Bale/Doneen Live Chat Session

5/8/2013

5:30-6:30 pm PST

Bradley Bale, MD

Intention of the live chats

- New data and slides
- Discuss “hot” topics
- Case study
- Review upcoming meetings
- Open discussion for remaining

New Studies!!!

Red Flags

RA and CVD

- RA pts have 68% increased risk for heart attack and 41% stroke
- Increased risk is independent of traditional CV risk factors and is related to systemic inflammation
- RA worldwide prevalence of ~1%; increases with age; 5% of women aged >60 yo have RA

Ma¨ki-Peta¨ja¨ K. M., PhD, et. al. Circulation. 11/2012;126:2473-2480

Why??

RA and CVD

- CABG RA pts demonstrate histologically greater mononuclear cell infiltration within the aortic media and adventitia

- This suggests a subclinical vasculitis in RA pts

Ma¨ki-Peta¨ja¨ K. M., PhD, et. al. Circulation. 2012;126:2473-2480

RA and CVD

- 17 RA pts; 34 controls (non-RA with stable CVD)
- FDG PET/computed tomography (CT) of aorta at baseline and post 8 wks anti-TNF rx in RA pts
- Aortic pulse wave velocity was also assessed as indictor of stiffness (endothelial function)

Ma¨ki-Peta¨ja¨ K. M., PhD, et. al. Circulation. 2012;126:2473-2480

RA and CVD

- RA pts had higher baseline aortic TBRs vs controls
  (2.02±0.22 vs 1.74±0.22) P=0.0001
- After rx, aortic TBR fell significantly
  (1.90±0.29) P=0.03
- After rx, proportion of inflamed aortic slices (defined as TBR >2.0 decreased from 50±33% to 33±27%, P=0.03

Ma¨ki-Peta¨ja¨ K. M., PhD, et. al. Circulation. 2012;126:2473-2480

RA and CVD

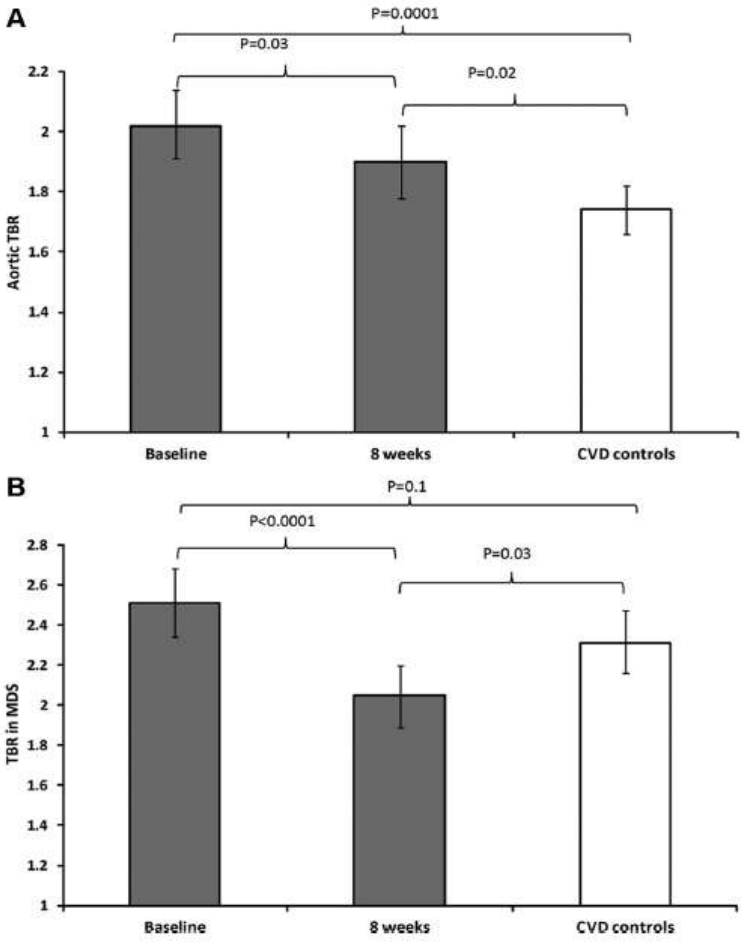
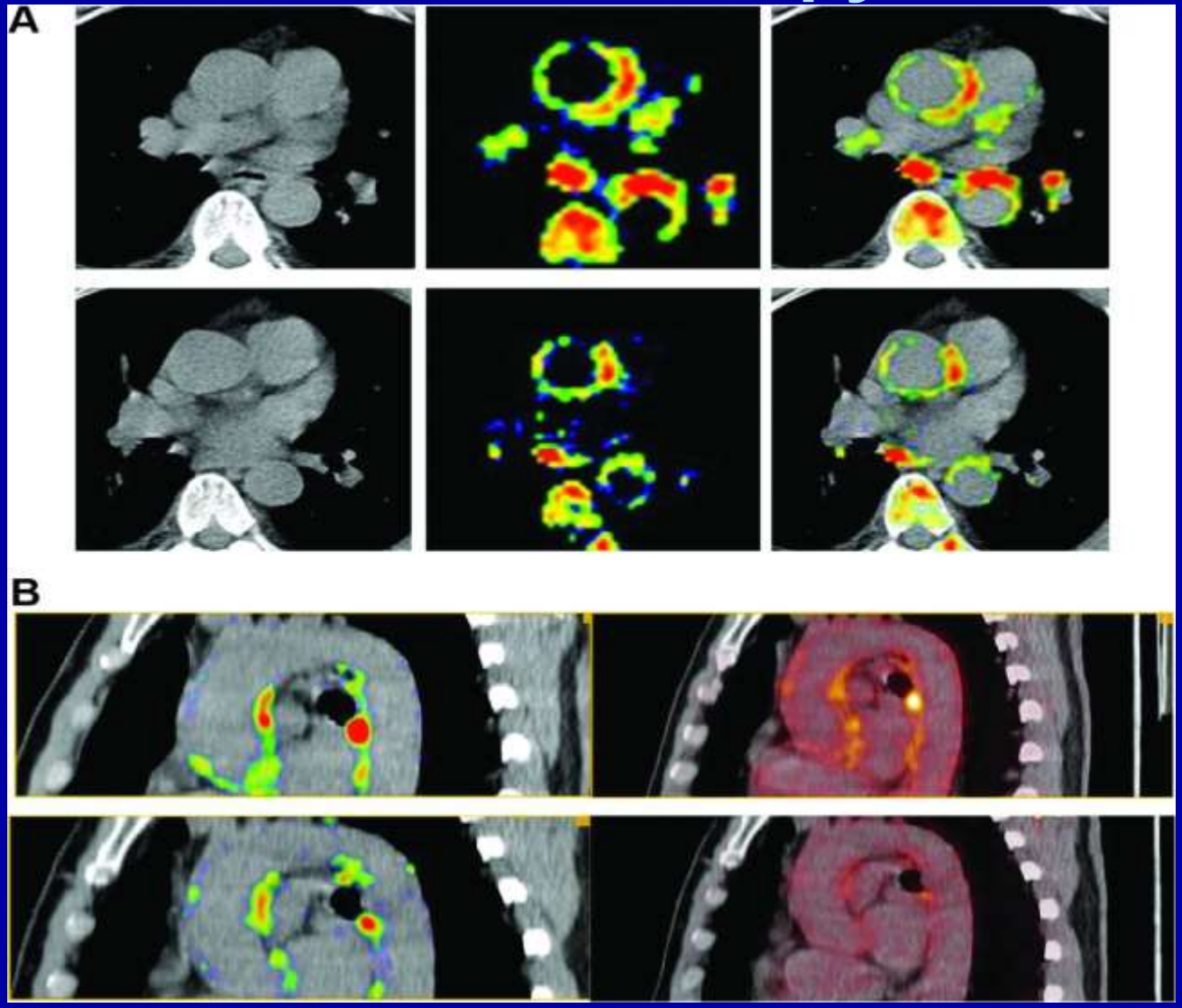


Figure 1. The effect of anti-TNF-α therapy on ^{18}F-FDG uptake. Seventeen RA subjects had ^{18}F-FDG PET/CT scans at baseline and 8 weeks after the initiation of the anti-TNF-α therapy. An age-matched control group (n=34) was scanned at baseline. **A,** tissue-to-background ratio (TBR) in the whole aorta. **B,** TBR in the most diseased segment (MDS) of the aorta. Bars represent means and 95% confidence intervals of means. ^{18}F-FDG-PET indicates ^{18}F-fluorodeoxyglucose positron emission tomography; CT, computed tomography; anti-TNF-α, anti-tumor necrosis factor α; and RA, rheumatoid arthritis.

Ma¨ki-Peta¨ja¨ K. M., PhD, et. al. Circulation. 2012;126:2473-2480

Typical PET/CT images before and after anti-TNF-α therapy.



Mäki-Petäjä K M et al. Circulation 2012;126:2473-2480

RA and CVD

- Aortic pulse wave velocity improved significantly with treatment

  9.09±1.77 to 8.63±1.42 m/s – P=0.04

- This enhancement correlated with the reduction of aortic TBR - (R=0.60, P=0.01)

Ma¨ki-Peta¨ja¨ K. M., PhD, et. al. Circulation. 2012;126:2473-2480

RA and CVD

Table 3. The Effect of Anti-TNF-α Therapy on Disease Activity, Inflammatory Markers, and Hemodynamics

	Baseline	8 wk	*P*
DAS28 score	6.52±0.78	4.38±1.61	<0.0001
CRP, mg/L*	11.0 (4.0–29.0)	3.0 (2.0–10.0)	0.007
ESR, mm/h*	22 (8.5–41.0)	13.0 (7.0–17.0)	0.04
MAP, mm Hg	104±11	104±12	0.9
Augmentation index, %	31±11	33±11	0.4
Brachial PWV, m/s	9.00±1.23	8.56±1.11	0.06
Aortic PWV, m/s	9.09±1.77	8.63±1.42	0.04
Baseline diameter, mm	3.94±0.59	3.91±0.68	0.8
FMD, %	3.54±2.34	6.66±3.17	0.003
GTN response, %	9.53±4.26	8.29±5.63	0.9

Values represent means±standard deviation. Significance was determined by using the paired Student *t* test, with the exception of skewed variables (*) where Wilcoxon signed rank test was used. n=17. DAS28 indicates disease activity score; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; MAP, mean arterial pressure; PWV, pulse wave velocity; FMD, flow-mediated dilatation; and GTN, glyceryl trinitrate.

Ma¨ki-Peta¨ja¨ K. M., PhD, et. al. Circulation. 2012;126:2473-2480

RA and CVD

- Suggests that RA pts exhibit a subclinical vasculitis.
- This helps account for the increased CVD risk seen in RA.

Ma¨ki-Peta¨ja¨ K. M., PhD, et. al. Circulation. 2012;126:2473-2480

What Provider Should Take Responsibility for RA Increased CV Risk?

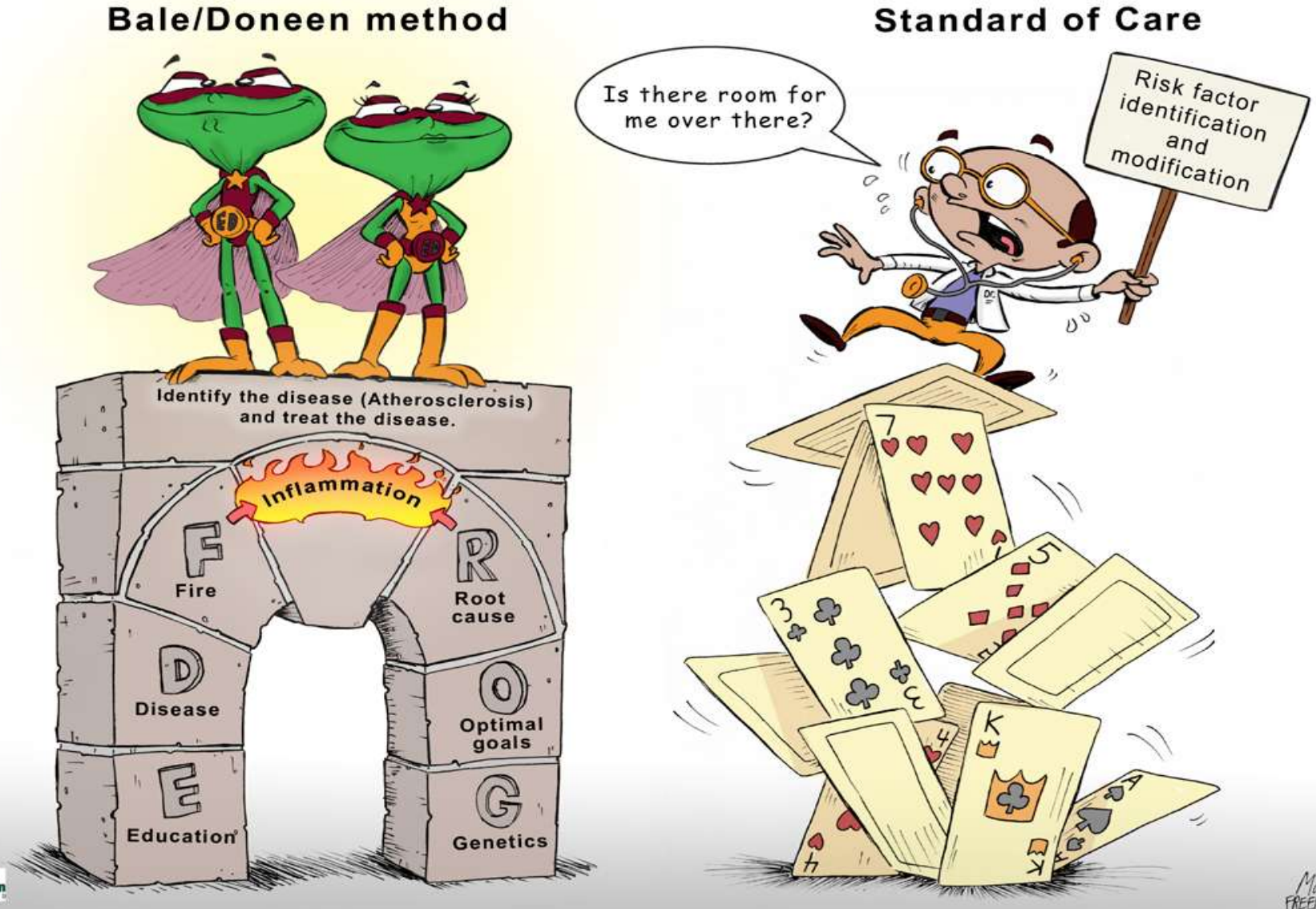
CV Risk Reduction Demands Coordinated Care in Pts with RA

- Rheumatologists may be well aware of the increased risk for CVD in RA pts, but a recent study suggests that they may be focusing on the rheumatic problem while passing the CV risk on to the primary care provider

- Better coordination of care is needed and perhaps more aggressive management of CV risk by the rheumatologist

Desai SS, Myles JM, and MJ Kaplan. Arthritis Research & Therapy, (2012)14:R270 doi:10.1186/ar4118.

What's the difference?



Adiponectin Paradox:
Higher Levels=Fewer CV Risk Factors
Higher Levels=Increased CV Risk

- 5,624 healthy pts; adiponectin at baseline; followed ~ 8 yrs.

- End point was all-cause mortality (801pts) ; MACE (502 pts)

Lindberg, S., et. al. 4/2013 *Amer. J of Cardio.* Volume 111, Issue 8: 1139 - 1145

Adiponectin Paradox:
Higher Levels=Fewer CV Risk Factors
Higher Levels=Increased CV Risk

High adiponectin was inversely associated with an increasing number of traditional CV risk factors

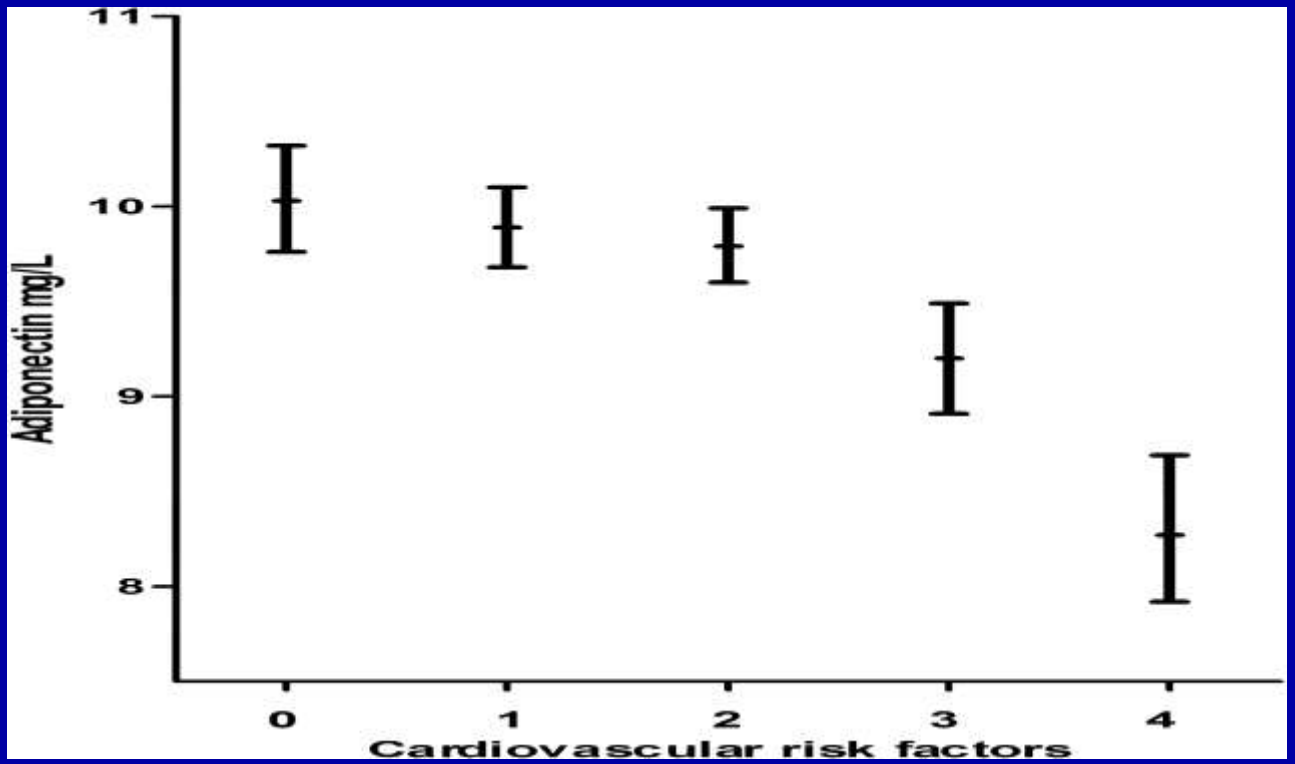
$p < 0.0001$

Lindberg, S., et. al. 4/2013 *Amer. J of Cardio.* Volume 111, Issue 8: 1139 - 1145

Adiponectin Paradox:

Higher Levels=Fewer CV Risk Factors

Higher Levels=Increased CV Risk



Plasma adiponectin levels dependent on numbers of traditional CV risk factors: (BP, DM, lipids, smoking) adjusted for age, gender, hsCRP, eGFR, BMI

Lindberg, S., et. al. 4/2013 *Amer. J of Cardio.* Volume 111, Issue 8: 1139 - 1145

Adiponectin Paradox:
Higher Levels=Fewer CV Risk Factors
Higher Levels=Increased CV Risk

HR for each 5 mg/L increase in adiponectin was 20% for death and 14% for MACE

HR- 1.20 (95% CI 1.14 to 1.27) p <0.0001

HR- 1.14 (95% CI 1.05 to 1.23) p <0.0001

Lindberg, S., et. al. 4/2013 *Amer. J of Cardio.* Volume 111, Issue 8: 1139 - 1145

Adiponectin Paradox:

Higher Levels=Fewer CV Risk Factors

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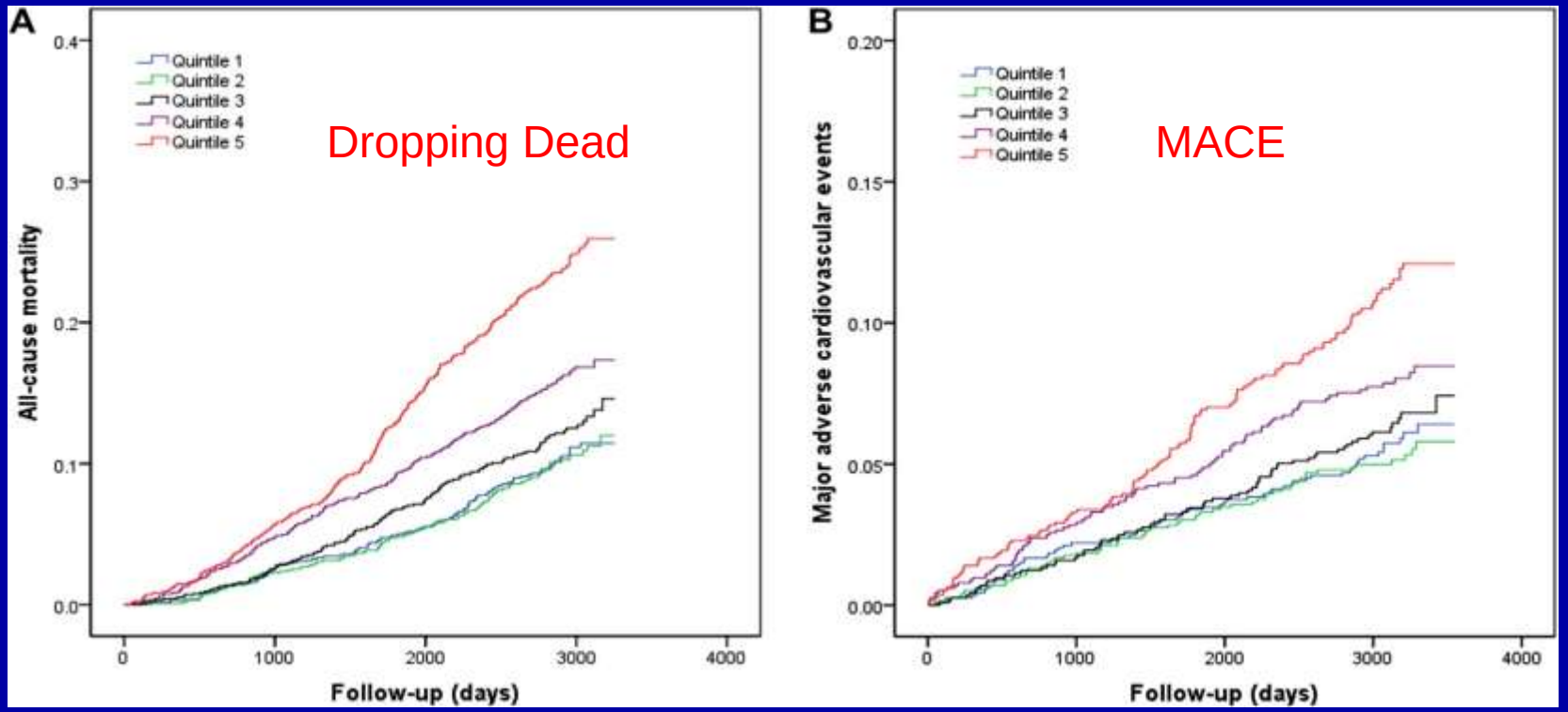


Kaplan-Maier plots of all-cause mortality and MACE according to adiponectin stratified in quartiles

Lindberg, S., et. al. 4/2013 *Amer. J of Cardio.* Volume 111, Issue 8: 1139 - 1145

Adiponectin Paradox:
Higher Levels=Fewer CV Risk Factors
Higher Levels=Increased CV Risk

Variable	All-cause Mortality		
	HR	95% CI	p Value
Low FRS, low adiponectin (n = 1,730)	1.0	—	—
Low FRS, high adiponectin (n = 381)	2.5	1.3–4.7	0.004

Cox proportional hazards regression models for risk of all-cause mortality according to FRS and high adiponectin (quintile 5) versus low adiponectin (quintiles 1 to 4)

Lindberg, S., et. al. 4/2013 *Amer. J of Cardio.* Volume 111, Issue 8: 1139 - 1145

BD Method Thoughts

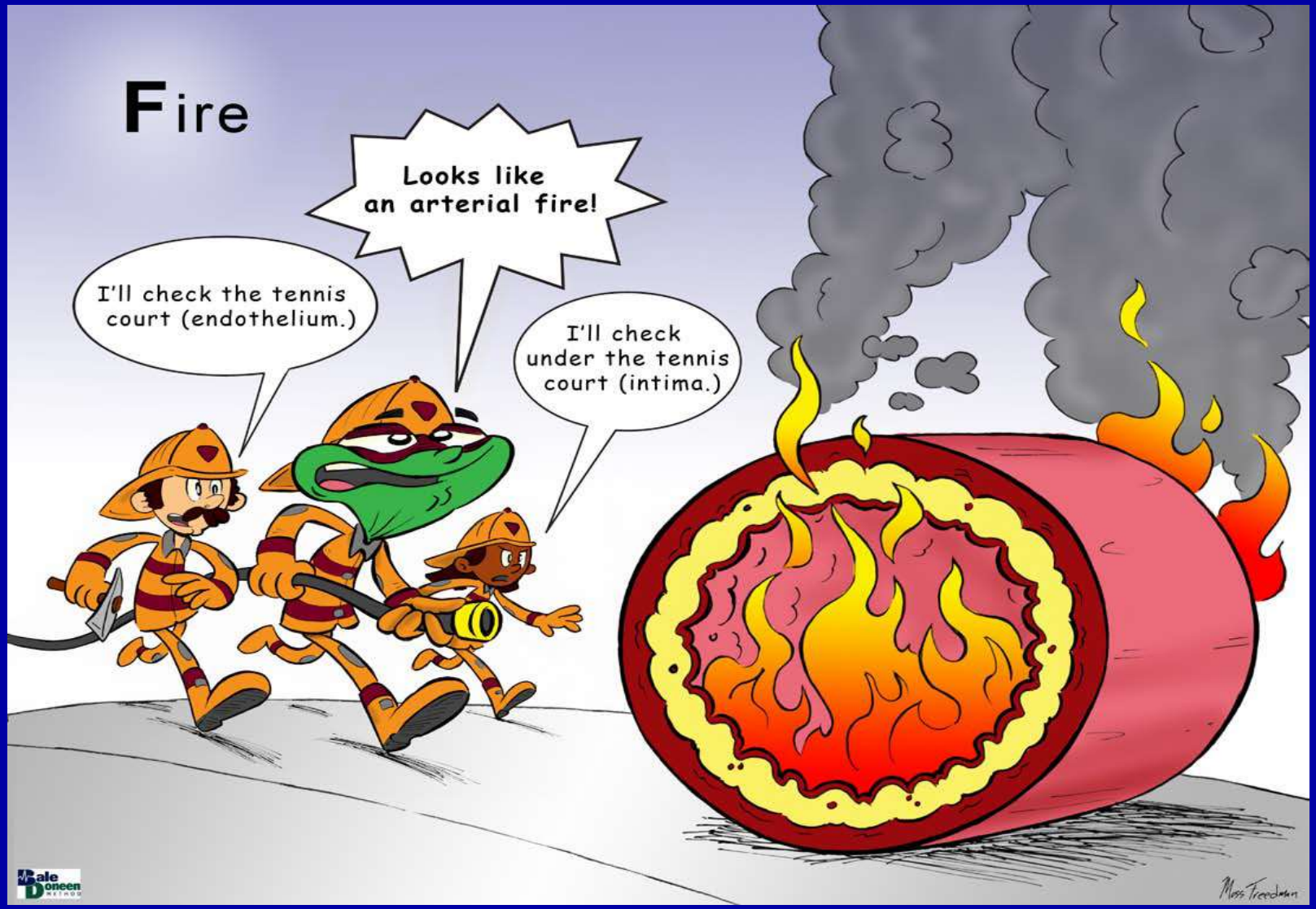
- Adiponectin probably not ready for use as a bio-marker ; if used, higher = worse risk

- Reinforces being on a disease platform as opposed to a CV risk factor platform

  disease is required for events

  risk factors can be low with a high event risk

Inflammation



trimethylamine N-oxide (TMAO)

- TMAO is an oxidant
- TMAO suppresses reverse cholesterol transport (RCT)
- TMAO may also promote atherosclerosis through increasing intimal macrophages and foam cell formation

Koeth, R. A., et. al. published online ***Nature Medicine*** 7 April 2013
doi:10.1038/nm.3145

trimethylamine N-oxide (TMAO)

- 1,876 stable pts undergoing elective CV evaluation demonstrated that TMAO predicted CVD risk independent of traditional risk factors and medications

- Pts. undergoing angiogram showed degree of CAD was associated with the TMAO levels

Wang. Z., et. al. Nature. 2011 April 7; 472(7341): 57–63

trimethylamine N-oxide (TMAO)

- Intestinal microbiota can generate TMAO from dietary lipid phosphatidylcholine (PC) - lecithin
- Foods rich in lecithin include: eggs, milk, liver, red meat, poultry, shell fish and fish.
- Metabolic pathway for dietary lecithin producing TMAO: PC → choline → TMA → TMAO

Wang. Z., et. al. Nature. 2011 April 7; 472(7341): 57–63

TMAO and L-carnitine

- Other nutrients possessing trimethylamine can generate TMAO from intestinal microbes
- L-carnitine contains a trimethylamine structure.
- L-carnitine ingestion is capable of generating TMAO

Koeth, R. A., et. al. published online ***Nature Medicine*** 7 April 2013
doi:10.1038/nm.3145

Carnitine

- Carnitine is endogenously produced from lysine and methionine
- Also may be ingested with foods such as, red meat and taken as supplements

Koeth, R. A., et. al. published online ***Nature Medicine*** 7 April 2013 doi:10.1038/nm.3145

L-carnitine Source is Mainly Endogenous

- Postprandial changes in endogenous L-carnitine and TMAO concentrations were modest, consistent with large total body pools of L-carnitine and TMAO in relation to the amounts of L-carnitine ingested and TMAO produced from ingestion.

Koeth, R. A., et. al. published online ***Nature Medicine*** 7 April 2013
doi:10.1038/nm.3145

L-carnitine is Beneficial

- L-carnitine (biologically active form) is essential in transporting fatty acids into the mitochondria to generate energy

- It exerts a substantial antioxidant action protecting against lipid peroxidation and oxidative stress induced on the myocardial and endothelial

- It is capable of increasing serum osteocalcin leading to reduced risk of osteoporosis

Koeth, R. A., et. al. published online ***Nature Medicine*** 7 April 2013
doi:10.1038/nm.3145

TMAO Production from Ingested L-carnitine Depends on Intestinal Flora

- Dietary habits (for example, vegan or vegetarian versus omnivore or carnivore) are associated with significant alterations in intestinal microbiota

- Vegans and vegetarians have a markedly reduced capacity to synthesize TMAO from oral carnitine

Koeth, R. A., et. al. published online ***Nature Medicine*** 7 April 2013
doi:10.1038/nm.3145

TMAO and L-carnitine

- 2,595 pts undergoing elective cardiac evaluation.
- Fasting plasma concentrations of L-carnitine associated with ASVD risk independent of known risk factors
- Elevated L-carnitine (4th quartile) concentration was an independent predictor of MACE within 3 yrs.
- No longer significant when adjusted for TMAO concent.
- No adjustment for F2 isoprostane (not measured)

Koeth, R. A., et. al. published online ***Nature Medicine*** 7 April 2013
doi:10.1038/nm.3145

TMAO and L-carnitine

- This data suggests the safety of chronic L-carnitine supplementation should be examined

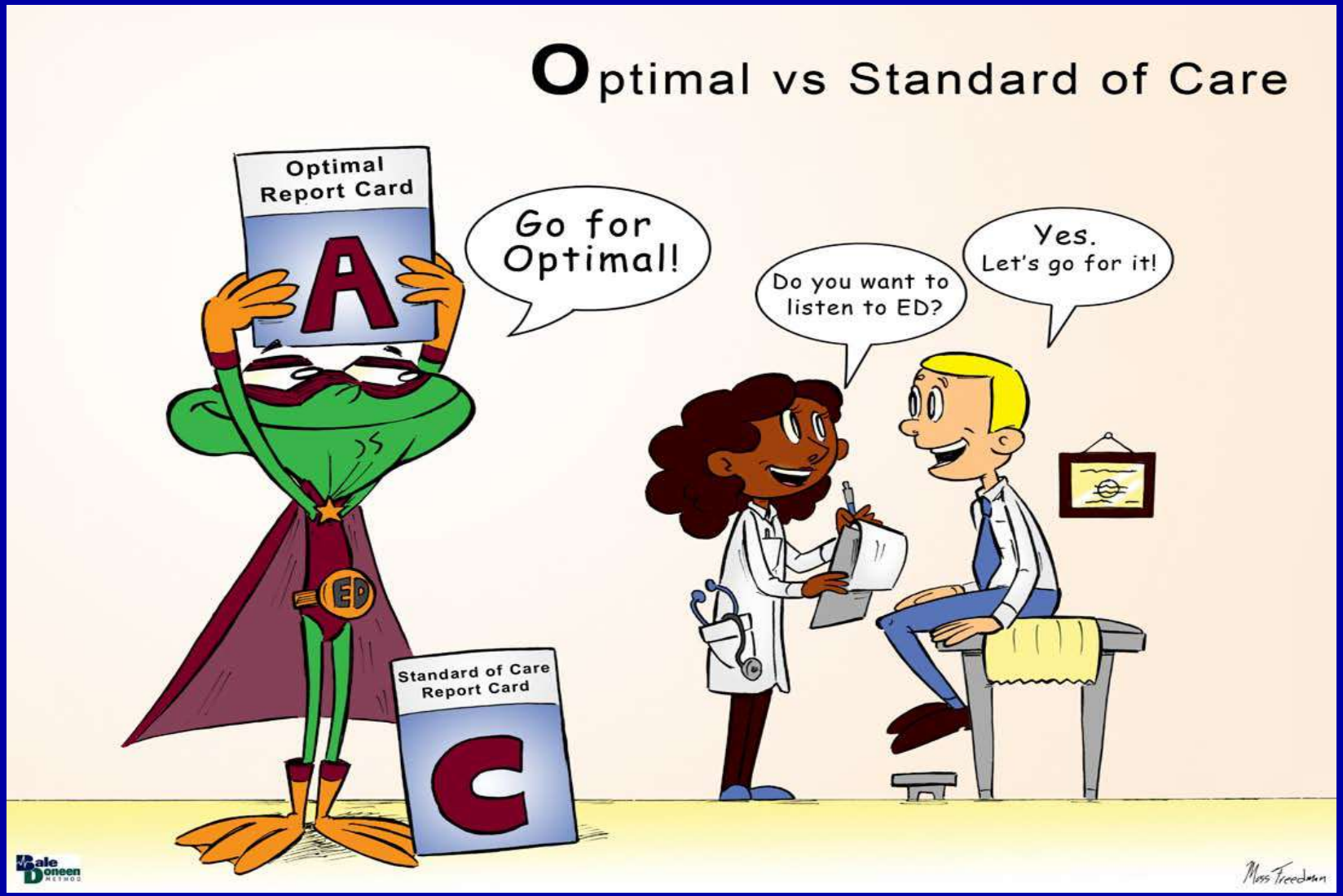
- High amounts of orally ingested L-carnitine may under some conditions increase TMAO and CV risk

Koeth, R. A., et. al. published online ***Nature Medicine*** 7 April 2013
doi:10.1038/nm.3145

BD Method Thoughts

- Story is evolving
- Prudent at this time to stop L-carnitine supplements unless the patient is a strict vegetarian and has a normal F2 isoprostane
- Already recommend limited red meat intake for numerous reasons

Optimal Care



BP Related to Timing of Caloric Intake

- 1,152 pts; 43 yo; 55% women; 5 day food diaries; 7 meals times (one was an ‘extra’); 10 yr. follow-up
- Higher energy intake at breakfast is associated with lower hypertension prevalence.
- Greater energy intake late in the evening is associated with higher hypertension prevalence.

Suzana Almoosawi, S., et. al. 4/2013 *Journal of Hypertension* 31:882–892

BP Related to Timing of Caloric Intake

- 242- 43yo hypertensives (HBPs); by age 53 there were 614 ; 89% not medically treated

- At age 43, non-HBPs consumed 14.5% of their daily energy intake at breakfast compared with 13.6% for HBPs : p=0.026

- HBPs also obtained 8.2% of intake at late evening compared to 7.3% for non-HBPs p=0.011

Suzana Almoosawi, S., et. al. 4/2013 *Journal of Hypertension* 31:882–892

BP Related to Timing of Caloric Intake

- SBP increased by 5 mmHg (95% CI 1.25–8.93) in highest quintile of energy at late evening compared with the lowest quintile –

  P for linear trend=0.016

- This was also related to an increase in DBP

Suzana Almoosawi, S., et. al. 4/2013 *Journal of Hypertension* 31:882–892

BD Method Thoughts

- “Hope is a good breakfast but a bad supper.” Francis Bacon, Sr. 1561-1626

- “Eat breakfast like a king, lunch like a prince, and dinner like a pauper” : Adelle Davis (American Nutritionist and Writer) 1904-1974

This can be very important!

hs-cTnI in Diabetics Predicts Major Adverse Clinical Event (MACE)

- 1,275 DM pts; elective angiograms; follow-up 3 yrs.; outcome all MACE; hs-cTnI levels <0.03ng/ml
- Subclinical myocardial necrosis = cTnI 0.009–0.029 ng/mL: 280 (22%) pts had cTnI in this hs range

TANG, W. H., MD, Hazen, S., MD, PhD, et. al. ***Diabetes Care***. Online 2/7/2013 DOI: 10.2337/dc11-1969

hs-cTnI in Diabetics Predicts MACE

- Purpose: to see if hs-cTnI is associated with MACE; also any relationship with glycemic control

- MACE : all cause death-129; nonfatal MI- 62; nonfatal stroke- 31

TANG, W. H., MD, Hazen, S., MD, PhD, et. al. ***Diabetes Care***. Online 2/7/2013
DOI: 10.2337/dc11-1969

hs-cTnI in Diabetics Predicts MACE

- A strong association observed btw levels of hs-cTnI and MACE

  after adjustment for traditional risk factors(FRS), CRP, creatinine clearance- remained significant

  HR- 1.48 (95% CI, 1.08–2.01) P = 0.013

- Weak correlation btw hs-cTnI

  glycemic control [A1c] (r = 0.06) P = 0.044

  insulin resistance [gluc/insulin] (r = 0.04) P = 0.094

TANG, W. H., MD, Hazen, S., MD, PhD, et. al. ***Diabetes Care***. Online 2/7/2013
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hs-cTnI in Diabetics Predicts MACE

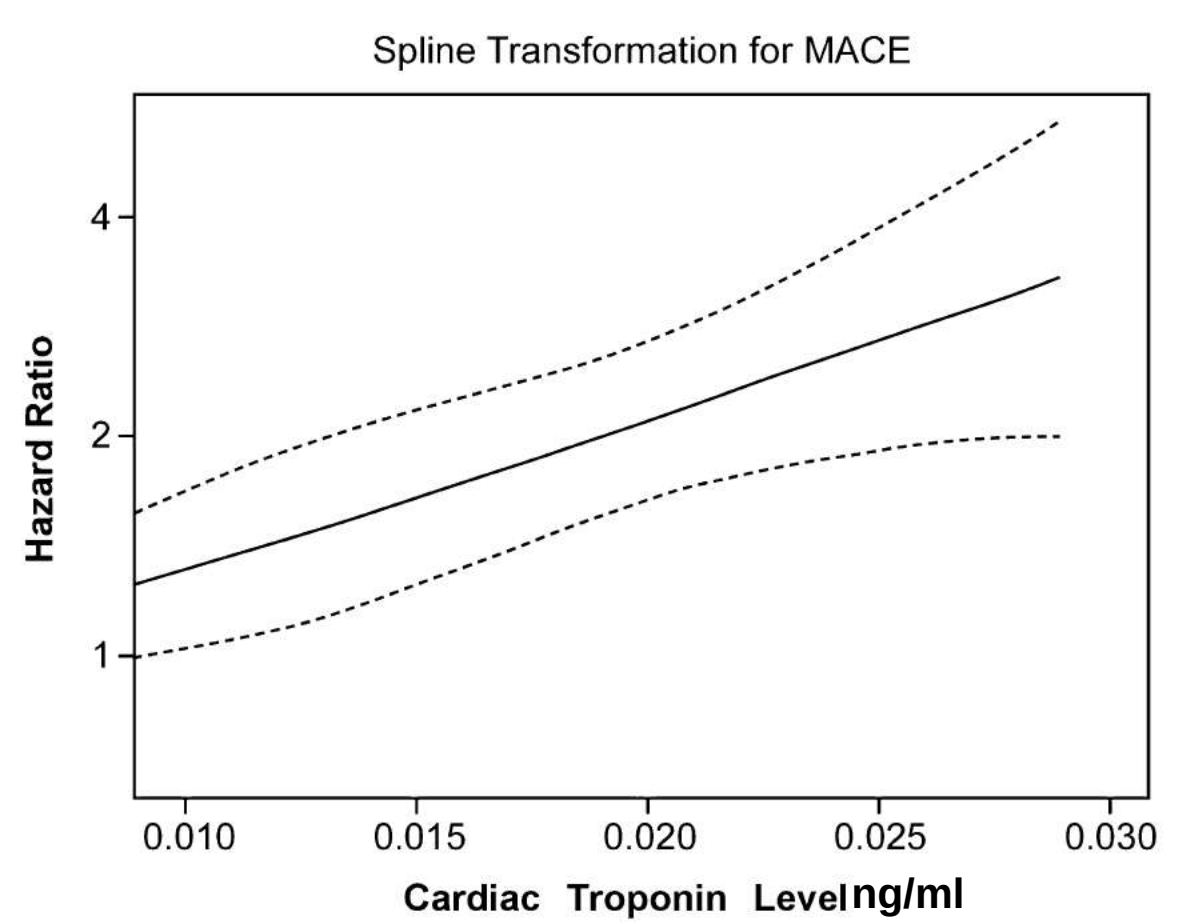
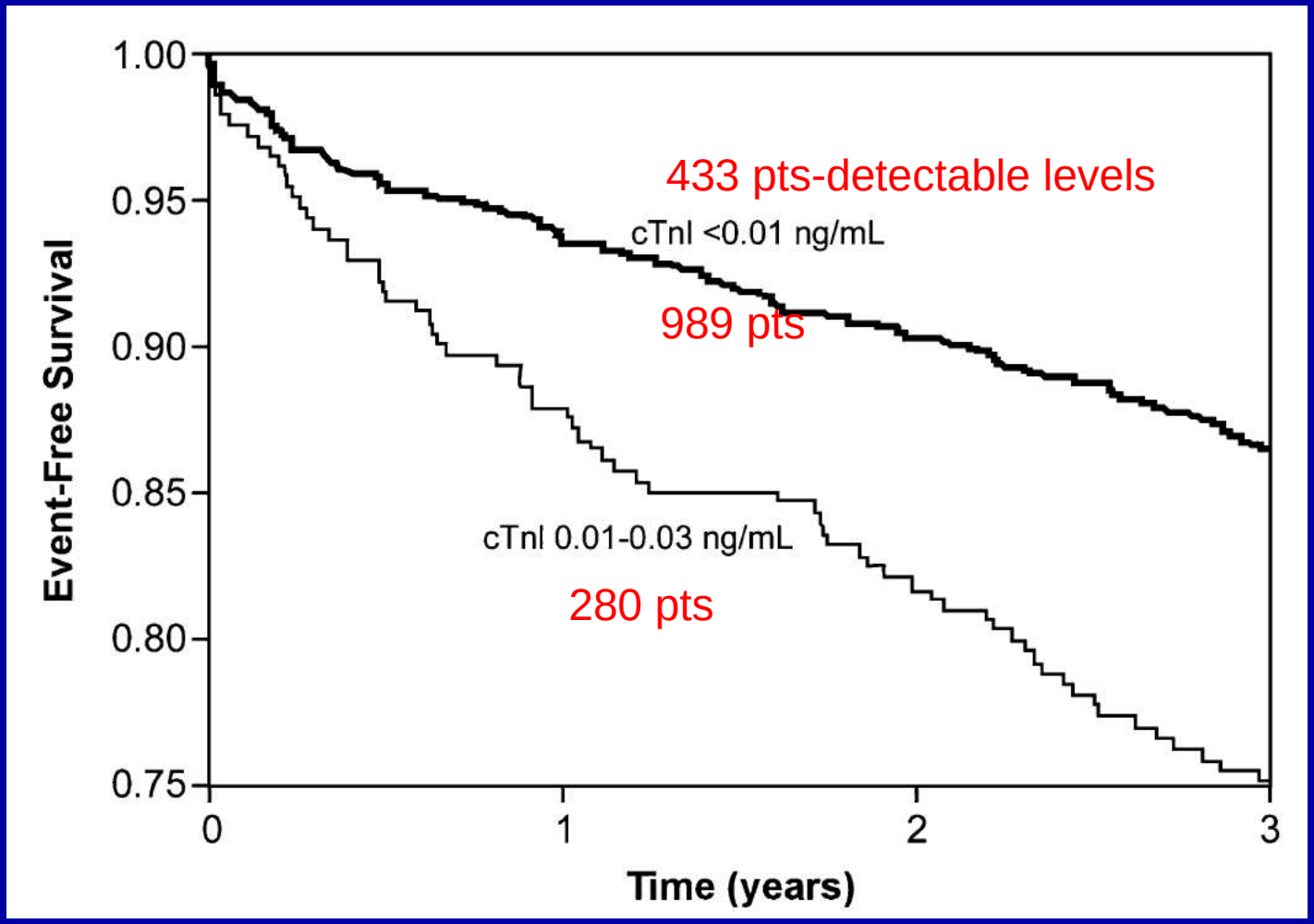


Figure 2—*Cubic spline curve of HRs for major adverse clinical events at 3 years with cTnI levels.*

TANG, W. H., MD, Hazen, S., MD, PhD, et. al. ***Diabetes Care***. Online 2/7/2013
DOI: 10.2337/dc11-1969

hs-cTnI in Diabetics Predicts MACE



Kaplan-Meier analysis for 3-year major adverse clinical events, stratified according to subclinical myocardial necrosis status (rounded to the nearest 0.001 ng/mL).

TANG, W. H., MD, Hazen, S., MD, PhD, et. al. ***Diabetes Care***. Online 2/7/2013
DOI: 10.2337/dc11-1969

hs-cTnI in Diabetics Predicts MACE

- Implies any hs-cTnI levels (713/1275- 56%) warrant global aggressive risk reduction efforts beyond glycemic control.

- Risk profile differences warrant different indications of preventive interventions.

TANG, W. H., MD, Hazen, S., MD, PhD, et. al. ***Diabetes Care***. Online 2/7/2013
DOI: 10.2337/dc11-1969

BD Method Thoughts

- A significant % of DM may be having ‘silent’ myocardial events
- Perhaps many of the above individuals are also having ‘silent’ cerbralvascular events
- hs-cTnI may be a good biomarker to follow in asx’ic DM patients as an indicator of ‘optimal’ CVD management

hs-cTnT Predicts Secondary Events in CAD Pts

- 984 stable CAD pts; all had baseline stress echo; follow-up 8 yrs.; 794 had detectable hs-cTnT; 317 pts had CV event
- Each doubling in hs-cTnT was associated with a 37% higher rate of CV events

HR- 1.37 (95% CI -1.14-1.65) P=0.001

Above adjusted for: clinical risk factors, baseline cardiac structure and function, NT pro-BNP and hsCRP

Heart and Soul Data

JAMA Intern Med. 4/8/2013;():1-7. doi:10.1001/jamainternmed.2013.116

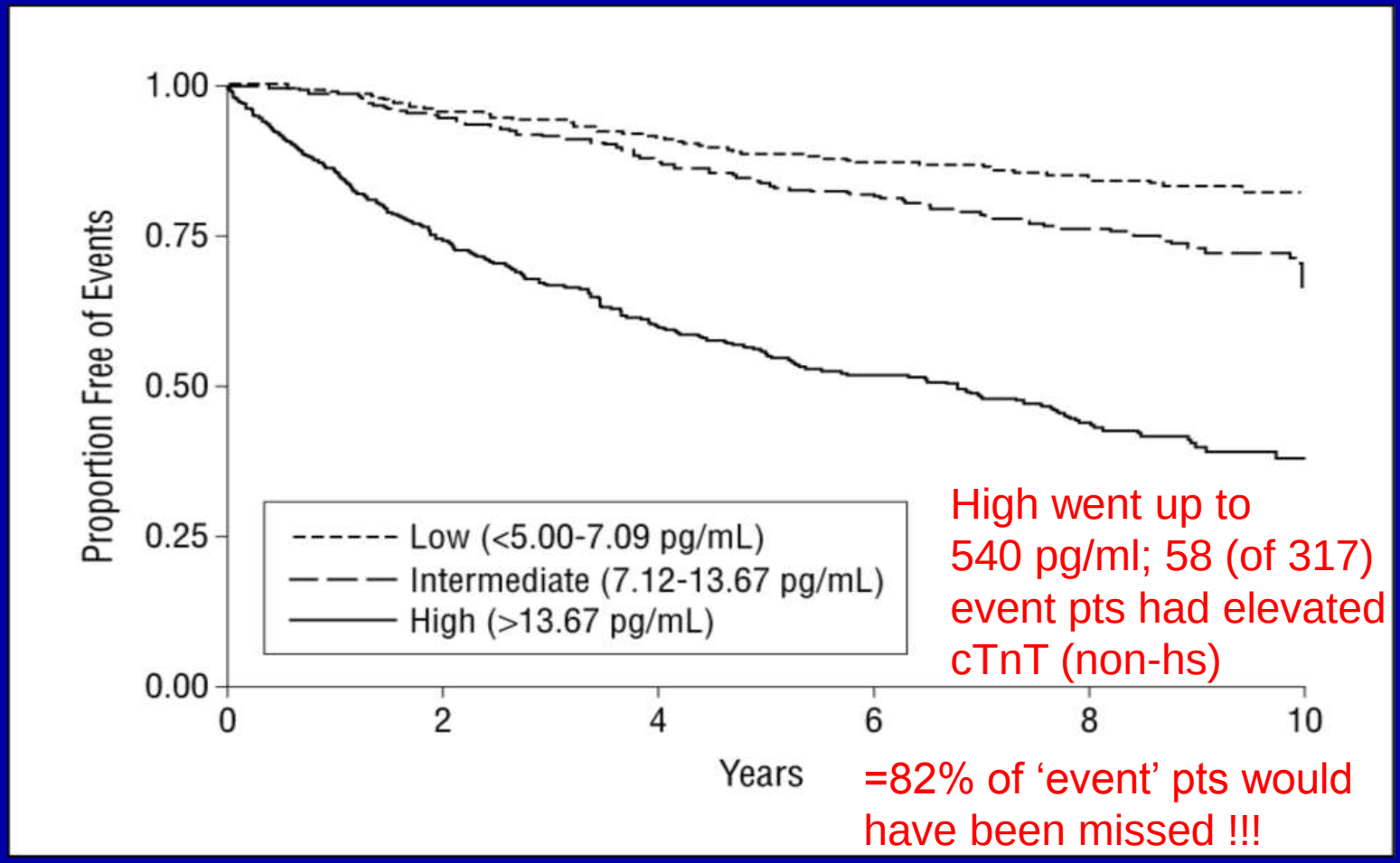
hs-cTnT Predicts Secondary Events in CAD Pts

- At baseline, higher hs-cTnT levels were associated with greater inducible ischemia and worse LV EF, left atrial function, diastolic function, LV mass, and treadmill exercise capacity.

- hs-cTnT remained independently predictive of secondary CV events from multiple abnormalities of cardiac structure and function.

JAMA Intern Med. 4/8/2013;():1-7. doi:10.1001/jamainternmed.2013.116

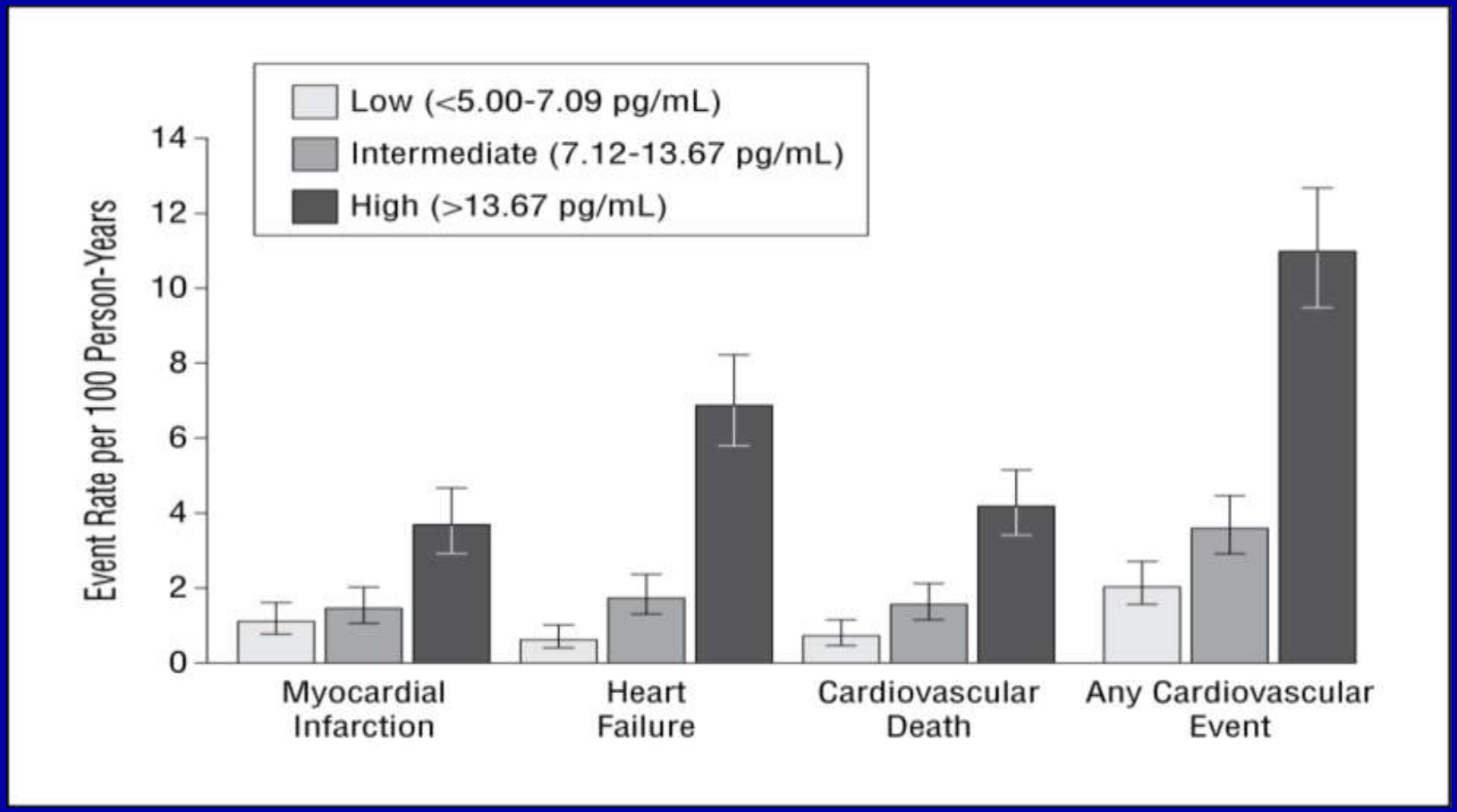
hs-cTnT Predicts Secondary Events in CAD Pts



Combined CV events (MI, HF, or CV death) by tertile of hs-cTnT P < .001

JAMA Intern Med. 2013;() 1-7. doi:10.1001/jamainternmed.2013.116

hs-cTnT Predicts Secondary Events in CAD Pts



Rates of CV events by tertile of hs-cTnT

Error bars indicate 95% confidence intervals for event rates. P < .001

JAMA Intern Med. 2013;() 1-7. doi:10.1001/jamainternmed.2013.116

BD Method Thoughts

- hs-cTnT in the intermediate or high range in patients with known CAD (included those with just ≥50% obstruction on angio) probably are having ‘silent’ myocardial damage

- hs-cTnT could be valuable in attempts to optimize care in CAD pts

hs-cTnT and NT pro-BNP Predict Stroke Risk

- 10,902 stroke free pts; followed 11 yrs.; 507 incident strokes; assessed baseline hs-TnT and NT pro-BNP as predictors of stroke
- Neither associated with lacunar or hemorrhagic stroke
- Both strongly associated with ischemic stroke (444 of 507) and cardioembolic (125 of 444) stroke
- NT pro-BNP was stronger with cardioembolic strokes with 58% occurring in the highest quintile

Folsom A R et al. Stroke 2013;44:961-967

ARIC data

TnT and NT pro-BNP Predict Stroke Risk

- hs TnT had a lower limit of detection of 0.003 µg/L, and values <0.003 µg/L were classified as the 'reference' group for HR

- Translates to lower limit of 3 pg/ml

Folsom A R et al. Stroke 2013;44:961-967

TnT and NT pro-BNP Predict Stroke Risk

Stroke Incidence by hsTnT Levels

	<3pg/ml HR	3-5pg/ml HR	6-8pg/ml HR	9-13pg/ml HR	>14pg/ml HR	P trend
# pts	3317	2605	2105	1411	912	
Total Stroke	reference	1.23	1.09	1.51*	1.85*	0.001
IS Stroke	reference	1.32	1.12	1.57*	2.04*	0.0003
Lacunar	reference	1.17	1.02	1.20	1.49	0.43
Non-L	reference	1.09	1.19	1.63*	2.02*	0.003
CardioEm	reference	2.03*	1.03	1.68*	2.63*	0.04
Hemorr.	reference	0.80	1.04	1.28	0.51	0.94

*Significant by 95% CI

- Adjusted for: age, sex, race, BMI, smoking, DM, systolic BP, BP med, HDL, TC, lipid med, CRP, Lp-PLA2, incident (AF, CAD, HF)

Folsom A R et al. Stroke 2013;44:961-967

TnT and NT pro-BNP Predict Stroke Risk

Stroke Incidence by NT pro-BNP Levels pg/ml

	<27.2 HR	27.3-51.9 HR	52-87.3 HR	87.4-155.1 HR	>155.1 HR	P trend
# pts	2063	2085	2058	2071	2073	
Total Stroke	reference	1.56*	1.32	1.44*	2.63*	<0.0001
IS Stroke	reference	1.48*	1.27	1.37	2.61*	<0.0001
Lacunar	reference	1.34	1.43	1.10	1.22	0.84
Non-L	reference	1.48	1.03	1.02	2.29*	0.004
CardioEm	reference	2.21	2.93	4.70*	9.01*	<0.0001
Hemorr.	reference	2.41	1.77	2.07	2.70	0.21

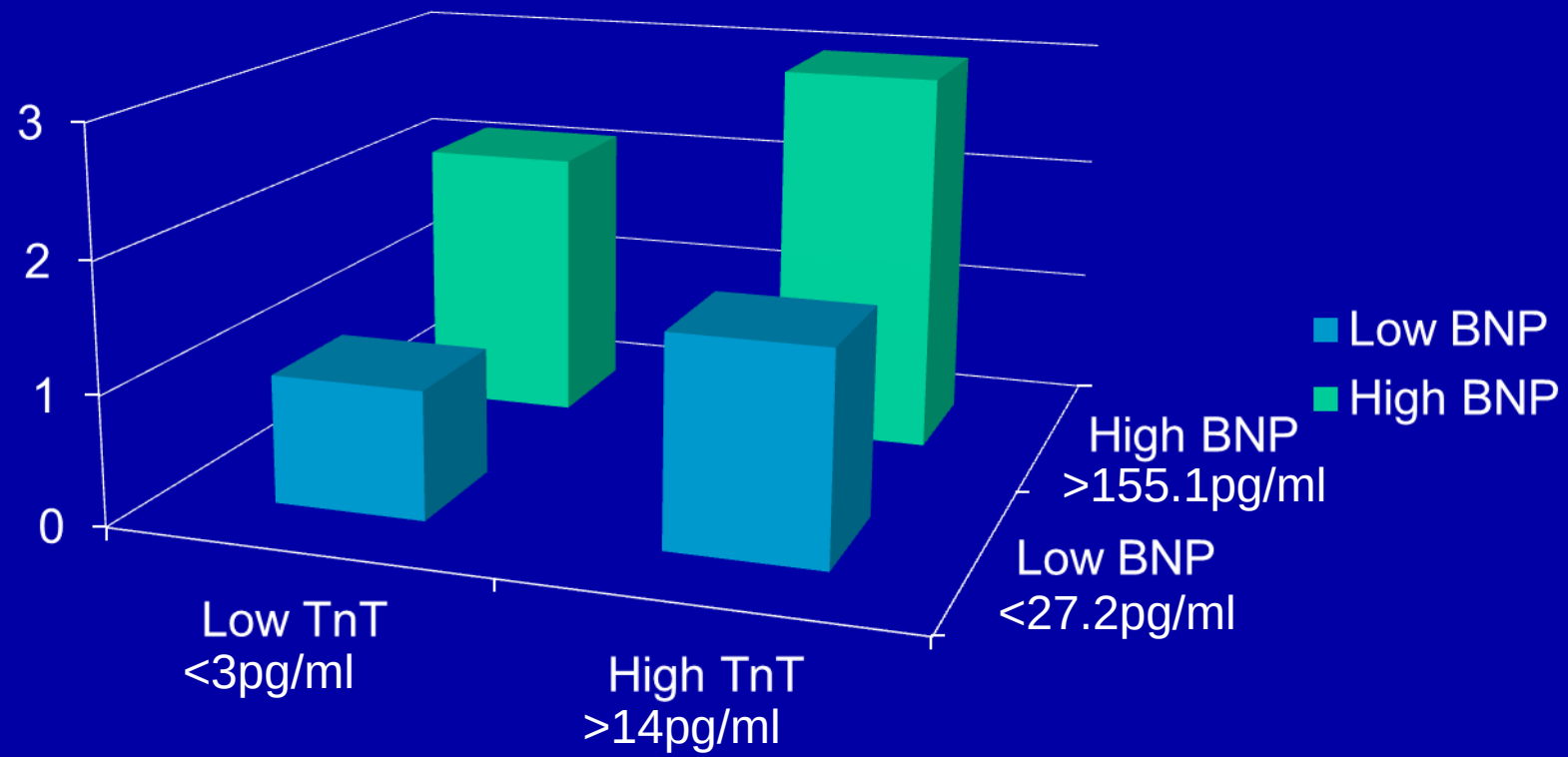
*Significant by 95% CI

- Adjusted for: age, sex, race, BMI, smoking, DM, systolic BP, BP med, HDL, TC, lipid med, CRP, Lp-PLA2, incident (AF, CAD, HF)

Folsom A R et al. Stroke 2013;44:961-967

TnT and NT pro-BNP Predict Stroke Risk

Risk of Ischemic Stroke: ~ 3 times increased risk with high TnT & NT pro-BNP



All values statistically significant via 95% CI and fully adjusted

Folsom A R et al. Stroke 2013;44:961-967

TnT and NT pro-BNP Predict Stroke Risk

- Higher levels of hsTnT and NT-proBNP in the general population independent of other measured risk factors are moderately strong risk markers for incident ischemic stroke (IS)

- TnT and NT-proBNP should not be considered causal factors for ischemic stroke

- The association of change in biomarkers with incident stroke was not determined

Folsom A R et al. Stroke 2013;44:961-967

BD Method Thoughts

- Already measure NT pro-BNP and recognize it predicts both MI and stroke risk – stroke most likely mainly from ‘silent’ arrhythmias

- hs-cTnT also appears valuable for stroke prediction possibly via indicating ‘silent’ CV events – both myocardial and indirectly cerebral

hs-TnI is Associated with CV risk Independent of Conventional Risk Markers and hs-TnT

- 3,623 stable CAD pts with preserved syst function
- 98.5% had hs-TnI conc. high enough to detect (1.2 pg/ml)
- median follow-up 5.2 yrs
- 203 CV deaths (included strokes) or HF hospitalizations; 209 nonfatal MIs

PEACE trial data

Omland, T., MD, PHD, MPH, et. Al. J Am Coll Cardiol. 3/2013; Vol. 61, No. 12:1240-49

hs-TnI is Associated with CV risk Independent of Conventional Risk Markers and hs-TnT

- Adjusting for conventional risk markers, NT pro-BNP and hs-TnT: hs-TnI in the 4th quartile compared with the lower 3 was assoc. with CV death or HF

  HR: 1.88; (95% CI: 1.33 - 2.66) p <0.001)

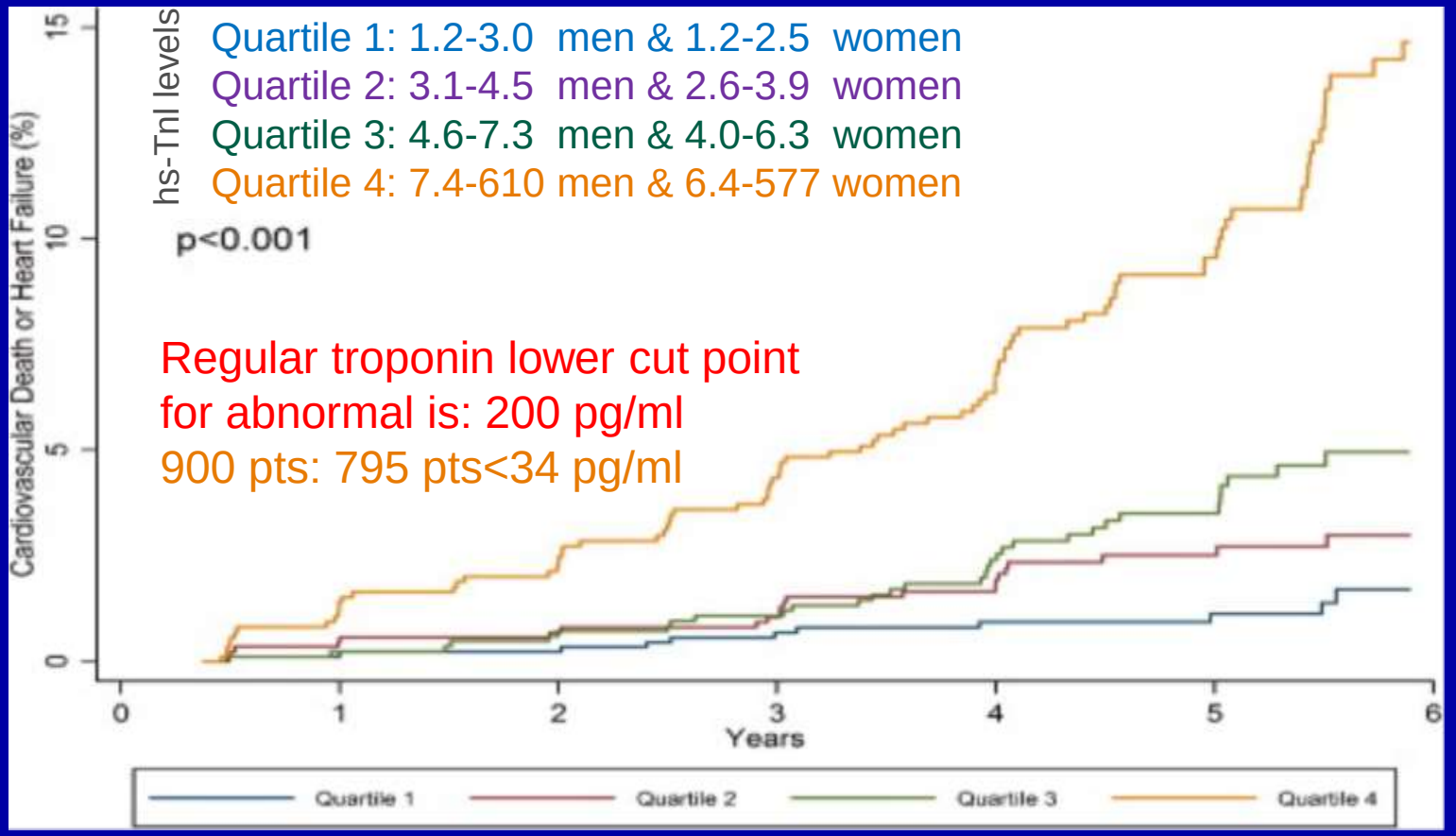
  with nonfatal MI

  HR: 1.44; (95% CI: 1.03 - 2.01) p=0.031)

- In the same models, hs-TnT conc. was assoc. with CV death or HF, but not MI

Omland, T., MD, PHD, MPH, et. Al. J Am Coll Cardiol. 3/2013; Vol. 61, No. 12:1240-49

hs TnI Predicts CV Risk in Stable CAD Pts.

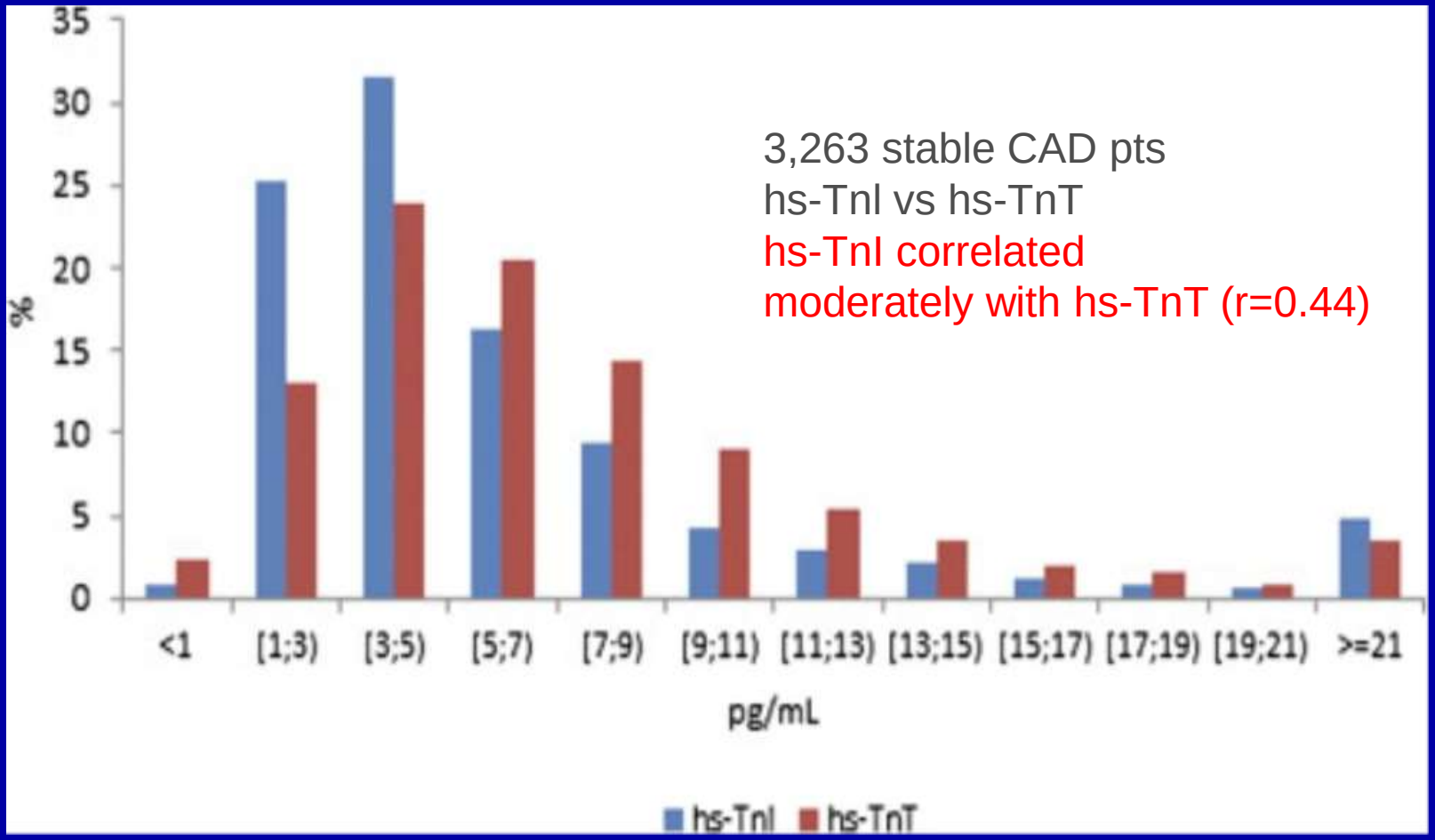


Risk for CV Death or HF by Baseline hs-TnI pg/ml Level

Strong and graded association between increasing quartiles

Omland, T., MD, PHD, MPH, et. Al. J Am Coll Cardiol. 2013; Vol. 61, No. 12:1240-49

hs TnI & hs TnT Levels Moderately Correlated



99th-percentile values of a general population are 15.6 pg/ml in women and 34.2 pg/ml in men for hs-TnI; 10.0 pg/ml in women and 14.2 pg/ml in men for hs-TnT.

Omland, T., MD, PHD, MPH, et. Al. J Am Coll Cardiol. 2013; Vol. 61, No. 12:1240-49

hs Troponin Predicts CV Risk in Stable CAD Pts.

- Prior AMI appeared to play a more important role for circulating hs-TnI levels than for hs-TnT levels.

- Renal function, age, and sex appeared to play a more important role for hs-TnT than for hs-TnI.

- ? Why: 1) the molecular size of troponin I is smaller than that of troponin T, which may facilitate transfer across the viable cell membrane 2) degradation may differ- in renal failure, the association with LV mass may be stronger for troponin T than for troponin I

Omland, T., MD, PHD, MPH, et. Al. J Am Coll Cardiol. 2013; Vol. 61, No. 12:1240-49

hs Troponin Predicts CV Risk in Stable CAD Pts.

- Both hs-TnI and hs-TnT are markers of subclinical cardiac injury (? released during ‘silent’ MIs)
- May reflect subtle differences in the etiology of cardiac injury and clearance mechanisms
- As such, they may be complementary rather than redundant biomarkers

Omland, T., MD, PHD, MPH, et. Al. J Am Coll Cardiol. 2013; Vol. 61, No. 12:1240-49

BD Method Thoughts

- hs-cTn appears to be an excellent marker for CV risk in ‘healthy’ pts, DM pts, stable CAD pts
- It appears to indicate IS stroke risk as well as myocardial risk
- It is too early to state whether ‘I’ or ‘T’ is superior and perhaps they will be complimentary

EDFROG IRA

Education	Genetics	Individual Management
Disease	Optimal	Risk factor response
Fire	Roots	Assess Disease Annually

Adults Lacking in Physical Activity

- Data from US in 2011; random phone based survey; 1 million called; 453,721 useable responders

- Guidelines:

1) aerobic (≥150 min/wk of moderate activity or ≥75 min/wk of vigorous activity).

2) muscle-strengthening (muscle-strengthening activities at least two times per week).

Harris CD, et al. Morb Mortal Wkly Rep 5/3/2013; 62:326-330

Adults Lacking in Physical Activity

- 80% of adults are not meeting the combined guidelines!!
- Gender: 23.4% of men and 17.9% of women meet combined goals
- Age: 30.7% aged 18–24 yrs to 15.9% aged ≥65 yrs
- Ethnic: Hispanic 18.4%; whites 20.7%; Blacks 21.2%

Harris CD, et al. Morb Mortal Wkly Rep 5/3/2013; 62:326-330

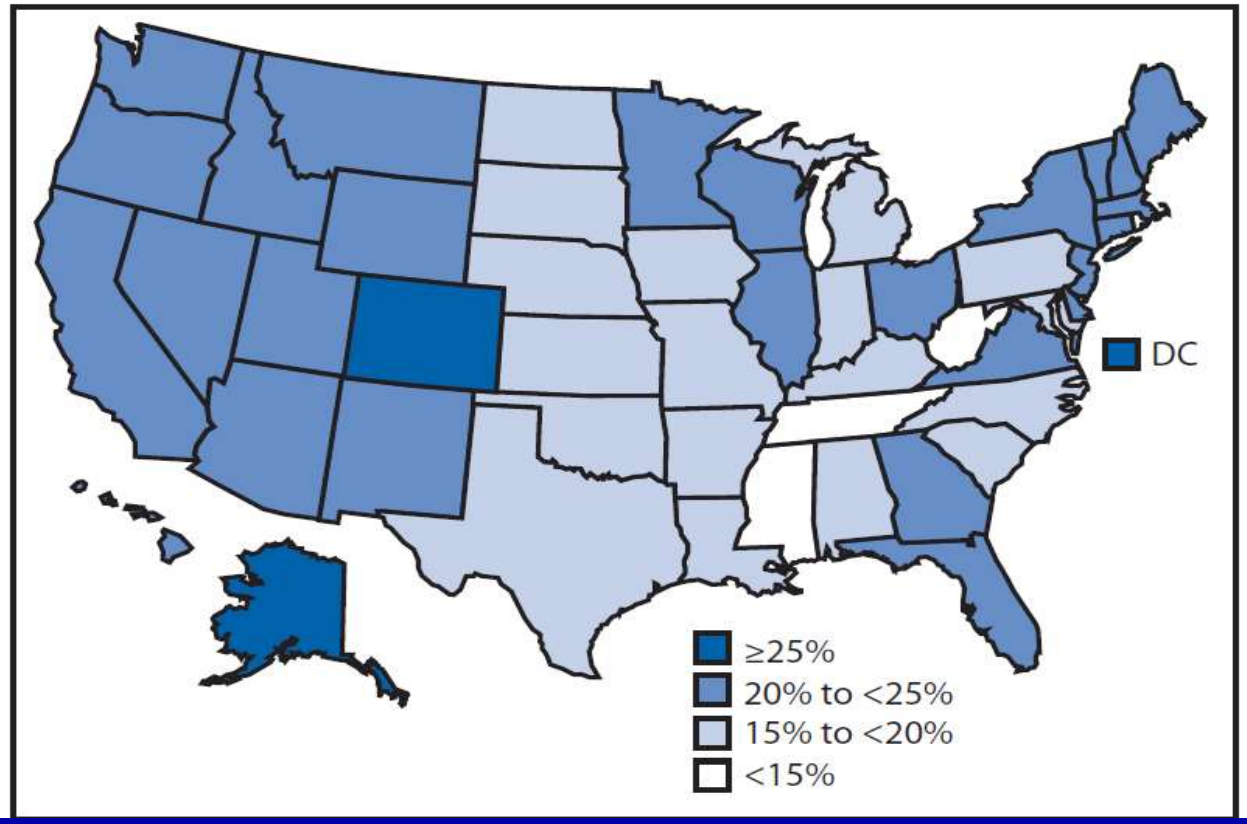
Adults Lacking in Physical Activity

- Education: college grads 27.4%; < high school 12%
- Weight: obese 13.5%; overweight 21.9%; underweight/normal weight 25.8%
- Separately: nationally, aerobic -51.6%; mm-strengthening 29.3%

Harris CD, et al. Morb Mortal Wkly Rep 5/3/2013; 62:326-330

Adults Lacking in Physical Activity

FIGURE. Proportion of U.S. adults meeting both aerobic and muscle-strengthening physical activity guidelines,* by state — Behavioral Risk Factor Surveillance System, United States, 2011



Harris CD, et al. Morb Mortal Wkly Rep 5/3/2013; 62:326-330

BD Method Thoughts

- Physical activity is a vital component of maintaining CV wellness
- Emphasize importance to patients and encourage a minimum of a 22 min. brisk walk each day; at least 2 days a week for strengthening of all major muscles
- May want to discuss autophagy and senescence in regard to arterial inflammation and longevity

Harris CD, et al. Morb Mortal Wkly Rep 5/3/2013; 62:326-330

What??

Randomized Comparison of High-Dose Oral Vitamins versus Placebo in the Trial to Assess Chelation Therapy (TACT)

Gervasio A. Lamas, MD, FACC

Professor of Clinical Medicine

Columbia University Division of Cardiology

Mount Sinai Medical Center

Miami Beach, FL

Design Rationale

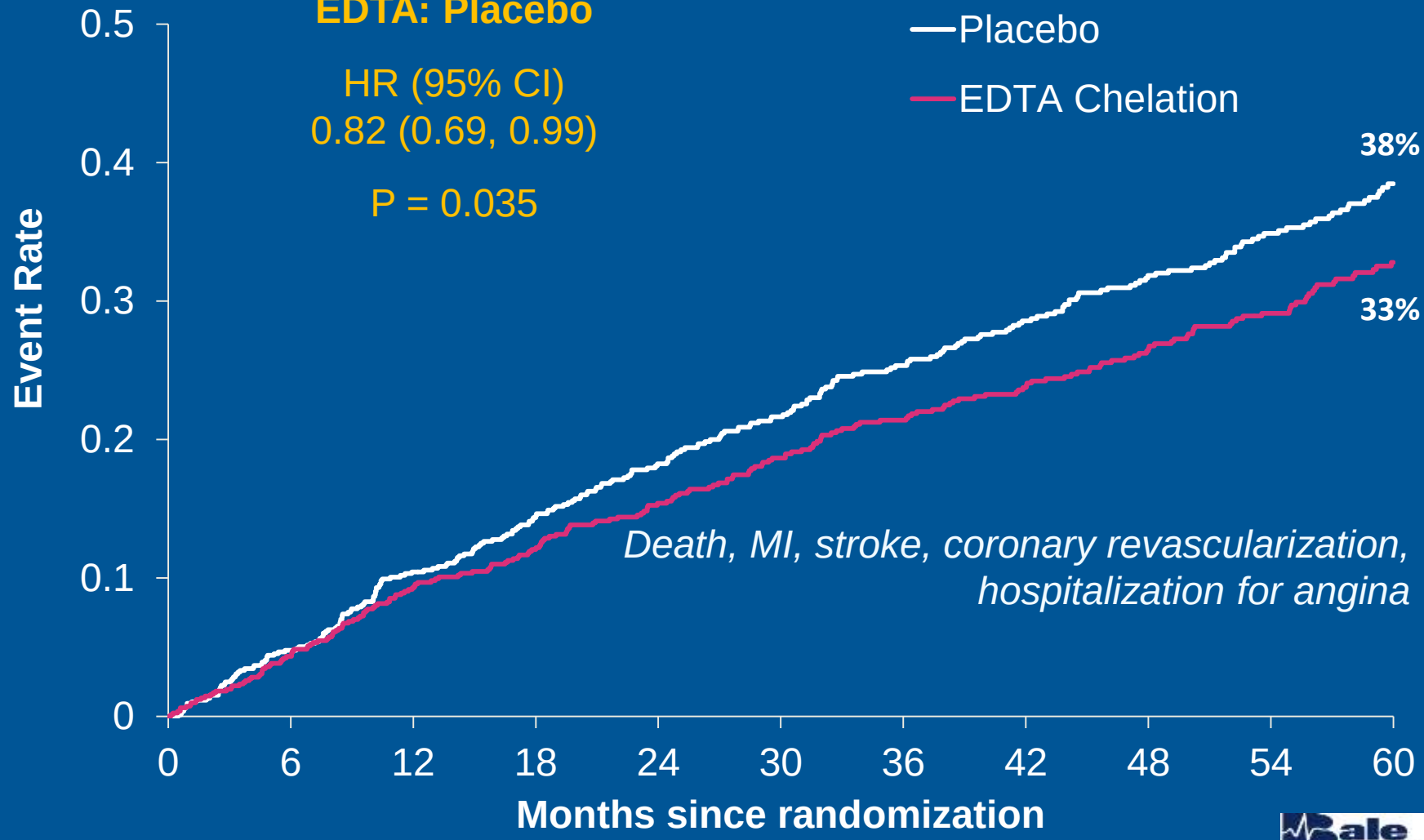
- 2 x 2 factorial trial, with 1708 patients randomized to 4 groups: ~425/group; mean rx 33.4 mos.

1. Active oral vitamins + active IV chelation
2. Placebo oral vitamins + active IV chelation
3. Active oral vitamins + placebo IV chelation
4. Placebo oral vitamins + placebo IV chelation

Eligibility: Post MI

- Age 50 or older
- MI > 6 weeks prior
- Creatinine ≤2.0 mg/dL
- No coronary or carotid revascularization within 6 months
- No active heart failure or heart failure hospitalization within 6 months
- No cigarette smoking within 3 months

Primary Endpoint Results for EDTA Chelation (presented at AHA 2012)



TACT: High-Dose Oral Treatment

3 caplets twice a day for the duration of the study.

Vitamin A
Vitamin C
Vitamin D_3
Vitamin E
Vitamin K
Thiamin
Niacin
Vitamin B_6
Folate
Vitamin B_{12}
Biotin
Panthothenic Acid

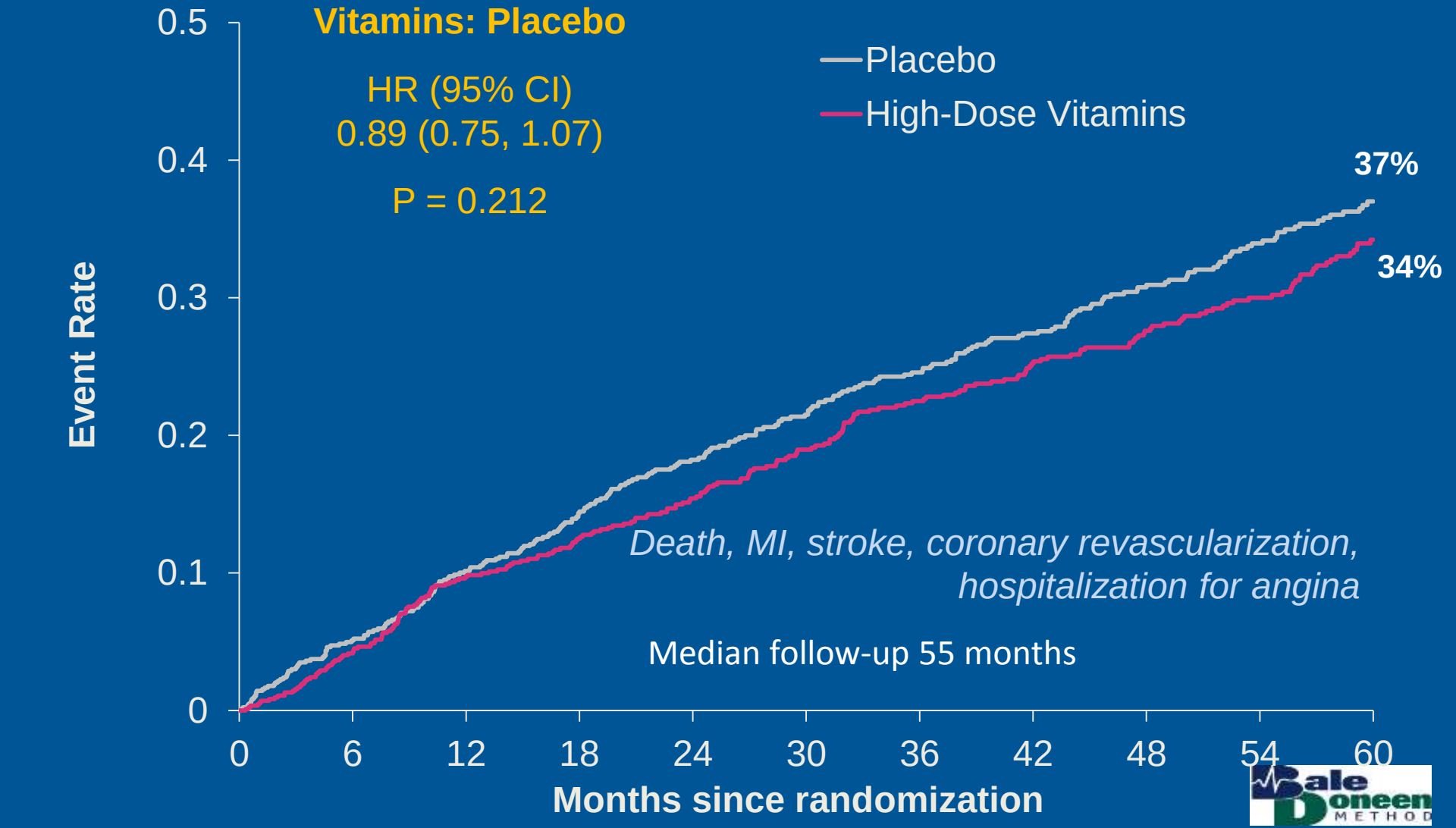
no carnitine; did have calcium

Calcium
Iodine
Magnesium
Zinc
Selenium
Copper
Manganese
Chromium
Molybdenum
Potassium
Choline
Boron
Inositol
PABA
Vanadium
Citrus Flavonoids

Double-blind active or placebo high dose vitamins were shipped from a central pharmacy to sites.

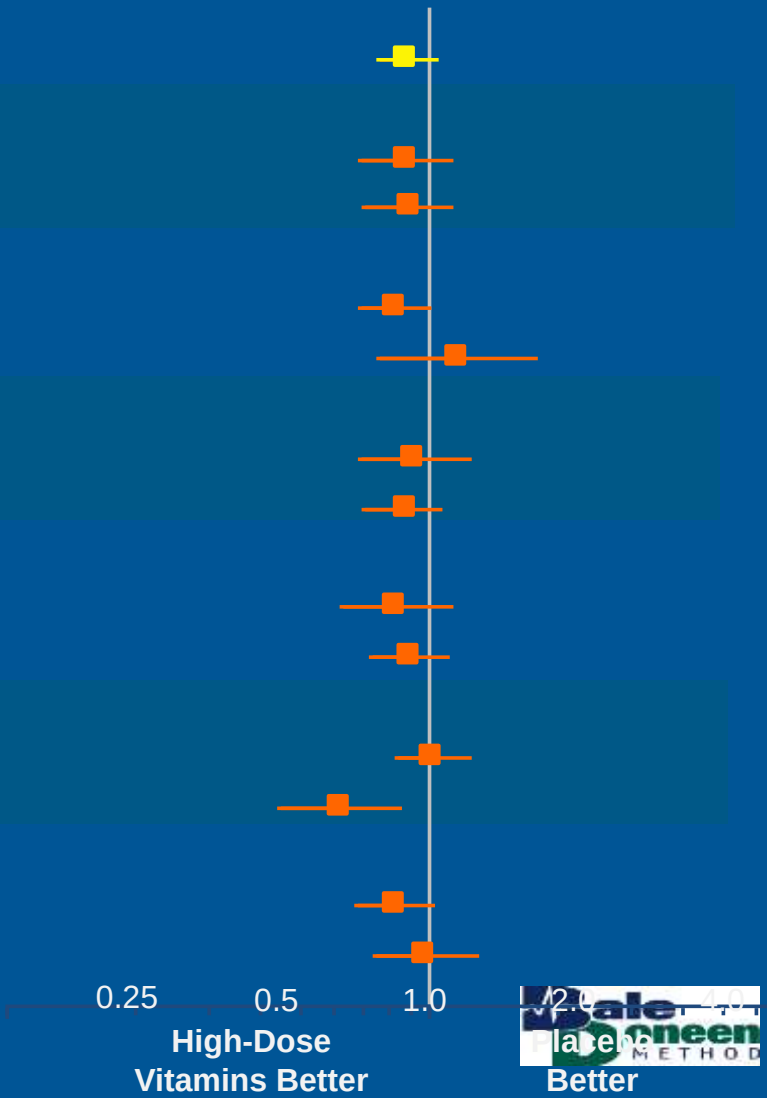
Lamas GA, Goertz C, Boineau R, et. al. Design of the Trial to Assess Chelation Therapy (TACT). Am Heart J. 2012 Jan;163(1):7-12.

Vitamin Primary Endpoint Results

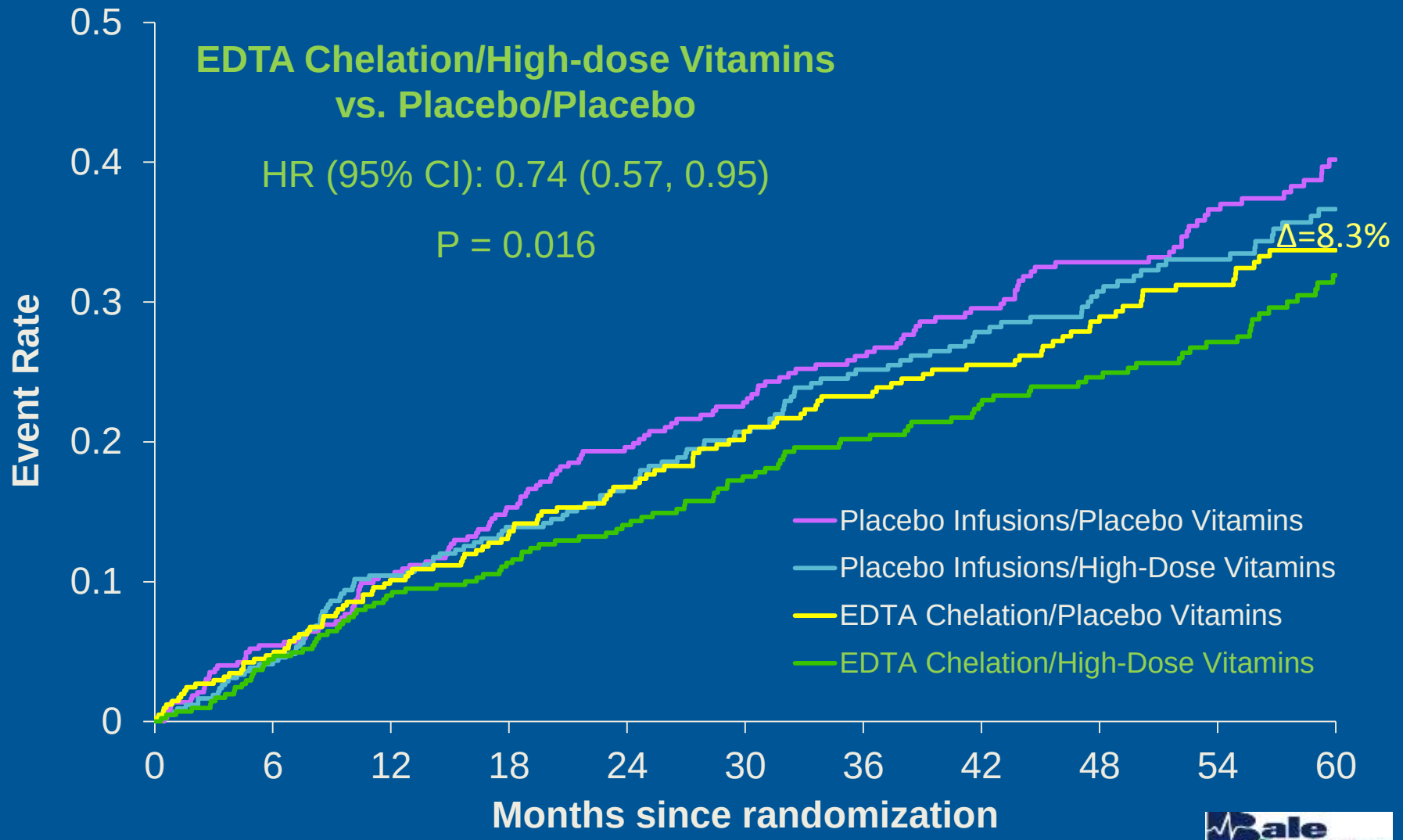


Subgroup Results for Vitamin Analyses

Participant Group	N	Interaction P-value	HR	95% CI
All participants	1708		0.89	0.75, 1.07
Infusions		0.94		
EDTA	839		0.89	0.68, 1.15
Placebo	869		0.90	0.7, 1.15
Gender		0.17		
Male	1409		0.84	0.69, 1.03
Female	299		1.17	0.75, 1.83
Anterior MI		0.79		
Yes	674		0.93	0.69, 1.26
No	1034		0.88	0.7, 1.09
Diabetes		0.72		
Yes	538		0.84	0.62, 1.14
No	1170		0.90	0.72, 1.12
Statins at baseline		0.01		
Yes	1248		1.03	0.84, 1.27
No	460		0.62	0.44, 0.87
CAM site		0.39		
Yes	1089		0.84	0.67, 1.05
No	619		0.99	0.74, 1.33



Primary Endpoint: Factorial Groups



Summary

- High dose oral vitamins reduced the composite outcome by 11%, which was not statistically significant.

- When combined with EDTA chelation, the small vitamin benefit was additive, and the combined effect was statistically significant.

Conclusions

- These findings should stimulate further research, but are not, by themselves, sufficient to recommend the routine use of chelation therapy and high-dose vitamins in post-MI patients.

Hot Topics

Can azithromycin do this??

Use of Azithromycin and Death from Cardiovascular Causes

- Cohort study 18 to 64 yo; data on filled prescriptions 1997-2010, causes of death, and pt characteristics.

- Estimated rate ratios for CV death causes, comparing 1,102,050 episodes of azithromycin use with no use of antibiotic agents (matched in a 1:1 ratio) and comparing with 7,364,292 episodes of penicillin V use

- Analysis was conducted with adjustment for propensity score. Total CV deaths: 6 – no rx; 17- azith.; 146 PCN

Henrik Svanström, M.Sc., et. Al. N Engl J Med 5/2/2013 Volume 368(18):1704-1712

Use of Azithromycin and Death from Cardiovascular Causes

- Risk of CV death with current 5 day course of azithromycin compared to no antibiotic was increased significantly

  rate ratio, 2.85- (95% CI, 1.13 to 7.24)

- Risk of CV death with azithromycin compared to penicillin V was not increased

  rate ratio, 0.93 (95% CI, 0.56 to 1.55)

Henrik Svanström, M.Sc., et. Al. N Engl J Med 5/2/2013 Volume 368(18):1704-1712

Use of Azithromycin and Death from Cardiovascular Causes

- Post hoc analysis, azithromycin use was compared with amoxicillin

  rate ratio- 0.60 (95% CI, 0.29 to 1.23)

Henrik Svanström, M.Sc., et. Al. N Engl J Med 5/2/2013 Volume 368(18):1704-1712

Use of Azithromycin and Death from Cardiovascular Causes: Conclusions

- Increased risk compared with no antibiotic use is entirely attributable to the risk of death associated with acute infection rather than with its treatment.

- Azithromycin is not associated with an increased risk of CV death in a general population of young and middle-aged adults.

Henrik Svanström, M.Sc., et. Al. N Engl J Med 5/2/2013 Volume 368(18):1704-1712

BD Method Thoughts

- Lethal arrhythmias from QT-interval prolongation are possible with azithromycin, other macrolides, and fluoroquinolones.

- This possibility should be kept in mind when prescribing antibacterial drugs to pts with preexisting CV risk factors

Cases???

Upcoming Presentations

Upcoming Presentations

- 5/17-18/2013 – BD Method Preceptorship; 17 hr. CME; Washington, DC
- 6/19/2013 – Amy and Brad – Webinar AAOSH 8pm EST
- 8/11/2013 – Brad– Florida Endocrine Society “2013 Post Graduate Update”; Orlando, FL (Amy enjoying her lake place with family!☺)
- 9/13-14/2013 – BD Method Preceptorship; 17 hr. CME; Lubbock, TX
- 9/20/2013 – Amy and Brad speaking at AAOSH; Las Vegas, NV
- 9/30/2013- Amy and Brad – American Osteopathic Association (AOA) – Brain Health/CVD Minorities; 1.5 hr. CME; Las Vegas, NV
- 10/12/2013 – Amy and Brad- International Academy of Biology, Dentistry and Medicine – Houston, TX

October 17-20/2013 – Dallas, TX

- 10/17 – Amy and Brad CEO Presentation
- 10/18 – Amy and Brad CHL Symposium
- 10/18 – Reunion dinner
- 10/19 – Reunion sessions
- 10/19 – Amy and Brad afternoon MDVIP talk

Open for Discussion