Bale/Doneen Live Chat Session

August 2011

Delivered: September 1st

5:30-6:30 pm PST

Amy L. Doneen MSN, ARNP

Outline for August Live Chat Session

New Data published in August 2011

1. AHA Prevention
2. Red Flags/Risk Factors
3. Disease/Structure
4. Homocysteine
5. Medication
6. Lifestyle
7. Two cases - 1. HDL subs, 2. IMT soft plaque

Primary Prevention and cost

Primary Prevention Strategies Cost Savings/Value

- Community-based Programs
- Worksite Wellness Programs
- School-based Programs
- Building bike and pedestrian trails
- Pedometer and Walking Programs
- Reducing sodium in food supply
- Obesity Management Programs
- Excise taxes on Tobacco

Weintraub WS et al. Circulation. July 25, 2011;124:000-000

Comprehensive Prevention Program

- *Community Based Programs - physical activity, improve nutrition, prevent smoking*
  - ROI of $5.60 per dollar spent within 5 years
- *Worksite wellness Programs*
  - Medical costs fall $3.27 per dollar spent x 1 yr
  - Absenteeism falls by $2.73 for dollar spent
- *School-based initiatives – healthy eating and physical activity*
  - Cost effectiveness is $900-$4305 per quality adjusted life year saved.

Weintraub WS et al. Circulation. July 25, 2011;124:000-000

Physical Activity

- *Building Bike and Pedestrian Trails:*
  - For every $1 invested in building trails, $3 saved in medical costs

- *Physical Activity programs (pedometers and walking programs)*
  - Incremental cost effectiveness ranging from $14,000-$69,000 per quality of life year saved.

Weintraub WS et al. Circulation. July 25, 2011;124:000-000

Diet Nutrition
Obesity Prevention
Tobacco Control/Prevention

- *Reducing Sodium in food supply with goal of 1500mg/day per person of sodium:*
  - Result in $26.2 billion in health care savings annually

- *Obesity Management Programs:*
  - ROI of $1.17 per dollar spent.

- *Tobacco Control and prevention:*
  - A 40% tax-induced cigarette price increase would reduce smoking by 15.2% by 2025
  - total cost savings of $682 billion

Weintraub WS et al. Circulation. July 25, 2011;124:000-000

AHA Preaches Prevention

- Review conducted by the AHA Advocacy Coordinating Committee

- "True healthcare reform will be realized only when we focus attention on disease prevention and not disease management," AHA president - **Dr Gordon F Tomaselli**

- Every $1 spent in wellness programs would save $3.27 in medical costs and $2.73 in absenteeism costs.

- "What we spend on cardiovascular disease is not sustainable. But we can afford to prevent it," - **Dr William S Weintraub**

Weintraub WS, et. al. *Circulation* 7/2011. DOI: 10.1161/CIR.0b013e3182285a81

Red Flags/Risk Factors

Women and Smoking

Stock Volatility

Increased risk of coronary heart disease among women smokers compared with men

- In a study of more than two million people, researchers showed that the pooled adjusted female-to-male relative risk of coronary heart disease in smokers vs nonsmokers is 25% higher in women.

- In the 75 cohorts, which included 2.4 million participants, the pooled adjusted female-to-male relative risk ratios of smoking compared with not smoking for coronary heart disease was 1.25 (95% CI 1.12-1.39, p<0.0001).

- The relative risk ratio increased by 2% for every additional year of study follow-up, a finding that suggests the longer a woman smokes, the greater her risk of developing coronary heart disease compared with a man who has smoked the same length of time.

Huxley RR, Woodward M. Cigarette smoking as a risk factor for coronary heart disease in women compared with men: a systematic review and meta-analysis of prospective cohort studies. *Lancet* 2011; (11) 60781-2.

Stock Volatility Increases CHD Mortality Risk

- Daily CHD death and stock performance data were collected from Shanghai btw 1/1/06-12/31/2008
- 22,272 CHD deaths
- Fewest deaths coincided with little to no change of the Stock *Index*.
- CHD deaths: in a 1-day lag model, each 100-point change of the *Index* corresponded to 5.17% (95% CI: 1.71-8.63) $p<0.01$

Wenjuan Ma, et. al. ***European Heart Journal***. 6/2011;32(8):1006-1011

cIMT and CV predictability

Carotid-Wall Intima–Media Thickness and Cardiovascular Events

Hypothesized that the IMT of the CCA and ICA would add to the predictive value of FRS regarding new-onset cardiovascular events.

Increased IMT of the CCA represents a form of atherosclerosis that is manifested as diffuse arterial-wall thickening, whereas increased IMT of the proximal ICA is a surrogate for focal atherosclerotic plaque.

Joseph F. Polak, M.D., M.P.H., Michael J. Pencina, Ph.D., Karol M. Pencina, Ph.D., Christopher J. O'Donnell, M.D., M.P.H., Philip A. Wolf, M.D., and Ralph B. D'Agostino, Sr., Ph.D.

The NEW ENGLAND JOURNAL of MEDICINE

Polak JF et al. N Engl J Med July 21, 2011;365:213-221

Study population:

Framingham Offspring Study cohort, composed of non-Hispanic whites, who were undergoing the sixth examination cycle, 2/1995 through 9/1998.

Of the 3532 persons seen during the clinic visit, 2946 had interpretable images of the internal carotid artery.

Mean CCA IMT: measured over a segment of the common carotid artery that was 1 cm long, located approximately 0.5 cm below the carotid-artery bulb, exclude plaque

Max IMT of Internal: Defined as the greatest intima–media thickness in either the right or left internal carotid artery extending from the bulb to 1 cm above the carotid sinus.

Plaque: defined as an intima–media thickness of more than 1.5 mm

Reproducibility: 37 participants. 0.94 for the mean IMT CCA and 0.76 for the Max IMT of Internal carotid artery.

Polak JF et al. N Engl J Med July 21, 2011;365:213-221

Results:

The results showed that the Framingham risk factors were all significant predictors of cardiovascular disease.

Addition of mean CCA IMT: was significantly associated with the risk of cardiovascular disease: HR per 1-SD increase in thickness, 1.13; 95% [CI], 1.02 to 1.24; P=0.02

Addition of maximum IMT of ICA was also significantly associated with the risk of cardiovascular disease: HR per 1-SD increase in thickness, 1.21; 95% CI, 1.13 to 1.29; P<0.001

When ICA IMT was added to the model, the predictability sign increased by 0.010 (95% CI, 0.003 to 0.016; P=0.003), from 0.748 (95% CI, 0.719 to 0.776) to 0.758 (95% CI, 0.730 to 0.785).

Polak JF et al. N Engl J Med July 21, 2011;365:213-221

Reclassification Index of FRS

Inclusion of max IMT of the ICA: (P<0.001)

5.8% for participants with cardiovascular events

1.8% for participants without cardiovascular events

7.6% overall

Addition of IMT of ICA but not for mean IMT of CCA (P=0.99)

0.4% for events

0.4% for nonevents

0.0% overall

ICA IMT sign increased the net reclassification index (P<0.05 for all)

6.7% for men and 9.2% for women

9.1% for persons ≤ 60 years old

7.6 % for persons ≥ 60 years old

Polak JF et al. N Engl J Med July 21, 2011;365:213-221

Predictive value of plaque

The presence of plaque (IMT > 1.5 mm in the internal carotid artery), was a significant independent predictor of cardiovascular events.

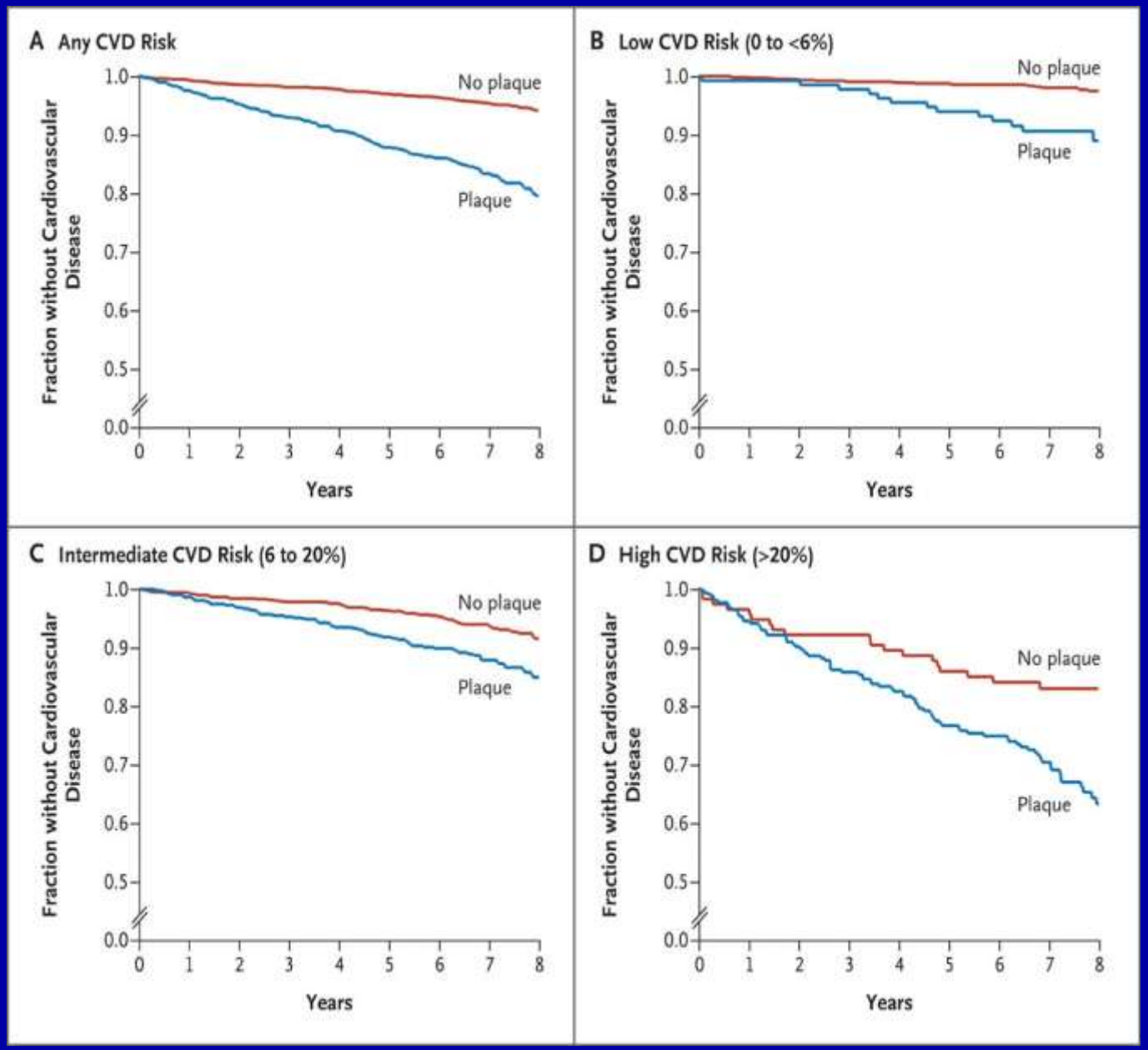
Increase of predictability from 0.748 to 0.762 (increase of 0.014; 95% CI, 0.003 to 0.025; P=0.02) (P=0.01)

Modest net reclassification index of 7.3%

Presence of plaque significantly improved the prediction of new-onset cardiovascular disease across all FRS categories.

Polak JF et al. N Engl J Med July 21, 2011;365:213-221

Probability of New-Onset (CVD) based on the presence of plaque in the ICA.



Polak JF et al. N Engl J Med July 21, 2011;365:213-221

CIMT Change as a Predictor of CV Events

Intervention	Ref. IMT trials	Result	Ref. event trials	Result	Congru.
Pravastatin	10-12,39,42	Benefit	54-56	Benefit	yes
Lovastatin	40,41	Benefit	53	Benefit	yes
Fluvastatin	43,46	Benefit	62	Benefit	yes
Rosuvastatin	13	Benefit	63	Benefit	yes
Simvastatin	44	Neutral	58,60	Benefit	no
Atorvastatin	45	Benefit	57,59,61	Benefit	yes
Niacin	47	Benefit	No data yet	NA	NA
Torceptrapib	48,49	Neutral	64	Harm	no
Ezetimibe	50	Neutral	65	Neutral	yes

Similarity between results from CIMT trials and event trials on the effects of lipid-modifying therapies strongly support the impact of changes in CIMT as a predictor of clinical events

Peters, S.A.E., et.al. ***Am J Cardiovasc Drugs***. 8/2/2011;11(4):253-263

Value of Carotid Intima-Media Thickness and Significant Carotid Stenosis as Markers of Stroke Recurrence (IMT-ARTICO)

Analyze outcome differences in stroke patients with high carotid IMT values compared with patients with significant carotid stenosis

Included 620 independent patients older than 60 years with a first-ever noncardioembolic stroke. Patients were followed-up for 1 year.

Primary end point was a composite of cardiovascular events and death.

Analyzed ultrasonographic data from 599 patients.

- 117 cases of carotid stenosis ≥50%
- 110 cases of mean CCA IMT of high IMT group ≥1.11 mm
- 372 control group - stroke patients with an IMT <1.11 mm, no SCS

Roquer, J et al, ARTICO Study, abstract 8.20.2011. Barcelona Span Hospital Universitari del Mar.

Results:

During follow-up, 88 patients (14.7%) had an end point event.

Male gender, diabetes, symptomatic PAD , ankle brachial index ≤0.9, SCS, and high IMT were related to the primary end point.

Factors related to primary end point of thrombotic stroke:

Peripheral Arterial Disease: (HR, 2.06; 95% [CI], 1.18–3.59; *P*=0.011)

Carotid Stenosis >50%: (HR, 3.02; 95% CI, 1.78–5.13; *P*=0.0001)

High mean IMT ≥1.11 mm: (HR, 1.86; 95% CI, 1.05–3.29; *P*=0.032)

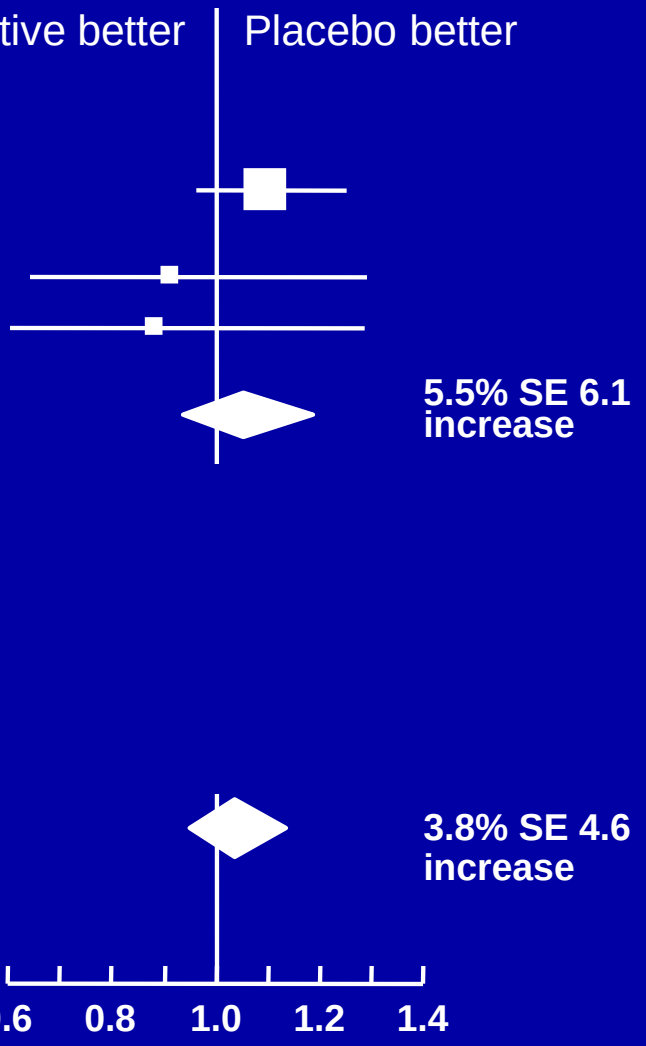
Roquer, J et al, ARTICO Study, abstract 8.20.2011. Barcelona Span Hospital Universitari del Mar.

Homocystine

- Marker vs Player?

Lowering Homocysteine does not reduce Mortality

Cause of death	Folate allocation: Active (n=6033)		Placebo (n=6031)	
CHD	463	(7.7%)	422	(7.0%)
Stroke	59	(1.0%)	65	(1.1%)
Other vascular	51	(0.8%)	58	(1.0%)
All vascular	**573**	**(9.5%)**	**545**	**(9.0%)**
All causes	**983**	**(16.3%)**	**950**	**(15.8%)**



12,000 stable post MI pts.; followed 6.7 yrs.
Homocysteine lowered average 28%;
30% baseline levels ≥14

SEARCH trial University of Oxford,Nuffield Department of Clinical Medicine

11/92008 www.ctsu.ox.ac.uk

Homocysteine Elevation Associated with Increased CV Risk

Post hoc analysis of 6450 participants from the Multi-Ethnic Study of Atherosclerosis (MESA)

Hard CHD events	**2.90 (1.69-4.95)**	**< 0.001**
HR for homocysteine >15 µmol/L vs <15 µmol/L		
All CVD events	1.79 (1.19-1.95)	0.006
Hard CHD events	2.22 (1.20-4.09)	0.01

Veeranna V, et al. *J Am Coll Cardiol* 8/30/2011; 58:1025-1033.

Homocysteine Elevation Associated with Increased CV Risk

Post hoc analysis of 6797 adults in the third **National Health and Nutrition Examination Survey** (NHANES 3)

End point	HR (95% CI	p
HR for homocysteine >15 µmol/L vs <15 µmol/L		
CVD deaths	2.72 (2.01-3.68)	< 0.001
CHD deaths	2.61 (1.83-3.73)	< 0.001

Veeranna V, et al. *J Am Coll Cardiol* 8/30/2011; 58:1025-1033.

Homocysteine: net reclassification improvement index (NRI) score

- Adding the biomarker led to significant reclassification of FRS:
- NRI of 0.35 (95% CI 0.17-0.53; p<0.001) in MESA
- NRI of 0.57 (95% CI 0.43-0.71; p<0.001) in NHANES 3.

Veeranna V, et al. *J Am Coll Cardiol* 8/30/2011; 58:1025-1033.

Criteria for New Biomarkers

- Relatively easy to measure ✓
- Add new information to traditional risk factors ✓
- Potential for changing therapy ✓
- Cost-effective ✓
- Predictive in different prospective cohorts ✓

Wang, T. J.,et. al. **Assessing the Role of Circulating, Genetic, and Imaging Biomarkers in Cardiovascular Risk Prediction** *Circulation* 8/2011, 123:551-565

Treatment information

- Chantix
- Diet of Soy Protein
- Exercise
- Optimism
- Actos – latest from FDA

Varenicline Increases CV Risk

- Meta-analysis;14 trials; 8,216 pts without CAD; 7 to 52 wks

Outcome	Varenicline (n=4908), n (%)	Placebo (n=3308), n (%)	Odds ratio (95% CI)
Serious CV events	52 (1.06)	27 (0.82)	1.72 (1.09-2.71)

1 in 10 on Chantix quit smoking; the NNT to cause 1 CV event is 28

FDA warning: varenicline may increase CV event risk in patients with CVD; based on study of 700 pts. with known CAD

Singh S, et. al. *CMAJ* 7/2011. Available at: http://www.cmaj.ca

Diet rich in soy proteins, viscous fibers, nuts, and vegetables is more effective than low saturated fat diet for LDL

- Randomized; 24-wk; 351 hyperlipid. pts (average LDL 171); two dietary interventions; outcome LDL reduction
- Standard diet (SD): low in sat. fat
- Portfolio diet (PD): plant sterols, soy protein, viscous fibers, and nuts. 6 mos. of dietary advice plus seven 40-minute counseling sessions (intensive group); two sessions (routine group)
- Results: PD – intensive: LDL down 26 mg/dL $p<0.001$

  PD- routine : LDL down 24 mg/dL $p<0.001$

  SD : LDL down 8 mg/dL

  PD versus SD was significant with $p<0.001$

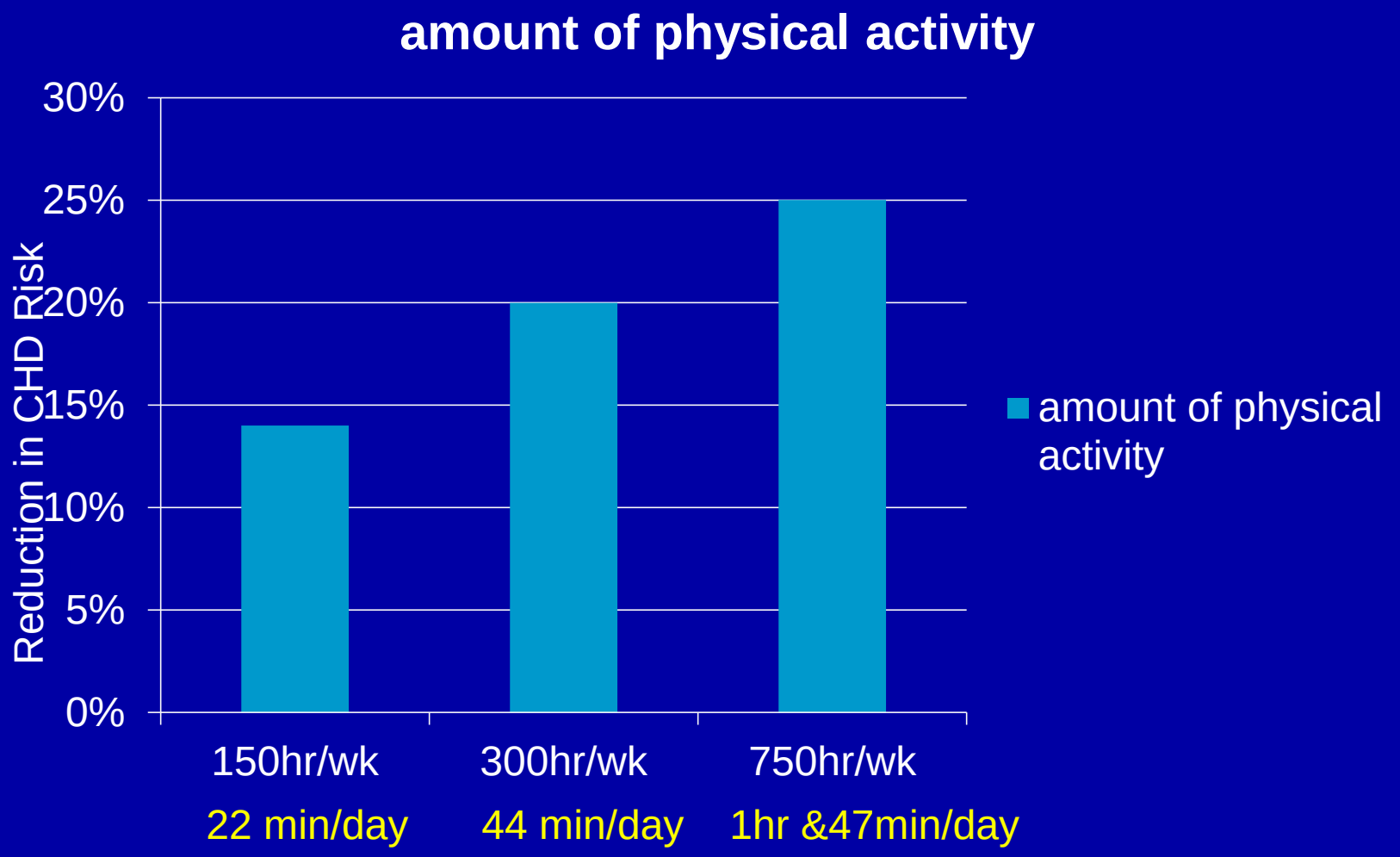
Jenkins DJ, et al. *JAMA* 8/24/2011; 306:831-839.

Exercise Amount Related to CHD Risk

- Meta-analysis 26 studies since 1995 evaluating CHD risk reduction from physical activity
- 150 min/wk reduces risk 14%
- 300 min/wk reduces risk 20%
- 750 min/wk reduces risk 25%
- Physical activity at any level lowers risk of CHD, compared with those who did nothing.

Sattelmair J, et. al. *Circulation* 8/1/2011; DOI: 10.1161/CIRCULATIONAHA.110.010710.
Available at: **http://circ.ahajournals.org**

Exercise Amount Related to CHD Risk



Sattelmair J, et. al. *Circulation* 8/1/2011; DOI: 10.1161/CIRCULATIONAHA.110.010710. Available at: **http://circ.ahajournals.org**

Optimism Reduces Stroke Risk

- Prospective 2 yr. observation of 6,044 adults ≥ 50 yo; 88 strokes
- Utilized an optimism measure ranging from 3 to 18
- Each unit increase in optimism associated with an OR of 0.90 for stroke (95% CI, 0.84 to 0.97) *p=0.01*
- Significant post fully adjusting for: age, behavioral, biological, and psychological stroke risk factors

Kim ES, et. al. *Stroke* 7/21/2011; DOI:10.1161/?STROKEAHA.111.613448.

Pioglitazone and Bladder Cancer Risk

- FDA AERS 1/04-12/09: 31 cases of bladder cancer in pio pts out of 37,841 AERs for pio
- Only 4 cases in pts on pio >24 mos.
- 24 cases involved multiple drug use

- Reporting odds ratio (ROR) is calculated by case/noncase methodology ('noncases' were all the AERs reported for pio - not bladder CA)

- ROR was only significant in older pts and in the yrs. '04, '06, '07, '08 – 4, 9, 5, 6 cases respectively
- Takeda is doing 10 yr. observational study

Piccinni, C., PhD, et. al. Diabetes Care 6/2011 Vol. 34: 1369-1371

Pioglitazone: FDA Warning

- Not start in pts with bladder cancer and used with caution in pts with a hx of bladder cancer
- If red color in their urine, notify provider
- If develop urinary urgency or pain, notify provider
- BD Method would add: use with caution in smokers; run urinalysis with routine labs

FDA Drug Safety Communication:
Updated drug labels for pioglitazone-containing medicines. August 4, 2011

Case 1 – statin and subs

GM is a 64 year old Caucasion woman with a history of non-Hodgkins lymphoma, hyperlipidemia and chronic sinusitis.

Family history: CAD father died of MI at 63

Bother with sudden death at 53

DM in mother and grandmother at older ages

She does not smoke and drinks 1-2 glasses of red wine per week, exercises 5 days per week walking 1 1/2 miles

Ht 5’4” Wt 184 BMI 32 Waist 40 inches, normotensive

Prior to her initial Berkeley lipid panel pertinent lipid therapy was simvastatin 20

Initial Berkeley Jan 2010:

TC 167	Apo E: 3/3
LDL 89	hsCRP: 5.3
HDL 44	Lp-PLA2: 105
TG 171	HDL 2B: 20%
Apo B 71	Insulin: 15

Simvastatin was continued. She was started on Niaspan 500 mg daily and titrated to 1000 mg daily which was the maximal dose she would tolerate.

At some point in her therapy due to cost, she changed to an OTC product (review of the label did indicate niacin and not inosital hexanicotinate or nicatinomide).

In subsequent laboratory findings:LDL, HDL, Apo B have improved. However, HDL 2b% and LDL 3a+b and LDL 4b had continued to rise.

The current treatment plan is to:

- Obtain 2 hour OGGT
- Change niacin to Niaspan (or Enduracin if Niaspan is not tolerated)
- Replace vitamin D

- Questions from Amy: Disease, Fire, Roots?

Question Regarding HDL 2b%

- Is there any evidence that rosuvastatin increases the HDL2b% subfraction specifically?

- If the patient is found to be insulin resistant, has to use of pioglitazone been shown to raise HDL2b% specifically in a non-insulin resistant patient?

Rosuvastatin 40mg is more effective than Atorvastatin 80mg with HDL Sub-particles

- large ă-1 and ă-2 HDLs decrease the risk of CHD and protect against progression of ASVD
- 306 hyperlipidemics; six weeks of rx
- The 2 large HDL particles were increased significantly higher for rosuvastatin than atorvastatin (ă-1, 24% vs 12%; ă-2, 13% vs 4%; p <0.001)
- In subjects with low HDL (<40 mg/dl for men, <50 mg/dl for women, n 99), increases in ă-1 were 32% versus 11%, and in ă-2, 21% versus 5% for rosuvastatin and atorvastatin, respectively

Asztalos, B.F., PhD, et. al. ***Am J Cardiol* 2007;99:681– 685**

Rosuvastatin 40mg is more effective than Atorvastatin 80mg for LDL Sub-particles

- 135 hyperlipidemics rx'ed with Crestor and 136 with Lipitor for 6 weeks
  - **sdLDL (-53% vs -46%); direct LDL (-52% vs -50%)**
  - **non-HDL (-51% vs -48%)**
  - **total cholesterol/HDL (-46% vs -39%)**

All in favor of Crestor p=0.01

Ai, M. et al., *Am J Cardiol* 2008;101:315-18.

Pioglitazone Improved CAD via Reducing TG/HDL

- Post hoc analysis 360 subjects in PERISCOPE
- Reduced progression of CAD was independently associated with improvements in the ratio of triglycerides to HDL among pioglitazone pts
- TG/HDL independently predicted change in total atheroma volume p=0.02

  adjusted for: sex,BP, history of PCI, hypercholesterolemia, **metformin** use, baseline HbA_{1C}, and baseline apoA-1.

Nicholls SJ, et. al., *J Am Coll Cardiol* 1/3/2011; 57:153-159.

HDL Ability to Perform Reverse Cholesterol Transport Enhanced with Pioglitazone

- 39 met. synd. pts; 16 pio for 12 wks. & 23 placebo; pio 30mg 6wks. then increased to 45mg

Rx	N	% change efflux	95% CI	p vs baseline	P vs placebo
Pio	16	11.3	1.8-20.8	0.02	0.04
Placebo	23	0.0	-6.2-6.1	0.99	

Increased HDL-C 14% : no significant association with change in efflux capacity ($r = 0.22$; $P = 0.18$

Khera, A. V., M.D., et. al. N Engl J Med 1/2011;364:127-35.

Case 2 – Soft Plaque

On serial CIMT, two areas of soft plaque are identified and I am asking what else could be done.

WG is 67 y/o Caucasian male diagnosed with coronary artery disease in 2000, at which time he had a stent placed. His additional problems are DM II (2009), HTN, hyperlipidemia, vitamin D deficiency (12, 2010).

His current medications are carvediolol 6.25 BID, Lipitor 40, Actos 15, Niaspan 1,000, Aspirin 325, Alfuzosin 10.

He is currently asymptomatic and his cardiologist feels he is doing fine. BP 122/64; overweight.

Labs:

Myeloperoxidase 193 (7/2010)

MACR 4.0 (7/2010), more recently 3.6

TG 129 (3/2011)

TG 69 (3/2011)

HDL 73, HDL2b 23% (3/2011; previously 14% in 6/10)

LDL 43, IIIa+b 11.9, IV 2.0 on BHL (3/2011)

A1c 6.4 (2011)

Vitamin D 42 (3/2011)

Creatinine 0.95

CIMT.

Feb, 2010, IMT 0.58, plaque burden 7.5

May 2011, IMT 0.50, plaque burden 5.9

BUT. Soft plaque present in left bulb and left IC in May 2011.

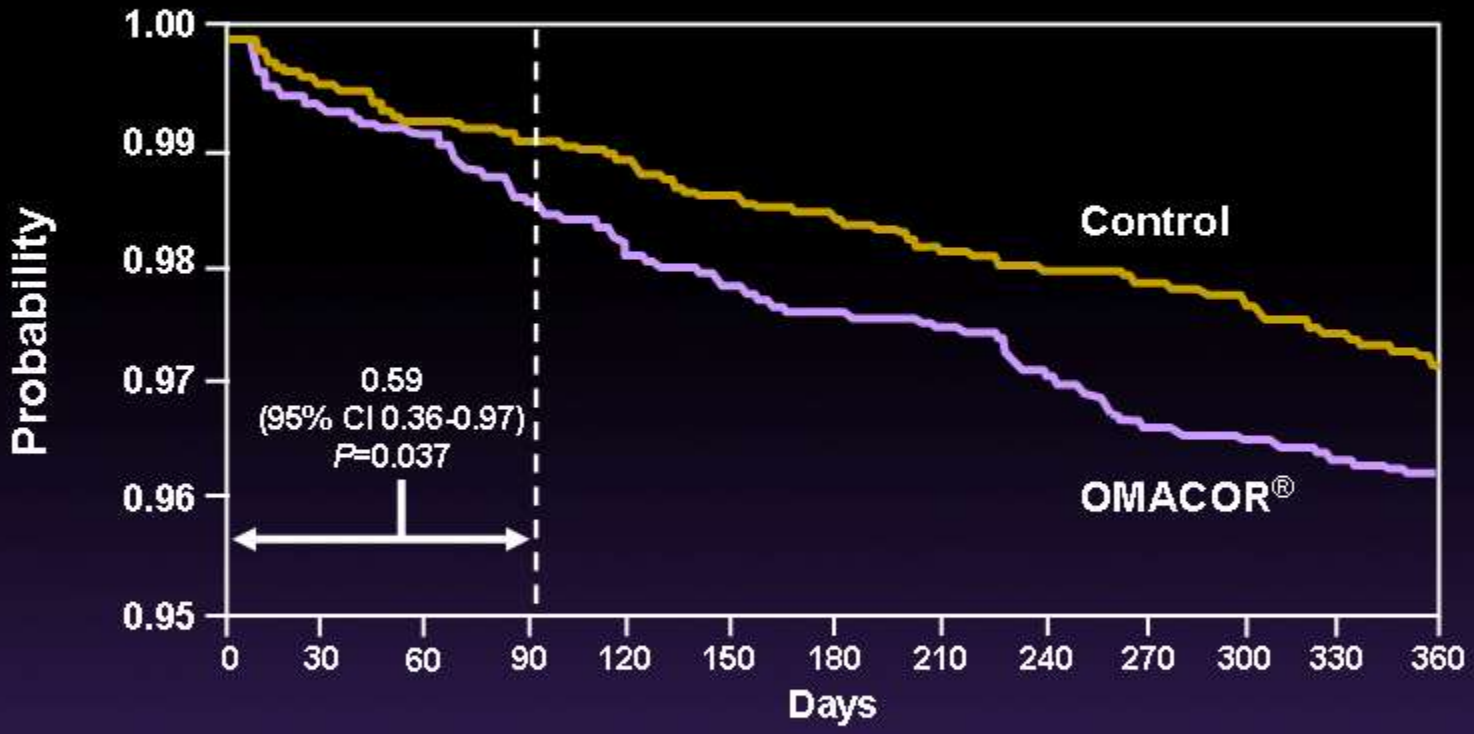
As stated initially, I am at a loss to explain the presence of soft plaque while every other parameter shows improvement, and I am at a loss to know what medication changes to offer him. I suppose the Actos could be increased, but I am concerned about hypoglycemia as the A1c drops, particularly in persons with established CAD.

Carvediolol 6.25 BID, Lipitor 40, Actos 15, Niaspan 1,000, Aspirin 325, Alfuzosin 10.

EDFROG

- 1. Education
- 2. Disease – tertiary (stent – CAD), ASVD/IMT - soft
- 3. Inflammation – hsCRP, MACR, Fibrin, Lp-PLA2, MPO
- 4. Root Causes - ?
  - Insulin resistance – yes/DM
  - Lipo(a) - ?
  - MPO - no
  - Vitamin D - treated
  - Periodontal disease ??
- 5. Optimal Goals – individualized goals
- 6. Genetics - KIF 6, 9P21, CYP2C19, LPA, Apo E , IL-1, haptoglobin?

GISSI-Prevenzione Trial
Early Effect on All-cause Mortality



Marchioli R et al. *Circulation*. 2002;105:1897-1903.

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Omega-3-acid ethyl esters

This slide is outside the approved indication for OMACOR® and may only be utilized in response to an unsolicited request.

Reliant PHARMACEUTICALS, INC.

L-carnitine in Combination with a Statin Lowers Lipo (a)

- 75 diabetics 30-70 yo; diets controlled; 4 months of therapy
- 37 – simva 20mg; 38 – simva 20mg plus L-carnitine 2g/day
- Mono simva group: baseline lipo (a) 30.4 $\pm$ 16.0 mg/dL
  4 mos lipo (a) 29.8 $\pm$ 15.8 mg/dL
- Combination group: baseline lipo (a) 31.7 $\pm$ 15.4 mg/dL
  4 mos lipo (a) 22.4 $\pm$ 15.7 mg/dL
- Difference between rx groups was significant with $p<0.05$
- Combo rx produced a 30% reduction in lipo (a)

Galvano, F., et. al. Expert Opinion Pharmacotherapy. 2009. 10(12):1875-1882

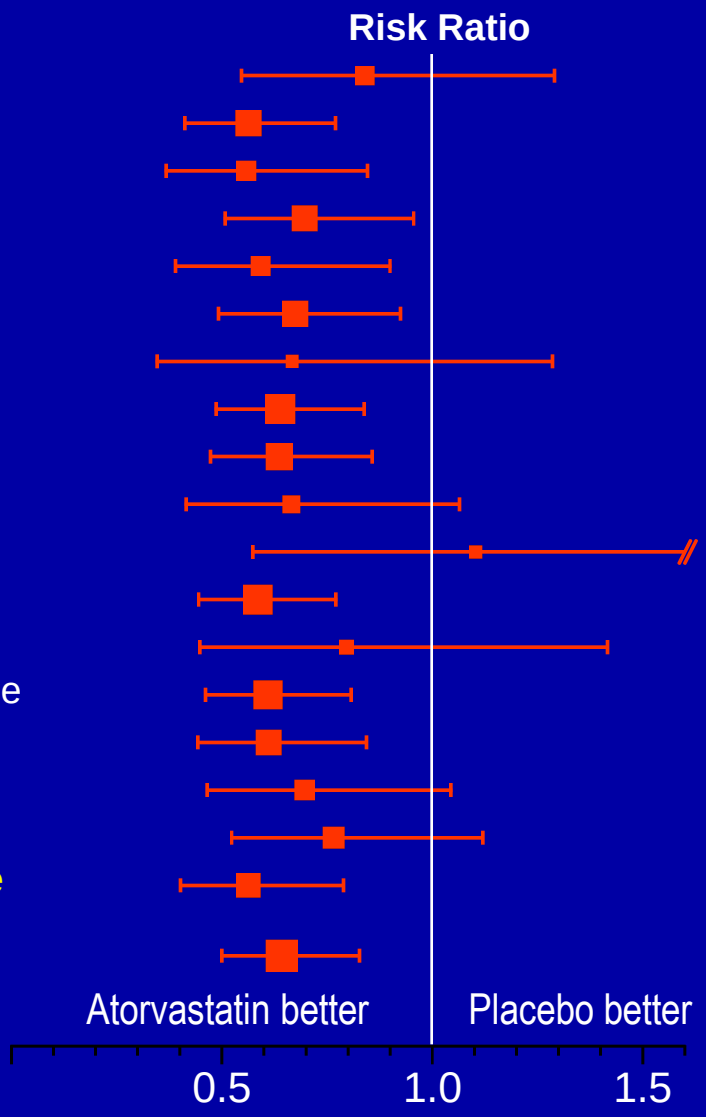
Atorvastatin Increases Insulin Resistance

- Randomized, blinded, placebo-controlled; 213 subjects; placebo or atorva 10,20,40,80mg; two months

- Atorva significantly increased fasting insulin (mean changes: 25%, 42%, 31%, and 45%, respectively) and A1c (2%, 5%, 5%, and 5%, respectively); compared baseline $p<0.05$ or placebo ($p=0.009$ for insulin and $p=0.008$ for A1c

Koh, K. et al., *J Am Coll Cardiol 9/*2010;55:1209-16

ASCOT Pre-specified Subgroups: Primary End Point



	Hazard Ratio
Diabetes	0.84 (0.55-1.29)
Nondiabetes	0.56 (0.41-0.77)
Current smoker	0.56 (0.37-0.85)
Noncurrent smoker	0.70 (0.51-0.96)
Obese	0.59 (0.39-0.90)
Nonobese	0.67 (0.49-0.92)
LVH	0.67 (0.35-1.29)
No LVH	0.64 (0.49-0.84)
Older (>60 years)	0.64 (0.47-0.86)
Younger (≤60 years)	0.66 (0.41-1.06)
Female	1.10 (0.57-2.12)
Male	0.59 (0.44-0.77)
Previous vascular disease	0.80 (0.45-1.42)
No previous vascular disease	0.61 (0.46-0.81)
Renal dysfunction	0.61 (0.44-0.84)
No renal dysfunction	0.70 (0.47-1.04)
With metabolic syndrome	0.77 (0.52-1.12)
Without metabolic syndrome	0.56 (0.40-0.79)
All patients	0.64 (0.50-0.83)

Area of squares is proportional to the amount of statistical information

Sever PS, Dahlöf B, Poulter N, Wedel H, et al, for the ASCOT Investigators. Lancet. 2003;361:1149-58

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.

The Oral Infections and Vascular Disease Epidemiology Study (INVEST)

- Overall periodontal bacterial burden was related to carotid IMT.
- This relationship was specific to causative bacterial burden and the dominance of etiologic bacteria (*A.a., P.g., T.f. T.d.*)
- Adjusted mean IMT values across tertiles of etiologic bacterial dominance were 0.84, 0.85, and 0.88 (P=0.002).

Desvarieux. ,M., et. al., Circulation, 2/28/2005; 111(5): 576

PD Pathogens Found in Carotid Atheroma

- 42 carotid endarterectomy specimens analyzed via DNA for PD pathogens
- *Porphyromonas gingivalis (78.57%, 33/42),*
- *Aggregatibacter actinomycetemcomitans (66.67%, 28/42)*
- *Tannerella forsythia (61.90%, 26/42)*
- *Eikenella corrodens (54.76%, 23/42)*
- *Fusobacterium nucleatum (50.00%, 21/42*
- *Campylobacter rectus (9.52%, 4/42)*
- *All had at least one; many had multiple pathogens*

Figuero, E., DDS, et. al.Journal of Periodontology; 8/2011. DOI: 10.1902/jop.2011.100719

Interleukin 1 (IL-1) polymorphisms Associated with Increased Risk of Coronary Artery Disease

- 504 patients referred for angiography for chest pain
- Patients classified as having 1-, 2-, or 3-vessel disease if angiography showed >50% stenosis
- Patients with no significant disease or mild disease (<30% stenosis) classified as controls
- *IL-1B allele 2, had an odds ratio that was almost as high as smoking (3.88)*

Am J Clin Nutr 2006;83(suppl):431S-5S; G.W. Duff

Points to consider when not seeing expected results on IMT

- 1. Are ALL root causes uncovered?
  - ? Lipo(a) – if yes, consider L-Carnitine and increase in Niaspan.
  - ? Periodontal (Oral DNA and IL-1) – if yes, consider local and systemic antiobiotic tx
- 2. Genetics?
- 3. Optimization of med selection based on co-morbidities - Omega 3, statin selection

Bale/Doneen: Upcoming meetings

Cleveland HeartLab & Bale/Doneen Reunion

September 15-17: Cleveland, OH