Bale/Doneen Live Chat Session

Amy Doneen MSN, ARNP

February 6, 2013

5:30-6:30 pm PST

Greetings from Spokane!

“You can only become truly accomplished at something you love. Don’t make money your goal. Instead pursue the things you love doing and then do them so well that people can’t take their eyes off of you.” - Maya Angelou

Outline for today's discussion

New Data:

- Red Flags
  - TV and Laziness
  - Waist and BMI
  - HTN & Pregnancy
  - Phosphorus and subclinical atherosclerosis
  - Phosphate and LVH
- Disease
  - Carotid plaque features – histology
  - Carotid Atherosclerosis = MI risk
  - Cognitive Decline in Women
- Roots
  - Smoking and Mortality and cessation trends
  - Silent MI's in T2DM
  - Obesity Myths, Presumptions, Facts
- Optimal Goals
  - 24 hour BP monitor and Cognitive Decline
- Treatment
  - Aspirin and Dementia prevention in women
  - Bupropion post MI
  - Dietary Flavonoids
  - Fructose vs Glucose
  - Ramipril and PAD
  - Heme Iron

Red Flags

Metabolic Syndrome in 40's linked to TV and lack of exercise at age 16

Northern Sweden – 888 participants assessed at age 43
Metabolic Syndrome identified in 26.9% of participants

Those who reported watching several TV shows per day compared to 1 show per week were twice as likely to have metabolic syndrome at age 43 (adjusted OR 2.14).

Those who reported leisure-time physical activity "several times per month" were twice as likely to have metabolic syndrome than those who reported "daily" leisure time physical activity in their teens (adjusted OR 2.31)

Wennberg P, Gustafsson, PE, et al. Diabetes Care Jan 22, 2013.

Waist measurement and BMI best predict heart disease death risk

15 547 participants with CAD from 5 studies, 3 continents – assessed for risk of mortality associated with either waist circumference or waist-to-Hip ratio (WHR). Excluded those with BMI < 18.5 kg/m2. Mean age 66, 55% men.

4699 deaths over median f/u of 4.7 years.

Subjects with normal weight but centrally obese had worst long-term survival.

BMI of 22 and WHR of 0.98 had higher mortality than a person with similar BMI but WHR of 0.89 (HR 1.10). BMI of 26 and WHR of 0.89 (HR of 1.20) BMI of 30 and WHR of 0.89 (HR of 1.61) BMI of 30 and WHR of 0.98 (HR of 1.27) ($p<.0001$ for all)

Being overweight by BMI does NOT lead to higher mortality in absence of central obesity.

Coutinho, T, et al. J Am Coll Cardiol Feb 5, 2012; 61:553-56.

Association between hypertensive disorders during pregnancy and end-stage renal disease

Methods: Insurance claims data from 1998 to 2009 to identify 26 651 women aged 19–40 years old who experienced hypertensive disorders during pregnancy; these women had no history of hypertension, diabetes, kidney disease or lupus.

Compared to 213 397 randomly selected women without hypertensive disorders during pregnancy as a comparison cohort; the frequency was matched by age and index year of pregnancy.

Compared the incidence of end-stage renal disease in the 2 cohorts

I-Kuan Wang MD, Chih-Hsin Muo MS, et al. Early release, published at www.cmaj.ca on January 21, 2013. Subject to revision.

Association between hypertensive disorders during pregnancy and end-stage renal disease

Results: Women with hypertensive disorders during pregnancy had a greater risk of chronic kidney disease and end-stage renal disease, with adjusted HRs of 9.38 (95% CI 7.09–12.4) and 12.4 (95% CI 8.54–18.0)

HR for end-stage renal disease was 2.72 (95% CI 1.76–4.22) after we also controlled for hypertension and diabetes.

Women with preeclampsia or eclampsia had a higher risk of end-stage renal disease (adjusted HR 14.0, 95% CI 9.43–20.7) than women who had gestational hypertension only (adjusted HR 9.03, 95% CI 5.20–15.7).

Interpretation: Women with hypertensive disorders during pregnancy were at a high risk of end-stage renal disease. The risk was much greater for women who had preeclampsia or eclampsia than those who had gestational hypertension only.

I-Kuan Wang MD, Chih-Hsin Muo MS, et al. Early release, published at www.cmaj.ca on January 21, 2013. Subject to revision.

Association between hypertensive disorders during pregnancy and end-stage renal disease

Adjusted HR (95% CI) for ESRD among women with (vs without) hypertensive disorders in pregnancy overall and by type of hypertensive disorder

Hypertensive disorders in pregnancy population	HR (95% CI)[a]	HR (95% CI)[b]
Overall	12.4 (8.54-18.0)	2.72 (1.76-4.22)
Preeclampsia/eclampsia (n=17 998)	14.0 (9.43-20.7)	3.19 (2.02-5.02)
Gestational hypertension (n=8653)	9.03 (5.20-15.7)	1.81 (0.99-3.30)

a. Adjusted for urban status, coronary artery disease, congestive heart failure, hyperlipidemia, and abruption b. After further adjustment for hypertension and diabetes during follow-up

Phosphorus levels are associated with subclinical atherosclerosis in the general population.

BACKGROUND: Elevated serum phosphorus has been linked to mortality among patients with renal failure. Aim to examine the association of serum phosphorus level with carotid atherosclerosis in the general population.

METHODS: Determined association of serum phosphorus levels with carotid intima-media thickness (cIMT) in **13,340** subjects 45-64 years old without known coronary heart disease, stroke, or renal disease from the Atherosclerosis Risk in Communities (ARIC) study.

Atherosclerosis. 2008 Aug;199(2):424-31. Epub 2008 Feb 21.

Phosphorus levels are associated with subclinical atherosclerosis in the general population.

RESULTS: Phosphorus levels were significantly associated with age, gender, diabetes mellitus, hypertension, hypercholesterolemia and fibrinogen levels ($p < 0.0001$ for each), but not with estimated glomerular filtration rate (eGFR).

Age- and sex-adjusted mean cIMT ranged from 0.718 to 0.736 mm for the lowest to the highest quintile of serum phosphorus (p-value for trend < 0.0001).

Relationship was attenuated but remained statistically significant after adjustment for atherosclerotic risk factors and eGFR (trend $p < 0.0001$) in men but not in women.

Conclusion: In a multivariable model, a one standard deviation increase in baseline serum phosphorus (0.48 mg/dL) was associated with a 0.012 mm increase in mean cIMT ($p < 0.007$) in men but not in women.

Atherosclerosis. 2008 Aug;199(2):424-31. Epub 2008 Feb 21.

Serum Phosphate and Left Ventricular Hypertrophy in Young Adults: The Coronary Artery Risk Development in Young Adults Study

Coronary Artery Risk Development in Young Adults study (n = 4,055).prospective, community-based. Phosphate levels were measured at year 0, and left ventricular hypertrophy assessed by echocardiography at year 5.

Results: The mean age was 25.0 years. Left ventricular hypertrophy was present in 4.5% of the population. As a continuous variable, the phosphate level was associated with left ventricular hypertrophy (odds ratio per standard deviation 1.27; 95% confidence interval 1.09–1.47; p = 0.0020).

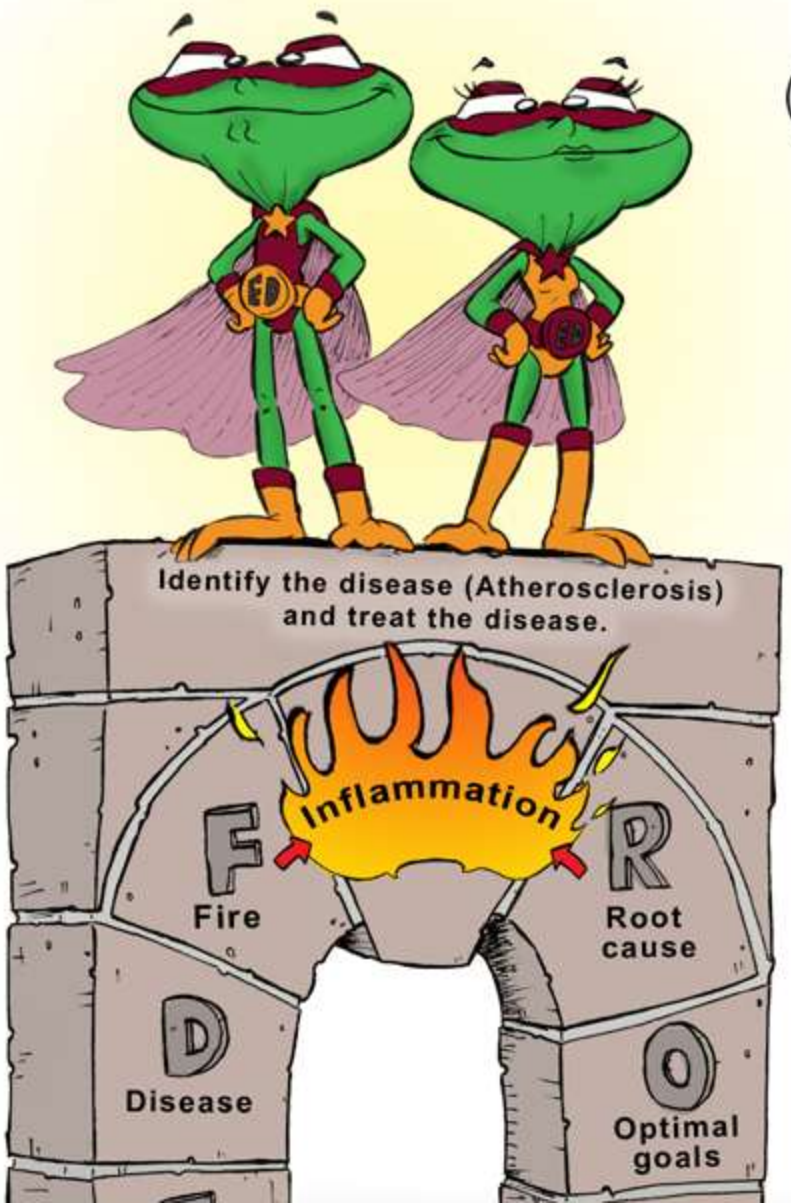
This association persisted after covariate adjustment (OR 1.30; 95% CI 1.10–1.54; p = 0.0018), and was most pronounced for fifth quintile phosphate levels (>4.0 mg/dl).

Conclusion: Phosphate level may be a risk factor for left ventricular hypertrophy in community-dwelling young adults.

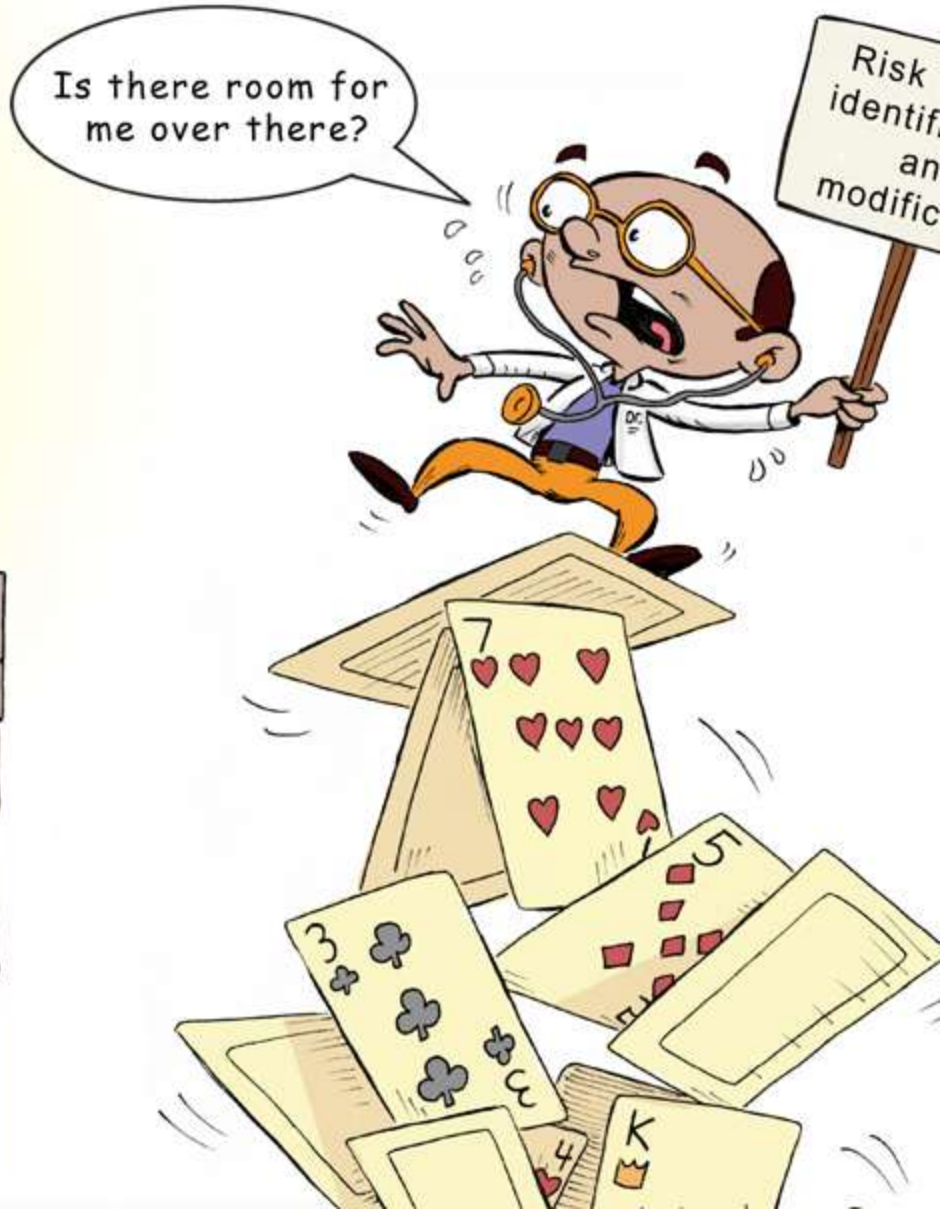
Kidney Blood Press Res 2009;32:37-44 (DOI: 10.1159/000203348)

What's the difference?

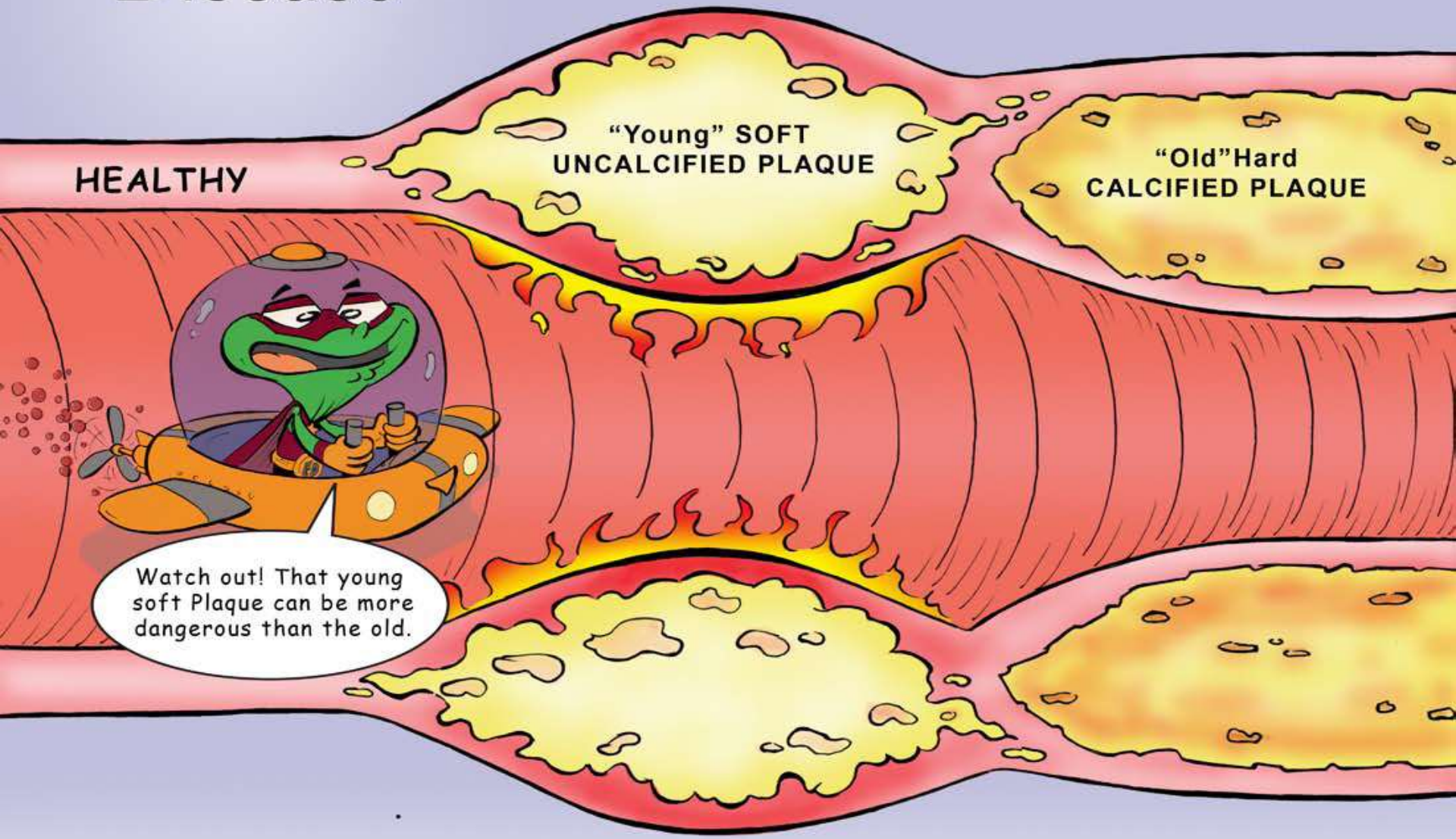
Bale/Doneen method



Standard of Care



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

Histological Features of Carotid Plaque in Patients With Ocular Ischemia Versus Cerebral Events

Question: *Does carotid plaque composition lend predictability to ischemic cerebral vascular events?*

Study carotid plaque composition in a large number of consecutive patients undergoing carotid endarterectomy for symptomatic stenosis to compare features in those who had cerebral events within the last 6 months versus those with ocular events only

D.P.J. Howard, G.W. van Lammeren et al. Stroke. published online 1.29. 2013; http://stroke.ahajournals.org/content/early/2013/01/29/STROKEAHA.112.678672

Histological Features of Carotid Plaque

Cerebral Events	Ocular Events
Greater macrophage staining	Smaller lipid core
Large lipid core	Larger fibrous content
Lower fibrous content	More calcified
Less Calcified	Lower macrophage staining.

Vulnerable plaques: Presence of thrombus, large lipid core, low fibrous content, intraplaque hemorrhage, and macrophage infiltration.

D.P.J. Howard, G.W. van Lammeren et al. Stroke. published online 1.29. 2013; http://stroke.ahajournals.org/content/early/2013/01/29/STROKEAHA.112.678672

Histological Features of Carotid Plaque

Cerebral Events

Tent to be associated with atheromatous, inflammatory plaques.

Ocular Events

Tend to produce smaller, fibrin-rich emboli

D.P.J. Howard, G.W. van Lammeren et al. Stroke. published online 1.29. 2013; http://stroke.ahajournals.org/content/early/2013/01/29/STROKEAHA.112.678672

Histological Features of Carotid Plaque in Patients With Ocular Ischemia Versus Cerebral Events

Table 3. Odds Ratios for Cerebral Symptoms Versus Monocular Symptoms for Nonoverlapping Plaque Characteristics

Study	OR	95% CI	*P* Value	Adjusted OR*	95% CI	Adjusted *P* Value*
Oxford Plaque Study (n=481)						
Plaque rupture	1.45	0.96–2.18	0.08	1.43	0.93–2.18	0.10
Foam cells	1.13	0.75–1.70	0.56	1.16	0.76–1.78	0.49
Heavy lymphocyte staining	1.63	1.07–2.47	0.02	1.62	1.05–2.48	0.03
Heavy cap macrophage staining	1.14	0.70–1.87	0.60	1.02	0.61–1.72	0.94
Thin cap (<200 μm)	1.12	0.70–1.80	0.64	1.08	0.66–1.77	0.76
Athero-Express Study (n=1159)						
Smooth muscle cells	0.76	0.54–1.08	0.13	0.80	0.56–1.16	0.24

CI indicates confidence interval; NA, not available; and OR, odds ratio.

*Adjusted for age, sex, diabetes mellitus, treated hypercholesterolemia, and hypertension.

D.P.J. Howard, G.W. van Lammeren et al. Stroke. published online 1.29. 2013; http://stroke.ahajournals.org/content/early/2013/01/29/STROKEAHA.112.678672

Histological Features of Carotid Plaque in Patients With Ocular Ischemia Versus Cerebral Events

Table 4. Odds Ratios for Presence of Multiple Vulnerable Plaque Characteristics (vs Zero Features) in Relation to Clinical Presentation in Pooled Sample: Cerebral Symptoms (n=1317) Versus Monocular Symptoms (n=323)

Plaque characteristics	Cerebral, n (%)	Ocular, n (%)	OR	95% CI	*P* Value	Adjusted OR*	95% CI	Adjusted *P* Value*
0 vulnerable plaque features	128 (9.7)	49 (15.2)	1.00			1.00		
1 vulnerable plaque feature	174 (13.2)	50 (15.5)	1.23	0.78–1.95	0.38	1.21	0.75–1.95	0.44
2 vulnerable plaque features	204 (15.5)	55 (17.0)	1.33	0.85–2.08	0.22	1.25	0.79–1.99	0.34
3 vulnerable plaque features	380 (28.9)	79 (24.5)	1.68	1.11–2.54	0.01	1.65	1.07–2.54	0.02
≥4 vulnerable plaque features	431 (32.7)	90 (27.9)	1.69	1.13–2.53	0.01	1.66	1.08–2.54	0.02

Data stratified by study group. χ^2 Linear-by-Linear association trend: P=0.002. CI indicates confidence interval; and OR, odds ratio.

*Adjusted for age, sex, diabetes mellitus, treated hypercholesterolemia, and hypertension.

D.P.J. Howard, G.W. van Lammeren et al. Stroke. published online 1.29. 2013; http://stroke.ahajournals.org/content/early/2013/01/29/STROKEAHA.112.678672

Histological Features of Carotid Plaque in Patients With Ocular Ischemia Versus Cerebral Events

Bale/Doneen Take-Away:

Plaque vulnerability based on histology validates our disease/inflammatory platform.

In this study the differences in ischemic events are likely attributable to the emboli formed by the different plaques and the anatomic and metabolic differences of the target organs.

D.P.J. Howard, G.W. van Lammeren et al. Stroke. published online 1.29. 2013; http://stroke.ahajournals.org/content/early/2013/01/29/STROKEAHA.112.678672

Carotid Atherosclerosis and Risk of Subsequent Coronary Event in Outpatients with Atherosclerosis

45,227 patients from the REACH Registry with 4-year follow-up. 23,364 with information on carotid atherosclerosis at baseline were analyzed.

Primary outcome was composite of fist occurrence of CV death, MI or Coronary Hospitalization.

REACH Registry: International, prospective, observational registry designed to provide up to 24 months of clinical follow-up of >68,000 outpatients from 5473 sites in 44 countries. After the initial follow-up, an additional 2-year extension was proposed, and 29 countries (3647 sites enrolled 45,227 more patients) decided to participate.

The present study included patients with 4-year follow-up and available carotid plaque status at baseline.

Sirimarco, G, Amarenco, P, et al. Stroke. Published online Jan 10, 2013. Stroke 2013;44:00-00.

Carotid Atherosclerosis and Risk of Subsequent Coronary Event in Outpatients with Atherosclerosis

Presence of carotid atherosclerosis:

1. cIMT ≥ 1 carotid plaque (defined as a distinct area with an IMT exceeding twice that of the neighboring sites)
2. Asymptomatic carotid stenosis ≥ 70%
3. History of carotid revascularization

Follow-up:

1. Primary: first occurrence of CV death, MI or CV hosp.
2. Secondary: first occurrence of MI (fatal or non-fatal).

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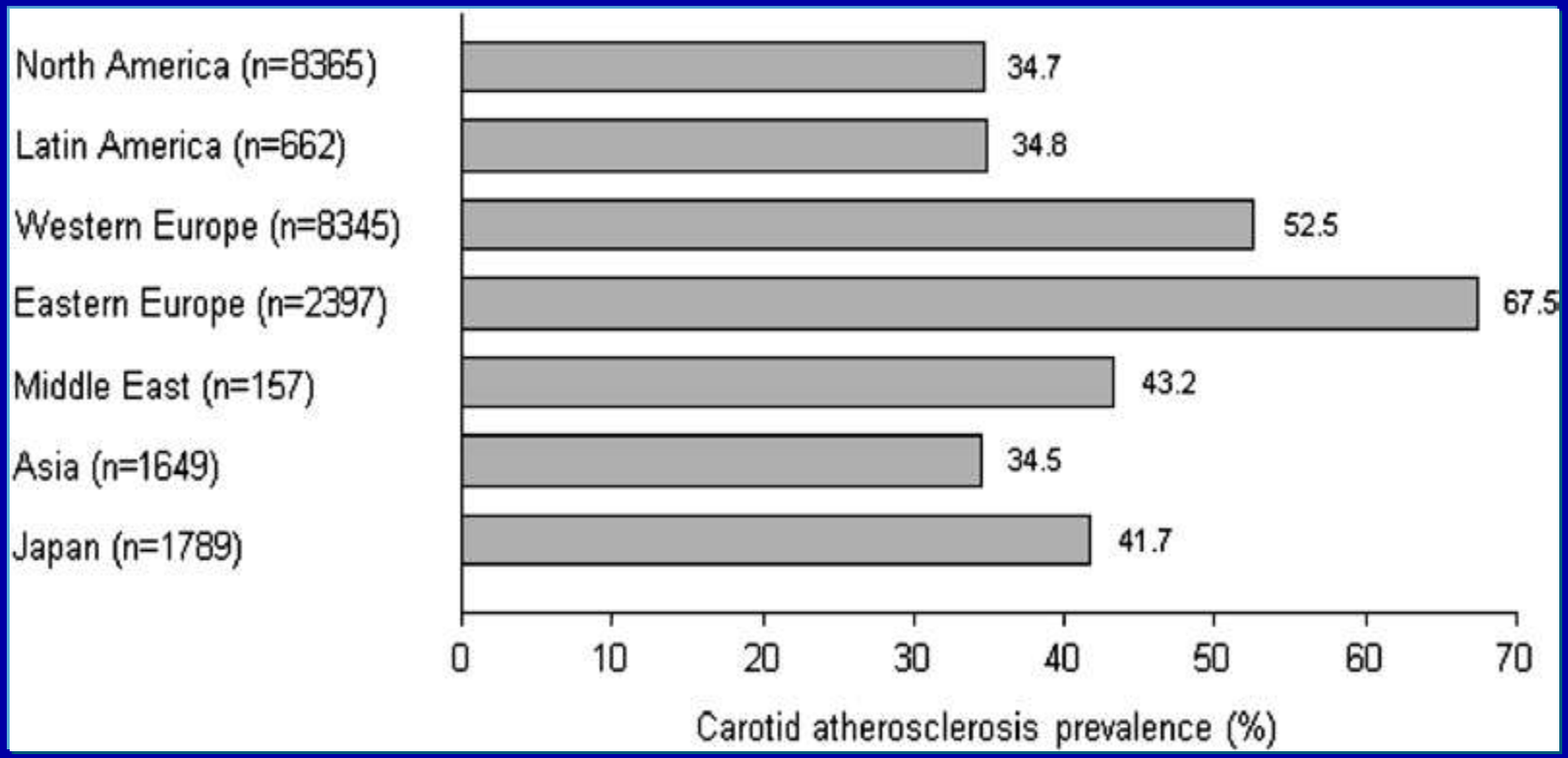
Carotid Atherosclerosis and Risk of Subsequent Coronary , Event in Outpatients with Atherosclerosis

Among 45,227 patients with 4 year follow-up, carotid atherosclerosis status was available for 23,364 patients (52%).



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Carotid Atherosclerosis and Risk of Subsequent Coronary Event in Outpatients with Atherosclerosis

		Carotid atherosclerosis rate %		
Characteristics	N, %	Absent	Present	P-value
Age >70 y	11 043 (47.4)	41.8	49.4	<0.0001
Men	15 071 (64.6)	43.3	47.3	<0.0001
Cardiovascular risk factors				
Diabetes mellitus	9725 (41.6)	47.2	42.7	<0.0001
Hypertension	19 249 (82.4)	40.1	46.3	<0.0001
Hyper lipids	16 754 (71.8)	46.2	44.9	0.09
Obesity BMI ≥30	6486 (28.1)	47.1	41.2	<0.0001
Current smoking	3571 (15.8)	44.1	50.0	<0.0001
Heart failure	3204 (13.9)	44.1	51.7	<0.0001
Atrial fibrillation	2462 (10.7)	44.6	48.8	0.0001
Vascular disease status				
CAD	12 982 (55.6)	46.6	44.1	0.0002
CVD	7973 (34.1)	37.5	59.9	<0.0001
PAD	3561 (15.2)	42.6	61.0	<0.0001

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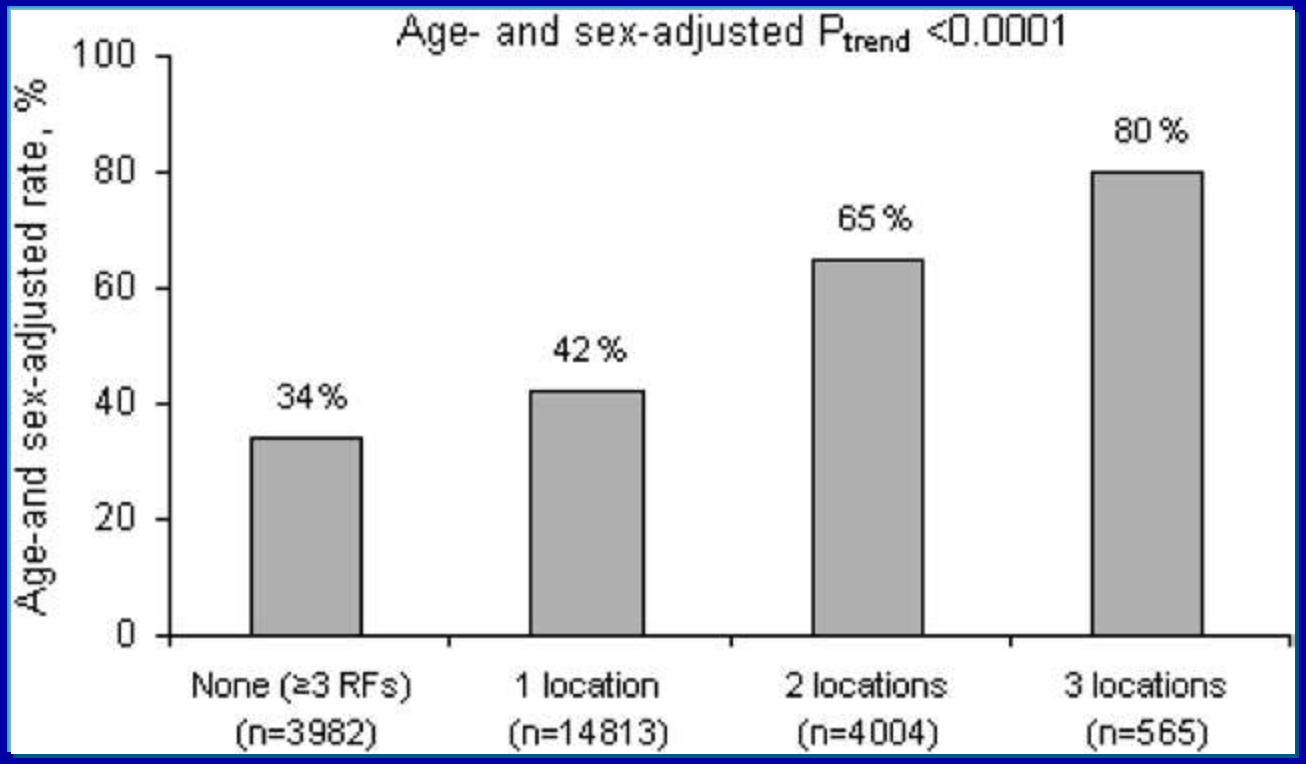
Carotid Atherosclerosis and Risk of Subsequent Coronary Event in Outpatients with Atherosclerosis

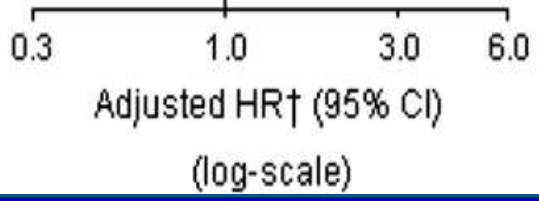


Age- and sex-adjusted rates of carotid atherosclerosis by number of symptomatic arterial disease locations at inclusion

Sirimarco, G, Amarenco, P, et al. Stroke. Published online Jan 10, 2013. Stroke 2013;44:00-00.

Carotid Atherosclerosis and Risk of Subsequent Coronary Event in Outpatients with Atherosclerosis

	Event Rate (%)* CA (–)	Event Rate (%)* CA (+)	Adjusted HR† (95%CI)	P-Value
CV death, non-fatal MI, coronary hospitalization				
None (≥3 risk factors) (n=3982)	10.9	10.4	1.18 (0.93-1.51)	0.18
1 location (n=14813)	20.4	20.6	0.99 (0.91-1.07)	0.81
2 locations (n=4004)	26.2	33.0	1.31 (1.14-1.50)	0.0001
3 locations (n=565)	31.2	40.6	1.41 (0.92-2.18)	0.12
Non-fatal/fatal MI				
None (≥3 risk factors) (n=3982)	3.7	3.2	1.12 (0.72-1.74)	0.62
1 location (n=14813)	4.9	5.2	1.15 (0.97-1.36)	0.11
2 locations (n=4004)	6.4	9.4	1.63 (1.22-2.18)	0.0009
3 locations (n=565)	9.5	14.9	1.91 (0.80-4.56)	0.14



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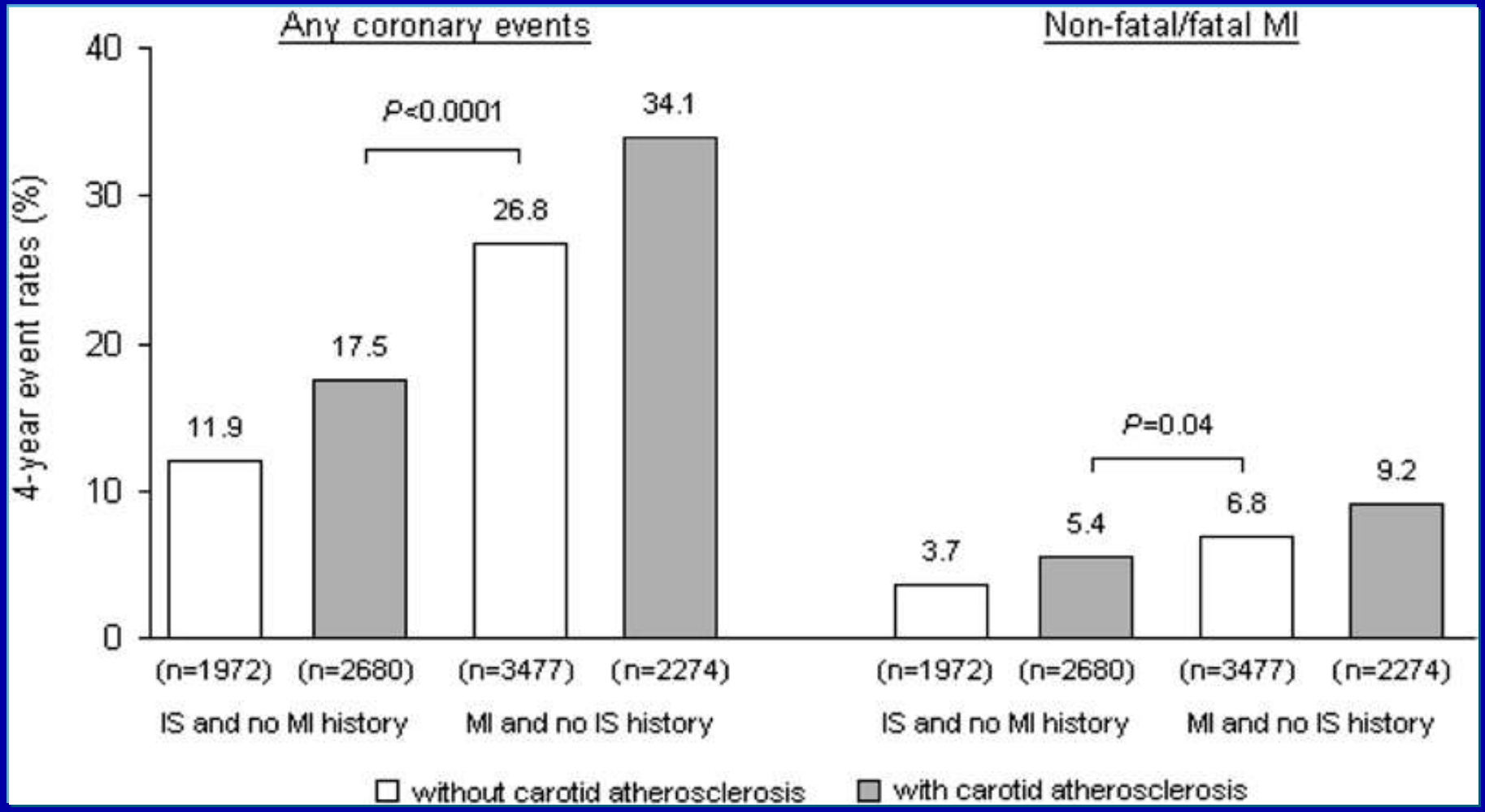

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Carotid Atherosclerosis and Risk of Subsequent Coronary Event in Outpatients with Atherosclerosis

"Plaques seem to appear later in the carotids than in the aorta and coronary arteries. Therefore, the phase of plaque formation in the 2 arterial territories may differ. Our findings that the mere presence of carotid atherosclerosis independently increases the risk of coronary events across various disease locations is in favor of carotid atherosclerosis being marker of disease severity"

Sirimarco, G, Amarenco, P, et al. Stroke. Published online Jan 10, 2013. Stroke 2013;44:00-00.

Carotid Atherosclerosis and Risk of Subsequent Coronary Event in Outpatients with Atherosclerosis

Bale/Doneen Take-Away:

If you find plaque in the carotid artery – pay attention! Your patient is at risk for a coronary event!

Sirimarco, G, Amarenco, P, et al. Stroke. Published online Jan 10, 2013. Stroke 2013;44:00-00.

Cardiac Disease Associated With Increased Risk of Nonamnestic Cognitive Impairment: Stronger Effect on Women

Objective To investigate the association of cardiac disease with amnestic and nonamnestic mild cognitive impairment

Design A prospective, population-based, cohort study with a median 4.0 years of follow-up.

Participants A total of 2719 participants were evaluated at baseline and every 15 months using the Clinical Dementia Rating scale, and neuropsychological testing. A diagnosis of normal cognition, MCI, or dementia was made by consensus. Cardiac disease at baseline was assessed from the participant's medical records.

Main Outcome Measures Cognitive Impairment – nonamnestic

JAMA Neurol. Jan 29, 2013;():1-9. doi:10.1001/jamaneurol.2013.607

Cardiac Disease Associated With Increased Risk of Nonamnestic Cognitive Impairment: Stronger Effect on Women

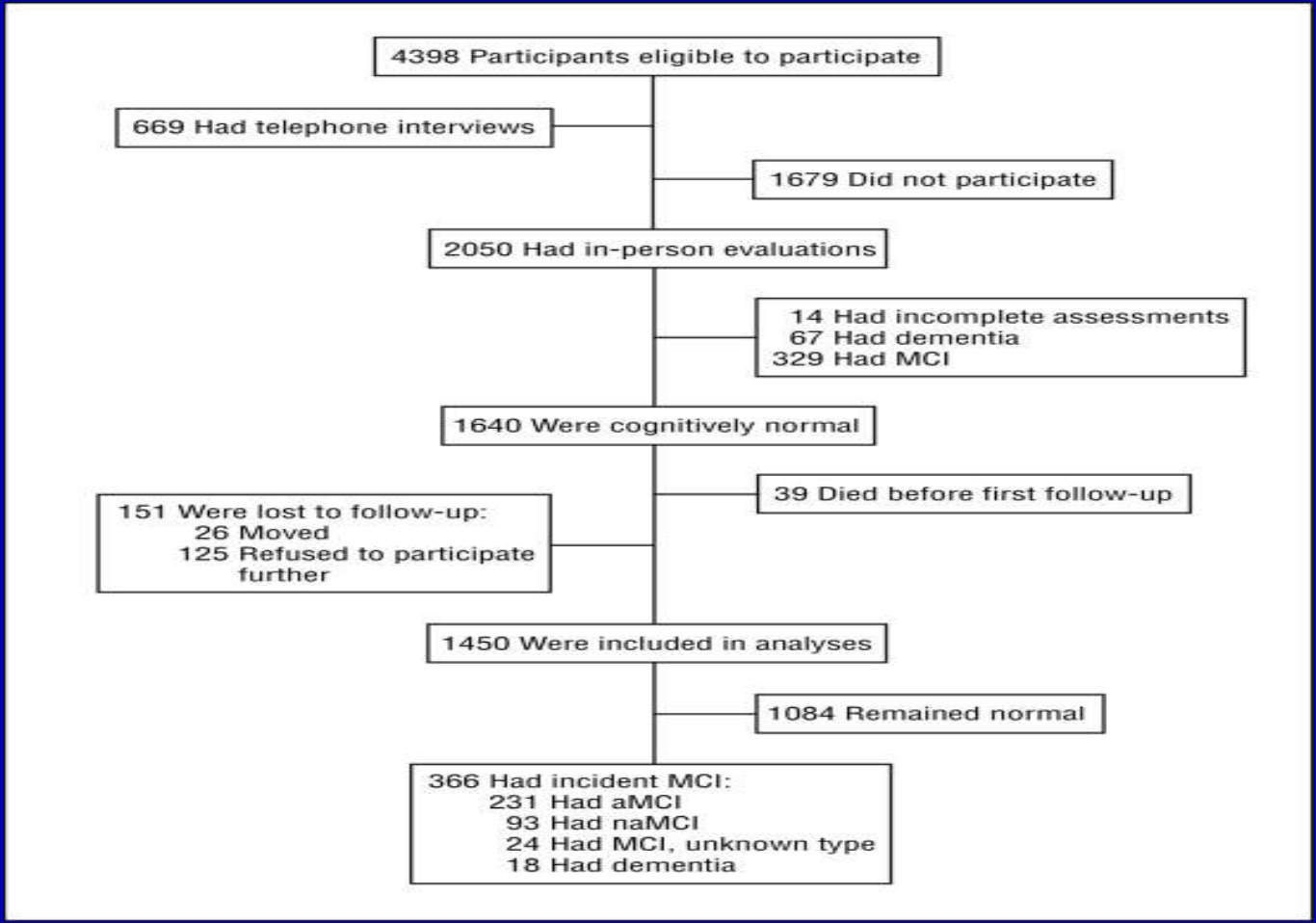


Figure Legend:

Figure 1. Study flowchart. There were 669 persons who participated only by telephone at baseline, and they were not included in the present study; 24 persons with mild cognitive impairment (MCI) participated by telephone at follow-up, and their MCI subtype is unknown; 18 developed dementia without an interim diagnosis of MCI. aMCI indicates amnestic MCI; and naMCI, nonamnestic MCI.

JAMA Neurol. Jan 29, 2013;():1-9. doi:10.1001/jamaneurol.2013.607

Cardiac Disease Associated With Increased Risk of Nonamnestic Cognitive Impairment: Stronger Effect on Women

Results: Of 1450 participants without MCI or dementia at baseline, 366 developed MCI.

Cardiac disease was associated with an increased risk of naMCI (hazard ratio, 3.07 [95% CI, 1.58-5.99]) for women but not for men (hazard ratio, 1.16 [95% CI, 0.68-1.99]).

Conclusions: Cardiac disease is an independent risk factor for naMCI; within-sex comparisons showed a stronger association for women.

Prevention and management of cardiac disease and vascular risk factors may reduce the risk of naMCI.

JAMA Neurol. Jan 29, 2013;():1-9. doi:10.1001/jamaneurol.2013.607

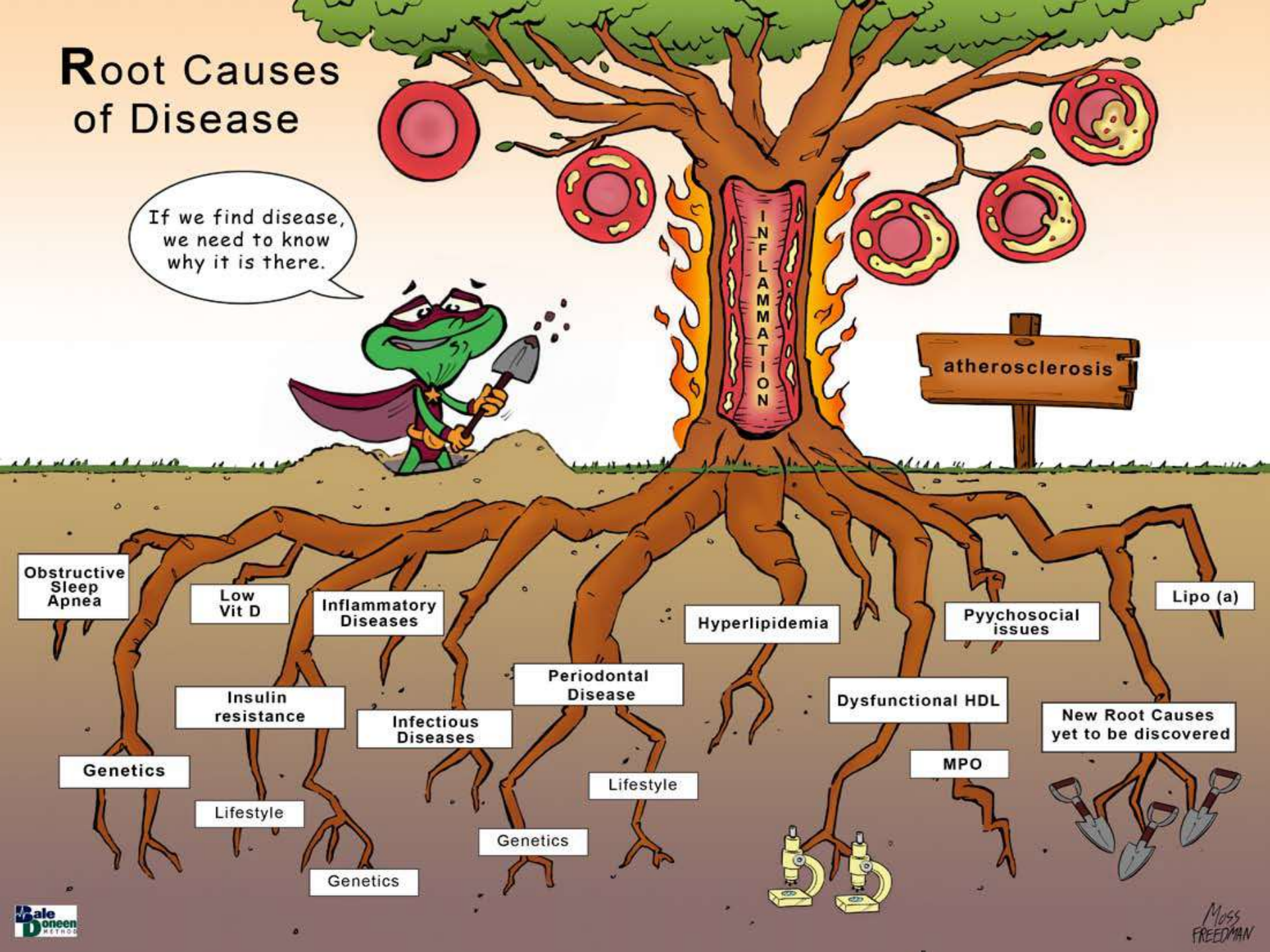
Cardiac Disease Associated With Increased Risk of Nonamnestic Cognitive Impairment: Stronger Effect on Women

Bale/Doneen Take-Away:

Cognitive Impairment is likely related to vascular health. Women are more inclined to struggle with microvascular atherosclerosis. Talk to your female patients about vascular dementia and the importance of treating systemic vascular disease with optimal medical and lifestyle Management.

Remember – atherosclerosis is sine qua non for a CV event – define 'events' globally to patients. Don't forget about microvascular atherosclerosis.

JAMA Neurol. Jan 29, 2013;():1-9. doi:10.1001/jamaneurol.2013.607


Root Causes of Disease
If we find disease, we need to know why it is there.
INFLAMMATION
atherosclerosis
Obstructive Sleep Apnea
Low Vit D
Inflammatory Diseases
Hyperlipidemia
Pyychosocial issues
Lipo (a)
Insulin resistance
Periodontal Disease
Dysfunctional HDL
New Root Causes yet to be discovered
Infectious Diseases
Genetics
MPO
Lifestyle
Lifestyle
Genetics
Genetics
Dale Boneen METHOD
MOSS FREEDMAN

Benefits of Smoking Cessation in the U.S.

Smoking and smoking-cessation histories from 113,752 women and 88,496 men aged 25 and older who were interviewed between 1997 and 2004.

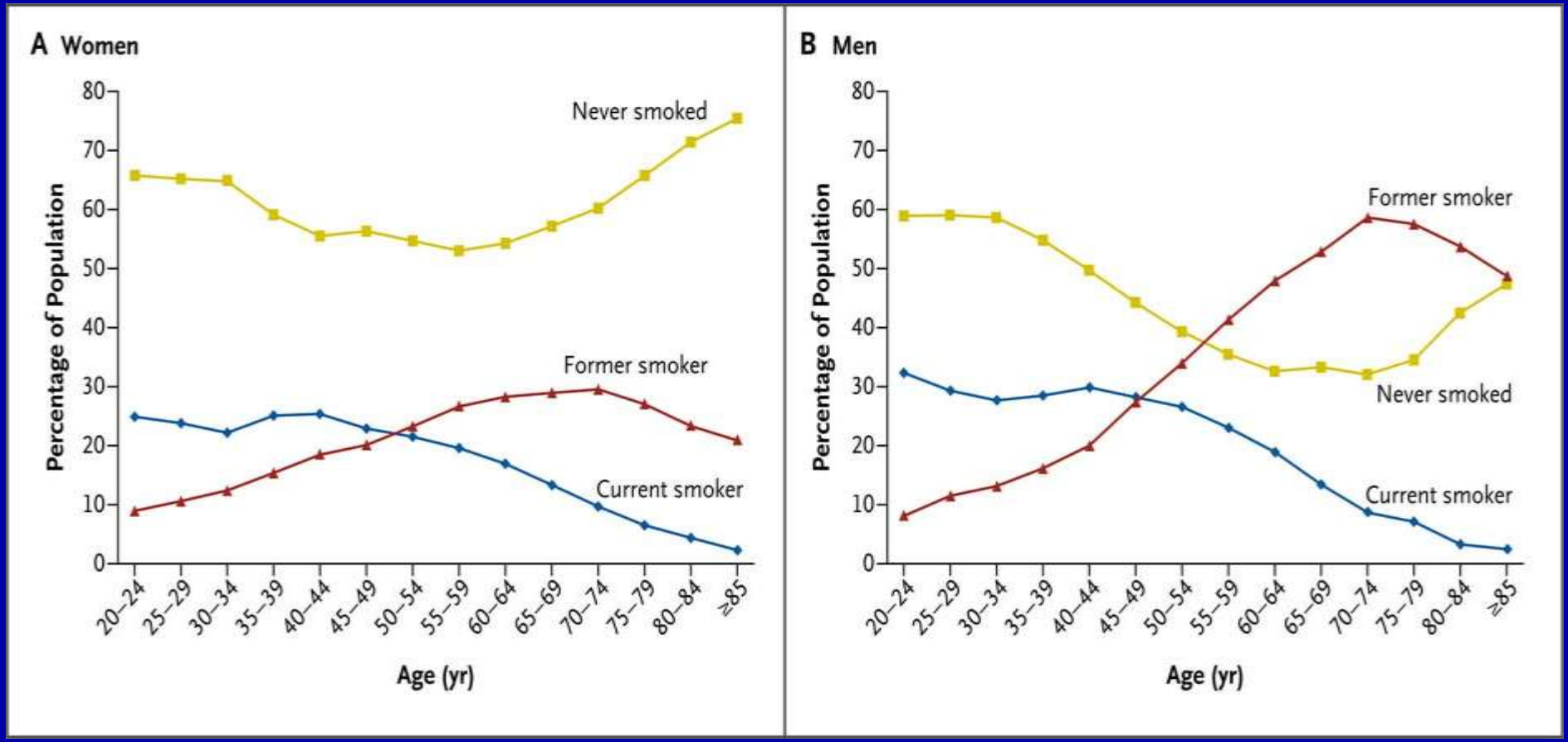
For participants who were 25-79 years of age, the rate of death from any cause among smokers was about three times that among those who had never smoked (HR for women 3.0; 99% CI, 2.4 to 3.1)

Smokers lose at least one decade of life expectancy as compared with those who have never smoked. Cessation before the age of 40 years reduces the risk of death associated with continued smoking by about 90%.

Jha, P, Ramasundarahettige, M., et al. N Engl J Med 368;4 January 24, 2013.

Benefits of Smoking Cessation in the U.S.

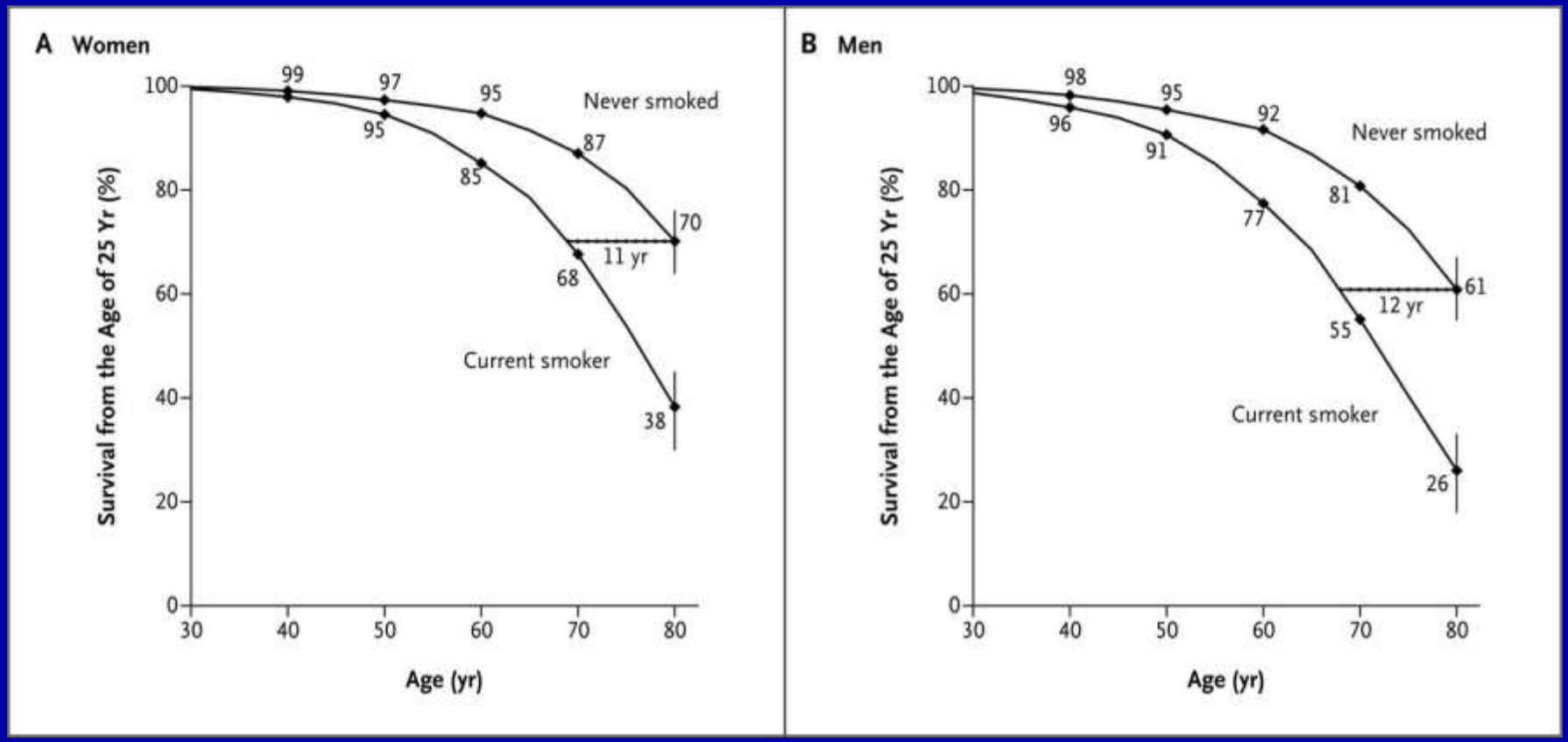
Age-Specific Proportions of Participants in the National Health Interview Survey (NHIS) According to Baseline Smoking Status, 1997–2004.



Jha, P, Ramasundarahettige, M., et al. N Engl J Med 368;4 January 24, 2013

Benefits of Smoking Cessation in the U.S.

Survival Probabilities for Current Smokers and for Those Who Never Smoked among Men and Women 25 to 80 Years of Age.



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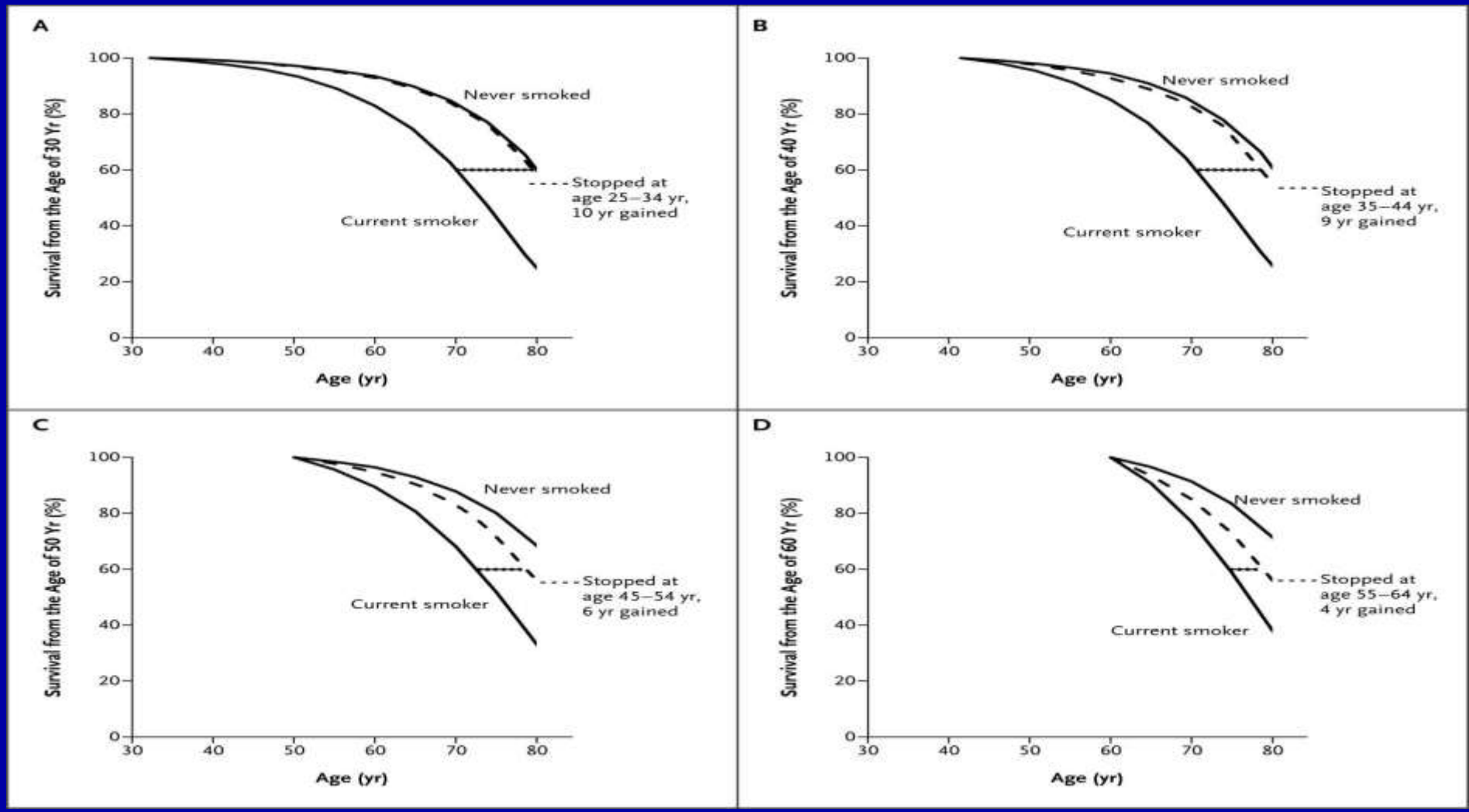
Benefits of Smoking Cessation in the U.S.

Effect of Smoking Cessation on Survival to 80 Years of Age, According to Age at the Time of Quitting.



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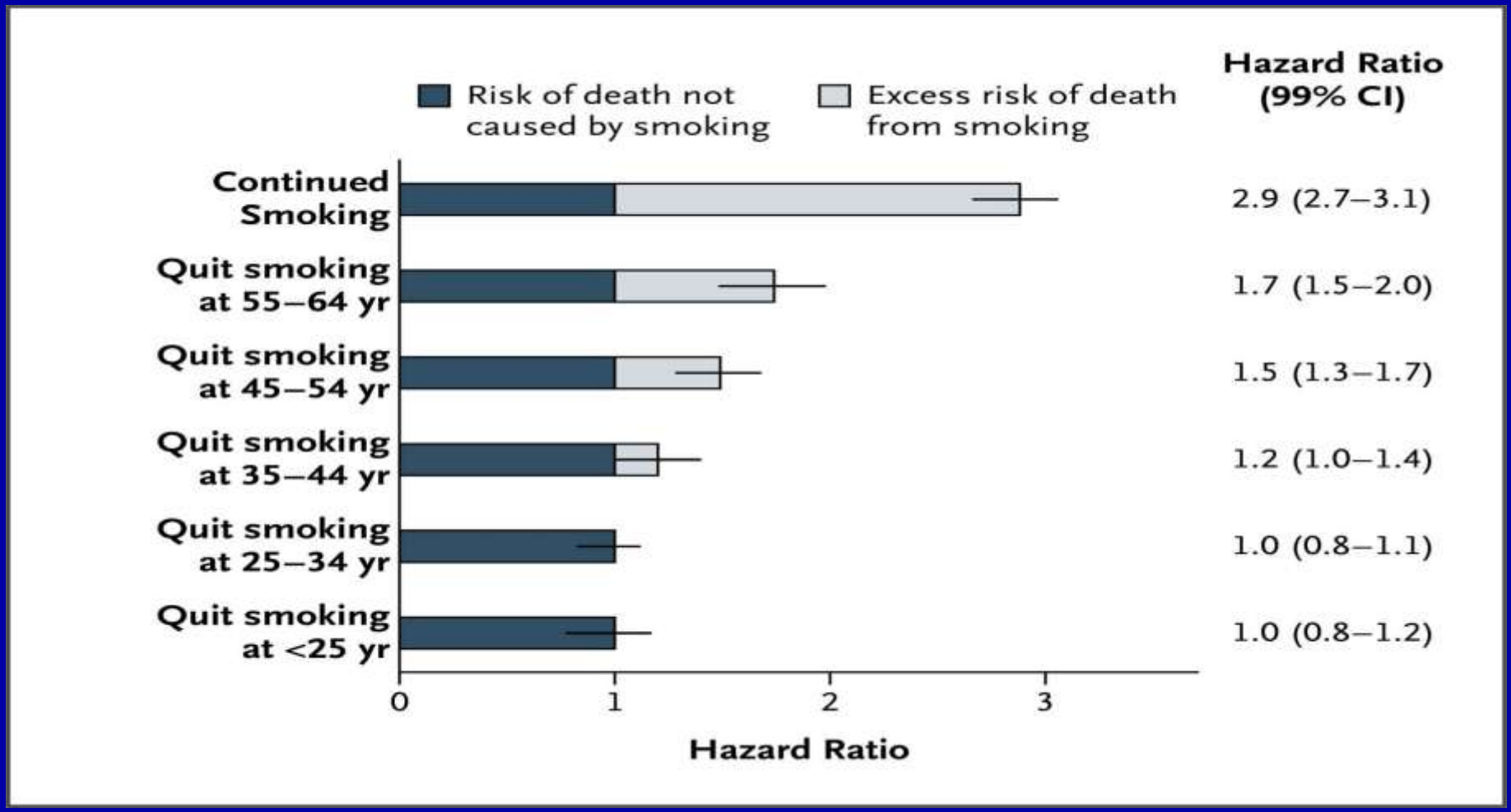
Benefits of Smoking Cessation in the U.S.

Risks of Death for Participants Who Continued to Smoke and for Those Who Quit Smoking According to Age at the Time of Cessation.



Jha, P, Ramasundarahettige, M., et al. N Engl J Med 368;4 January 24, 2013

Benefits of Smoking Cessation in the U.S.

Adjusted Hazard Ratios for Various Causes of Death among Current Smokers, as Compared with Those Who Never Smoked, among Women and Men 25 to 79 Years of Age.

Table 2. Adjusted Hazard Ratios for Various Causes of Death among Current Smokers, as Compared with Those Who Never Smoked, among Women and Men 25 to 79 Years of Age.*

Cause of Death	Women				Men			
	Never Smoked	Current Smoker	Adjusted Hazard Ratio (99% CI)	Deaths Attributable to Smoking among Smokers	Never Smoked	Current Smokers	Adjusted Hazard Ratio (99% CI)	Deaths Attributable to Smoking among Smokers
	no. of deaths			*no. (%)*	*no. of deaths*			*no. (%)*
Lung cancer	61	267	17.8 (11.4–27.8)	252 (94)	44	348	14.6 (9.1–23.4)	324 (93)
Cancers other than lung cancer	544	258	1.7 (1.4–2.1)	106 (41)	280	317	2.2 (1.7–2.8)	173 (55)
All cancers	605	525	3.2 (2.6–3.9)	360 (69)	324	665	3.8 (3.1–4.8)	491 (74)
Ischemic heart disease	382	251	3.5 (2.7–4.6)	179 (72)	285	416	3.2 (2.5–4.1)	288 (69)
Stroke	150	88	3.2 (2.2–4.7)	60 (69)	74	66	1.7 (1.0–2.8)	27 (40)
Other vascular disease	252	137	3.1 (2.2–4.4)	93 (68)	141	161	2.1 (1.5–3.0)	84 (52)
All vascular diseases	784	476	3.2 (2.7–3.9)	328 (69)	500	643	2.6 (2.1–3.2)	395 (61)
Respiratory diseases	119	206	8.5 (6.1–11.8)	182 (88)	45	188	9.0 (5.6–14.4)	167 (89)
Other medical disorders not shown above	581	277	2.2 (1.7–2.8)	151 (55)	295	370	2.2 (1.7–2.9)	205 (55)
All medical disorders	2089	1484	3.0 (2.7–3.3)	986 (66)	1164	1866	2.9 (2.5–3.2)	1211 (65)
Accidents and injuries	101	95	3.9 (2.4–6.2)	0	119	164	2.1 (1.4–3.0)	0
All causes†	2190	1579	3.0 (2.7–3.3)	986 (62)	1283	2030	2.8 (2.4–3.1)	1211 (60)

* Hazard ratios were adjusted for age, educational level, alcohol consumption, and body-mass index.
† Deaths attributable to smoking were determined with the use of the hazard ratios for all medical causes of death. With the exclusion of the 199 women and 222 men who had quit smoking less than 5 years before their deaths and the exclusion of the 1795 women and 2184 men who reported a history of coronary heart disease, stroke, or cancer, the hazard ratios for all-cause mortality were 3.1 for women and 2.8 for men.

Jha, P, Ramasundarahettige, M., et al. N Engl J Med 368;4 January 24, 2013

Silent myocardial infarction in type 2 diabetes

5,102 patients in the 30-year UK Prospective Diabetes Study (UKPDS)

Determine the prevalence of silent myocardial infarction (SMI) in people with newly-diagnosed type 2 diabetes (T2D).

One in six UKPDS patients with newly-diagnosed T2D had evidence of SMI, which was independently associated with an increased risk of fatal MI and all-cause mortality.

This study shows that evidence of a SMI at the time of diagnosis of T2D is significantly associated with a 49% increased rate of subsequent fatal MI and a 26% increased rate of all cause mortality after adjustment for conventional cardiovascular risk factors.

Davis, T, Coleman, R, Holman, R. et al. UKPDS 79. Circulation Published online January 29, 2013.

Silent myocardial infarction in type 2 diabetes

Bale/Doneen Take-Away:

Silent ischemia is a reality in newly diagnosed T2 DM. Strongly recommend getting perfusion imaging on new DM in your practices.

Remember: some of these folks will be diagnosed diabetes via a OGTT!

Also – do your due diligence to properly identify primary-secondary-tertiary in ALL patients!

Davis, T, Coleman, R, Holman, R. et al. UKPDS 79. Circulation Published online January 29, 2013.

Myths, Presumptions, and Facts about Obesity

7 Obesity Myths

1. Small sustained changes in energy intake or expenditure will produce large, long-term weight changes.

2. Setting realistic goals for weight loss is important, because otherwise patients will become frustrated and lose less weight.

3. Large, rapid weight loss is associated with poorer long-term weight-loss outcomes, as compared with slow, gradual weight loss

Casazza, K, Fontaine, K, et al. The N Engl J Med 368;5 January 31, 2013.

Myths, Presumptions, and Facts about Obesity

7 Obesity Myths

4. It is important to assess the stage of change or diet readiness in order to help patients who request weight loss treatment.

5. Physical-education classes, in their current form, play an important role in reducing or preventing childhood obesity.

6. Breast-feeding is protective against obesity.

7. A bout of sexual activity burns 100-300 kcal for each participant.

Casazza, K, Fontaine, K, et al. The N Engl J Med 368;5 January 31, 2013.

Myths, **Presumptions**, and Facts about Obesity

6 Obesity Presumptions (neither proven or disproven)

1. Regularly eating (vs skipping) breakfast is protective against obesity.

2. Early childhood is the period in which we learn exercise and eating habits that influence our weight throughout life.

3. Eating more fruits and vegetables will result in weight loss or less weight gain, regardless of whether any other changes to one's behavior or environment are made.

Casazza, K, Fontaine, K, et al. The N Engl J Med 368;5 January 31, 2013

Myths, **Presumptions**, and Facts about Obesity

6 Obesity Presumptions (neither proven or disproven)

4. Weight cycling (yo-yo dieting) is associated with increased mortality

5. Snacking contributes to weight gain and obesity

6. The built environment, in terms of sidewalks and park availability, influence the incidence or prevalence of obesity.

Casazza, K, Fontaine, K, et al. The N Engl J Med 368;5 January 31, 2013.

Myths, Presumptions, and **Facts** about Obesity

9 Facts about Obesity

1. Although genetic factors play a large role, heritability is not destiny.
2. Diets very effectively reduce weight, but trying to go on a diet or recommending that someone go on a diet generally does not work well in the long term.
3. Regardless of body weight or weight loss, an increased level of exercise increases health.
4. Physical activity or exercise in a sufficient dose aids in long-term weight maintenance.
5. Continuation of conditions that promote weight loss promotes maintenance of lower weight

Casazza, K, Fontaine, K, et al. The N Engl J Med 368;5 January 31, 2013.

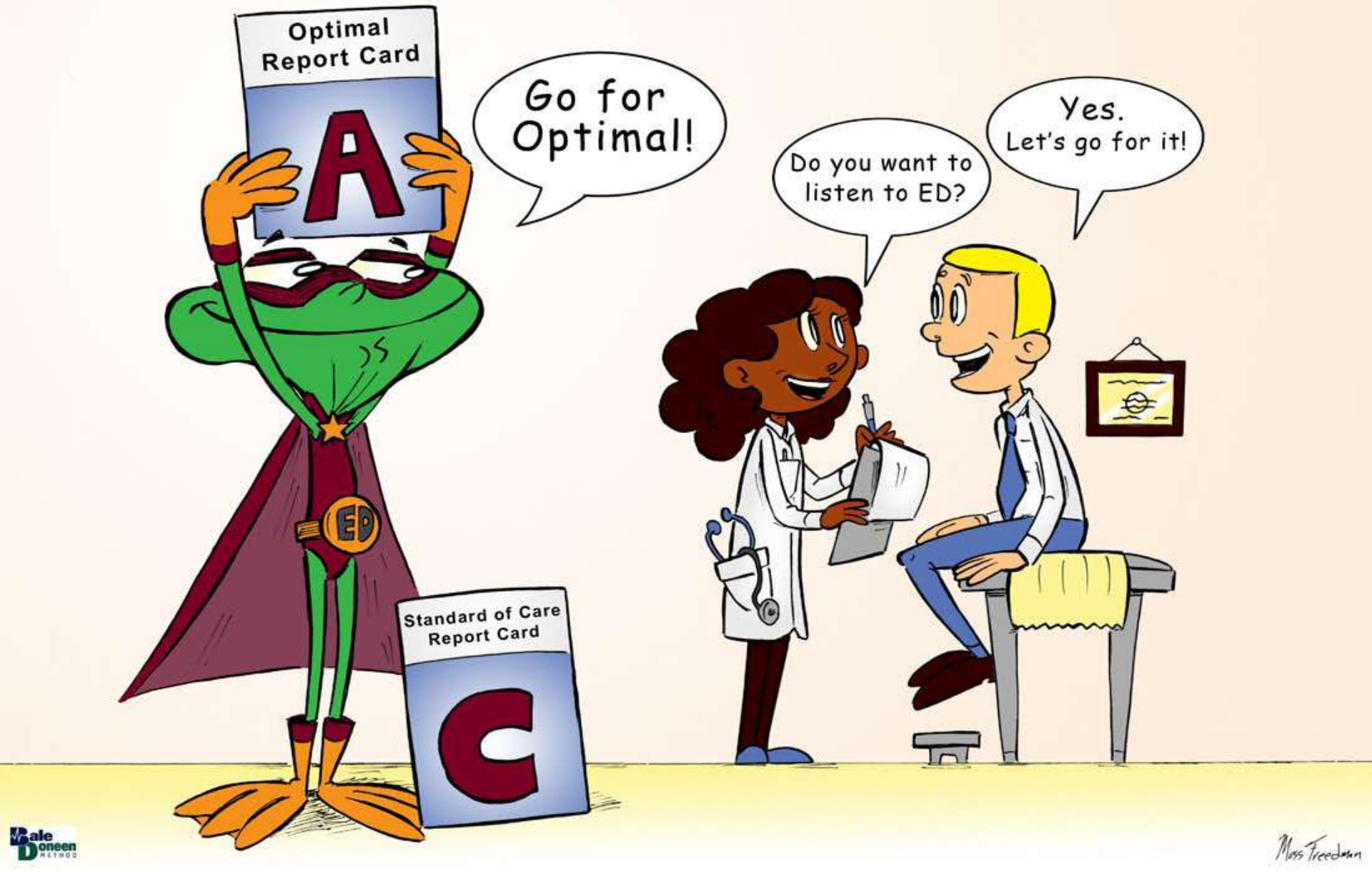
Myths, Presumptions, and **Facts** about Obesity

9 Facts about Obesity

6. For overweight children, programs that involve the parents and the home setting promote greater weight loss or maintenance.
7. Provisions of meals and use of meal-replacement products promote greater weight loss.
8. Some pharmaceutical agents can help patients achieve clinically meaningful weight loss and maintain the reduction as long as the agents continue to be used.
9. In appropriate patients, bariatric surgery results in long-term weight loss and reductions in the rate of incident diabetes and mortality.

Casazza, K, Fontaine, K, et al. The N Engl J Med 368;5 January 31, 2013.

Optimal vs Standard of Care



24 hour BP & Brain Volume Reduction: A cross-Sectional Elderly Population-based study.

On the basis of a cross-sectional design, 24-hour ambulatory BP measurements, as well as brain morphology from 3-D MRI, were assessed among 183 participants (mean, 65±0.6 years; 62.4% women).

Adjustments: Sex, use of antihypertensive drugs, duration of hypertension, leukoaraiosis, BMI, education level, and total brain matter volume.

Blood pressure related decreases in gray matter volume were significantly associated with a decline in executive function performance.

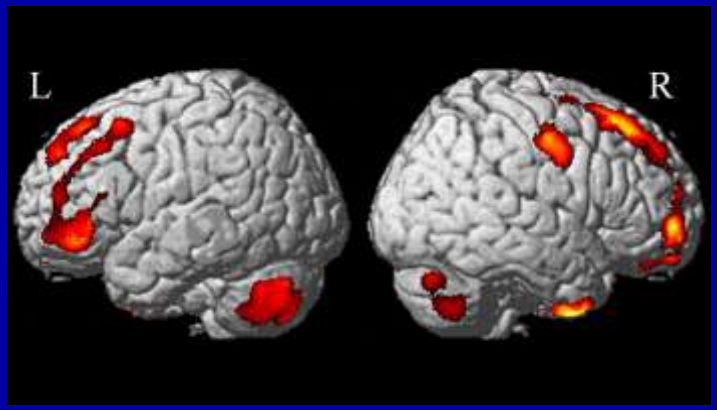
The association of high blood pressure with brain volume reduction may in part explain blood pressure-related cognitive decline leading to dementia.

Celle, S., Annweiler, C., Pichot, V., et al. Hypertension AHA. 10.8.2012.

24 hour BP & Brain Volume Reduction: A cross-Sectional Elderly Population-based study.

Bale/Doneen Take-Away:

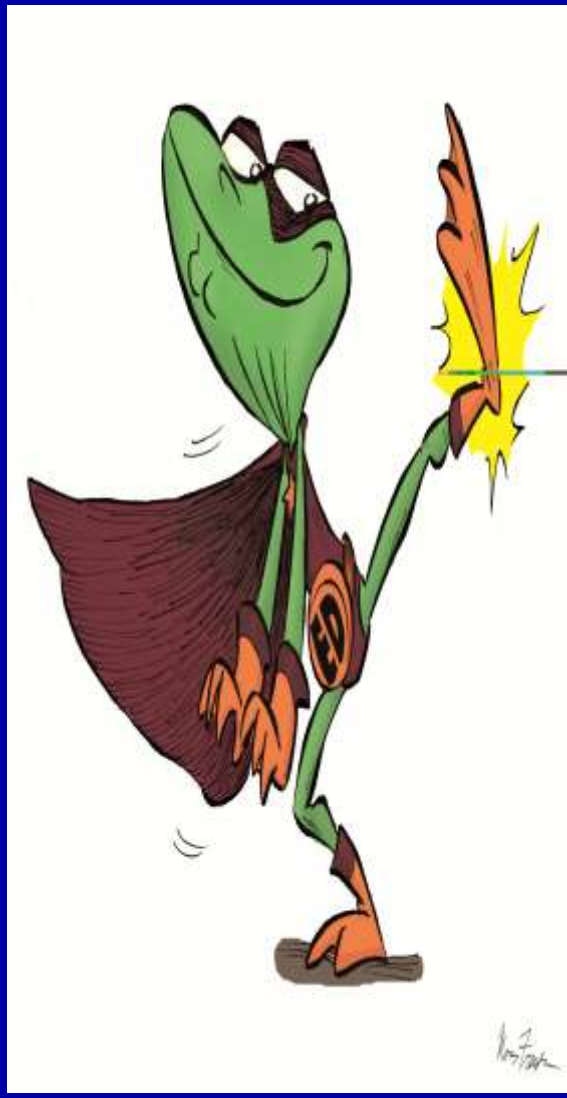
Blood Pressures – keep OPTIMAL goals in mind when assessing blood pressure. Optimal = individualized goals. Patients are most fearful of loss of brain function! Educate them to monitor pressures at home – stay engaged in therapy.



Celle, S., Annweiler, C., Pichot, V., et al. Hypertension AHA. 10.8.2012.

EDFROG IRA

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



TREATMENT

Low dose aspirin prevents cognitive decline in women with high CV risk.

Prospective Study of Women from the Swedish Population Register, included 681 women aged 70–92 years. Excluded: with dementia, on warfarin or clopidogrel

95.4% (N=601) had a high cardiovascular risk (CVD), defined as ≥ 10% FRS. 129 used low-dose ASA (75–160 mg daily) at baseline. (489 women x 5 years)

Primary Outcome: Cognitive decline and dementia incidence in relation to the use of low-dose ASA and cardiovascular risk factors.

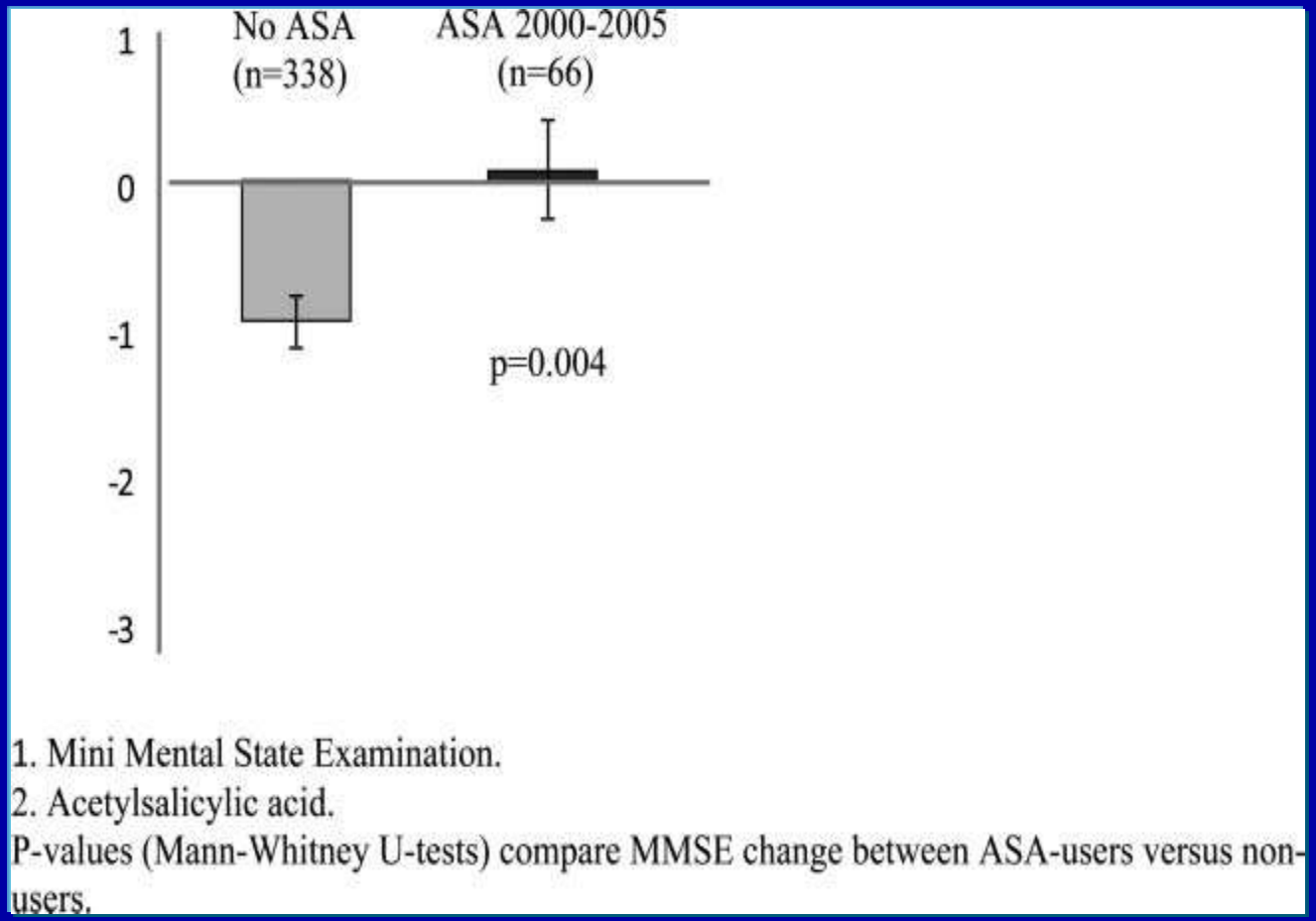
Cognition was measured using the Mini Mental State Examination (MMSE), word fluency, naming ability and memory word tests.

Dementia was diagnosed according to the DSM-III-R criterion.

Results: Women on regular low-dose ASA declined less on MMSE at follow-up than those not on ASA. (p=0.004 compared with never users; n=66 vs n=338).

Kern, S., Skoog, I, et al. BMJ. Open Oct 8, 2012. bmjopen-2012-001288

Low dose aspirin prevents cognitive decline in women with high CV risk.



1. Mini Mental State Examination.
2. Acetylsalicylic acid.
P-values (Mann-Whitney U-tests) compare MMSE change between ASA-users versus non-users.

Change in Mini Mental State Examination (MMSE) by ASA use in women followed from 2000 to 2005 p Values compare MMSE change between ASA-users versus non users

Kern, S., Skoog, I, et al. BMJ. Open Oct 8, 2012. bmjopen-2012-001288

Buproprion for Smoking Cessation in patients with Acute Coronary Syndrome – no quick fix!.

Double-blind, randomized controlled trial, 8 weeks of treatment with bupropion SR or placebo for smokers hospitalized with ACS as an adjunct to nurse led hospital- and telephone-based support.

Primary efficacy outcome was smoking abstinence at 1 year.

Results: A total of 151 patients were enrolled; all but 2 completed follow-up. Abstinence rates at 3 months were 45% and 44% in the bupropion SR and placebo groups, respectively (*P*=.99); 37% vs 42% (*P*=.61) at 6 months; and 31% vs 33% (*P*=.86) at 1 year. On multivariate analysis, an invasive procedure performed during index hospitalization was an independent predictor for smoking abstinence at 1 year (odds ratio [OR], 4.2; 95% confidence interval [CI], 1.22-14.19).

Conclusion: In hospitalized patients with ACS who received continuous, intensive nurse counseling about smoking cessation, bupropion did not increase the rates of smoking abstinence.

Planer, D., Lev, I, et al. Arch Intern Med/Vol 171 No. 12. June 27, 2012

Buproprion for Smoking Cessation in patients with Acute Coronary Syndrome – no quick fix!.

Bale/Doneen Take-Away:

A heart attack is a motivator for ALL patients to quit smoking. There is NO quick fix for cessation long term except continued support and counseling. It is the job of the out-patient prevention minded provider to take on this challenge. Remember – 5-A's.

Planer, D., Lev, I, et al. Arch Intern Med/Vol 171 No. 12. June 27, 2012

Dietary Flavonoids and reduced MI risk in young and middle-aged women.

93 600 women 25 to 42 years of age from the Nurses' Health Study (NHS) II who were healthy at baseline (1989) to examine the relationship between flavonoids and the risk of MI.

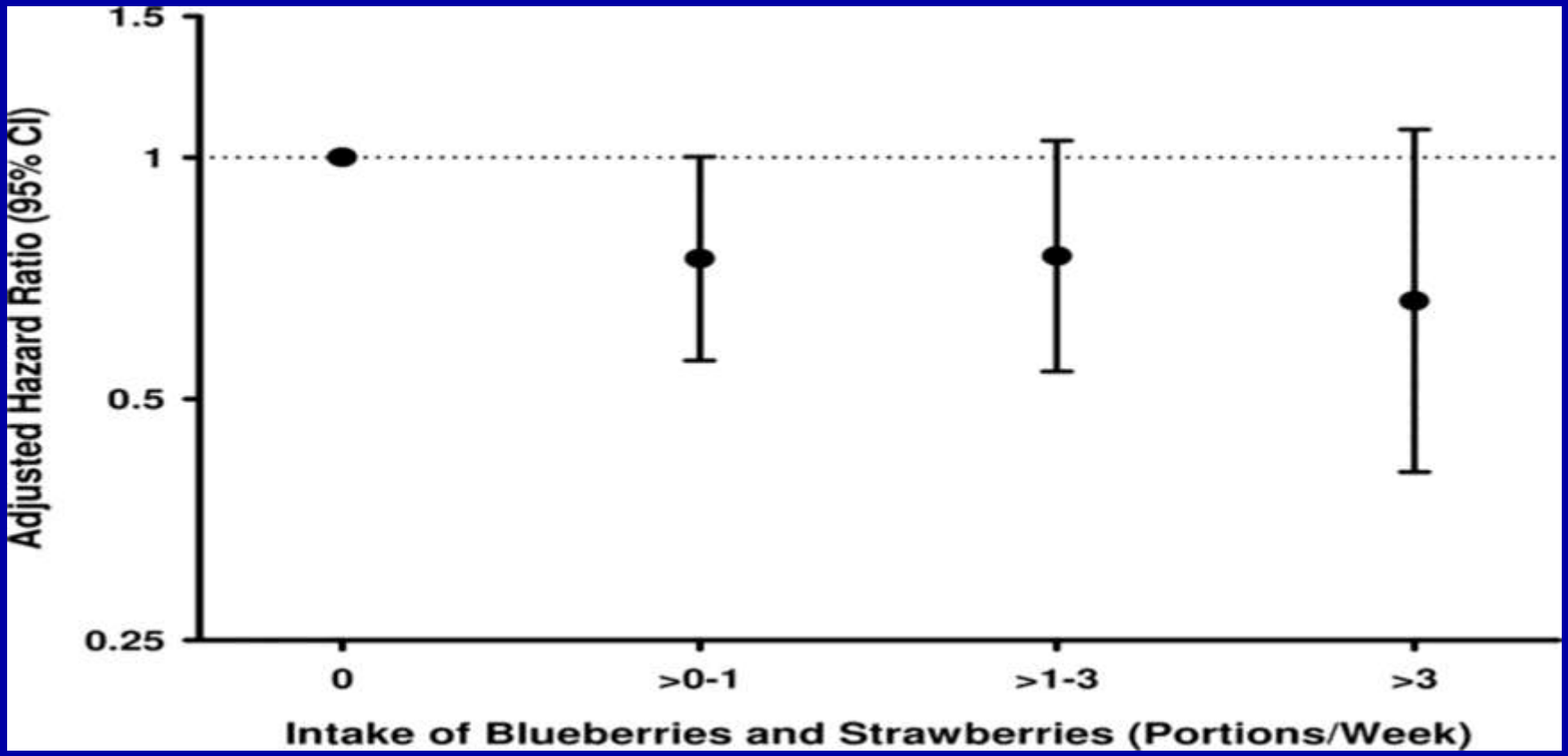
Intake of flavonoid subclasses was calculated from validated food-frequency questionnaires collected every 4 years using an updated and extended US Department of Agriculture database.

During 18 years of follow-up, 405 cases of MI were reported. An inverse association between higher intake of flavonoids and risk of MI was observed (hazard ratio, 0.68; 95% confidence interval, 0.49–0.96; *P*=0.03, highest versus lowest quintiles)

Combined intake of 2 flavonoid-rich foods, blueberries and strawberries (>3 servings per week), tended to be associated with a decreased risk of MI (hazard ratio, 0.66; 95% confidence interval, 0.40–1.08) in a comparison of those with lower intake.

Cassidy, A, Mukamal, K, et al. Circulation. Jan 16, 2013. 127:188-196

Dietary Flavonoids and reduced MI risk in young and middle-aged women.



Multivariate-adjusted relative risk of myocardial infarction according to combined intake of strawberries and blueberries in the Nurses' Health Study II. Model adjusted for age, physical activity, smoking, body mass index, alcohol, energy, menopausal status

Cassidy, A, Mukamal, K, et al. Circulation. Jan 16, 2013. 127:188-196

Dietary Flavonoids and reduced MI risk in young and middle-aged women.

Bale/Doneen Take-Away: Eat blueberries and strawberries at least 3 times per week and lower your heart attack risk!
Anthocyanin (flavonoid in these berries) – whole foods!

Cassidy, A, Mukamal, K, et al. Circulation. Jan 16, 2013. 127:188-196

Fructose and Glucose Ingestion Affect Appetite Pathways in the Brain Differently

Fructose (usually in the form of high-fructose corn syrup) is added to processed foods and beverages because it is more intensely sweet than glucose — and its consumption has risen dramatically in parallel with obesity.

Investigators recruited 20 normal-weight, healthy young adults to assess the effects of fructose versus glucose ingestion on cerebral blood flow as a proxy for neuronal activity (measured with functional magnetic resonance imaging [fMRI]) in areas associated with appetite control; levels of satiety hormones also were measured

Page KA et al. Effects of fructose vs glucose on regional cerebral blood flow in brain regions involved with appetite and reward pathways. JAMA 2013; 309:63

Fructose and Glucose Ingestion Affect Appetite Pathways in the Brain Differently

In two blinded sessions, participants consumed 75 g of either glucose or fructose (equivalent to two 12-oz beverages) after overnight fasts, then underwent fMRI and blood sampling.

Page KA et al. Effects of fructose vs glucose on regional cerebral blood flow in brain regions involved with appetite and reward pathways. JAMA 2013; 309:63

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Fructose and Glucose Ingestion Affect Appetite Pathways in the Brain Differently

Changes in blood flow in brain areas associated with hunger and reward (i.e., hypothalamus, thalamus, insula, cingulate cortex, fusiform gyrus, and striatum) differed significantly, depending on whether glucose or fructose had been ingested.

Complex fMRI analyses suggested that these differences in blood flow delineated areas that preferentially promote glucose-induced satiety.

Compared with glucose, fructose was associated with lower peak levels of hormones associated with satiety (e.g., insulin, glucagon-like polypeptide 1).

Page KA et al. Effects of fructose vs glucose on regional cerebral blood flow in brain regions involved with appetite and reward pathways. JAMA 2013 309:63

Heme Iron Intake and Stroke Risk.

Two forms of dietary iron: heme and non-heme.
Heme iron is derived from hemoglobin (animal source)
Non-Heme Iron does not come from an animal source.

	Heme iron	Non-heme iron
What is it?	Heme iron is found in foods that contained hemoglobin – animal foods including red meats, fish and poultry.	Non-heme iron is the form of iron found in all other, non-meat based foods.
Iron sources in food	A serving of chicken livers, clams, or roasted beef tenderloin contains all the iron you need for a day.	Non-heme iron can be found in vegetables, grains, iron-fortified breakfast cereal, lentils and beans.
Iron absorption	One of the biggest benefits is that heme iron is absorbed better than non-heme iron, and its absorption isn't affected by anything else you eat. We absorb approximately 15-35% of the heme iron we eat, which is a lot!	Non-heme iron is not absorbed by the body as well as heme iron. Only 2 - 20% of non-heme iron is absorbed.

Heme Iron Intake and Stroke Risk.

Prospective Cohort of Swedish Men included 38 859 men, aged 45 to 79 years, no history of stroke, coronary heart disease, or cancer at baseline.

Results— 11.7 years follow-up, 3097 incident cases of stroke,

The association was confined to men with BMI <25
Total Stroke: HR 1.40 (95% CI, 1.17–1.68; *P* trend<0.001)
Cerebral Infarct: HR 1.38 (95% CI, 1.13–1.70; *P* trend=0.001)

Conclusions—Findings from this prospective study indicate that a high heme iron intake, particularly in normal weight individuals, may increase the risk of stroke

Kaluza, J., Wolk, A., et al. Heme Iron Intake and Risk of Stroke: A Prospective Study of Men. Stroke. January 10, 2013.

Heme Iron Intake and Stroke Risk.

Men in the highest quintile of heme iron intake consumed 2.6-times more red meat than those in the lowest quintile (149±79 versus 58±29 g/d),

The potential adverse effect of heme iron may be attributed to its pro-oxidative properties. It catalyzes the conversion of superoxide and hydrogen peroxide into hydroxyl radicals in the Fenton reaction.

There is evidence that increased iron accumulation in endothelial cell in the brain can contribute to stroke progression and worse prognosis among patients.

Kaluza, J., Wolk, A., et al. Heme Iron Intake and Risk of Stroke: A Prospective Study of Men. Stroke. January 10, 2013.

Heme Iron Intake and Stroke Risk.

	Heme Iron Milligrams per serving	% DV*
Chicken liver, pan-fried, 3 ounces	11.0	61
Oysters, canned, 3 ounces	5.7	32
Beef liver, pan-fried, 3 ounces	5.2	29
Beef, chuck, blade roast, lean only, braised, 3 ounces	3.1	17
Turkey, dark meat, roasted, 3 ounces	2.0	11
Beef, ground, 85% lean, patty, broiled, 3 ounces	2.2	12
Beef, top sirloin, steak, lean only, broiled, 3 ounces	1.6	9
Tuna, light, canned in water, 3 ounces	1.3	7

National Institute of Health. Taken from On-line source 2.6.2013

Heme Iron Intake and Stroke Risk.

Bale/Doneen Take-Away:

Red meat is highly correlated with heme iron intake.

Watch F2-isoprostane levels and consider the possibility that heme iron may be a factor for stroke risk!

No “magic” level of acceptable amount of heme-iron intake was offered in the trial but statistical sign risk started at 1.46 mg/day of Heme Iron intake.

Kaluza, J., Wolk, A., et al. Heme Iron Intake and Risk of Stroke: A Prospective Study of Men. Stroke. January 10, 2013.

Ramipril improves PAD

212 patients with PAD. Randomized, double-blind, placebo-controlled trial. mean age, 65.5 [SD, 6.2] years.

Intervention Randomized to receive 10 mg/d of ramipril (n=106) or matching placebo (n=106) for 24 weeks.

Main Outcome Measures Maximum and pain-free walking times were recorded during a standard treadmill test.

The Walking Impairment Questionnaire (WIQ) – assess walking

Short-Form 36 Health Survey (SF-36) –assess quality of life

Why? 27 million people in Europe and North America with PAD and 1/3 with intermittent claudication (pain with walking and relieved with rest).

Only 2 drugs currently approved by the FDA to improve walking distance– pentoxifylline and cilostazol – increase walking distance by 15%-25% respectively.

Ahimastos, A., Walker, P., et al. JAMA, 2.6.2013. Vol 309, Nol. 5 453-460

Table 2. Primary and Secondary Outcome Measures of the Study Population[a]

Outcome Measure	No. of Participants	Value		Mean (95% CI)[b]		*P* Value[c]
		Baseline	6 mo	Within-Group Changes	Between-Group Difference	
Primary outcome measures, mean (SD)						
PFWT, s						
Placebo	106	142 (54)	156 (57)	14 (6 to 21)	75 (60 to 89)	<.001
Ramipril	106	140 (61)	229 (85)	88 (76 to 101)		
MWT, s						
Placebo	106	238 (71)	259 (80)	23 (13 to 36)	255 (215 to 295)	<.001
Ramipril	106	234 (91)	512 (235)	277 (238 to 316)		
Secondary outcome measures, limiting-leg ABI, mean (SD)						
At rest						
Placebo	106	0.55 (0.14)	0.54 (0.16)	0.00 (−0.02 to 0.02)	0.10 (0.08 to 0.13)	<.001
Ramipril	106	0.57 (0.14)	0.64 (0.13)	0.08 (0.06 to 0.09)		
Following exercise						
Placebo	106	0.43 (0.12)	0.42 (0.16)	0.00 (−0.03 to 0.18)	0.11 (0.08 to 0.14)	<.001
Ramipril	106	0.45 (0.14)	0.52 (0.14)	0.07 (0.05 to 0.09)		
WIQ scores, median (IQR)[d]						
Distance score						
Placebo	106	6.1 (2.7 to 11.2)	4.7 (2.3 to 7.4)	−1.1 (−4.2 to 0.0)	13.8 (12.2 to 15.5)	<.001[e]
Ramipril	106	6.3 (3.9 to 19.7)	16.9 (13.4 to 31.8)	9.9 (8.3 to 12.1)		
Speed						
Placebo	106	10.9 (6.5 to 17.4)	6.9 (3.3 to 10.9)	−3.3 (−4.0 to 0.0)	13.3 (11.9 to 15.2)	<.001[e]
Ramipril	106	7.6 (6.5 to 14.4)	20.1 (15.2 to 30.2)	10.9 (7.6 to 12.0)		
Stair climbing						
Placebo	106	16.8 (15.3 to 38.7)	16.7 (12.6 to 21.0)	−4.2 (−8.4 to 0.0)	25.2 (25.1 to 29.4)	<.001[e]
Ramipril	106	16.8 (15.7 to 37.8)	41.9 (31.0 to 67.1)	20.9 (16.8 to 25.2)		
SF-36 scores, median (IQR)[f]						
Physical Component Summary						
Placebo	106	31.4 (30.9 to 32.7)	32.5 (31.8 to 33.0)	0.2 (−0.4 to 1.8)	8.2 (3.6 to 11.4)	.02[e]
Ramipril	106	32.3 (30.4 to 33.1)	41.4 (32.8 to 48.6)	6.3 (0.0 to 19.0)		
Mental Component Summary						
Placebo	106	47.8 (34.7 to 64.3)	48.5 (33.2 to 66.8)	0.1 (−0.5 to 0.3)	0.5 (−0.7 to 1.1)	.74[e]
Ramipril	106	44.1 (33.7 to 62.2)	49.2 (35.1 to 62.5)	1.8 (0.0 to 3.9)		
Volume flow, limiting-leg ABI, mL/min						

Ramipril and PAD

Results (compared to placebo at 6 months) Ramipril was associated with:

1. 75-second (95% CI, 60-89 seconds) increase in mean pain-free walking time (*P*.001)
2. 4.25 min (95% CI, 215-295 seconds) increase in maximum walking time (*P*.001).
3. Improved speed score, median distance score, stair climbing, physical component summary score (p = 0.001 for all)

Conclusions and Relevance

Among patients with intermittent claudication, 24-week treatment with ramipril resulted in significant increases in pain-free and maximum treadmill walking times compared with placebo.

This was associated with a significant increase in the physical functioning.

Ahimastos, A., Walker, P., et al. JAMA, 2.6.2013. Vol 309, Nol. 5 453-460

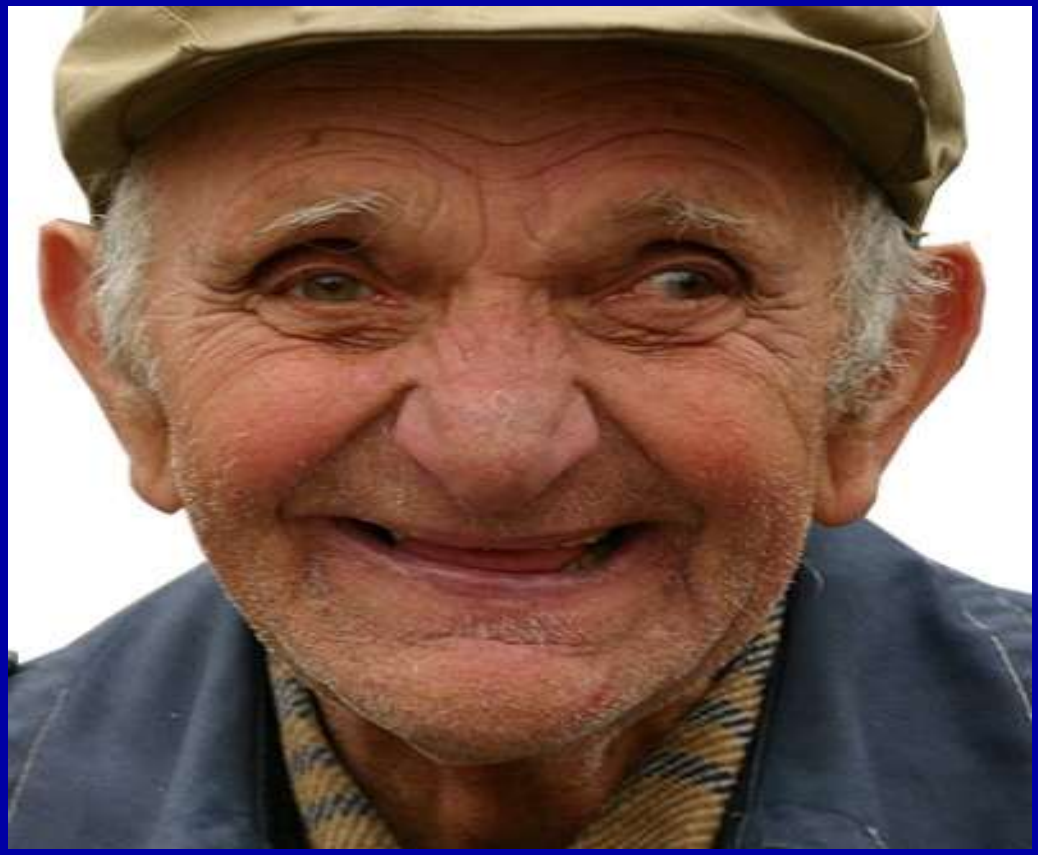
Ramipril and PAD

Bale/Doneen Take-Away:

Ramipril has long been in our tool kit for endothelial health, BP benefit, stroke and heart attack benefit – HOPE trial. Always remember, we are treating systemic vascular disease and this is one more illustration that our selection of medication does have systemic merit. Ramipril is the superior ACE and first line therapy for anyone with atherosclerosis.

Ahimastos, A., Walker, P., et al. JAMA, 2.6.2013. Vol 309, Nol. 5 453-460

Case:



Email: Hi Amy! Happy New Year!
I wanted to update you on the patient we discussed before the holiday. The energetic 80 yo gentleman with a h/o CAD and stenting in 2010 who was experiencing new SOB on his uphill walks that time correlated to a tooth abscess developing the last couple months. So… his cardiologist agreed to do a Stress test that although it was read as "normal" did have some inhomogeneity in the apical perfusion just not enough to call a perfusion defect.

His Vascular inflammation markers are as follows: HD troponin 4.6, NT-proBNP 336, Lp-PLA2 270 H, hs-CRP 1.9.
He is on Lisinopril, Omega 3s, ASA and Crestor +CoQ10.

Do you think I can allow him to proceed with the dental extraction and add Niaspan? Or should I try to get him Niaspan and get the Plac2 down first? I hate to have him harboring the abscess but I'm not sure if extracting the tooth may push him over the inflammation edge!
Thanks so much for you assistance with this tricky case :)

Phone call from me: Work first of artery wall stability and Make sure correct treatment for tooth infection.

E-mail response:
He has had complete improvement of the tooth pain on Clindamycin but has finished the course now. His statin is Crestor, I think 10 mg.

Plan: discussed: Niaspan: had previous CK – willing to try again but cautious. Willing to go to 15-20 mg Crestor and tolerates well. Recheck labs in 2 weeks BEFORE proceeding with the extraction. I can re-check PLAC2 but don't have a lab source for MPO here.

2/4/2013: Hi Amy,

Just wanted to give you f/u on our 80 yo gentleman with the dental abscess, exertional SOB and plac2 of 270……

Crestor at 20mg did the trick. Plac2 is now 180! And SOB symptoms are gone. So, I'll have him get the tooth extracted now then he needs a ventral hernia repaired and minor foot surgery. After all of those are done, I expect I can drop the Crestor back down to 10mg and maybe check the markers again a month after that change and perhaps again 3 mo after that if all stays well?