Bale/Doneen Live Chat Session

Amy Doneen MSN, ARNP

May 9, 2012

5:30-6:30 pm PST

Where are we heading?

AHA Goal of 20% Improved CV Health by 2020 Unrealistic

35,059 CVD free individuals; NHANES 1988-94 baseline; 2 yr. surveys for improvement trends from 1999-2008

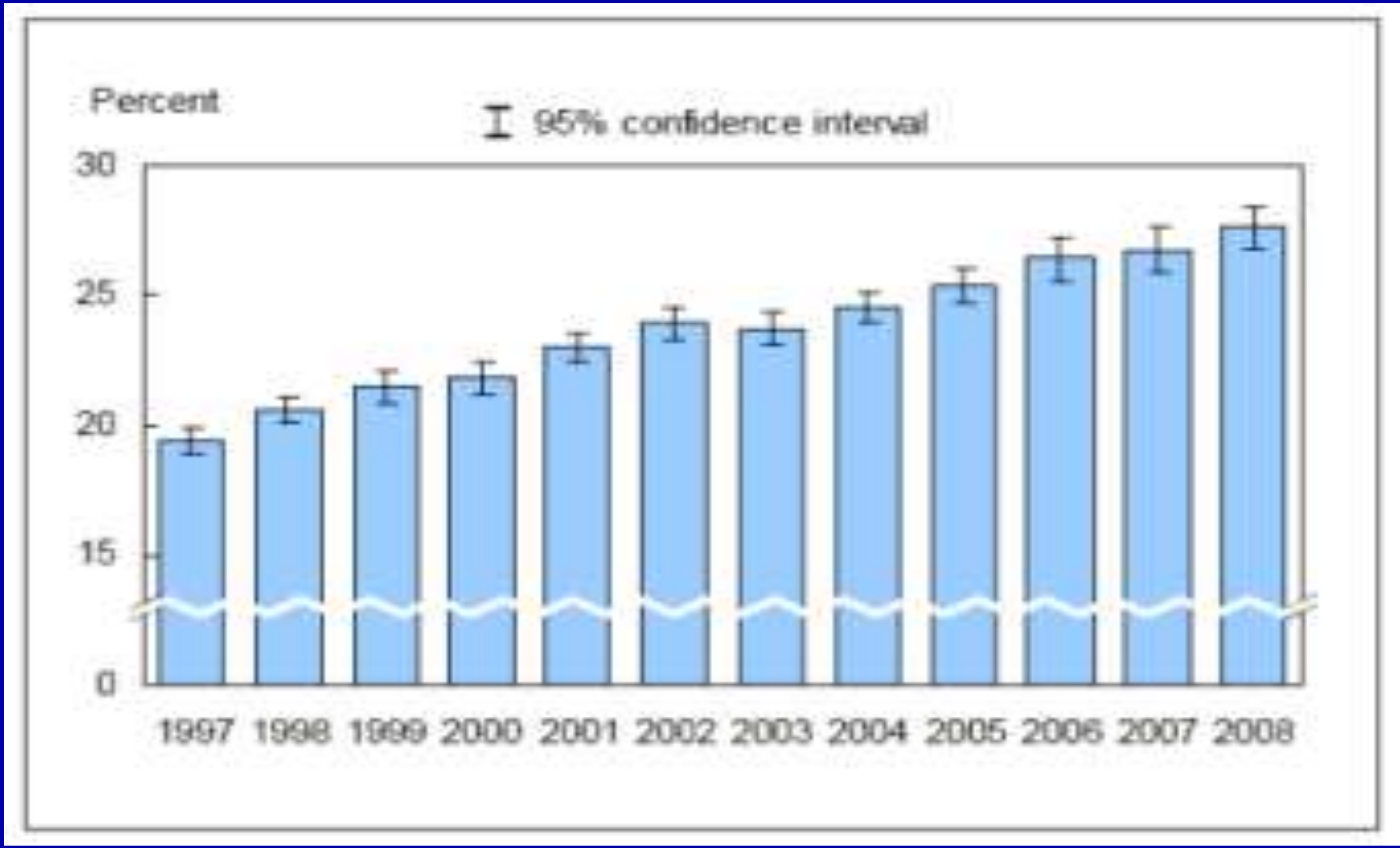
Calculated CV health based on seven parameters: smoking, diet, exercise, BMI, glucose, BP, TC

Smoking, TC, BP improving; exercise & diet stagnant; BMI and glucose getting worse

If current trends continue, will only be a 6% improve by 2020

Mark D. Huffman, et. al. *Circulation published online April 30, 2012*
http://circ.ahajournals.org/content/early/2012/04/30/CIRCULATIONAHA.111.070722

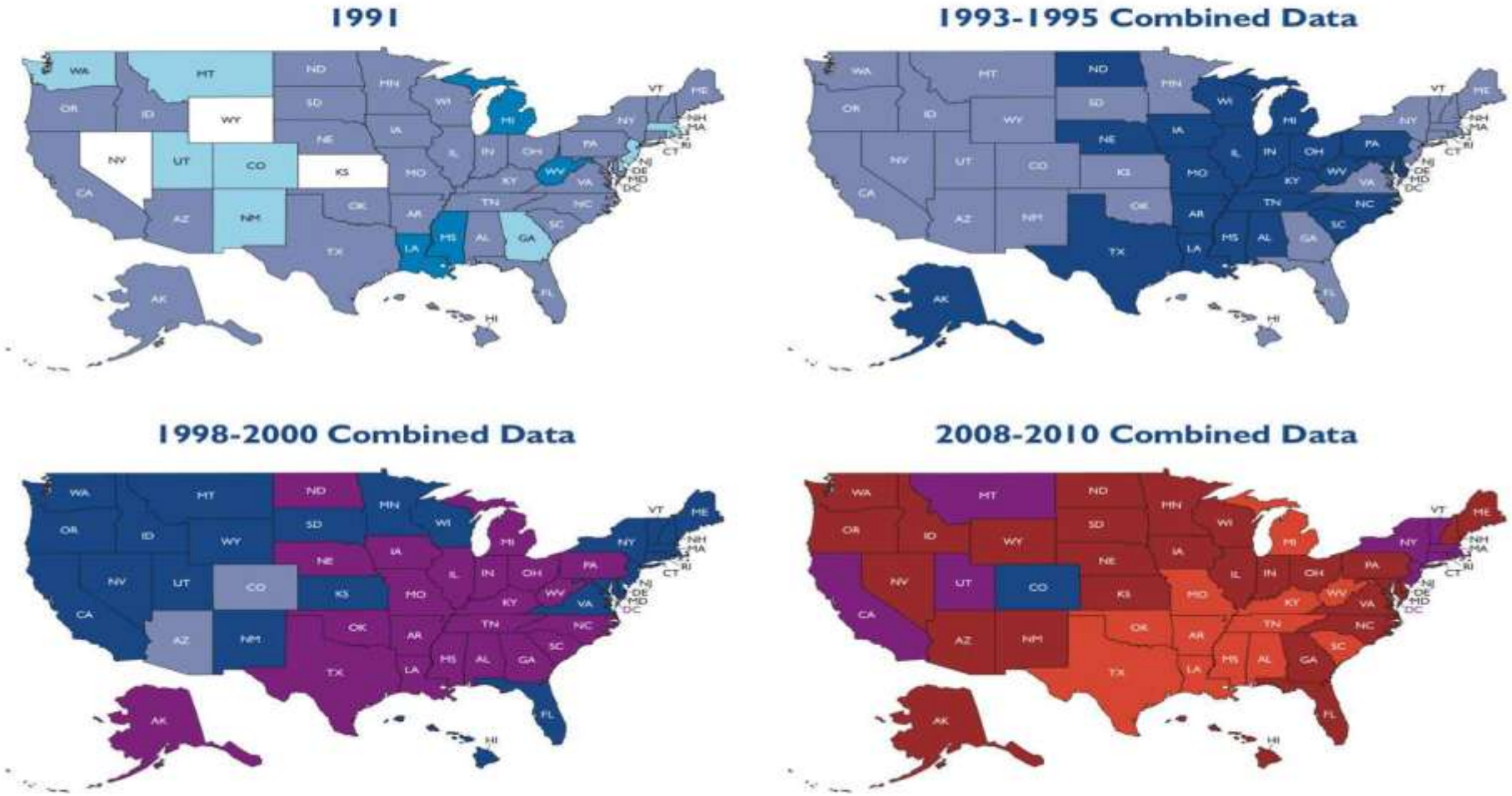
Obesity trends….



OBESITY TRENDS* AMONG U.S. ADULTS

BRFSS, 1991, 1993-1995, 1998-2000, and 2008-2010 Combined Data

(*BMI >30, or about 30lbs overweight for 5'4" person)



BP Poorly Controlled in Cardiology Practices

5,979 hypertensives routinely followed by 47 cardiologists; one year follow-up

1/3 had poor BP control (≥140/90)

1/3 of these had no documented plan of how to get control

Using the patient's average BP record did not change results

Huge opportunity to reduce CV risk!

Who claims responsibility?

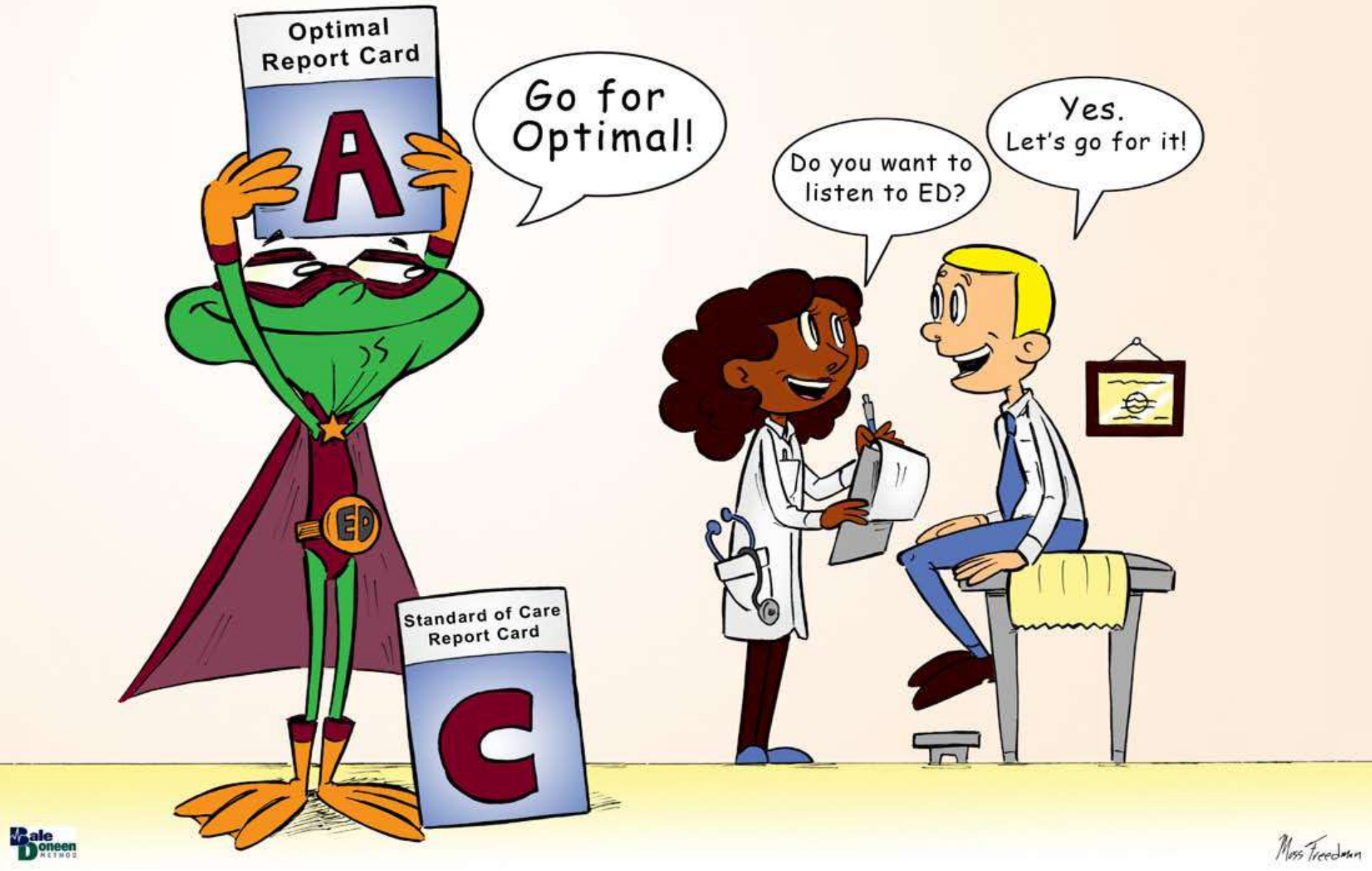
Ann Marie Navar-Boggan, MD, PhD, et. al. ***Circ Cardiovasc Qual Outcomes. 5/1/2012;5:00-00.*** DOI: 10.1161/CIRCOUTCOMES.111.963488

Complexity of Coronary Events

- One million Americans suffer acute coronary events annually and 400,000 die from those events
- It is estimated that over the next two decades healthcare dollars spent for CVD will triple: from $273 billion to $818 billion
- More effective solutions for prevention are needed

Arbab-Zadeh A et al. Circulation 3/6/2012;125:1147-1156

Optimal vs Standard of Care



Improving BP Control through a Clinical Pharmacist Outreach Program: a Clinical Pharmacist Outreach Program in Diabetes Patients in Two-High Performing Health Systems

Prospective, 16 primary care teams at five medical to the AIM intervention or usual care. Primary outcome: change in systolic BP (SBP), comparing 1,797 intervention to 2,303 control team patients, from 6-months preceding to 6-months following the 14-month intervention period.

The mean SBP decrease from 6 months prior to 6 months after the intervention period was approximately 9 mm Hg in both arms. Mean SBPs of eligible intervention patients were 2.4 mm Hg lower (95% CI: -3.4 to -1.5; p<.001) immediately after the intervention than those achieved by control patients.

Conclusions – Many programs are effective – BP control CAN be achieved!!

Heisler et al. Circulation published online May 8, 2012

Happy Mother's Day!

Meta-Analysis of Statin Effects in Women vs Men

Evaluate the effect of statins in decreasing CV events in women and men.

18 randomized clinical trials of statins with sex-specific outcomes

(N =141,235, 40,275 women, 21,468 cardiovascular events)

The benefit of statins was statistically significant in both sexes, regardless of the type of control, baseline risk, or type of endpoint and in both primary and secondary prevention.

All-cause mortality was also lower with statin therapy both in women and men without significant interaction by sex (p for interaction 0.4457).

Kostis, W, Cheng, J. Journal of Am Col of Card.
Meta analysis of Statin Effects in Women Versus Men. April 2012;59:572-82.

CREATE: Differences in baseline characteristics, treatments, and outcome between men & women

Characteristic or outcome	Men	Women	p
Time from symptoms to hospital (min)	340	415	< 0.0001
Angiography (%)	24	19.3	< 0.0001
Any revascularization (%)	52.7	37.5	< 0.0001
Thrombolysis (%)	44.9	30.9	< 0.0001
Antiplatelet drugs (%)	98.3	97.6	0.003
Beta blockers (%)	60.5	59.7	0.314
ACE inhibitors/ARBs (%)	56.4	54.6	0.023
Lipid-lowering drugs (%)	53	50.6	0.004
Death at 30 d (%)	6.2	8.6	< 0.0001

Prospective enroll n=20,468 across 89 centers in 50 Indian cities
Dr. Pais, WCC Dubai April 28, 2012

2009 Joint Statement

American Heart Association®
Fighting Heart Disease and Stroke

April 18, 2012

= ?

NEW YORK (CNN) 4/20/12
HEADLINE

"In a recent study, the American Heart Association said the link between gum disease and heart disease is a little hard to swallow. "

AJC-JOP Editors' Consensus Paper

Collaboration between Periodontists and Cardiologists

Dentistry and Medicine Work Together to Improve Patient Care – July 2009

1. Confirms the connection between periodontal disease and cardiovascular disease.

2. The underlying biologic and inflammatory mechanisms that may be the basis for the connection are explained.

3. Clinical recommendations for treating patients with periodontal disease or cardiovascular disease.

American Heart Association
Periodontal Disease & Cardiovascular Disease

"After extensive review of all the literature in this field, we were not able to find any real scientific evidence that periodontal disease causes atherosclerosis or that treating periodontal disease has any long-term effect on atherosclerosis or heart disease. Although we also haven't proved that the link is not causative, it would seem that if it were causative, it would be a small relationship. And it does not appear to be worth creating too much stress about it."

"Our message is that while good oral hygiene is obviously still important, patients should not be distracted by periodontal disease in trying to lower their rates of heart attack and stroke. Rather, they should focus on the well-known causes of heart disease such as hypertension, obesity, and high cholesterol. Reducing these things can make a real difference."

Lockhart P B, Bolger AF, et al A scientific statement from the American Heart Association. Circulation April 18 2012;

Bale/Doneen/Nabors White Paper
April 24, 2012

A significant challenge in evaluating a cause and effect relationship between these two diseases is that PD is not consistently nor universally defined. This results in substantial variation in definitive clinical diagnoses. An objective and uniform definition of PD from its biological phenotype would be helpful in order to establish a formal cause and effect relationship with CVD.

The literature confirms that the inflammatory milieu resulting from PD contributes to the systemic vascular burden of inflammation, as documented by various biomarkers including highly sensitive c-reactive protein (hsCRP), lipoprotein-associated phospholipase A-2 (Lp-PLA2), fibrinogen, and myeloperoxidase (MPO).

PD should be Assessed and Treated in Programs Designed to Maintain CV Wellness

- Level A evidence that PD is associated with arterial disease
- Available evidence shows a trend toward reducing CV risk with the therapy of PD

Peter B. Lockhart, et. al. *Circulation published online April 18, 2012*
DOI: 10.1161/CIR.0b013e31825719f3

Fusobacterium nucleatum (Fn) Increases Permeability of Endothelium

Fn adheres to and invades endothelial cells via a novel surface adhesin –FadA. Vascular endothelial (VE)-cadherin is a cell–cell junction molecule. This molecule is the receptor for Fn's FadA

The union of cadherin & FadA causes a relocation of VE-cadherin away from the cell–cell junctions.

As a result, endothelial permeability increases allowing the bacteria to enter the arterial wall

Fn may serve as an 'enabler' for other microorganisms explaining why Fn is often found in mixed infections.

Yann Fardini, et. al. *Molecular Microbiology* 11/2011 82(6):1468–1480

Oral Health Associated with Overall Mortality Risk in Elderly

- 5,611 older adults; 69% women; median age 81; followed 17 yrs with median 9 years; mortality was end point

- Evaluated for association with oral hygiene, frequency of routine dental visits, preservation of teeth

Annlia Paganini-Hill, et. al. Journal of Aging Research
Volume 2011, Article ID 156061, 10 pages doi:10.4061/2011/156061

Oral Health Associated with Overall Mortality Risk in Elderly: Number of Teeth

After adjusting for: age at entry, smoking, alcohol, caffeine, activity level, BMI, BP, angina, heart attack, stroke, diabetes, rheumatoid arthritis, and cancer.

0 to 15 teeth had a significant 20% higher mortality risk compared to those with 26-32 teeth

Dentures eliminated the significance with zero teeth

Annlia Paganini-Hill, et. al. Journal of Aging Research
Volume 2011, Article ID 156061, 10 pages
doi:10.4061/2011/156061

Oral Health Associated with Overall Mortality Risk in Elderly: Hygiene Habits

After adjusting for: age at entry, smoking, alcohol, caffeine, activity level, BMI, BP, angina, heart attack, stroke, diabetes, rheumatoid arthritis, and cancer.

Not brushing at bedtime significantly increased risk by 20%

Not flossing daily significantly increased risk by 28%

Not brushing daily had a significant 41–91% increased risk compared with brushing times daily

Annlia Paganini-Hill, et. al. Journal of Aging Research
Volume 2011, Article ID 156061, 10 pages
doi:10.4061/2011/156061

Oral Health Associated with Overall Mortality Risk in Elderly: Dental Visits

- Not seeing a dentist in a year versus visiting a dentist twice a year was associated with a (25–50%) increased risk even if dentured

- The risk was slightly higher in men and in those with teeth than in those with dentures.

Annlia Paganini-Hill, et. al. Journal of Aging Research
Volume 2011, Article ID 156061, 10 pages
doi:10.4061/2011/156061

Oral Health is Associated with Risk of Dying

- Bottom line:
  1) Try to keep at least 16 teeth; ? dentures
  2) brush before bed and use dental floss
  3) see a dentist at least twice a year

Annlia Paganini-Hill, et. al. Journal of Aging Research
Volume 2011, Article ID 156061, 10 pages
doi:10.4061/2011/156061

Announcing New Course for Dental & Medical Providers!

Medical/Dental Arteriology
Bale/Doneen/Nabors

Las Vegas Institute

November 2, 2012

6.25 hour CME course - AAFP

Medical/Dental Arteriology
Bale/Doneen/Nabors

$995 for dentists and medical providers

$595 for hygienists

“Team” Discounts available

Early Bird before June 1st receive $100 discount

To register:

www.baledoneen.com

Testosterone: Potential CV Harm

- Testosterone abuse may increase arterial blood pressure, leading to left ventricular hypertrophy
- Testosterone abuse has been associated with myocardial infarction because of coronary vasospasm or thrombosis.
- Mechanisms of how exogenous, as opposed to endogenous, testosterone contributes to increased in cardiovascular risk, and coagulatory activation, as well as accelerated progression of coronary artery disease.

Matthias Barton, et. al. *Hypertension published online May 7, 2012*

Testosterone: Potential CV Harm

- Therapeutic use of testosterone is somewhat controversial with conflicting data.
- The use of anabolic steroids (AS) outside of therapeutic prescription has raised significant concerns about negative CV health consequences.
- Scientific data detailing the association of AS use and CVD prevalence, morbidity and mortality are limited and controversial.

Peter Angell, et. al. Sports Med 2/2012; 42 (2): 119-134

Testosterone: Controversial Topic

- The only substantial and growing database related to the association between AS use and the presence of CVD is provided by case study reports.

- The developing list of case studies provides compelling evidence of the significant, and often fatal, association between AS and CVD.

Peter Angell, et. al. Sports Med 2/2012; 42 (2): 119-134

Table I. Case study events in anabolic steroid users and reported presence of risk factors[a]

Event	Case studies [cardiovascular disease risk factors present][b]
Stroke	Frankle et al.[16] [↓HDL, ↑liver enzymes]; Mochizuki et al.,[17] Kennedy et al.,[18] Akhter et al.,[19] Sahraian et al.,[20] Santamarina et al.[21] [↑Apo B]
Myocardial infarction	McNutt et al.[22] [↑LDL, ↓HDL]; Bowman[23] [↑TC, ↓HDL]; Ferenchick and Adelman[24] [family history]; Kennedy[25] [↑TC, ↓HDL, smoker]; Appleby et al.[26] [smoker, ↑BP]; Huie[27] [family history, ↑ALT, ↑ASP, ↑CK]; Fisher et al.,[28] Goldstein et al.,[29] Fineschi et al. (pt 1),[30] Gunes et al.[31] [↓HDL]; Angelilli et al.[32] [↑Trig, history of hypertension]; Wysozcanski et al.[33] [↑BP, ↑CK, ↓HDL]; Lunghetti et al.[34]
Sudden death	Luke et al.,[35] Campbell et al.,[36] Hausmann et al.,[37] Madea and Grellner[38] [↑BP, ↑TC and LDL, ↓HDL ↑Trig]; Fineschi et al., (pts 3 and 4)[39]
Thromboembolism	Laroche[40] [smoker]; Gaede and Montine,[41] Jaillard et al.,[42] Mewis et al.[43] [↑LDL]; Nieminen et al., (pt 4)[44]; Palfi et al.,[45]; Falkenberg et al.,[46] [pt 2: smoker]; Hourigan et al.,[47] McCarthy et al.,[48] Ment and Ludman[49] [smoker, ↑TC]; Alhadad et al.[50] [protein C deficiency]; Liljeqvist et al.,[51] Frogel et al.[52]
Cardiac hypertrophy	Nieminen et al., (pt 2)[44] Mark et al.[53]
Cardiomyopathy	Ahlgrim and Guglin[54] [↑ALT and AST]; Bispo et al.[55]
Endocarditis	Nieminen et al.[44] [pt 1: ↓HDL] ; Fineschi et al.[39] (pts 1 and 2), Frogel et al.[52]
Atrial fibrillation	Sullivan et al.[56] [Tachycardia, ↑CK].
Heart failure	Clark and Schofield[57] [Sinus Tachycardia, ↑ALT, AST]
Subdural haematoma	Alaraj et al.,[58] Alhadad et al.[50] [protein C deficiency].

a Case studies where no cause of death is reported or ascertained are grouped under 'sudden death' whereas those case studies where death is attributed to a myocardial infarction are grouped accordingly.

b Where there are no risk factors cited after a study, no observations of negative results of CV risk factors were reported.

ALT = alanine transaminase; **Apo B** = apolipoprotein B; **AST** = aspartate transaminase; **BP** = blood pressure; **CK** = creatine kinase; **HDL** = high-density lipoprotein; **LDL** = low-density lipoprotein; **pt(s)** = patient(s); **TC** = total cholesterol; **Trig** = triglycerides; ↑ indicates increase; ↓ indicates decrease.

Peter Angell, et. al. Sports Med 2/2012; 42 (2): 119-134

Table III. Studies showing affects of anabolic steroids on cardiac structure

Study	Groups vs controls [n]	Parameters measured	Findings
Urhausen et al.[89]	ASU [14] vs BC [7]	Total heart volume, LVM, LVD, LVPW, IVS, LVWT : D, LVM : LVV	Total heart volume and LVM: no difference LVD: ASU ↓ ** vs BC LVPW, IVS, LVWT : D and LVM : LVV: ASU ↑ ** vs BC
Sachtleben et al.[90]	ASU (on and off cycle) [11] vs BC [13]	LVM, LV and IVS wall thicknesses, LVD (s and d)	LVM and IVS thickness: ASU (on) ↑ * vs ASU (of LVM, IVS and LV posterior wall thickness: ASU (on) ↑ * vs BC
Dickerman et al.[91]	ASU [8] vs BC [8]	LV wall thickness	LV wall thickness: 6/6 ASU >11 mm 3/7 BC > 11 mm
Hartgens et al.[92]	ASU [17] vs BC [15]	LVD, LVM, LVMI, IVS, RVD, LVPW	No significant differences observed.
Nottin et al.[93]	ASU [6] vs BC [9] vs SC [16]	LVD (s and d), LVM, LVV(s and d), LV wall thicknesses	LVM and LVD: SU ↑ * vs BC and SC LVV (s and d): ASU ↑ ** vs SC LV wall thicknesses: no significant difference between groups
D'Andrea et al.[94]	ASU [20] vs BC [25] vs SC [25]	LVM, LVD	LVM and LVD: no significant difference betwee groups
Kasikcioglu et al.[95]	ASU [12] vs BC [14]	LV and RV	LVM: ASU ↑ * vs BC RVD: ASU ↓ * vs BC
Baggish et al.[96]	ASU [12] vs BC [7]	IVS, LVPW, LVD, LVM	No significant differences observed

ASU = anabolic steroid user; **BC** = bodybuilding control; **IVS** = inter-ventricular septum; **LV** = left ventricle; **LVD** = LV diameter; **LVD** = le ventricular diameter; **LVM** = left ventricular mass; **LVPW** = left ventricular posterior wall; **LVV** = left ventricular volume; **LVWT** = left ventricul wall thickening; **RV** = right ventricle; **RVD** = RV diameter; **s** = end systole; **d** = end diastole; **SC** = sedentary control; ↑ indicates increas ↓ indicates decrease; * $p < 0.05$, ** $p < 0.01$.

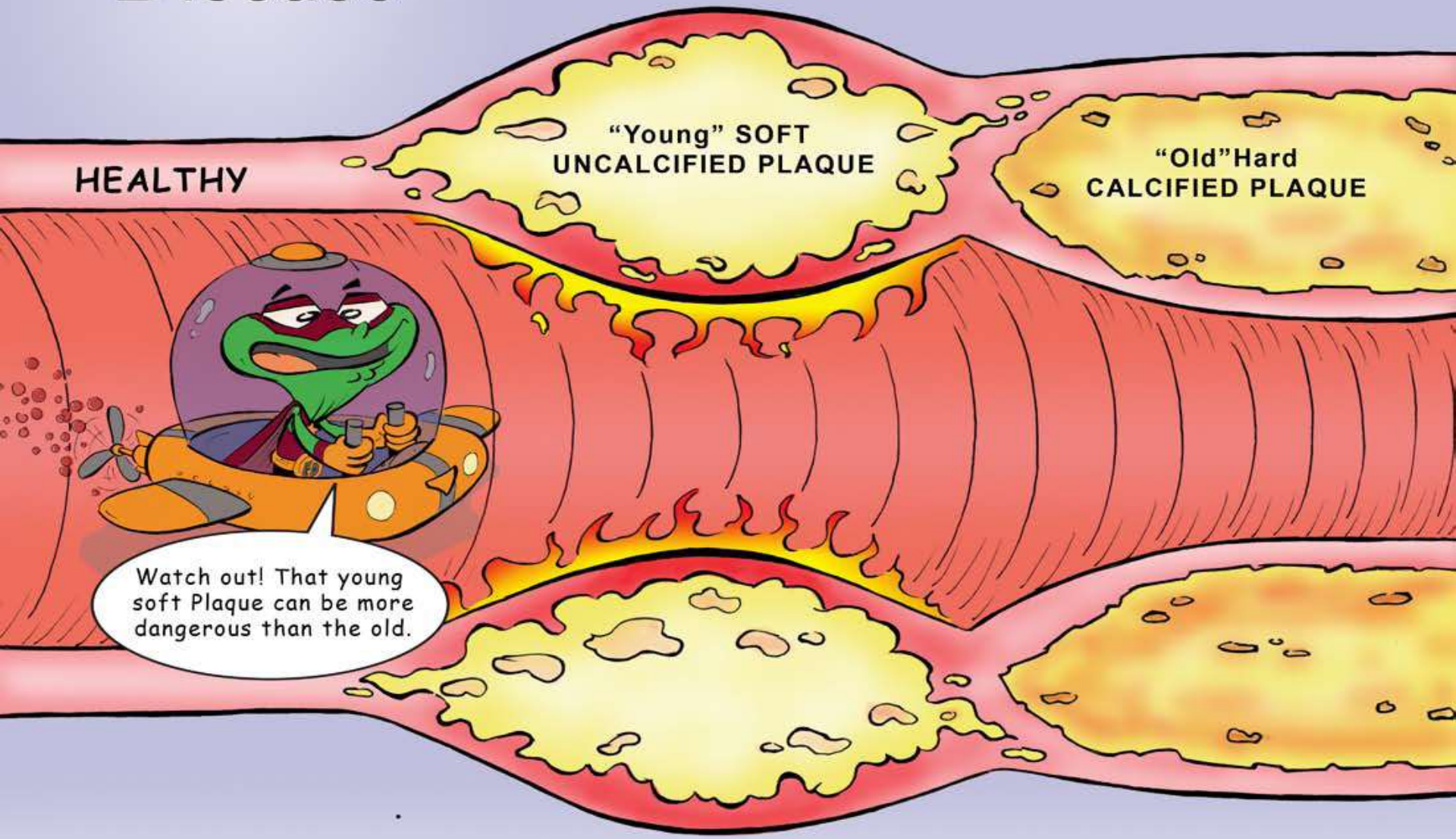
Peter Angell, et. al. Sports Med 2/2012; 42 (2): 119-134

Testosterone: Potential CV Harm

- The burgeoning body of case-study reports of CV events and disease endpoints, raises significant concerns about the CV health consequences of anabolic steroid use.

Peter Angell, et. al. Sports Med 2/2012; 42 (2): 119-134

Disease



Plaque formation is an active process and its consistency changes over time. Some technologies (X-Rays) can only see hard calcified disease while others like ultrasounds can spot soft disease.

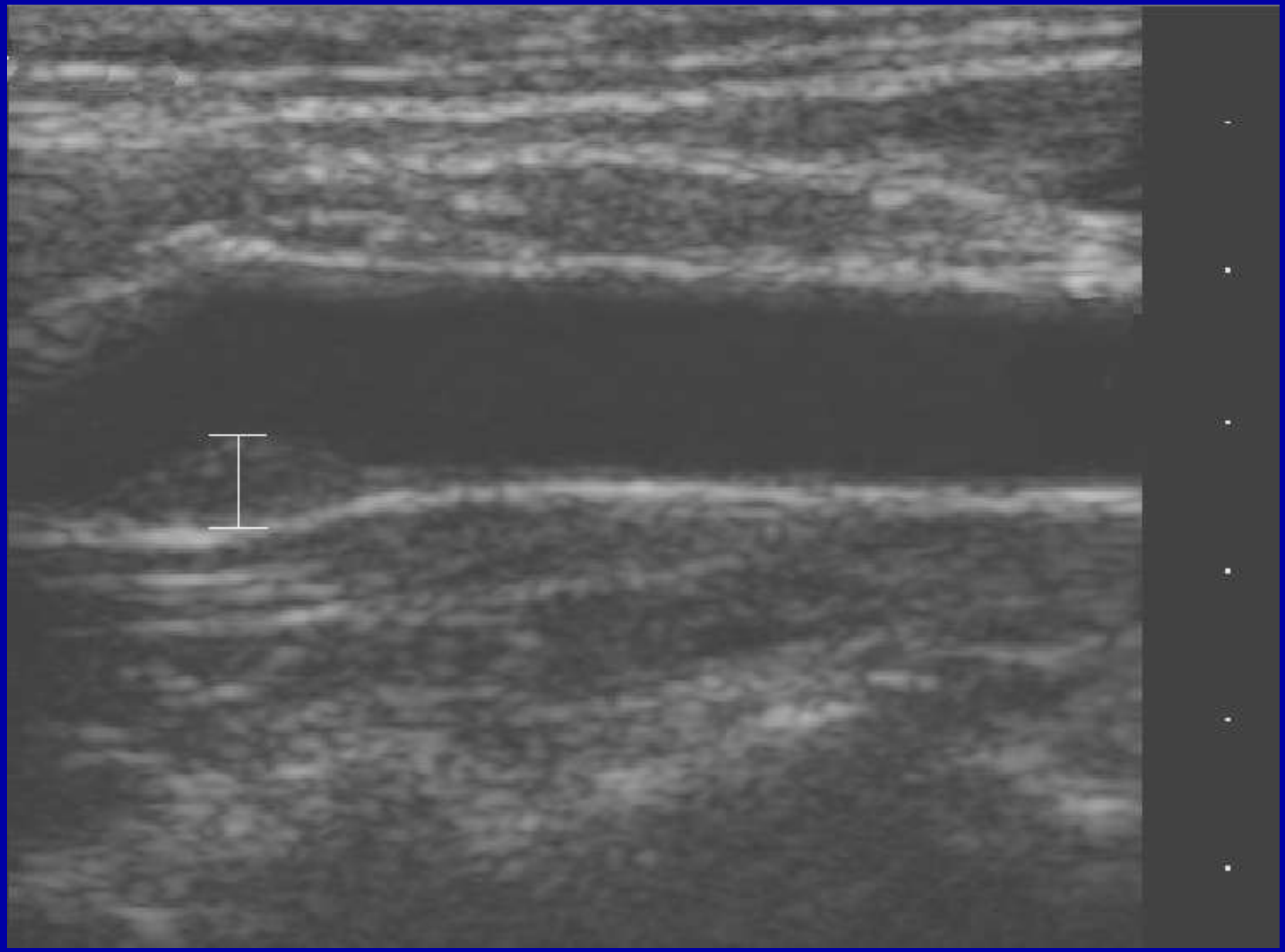
Dale Doneen METHOD

Moss Freedman

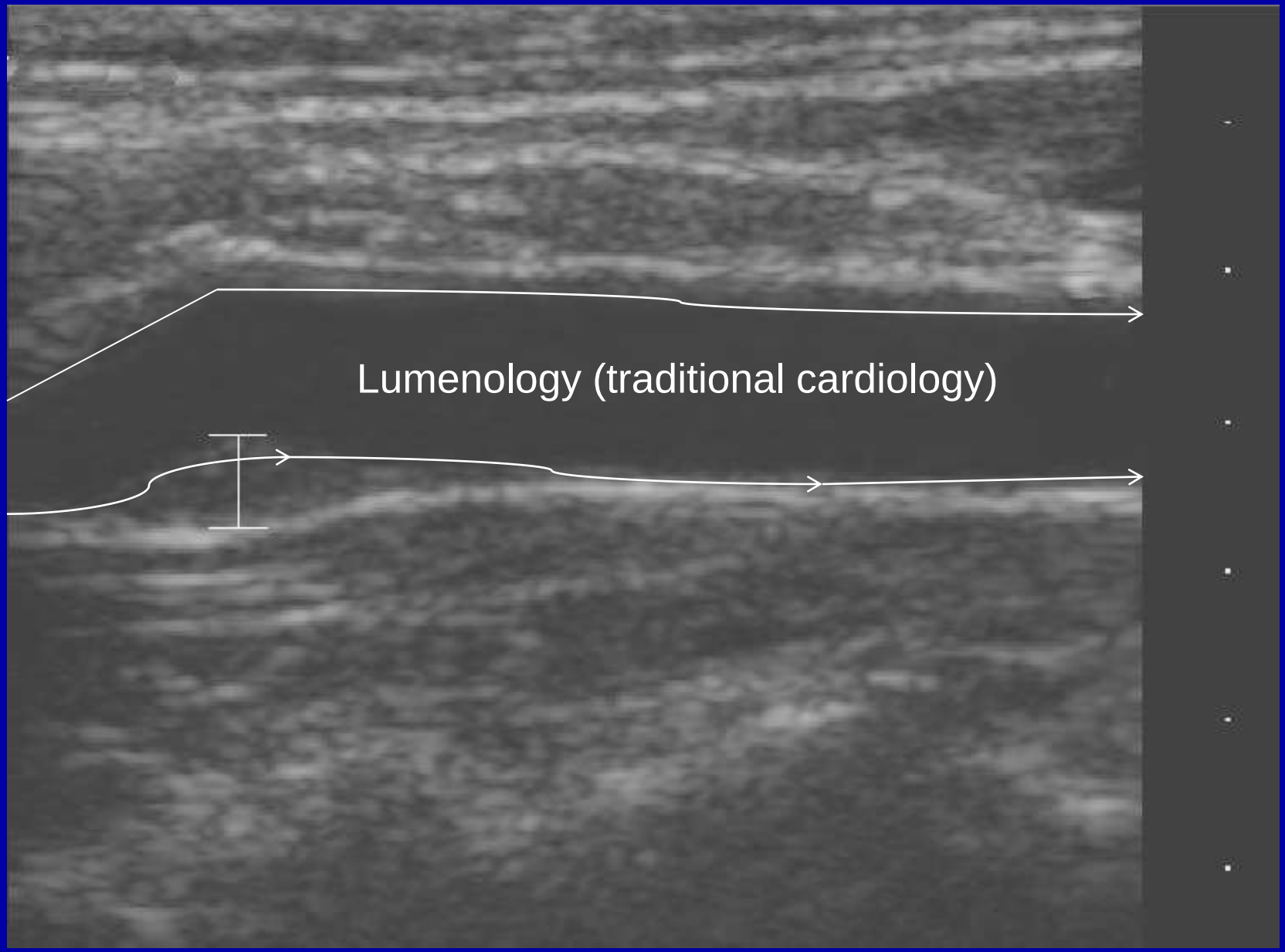
Defining our specialty

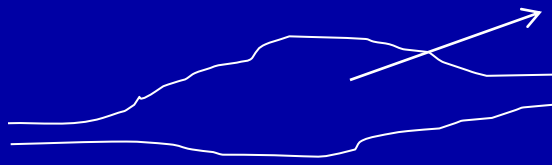
- *A **lumenologist**?*
  - ***Is the lumen open?***
    - ***Stress testing***
    - ***Angiography***
    - ***Carotid Duplex Imaging***
    - ***ABI***
- *An **arteriologist**?*
  - ***Is disease present?***
    - ***IVUS***
    - ***CACS***
    - ***Carotid IMT***
    - ***Femoral IMT***
    - ***AAA for calcium***

Clearly it takes a partnership!

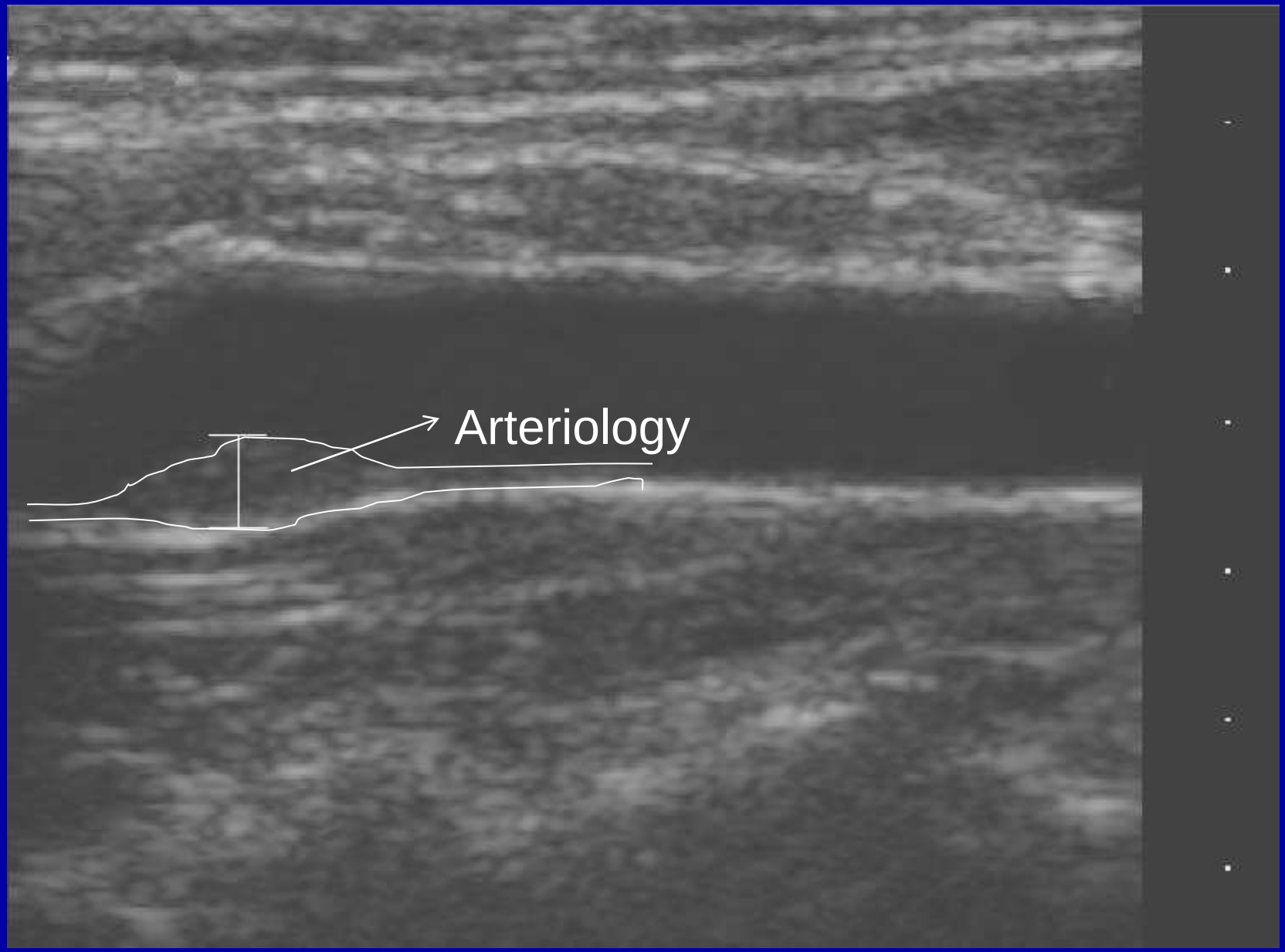



Lumenology


Lumenology (traditional cardiology)



Arteriology (Bale/Doneen Method)


Arteriology

Define each patient

Definition:

- Primary Prevention
- Secondary Prevention
- Tertiary Prevention

Goal of treatment:

- Prevent plaque
- Prevent rupture
- Prevent recidivism

What's the difference?

Bale/Doneen method

Standard of Care

Click to return to normal

GroupHealth.

Subject: labs

To: [redacted]
From:
Received:

James, your labs returned showing you cholesterol is a bit elevated. Using this data I have calculated your Framingham score, a cardiac risk score:

5-YEAR CVD RISK - 2.8%
10-YEAR CVD RISK - 6.3%

Based on:
-Cholesterol: 233 mg/dL (1/21/11)
-HDL: 46 mg/dL (1/21/11)
-Blood Pressure (untreated): 120/80 (1/21/11)
-Tobacco: No
-Diabetic: No
-Family History CHD: No

Estimated risks not accurate for patients with known ASCVD

The above helps guide us regarding what we should do in terms of treatment. It is generally accepted that a statin cholesterol-lowering drug should be started if your 10 year risk approaches 20%. Yours is much lower than that. With that said, both your total cholesterol and LDL (the "bad" cholesterol) are somewhat elevated. My recommendation is that you attack this via diet and exercise, and then repeat the study in a year. If you wanted to be very conservative a cholesterol lowering drug could be started now. Let me know how you would like to proceed.

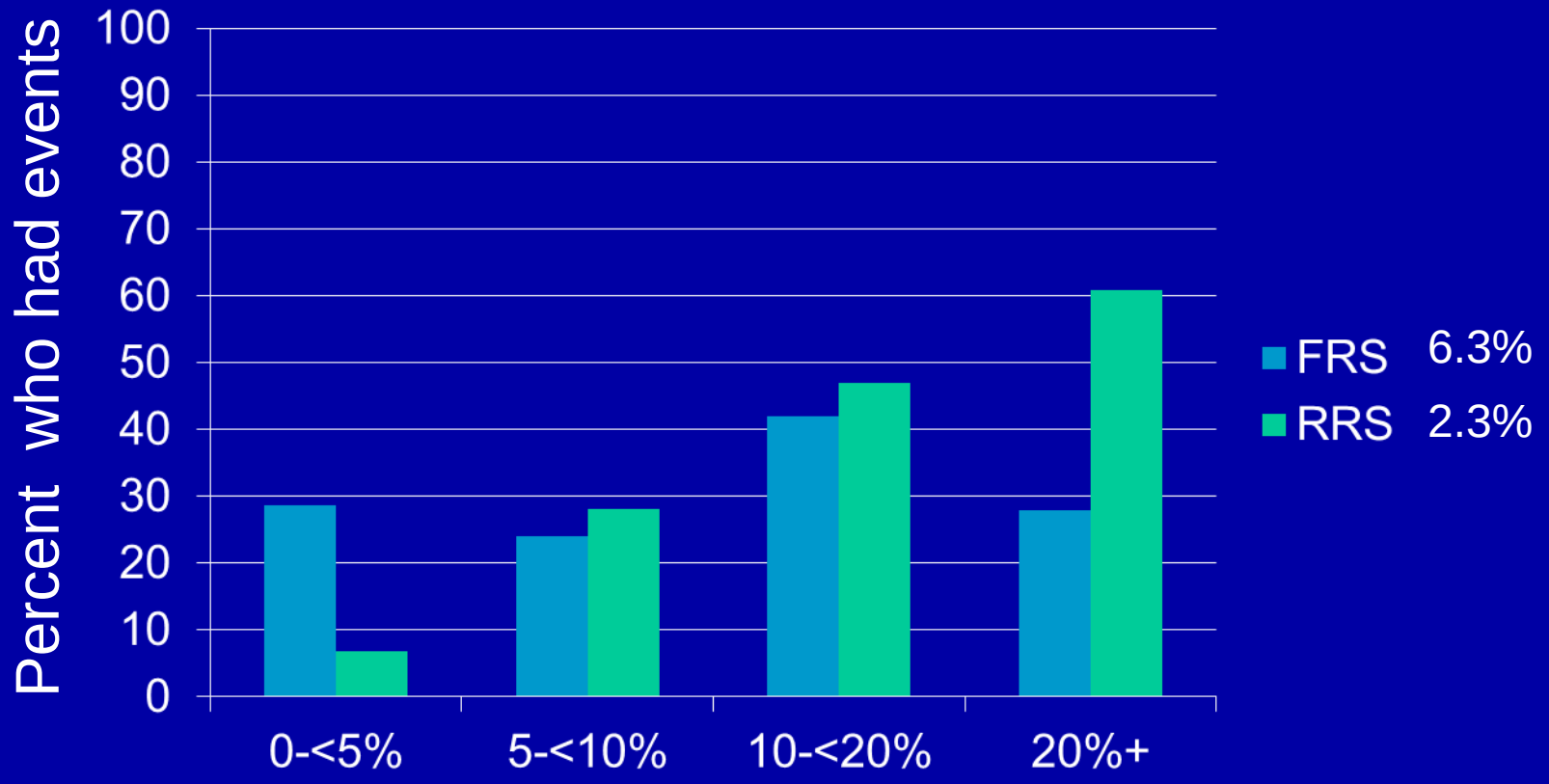
Robert [redacted] MD

RRS (give him a high hsCRP of 3.0) = 2.3% 10 year

You can reply to most messages for 30 days. Certain messages won't have a reply button; see About This Service.

BACK TO MESSAGE LIST

FRS and RRS Frequently Fail to Indentify Who Will Have an Event



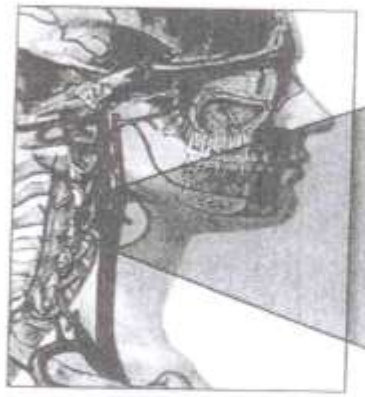
Cook N R et al. Circulation 4/2012;125:1748-1756

Bale/Doneen Method Advice

- Calculate the RRS instead of the FRS
- Realize a ‘non-high risk’ score does not rule out the chance of an event
- The presence of an atheroma is essentially a *conditio sine qua non* for an event.
- Screen for subclinical atherosclerosis

Visualized Plaque and Atherosclerotic Burden Assessment

Name: [redacted] JAMES DOB: [redacted] Age: 45 Gender: Male Date: 3/7/12



Right

Plaque Description

1.156mm Soft Homogeneous

1.072mm Heterogeneous

Left

Plaque Description

1.056mm Heterogeneous
1.072mm Heterogeneous

*Carotid velocities are provided on reverse

*Plaque noted above was measured through arterial area diameter reduction, which is deliberated by measuring the circumference of the outside of the vessel subtracting any visible stenosis.

Carotid - IMT

Your average Carotid-IMT is **0.726.**

You are a *45* year old with arteries of a **57** year old Male.

This graph indicates your percentile score for similar sex and age.

A C-IMT of less than 0.60mm is generally considered healthy.

Technical Notes:

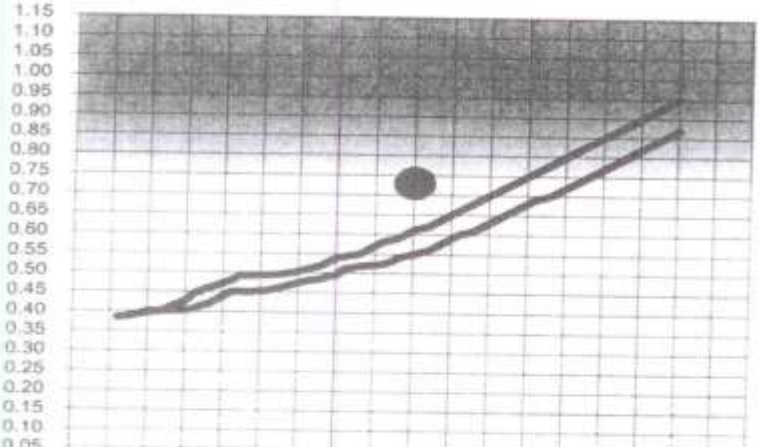
45 year old Male for cardiovascular risk stratification.

Physicians Notes:

Current CIMT Measurement

Date	Age	CIMT	Percentile
Mar 2012	45	0.726	82nd

Mean Distal 1 cm CCA IMT of General Population with No Coronary Heart History



Sub-clinical Atherosclerosis Predicts CV Risk

- 10,000 healthy subjects followed 10 yrs.; 40% female; aged 35-65 yo; base line B-mode US carotids and femorals

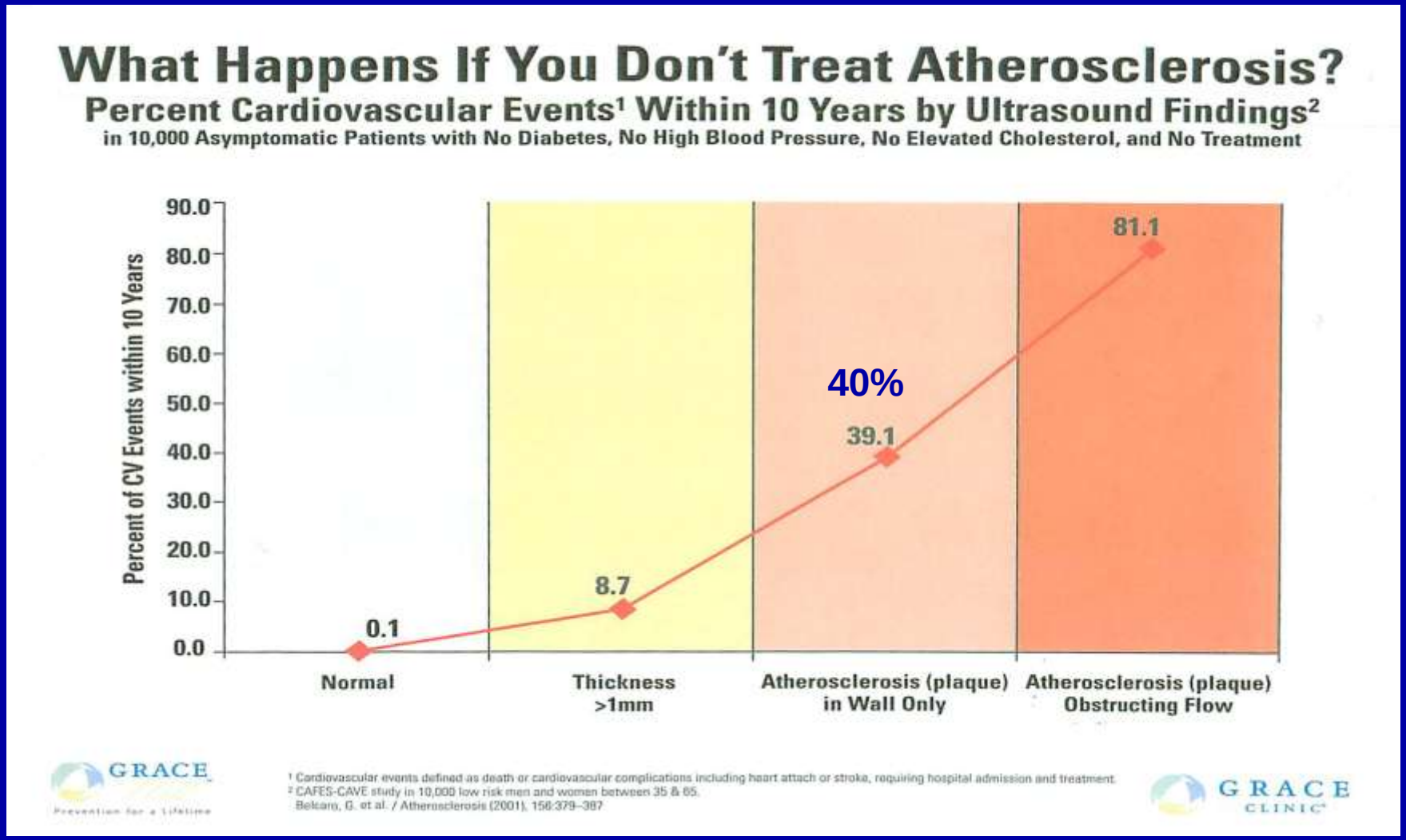
- No treatment allowed over 10 years -

- Class 1 (normal artery): 7989 subjects – 10 CV events
- Class 2 (wall thickening): 930 subjects - 81 CV events
- Class 3 (disease present): 611 subjects – 239 CV events
- Class 4 (stenotic disease): 470 subjects – 381 CV events

- Respective incidence: 0.1%; 8.6%; 39.8%; 81.1%

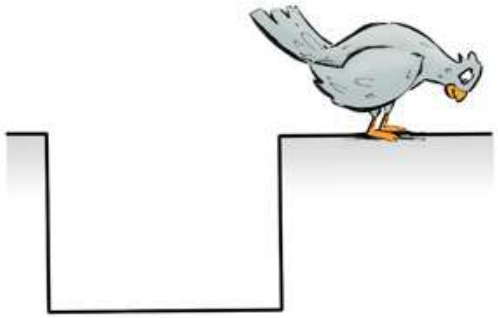
Belcaro, G., et. al. CAFES-CAVE Study. ***Atherosclerosis*** 2001. 156:379-387

The Risk of Not Treating Plaque



Belcaro, G., et. al. ***Atherosclerosis*** 2001. Vol. 156:379-387

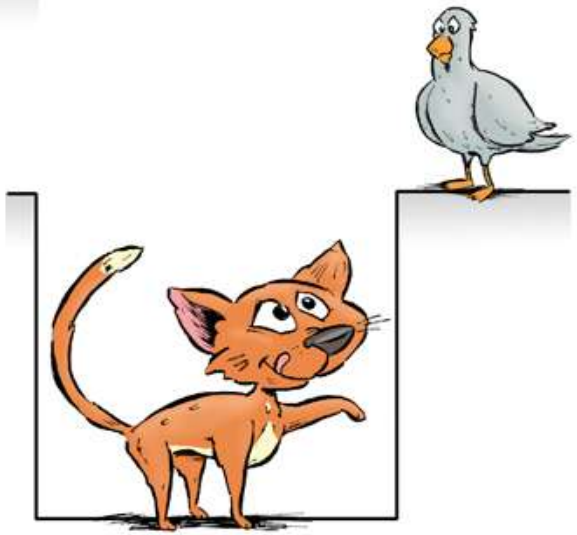
Patient Identification



Primary

No disease.

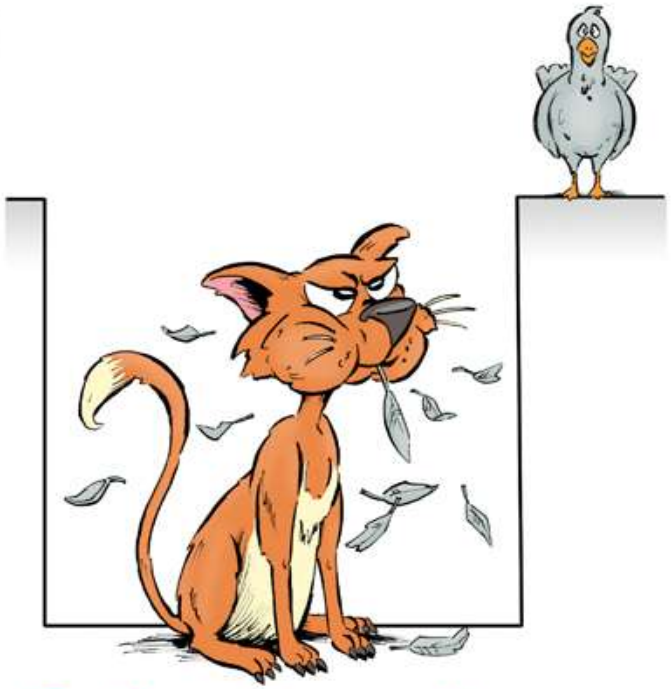
Your gutter is cat free and
we work to keep it that way.



Secondary

Disease but no heart attack or stroke.

The cat is in the gutter. We need
to make sure it doesn't get out



Tertiary Prevention

Patient has had a heart attack or stroke.

The cat has gotten out of the gutter once before;
we need to make sure it doesn't happen again.

Bale Doneen METHOD

Moss Freedman

New Carotid data

- Boss et al. Internal Carotid Calcification
- Herder et al. Tromso Study: IMT & TPA
- Kuo et al. Non-traditional RF to plaque variability

Internal Carotid Artery Calcification

- 2,495 pts; mean age 70 yo; 50% female; CT scan for calcification in intracranial internal carotid arteries (ICAC)

- Prevalence of ICAC was 82.2%

- In women, presence independently associated with:

  DM- OR 2.02 (95%CI, 1.29-3.17)

  BP –OR 1.79 (95%CI, 1.20-2.68)

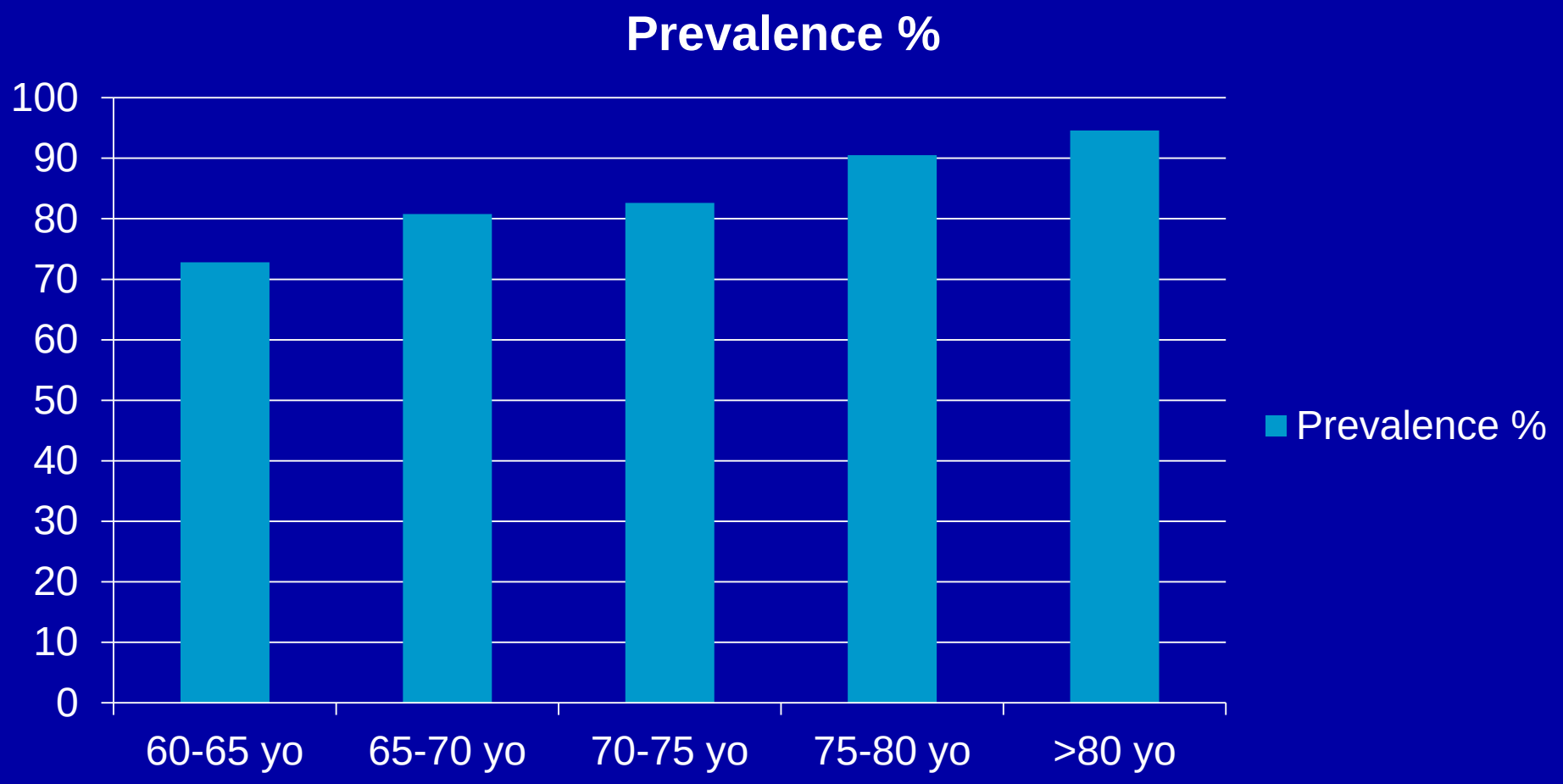
- In men, presence independently associated with:

  Excessive alcohol- OR 1.74 (95%CI, 1.28-2.37)

  Smoking - OR 1.72 (95%CI, 1.10-2.70)

Daniel Bos, MD, et. al. ***Stroke. 5/8/2012;43:00-00***
http://stroke.ahajournals.org/content/early/2012/05/07/STROKEAHA.111.648667

Internal Carotid Artery Calcification



Daniel Bos, MD, et. al. ***Stroke. 5/8/2012;43:00-00***
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Internal Carotid Artery Calcification

Table 3. Cardiovascular Risk Factors and Intracranial Carotid Artery Calcification

	Differences in Calcification Volume			
	Model 1	*P* Value	Model 2	*P* Value
Men				
Age	0.05 (0.04–0.06)	<0.001	0.04 (0.04–0.05)	<0.001
Obesity	0.22 (0.08–0.35)	0.002	0.11 (−0.03–0.25)	0.127
Hypertension	0.17 (0.04–0.30)	0.009	0.04 (−0.09–0.17)	0.560
Diabetes mellitus	0.40 (0.24–0.57)	<0.001	0.31 (0.14–0.47)	<0.001
Hypercholesterolemia	0.27 (0.16–0.38)	<0.001	0.15 (0.04–0.27)	0.010
HDL<1 mmol/l	−0.05 (−0.19–0.10)	0.528	−0.09 (−0.23–0.06)	0.247
Excessive alcohol intake	0.20 (0.08–0.31)	0.001	0.18 (0.07–0.30)	0.002
Smoking (ever vs never)	0.34 (0.20–0.49)	<0.001	0.26 (0.12–0.40)	<0.001
History of cardiovascular disease	0.48 (0.34–0.62)	<0.001	0.35 (0.20–0.50)	<0.001
Women				
Age	0.06 (0.05–0.06)	<0.001	0.05 (0.04–0.06)	<0.001
Obesity	0.05 (−0.07–0.16)	0.431	−0.03 (−0.15–0.08)	0.571
Hypertension	0.29 (0.17–0.41)	<0.001	0.21 (0.10–0.33)	0.001
Diabetes mellitus	0.27 (0.11–0.44)	0.001	0.20 (0.04–0.37)	0.018
Hypercholesterolemia	0.26 (0.16–0.36)	<0.001	0.20 (0.10–0.30)	<0.001
HDL<1 mmol/l	0.10 (−0.12–0.32)	0.373	0.02 (−0.20–0.24)	0.860
Excessive alcohol intake	0.01 (−0.14–0.15)	0.925	−0.03 (−0.17–0.12)	0.740
Smoking (ever vs never)	0.06 (−0.05–0.16)	0.288	0.01 (−0.09–0.11)	0.810
History of cardiovascular disease	0.66 (0.48–0.85)	<0.001	0.61 (0.42–0.80)	<0.001

Values represent differences in standardized calcification volume Ln(calcification+1.0 mm^3) per unit increase of the cardiovascular risk factors with 95% CI.

Daniel Bos, MD, et. al. ***Stroke. 5/8/2012;43:00-00***
http://stroke.ahajournals.org/content/early/2012/05/07/STROKEAHA.111.648667

CIMT versus Carotid Plaque: Tromso Study

CCA-IMT and Carotid Plaque have different relationships to CV risk factors as well as clinical end points.

Although highly correlated, plaque and IMT may reflect different genetic and biological aspects of atherogenesis with distinctive relations to cardiovascular risk factors and to clinical vascular disease.

The role of CCA-IMT only as a marker of atherosclerosis has been questioned.

Carotid Plaque Burden can be measured as a continuous variable as the sum of all plaque areas in the artery (TPA)

Marit Herder, et. al. ***Stroke. 5/1/2012;43:00-00***
http://stroke.ahajournals.org/content/early/2012/04/30/STROKEAHA.111.646596

Long term risk factors related to cIMT progression – Tromso study

2743 people (52% women) followed 13 years.

Baseline: IMT and TPA (total plaque area), TC, HDL, BP, BMI, smoking, DM, CVD.

Follow-up: TC, SBP, smoking were stronger predictors of TPA than of IMT

CVD risk factors of TC, smoking, SBP were stronger long-term predictors of TPA and TPA progression than CCA-IMT.

Herder, M., Johnse, S., Stroke. May 1, 2012. http://stroke.ahajournals.org.

CIMT versus Carotid Plaque - Tromso

- IMT is strongly related to age and BP; mainly represents a hypertrophic adaptive response of smooth muscle cells in the tunica media to high shear stress
- IMT as a marker of atherosclerosis has been questioned, especially when measurements include the CCA-IMT only
- IMT was not associated with ischemic stroke risk after adjustment for other CV risk factors

Marit Herder, et. al. ***Stroke. 5/12012;43:00-00***
http://stroke.ahajournals.org/content/early/2012/04/30/STROKEAHA.111.646596

CIMT versus Carotid Plaque - Tromso

- Plaques usually occur at sites of low shear and nonluminar turbulent flow such as in the carotid bulb and the proximal internal carotid artery

- Total plaque area (TPA) is more strongly associated with traditional CV risk factors and a stronger predictor of CAD

- Autopsy and US studies have demonstrated that carotid plaque is more strongly correlated to atherosclerosis in other vascular beds than is IMT

Marit Herder, et. al. ***Stroke. 5/12012;43:00-00***
http://stroke.ahajournals.org/content/early/2012/04/30/STROKEAHA.111.646596

NOMAS substudy – Identifying risk factors for plaque variability

- 1790 stroke-free individuals (mean age, 69; 60% women; 61% Hispanic, 19% black, 18% white) were assessed for total plaque area (TPA) burden using 2-dimensional carotid ultrasound imaging.
- Model 1: traditional risk factors: age, sex, low-density lipoprotein cholesterol, diabetes mellitus, pack-years of smoking, blood pressure
- Model 2, an addition of socioeconomic and less traditional risk factors.
- Framingham heart risk score and the NOMAS Global Vascular Risk Score to the TPA were explored.

Kuo, F., Gardener, H, et al. *Stroke. May 1, 2012;43:00-00*

Nomas Substudy results:

Prevalence of carotid plaque was 58%. Mean TPA was 1319 mm2.

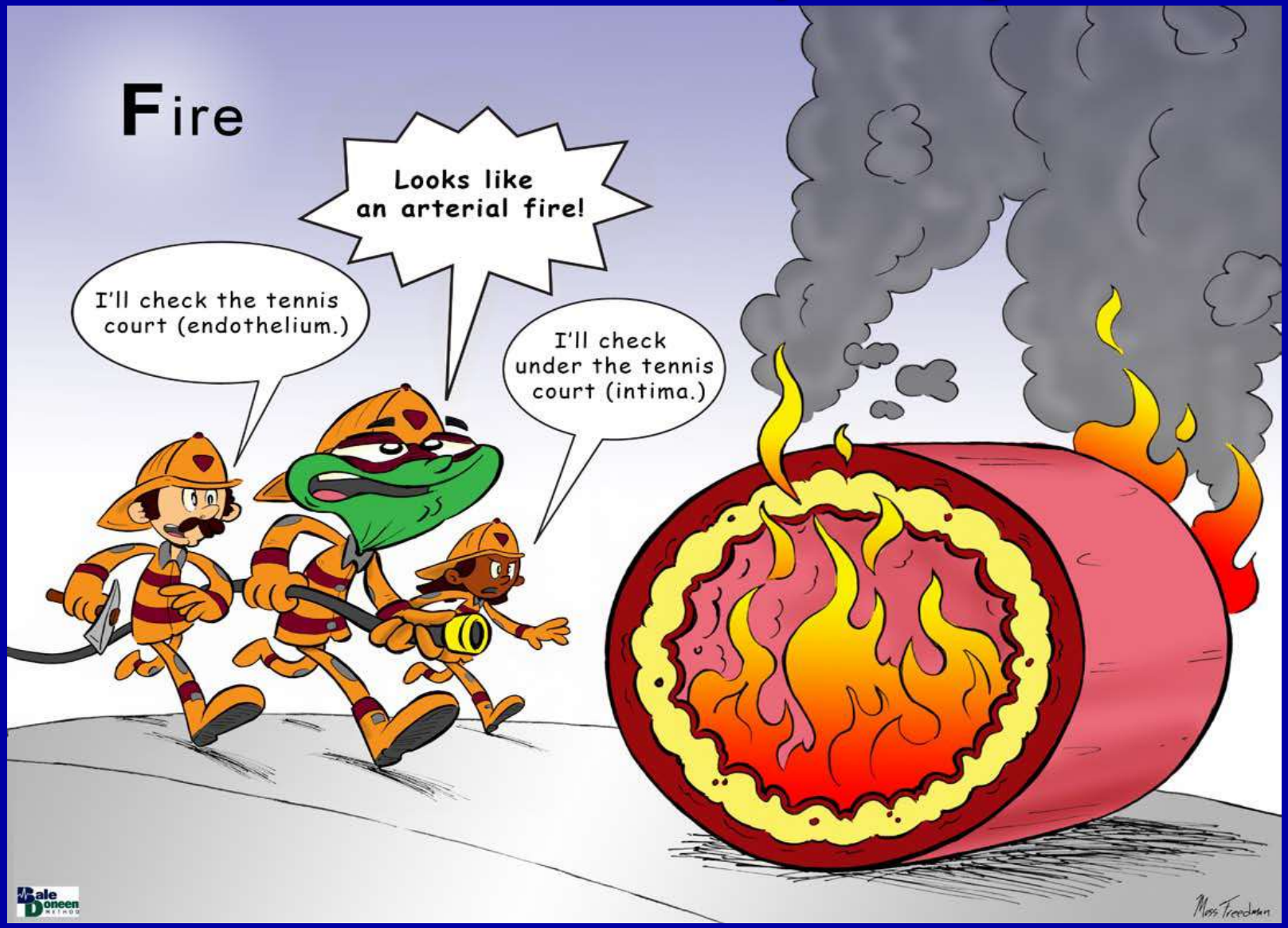
- Model 1 explained 19.5% of the variance in TPA burden
- Model 2 explained 21.9% of TPA burden.

- FRS explained 18.8% and NOMAS global vascular risk score 21.5% of the TPA variance.

Environmental and genetic factors play an important role in the determination of atherosclerotic plaque. Identification of these factors may lead to new approaches to prevent stroke and cardiovascular disease.

Kuo, F., Gardener, H, et al. *Stroke. May 1, 2012;43:00-00*

Inflammation – anything new?



Microalbumin/creatinine (MACR) Monitoring has Prognostic Value

- 393 hypertensive diabetics; assessed CV mortality prognostic value of changes in urinary albumin excretion (UAE); yearly for ten yrs

- In Cox regression model that included baseline UAE and CVD history the 10-yr predicted CV mortality:

  decrease in UAE of 2 logs at 1 year was 4.7% (95% CI 1.4% to 7.8%)

  increase in UAE of 2 logs at 1 year was 24.5% (95% CI 10.1% to 36.5%) 5 times more likely to be dead

- Data support serial UAE values have prognostic value independent of traditional CV risk factors

Raymond O. Estacio, MD, et. al. **Am J Cardiol 2012;xx:xxx – in press**

Microalbumin/creatinine (MACR) Monitoring has Prognostic Value

- Study adds to the evidence that changes within the normoalbuminuric range are independently associated with adverse CV outcomes
- There is need to redefine “normal” and “abnormal”
- There was continuous association between MACR and CV outcomes starting at just 4.4 well below the 30 cutoff

Raymond O. Estacio, MD, et. al. **Am J Cardiol 2012;xx:xxx – in press**

Periodontal Disease (PD) Associated with Microalbumin-creatinine Ratio (MACR)

- 242 non-rx'ed hypertensive patients 51 ± 9 yo;
  two nonconsecutive overnight urines for MACR

- Utilized 3 PD indexes (PDI):
  1) mean clinical loss of attachment (MCLA)
  2) maximum probe depth
  3) gingival bleeding index

- PDIs effected MACR independent of BP; MCLA strongest association

Tsioufis, C., et. al. Am J Cardiol. 1/2011;107(1):52-8.

MACR Improvement Associated with Reduction in CV Event Risk

- 1513 diabetics with BP and nephropathy; 6 month assessment; post hoc analysis
- Among all available baseline risk markers, albuminuria was the strongest predictor of CV outcome.
- Every 50% decrease in albuminuria reduced the risk of CV events by 18% (95% CI - 9% to 25%)

De Zeeuw D, et. al. *Circulation 2004;110:921–927*

Lp-PLA2 is Associated with LysoPC which is Correlated with Plaque Inflammation

- 162 endarterectomy pts; carotid plaques evaluated for inflammation and levels of Lp-PLA2 and lysoPC
- Lp-PLA2 was correlated with LysoPC levels; both assoc. with higher levels of IL-6, IL-1 beta, MCP, TNF-alpha, increased macrophages, increased lipids and decreased smooth muscle cells
- Both higher in symptomatic plaques - Suggests that Lp-PLA2 plays a key role in plaque inflammation and vulnerability.
- Supports Lp-PLA2 inhibition as a strategy for the prevention of cardiovascular disease.

Isabel Gonçalves, et. al. ***Arterioscler Thromb Vasc Biol. 5/2012;32:00-00***
http://atvb.ahajournals.org/content/early/2012/04/12/ATVBAHA.112.249854

Lp-PLA2 is Associated with LysoPC which is Correlated with Plaque Inflammation

- Study fits with recent publication showing the vast majority of Lp-PLA2 is manufactured in the plaque; plasma levels do not correlate strongly (r value was positive, but only 0.30 – weak)
- Study supports the strong signal that Lp-PLA2 is a 'player'
- As a 'player', it is a target of therapy
- At present, clinically we are forced to rely on the plasma level as a judge of effectiveness; at least there is a positive correlation

Isabel Gonçalves, et. al. ***Arterioscler Thromb Vasc Biol. 5/2012;32:00-00***
http://atvb.ahajournals.org/content/early/2012/04/12/ATVBAHA.112.249854

Lp-PLA2: BD Method

- PLAC-2 is important to follow routinely
- It appears to be causal of atherosclerosis and therefore, a direct target of therapy
- We need to utilize plasma levels clinically although arterial wall concentrations may be different

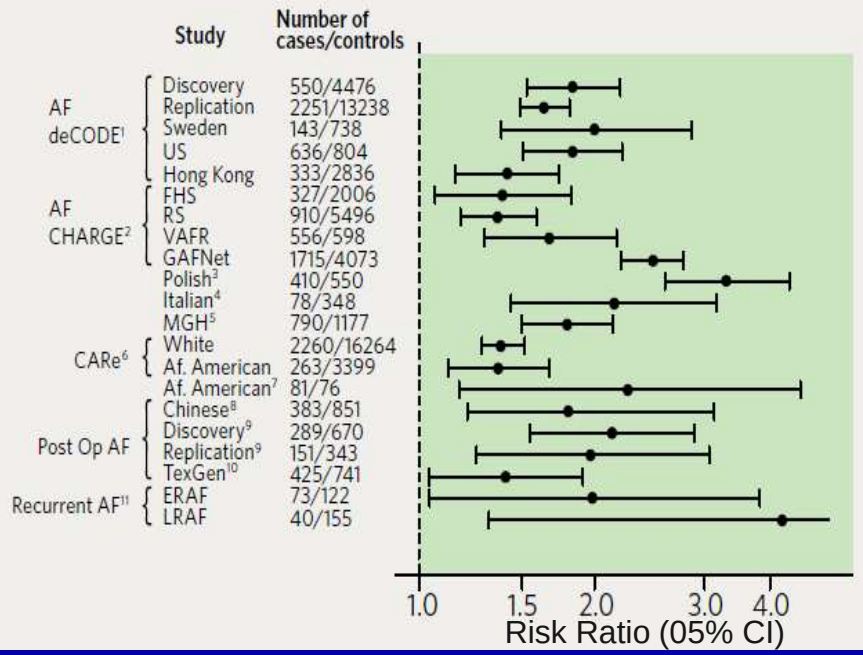
Genetics

New Genetic offering from BHL

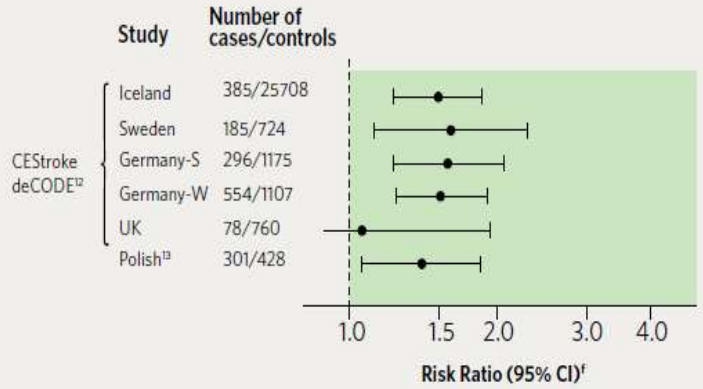
The 4q25 rs2200733 Risk Allele

- The rs2200733 risk allele has been shown to be associated with a 1.7x increased risk of AF and a 1.5x increased risk of CE stroke
- This risk is independent of the rs10033464 risk allele

AF Risk and 4q25 rs2200733

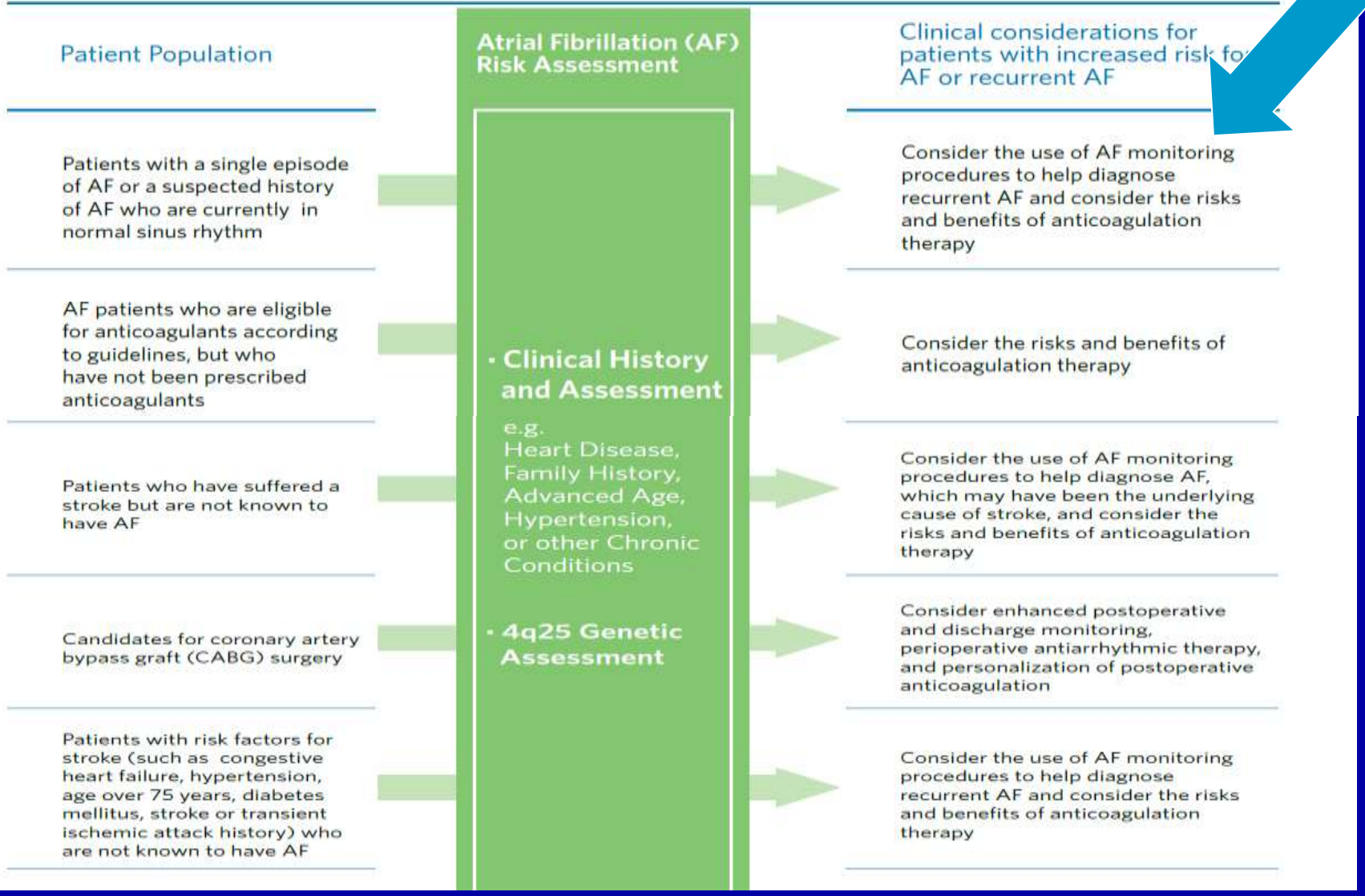


CE Stroke Risk and 4q25 rs2200733

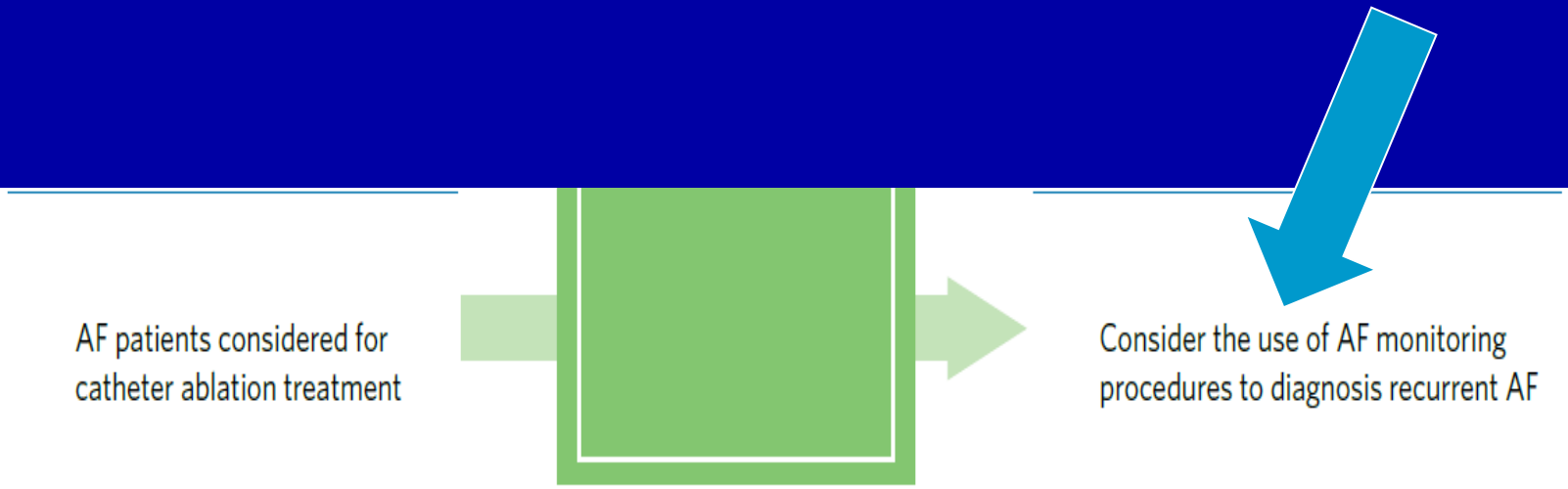


Patient Populations and Potential Clinical Considerations

4q25-AF Risk genotyping provides information that can help predict increased risk of AF and CE stroke related to AF. Physicians may benefit from knowledge of their patient's increased AF risk, and wish to consider additional clinical follow-up for those patients.



Patient Populations and Potential Clinical Considerations



The materials and data presented herein are for informational purposes only. Health care providers should rely on their learning, education, experience, and knowledge of a patient's clinical status when determining how to diagnose and treat a patient.

Warfarin to Dabigatran: safety

113 patients switched from warfarin to dabigatran. clinical events that necessitated medication withdrawal from the first six months on dabigatran were compared with a six-month previous warfarin treatment period.

Warfarin: 1 event (0.88%) drug discontinuation—hospitalized due to high INR.

Dabigatran: 13 events (11.5%) - one treatment-related death (GI bleed), four other bleeding episodes (two GI bleeds, one rectus sheath hemorrhage, one intracranial hemorrhage associated with trauma), one deep venous thrombosis, one atrial thrombus, one transient ischemic attack, one skin rash, and four patients with GI symptoms.

These adverse reactions were more common in older patients and in females.

Wurster MW. Dabigatran use in the real world: Preliminary results of a prospective trial comparing outcomes with dabigatran and warfarin therapy. Research abstracts. Am J Hematol 2012; 87:S146-S200.

Very Low Doses of Omega 3's May not be Beneficial

- Meta-analysis 14 omega-3 trials; 20,485 pts.; follow-up generally one to as long as 4.7 years
- 89% of the treated individuals received an average of 0.72 grams of omega-3/day (EPA-DHA)
- Only significant CV benefit was reduction in CV death: RR -0.91 (95% CI, 0.84-0.99)

Sang Mi Kwak, MD, et. al. Arch Intern Med. Published online April 9, 2012. doi:10.1001/archinternmed.2012.262

Omega 3 and LV function

133 chronic HF, minimally symptomatic patients were randomly assigned 2g n-3 PUFAs or placebo

LV function and functional capacity were assessed pre & 12 mo.

	Placebo	2 g N-3 PUFA	P-value
LV EF	Drop by 5%	Increase by 10.4%	P<0.001
Peak VO2	Drop by 4.5%	Increase by 6.2%	P<0.001
Exercise Duration	Drop by 4.8%	Increase by 7.5%	P<0.001
HF Classification (NY Heart Assoc)	1.83±0.38 to 2.14 ±0.65	1.88±0.33 to 1.61±0.49	P<0.001
Hosp. rates	30%	6%	P=0.0002

Nodari et al. Journal of Amer College of Cardiogy. Vol. 57, No 7 2/2011

Case Submission – Dr. Rocky Patel, MD - Arizona

6/2011: 68 yo Male established in 6/11, h/o htn (treated) and hi cholesterol in past, h/o PD in past who is statin phobic (myalgia with pravastatin in past). BP 132/82 wt 194 BMI 32.28

Meds Moxepril 15 qd, Cialis 20 mg, ASA 81 mg qd, Nasonex NS, Astelin

Labs: Initial: TC 165 TG 75 LDL 97 HDL 53 APOB 72

hsCRP 6.9, LpPLA2 203 Vit d 49 mcalb/cr 7.3, mpo 571, F2 WNL,

KIF trp/arg, 9p21 aa-gg, APOE 3/3, FBS 104, 1 hr 142, 2 hr 94.

CIMT 59th%, plaque 1.8mm rt bulb het , 1.4 mm lt bulb

6/2011: Dr. Patel's treatment plan:

Action Plan:

1. Periodontal evaluation and treatment
2. start:

RRY	Pomegranite extract
Pyconogenol	Resveratrol
Grapeseed	VN Blood Sugar Support

3. Continue ACE 1
4. Lower carb diet and wt loss

2/2012: Dr. Patel's plan cont:

Patient is status post PD treatment -

BP 124/78 wt 186.7 BMI 32.09

Meds: no changes

Labs: TC 166 TG 66 LDL-D 76 HDL 52 HbA1C 5.5

LpPLA2 remains elevated at 209, hsCRP 0.9.

Oral DNA test after treatment has all pathogens below threshold and plaque index less than 35% (low)

Question:

Despite PD treatment, LpPLA2 remains elevated with discordance with CRP. Time to convince this patient to go on statin therapy? Why LpPLA2 remains elevated, not enough time?

Dr. Patel's question -

"I think it is plain and simple, he has no other reason for elevated Lp-PLA2. I find it surprising though, that his had discordance with CRP."

"It makes me ponder if his PD is still active in some way even though bacteria are below threshold, which is why I find this case interesting. I know I will not have a problem "convincing" to go on statin therapy. But we will optimize have vit d/coq10 status and then start very slowly, probably with 2-3x/week dosing statin and assess tolerablity"

Dr. Patel in the news…..

- http://www.azfamily.com/news/One-womans-weight-loss-secret-how-she-dropped-150-pounds-150643965.html