Assessment of CVS Risk

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Auckland City Hospital

& Auckland Heart Group:

Mercy Hospital

NZMA GP CME Conference, Rotorua 9-12 June 2011

Assessment of CVS Risk

1. It’s not easy!
2. Methods differ
3. [Suggest you]
   Do it this way!

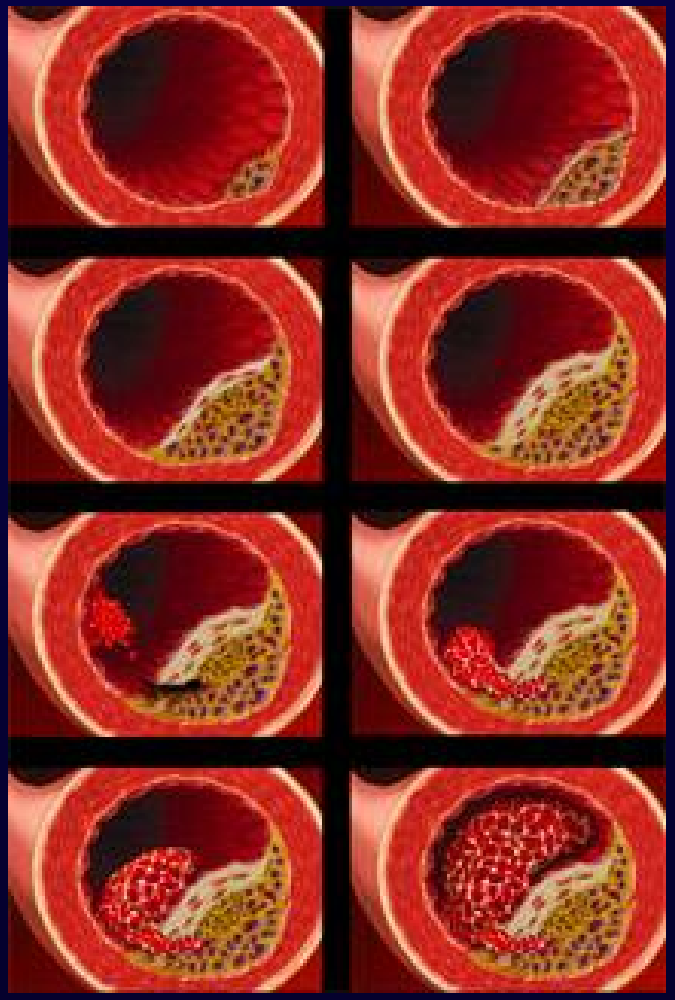
+ Bullet Points!

CVS Patients are NOT always Obvious!

Case History 1

William Jefferson Clinton

BILL CLINTON

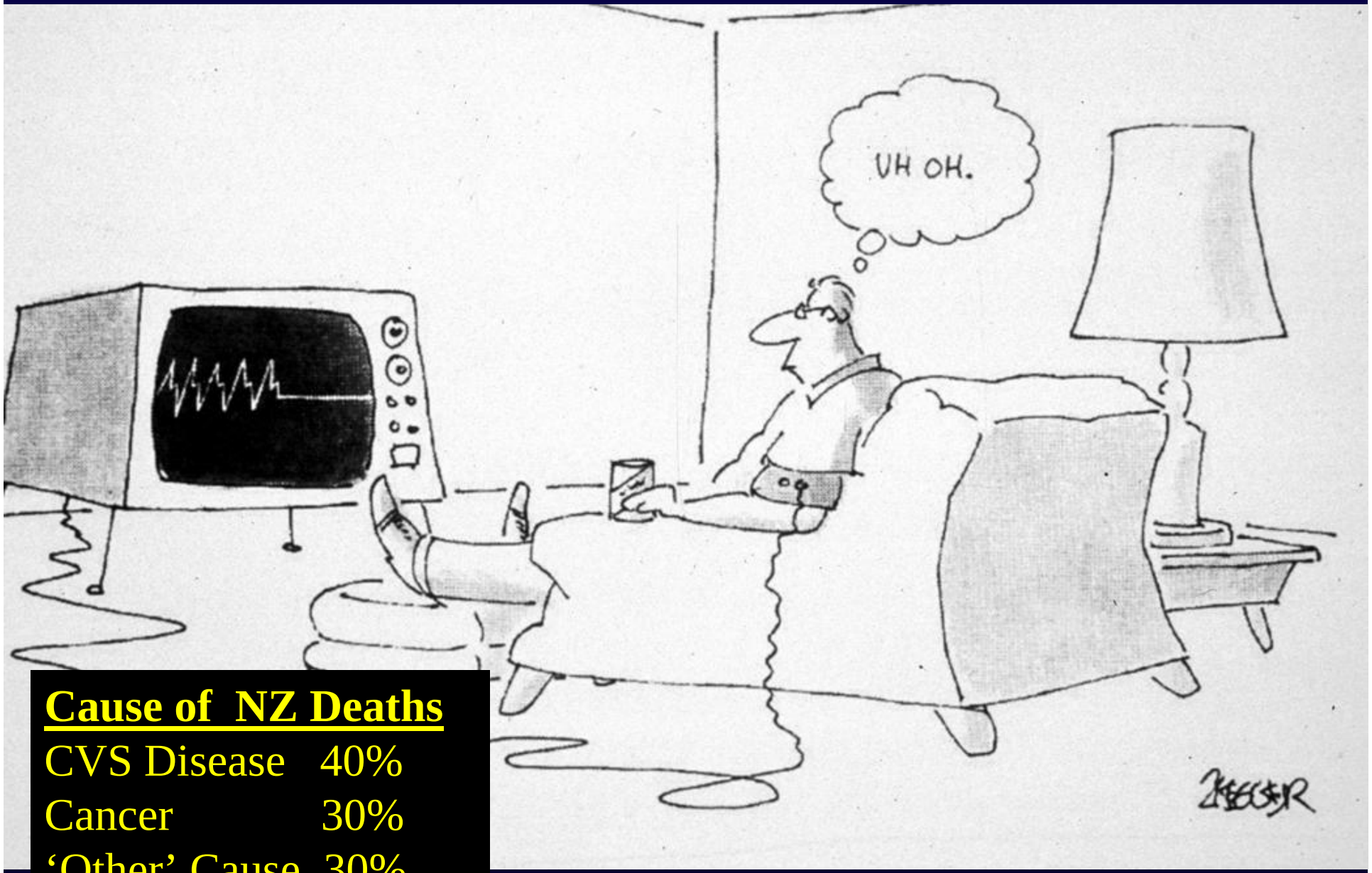


Coronary Heart Disease:
We're not good at CVS risk assessment!

William Jefferson Clinton

Emergency Bypass Surgery @ age 58 years

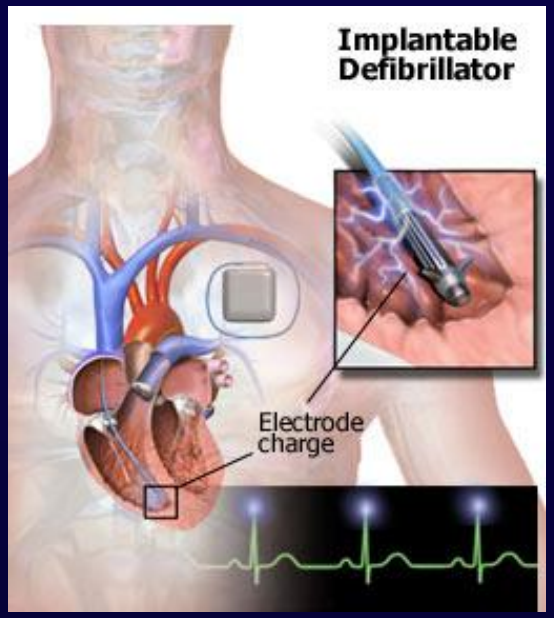
CVS Disease: A Major Problem in New Zealand



Cause of NZ Deaths

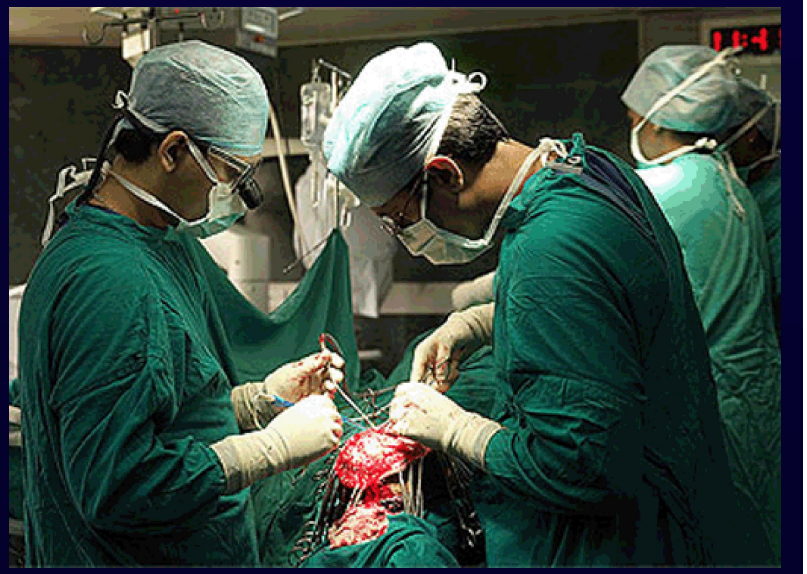
CVS Disease	40%
Cancer	30%
'Other' Cause	30%

CVS Disease Prevention?



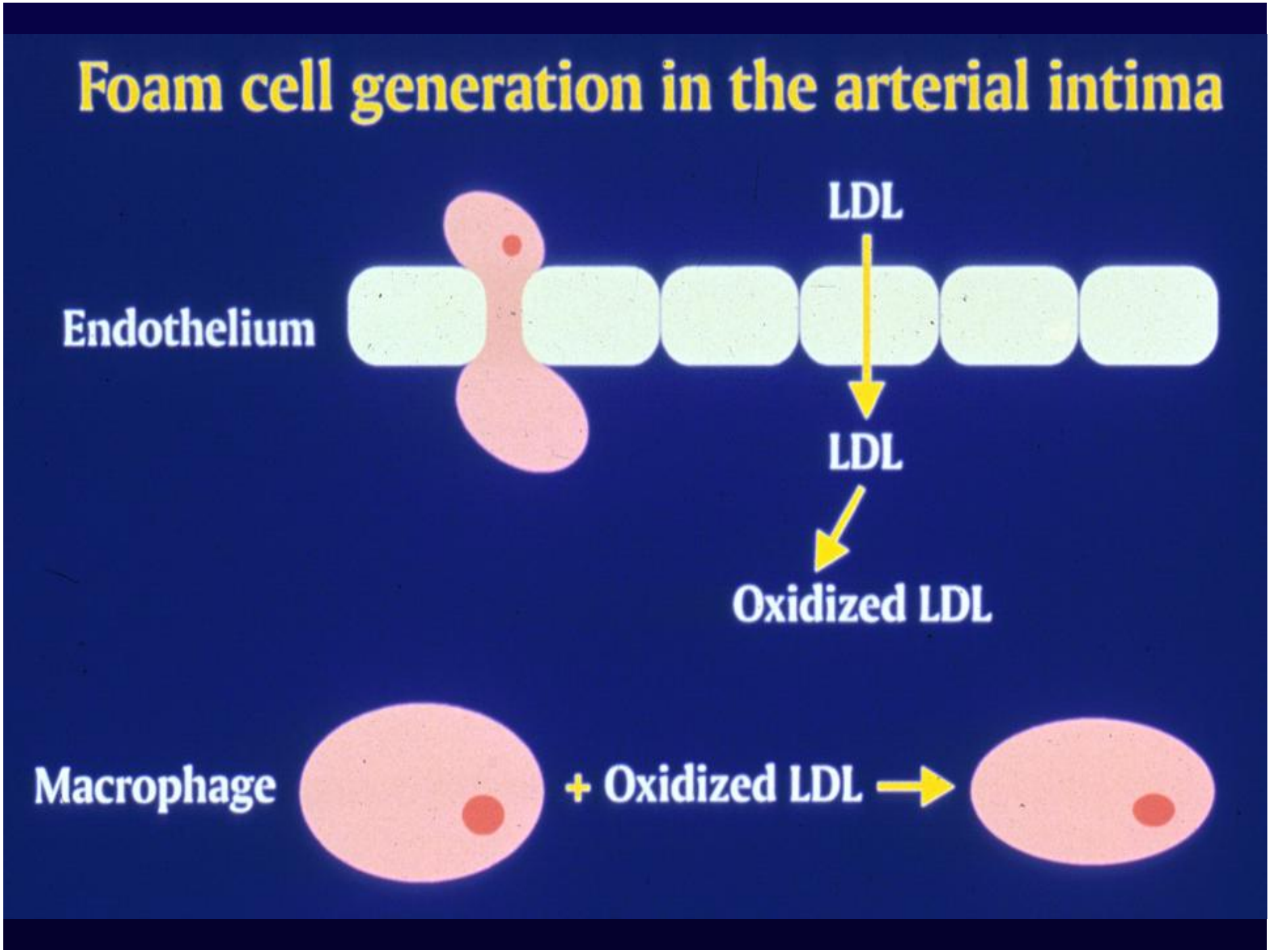
or

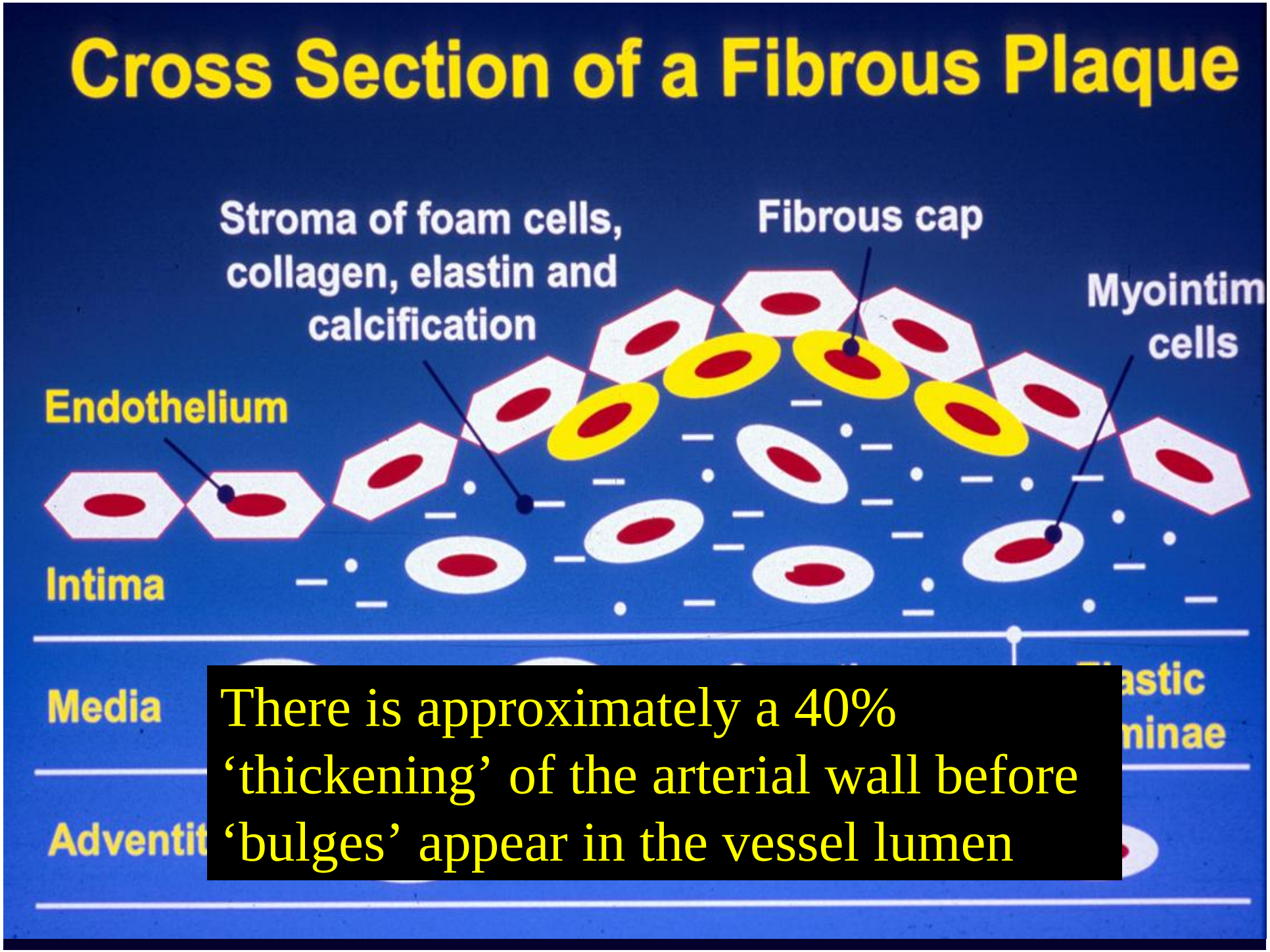
Expensive ‘Cure’!



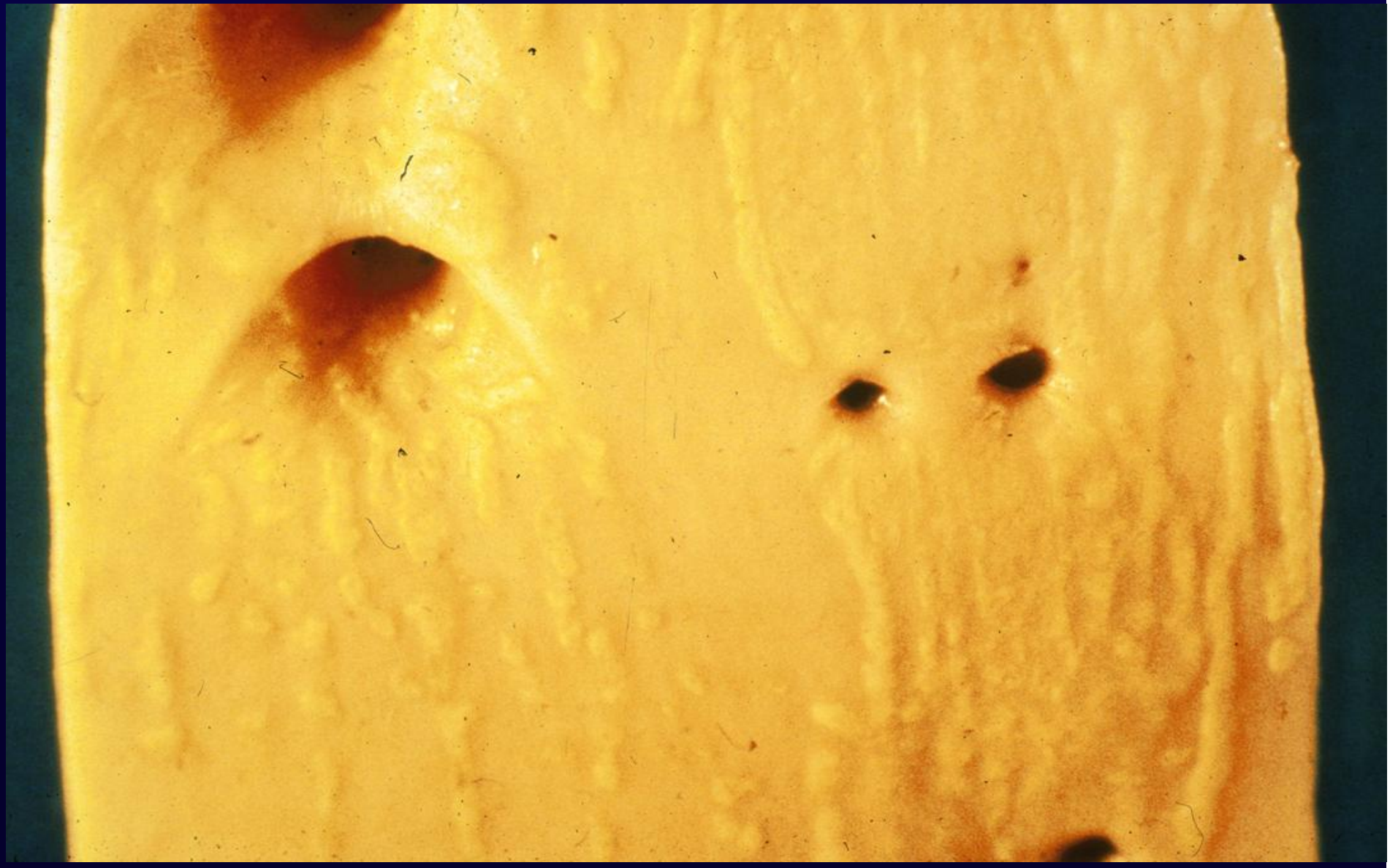
Bullet Points 1

- CVS Risk assessment is not easy
- BUT it is very important for our NZ population!

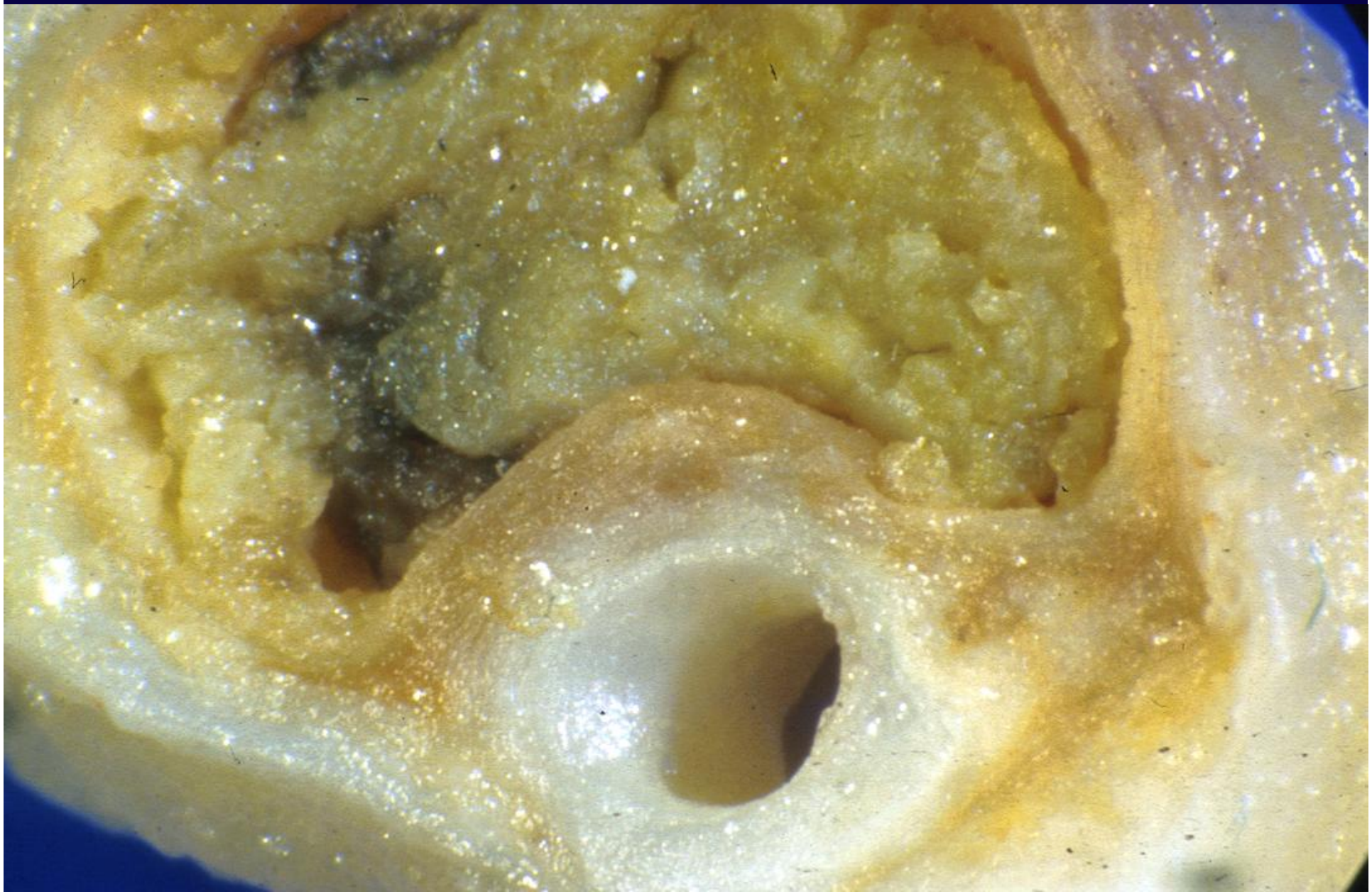

Foam cell generation in the arterial intima
LDL
Endothelium
LDL
Oxidized LDL
Macrophage
+ Oxidized LDL


Cross Section of a Fibrous Plaque
Stroma of foam cells, collagen, elastin and calcification
Fibrous cap
Myointim cells
Endothelium
Intima
Media
There is approximately a 40% 'thickening' of the arterial wall before 'bulges' appear in the vessel lumen

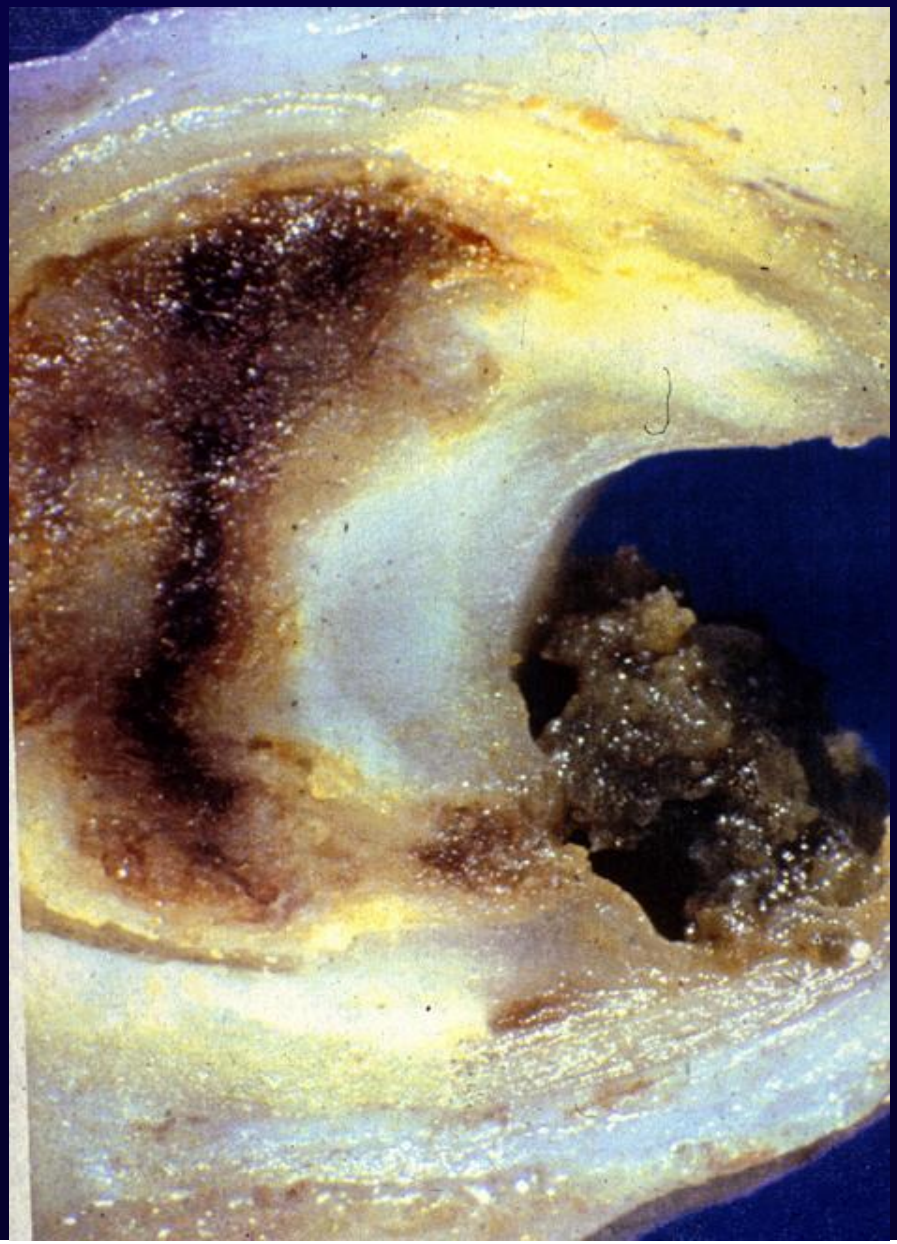
Atheromatous Fatty Streaks



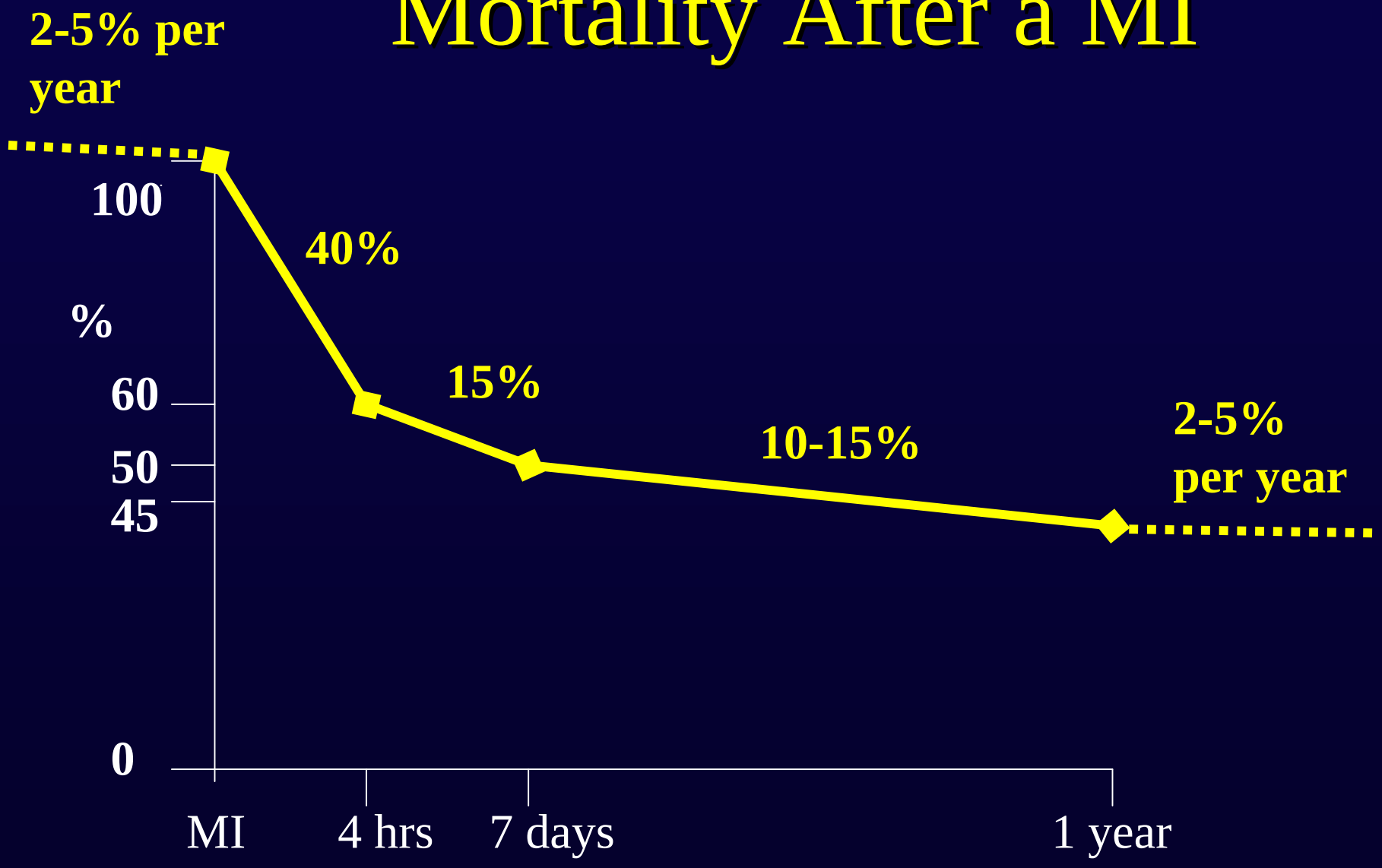
Severe Coronary Stenosis



Ruptured Plaque: Partial Occlusion



Mortality After a MI



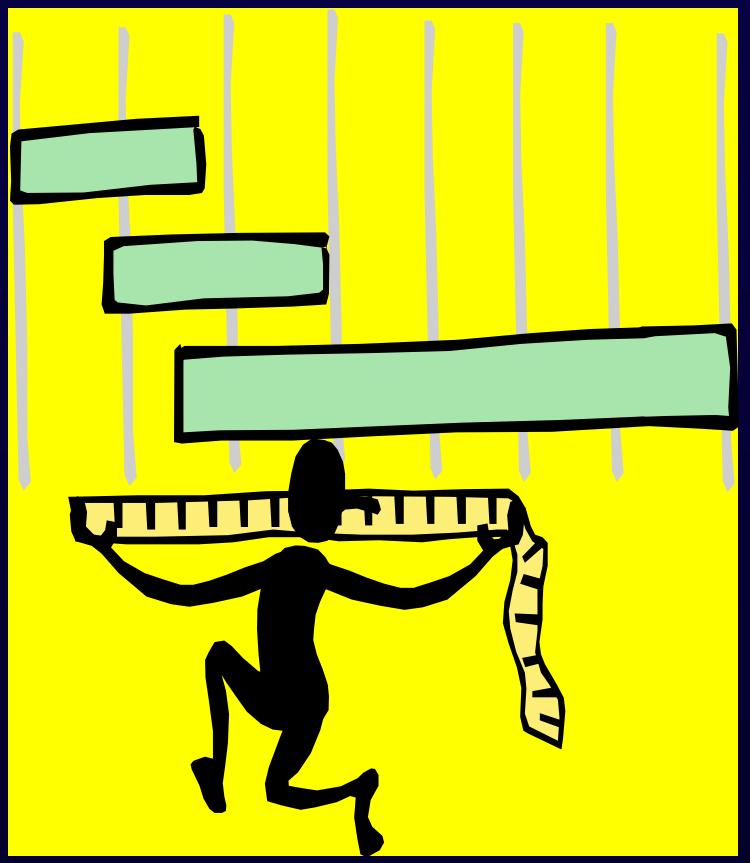
Bullet Points 2

- Atherosclerosis is a highly complex, poorly understood, ageing/disease process
- [It may be difficult to predict CVS events!]

How do we Assess CVS Risk in New Zealand Today?

Framingham-Based CVS Risk Tables: Risk Factors Used in NZ

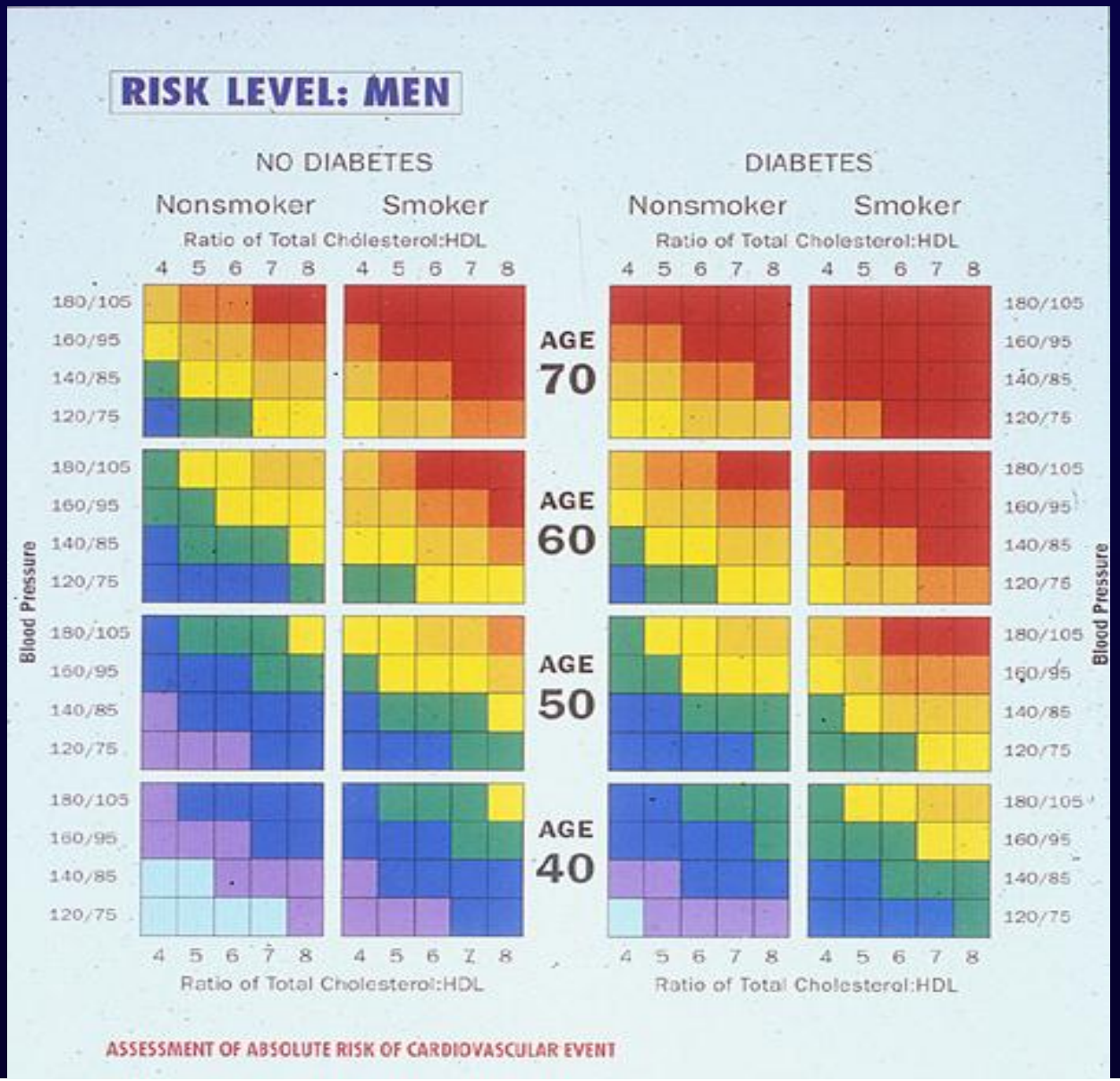
- Age (decades)
- Gender
- Diabetes Status (Y/N)
- Hypertension
- Smoker (Y/N)
- Total Cholesterol/HDL Ratio



Additional 5% CVS Risk Factors: 2003/2009 NZ Guidelines

Family history of premature coronary heart disease or ischaemic stroke in a first-degree male relative before the age of 55 years or a first-degree female relative before the age of 65 years
Maori
Pacific peoples or people from the Indian subcontinent
People with both diabetes and microalbuminuria
People who have had type 2 diabetes for more than 10 years or who have an HbA1c consistently greater than 8%
(People with the metabolic syndrome) GONE 2009
IF Total Cholesterol $\geq$ 8 then risk $\geq$ 15%
if Total Cholesterol/ HDL $\geq$ 8 then risk $\geq$ 15%
if BP consistently $\geq$ 170/100 then risk $\geq$ 15%

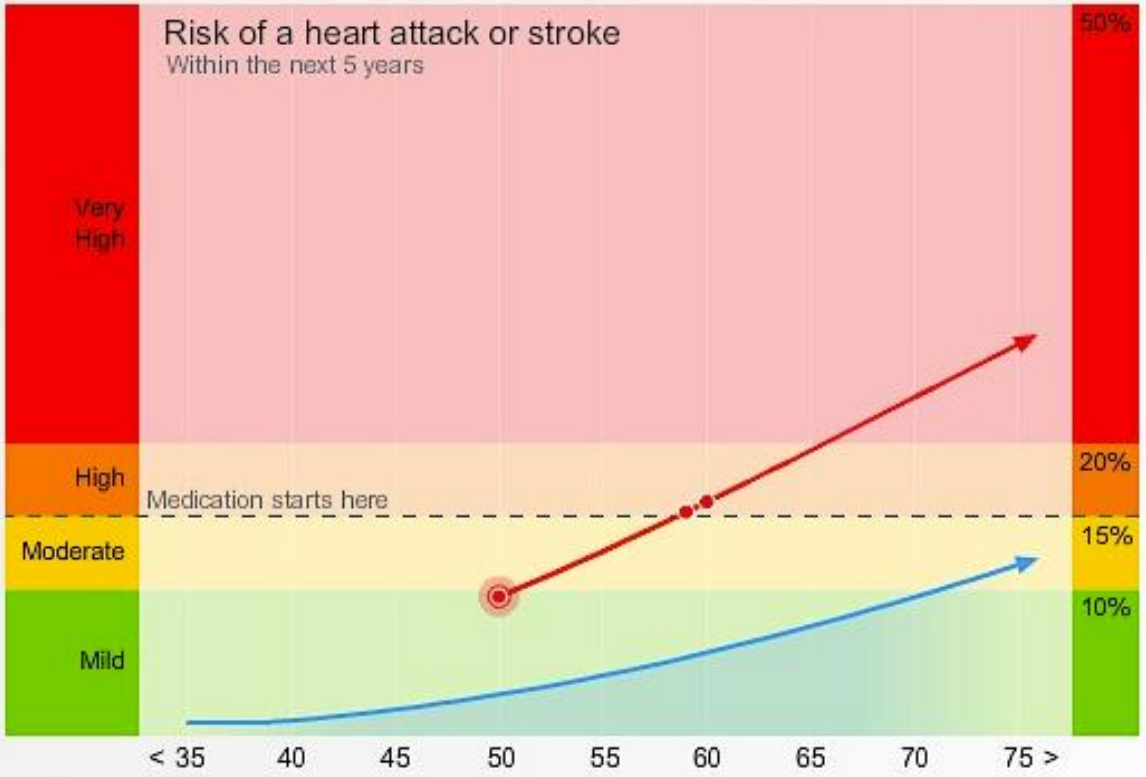
Framingham-Based Risk Tables



Your Heart Forecast

Step 3

◀ Prev



You can reduce your risk of a heart attack or stroke by...

- not smoking
- eating a healthy heart diet
- 'Push-Play' by being active for at least 30 minutes on most days of the week

This will help you to feel good and lower your blood pressure and cholesterol.

You can adjust these factors on the next page to see what they can do for your risk of a heart attack or stroke.

Next ▶

Your current risk right now

Your projected risk if no changes are made

Point where heart pills are recommended (15% risk)

Your ideal risk zone
(Based on Non-Smoker, TC/HDL ratio:4, BP: 120/80)

Heart Foundation

THE UNIVERSITY OF AUCKLAND
FACULTY OF MEDICAL AND HEALTH SCIENCES

CVS Risk Assessment by Framingham

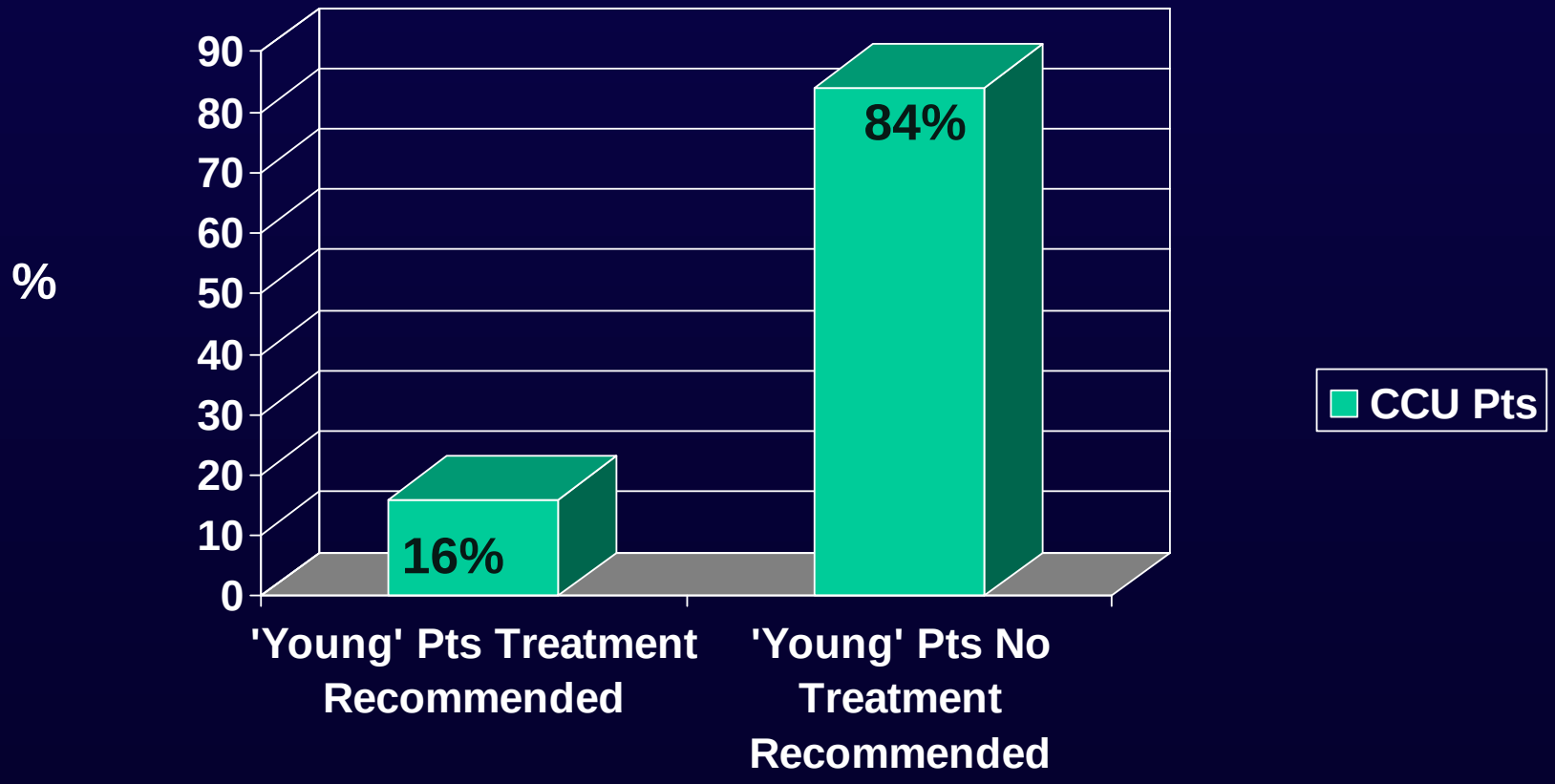
1. Identifies older patients at higher risk who can benefit if they are more vigorously treated
2. BUT, a tendency to ‘predict the inevitable’ and treat an elderly, population with multiple risk factors
   - Prolong life by 5 years from 75 to 80 years (good)
3. Younger patients with a high ‘total life risk’ are not identified
   - Prolong life by 35 years from 45 to 80 years (v good!)

Can the Framingham Tables Predict CVS Risk in Young ACS Patients in New Zealand?

Auckland City Hosp CCU Pts 1 June 06 to 30 June 07

J Looi, CJ Ellis et al CSANZ 2008

Pts with NZ Framingham CVS Risk > 15% over 5 Years



'Young' (male<55, female<65 years) n = 229 pts, no prior CVS disease

Results

J Looi, CJ Ellis et al CSANZ 2008

	Young patients (n=229)	
Treatment received		
-medical	51 (22%)	
-angioplasty	144 (63%)	
-CABG	31 (14%)	
-angioplasty followed by CABG	2 (1%)	

Only 16% Pts would have been recommended to receive preventative therapy before their MI

Bullet Points 3

- The Framingham-based NZ Guidelines are significantly inaccurate
- The use of a ‘5-year’ risk assessment is illogical for an ageing process which takes decades to develop; consider a ‘life-time risk’
- High risk younger patients are often untreated with this [short-sighted] approach
- Threshold:
  - 15% in 5 years is 30% in 10 years = treat
  - Overseas: 20% in 10 years: 2%/year = treat

We will soon have the ‘PREDICT’ New Zealand Data, so we won’t need to use Framingham Tables

[Unfortunately Wrong]

Methods Since 2002 cardiovascular risk assessments have been undertaken as part of routine clinical care in many New Zealand primary care practices using PREDICT, a web-based decision support programme for assessing and managing cardiovascular risk. Individual risk profiles from PREDICT were electronically and anonymously linked to national hospital admissions and death registrations in January 2008.

PREDICT Data: GP or Practice Nurse completes via computer

Factors: Age, Sex, Diabetes, Smoking status, Systolic BP, total cholesterol/HDL Cholesterol ratio, height, weight, ethnicity:

Patient Numbers: Only 14% of eligible people were enrolled in the cooperating GP PHOs [PREDICT 10 Paper]

-Uncertain how this cohort was selected i.e. low or high risk?

Definition of CVS Disease: End Points

Framingham (Described)

[n=383:Type unknown]

- Myocardial Infarction, Angina, 'coronary insufficiency'
- Ischaemic stroke, Transient ischaemic attack
- Peripheral vascular disease
- 'Congestive heart failure'
- Cardiovascular-related death

PREDICT (ICD 10 AM Codes)

[n=2327:total, n=1374: 1st CVS]

- Coded by house surgeon & hospital coders
- ? Accuracy

The 2 Studies endpoints are *very* different *and* collected differently

PREDICT ICD 10 AM Codes: Endpoints (1)

Outcomes	ICD–10–AM codes	Number of first events (N)*
Coronary heart disease Cardiac arrest or sudden cardiac death	I20–I25 (except I252) Acute coronary syndromes, chronic ischemic heart diseases E1053, E1153, E1453 Coronary heart disease I461 Sudden cardiac death, so described R96 Other sudden death, cause unknown R98 Unattended death 3530400–3530501 Coronary angioplasty or stent 3531000–531005 Percutaneous coronary intervention	770
Coronary procedures	3849700–3850304, 9020100–9020103 Coronary artery bypass 3863700 Re-operation for reconstruction of occluded coronary artery 3845619 Other intrathoracic procedures on arteries of heart without cardiopulmonary bypass 3865308 Other intrathoracic procedures on arteries of heart with cardiopulmonary bypass 3850500 Open coronary endarterectomy I63 Cerebral infarction I64 Stroke, not specified as haemorrhage or infarction I66 Occlusion and stenosis of cerebral arteries, not resulting in cerebral infarction I678 Other specified cerebrovascular diseases I693 Sequelae of cerebral infarction I694 Sequelae of stroke, not specified as haemorrhage or infarction I698 Sequelae of other and unspecified cerebrovascular diseases	301

PREDICT ICD 10 AM Codes: Endpoints (2)

Ischaemic cerebrovascular disease	G45 (except G453), G46 Transient ischaemic attack I670 Dissection of cerebral arteries, nonruptured I671 Cerebral aneurysm, nonruptured	1098
Peripheral arterial disease	I65 Occlusion and stenosis of precerebral arteries I71 Aortic aneurysm and dissection (other arterial dissection I72 Other aneurysm I74 Arterial embolism and thrombosis	120
Peripheral procedures	I739 Peripheral vascular disease, unspecified I7021, I7022, I7023, I7024 Intermittent claudification, gangrene, or diabetic peripheral angiopathy with or without gangrene 330–331 Repair aneurysm 3270000–3276318 Artrial bypass graft 3350000–3355400 Endarterectomy and patch graft artery 3380000–3380612 Embolectomy/thrombectomy 3531200–3531501 Arterial atherectomy 3855000–3857101, 3857200, 3870600, 3870601, 3871200 (Repair/replacement of aorta) 9023000 Embolectomy or thrombectomy of other artery 9022900 Other endarterectomy	38
Total		**2327**

*One person may have multiple ICD codes for a first cardiovascular event.

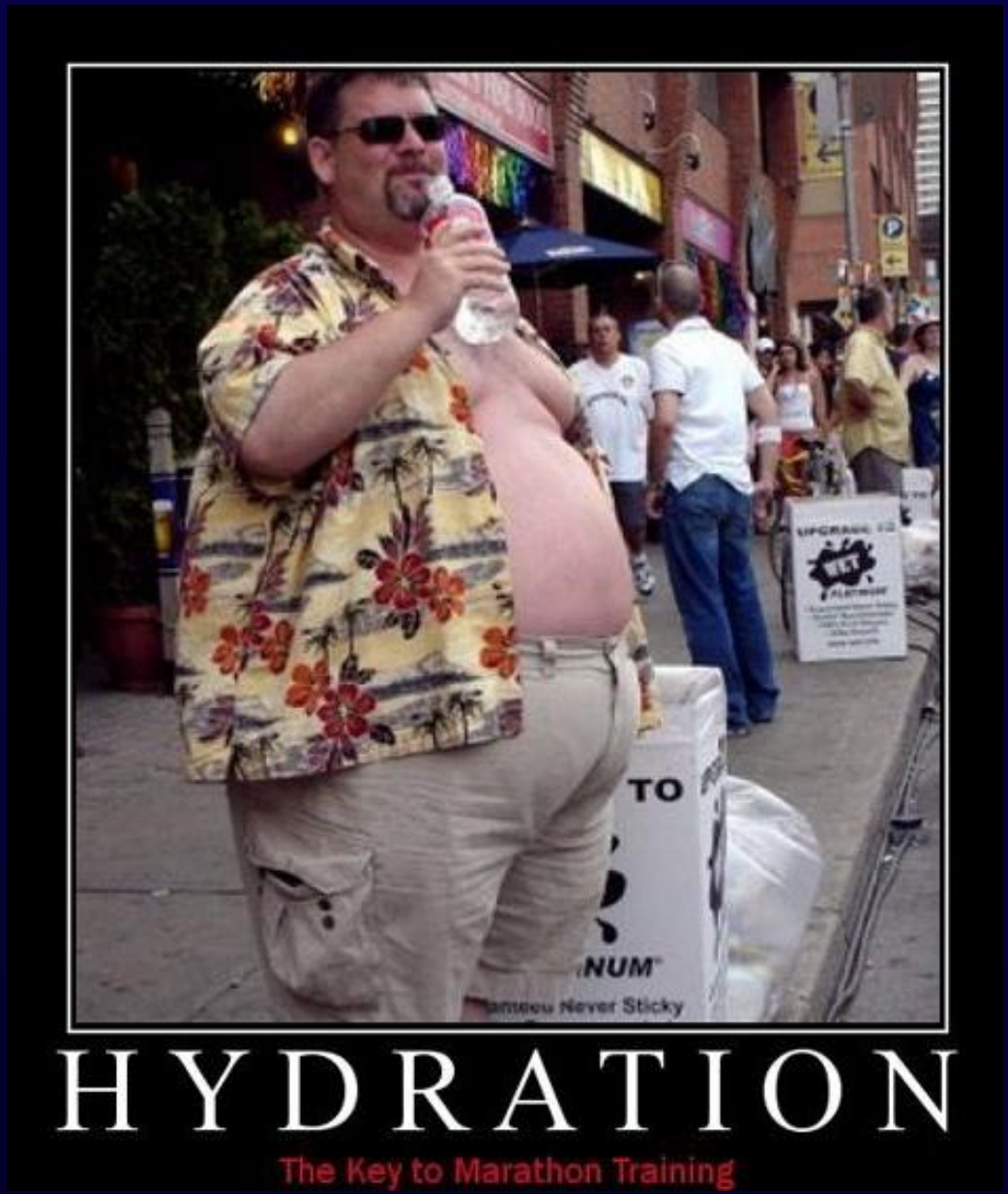
Some Problems with PREDICT 10 Comparison Study: "Framingham vs. New Zealand Data"

- Whereas Framingham data collected by biannual FU with electrocardiograms (Nurse)
- PREDICT cohort is based on public hospital admissions
- Hence some un-recorded community events:
  - Silent MI, UAP, TIAs (in community)
  - Strokes (elderly pts admitted to private 'nursing' hospitals: not coded)
  - Private hospital admissions:
    - PCIs or CABGs (not coded)
    - MIs/ UAP (not coded)
    - PVD procedures etc (not coded)
- ANY Private hospital ICD 10 AM coded procedure NOT routinely accounted for in PREDICT

Bullet Points 4

- The best Epidemiological models of CVS risk assessment are inaccurate
- PREDICT has some useful ideas, but is fundamentally flawed in design, relying on weak endpoints to drive the study
- Epidemiological CVS risk assessment: are we missing something?

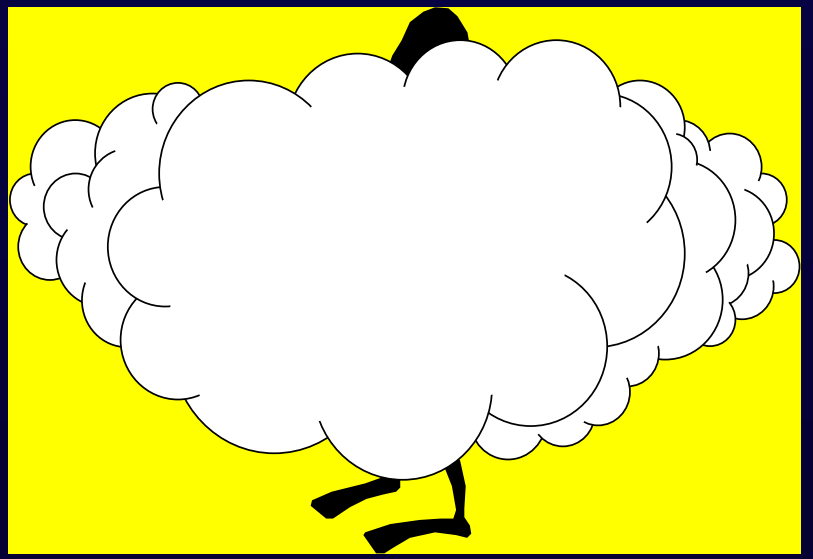
Assessment of CVS Risk: Are We Missing Something?



Assessing CVS Risk

Atherosclerosis:

- Highly complex ageing process
- Poorly understood
- Develops over many decades



Atherosclerosis: Environmental AND Genetic Influences

Each step in the complex development of atheroma will probably have a genetic & environmental influence:

- LDL cholesterol amount & type
- Other risk factors amount & type
- Intimal Proteoglycan type
- Oxidation load & protection
- Degree of inflammation in the Intima
- Plaque rupture initiators
- Blood clotting tendency
- etc

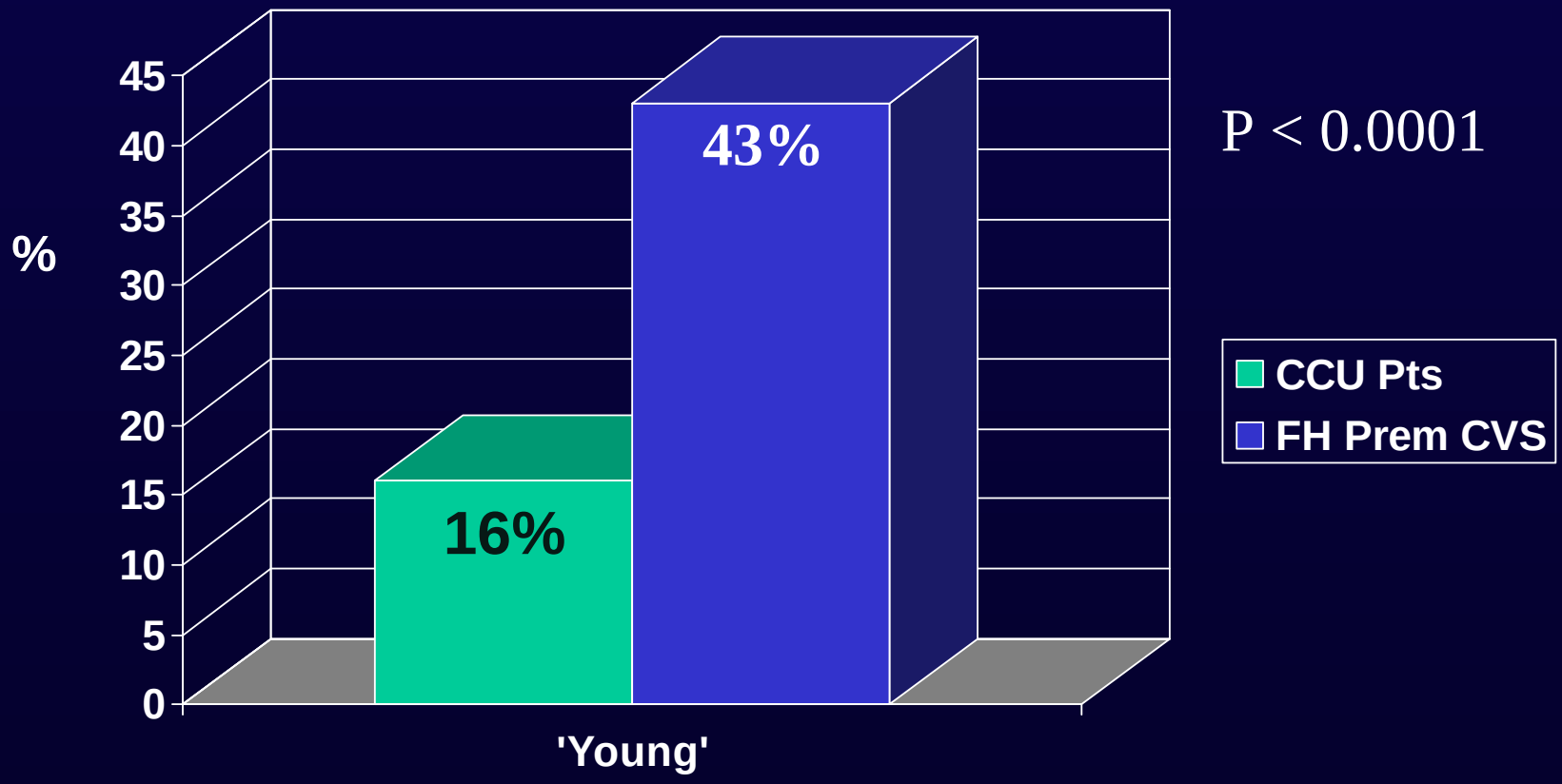
Causes of Atherosclerosis

1. Lifestyle
2. Genetic (Family History)

Auckland City Hosp CCU Pts 1/6/06 to 30/6/07

J Looi, CJ Ellis et al CSANZ 2008

Pts with NZ Framingham CVS Risk > 15% over 5 Years



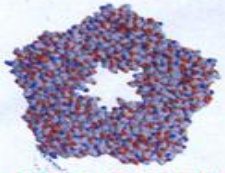
['Young' (male<55, female<65 years) n = 229 pts, no prior CVS disease]

Emerging Risk factors for CVS Disease

Beyond Cholesterol

Inflammation is emerging as a major risk factor—and not just in heart disease

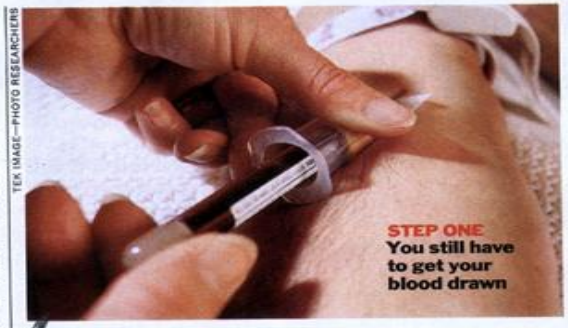
By ALICE PARK



C-REACTIVE PROTEIN

ASK ANY HEART DOCtor the best way to avoid a heart attack, and he will probably tell you to lower your cholesterol and exercise more. What he's not likely to tell you is that despite cholesterol's well-earned reputation as the heart's primary nemesis, half of all heart attacks occur in people with normal cholesterol levels. That's because though scientists have identified some 250 other risk factors, from obesity to gum disease, they have never found a better indicator of the health of one's cardiovascular system than the levels of good and bad cholesterol in the blood.

Until now. In a groundbreaking study published in the *New England Journal of Medicine* last week, doctors from Boston's Brigham and Women's Hospital showed that a simple blood test, called CRP, that measures the presence and intensity of inflammation in the walls of the blood vessels is as good as and in some cases better than cholesterol levels at predicting which patients are most likely to suffer a heart attack or stroke.



TEK IMAGE—PHOTO RESEARCHERS

STEP ONE
You still have to get your blood drawn

The study, led by Dr. Paul Ridker, director of the hospital's center for cardiovascular-disease prevention, is likely to be the talk of the annual meeting of the American Heart Association this week in Chicago. Not only does it provide the strongest evidence to date that inflammation plays a key role in heart disease, but it also supports the growing suspicion among medical researchers that inflammation is a major culprit behind a wide range of disorders, including cancer.

Inflammation is the body's basic emergency-response system. When anything threatens the body's health—from disease-causing germs to the buildup of fatty plaque in the walls of a heart vessel—the immune system sends in wave after wave of cells to swarm and destroy the invader. In the blood vessels, layers of these immune cells pile up, creating lesions that become increasingly unstable and may eventually rupture, triggering a heart attack. How sensitive this alarm system is depends on such things as diet, stress and one's genetic predisposition.

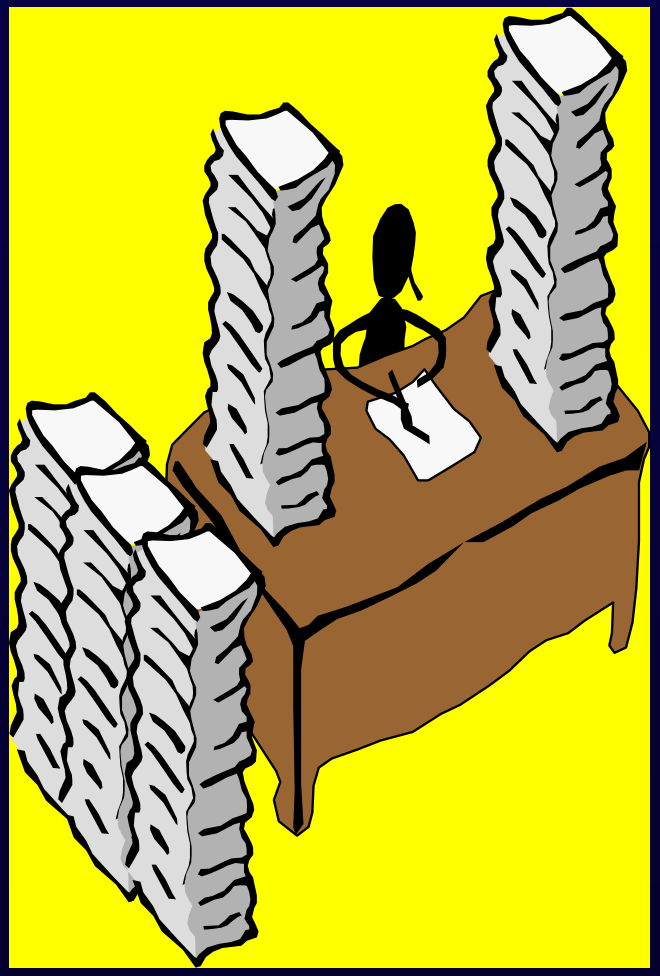
CRP, for C-reactive protein, is a substance manufactured by the liver in response to the immune system's alarms. It can easily be picked up in the blood and provides a convenient measure of how inflamed the heart arteries may be. Ridker's team, which pioneered the study of CRP's role in heart disease, tracked the levels of both CRP and LDL ("bad" cholesterol) in nearly 28,000 women for eight years. They

TIME Magazine 2003: Highly Sensitive CRP

Emerging Risk Factors for CVS Disease

Some Risk Factors Not Used in Framingham

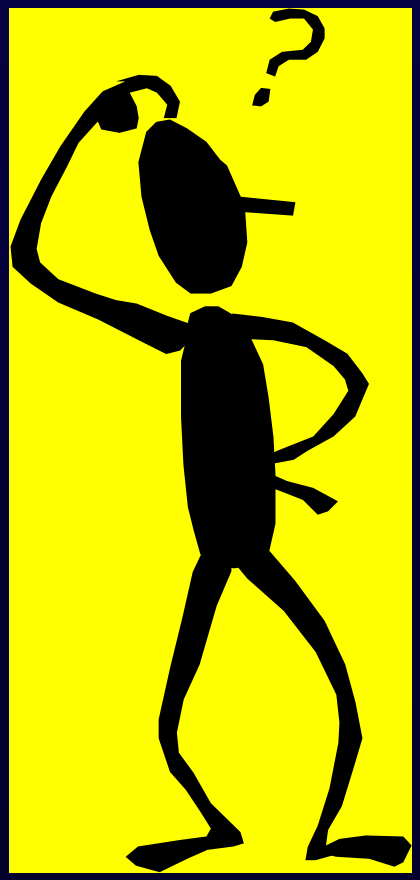
- Atherogenic markers
  - eg Lp(a), LDL size, Homocysteine
- Thrombogenic markers
  - eg Fibrinogen, Leiden factor
- Inflammatory markers
  - eg “Sensitive” CRP, IL-6
- Psycho-social Markers
  - Deprivation, Ethnicity
- ‘Lifestyle’
  - Obesity, physical fitness



Bullet Points 5

- A Family History of premature CVS Disease increases CVS risk by 2 to 4 times
- Use Family History!
- Most ‘emerging’ CVS risk factors are hard to use for an individual patient
- Don’t use them [much]

Are We Surprised that Epidemiological Studies Struggle to Accurately Detect CVS Risk for Individuals in New Zealand?



Illogical Process?

In Other Areas of Medicine, we *'Look for Disease'*

- Breast Cancer: Mammogram
- Colon Cancer: Colonoscopy

BUT

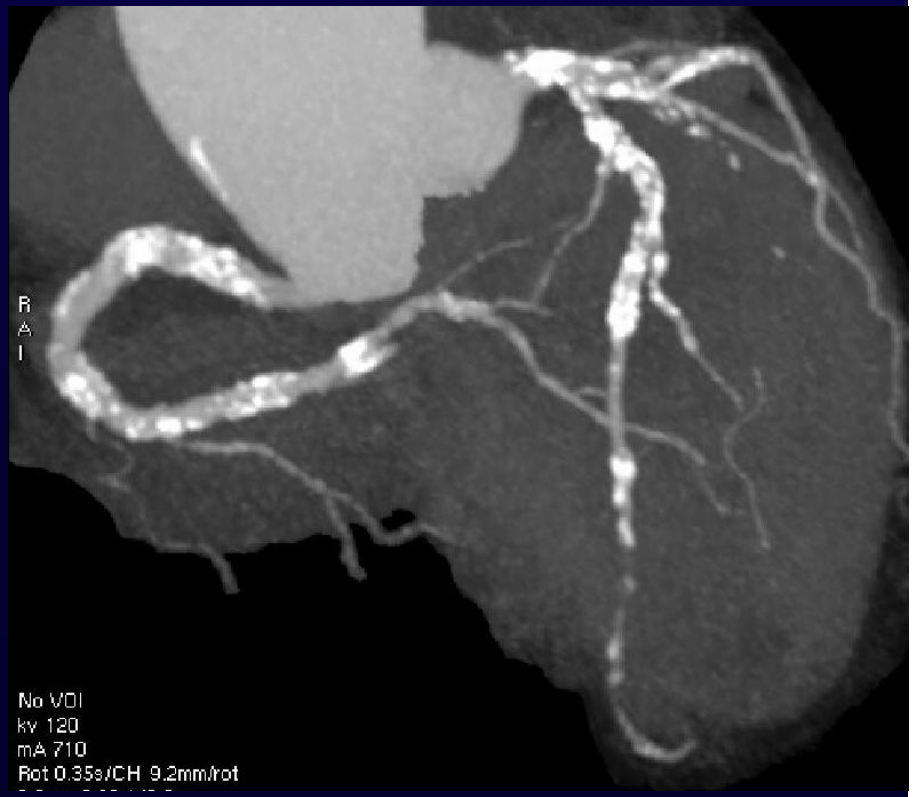
- Coronary Artery Disease: 'Coloured Charts' or Equations?

What happens if we *'Look for Disease'* in Coronary Artery Disease?

- Calcium Scoring
- CT Cardiac Angiography

Calcified Coronary Arteries

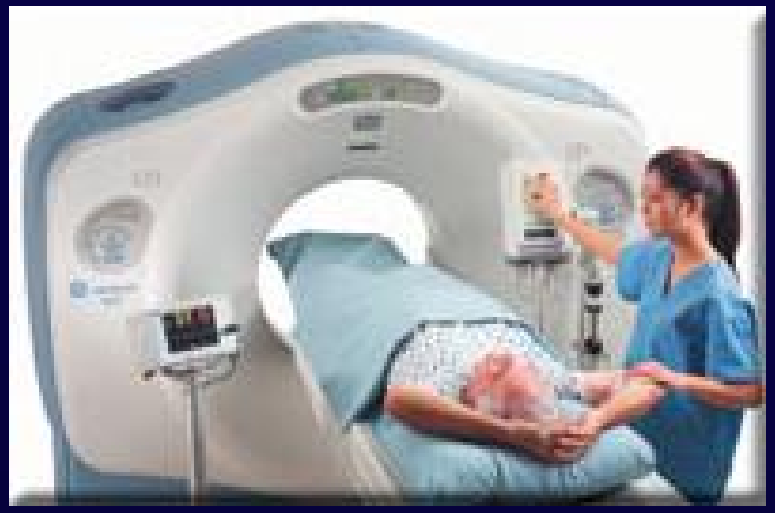
- Intuitive for CVS Risk
  - *Look for disease*
  - Concept used elsewhere
- Coronary Atherosclerosis & calcification is the ‘End Product’ of all CVS risk factors [known or unknown]

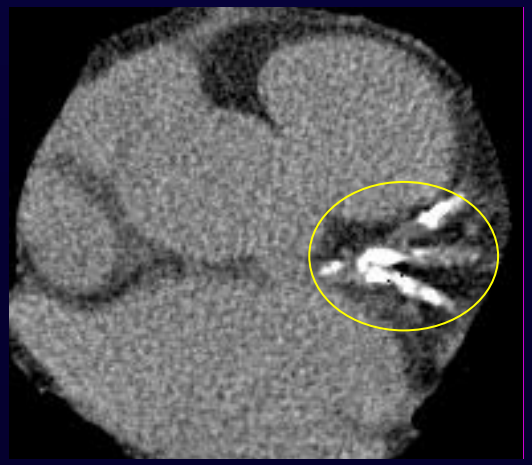


“Is Coronary Calcium Scoring: the Logical Way to Assess CVS Risk?”

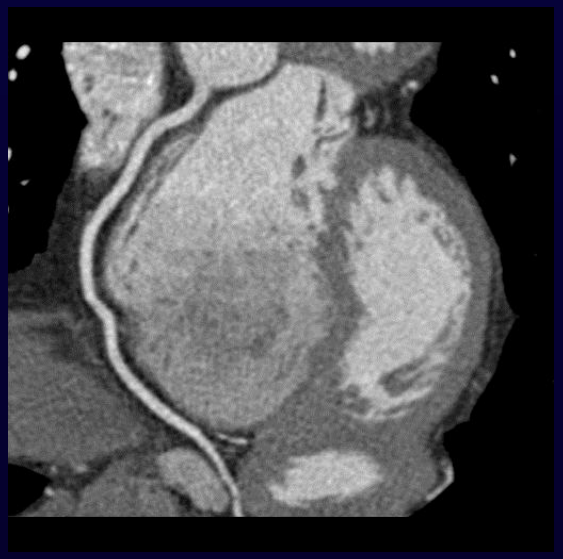
“Coronary Calcium Scoring: is challenging the established [and entrenched?] epidemiological concepts of CVS risk assessment ”

CTA Patients have 2 ‘scans’

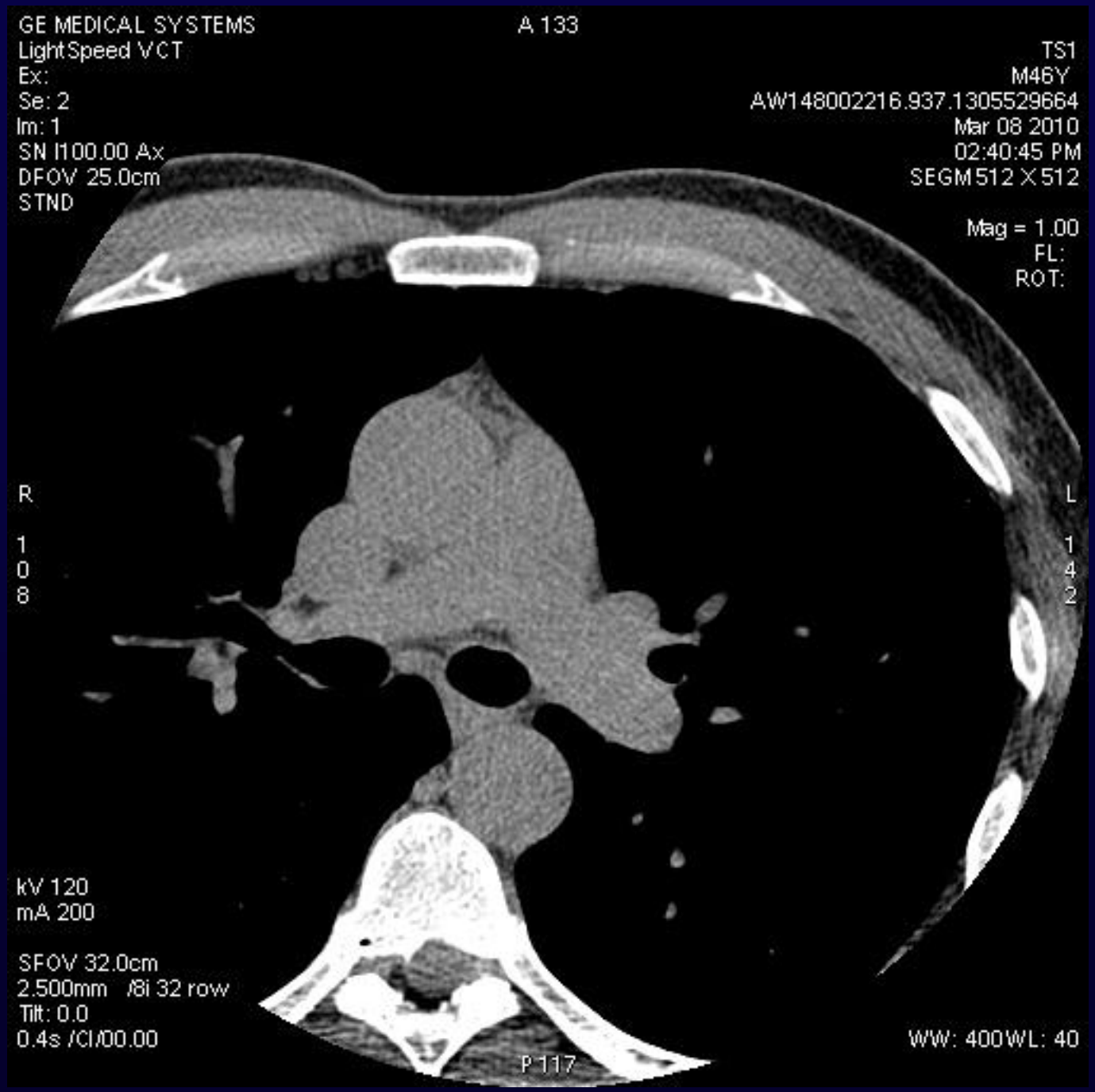




1. Calcium Score



2. Main Scan


GE MEDICAL SYSTEMS
LightSpeed VCT
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M46Y
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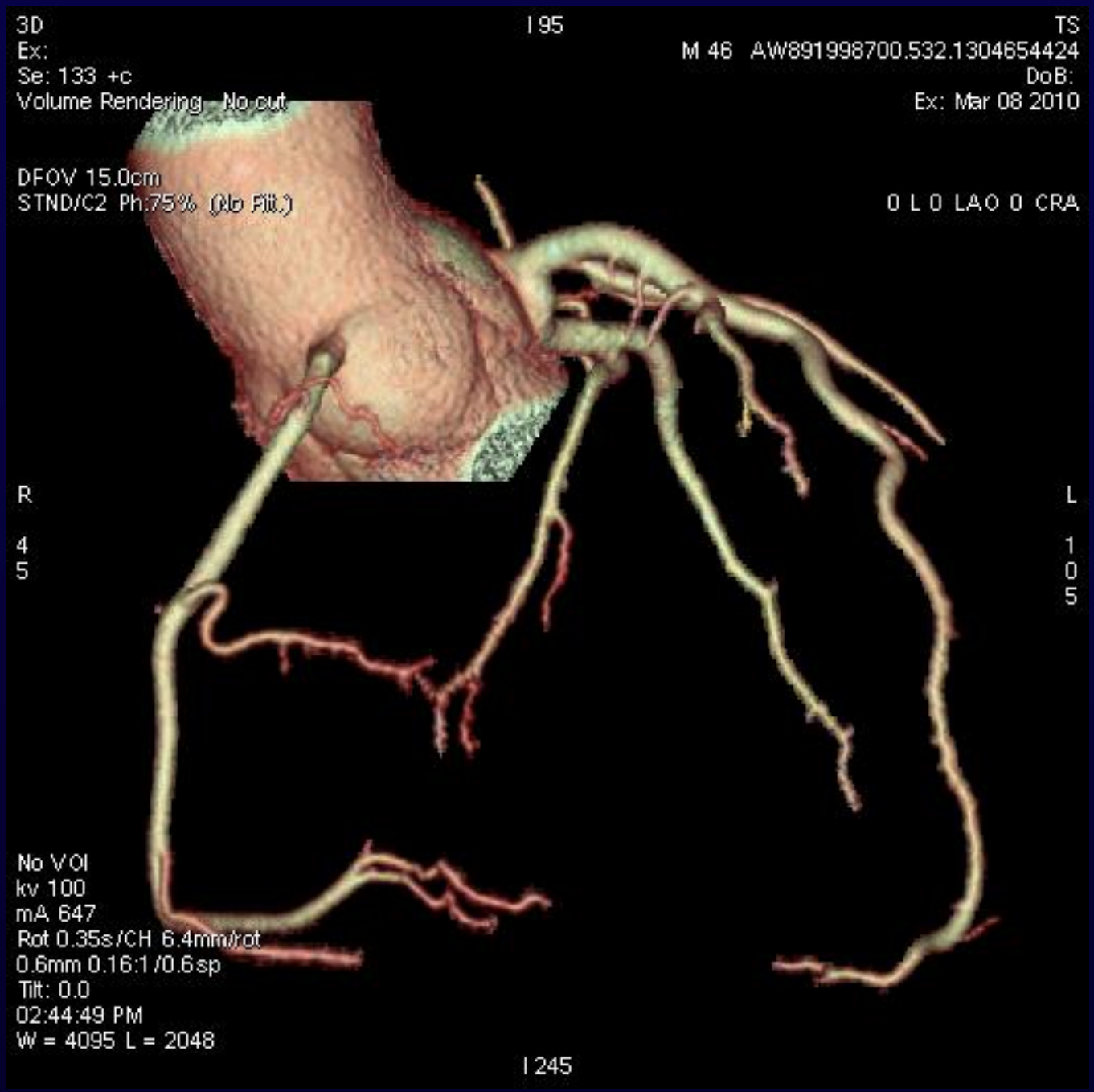
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DoB:
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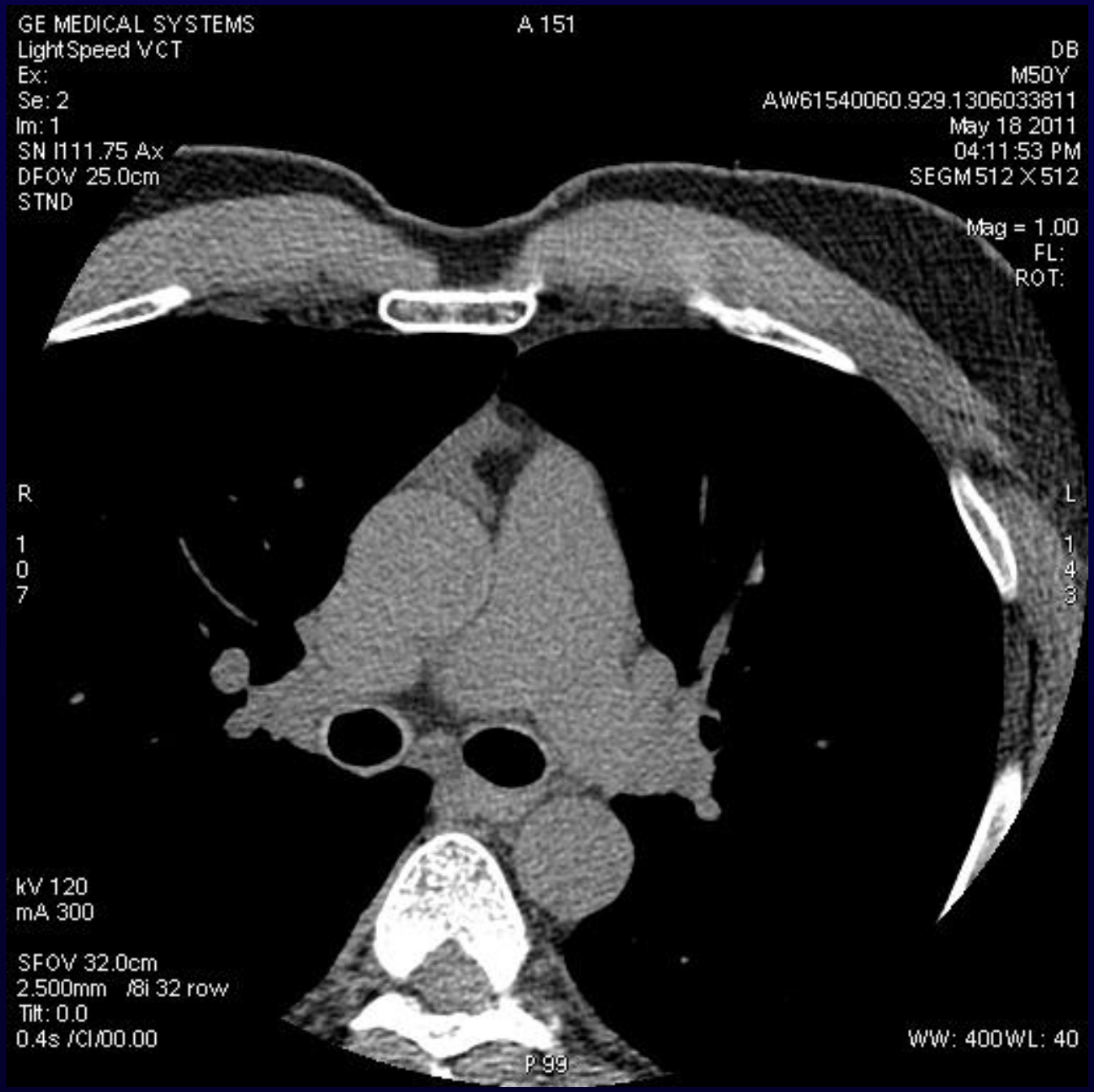
GE MEDICAL SYSTEMS
LightSpeed VCT
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Mag = 1.00
FL:
ROT:
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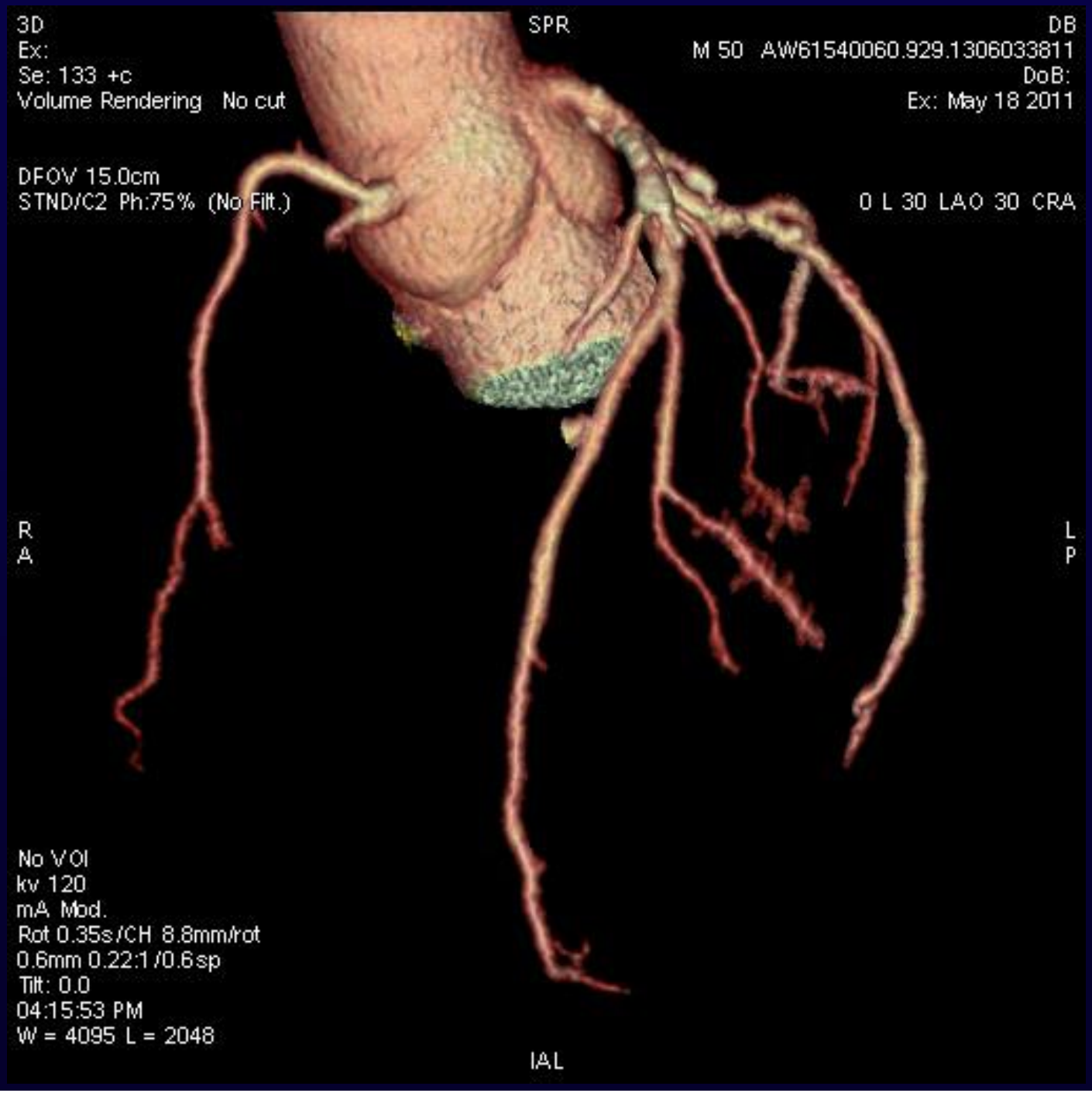
4
3
kV 120
mA 300
SFOV 32.0cm
2.500mm /8i 32 row
Tilt: 0.0
0.4s /CI/00.00
P 99
WW: 400 WL: 40


3D
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STND/C2 Ph:75% (No Filt.)
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A
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No VOI
kv 120
mA Mod.
Rot 0.35s/CH 8.8mm/rot
0.6mm 0.22:1/0.6sp
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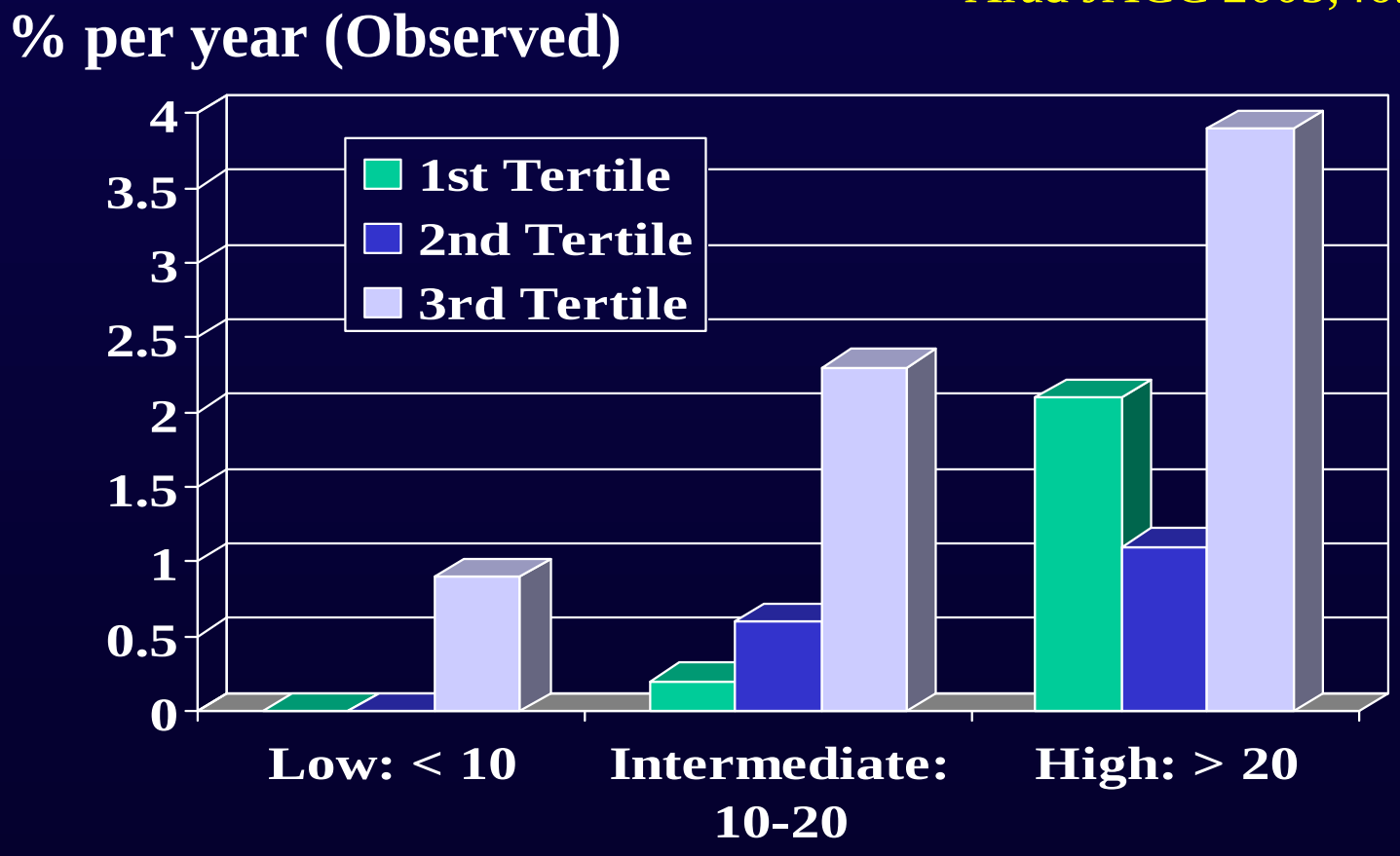
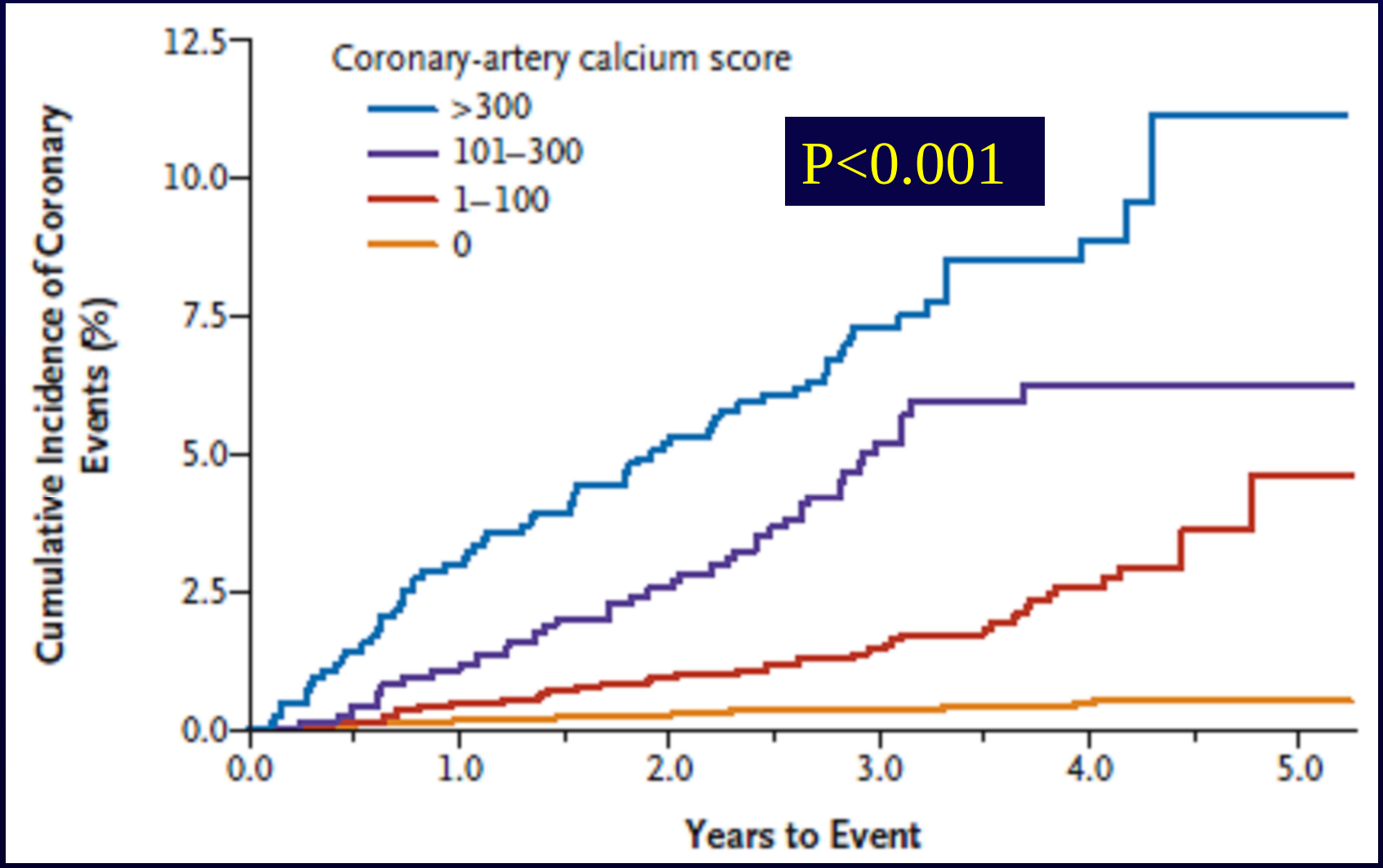
04:15:53 PM
W = 4095 L = 2048
IAL

St Francis Heart Study: Coronary Event Rates as a function of Calcium Score within Framingham Risk Groups

Arad JACC 2005;46:158-65



Calcium Score & Any Coronary Events: MESA Study NEJM 2008;358:1336-45



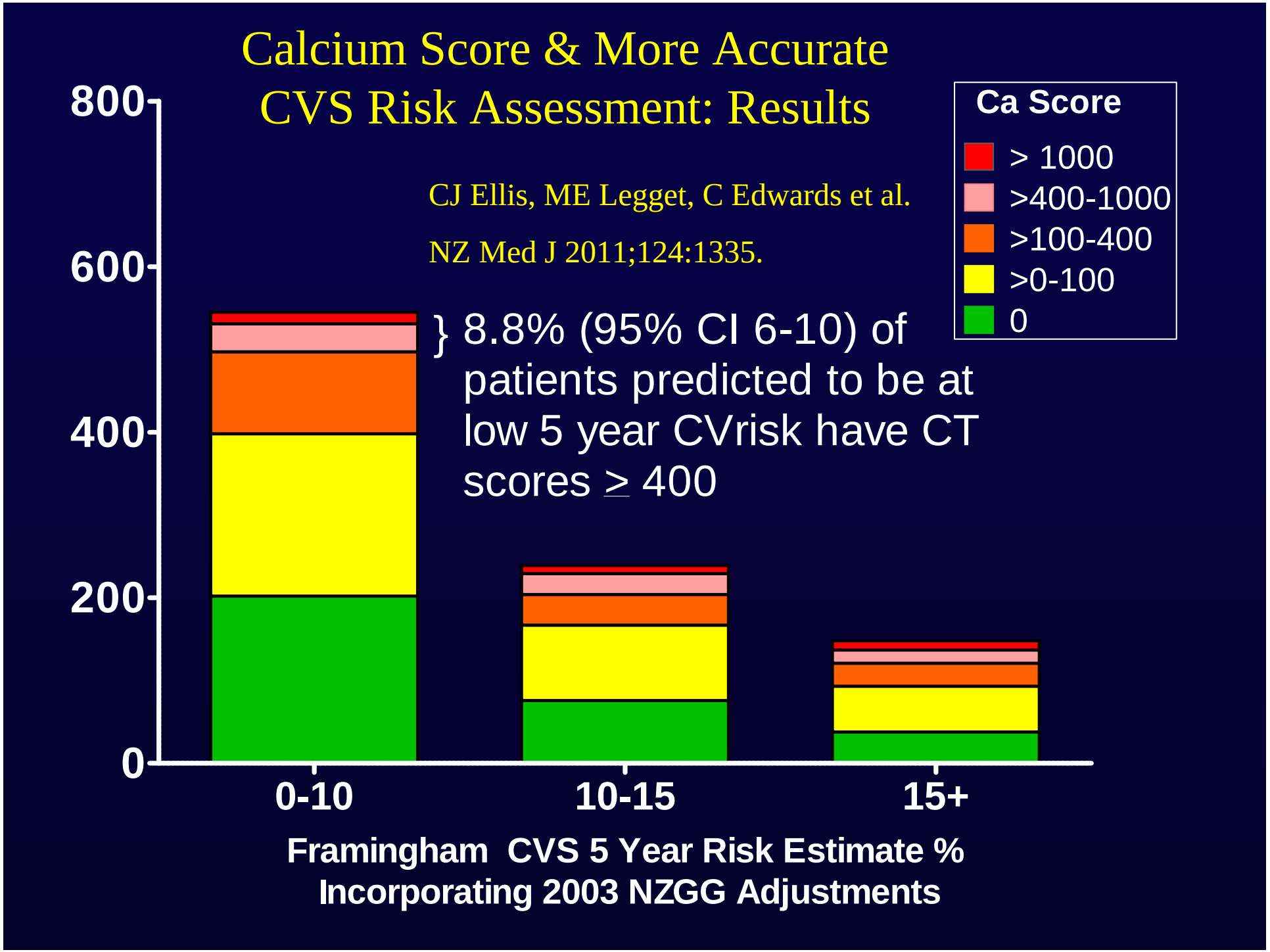
THE NEW ZEALAND MEDICAL JOURNAL
Journal of the New Zealand Medical Association

High calcium scores in patients with a low Framingham risk of cardiovascular (CVS) disease: implications for more accurate CVS risk assessment in New Zealand

Chris J Ellis, Malcolm E Legget, Colin Edwards, Niels Van Pelt, John A Ormiston, Jonathan Christiansen, Helen Winch, Mark Osborne, Greg Gamble

NZMJ 27 May 2011, Vol 124 No 1335; ISSN 1175 8716
URL: http://www.nzma.org.nz/journal/124-1335/4676/

Calcium Score & More Accurate CVS Risk Assessment: Results

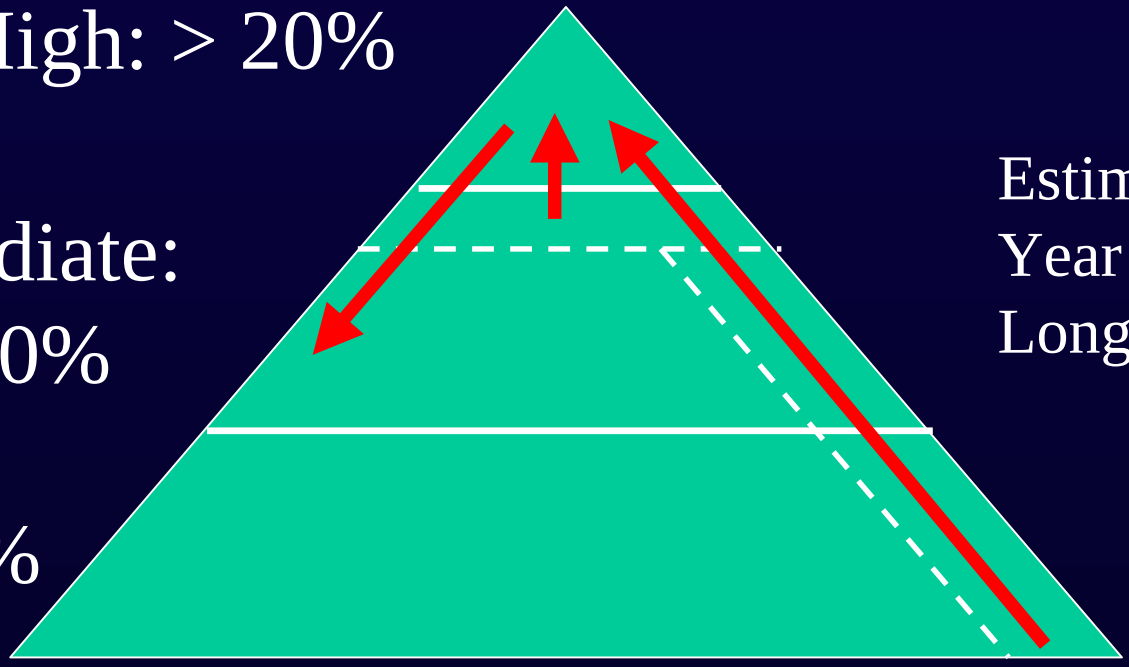


Potential Identification of more High & Low-Risk Individuals using Calcium Scoring

High: > 20%

Intermediate: 10% - 20%

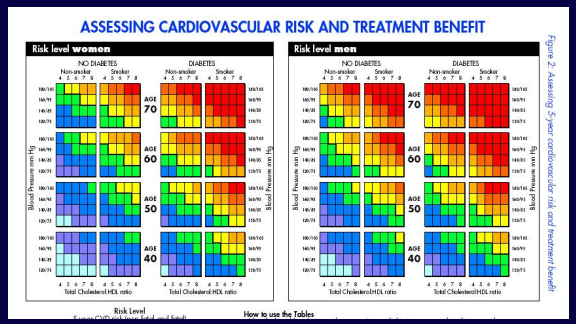
Low: < 10%



Estimated 10-Year **AND** Long-Term Risk

Bullet Points 5

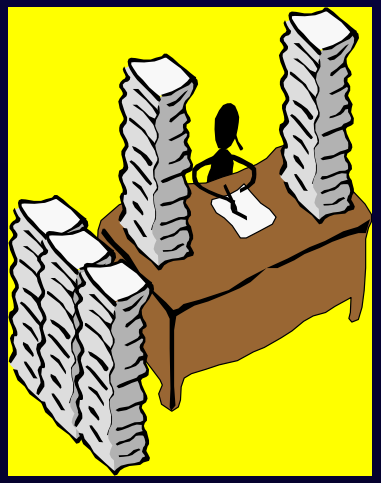
- ‘Looking for Disease’ to assess CVS risk is logical
- Whatever the risk factors & genetic drive, if there is advanced atherosclerosis present, there is increased CVS risk
- Breast screening, cervical screening, colon screening; possibly Calcium score/Cardiac CT screening in the future? [This has started overseas]



Framingham-Based:
5 or 10-Year Risk &
"Lifetime-Risk"

Family History

CVS Risk Assessment



"Modern Risk Factors"

Calcium Scoring (& CT Angiography)

Assessment of CVS Risk

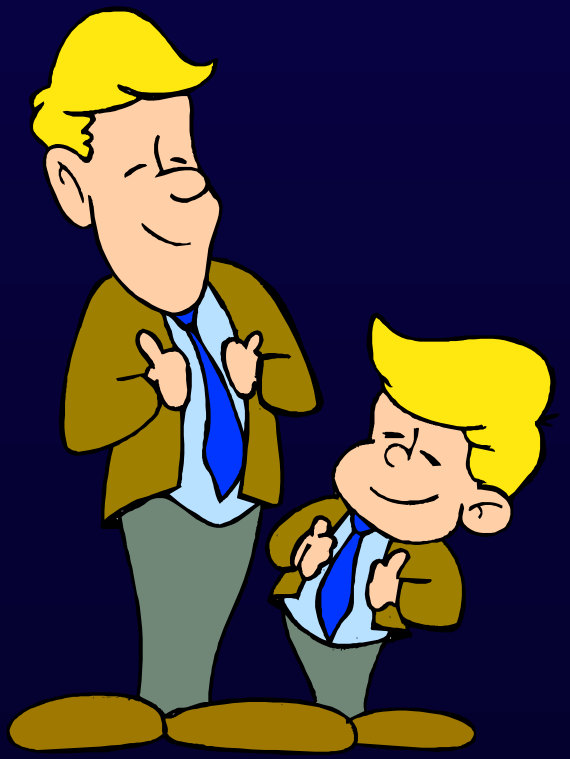
1. It’s not easy!
2. Methods differ
3. [Suggest you] Do it this way!

Clinicians Approach to CVS Risk Assessment 1

- Consider the lifetime of a patient
- In the early 20s check the cholesterol level ($7)
  - This will identify FH pts who need early statin treatment
- Encourage healthy lifestyle choices; with time it becomes clear who is being unhealthy!
- Obtain a clear family history; this will be updated over time

Clinicians Approach to CVS Risk Assessment 2

- Identify the age when CVS risk assessment will next be done
  - E.g. at 30 years, then 40 years, then every 5 years
- Negotiate, discuss, explain with each assessment
  - Patients need to have ‘buy in’ to the process
  - They may wish for a more/less vigorous approach than yours!



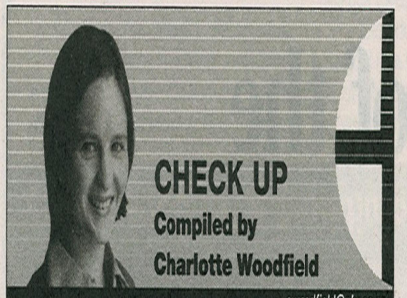
Clinicians Approach to CVS Risk Assessment 3

- Use the Framingham score in middle-age & older years
  - IF a high score, very likely a high risk, treat with a statin!
  - IF a low score, be sceptical & look for other clues e.g. Family History
  - Remain a clinician and consider the patients health, not Guideline ‘recipe’ medicine
- Discuss the potential use of statins ahead of time
  - Statins really do work!

Clinicians Approach to CVS Risk Assessment 4

- Discuss an ‘unclear zone’ with a patient: when statins could be started or deferred: the risk is only modest
  - Patients wishes often guide the management at this point
- Discuss the important use of statins when the risk is higher
  - Statins really do work!

Executive health+



CHECK UP
Compiled by Charlotte Woodfield

cwoodfield@nbr.co.nz

Burgers could cause craving

A six-month high-fat diet could cause permanent and potentially addictive brain change. In a study by the University of Pennsylvania School of Medicine, mice fed a high-fat diet for more than six months suffered irreversible changes in brain areas associated with reward and pleasure. Fatty foods tap the pleasure centres of the brain, the same areas triggered by cocaine or heroin. The researchers found the diet altered the genes involved with reward, possibly promoting cravings for fatty foods. Study senior author Teresa Reyes, PhD, said the results gave further insight into the health consequences of long-term, high-fat diets. "[They] suggest one explanation for why some people face such difficulty in the path to weight loss and healthier eating," Ms Reyes said.

Cuppa keeps away diabetes

On the plus side, that morning coffee could be warding off diabetes. New research from UCLA has linked increased coffee consumption with a decreased likelihood of developing type 2 diabetes. According to a report in medical journal *Diabetes*, women who drink at least four cups of coffee a day are less than half as likely to develop diabetes as non-coffee drinkers. Drinking coffee increases levels of sex hormone-binding globulin (SHBG) in the blood. The protein regulates the body's sex hormones, testosterone and estrogen, which have long been thought to play a role in the development of type 2 diabetes. Study co-author Dr. Simin Liu, a UCLA professor of epidemiology and medicine, said the protein's presence in the blood indicated a diabetes risk. The study indicated such risk could be con-

Statin benefits low for those without heart disease

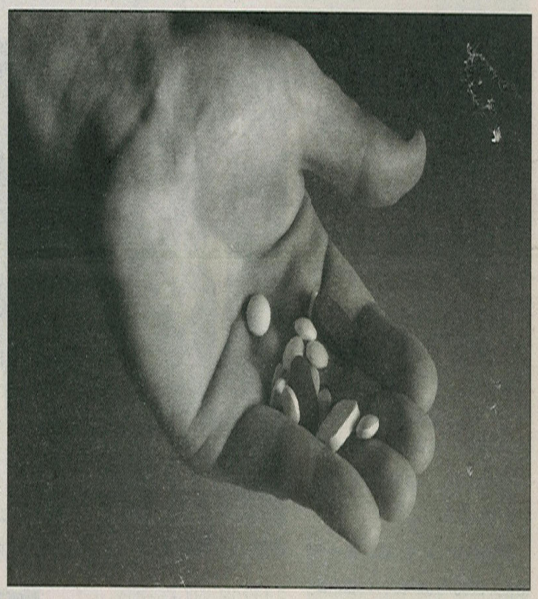
Charlotte Woodfield

Prescribing cholesterol-lowering statins poses risks to the mostly healthy, says a new report published by the Cochrane Library.

Traditionally, statins are given to those at high risk of heart attacks. Amy Thompson, senior cardiac nurse at the British Heart Foundation, said statins had huge benefits for people with heart and circulatory disease. "[For] those who are high risk they help to reduce the risk of heart disease including heart attacks."

Approximately 400,000 New Zealanders take statins to manage their cholesterol levels. Government drug funder Pharmac lowered the drug's price by 90% last year to allow wider access.

In the UK at present, statins are advised for anyone believed to have a 20% chance of developing heart disease in the next 10 years. New Zealand guidelines recommend statins be used when the risk of developing cardiovascular disease in the next five years rises to 15-20%, an equivalent figure



WEIGHING OPTIONS: New research has shown a range of side effects in test cases

American medical research group Mayo Clinic suggested statins could protect against prostate cancer and erectile dysfunction. Men who took statins were three times less likely to develop the inflammation which led to prostate cancer.

In this most recent study, published last year in the *British Medical Journal*, Nottingham University researchers examined more than two

for people with, or at high risk of heart disease, the benefits of statins far outweigh this risk." A report last year in the New Zealand publication *Best Practice Journal* agreed. "The absolute benefit of treatment is proportional to the underlying absolute risk."

The Cochrane Library study reviewed the evidence from 14 trials. According to a recent BBC News arti-

The Cochrane Library 2011, Issue 1

Statins for the primary prevention of cardiovascular disease (Review)

Taylor F, Ward K, Moore THM, Burke M, Davey Smith G, Casas JP, Ebrahim S

THE COCHRANE COLLABORATION®

14 Trials

72 Pages

Cochrane: Total Mortality: 16% Risk Reduction [0.73-0.96]

Analysis 2.1. Comparison 2 Mortality and Morbidity, Outcome 1 Total Mortality.

Review: Statins for the primary prevention of cardiovascular disease

Comparison: 2 Mortality and Morbidity

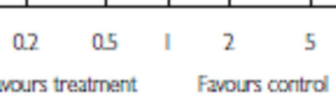
Outcome: 1 Total Mortality

Study or subgroup	Statin Therapy Group n/N	Usual Care or Placebo n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
ACAPS 1994	0/460	4/459		1.0 %	0.11 [0.01, 2.05]
Adult Japanese MEGA Study	57/3958	81/4051		18.5 %	0.72 [0.51, 1.01]
AFCAPS/TexCAPS 1998	80/3304	77/3301		17.8 %	1.04 [0.76, 1.41]
ASPEN 2006	44/959	40/946		9.3 %	1.09 [0.71, 1.65]
CARDS 2004	61/1428	82/1410		19.1 %	0.73 [0.53, 1.01]
KAPS 1995	4/214	5/212		1.2 %	0.79 [0.22, 2.91]
PREVEND IT 2004	10/433	8/431		1.9 %	1.24 [0.50, 3.12]
WOSCOPS 1997	106/3302	135/3293		31.2 %	0.78 [0.61, 1.01]
Total (95% CI)	**14058**	**14103**		**100.0 %**	**0.84 [0.73, 0.96]**

Total events: 362 (Statin Therapy Group), 432 (Usual Care or Placebo)

Heterogeneity: $Chi^2 = 7.57$, $df = 7$ ($P = 0.37$); $I^2 = 8\%$

Test for overall effect: $Z = 2.53$ ($P = 0.011$)



Cochrane: Total CHD Events: 18% Risk Reduction [0.65-0.79]

Analysis 2.4. Comparison 2 Mortality and Morbidity, Outcome 4 Total Number of CHD Events.

Review: Statins for the primary prevention of cardiovascular disease

Comparison: 2 Mortality and Morbidity

Outcome: 4 Total Number of CHD Events

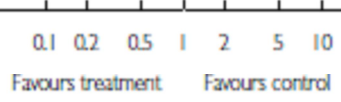
Authors *judgement* was not to use statins

Study or subgroup	Statin Therapy Group n/N	Usual Care or Placebo n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
ACAPS 1994	5/460	9/459		1.0 %	0.55 [0.19, 1.64]
Adult Japanese MEGA Study	184/3958	280/4051		30.2 %	0.67 [0.56, 0.81]
AFCAPS/TexCAPS 1998	163/3304	215/3301		23.5 %	0.76 [0.62, 0.92]
ASPEN 2006	72/959	75/946		8.2 %	0.95 [0.69, 1.29]
CAIUS 1996	3/151	2/154		0.2 %	1.53 [0.26, 9.03]
CARDS 2004	51/1428	77/1410		8.4 %	0.65 [0.46, 0.92]
HYRIM 2004	6/142	9/143		1.0 %	0.67 [0.25, 1.84]
PHYLLIS A 2004	0/126	3/127		0.4 %	0.14 [0.01, 2.76]
PHYLLIS B 2004	1/128	0/127		0.1 %	2.98 [0.12, 72.39]
WOSCOPS 1997	174/3302	248/3293		27.1 %	0.70 [0.58, 0.84]
Total (95% CI)	**13958**	**14011**		**100.0 %**	**0.72 [0.65, 0.79]**

Total events: 659 (Statin Therapy Group), 918 (Usual Care or Placebo)

Heterogeneity: $Chi^2 = 7.01$, $df = 9$ ($P = 0.64$); $I^2 = 0.0\%$

Test for overall effect: $Z = 6.61$ ($P < 0.00001$)



Statin Therapy?

It's all about Assessing CVS Risk:

The more the risk, the more the benefit and

The less the risk, the less the benefit

Cholesterol Treatment Trialists (CTT) Collaborators 2010 Paper

Lancet 2010; 376: 1670-81

Efficacy and safety of more intensive lowering of LDL cholesterol: a meta-analysis of data from 170 000 participants in 26 randomised trials

*Cholesterol Treatment Trialists' (CTT) Collaboration**

Lancet 2010; 376: 1670–81

Published Online November 9, 2010 DOI:10.1016/S0140-6736(10)61350-5

See Comment page 1622

See Articles page 1658

*Collaborators are listed at the end of the paper

Correspondence to: Clinical Trial Service Unit and Epidemiological Studies Unit (CTSU), Richard Doll Building, Old Road Campus, Roosevelt Drive, Oxford OX3 7LF, UK ctt@ctsu.ox.ac.uk

or National Health and Medical Research Council (NHMRC)

Summary

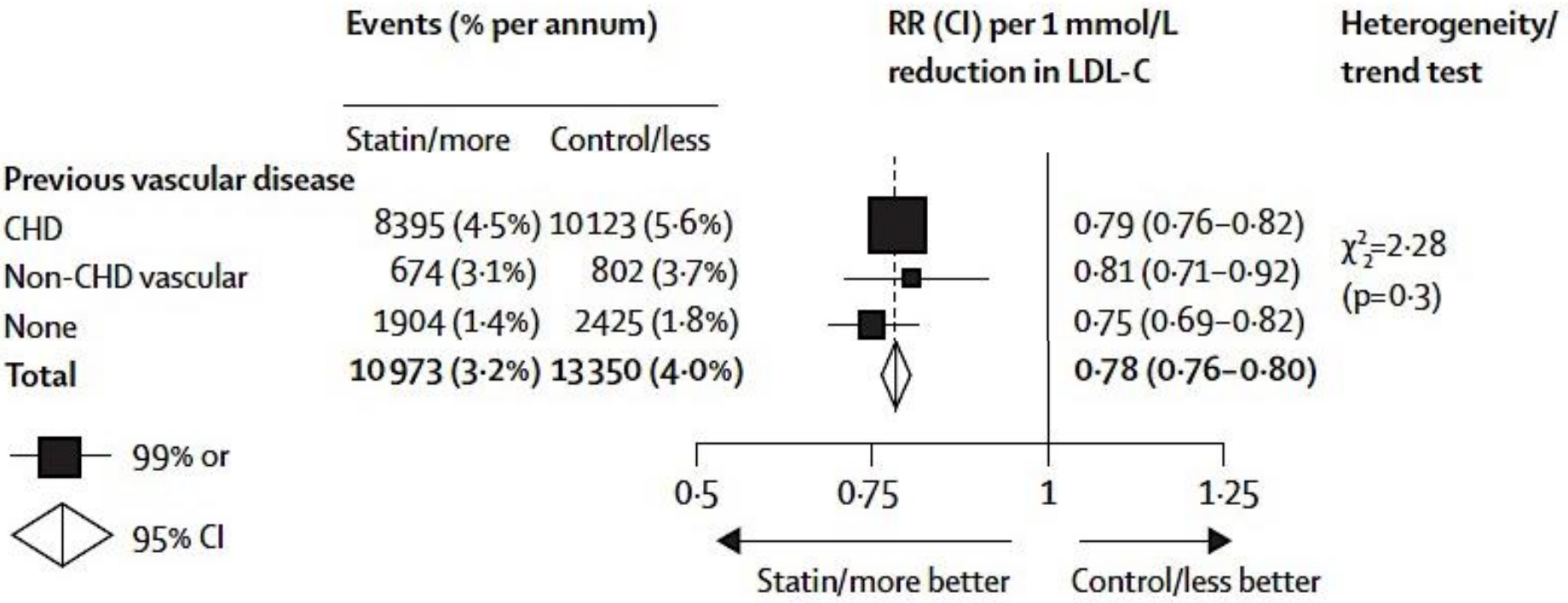
Background Lowering of LDL cholesterol with standard statin regimens reduces the risk of occlusive vascular events in a wide range of individuals. We aimed to assess the safety and efficacy of more intensive lowering of LDL cholesterol with statin therapy.

Methods We undertook meta-analyses of individual participant data from randomised trials involving at least 1000 participants and at least 2 years' treatment duration of more versus less intensive statin regimens (five trials; 39 612 individuals; median follow-up 5·1 years) and of statin versus control (21 trials; 129 526 individuals; median follow-up 4·8 years). For each type of trial, we calculated not only the average risk reduction, but also the average risk reduction per 1·0 mmol/L LDL cholesterol reduction at 1 year after randomisation.

Findings In the trials of more versus less intensive statin therapy, the weighted mean further reduction in LDL cholesterol at 1 year was 0·51 mmol/L. Compared with less intensive regimens, more intensive regimens produced a highly significant 15% (95% CI 11–18; p<0·0001) further reduction in major vascular events, consisting of separately significant reductions in coronary death or non-fatal myocardial infarction of 13% (95% CI 7–19; p<0·0001), in coronary revascularisation of 19% (95% CI 15–24; p<0·0001), and in ischaemic stroke of 16% (95% CI 5–26; p=0·005). Per 1·0 mmol/L reduction in LDL cholesterol, these further reductions in risk were similar to the proportional reductions in the trials of statin versus control. When both types of trial were combined, similar

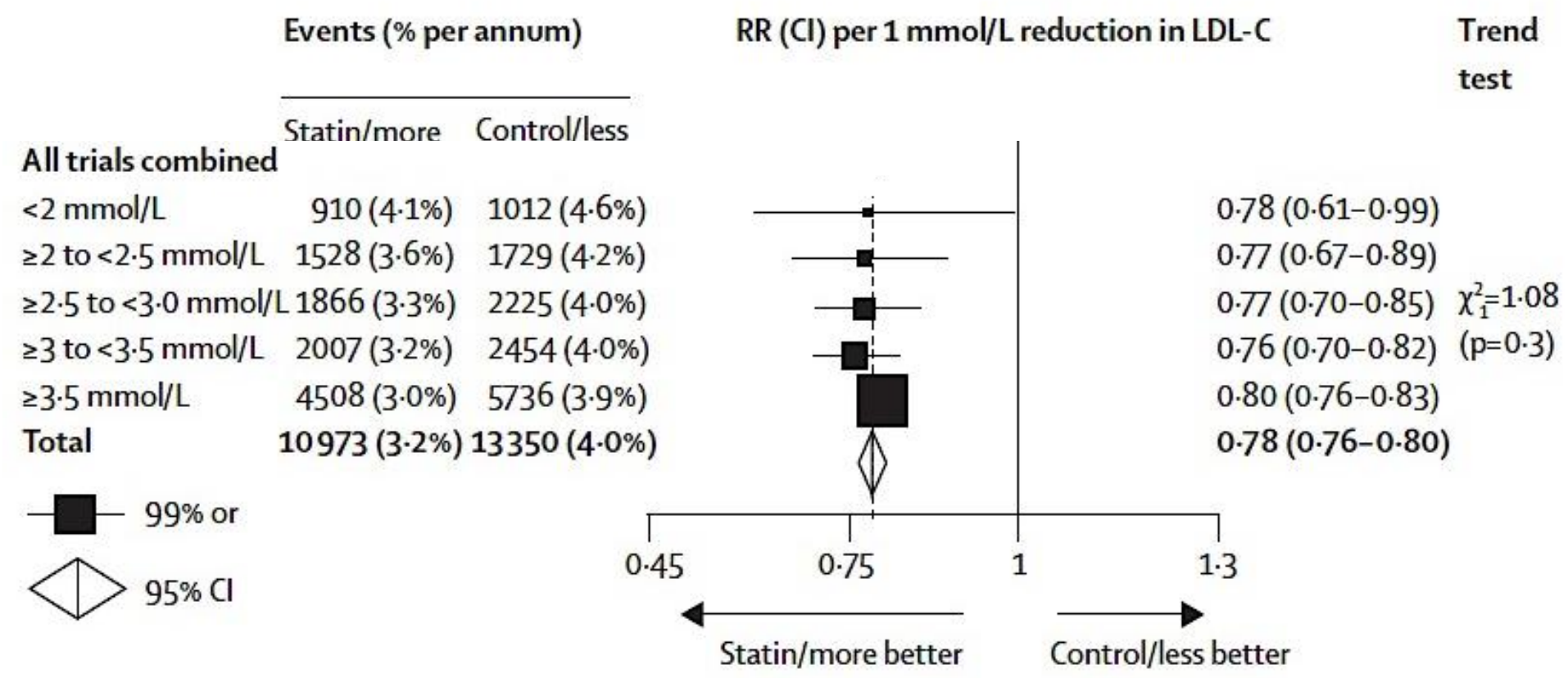
THE Statin Paper

Effects of statins on major vascular events for subjects with and without CHD



CTT Collaboration, *Lancet*, 2010;376:1670-81

Effects of statins on major vascular events by LDL cholesterol level before treatment



CTT Collaboration, *Lancet*, 2010;376:1670-81

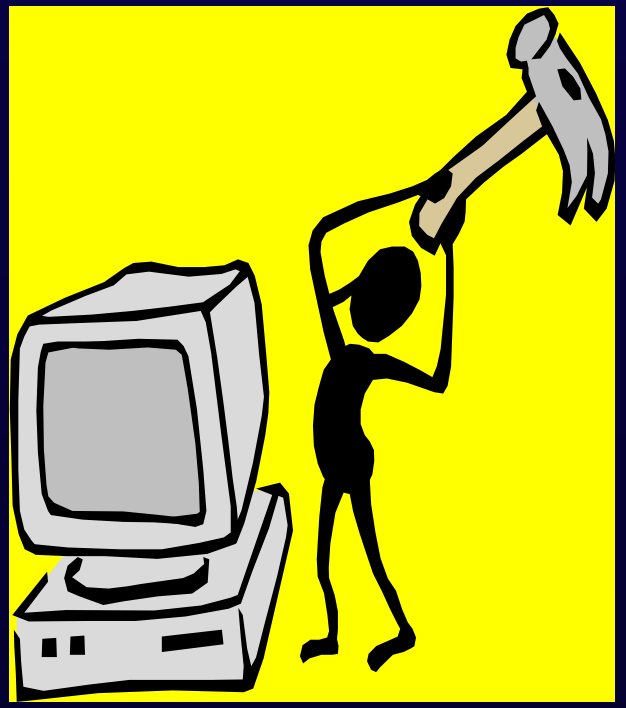
CTT Lancet 2010 Interpretation

Lancet 2010; 376: 1670-81

- Statin therapy *safely* reduces 5-year incidence of major CVS events by *'just over'* 1/5 per 1.0 mmol/l reduction in LDL cholesterol
- *There was no evidence of any threshold within the cholesterol range studied, suggesting that reduction of LDL cholesterol by 2-3mmol/l would reduce risk by about 40-50%*

Vascular Prevention Strategies: ‘Primary’ or ‘Secondary’

- As we all have some coronary atheroma by the age of 50 years
- The distinction between ‘primary’ & ‘secondary’ prevention is convenient, for patient management, but not scientifically accurate.

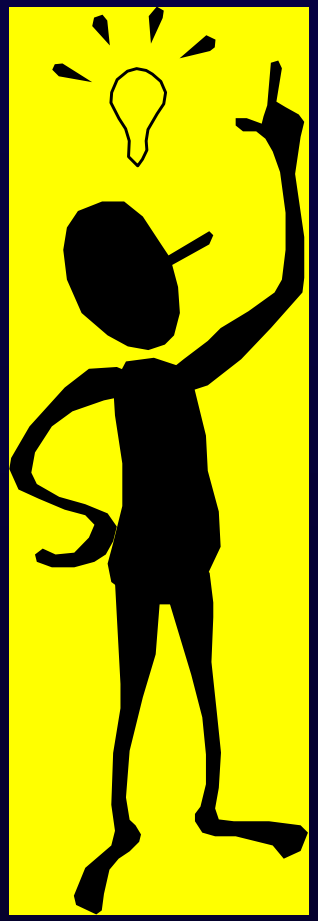


Primary or Secondary Prevention?

Q. “What is the difference between primary & secondary prevention of CVS Disease?”

A. “About 2 seconds!”

[The time it takes for a plaque to rupture]



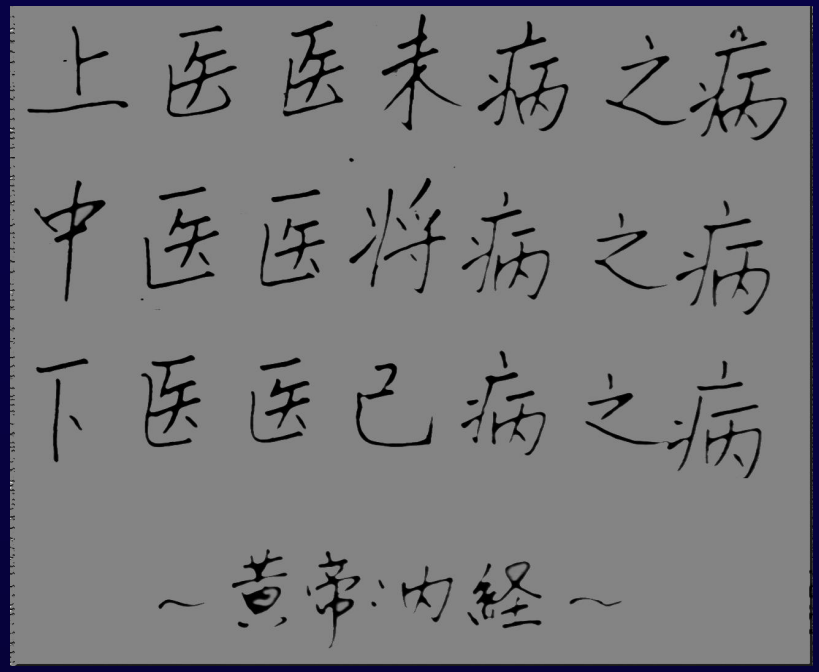
Bullet Points 6

- Encourage high risk patients to take a statin
- Check blood tests for lipids, CK, LFTs 4 weeks after starting and after any change in dose
  - Patients expect to be carefully monitored if starting preventative therapy
  - Encourages trust and interest
- Some patients may be helped by a Cardiology assessment, including a Calcium score/CT Cardiac angiogram
  - ‘Individualised’ CVS risk assessment is likely to be the future of this area

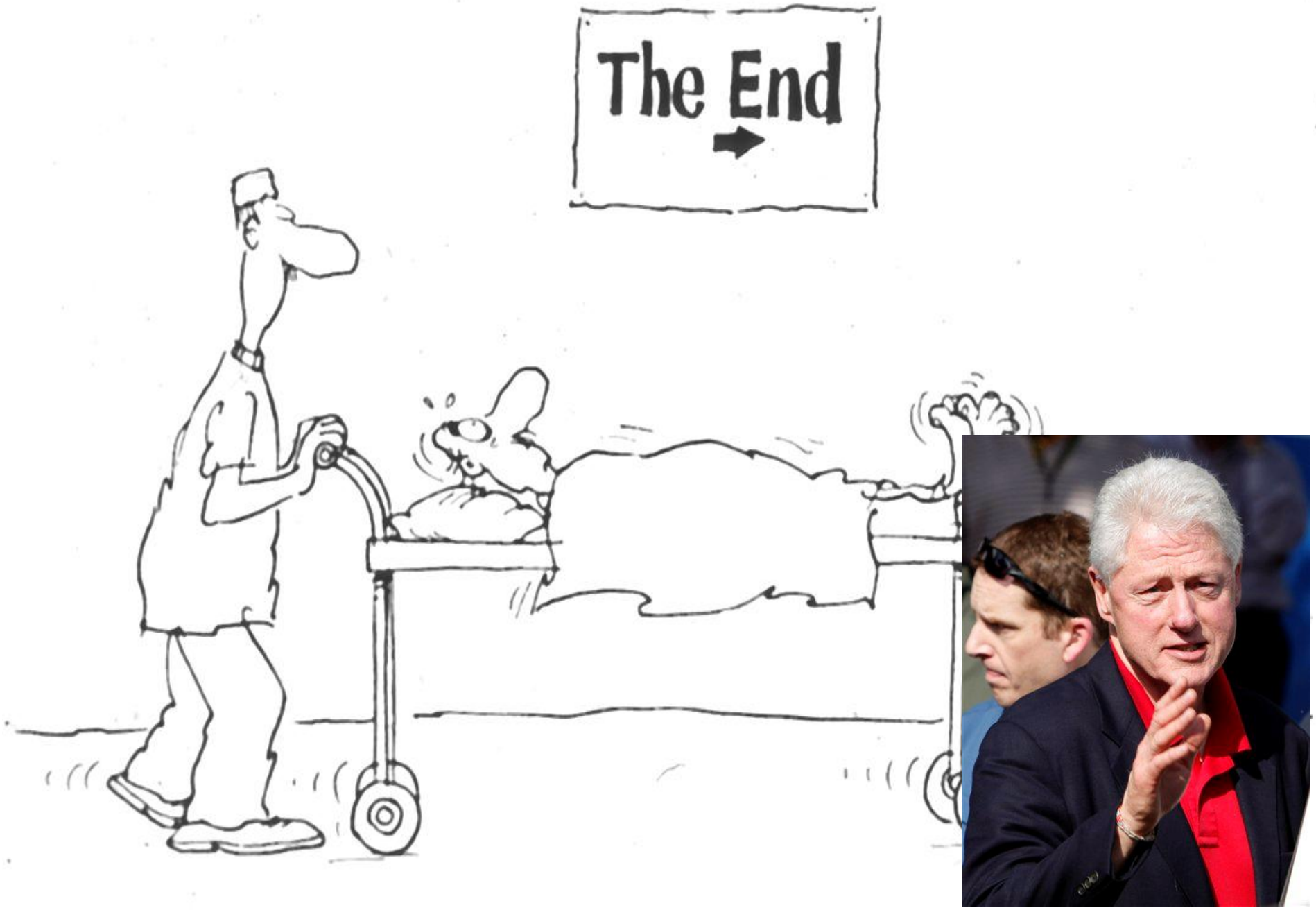
Bullet Points 7

- Remain a Clinician
  - Avoid Guideline driven ‘recipe’ medicine [it doesn’t work]
- Some patients may be helped by a Cardiology assessment
  - Including a Calcium score/CT Cardiac angiogram
- ‘Individualised’ CVS risk assessment, with Calcium scoring/CT Cardiac angiography is likely to be the future
  - It focuses the problem to those who *actually develop* significant atherosclerosis

SCCT International Scientific Meeting: Las Vegas 14-17 July 2010



Superior doctors prevent the disease.
Mediocre doctors treat the disease
before evident.
Inferior doctors treat the full-blown disease.
--Huang Dee: Nai-Ching
(2600 BC First Chinese Medical Text)

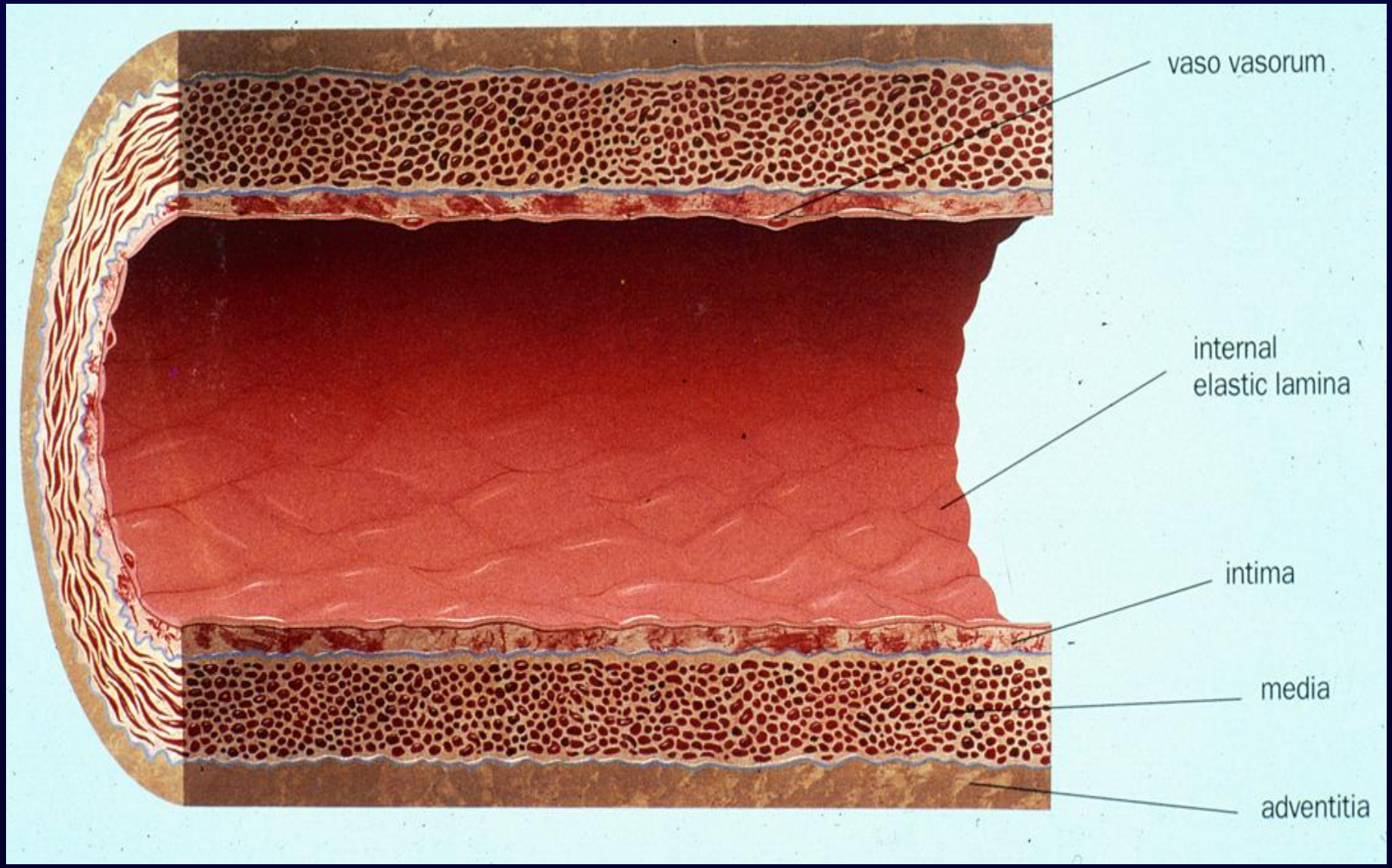

The End

Framingham Heart Study:
Basic CVS Risk Model

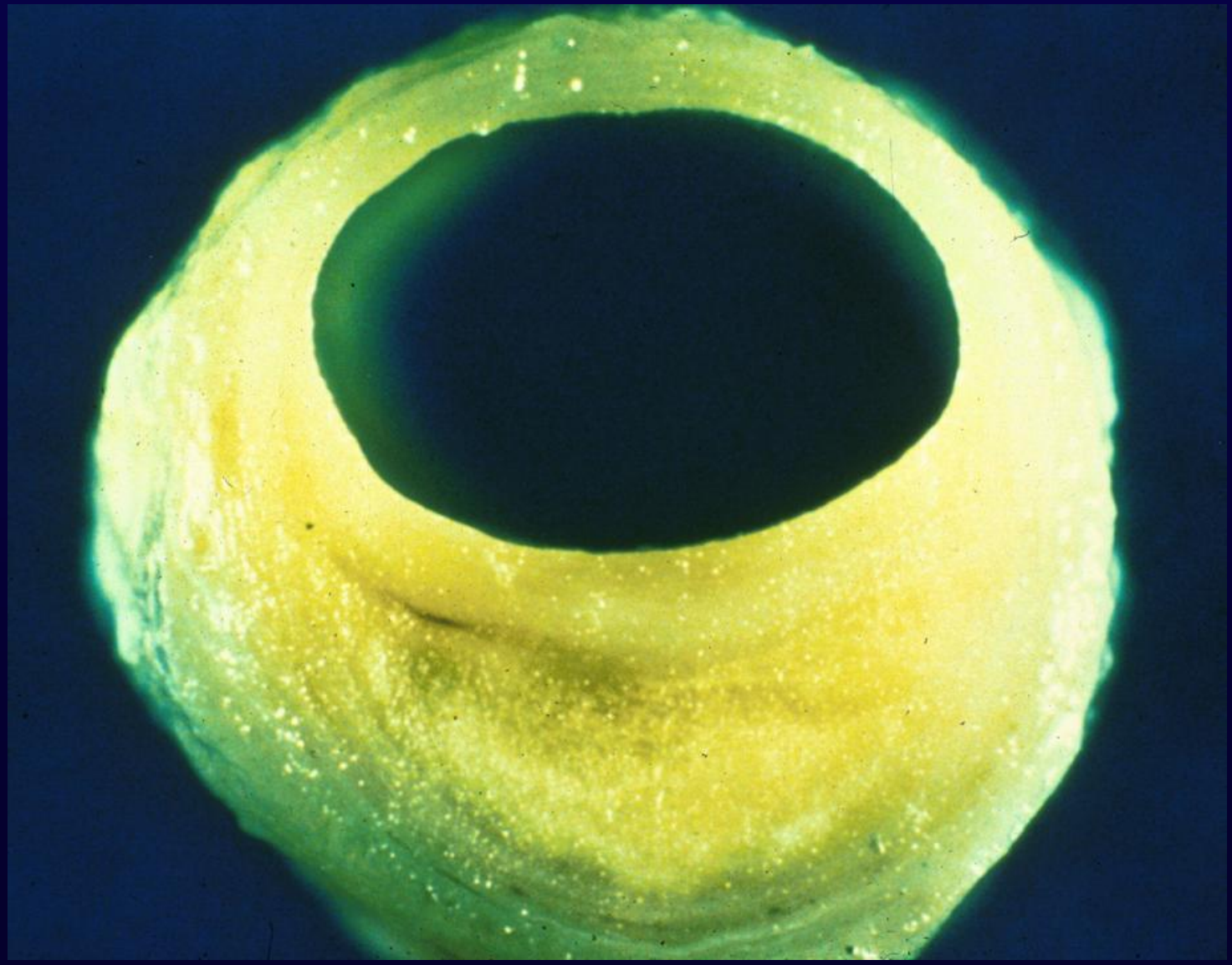
Anderson et al. Am Heart J 1990; 121; 293-8.

- Selected subjects from the ‘original’ and ‘offspring’ Framingham cohort used: 5573 subjects
- Aged 30 to 74 years at baseline examination from 1968-1975 & free from CVS disease
  - At least 12 years of FU achieved, from baseline
  - Endpoints: MI, CHD Death, angina, ‘coronary insufficiency’, stroke, TIA, ‘congestive heart failure’, ‘peripheral vascular disease’ (Recorded by Research Nurse)
  - 4 to 12 years CVS risk could be assessed
- Anderson equation used for 1996 NZ CVS Risk Guidelines
  - 5-Year CVS Risk advocated

Normal Coronary Artery

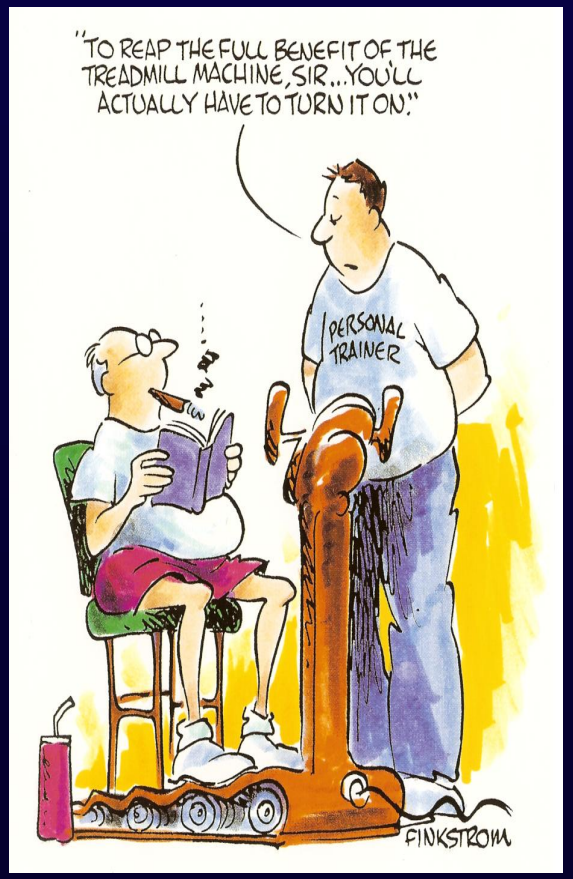


Moderate Coronary Stenosis: Approx 50%



Vascular Prevention Strategies: ‘Primary’ or ‘Secondary’

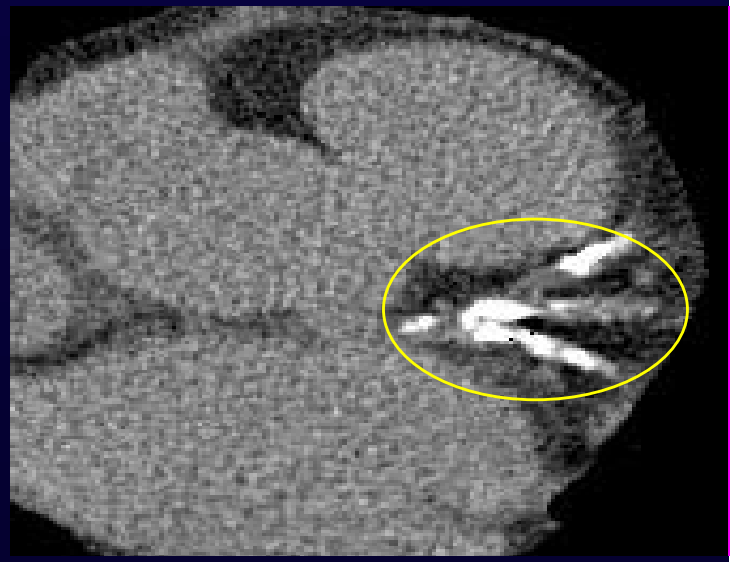
- We all have some coronary atheroma (intimal thickening) by the age of 50 years
  - (IVUS Studies)
- There is a spectrum of the severity of atheroma in people
- The distinction between ‘primary’ & ‘secondary’ prevention is only convenient for patient management
  - Not an accurate way to understand CVS risk
- There is a spectrum of CVS risk in people
  - The higher the risk, the more benefit in being pro-active with risk factor management


"TO REAP THE FULL BENEFIT OF THE TREADMILL MACHINE, SIR... YOU'LL ACTUALLY HAVE TO TURN IT ON."
PERSONAL TRAINER
FINKSTROM

Coronary Calcium Score: Agatston Method

Agatston et al JACC 1990;15:827-832.

- 30-40 contiguous slices obtained at 3mm intervals down the heart to include the entire coronary tree (ECG ‘gated’)
- ‘Agatston score’: Algorithm using *density* of calcium (Hounsfield Units) and the *volume* of calcified area
- ‘Effective’ radiation dose of <1mSv/Scan (Mammography approx 1mSv)



St Francis Heart Study

Arad et al. JACC 2005;46: 158-65, 166-72.

St Francis Heart Hospital, New York, 1st prospective, population-based study:

- 4,613 asymptomatic people aged 50-70 years FU at 4.3 years,
- Mean age 59 (± 6) years, 65% male, BMI 28 (±5), LDL 3.6mmol/l, 10% smokers, 6% diabetes, 34% hypertension, Median CRP 1.84 (0.89-3.96)
- 119 CVS events
- Pts with a CVS Event had a higher CS (Agatston units) at baseline:
  - median 384 (127-800) vs 10 (0-86) $p<0.0001$

St Francis Heart Study

Arad et al. JACC 2005;46: 158-65, 166-72.

Using a Coronary Calcium Score (CS) threshold of ≥ 100 Agatston units RR (95%CI):

- 9.6 (6.7 – 13.9) for all CVS events
- 11.1 (7.3 – 16.7) for all CAD events
- 9.2 (4.9 – 17.3) for all non-fatal MI & death

Calcium Score (CS) predicted:

- CVS events independently of Framingham Risk factors and CRP (p=0.004)
- Was superior to the Framingham Risk Equation (Receiver-operator curve 0.79 ± 0.03 vs 0.69 ± 0.03, p=0.0006)
- Enhanced stratification of Framingham Risk categories, low, intermediate, high risk (p<0.0001)

Results

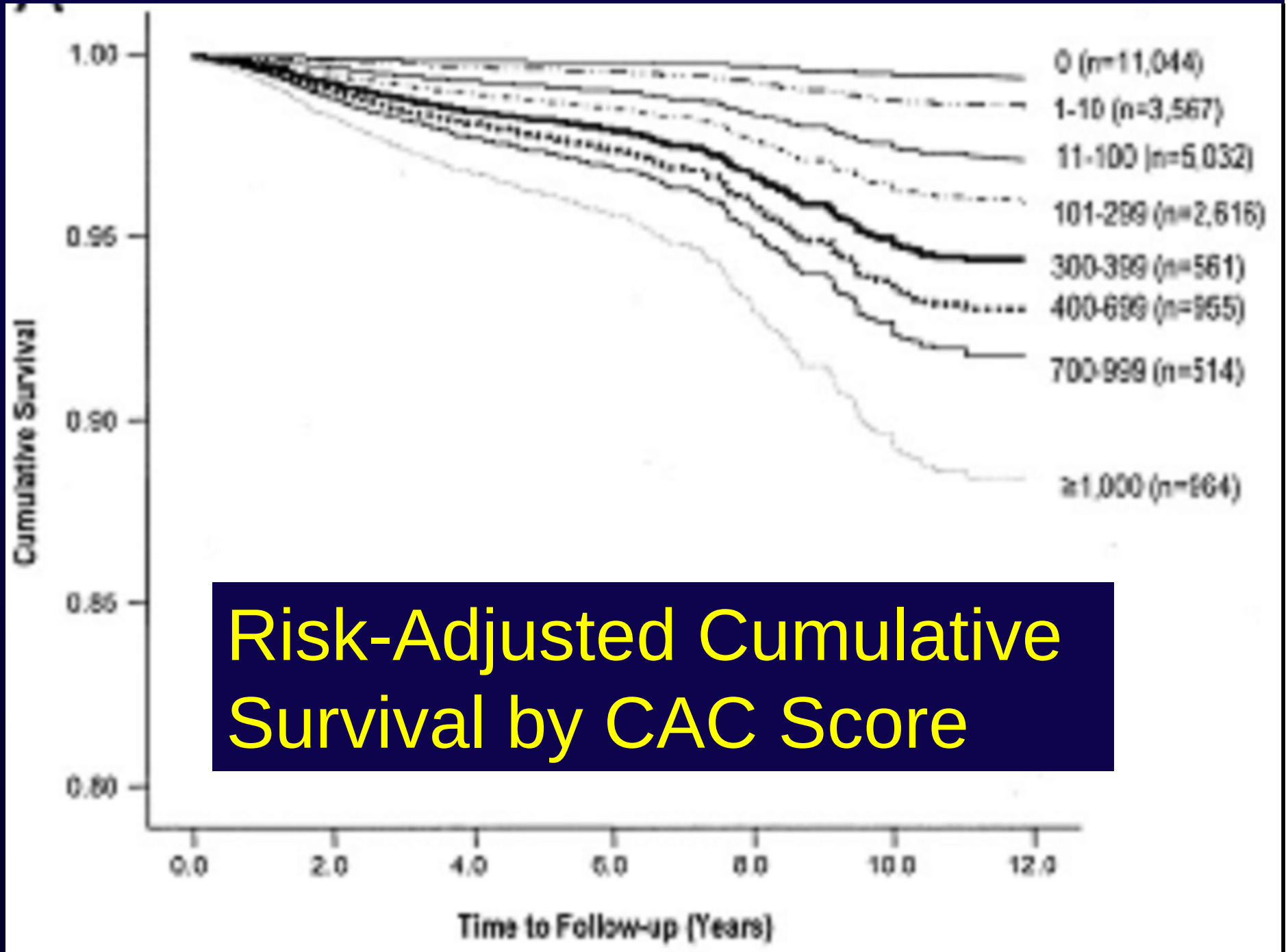
"During a mean follow-up of 6.8 +/-3 years, the death rate was 2% (510 deaths).

The CAC Score was an independent predictor of mortality in a multivariable model

- controlled for age, gender, ethnicity, and cardiac risk factors, $p < 0.0001$.

Risk-Adjustment Cumulative Survival by CAC Score

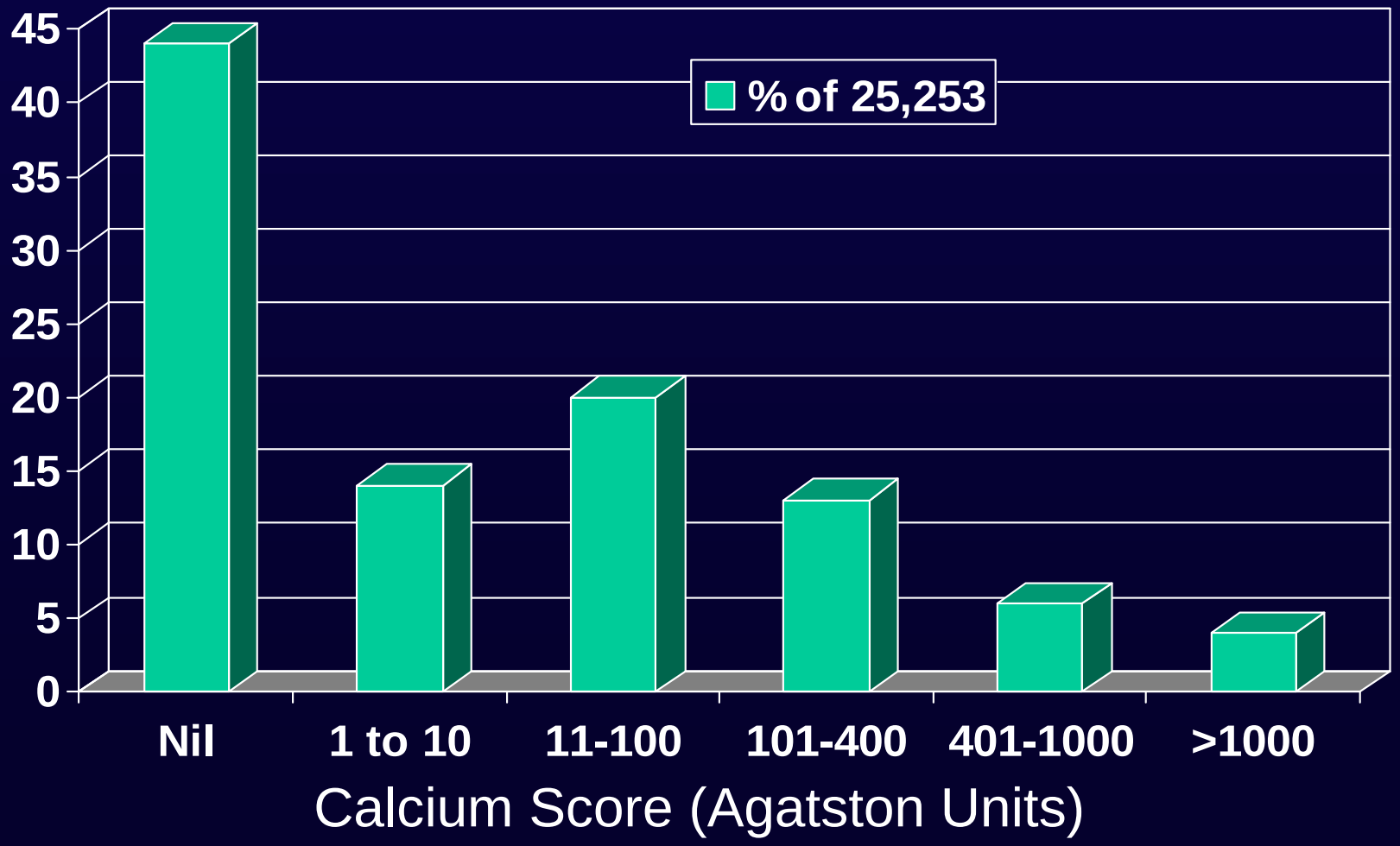
- Age
- Hypercholesterolaemia
- Diabetes M
- Smoking
- Hypertension
- FH Premature CHD
  - (Men < 55, Women < 65 Years)



Risk-Adjusted Cumulative Survival by CAC Score

Largest Study (25,253 Patients): Range of Calcium Scores

Budoff et al 2007 JACC

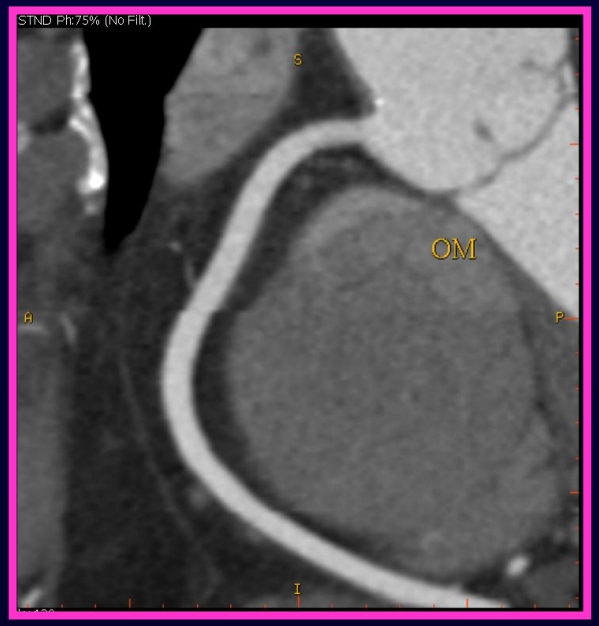


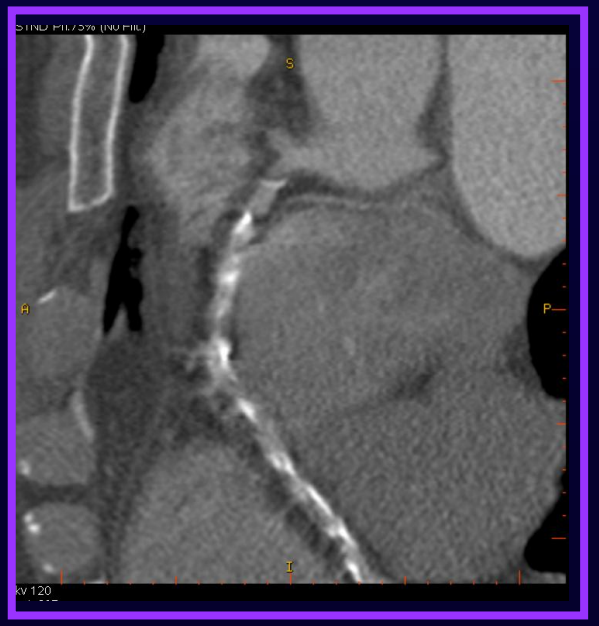
High Calcium Scores in Patients with low Framingham Risk of CVS Disease: The Auckland Experience of 1000 Consecutive Patients at Mercy Hospital

CJ Ellis, ME Legget, C Edwards, N Van Pelt, JA Ormiston, J Christiansen, H Winch, M Osborne, G Gamble.

	Patient A	Patient B
Framingham Risk	Low	Low [BUT Strong FH]
Calcium score	Zero	867 Agatston U: > 90th Percentile

MULTISLICE CT CORONARY ANGIOGRAPHY: Risk Assessment





Coronary Calcium Scoring: the Logical Way to Assess CVS Risk? : Summary

- Atherosclerosis is a complex ageing process
  - Genetic & environmental factors are important
  - Assessment of CVS risk is difficult
- Epidemiological *population* studies do not accurately translate to an *individual's* risk of CVS disease, particularly in the young
- Various risk factors are being studied
  - EG. Inflammatory markers, reflecting markers of plaque rupture
- The current, International trend is to 'individualise risk'
  - Add: 'Modern' Risk Factors
  - Add: Calcium score: It does seem logical!
  - Further momentum is likely to come from other CT cardiac angiogram studies of atheromatous plaque burden

Which Test is Appropriate?

CT Cardiac Angiogram

- Equivocal symptoms
- Equivocal ECG changes
- $1600
- (Usually) SX-funded
- Excellent test for selected patients
- ‘Rule Out’ significant coronary disease

Calcium Score (Alone)

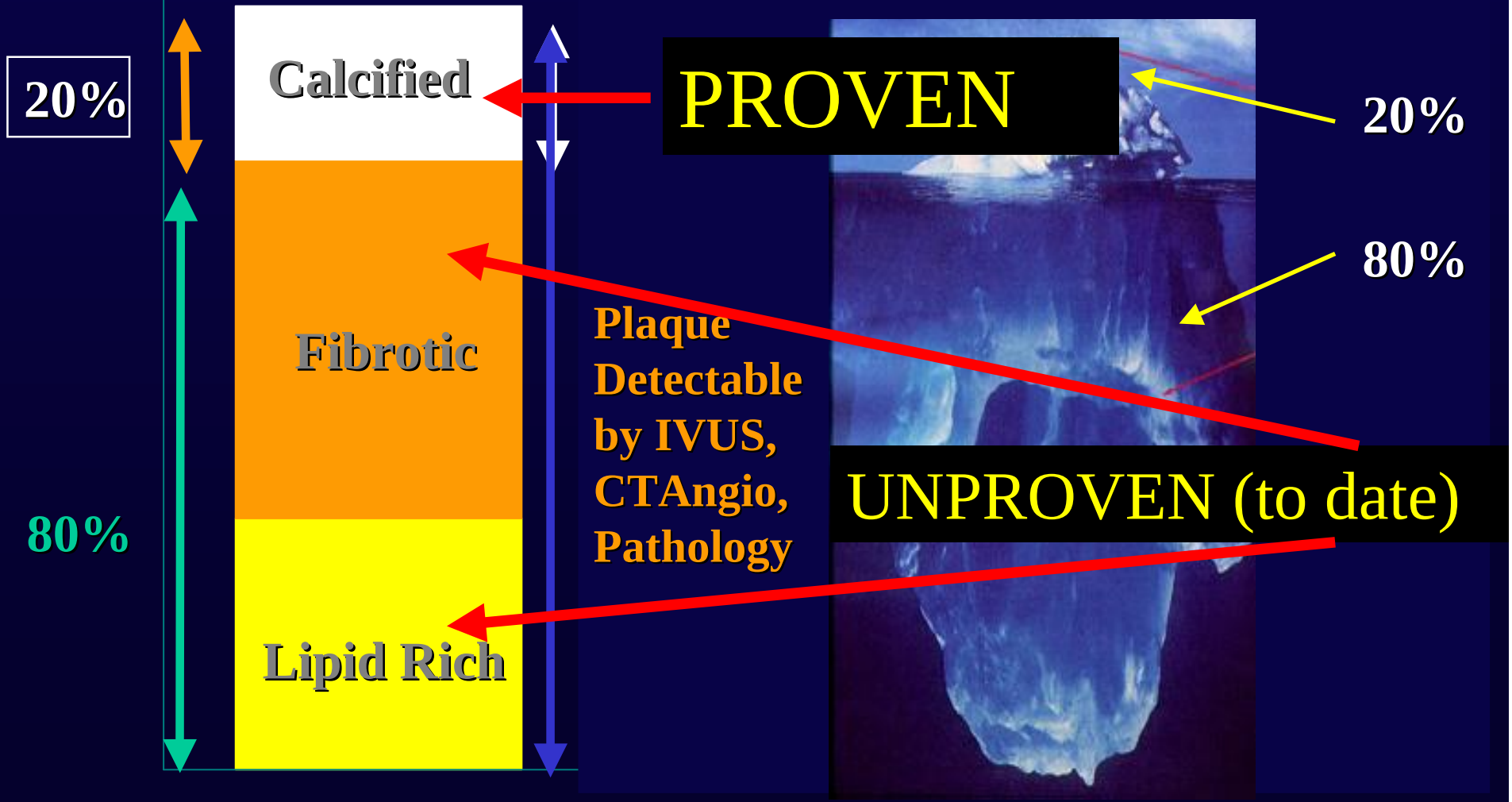
- Asymptomatic (ONLY)
- $500
- NOT SX-funded
- ‘Screening’
- The most accurate CVS risk assessment tool

Some Problems with End-Points in the Framingham CVS Risk Equation

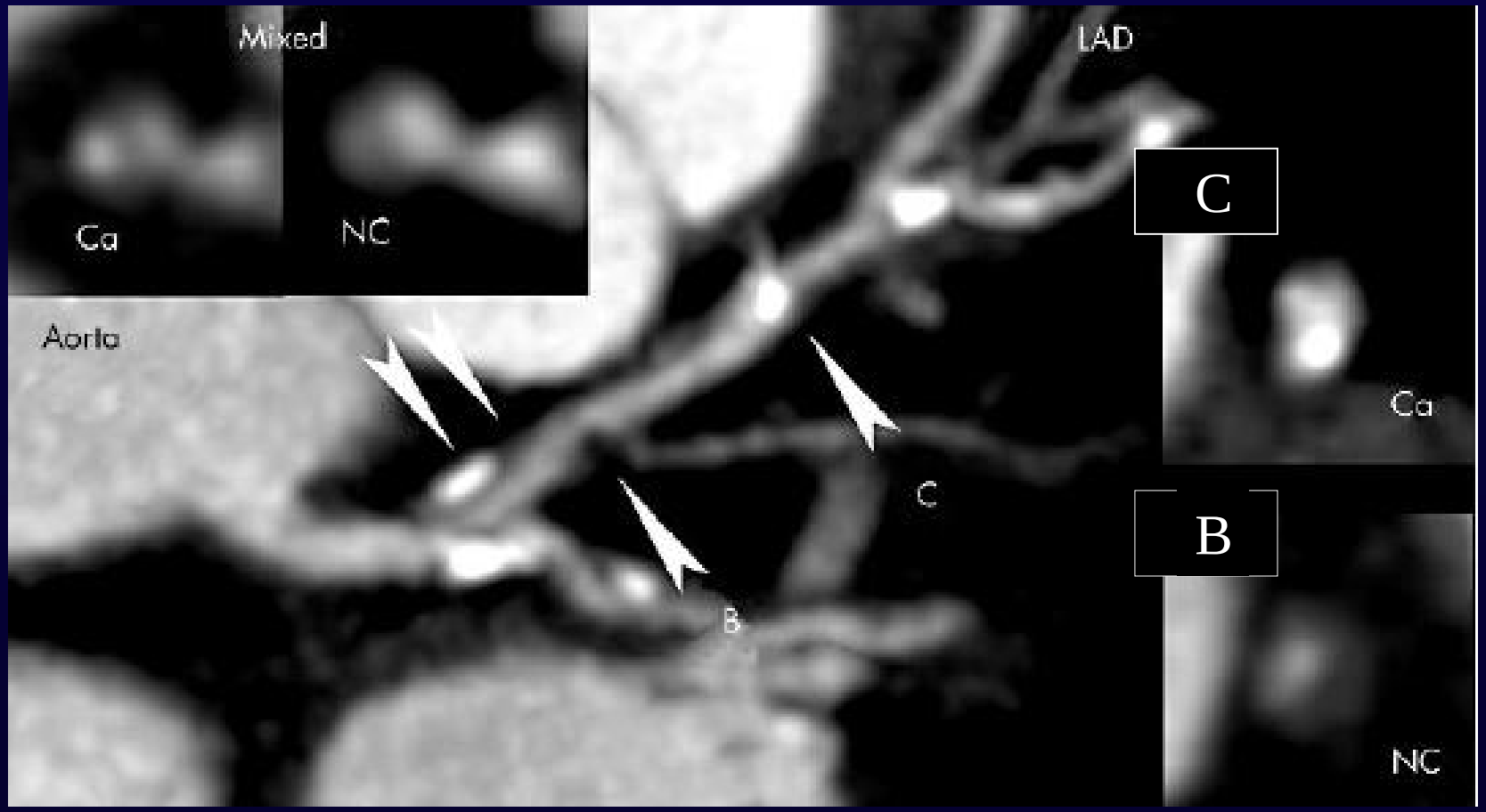
- Few Endpoints in NZ Equation
  - 383 in total [although carefully collected]
- Endpoints:
  - Myocardial Infarction, New Angina
  - Ischaemic stroke, Transient ischaemic attack
  - Peripheral vascular disease
  - Congestive heart failure
  - Cardiovascular-related death
- Problems with definitions, accuracy, how/who assessed these 30-50 years ago
- Number & Type of Endpoints never published
- No Confidence limits around data points

Correct concept, Not ‘Accurate’ Science

Coronary Calcium Score & Coronary Artery Plaque :Risk Assessment



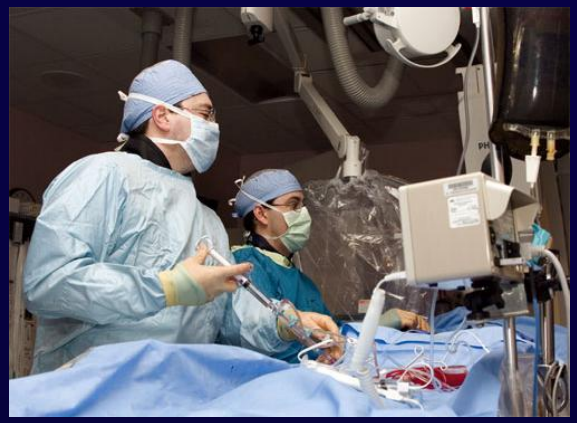
CT Angiography: Calcified and non-calcified plaques

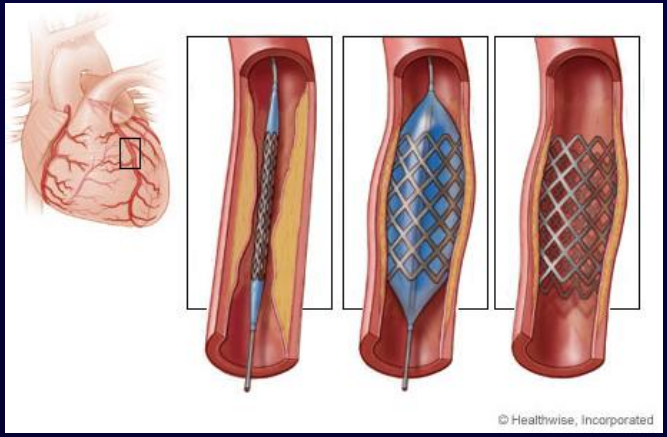


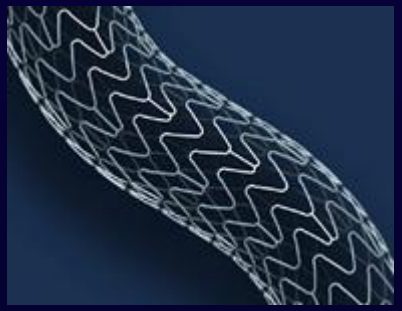
Contribution to CVS Risk is Unclear at this stage

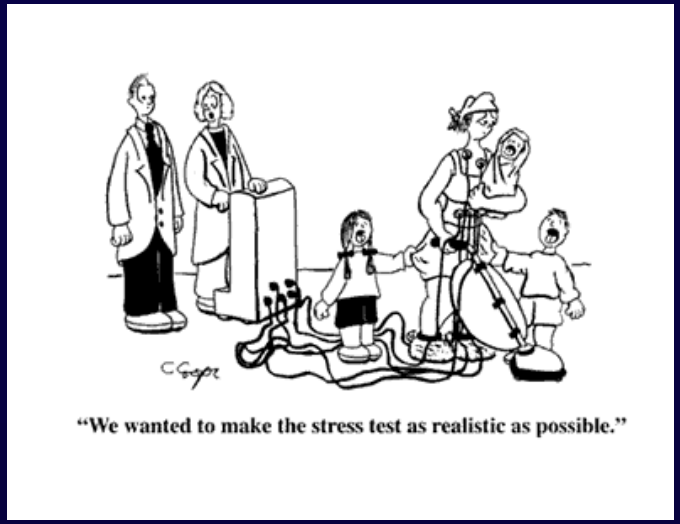

Be Heart Healthy...
Sleep With A
Cardiologist.


©Marty Bucella
www.martybucella.com
"You know, if I do give you a heart, you'll have to start watching your cholesterol."

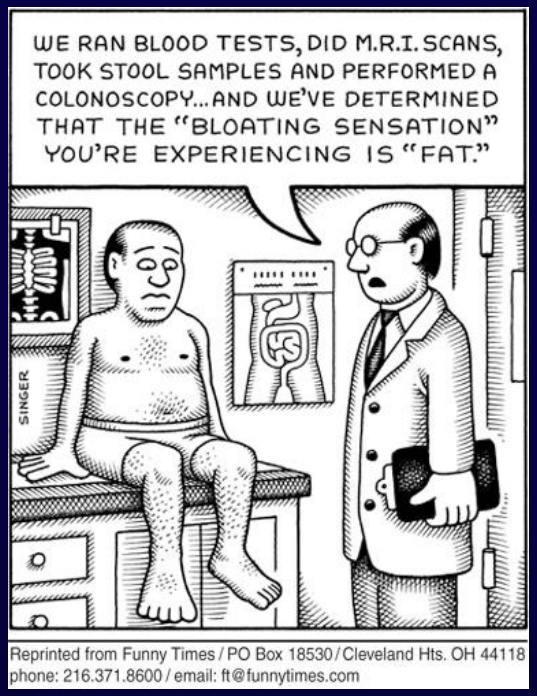



© Healthwise, Incorporated

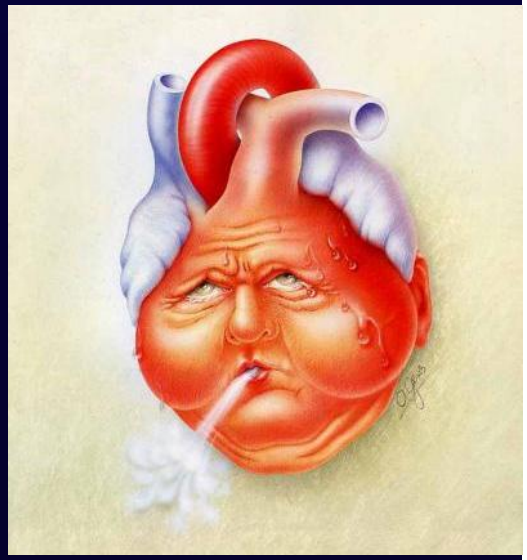


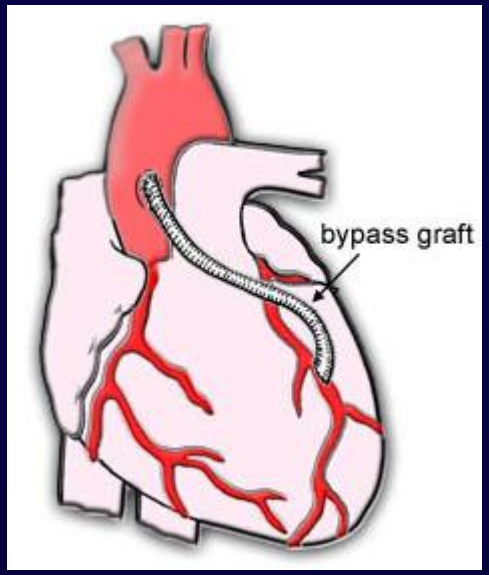


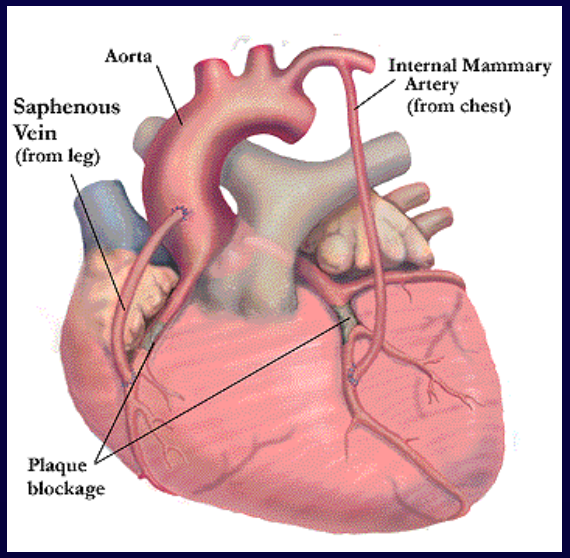
"We wanted to make the stress test as realistic as possible."

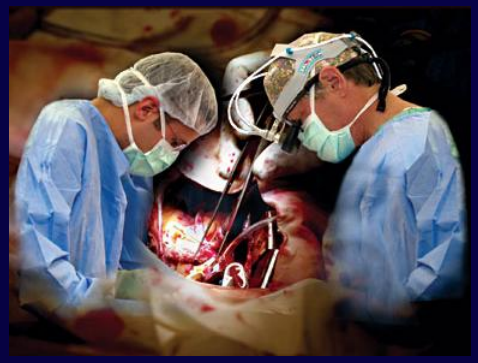


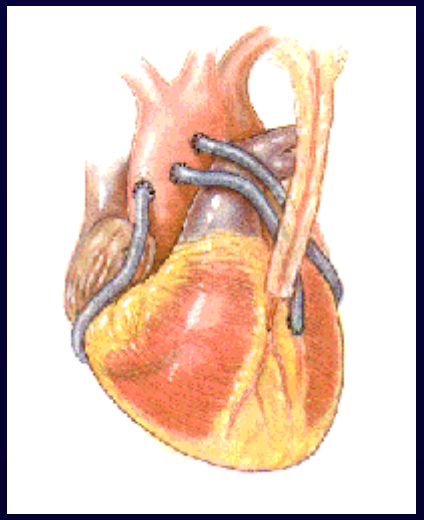
"Off hand, I'd say you're suffering from an arrow through your head, but just to play it safe, I'm ordering a bunch of tests."

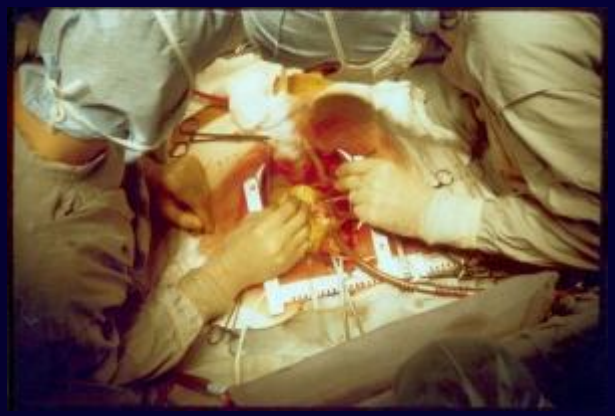



bypass graft


Aorta
Internal Mammary Artery (from chest)
Saphenous Vein (from leg)
Plaque blockage

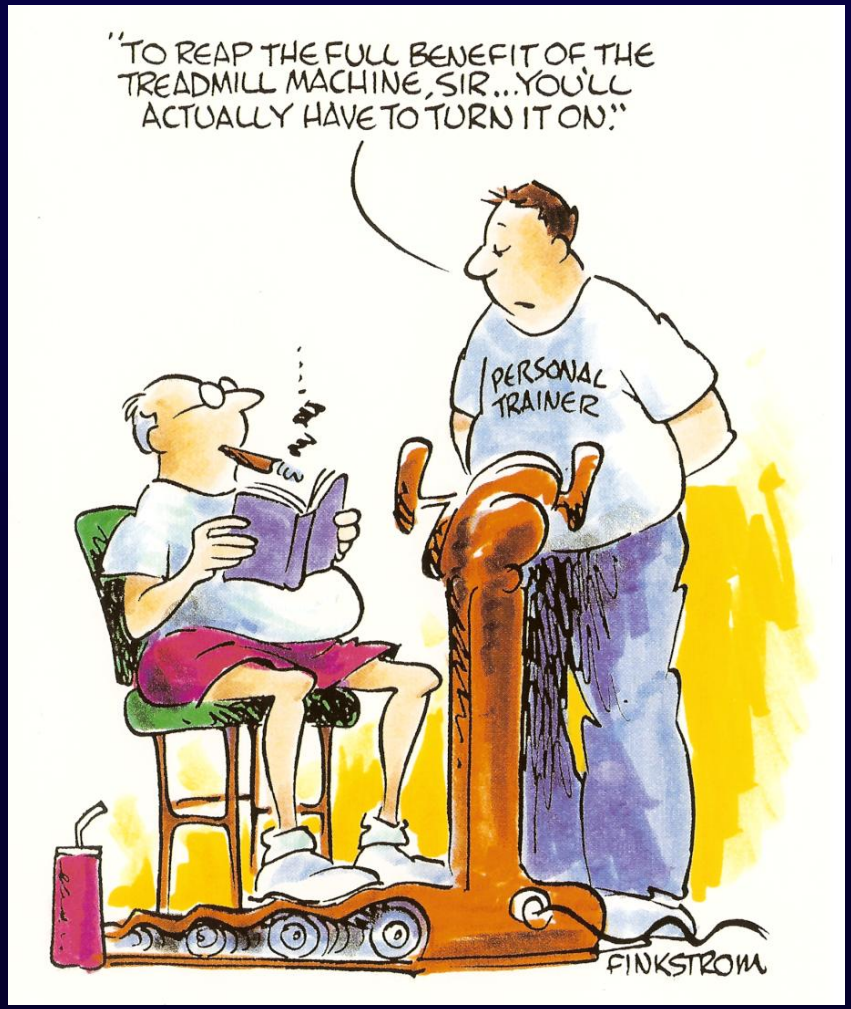


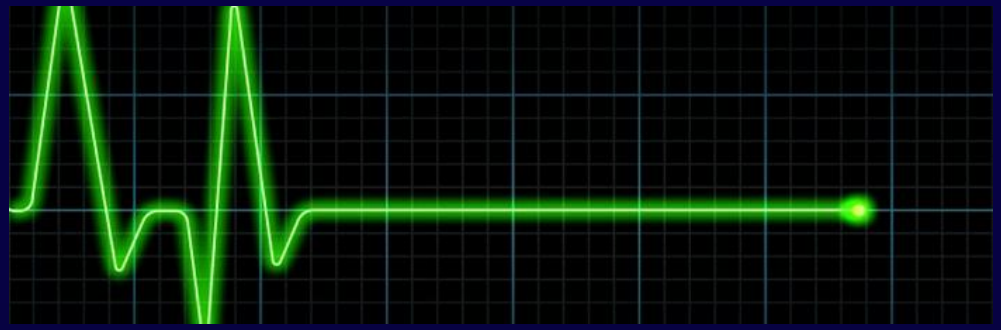




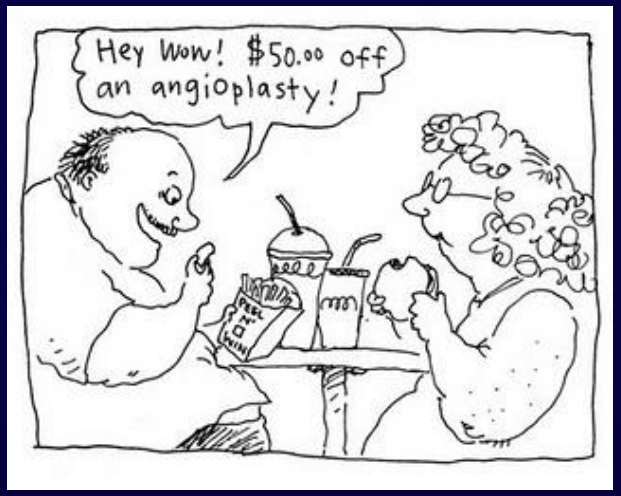
How to (Try to) Prevent CVS Events in Your Patients

- Businessman age 60 years
  - Crescendo angina 2003
  - Seen urgently, angiogram that evening
  - OM Stent, statin, aspirin, ACE
  - 2004 stopped FU, no statin……
- Businessman age 67 years
  - This week CCU, ACH
  - VF Arrest in ED, ACH…..23.30
  - Left main plaque rupture, LAD occluded, Circumflex severe
  - Stents, POBA, survival…...01.30
  - Doctor exhaustion!






I BEAT
ANOREXIA
This image is hosted on
ebaumsworld.com


Hey Wow! $50.00 off
an angioplasty!

Definition of CVS Disease: End Points

Framingham (Described)

[n=383:Type unknown]

- Myocardial Infarction, Angina, 'coronary insufficiency'
- Ischaemic stroke, Transient ischaemic attack
- Peripheral vascular disease
- 'Congestive heart failure'
- Cardiovascular-related death

PREDICT (ICD 10 AM Codes)

[n=2327:total, n=1374: 1st CVS]

- Coded by house surgeon & hospital coders
- ? Accuracy

The 2 Studies endpoints are *very* different *and* collected differently

Coronary Calcium & Coronary Events: MESA Study NEJM 2008;358:1336-45

Study

- Multi-Ethnic Study of Atherosclerosis (MESA: NHBLI Funded) investigates the prevalence, correlates and progression of subclinical CVS disease (Calcium score)
- Population-based sample from 6 urban communities (n=6722), no clinical CVS disease at entry:
  - White (38.6%)
  - Black (27.6%)
  - Hispanic (21.9%)
  - Chinese (11.9%)
- Median 3.8 years FU, 162 coronary events, 89 ‘major’ (MI/death from IHD)

CTT 2010 Lancet Paper. *Also* www.ctsu.ox.ac.uk/projects/ctt

	Number of patients	Treatment comparison (mg per day)	Median follow-up in survivors (years)*	Baseline LDL-C (mmol/L)	LDL-C difference at 1 year (mmol/L)	Women (%)	Diabetes (%)	Prior CHD (%)	Other vascular disease (%)†	No prior vascular disease (%)‡
More versus less statin										
PROVE-IT	4162	A80 vs P40	2·1	2·62§	−0·65	911 (22%)	734 (18%)	4162 (100%)	328 (8%)	0
A to Z	4497	S40 then S80 vs placebo then S20	2·0	2·09§	−0·30	1100 (24%)	1059 (24%)	4497 (100%)	479 (11%)	0
TNT	10 001	A80 vs A10	5·0	2·52	−0·62	1902 (19%)	1501 (15%)	10 001 (100%)	1537 (15%)	0
IDEAL	8888	A40–80 vs S20–40	4·8	2·64§	−0·55	1702 (19%)	1069 (12%)	8888 (100%)	971 (11%)	0
SEARCH	12 064	S80 vs S20	7·0	2·50	−0·39	2052 (17%)	1267 (11%)	12 064 (100%)	1062 (9%)	0
Subtotal (5 trials)	39 612	NA	5·1‖	2·53‖	−0·51‖	7667 (19%)	5630 (14%)	39 612 (100%)	4377 (11%)	0
Statin versus control										
SSSS	4444	S20–40 vs placebo	5·4	4·88	−1·77	827 (19%)	202 (5%)	4444 (100%)	126 (3%)	0
WOSCOPS	6595	P40 vs placebo	4·8	4·96	−1·07	0	76 (1%)	338 (5%)	193 (3%)	6096 (92%)
CARE	4159	P40 vs placebo	5·0	3·58	−1·03	576 (14%)	586 (14%)	4159 (100%)	0	0
Post-CABG	1351	L40–80 vs L2·5–5	4·3	4·02	−1·07	102 (8%)	116 (9%)	1351 (100%)	37 (3%)	0
AFCAPS/TexCAPS	6605	L20–40 vs placebo	5·2	3·89	−0·94	997 (15%)	155 (2%)	10 (<1%)	9 (<1%)	6586 (>99%)
LIPID	9014	P40 vs placebo	6·0	3·88	−1·03	1516 (17%)	782 (9%)	9014 (100%)	905 (10%)	0
GISSI-P	4271	P20 vs no treatment	2·0	3·92	−0·35	587 (14%)	582 (14%)	4271 (100%)	179 (4%)	0
LIPS	1677	F80 vs placebo	3·9	3·42	−0·92	271 (16%)	202 (12%)	1677 (100%)	142 (8%)	0
HPS	20 536	S40 vs placebo	5·4	3·38	−1·29	5082 (25%)	5963 (29%)	13 386 (65%)	8865 (43%)	3161 (15%)
PROSPER	5804	P40 vs placebo	3·3	3·79	−1·04	3000 (52%)	623 (11%)	1881 (32%)	1026 (18%)	3254 (56%)
ALLHAT-LLT	10 355	P40 vs usual care	4·9	3·76	−0·54	5051 (49%)	3638 (35%)	1188 (11%)	1788 (17%)	8037 (78%)
ASCOT-LLA	10 305	A10 vs placebo	3·3	3·44	−1·07	1942 (19%)	2527 (25%)	15 (<1%)	1435 (14%)	8860 (86%)
ALERT	2102	F40 vs placebo	5·5	4·14	−0·84	715 (34%)	396 (19%)	400 (19%)	241 (11%)	1702 (81%)
CARDS	2838	A10 vs placebo	4·1	3·03	−1·14	909 (32%)	2838 (100%)	9 (<1%)	97 (3%)	2738 (96%)
ALLIANCE**	2442	A10–80 vs usual care	4·7	3·80	−1·16	434 (18%)	540 (22%)	2442 (100%)	162 (7%)	0
4D**	1255	A20 vs placebo	4·0	3·25	−0·89	578 (46%)	1255 (100%)	630 (50%)	666 (53%)	344 (27%)
ASPEN**	2410	A10 vs placebo	4·0	2·93	−0·99	811 (34%)	2410 (100%)	578 (24%)	302 (13%)	1663 (69%)
MEGA**††	8214	P10–20 vs usual care	5·0	4·05	−0·67	5547 (68%)	1686 (21%)	42 (<1%)	53 (<1%)	8119 (99%)
JUPITER**	17 802	R20 vs placebo	2·0	2·70	−1·09	6801 (38%)	76 (<1%)	0	0	17 802 (100%)
GISSI-HF**	4574	R10 vs placebo	4·2	3·06	−0·92	1032 (23%)	1196 (26%)	1797 (39%)	4574 (100%)	0
AURORA**	2773	R10 vs placebo	4·6	2·58	−0·99	1050 (38%)	731 (26%)	659 (24%)	743 (27%)	1663 (60%)
Subtotal (21 trials)	129 526	NA	4·8‖	3·70‖	−1·07‖	37 828 (29%)	26 580 (21%)	48 291 (37%)	21 543 (17%)	70 025 (54%)
Total (26 trials)	169 138	NA	4·9‖	NA	NA	45 495 (27%)	32 210 (19%)	87 903 (52%)	25 920 (15%)	70 025 (41%)

CTT 2010 Lancet Paper: 22% Reduction in Any Major CVS Event

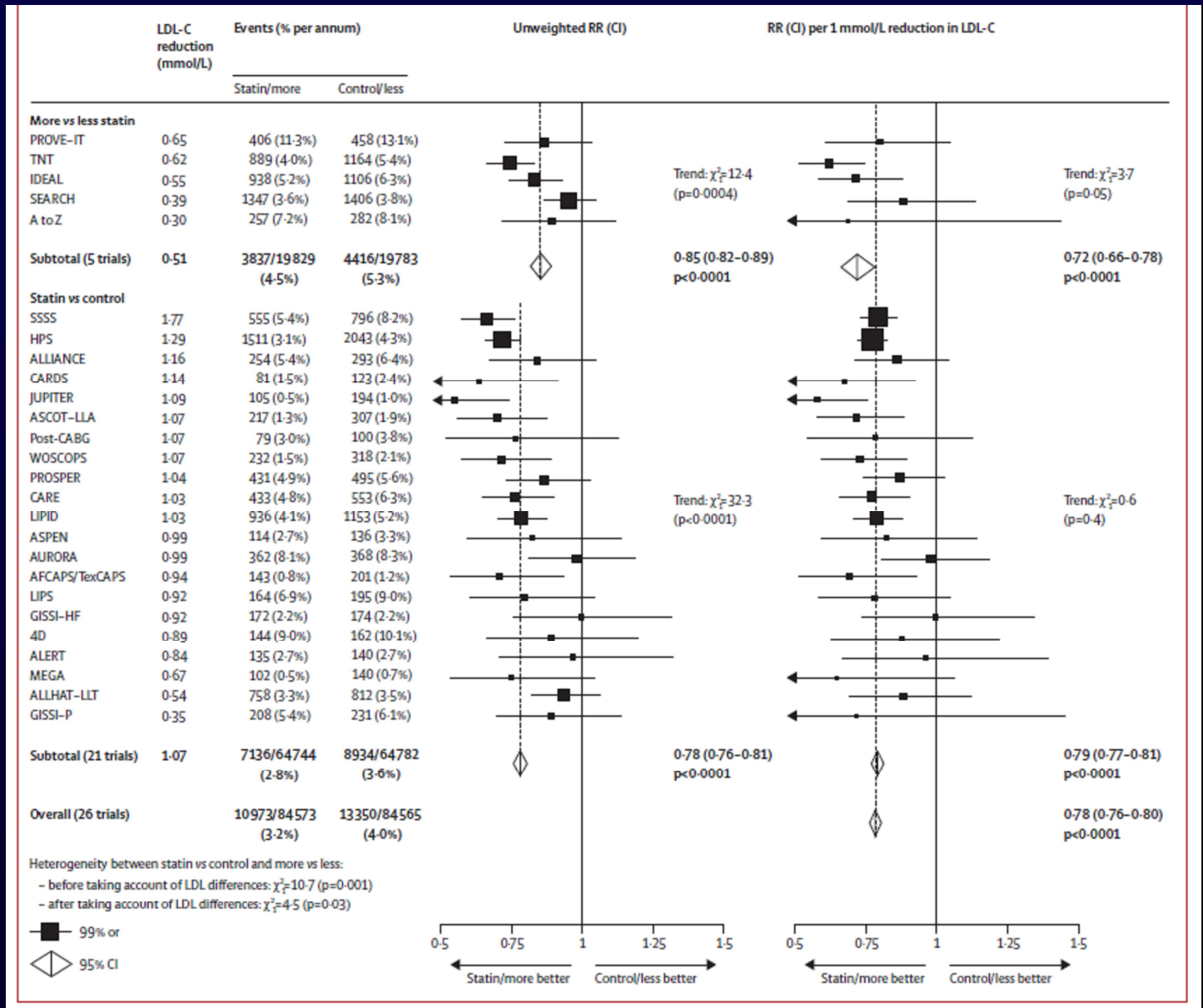
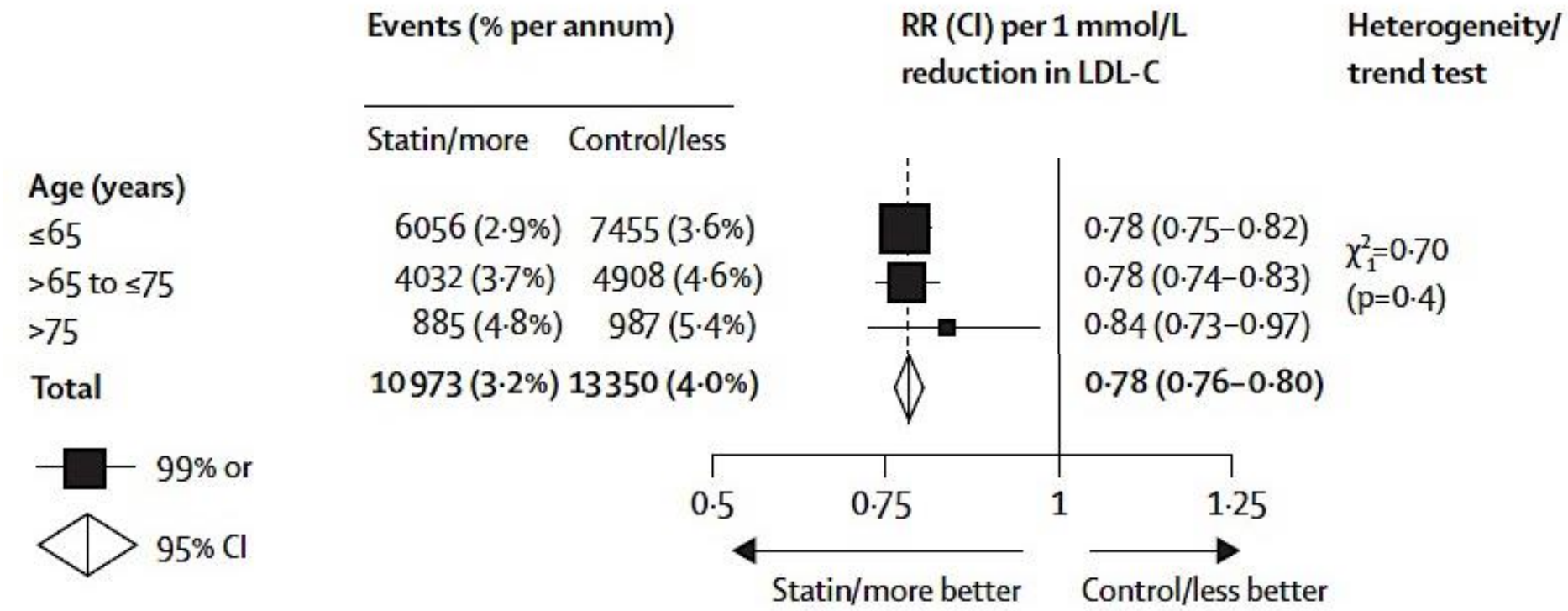


***Figure 1*: Effects on any major vascular event in each study**

In the left panel, unweighted rate ratios (RRs) for each trial of the comparison of first event rates between randomly allocated treatment groups are plotted along with 99% CIs. Trials are ordered according to the absolute reduction in LDL cholesterol (LDL-C) at 1 year within each type of trial comparison (more *vs* less statin and statin *vs* control). In the right panel, rate ratios are weighted per 1·0 mmol/L LDL cholesterol difference at 1 year. Subtotals and totals with 95% CIs are shown by open diamonds.

Effects of statins on major vascular events by age



CTT Collaboration, *Lancet*, 2010;376:1670-81

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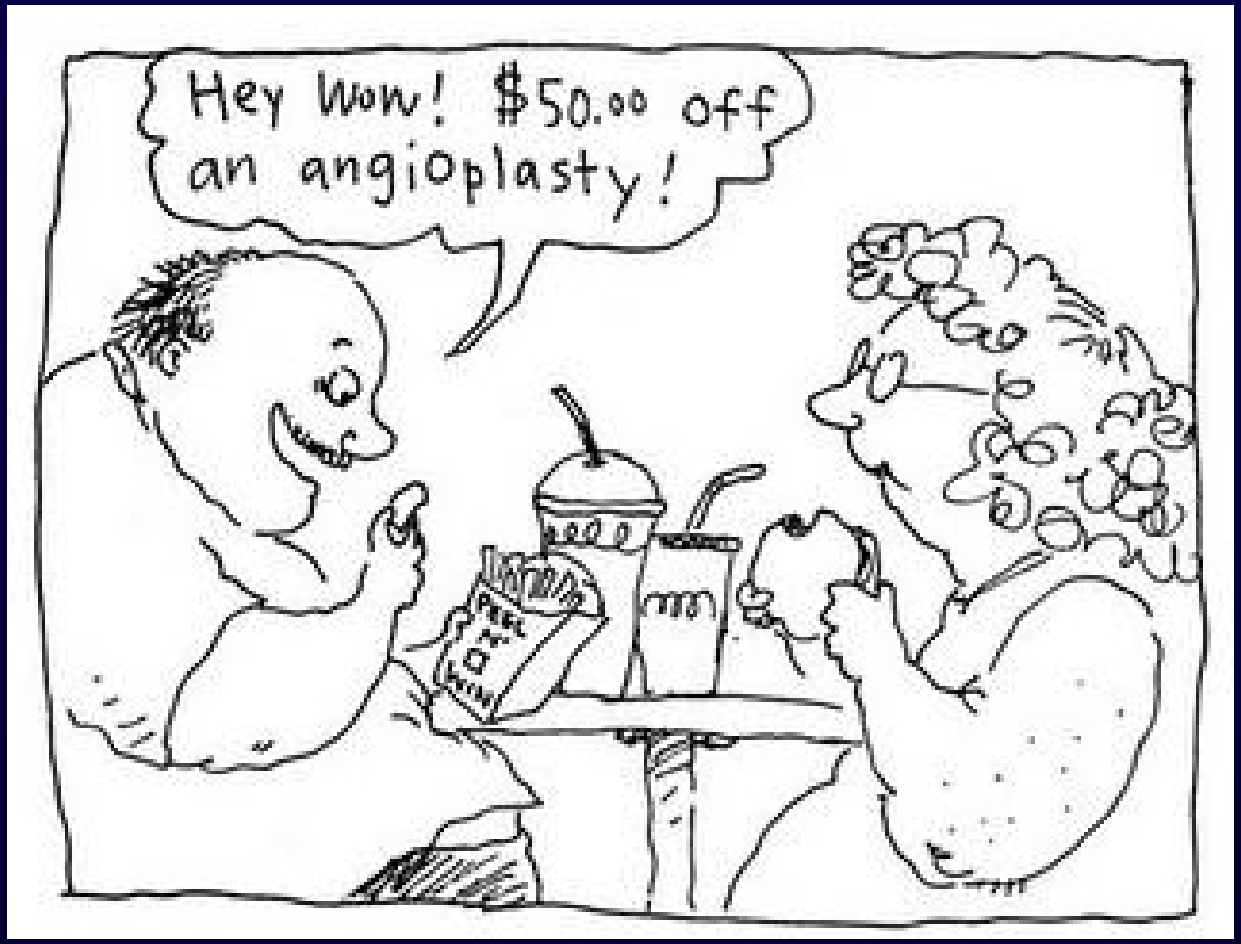
Potential Conflict of Interest



- Please note that the Cardiac CT & Calcium Scoring Experience is a part of my private, as well as my public practice.
- I am the NZ representative on the International Society of CVS CT (SCCT)