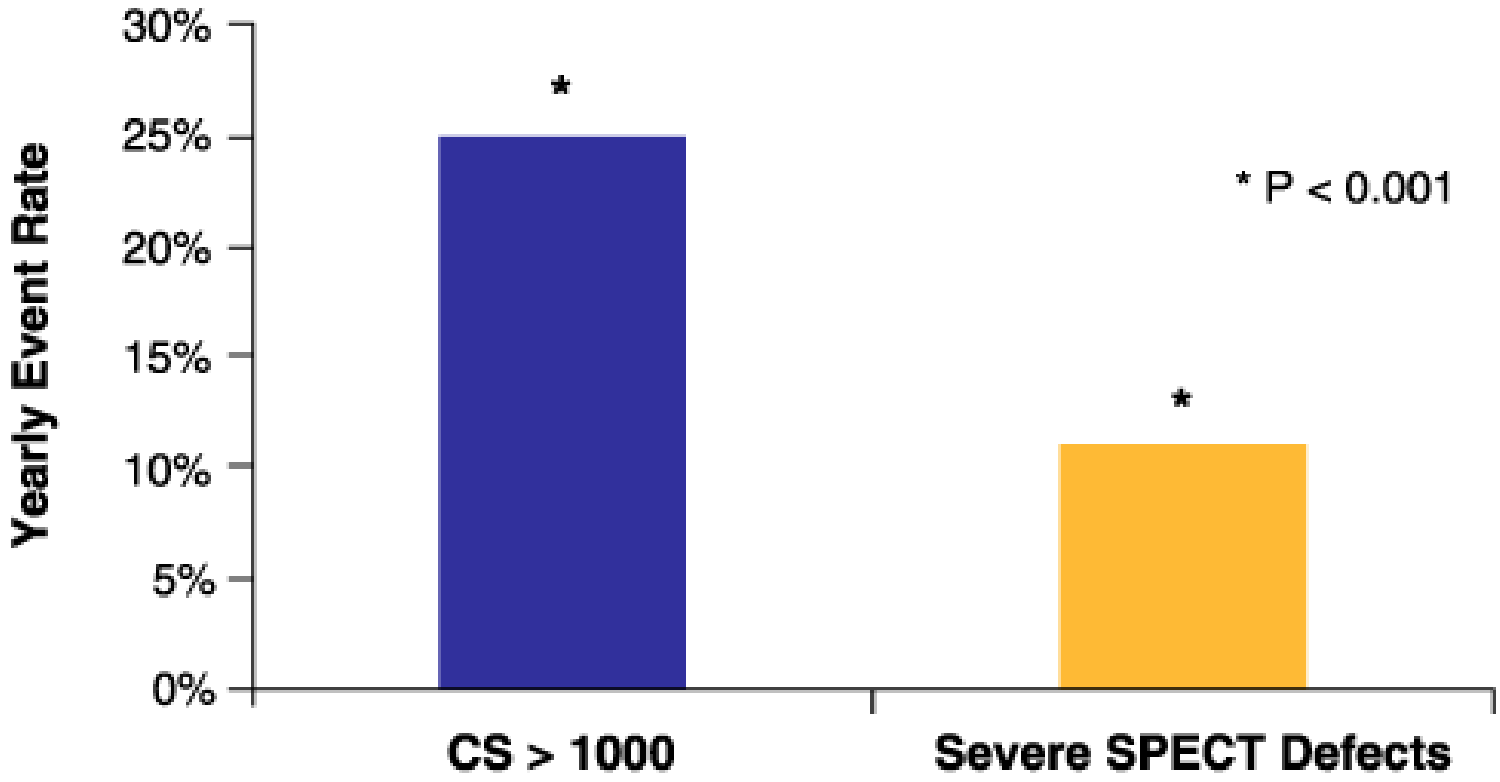


Raggi P, Cooil B, Callister TQ. Use of electron beam tomography data to develop models for prediction of hard coronary events. Am Heart J 2001;141:375-82



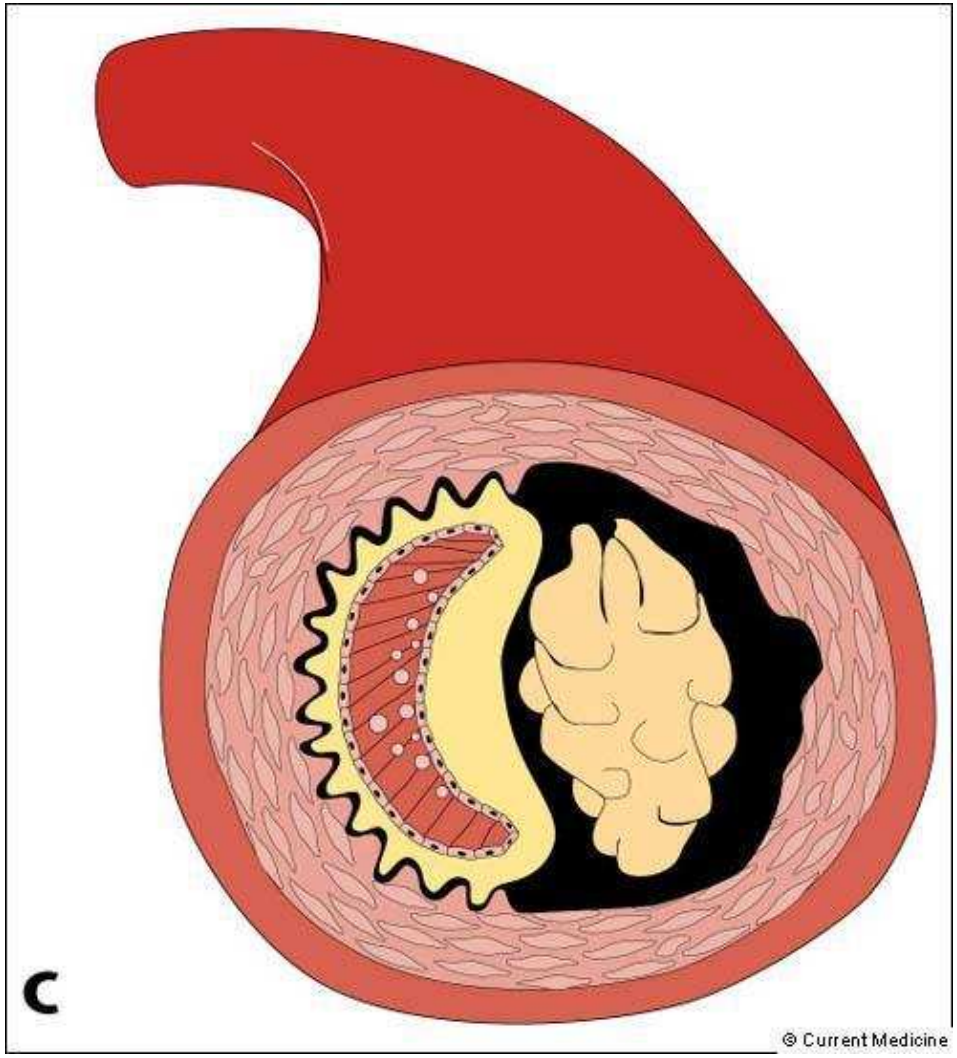
Greenland P, LaBree L, Azen SP, Doherty TM, Detrano RC. Coronary artery calcium score combined with Framingham score for risk prediction in asymptomatic individuals. JAMA 2004;291:210-15

Rate of MI and Death in Asymptomatic Patients with CS>1000 and Symptomatic Historical Controls



Wayhs R, Zelinger A, Raggi P. High coronary artery calcium scores pose an extremely elevated risk for hard events. J Am Coll Cardiol. 2001;39;225-230

The atherosclerotic process (C)



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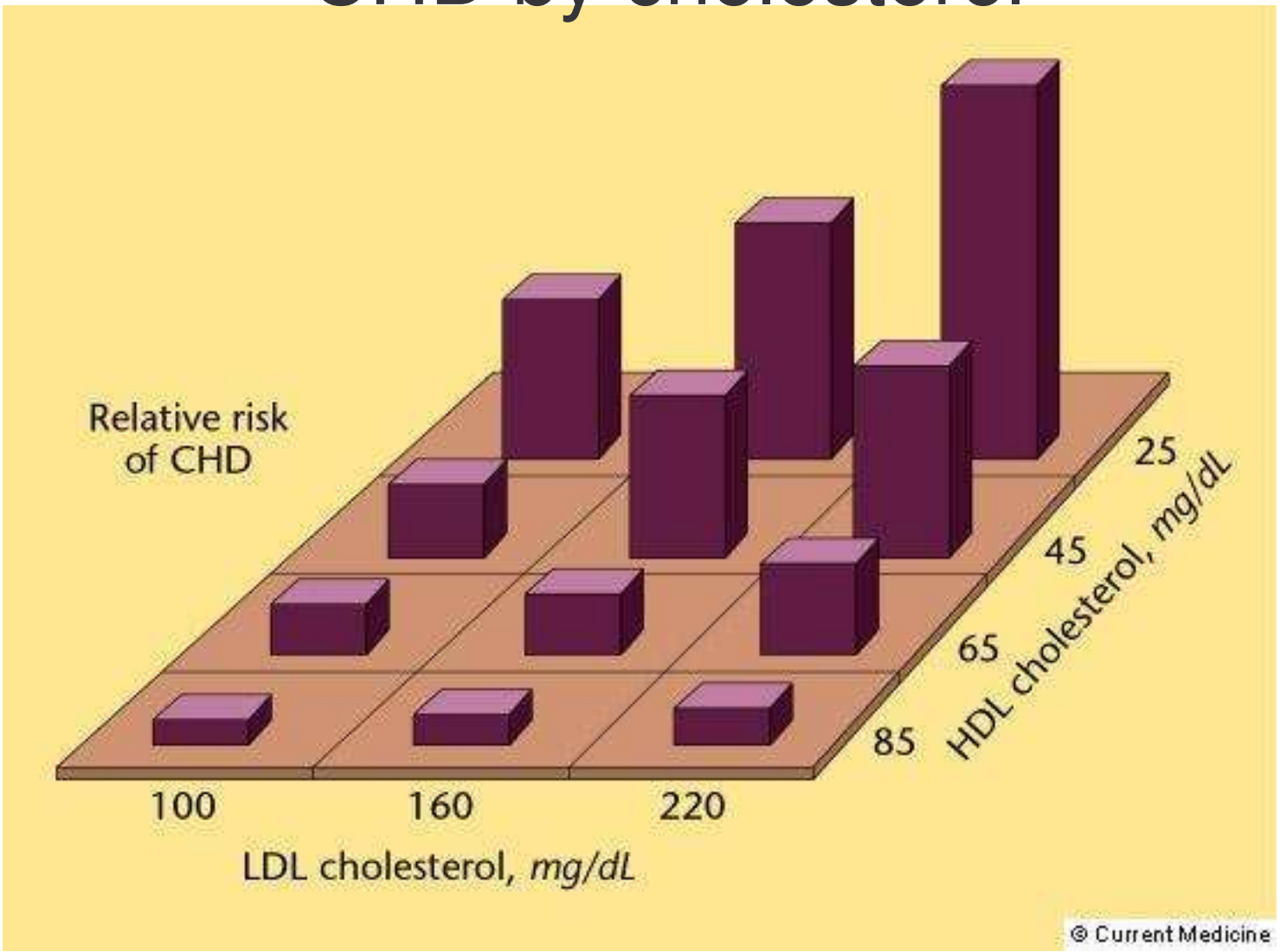
The Framingham Heart Study: risk of CHD by cholesterol



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