You Don't Look a Day Over 50 – *Do Your Arteries?*

Using Ultrasound to Evaluate Arterial Age

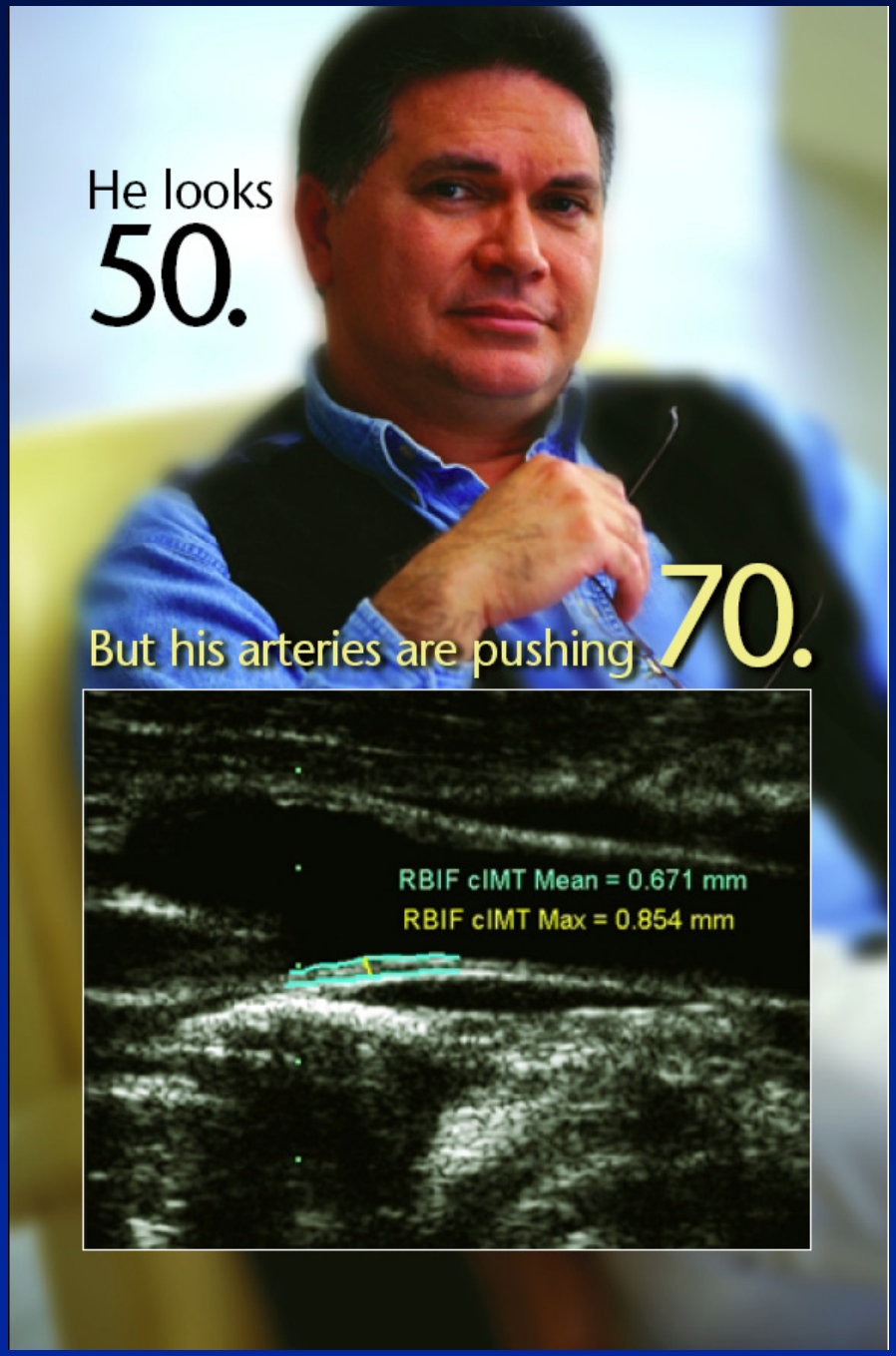
James H. Stein, M.D.

Professor of Medicine, Cardiovascular Medicine Division
UW School of Medicine and Public Health
Director, Preventive Cardiology
UW Health Heart and Vascular Care

UW Health
University of Wisconsin
Heart and Vascular Care

Conflict of Interest Disclaimer

- Research grants
  - Siemens Medical Solutions
  - Sonosite
- Intellectual property royalties
  - WARF (carotid US and CVD risk prediction)


He looks
50.
But his arteries are pushing 70.
RBIF cIMT Mean = 0.671 mm
RBIF cIMT Max = 0.854 mm

Cardiovascular (CV) Disease
The Problem in the United States

- Each year, approximately 1.2 million Americans have a heart attack – 1/3 die
- Every day, nearly 1800 Americans die of CV disease

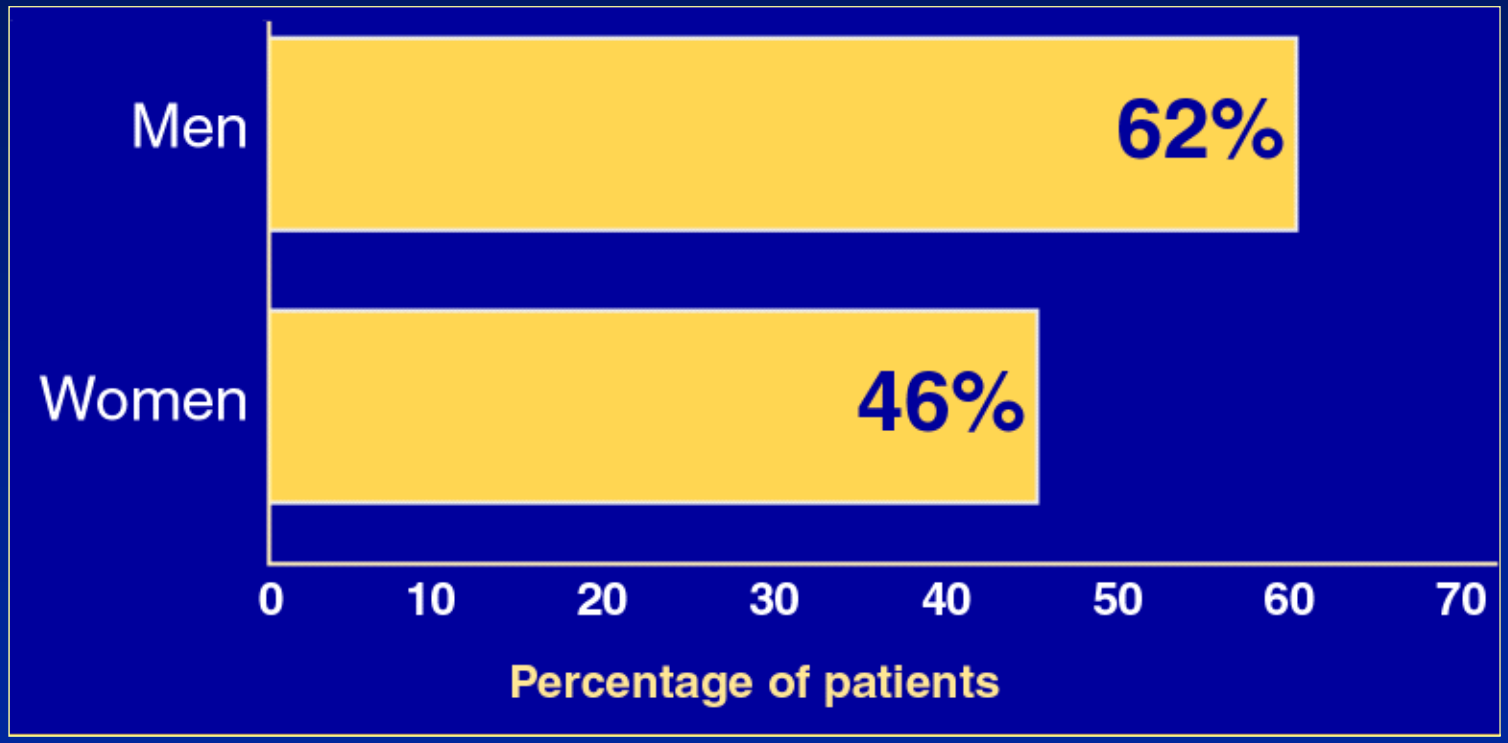
= 1 heart attack every 20 seconds

= 1 death every 48 seconds

AHA Heart and Stroke Facts, 2006

The Diagnosis of Heart Disease Frequently Comes Too Late …

First Symptom* of Heart Disease is *Heart Attack or Death



Levy D, et al . Textbook of Cardiovascular Medicine, 1998, Topol EJ (ed.)

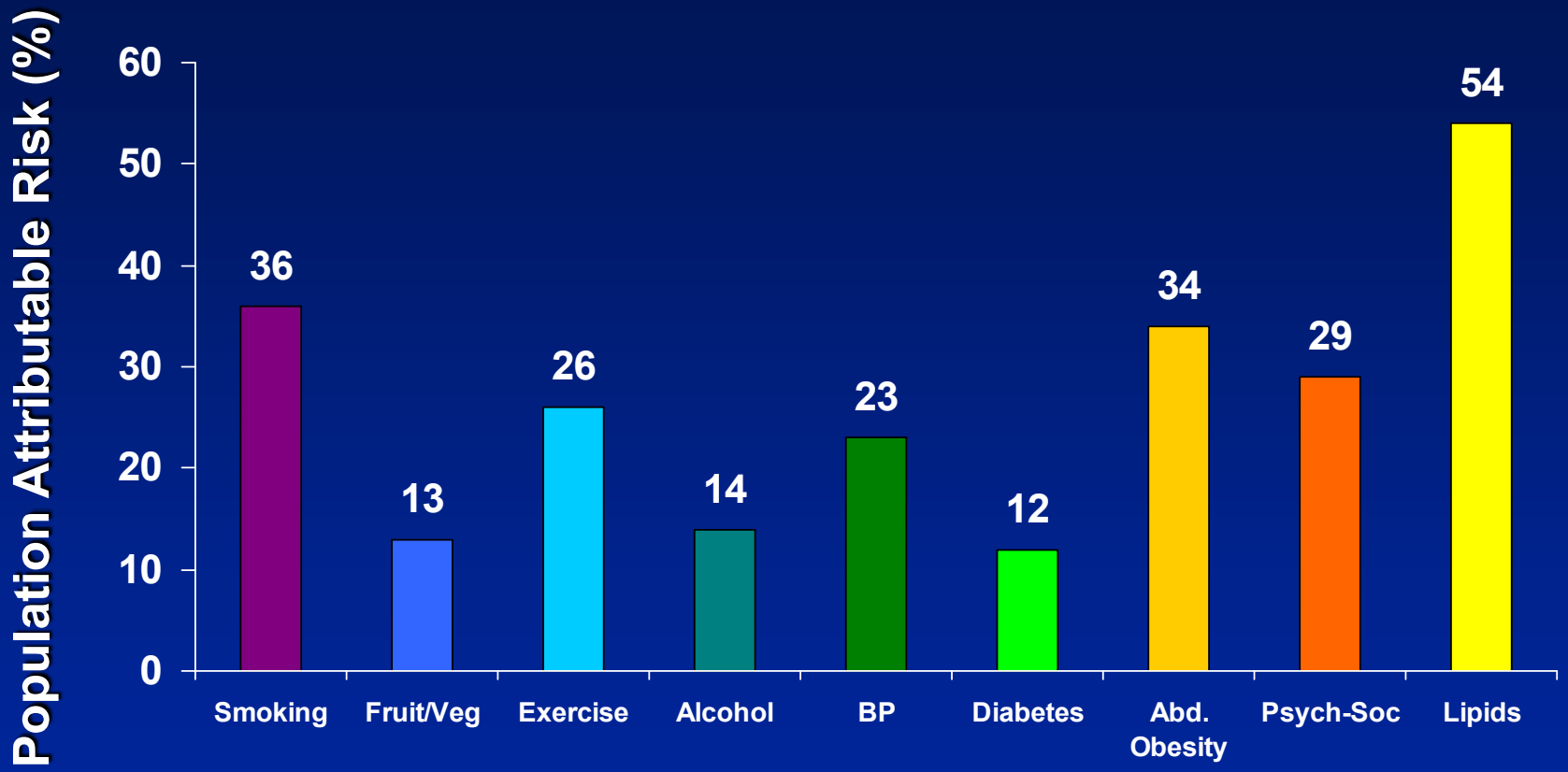
How Do We Determine Who is at Risk?

- Risk factors
- Treadmill stress testing
- Newer tests

Major Risk Factors for CV Disease

- Non-modifiable
  - Aging
  - Gender
  - Family history
- Modifiable
  - High cholesterol
  - High blood pressure
  - Cigarette smoking
  - Diabetes mellitus
  - Adverse lifestyle habits

INTERHEART
Risk of Heart Attack



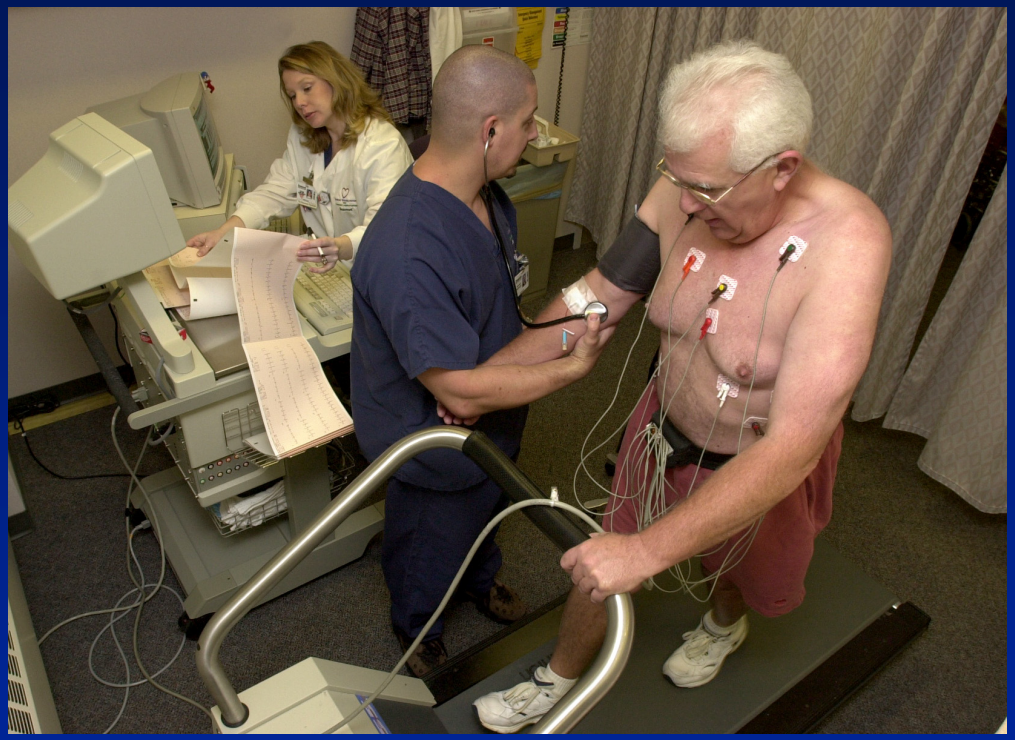
- All risk factors = 90%
- All lifestyle = 63%

Yusuf S, et al. Lancet 2004;364:937

So What's The Problem?

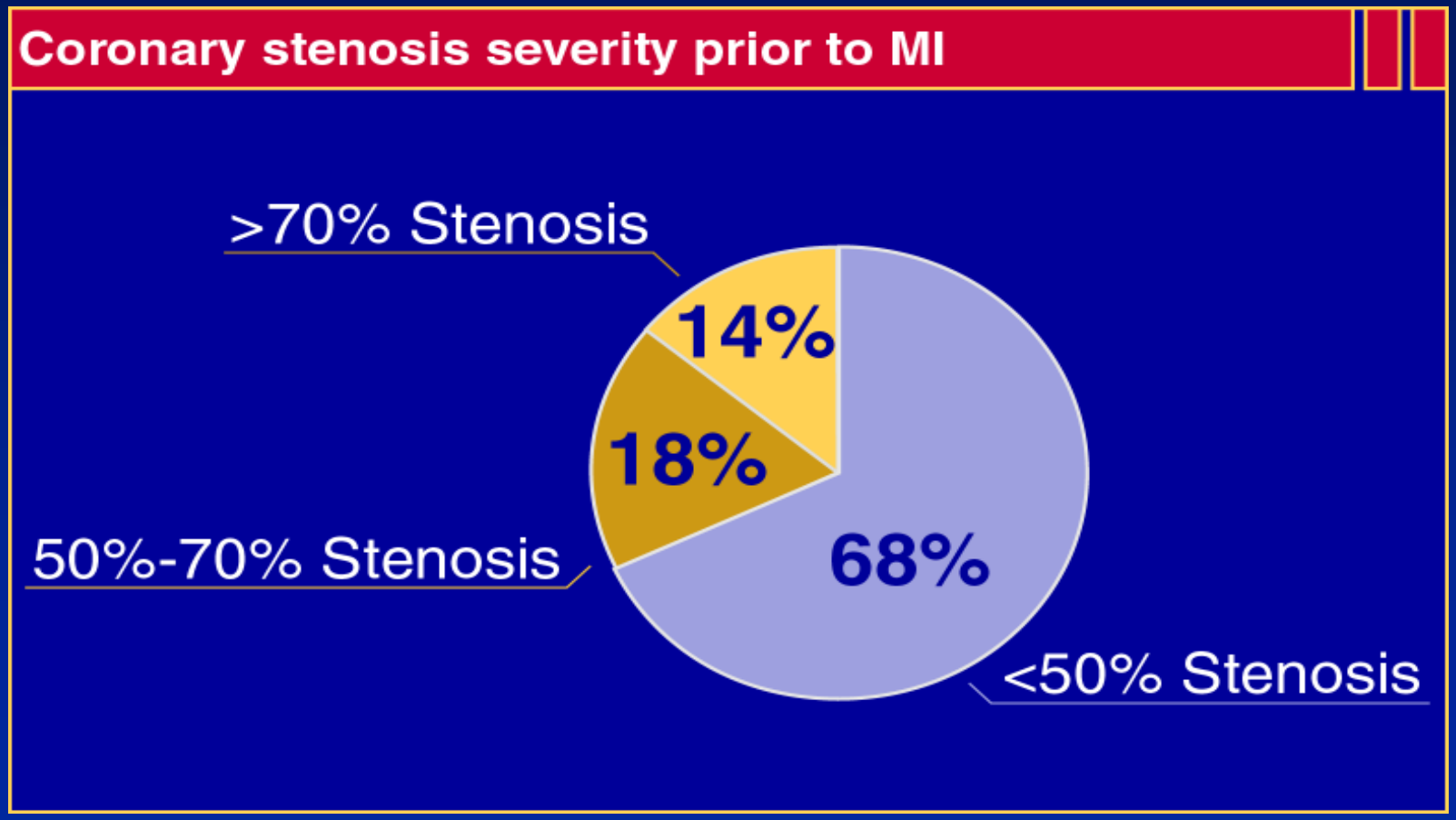
- Risk factors accurately predict risk in *populations*, but may not be adequate in *individuals*
- At every level of risk factor exposure, substantial variation in degree of atherosclerosis
  - Genetic susceptibility (*e.g.* family history)
  - Lifestyle habits
  - Duration of exposure

Treadmill Stress Testing



"But She Just Passed A Stress Test!"

Most Heart Attacks are Caused by Minor Blockages



Adapted from Falk E, et al. Circulation, 1995

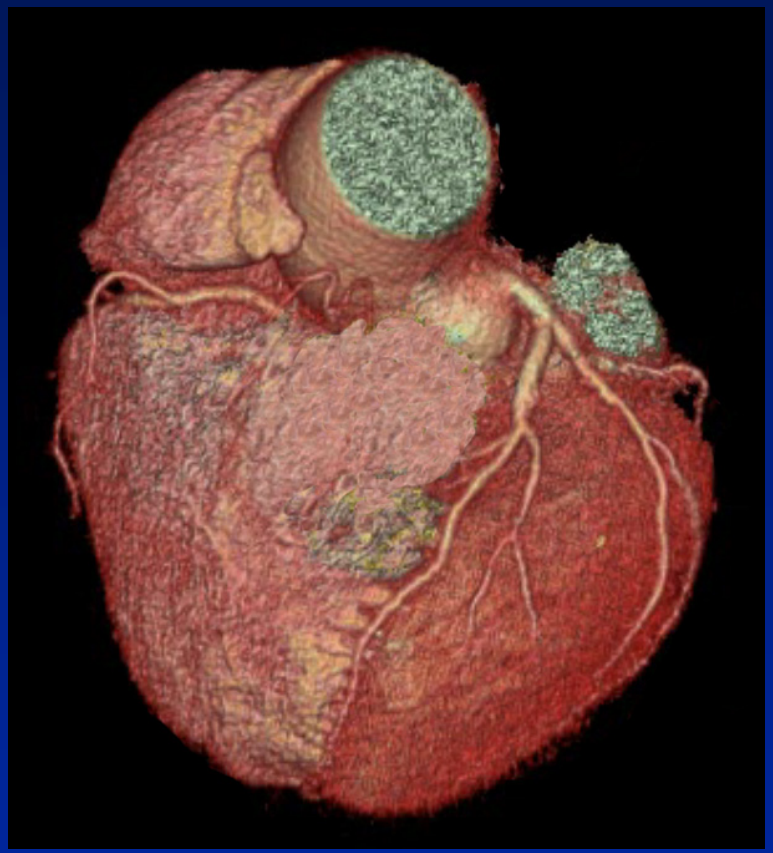
The Plumbing Problem

Stress Testing Doesn't Identify Minor Blockages

Transition to a Heart Attack

The Challenge: How Can We Safely Look Into Your Arteries?

CT Angiography



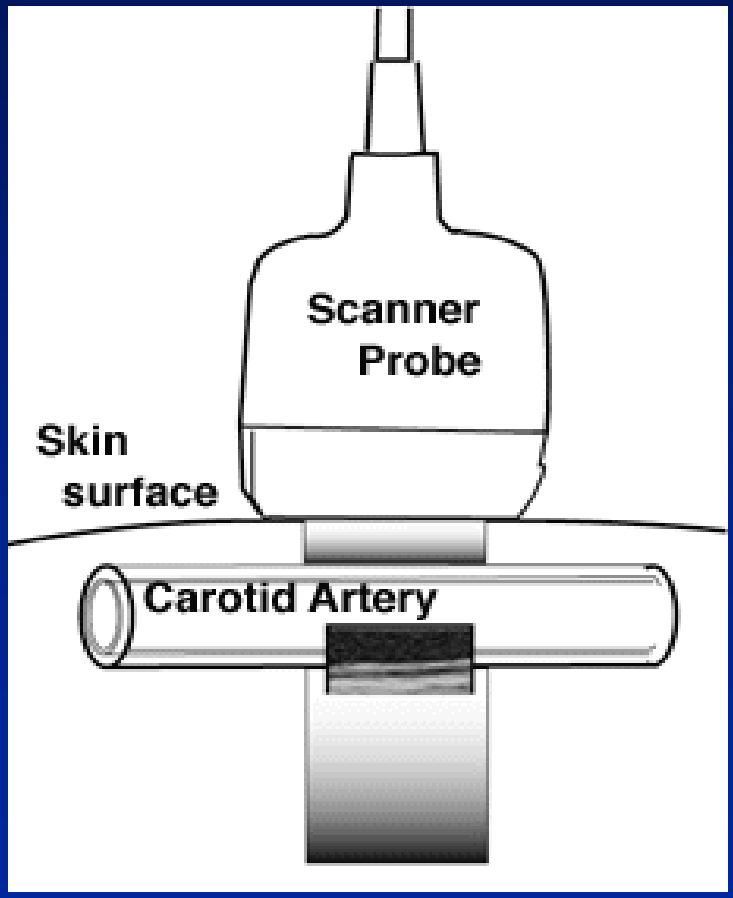
Diagnostic test for people with chest pain - <u>Not a screening test</u>

The Solution: Look at the Carotid Arteries

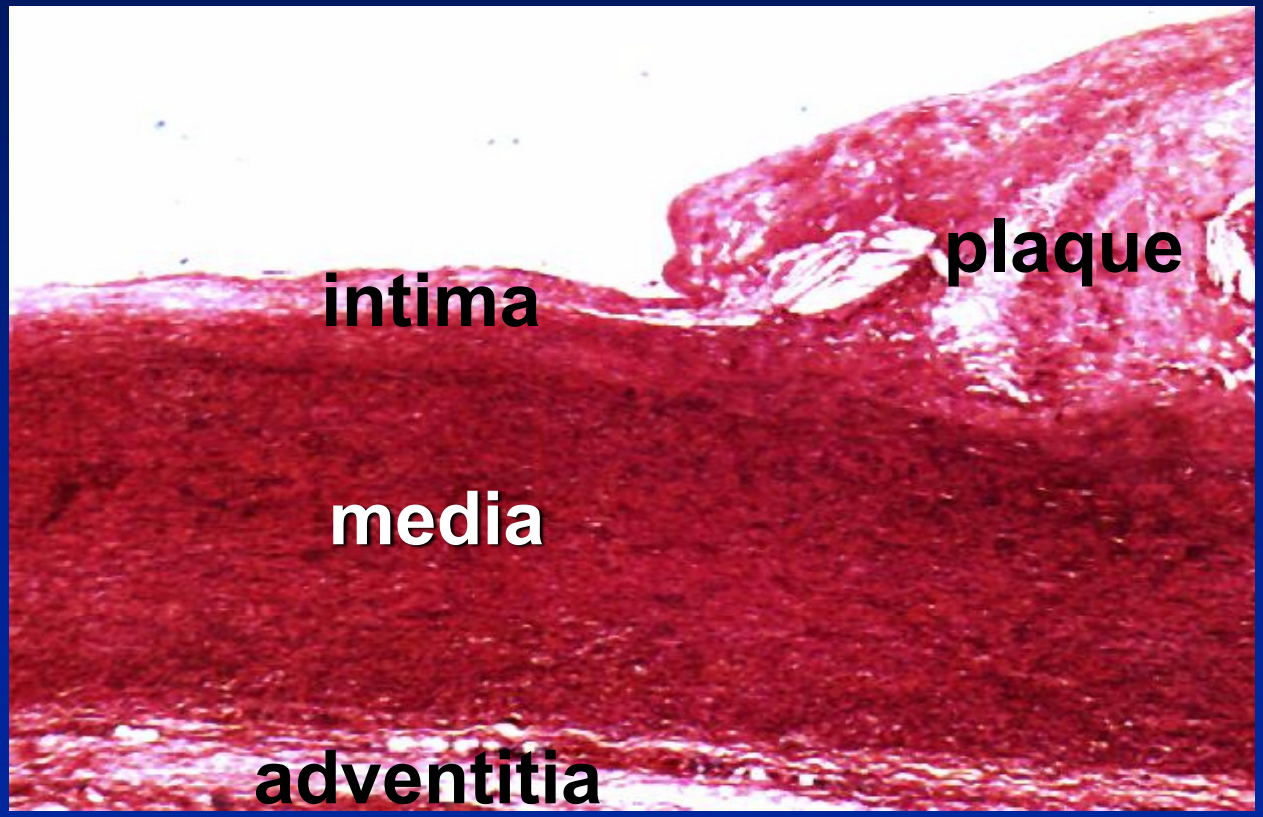
- Carotid arteries are a "window" to the coronary arteries
- Same risk factors
- Atherosclerosis of the carotid and coronary arteries ≅ any two coronary arteries

Young W, et al. Am J Cardiol 1960;6:300
Chambers BR, et al. N Engl J Med 1986;315:860
Chimowitz MI, et al. Stroke 1994;25:759

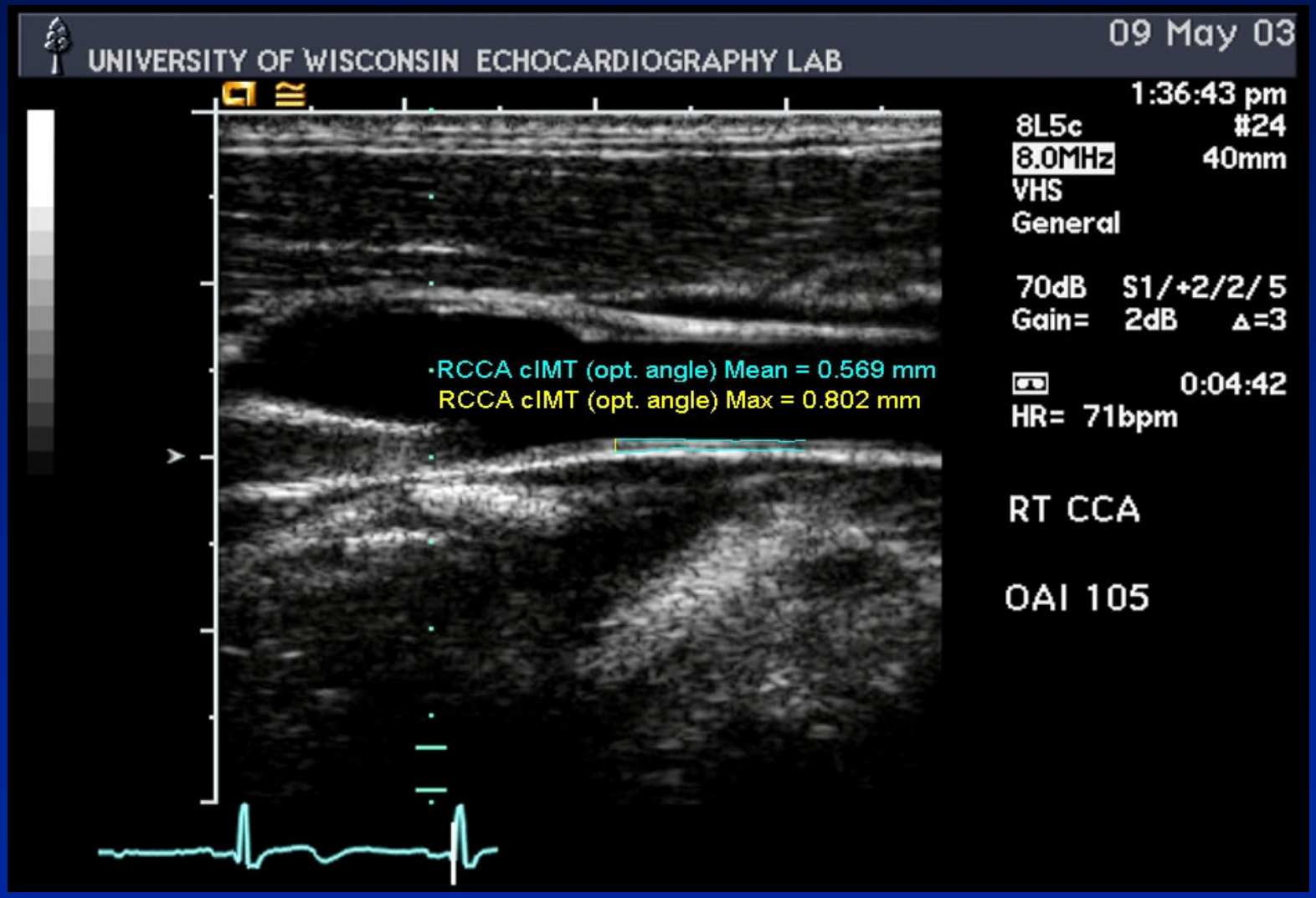
The Technique: Carotid Ultrasound



A Solution: Ultrasound Assessment of Carotid Intima-Media Thickness (IMT)

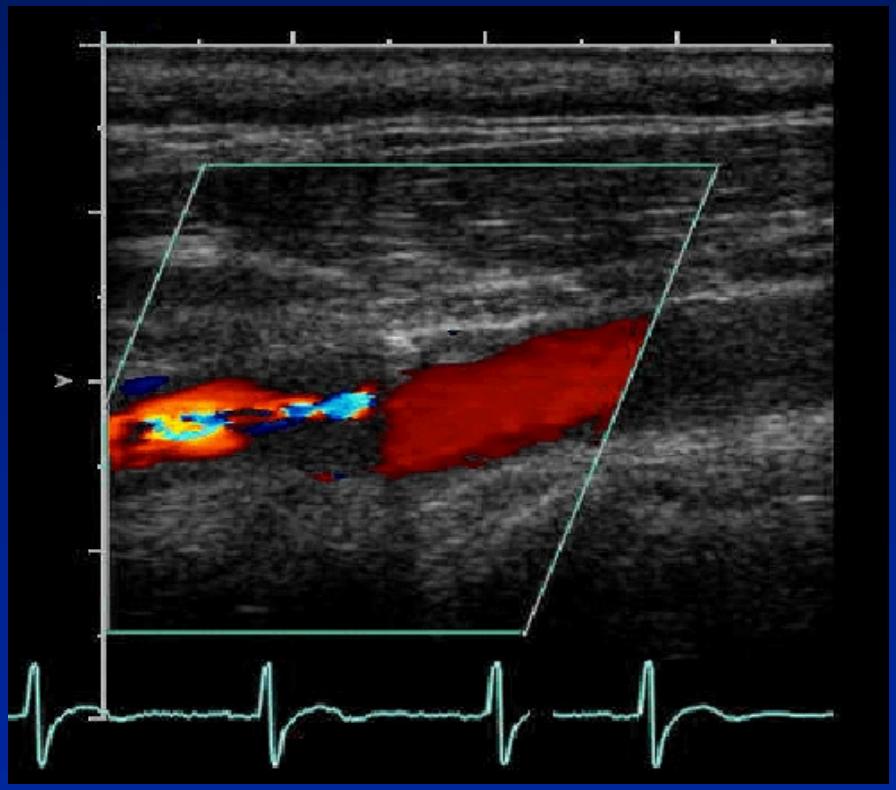


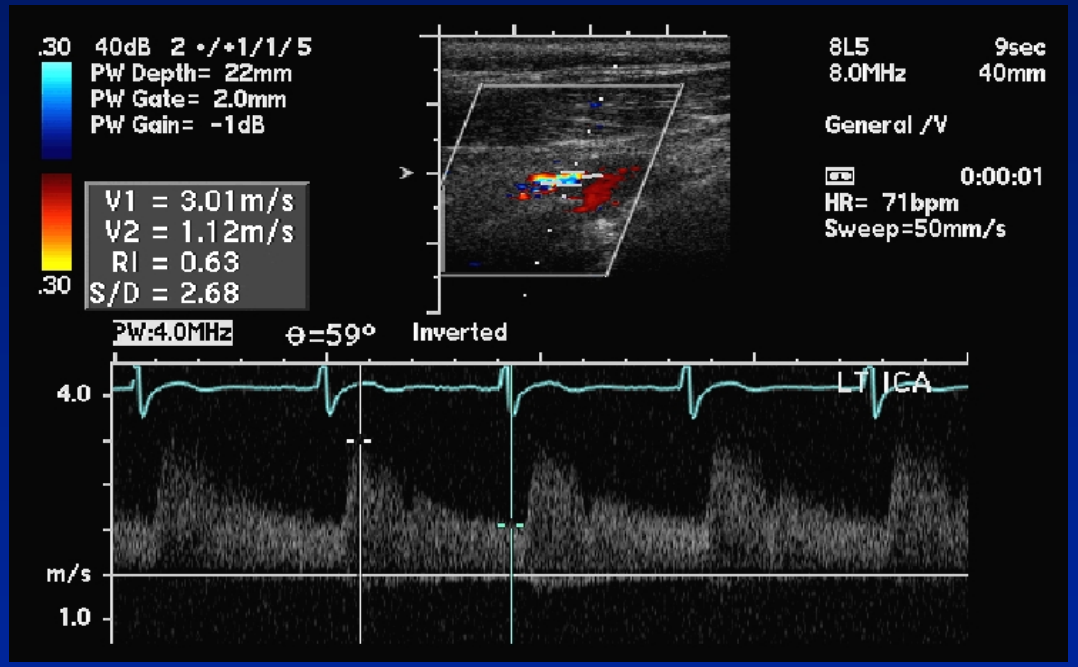
Measurement of Carotid IMT



Carotid Ultrasound: Window To The Heart

Carotid Artery Duplex Ultrasound

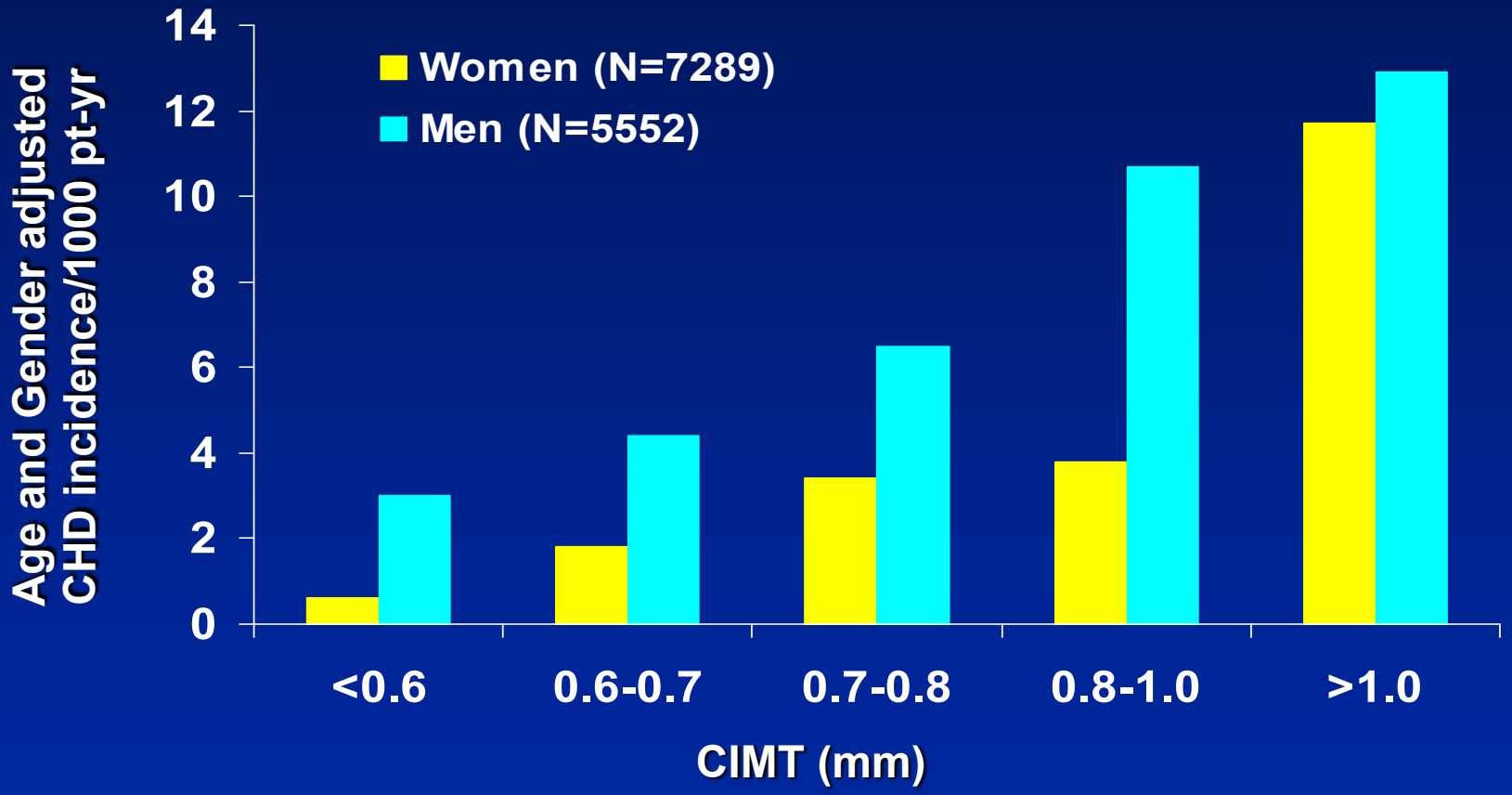




Advantages of Carotid Ultrasound as a Risk Prediction Tool

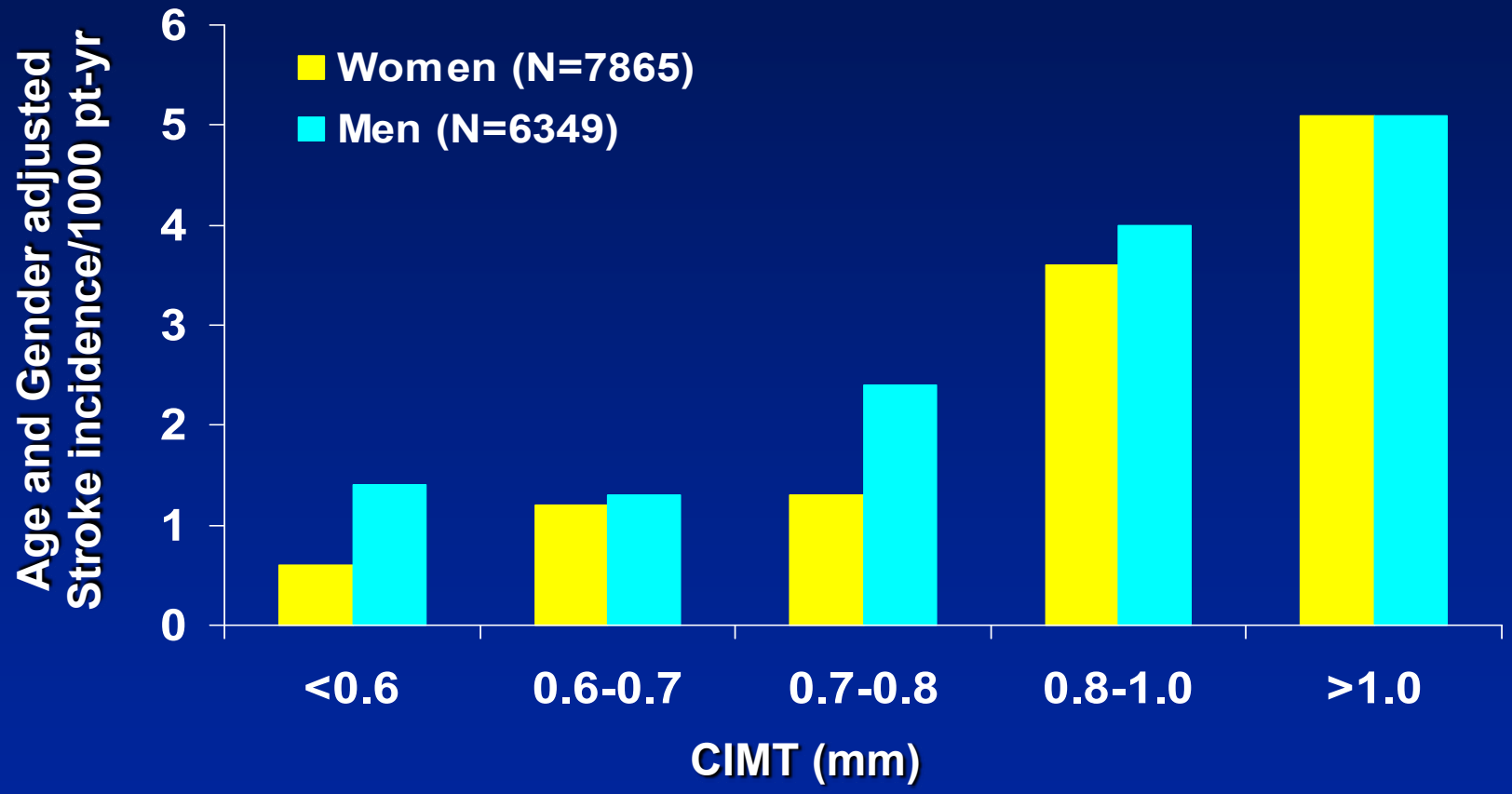
- Completely noninvasive – no radiation, no harmful exposures, no known biological effects
- Identifies range of disease – increased CIMT, non-occlusive plaque, stenosis
- Predicts future heart attacks, death from heart disease, and stroke, with incremental predictive power
- Track serial changes
- Recommended by NCEP, AHA, ACC, ASE, SVM, and ESC to assist with CVD risk assessment

Carotid IMT Predicts Heart Attacks and Death from Heart Disease



Chambless LE, et al. Am J Epidemiol 1997;146:483

Carotid IMT Predicts Future Strokes



Chambless LE, et al. Am J Epidemiol 2000;151:478

ASE CONSENSUS STATEMENT

Use of Carotid Ultrasound to Identify Subclinical Vascular Disease and Evaluate Cardiovascular Disease Risk: A Consensus Statement from the American Society of Echocardiography Carotid Intima-Media Thickness Task Force

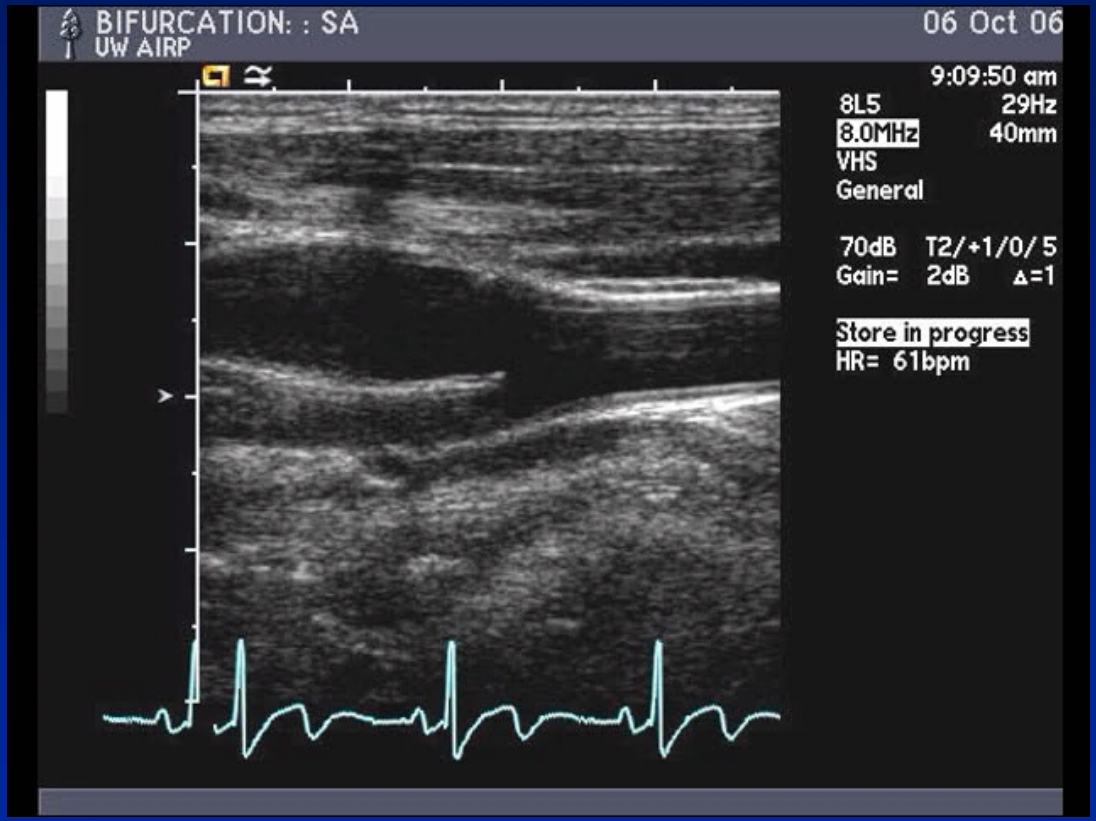
Endorsed by the Society for Vascular Medicine

James H. Stein, MD, FASE, Claudia E. Korcarz, DVM, RDCS, FASE, R. Todd Hurst, MD, Eva Lonn MD, MSc, FASE, Christopher B. Kendall, BS, RDCS, Emile R. Mohler, MD, Samer S. Najjar, MD, Christopher M. Rembold, MD, and Wendy S. Post, MD, MS,

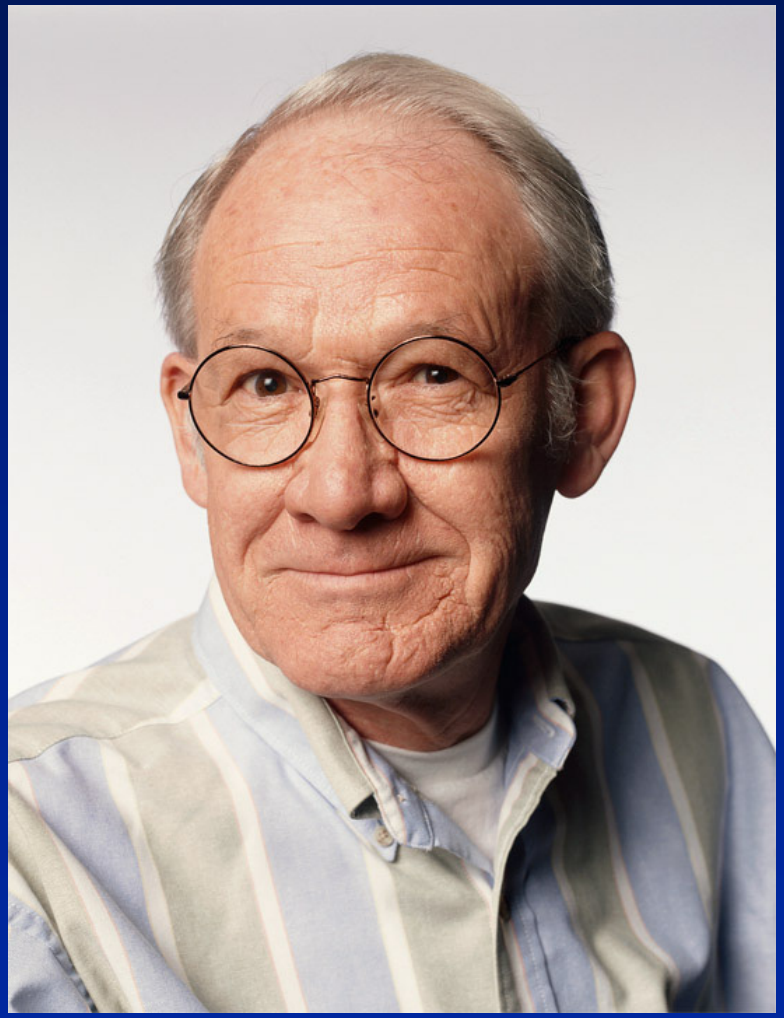
Madison, Wisconsin; Scottsdale, Arizona; Hamilton, Ontario, Canada; Philadelphia, Pennsylvania; Baltimore, Maryland; and Charlottesville, Virginia

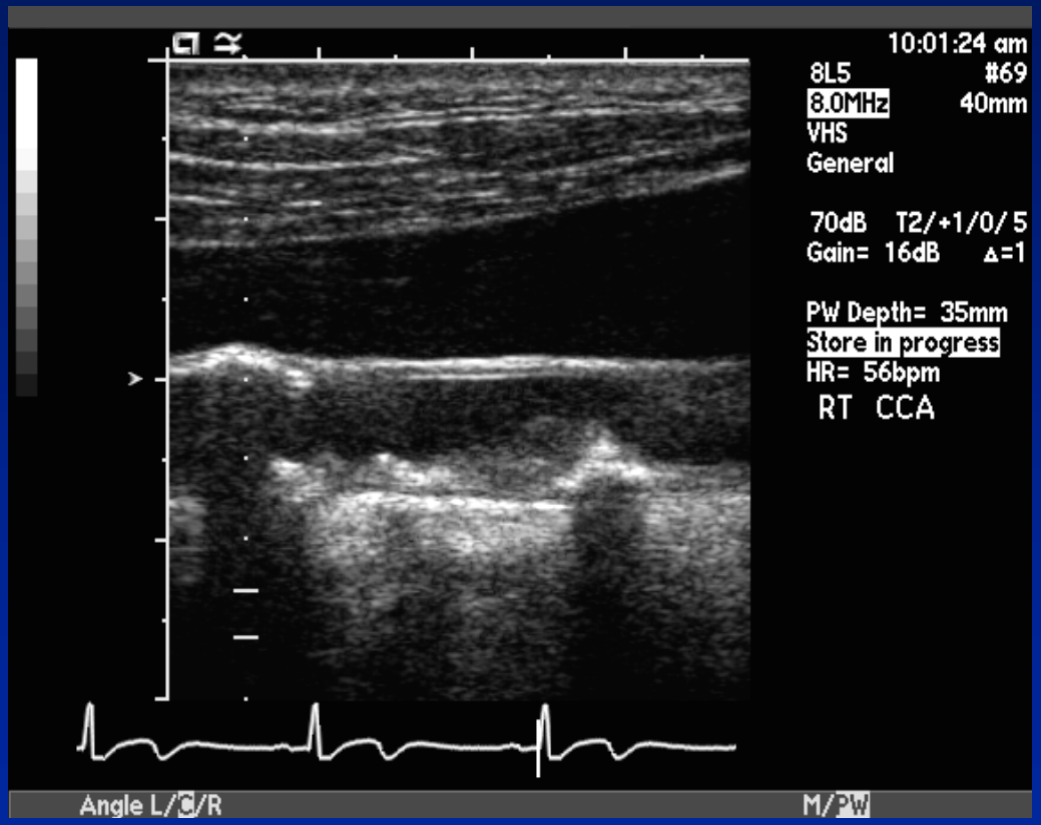
Stein JH, et al. J Am Soc Echocardiogr 2008;21:93

Determination of “Vascular Age”

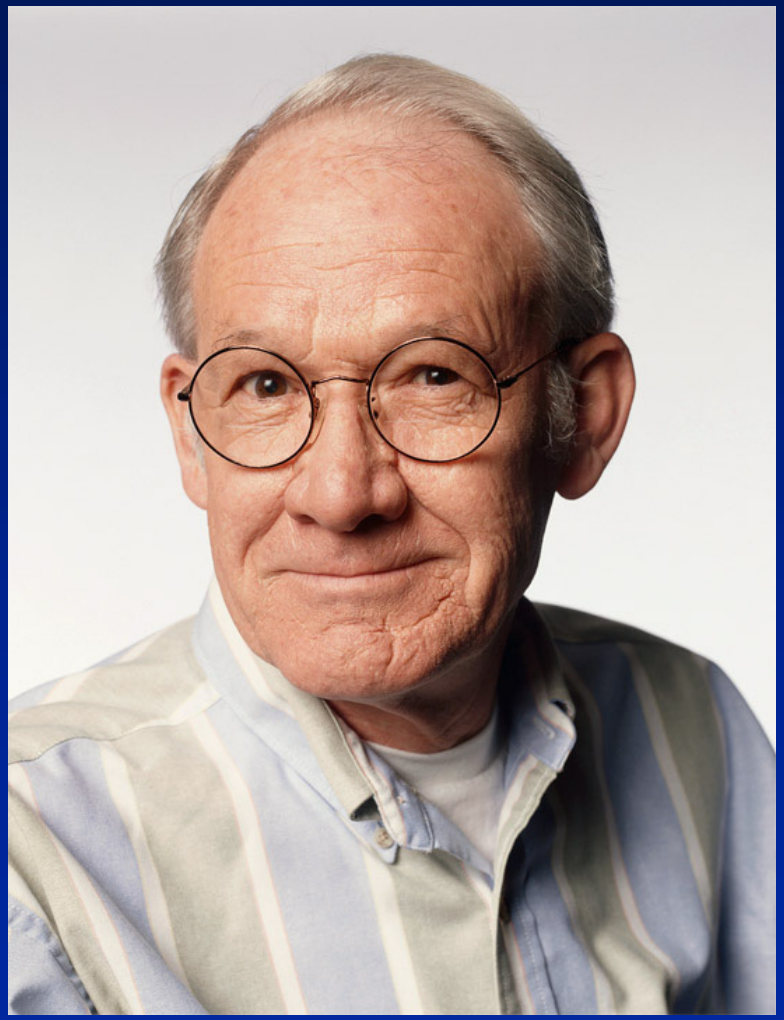


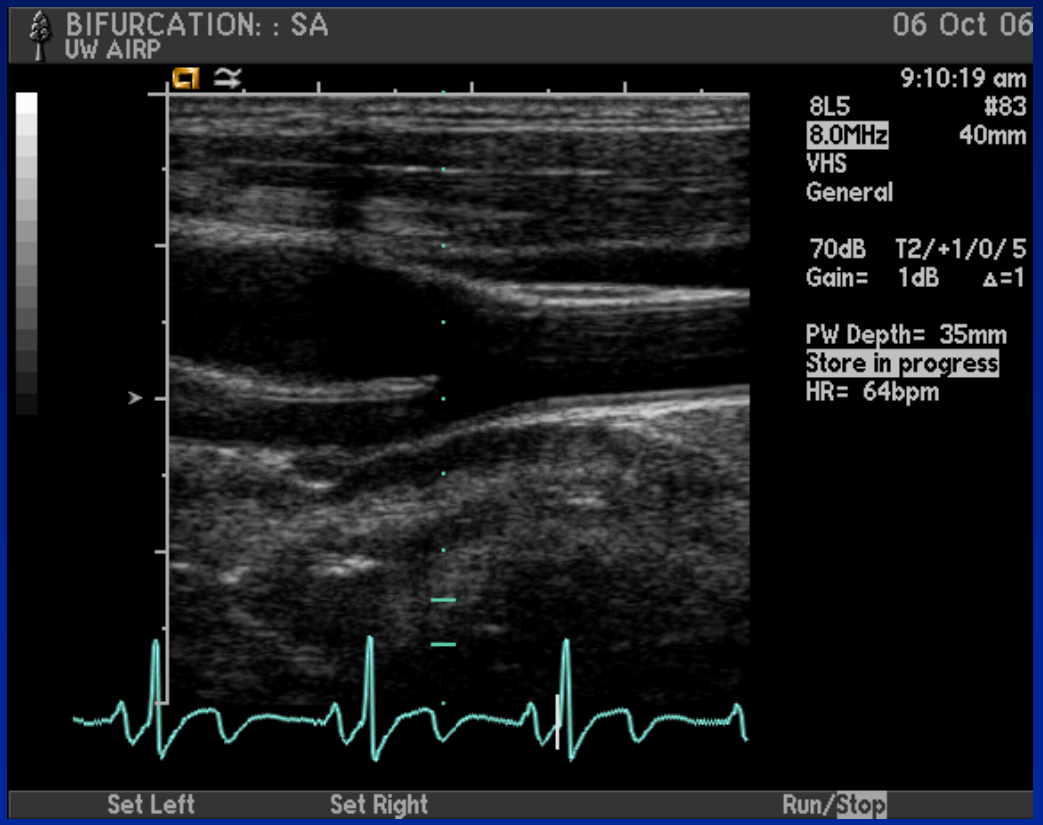
Determination of “Vascular Age”



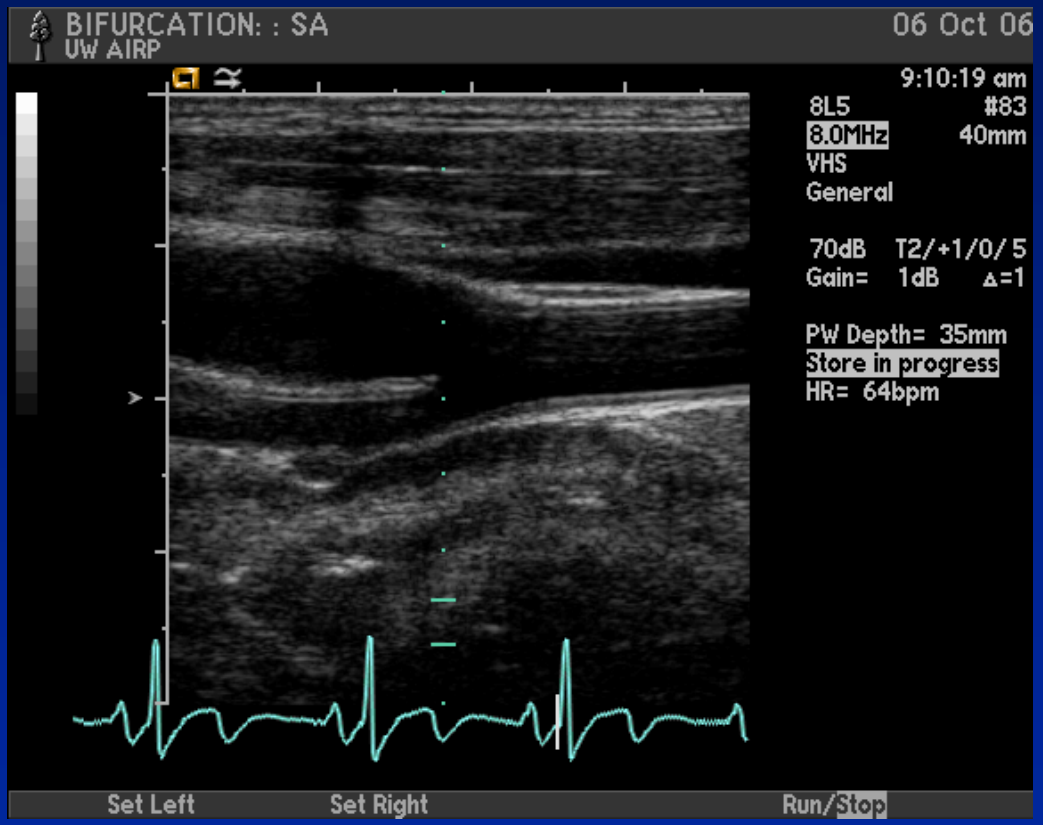


Determination of “Vascular Age”



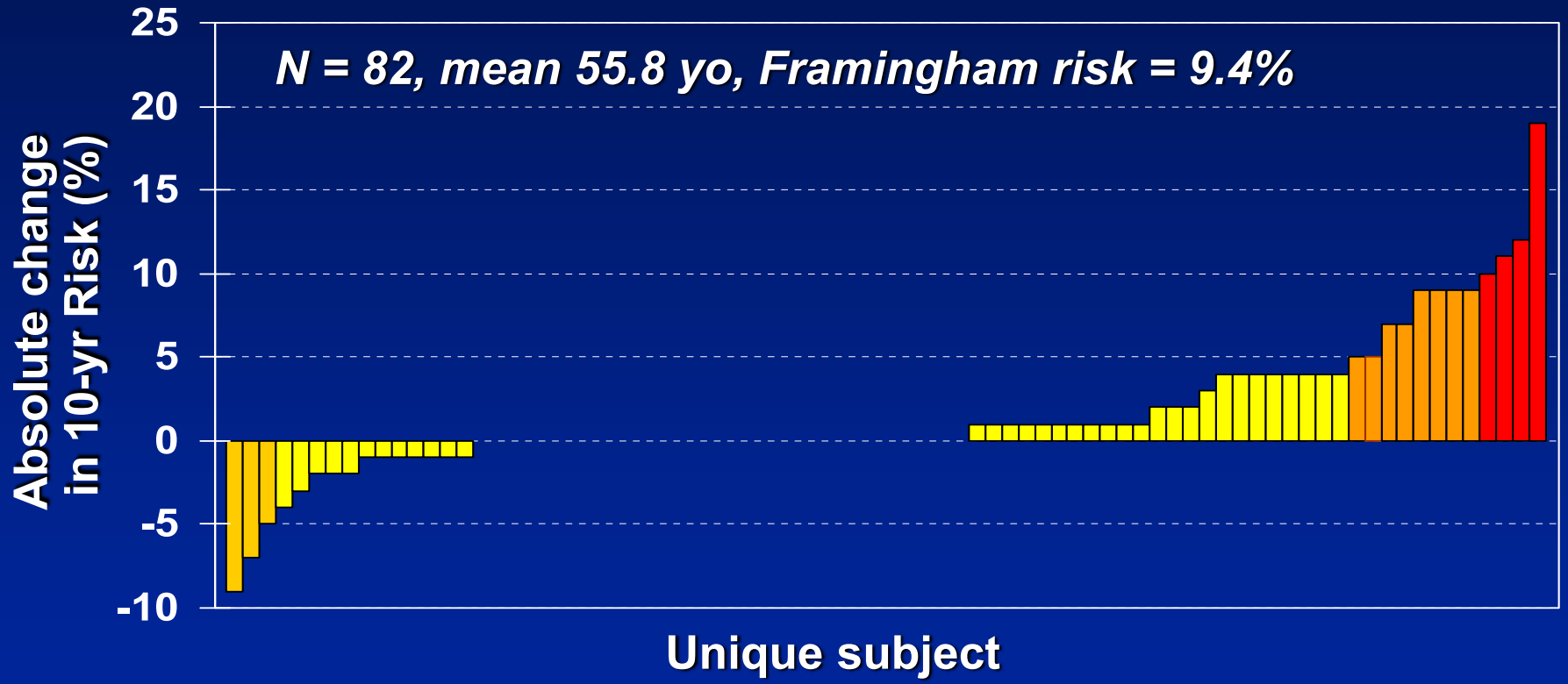


Determination of “Vascular Age”



Vascular Age Alters CV Risk

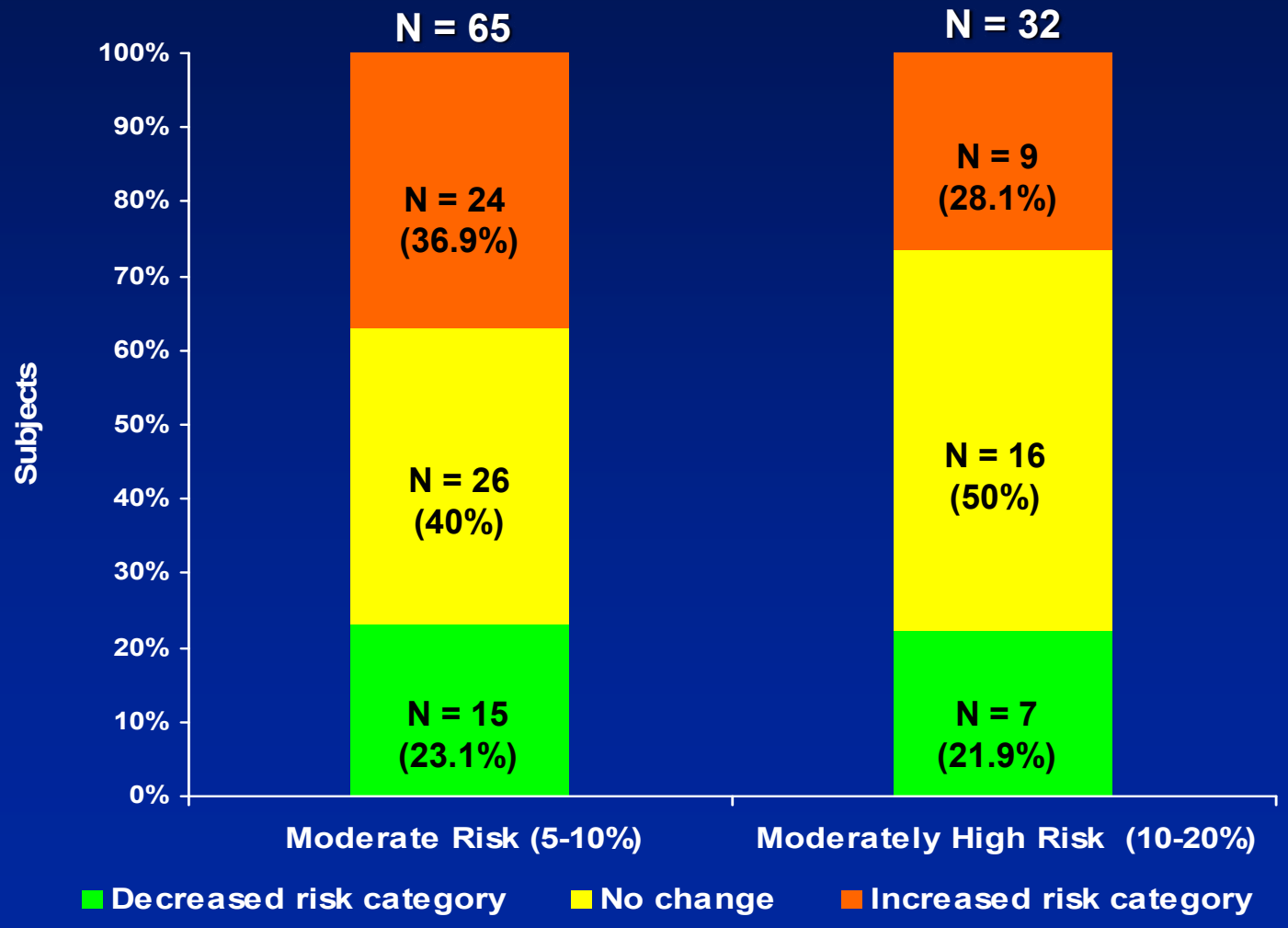
Change in Predicted 10-Year CHD Risk



- Substituting VA ↑ CHD risk in 37 (46%); ↓ in 17 (20%)
- Intermediate risk: 36% re-classified higher, 14% lower risk

Stein JH, et al. Clin Card 2004; 27:388

Vascular Age Alters CV Risk In Untreated Intermediate Risk Patients

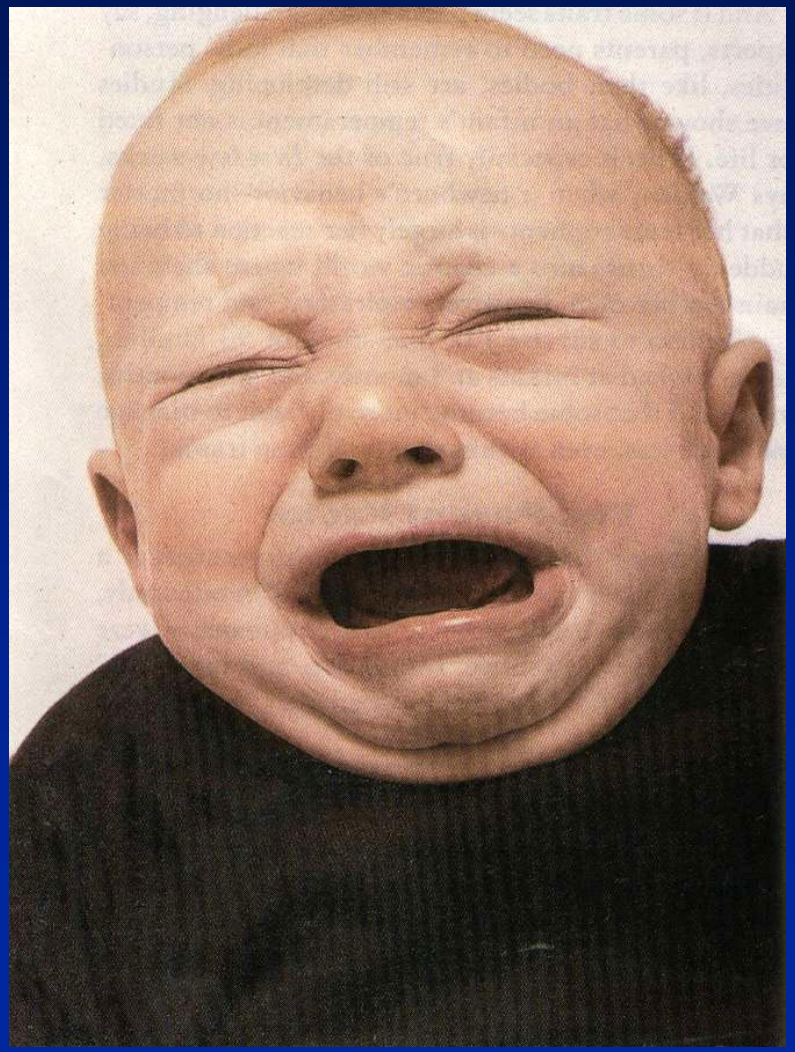


Gepner AD, et al. J Am Soc Echocardiogr 2006; 19:1170

Why Not More?
Barriers to Clinical Use

- Small measurements: <1 pixel
  - High-end ultrasound instrumentation
  - Highly standardized protocols for performing and interpreting studies → highly trained scanners and readers
- Time-consuming
- Expensive
- No insurance reimbursement
- Results not integrated with treatment

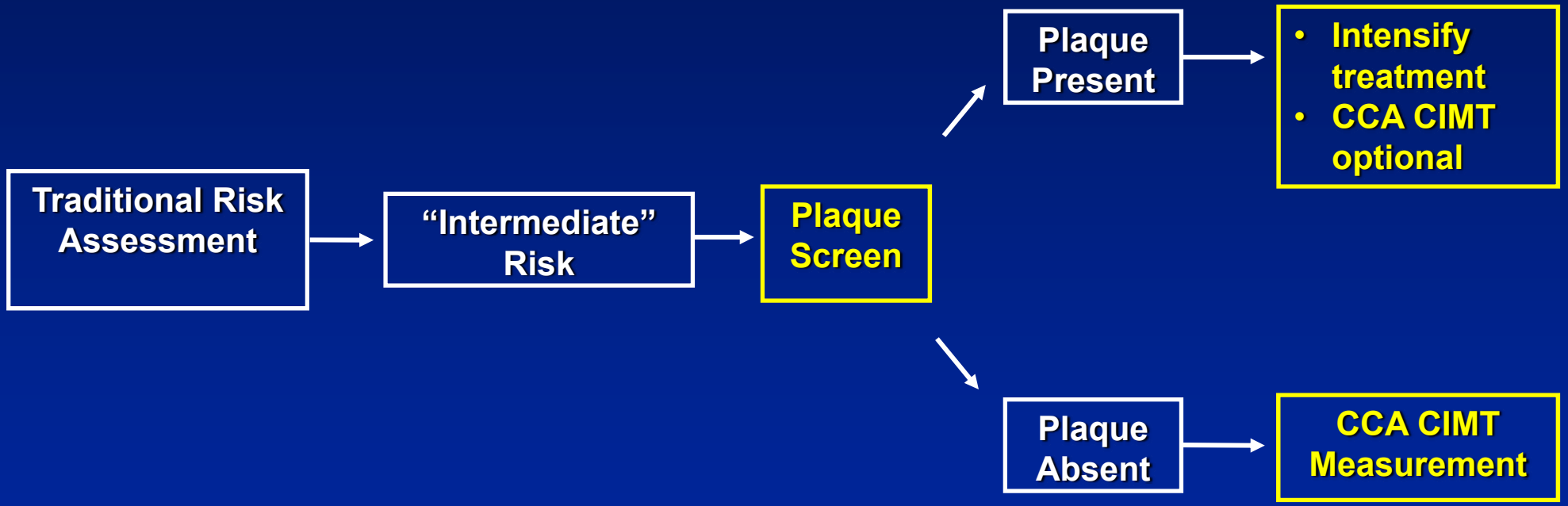
Solution #1:
Insurance Coverage



- Medicare 0126T
- Local carriers
- Office practice
  - Non-sonographer clinicians
  - Abbreviated scanning protocols
  - Border detection programs

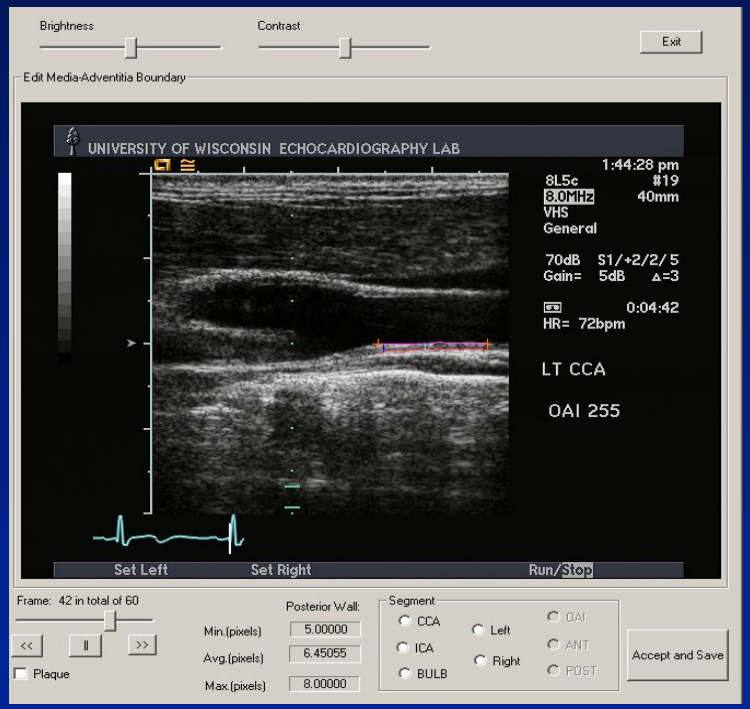
Solution #2:
Less Expensive Instrumentation

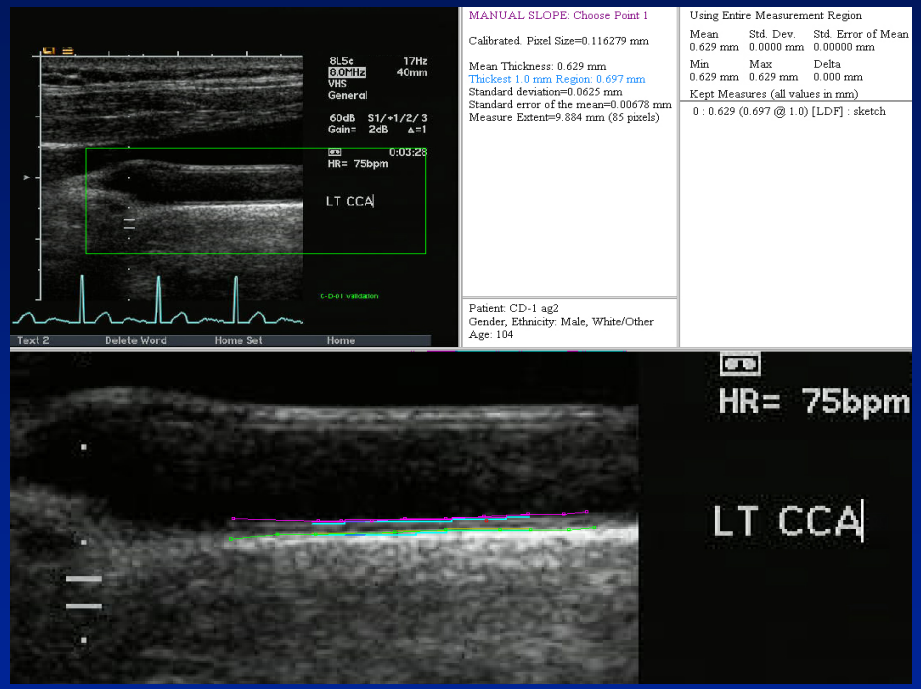
Solution #3: Abbreviated Scanning Protocols



Gepner AG, et al. J Am Soc Echocardiogr 2007; 20:1269

Solution #4:
Border Detection Programs





- Improve reproducibility
- Decrease reading time, esp. for less experienced reader

Stein JH, et al. J Am Soc Echocardiogr 2005;18:244
Gepner AG, et al. J Am Soc Echocardiogr 2006;19:223

Why Might Atherosclerosis Imaging Help Get Patients to Goal?

- Pop psychologist thinks it will "**motivate**" the patient to "get with the program" or "take his health seriously"
- Rationale for providing personalized biomarker feedback is to identify a **threat** and use that to **affect behaviors** on a deeper emotional or subconscious level
- "**Teachable moment**" concept: increased readiness for change after life-threatening event

It Just Makes Sense, Doesn't It?

- "You need to scare him so he starts taking his medicines."
- "I hope this scare will make him finally take off some weight."
- "I'm going to show him a picture of his artery – that will get his attention."
- It makes sense to doctors.

Limitations of All New Non-Invasive Imaging Tests for CVD Risk Assessment

- Limited data that using these tests in clinical practice improves patient outcomes
  - Moderate evidence that they change physician behavior – aspirin, cholesterol medications
  - Some evidence that they may affect patient motivations, intentions, and in some studies adherence - inconsistent

Solution #6: Integration With Clinical Practice

- OPACA, Phase III
- N = 253, 58.1 (6.6) years old
- Framingham 10-year CV risk = 6.1 (5.2)%
- When ↑ CIMT or plaque were detected, physicians were more likely to prescribe:
  - Aspirin (OR 6.3 and 4.8, $p<0.001$)
  - Lipid-lowering therapy (OR 2.9 and 7.4, $p<0.001$)

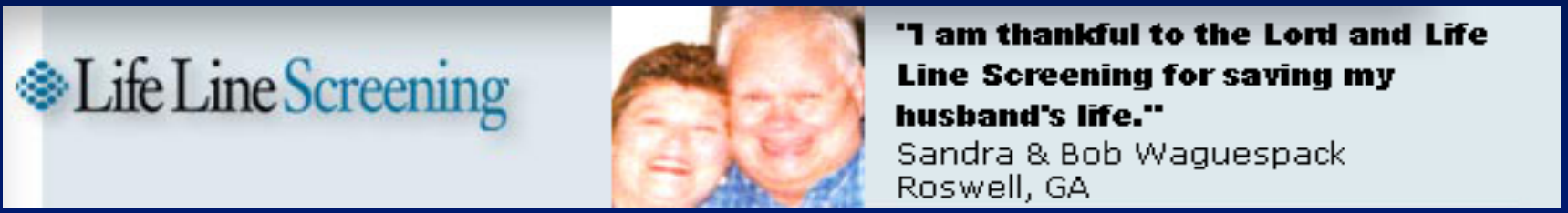
Korcarz CE, et al. J Am Soc Echocardiogr 2008; 21:1156

OPACA Phase III

- Subjects with abnormal findings were more likely to report increases in
  - Plans to take lipid-lowering medication ($p=0.002$)
  - Perceived likelihood of having ($p=0.004$) or developing ($p<0.001$) heart disease
- Even subjects *without* ultrasound abnormalities reported increased motivation to exercise ($p=0.003$) and make dietary changes ($p=0.051$)

Korcarz CE, et al. J Am Soc Echocardiogr 2008; 21:1156

Commercial Community Screening Programs



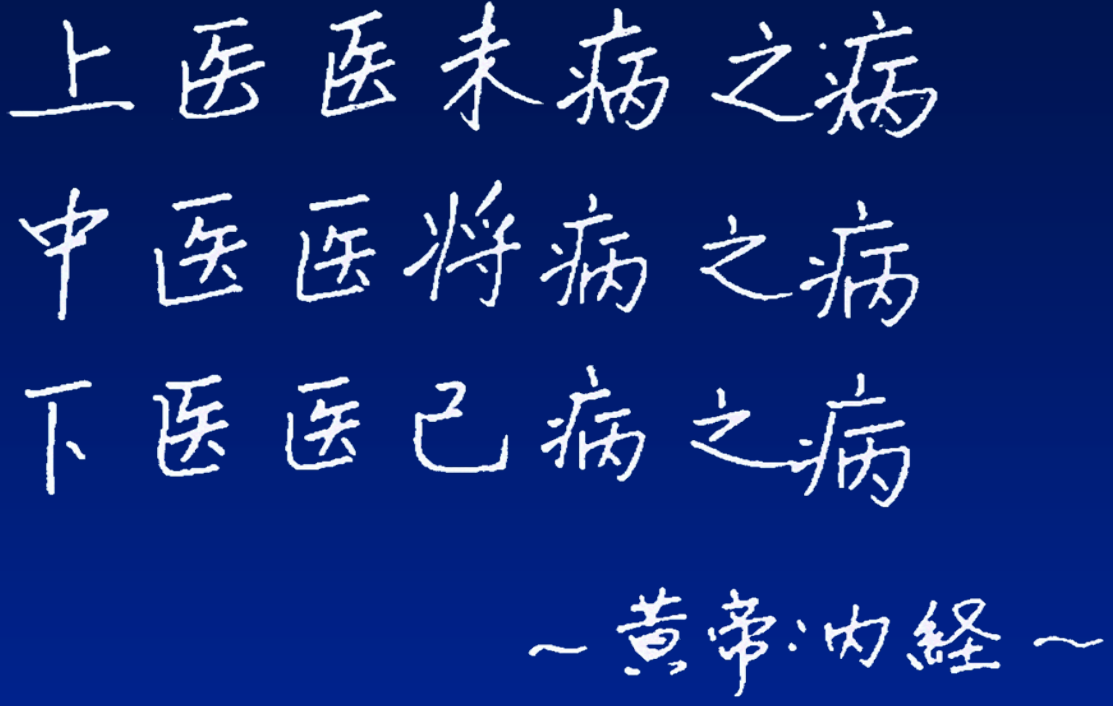
- Not CIMT test
- Not evidence-based – screen anyone
  - Scare tactics
  - Recommend repeat exams
- Limited physician supervision
- Patient ordered
- Quality control

The Perfect Risk Assessment

Rock crystal sphere, on a Japanese silver stand.
19th century China.

Carotid Artery Screening
What Will the Future Bring?

- Office-based testing
- Non-sonographer clinicians
  - Portable devices
  - Semi-automatic border detection
- Need research to identify types of patients who will benefit from screening
- Need proof that finding disease early really helps



Inferior doctors treat the full blown disease.
Mediocre doctors treat the disease before evident.
Superior doctors prevent the disease.

- Huang Dee: Nai-Ching (2600 B.C. 1st Chinese Medical Text)

Back up

Understanding The Effects of Personal Information on Behavior

- Used to counteract perceptions of invulnerability to health consequences of adverse behavior
- Raising threat perception and fear can motivate behavioral change
- Extended Parallel Process Model: people engage in protective behaviors when they
  - Perceive themselves to be at risk of a threat (threat appraisal), and
  - Feel they can reduce the threat (efficacy appraisal)

Shahab L, et al. Br J Health Psychol 2007; 12:275

Understanding The Effects of Personal Information on Behavior

- Step 1: Threat appraisal
  - How severe is the threat?
  - How susceptible am I?
- Step 2: Efficacy appraisal
  - Assess ability to perform a behavior (self-efficacy)
  - That can avert the threat (response efficacy)
- When both are high
  - Danger control processes lead to acceptance of a threat message (*i.e.* "stop smoking")
  - Fear from threat appraisal may lead to a behavioral solution (*i.e.* cessation)

Shahab L, et al. Br J Health Psychol 2007; 12:275

Understanding The Effects of Personal Information on Behavior

- But: when threat appraisal is high and efficacy appraisal is low
  - Fear may lead to a cognitive solution (*i.e.* avoidance)
  - Fear control processes may lead to rejection of the threat message
- Personalized biomarker feedback showing harm may have maximal effect if visual, by avoiding "disengagement beliefs" that distort meaning of potentially motivating information
- But if self-efficacy is low, motivational change is unlikely

Shahab L, et al. Br J Health Psychol 2007; 12:275

Biomarker Feedback and Psychology in Action: Smoking Cessation

- A small study (N=153) randomly assigned smokers to SC or SC + carotid ultrasound, with a picture of their plaques
- Smoking cessation rates were 22.2% in those with plaques (p=0.003)
- Follow-up pilot RCT (N=23), visual vs. verbal feedback, the intervention increased
  - Perception of smoking-related illness
  - Smoking cessation behavior and intention
- **Mediated by self-efficacy**: intention only increased in people with high levels (p<0.03)

Bovet P, et al. Prev Med 2002; 34:215
Shahab L, et al. Br J Health Psychol 2007; 12:275

Solution #6: Integration With Clinical Practice OPACA Phase III

- N = 253, 58.1 (6.6) years old
- Framingham 10-year CV risk = 6.1 (5.2)%
- When ↑ CIMT or plaque were detected, physicians were more likely to prescribe:
  - Aspirin (OR 6.34 and 4.84, $p<0.001$)
  - Lipid-lowering therapy (OR 2.93 and 7.40, $p<0.001$)

Korcarz CE, et al. J Am Soc Echocardiogr 2008; 21:1156

OPACA Phase III

- Subjects with abnormal findings were more likely to report increases in
  - Plans to take lipid-lowering medication ($p=0.002$)
  - Perceived likelihood of having heart disease ($p=0.004$)
  - Perceived likelihood of developing heart disease ($p<0.001$)
- Even subjects without ultrasound abnormalities reported increased motivation to exercise ($p=0.003$)

Korcarz CE, et al. J Am Soc Echocardiogr 2008; 21:1156

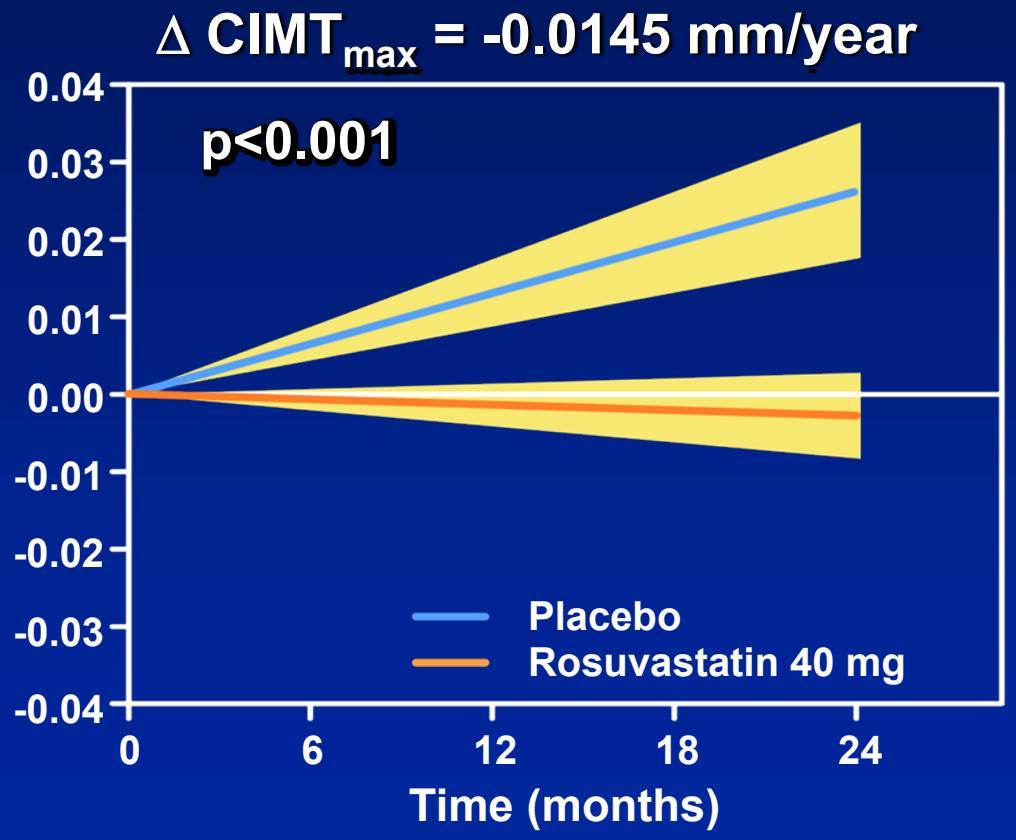
Is Treatment Justified?

Statin Therapy in "Low Risk" Patients

- METEOR
- N = 984 subjects
- Only risk factor = age

OR

- FRS <10%
- Focal CIMT >1.2 mm
- LDL-C 120-190 mg/dL



Crouse JR, et al. JAMA 2007; 297;1344

CIMT Regression on Statin Therapy Predicts CV Event Reduction

Trial (N)	Statin	Δ CIMT Progression (mm/yr)	CVD Event	OR [95% CI]
ACAPS (N=919)	Lovastatin	-0.015 (p=0.001)	CVD Death, MI, Stroke	0.34 [0.12, 0.69]
KAPS (N=447)	Pravastatin	-0.014 (p=0.005)	CVD Death, MI, Stroke	0.57 [0.22, 1.47]
PLAC-II (N=151)	Pravastatin	-0.009 (p=0.44)	Clinical Coronary Events	0.37 [0.11, 1.24]
CAIUS (N=305)	Pravastatin	-0.014 (p=0.0007)	CVD Death, MI	1.02 [0.14, 7.33]
REGRESS (N=255)	Pravastatin	-0.030 (p=0.002)	Clinical Events	0.51 [0.24, 1.07]
BCAPS (N=793)	Fluvastatin	-0.008 (p=0.002)	CVD Death, MI, Stroke	0.64 [-0.24, 1.66]
FAST (N=164)	Pravastatin	(p<0.001)	CVD Death, MI	0.32 [0.10, 1.06]
Pooled Estimate		**-0.012 [-0.016, -0.007]***		**0.48 [0.30, 0.78]**

** 95%CI, estimate excludes FAST*

Espeland MA, et al. Current Controlled Trials in Cardiovascular Medicine 2005;6:3

Prospective Studies Relating CIMT to Incident CV Events in Asymptomatic Individuals

Study	N	Age	Yrs	CV Event	Cutpoint	Adjusted RR (95% CI)
ARIC	12,841	45-64	5	MI, CHD death	tertile	W: 2.53 (1.02-6.26) M: 2.02 (1.32-3.09)
	14,214	45-64	7	stroke	tertile	W: 2.32 (1.09-4.94) M: 2.24 (1.26-4.00)
CAPS	5,056	19-90	4	MI, stroke, death	quartile	1.85 (1.09-3.15)
CHS	4,476	>65	6	MI	quintile	3.61 (2.13-6.11)
				stroke	quintile	2.57 (1.64-4.02)
KIHD	1,257	42-60	3	MI	>1.0 mm	2.1 (0.8-5.2)
Yao City	1,289	60-74	5	stroke	quartile	4.9 (1.9-12.0)
MDCS	5,163	46-68	7	MI, CHD death	tertile	1.50 (0.81-2.59)
Rotterdam	6,389	>55	7-10	MI	quartile	1.95 (1.19-3.19)

Modified from Lorenz MW, et al. Circulation 2007; 115:459

Prospective Studies Relating Carotid Plaque Presence to Incident CV Disease in Asymptomatic Individuals

Study	N	Age	Yrs	Event	Adjusted HR
ARIC	12,375	45-64	7	MI, CHD death	2.96 (1.54-3.30)
KIHD	1,288	42-60	≤2	MI	4.15 (1.5-11.47)
MDCS	5,163	46-68	7	MI, CHD death	1.81 (1.14-2.87)
Yao City	1,289	60-74	5	Stroke	3.2 (1.4-7.1)
Northern Manhattan	1,939	>40	6	Stroke	3.1 (1.1-8.5)
Rotterdam	6,389	>55	7-10	MI	1.83 (1.27-2.62)

Modified from Wyman WA, et al. Vascular Medicine 2006; 11:123