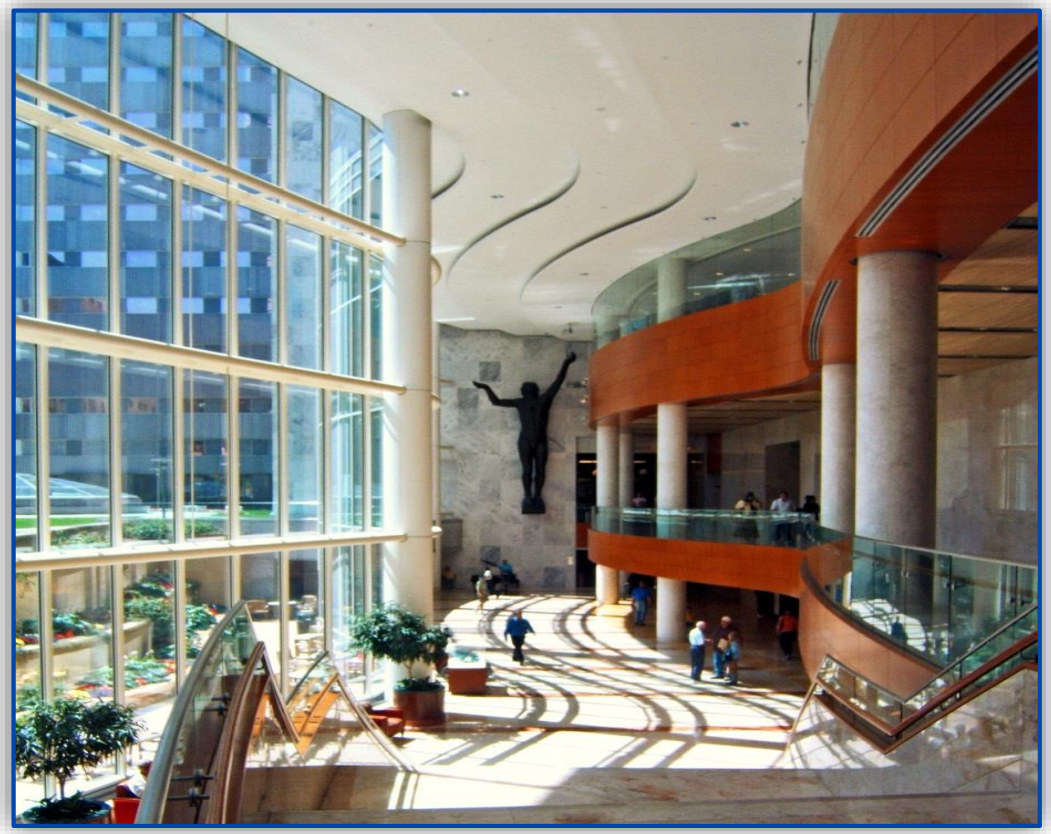

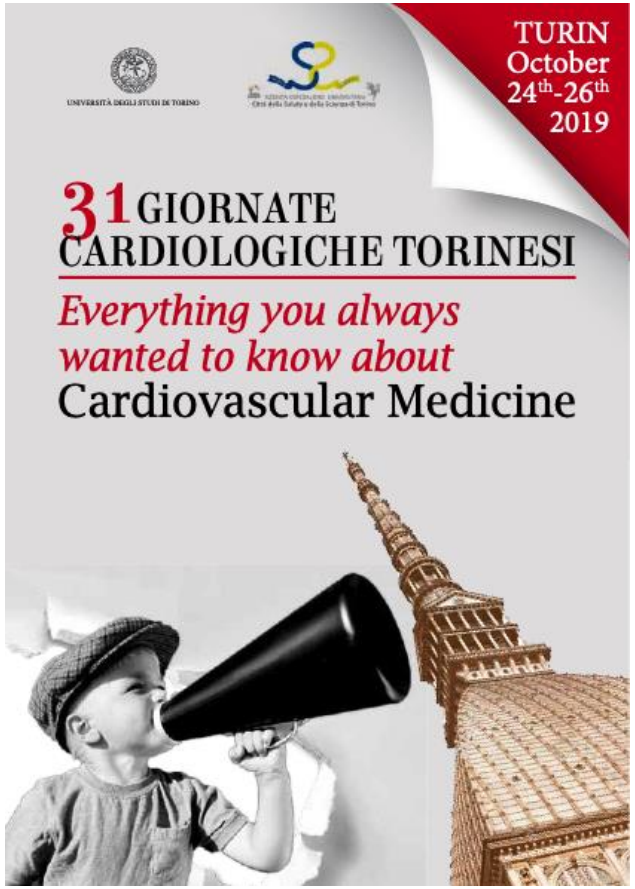

Non traditional risk factors for CAD

Amir Lerman, MD

Barbara Woodward Lips Endowed Professor

Director Cardiovascular Research Center

Mayo Clinic, Rochester, MN

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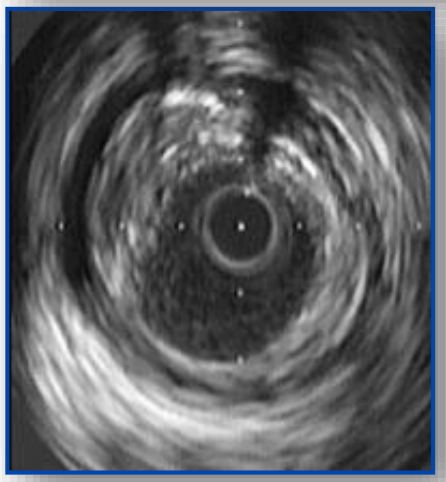
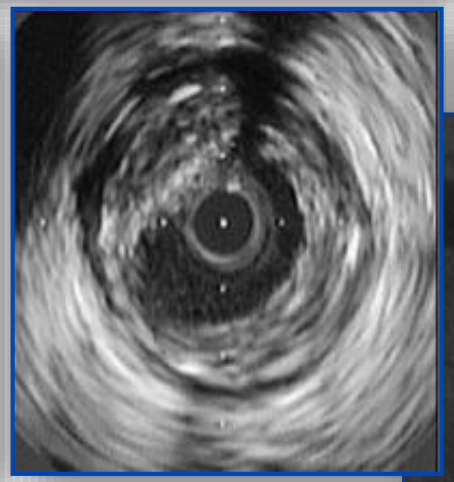
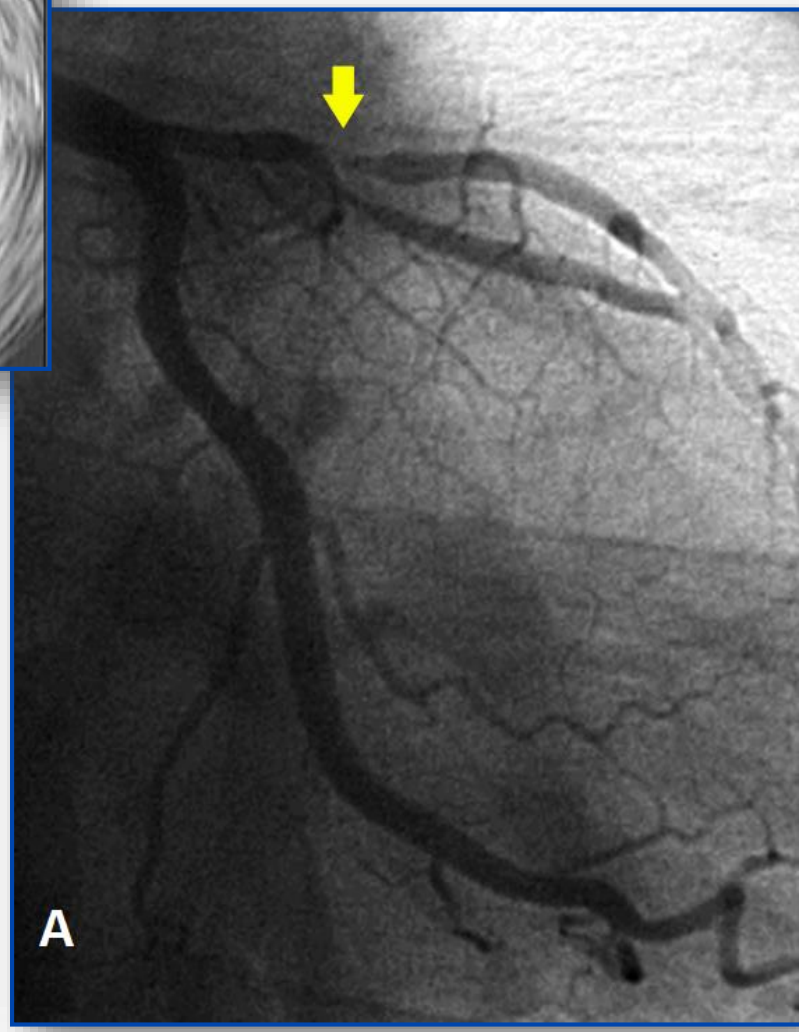
- 62-year-old male

- History of obesity and remote history smoking presetting with increasing episodes of chest pain on exertion
- High stress at work
- No family history
- Negative stress test







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Traditional risk factors and Atherosclerosis

Smoking | Hypertension | Hypercholesterolemia | Age | Diabetes

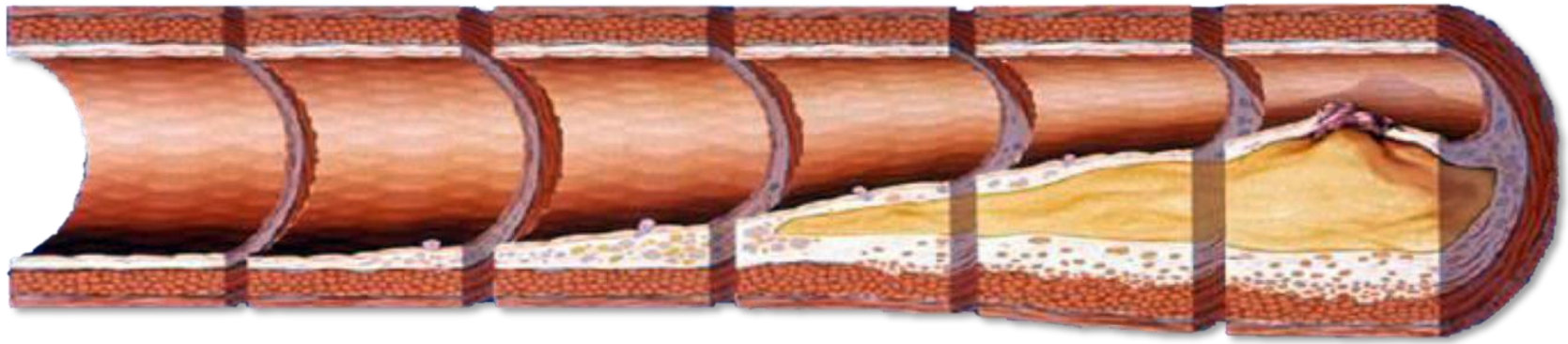
Enviromental

Mental stress

Inflammation

Inflammation & oxidative stress

Endothelial dysfunction: The risk of the risk factors



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Special Report

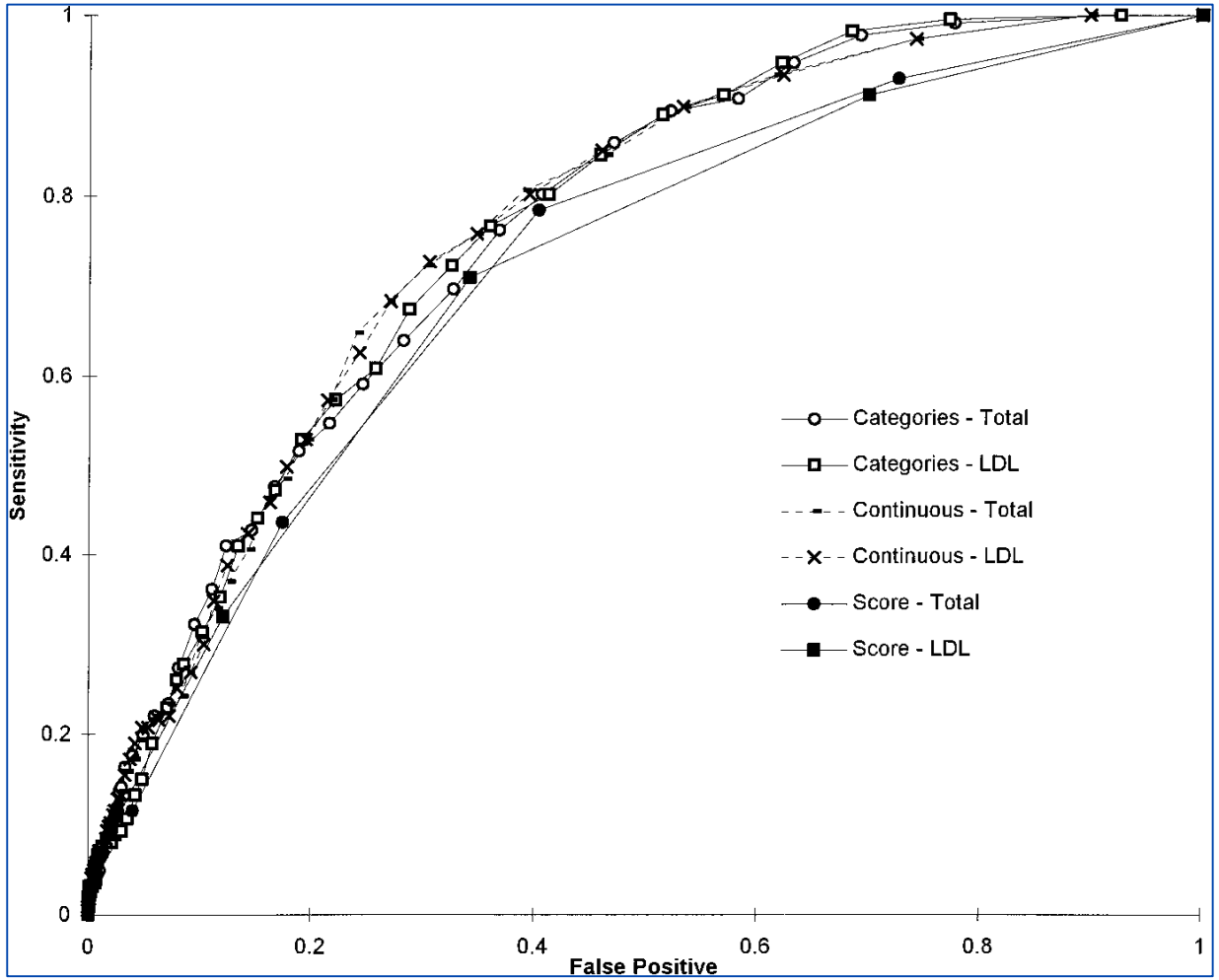
Prediction of Coronary Heart Disease Using Risk Factor Categories

Peter W.F. Wilson, MD; Ralph B. D'Agostino, PhD; Daniel Levy, MD; Albert M. Belanger, BS; Halit Silbershatz, PhD; William B. Kannel, MD

Background—The objective of this study was to examine the association of Joint National Committee (JNC-V) blood pressure and National Cholesterol Education Program (NCEP) cholesterol categories with coronary heart disease (CHD) risk, to incorporate them into coronary prediction algorithms, and to compare the discrimination properties of this approach with other noncategorical prediction functions.

Methods and Results—This work was designed as a prospective, single-center study in the setting of a community-based cohort. The patients were 2489 men and 2856 women 30 to 74 years old at baseline with 12 years of follow-up. During the 12 years of follow-up, a total of 383 men and 227 women developed CHD, which was significantly associated with categories of blood pressure, total cholesterol, LDL cholesterol, and HDL cholesterol (all $P<.001$). Sex-specific

Receiver operating characteristic curves for prediction of CHD in Framingham men over a period of 12 years



Established at 1948 (Life expectancy in the USA, at that year was 65 years

The population-based sample used for this report included 2489 men and 2856 women 30 to 74 years old at the time of their Framingham Heart Study examination in 1971 to 1974.

Clinicians should exercise caution in generalizing from experience of the Framingham Study, a community sample of white subjects drawn from a suburb west of Boston.

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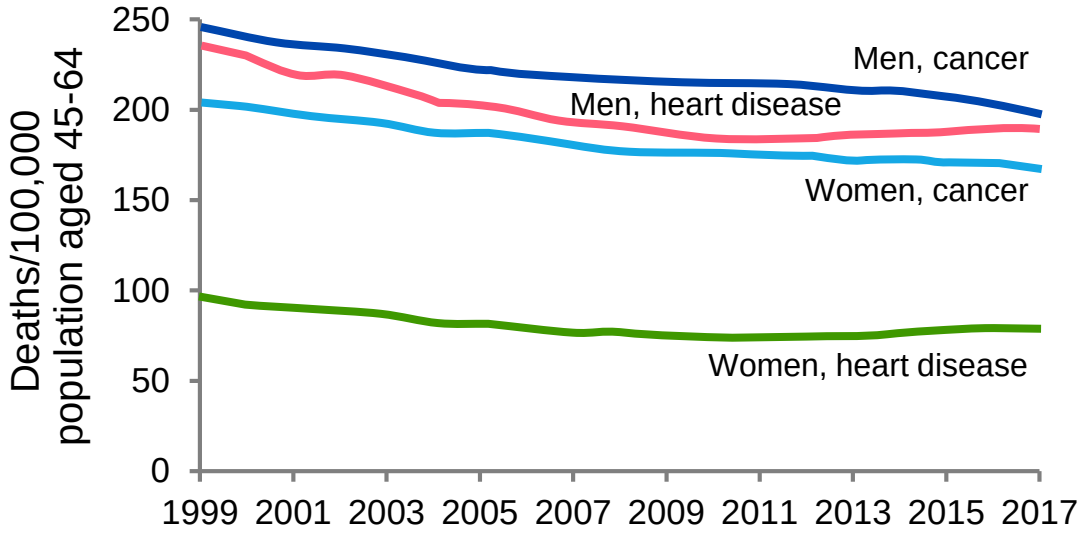
National Vital Statistics Reports

Volume 68, Number 5 May 22, 2019

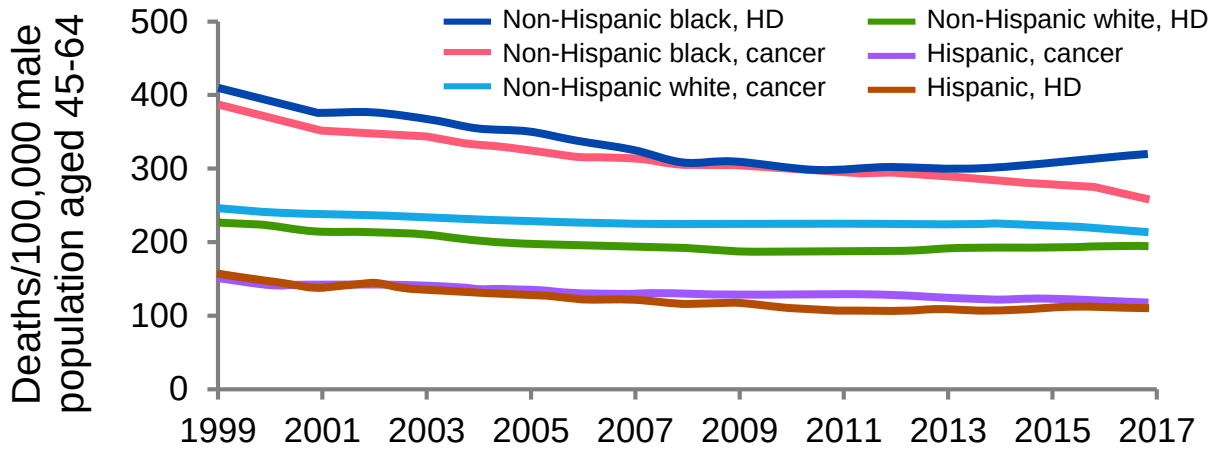
Trends in Cancer and Heart Disease Death Rates Among Adults Aged 45–64: United States, 1999–2017

by Sally C. Curtin, M.A., Division of Vital Statistics

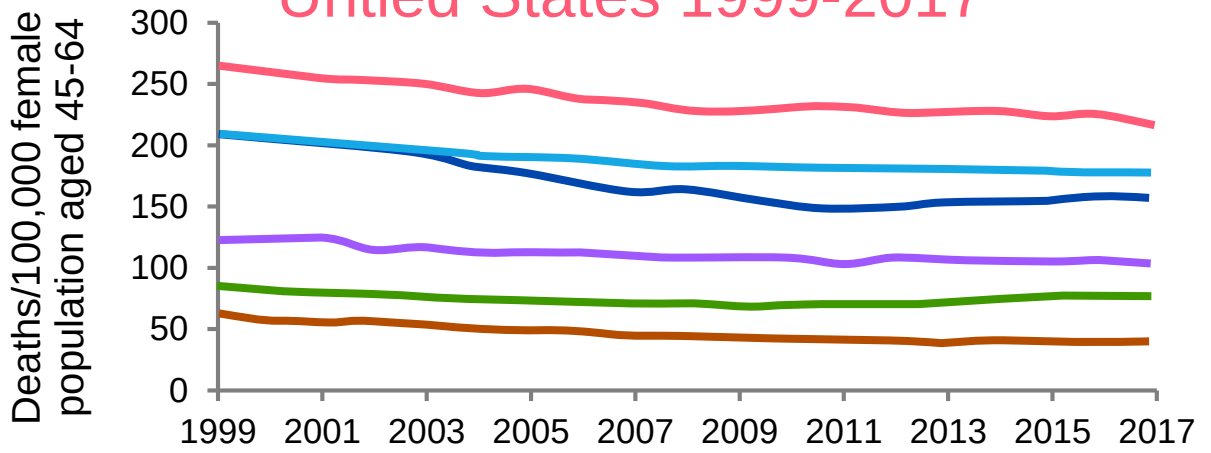
Death Rates for Cancer and Heart Disease Among Adults Aged 45-64, by Sex
Untied States 1999-2017



Death Rates for Cancer and Heart Disease (HD) Among Men Aged 45-64, by Race and Ethnicity
Untied States 1999-2017



Death Rates for Cancer and Heart Disease Among Women Aged 45-64, by Race and Ethnicity
Untied States 1999-2017



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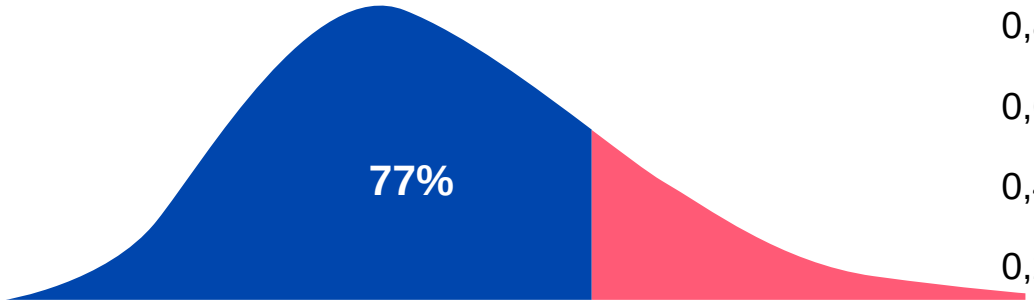
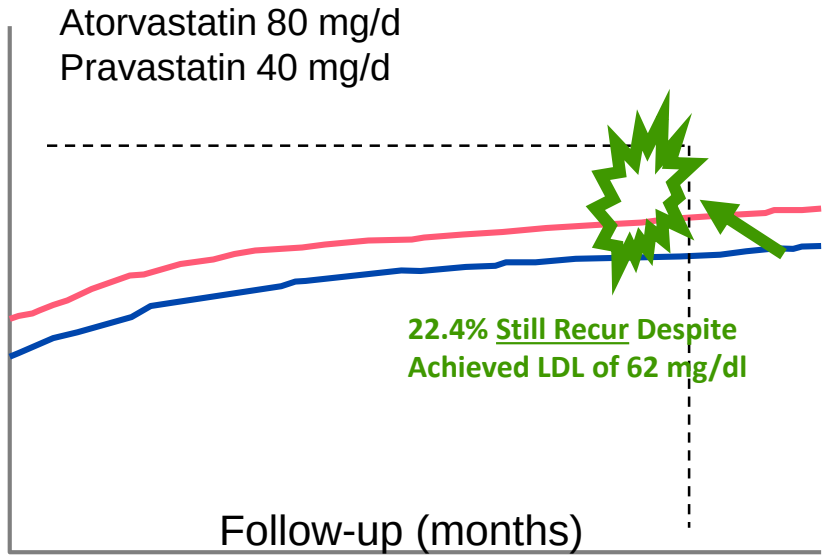
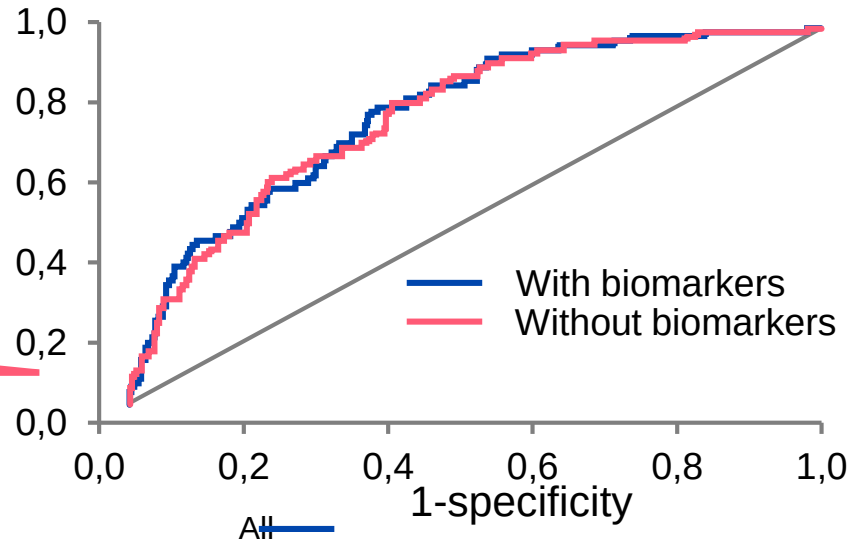
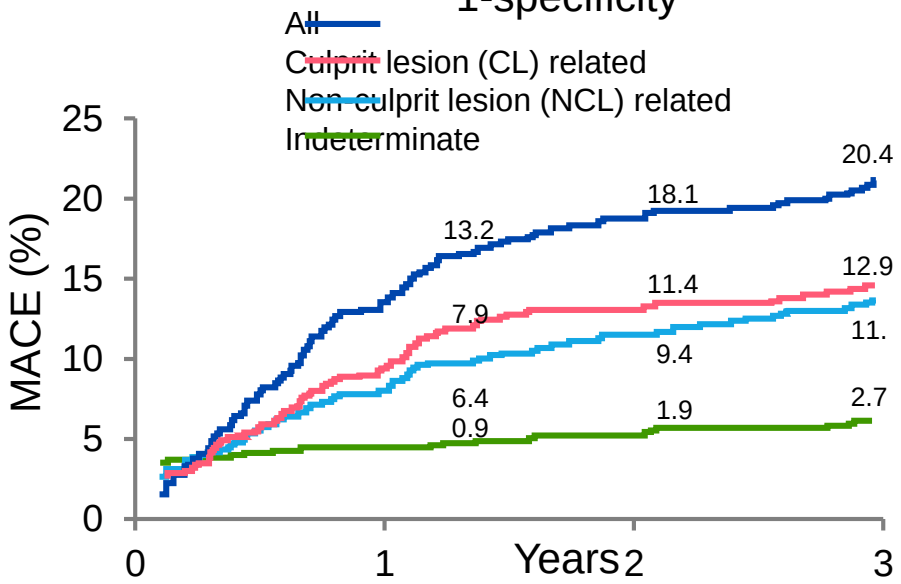
Traditional Risk Factors Markers and Imaging Fail in Identifying Vulnerable Patient

Of 136,905 patients hospitalized with CAD, 77% had normal LDL levels below 130 mg/dL









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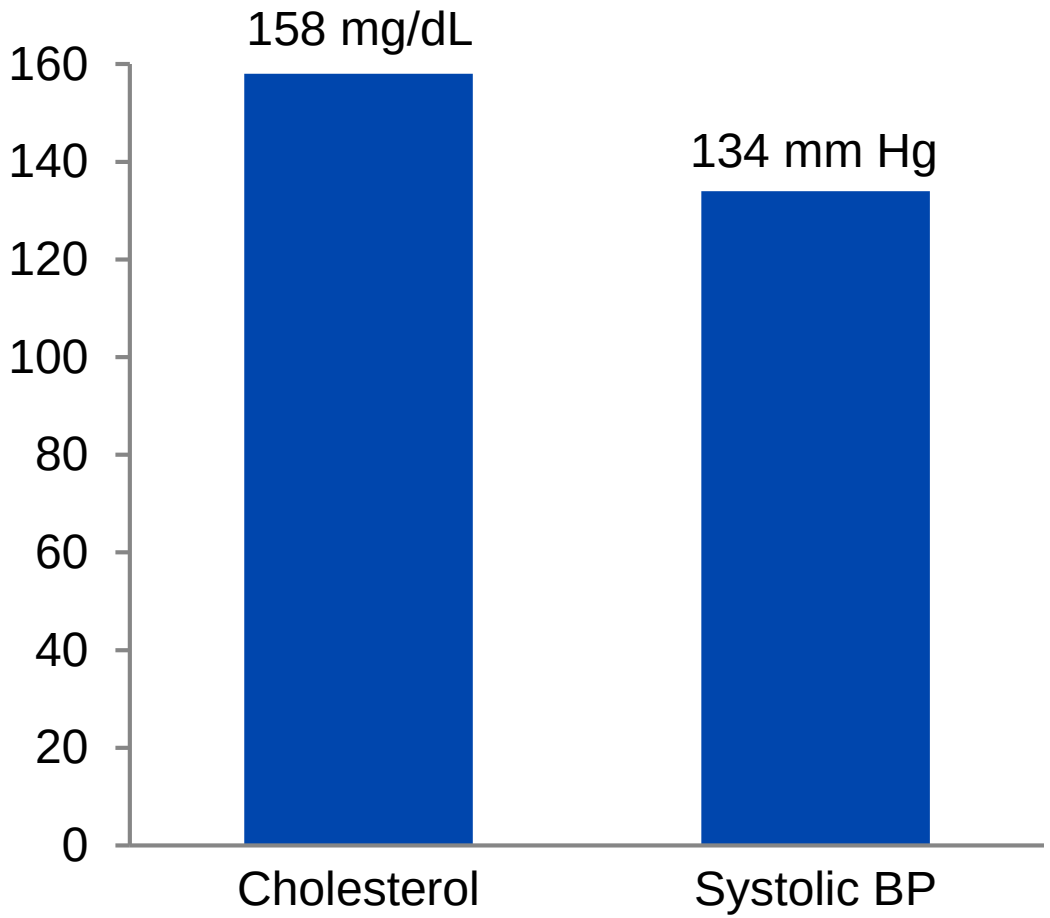
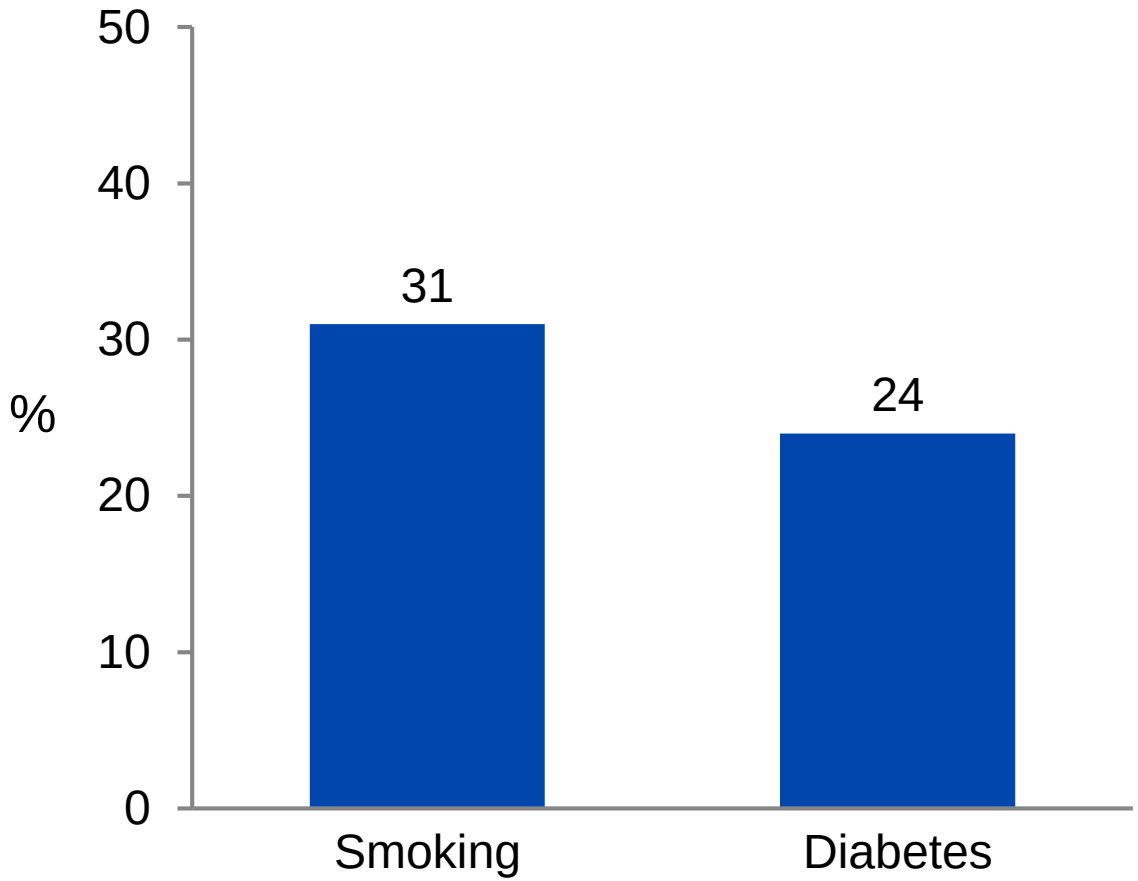
Conventional Risk Factors in Patients Presenting With STEMI



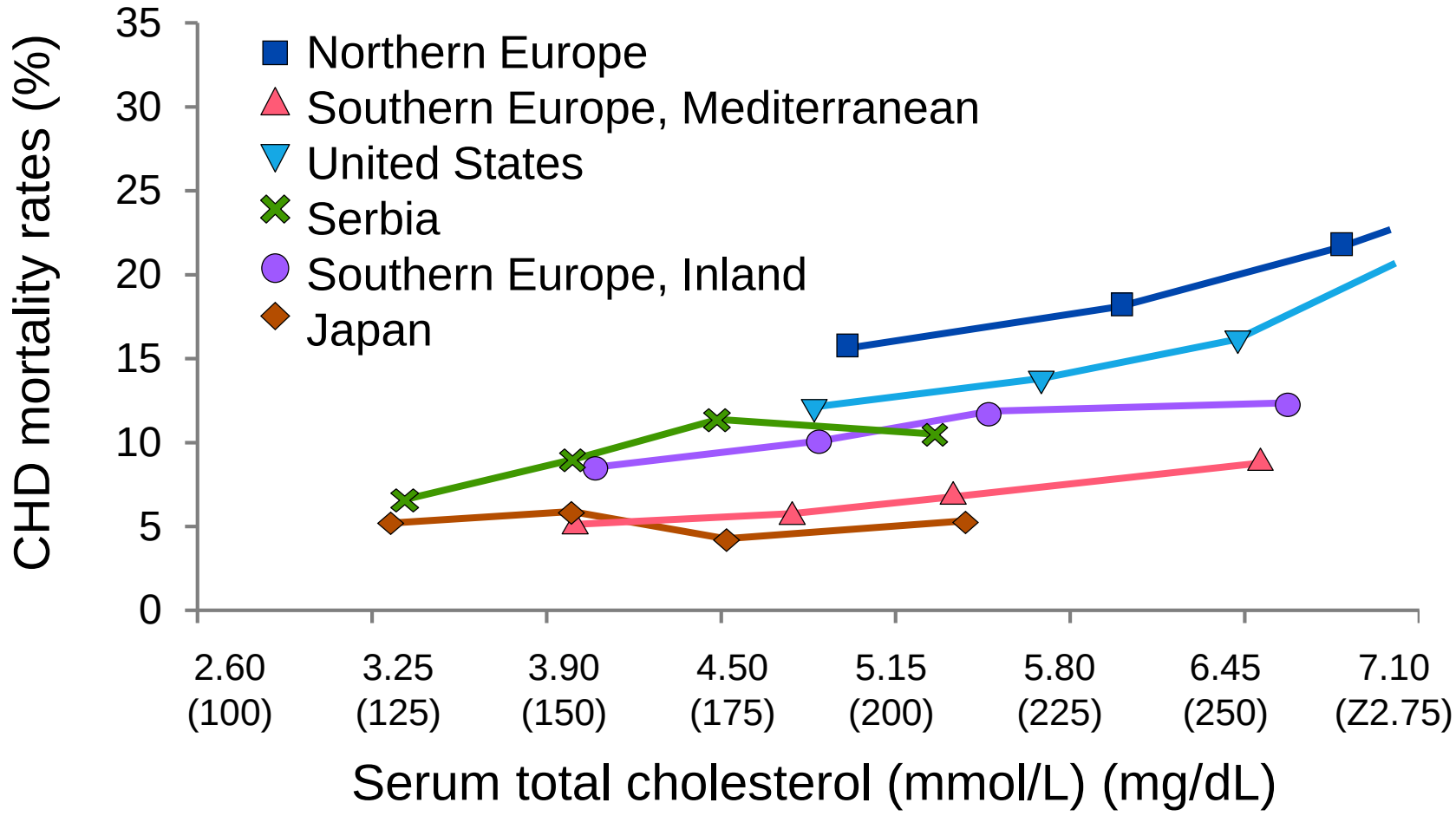


Mayo PCI. STEMI database

Serum Cholesterol and Mortality in Different Countries.

7 Countries – 25-Year Follow-Up Study

CHD Mortality



Verschuren: JAMA, 1995

Vulnerable

Vessel
Mind
Blood

It takes two to Tango

+

=

Trigger events

- **Emotional stress**
- **Physical activity**

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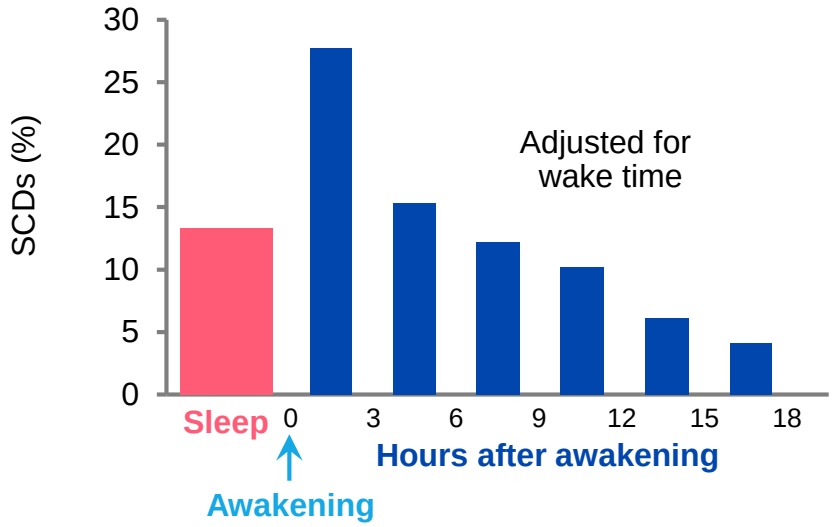
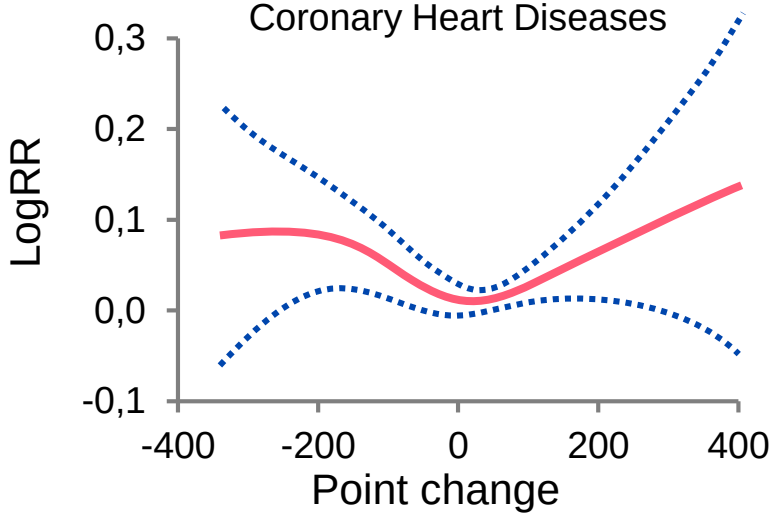
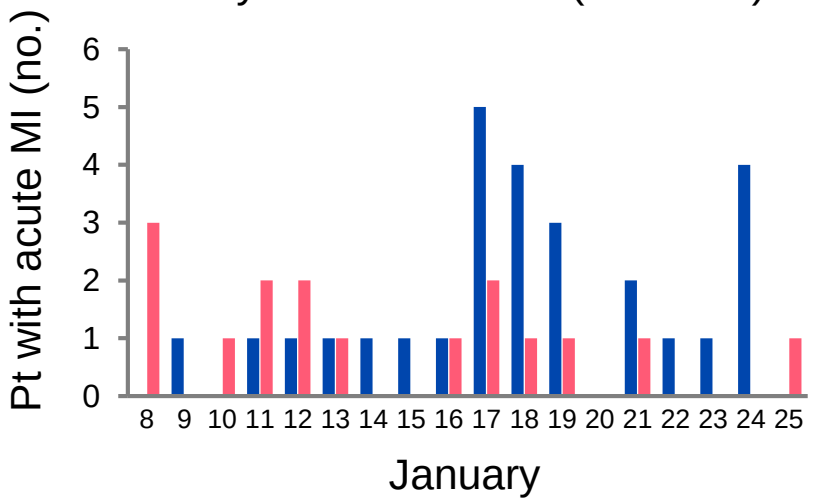
Awake Time and SCD



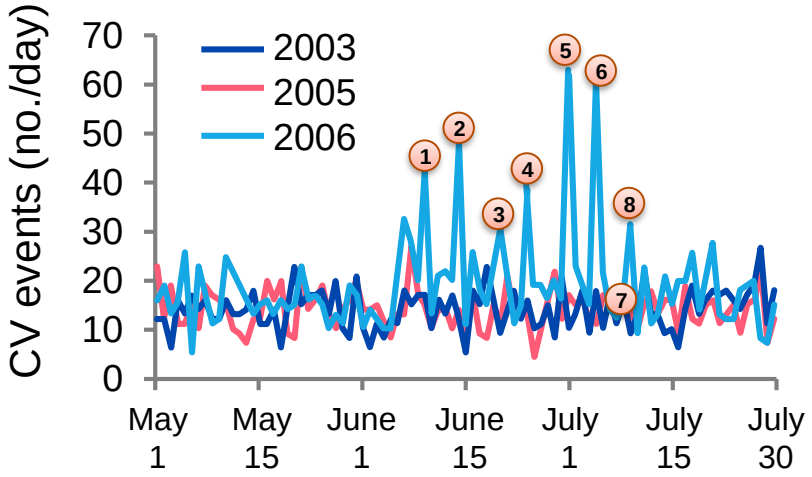
Shanghai Stock Exchange Composite Index Change with Daily Deaths of Coronary Heart Diseases



Daily Incidence of MI (Gulf War)



Cardiovascular Events during World Cup Soccer



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JAMA Network | Open

Original Investigation | Cardiology

Association of Optimism With Cardiovascular Events and All-Cause Mortality

A Systematic Review and Meta-analysis

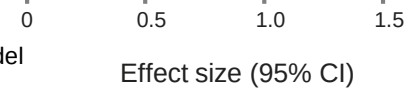
Alan Rozanski, MD; Chirag Bavishi, MD, MPH; Laura D. Kubzansky, PhD; Randy Cohen, MD

OBJECTIVE To conduct a meta-analysis and systematic review of the association between optimism and risk for future cardiovascular events and all-cause mortality.

RESULTS The search yielded 15 studies comprising 229 391 participants of which 10 studies reported data on cardiovascular events and 9 studies reported data on all-cause mortality. The mean follow-up period was 13.8 years

Association Between Optimism and Cardiovascular (CV) Events

Source	Effect size (95% CI)	Weight (%)
Anthony et al,[11] 2016	0.94 (0.86-1.02)	12.37
Boehm et al,[10] 2011	0.69 (0.47-0.91)	9.75
Giltay et al,[13] 2006	0.57 (0.31-0.83)	8.64
Giltay et al,[14] 2004	0.23 (0-0.46)	9.53
Hansen et al,[15] 2010	0.58 (0.25-0.90)	7.40
Kim et al,[16] 2011	0.89 (0.82-0.96)	12.50
Kim et al,[17] 2016	0.62 (0.49-0.75)	11.55
Kubzansky et al,[6] 2001	0.44 (0.20-0.68)	9.19
Nabi et al,[18] 2010	0.52 (0.20-0.84)	7.50
Tindle et al,[19] 2009	0.76 (0.63-0.89)	11.55
Overall	0.65 (0.51-0.78)	



Heterogeneity: $\tau^2 = 0.04$, $I^2 = 87.4\%$
Random-effects Hartung-Knapp-Sidik-Jonkman Model

Association Between Optimism and All-Cause Mortality

Source	Effect size (95% CI)	Weight (%)
Anthony et al,[11] 2016	0.99 (0.95-1.03)	15.37
Brummett et al,[7] 2006	0.86 (0.79-0.94)	13.35
Engberg et al, [12] 2013 (men)	0.91 (0.71-1.11)	5.92
Engberg et al,[12] 2013 (women)	0.85 (0.74-0.97)	10.45
Giltay et al,[14] 2004	0.71 (0.48-0.94)	5.05
Grossardt et al,[8] 2009	0.85 (0.76-0.95)	11.88
Mosing et al,[9] 2012	0.72 (0.50-0.94)	5.21
Tindle et al,[19] 2009	0.86 (0.79-0.93)	13.72
Kim et al,[17] 2016	0.91 (0.85-0.97)	14.42
Weiss-Faratci et al,[20] 2017	0.67 (0.43-0.91)	4.61
Overall	0.86 (0.80-0.92)	

Heterogeneity: $\tau^2 = 0.01$, $I^2 = 73.2\%$
Random-effects Hartung-Knapp-Sidik-Jonkman Model

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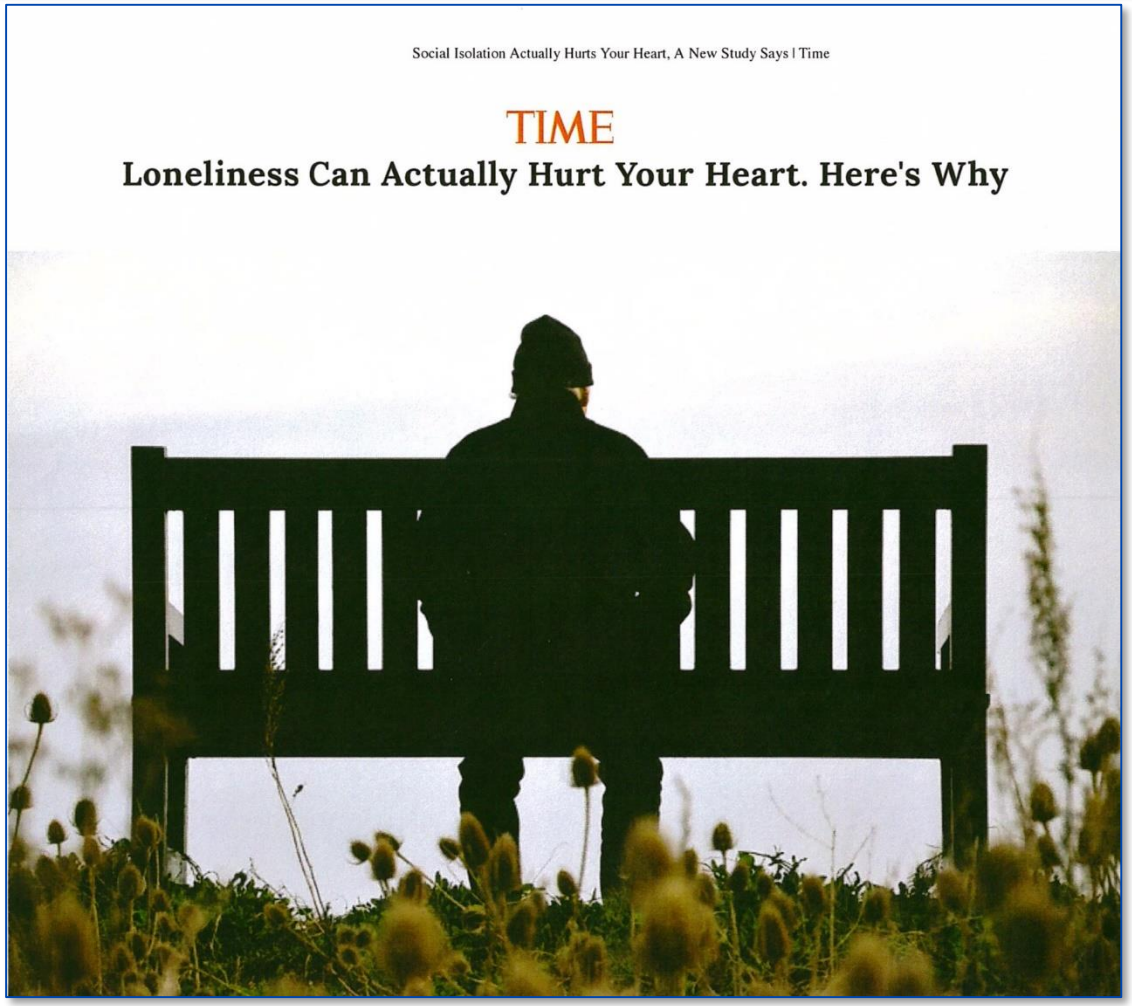
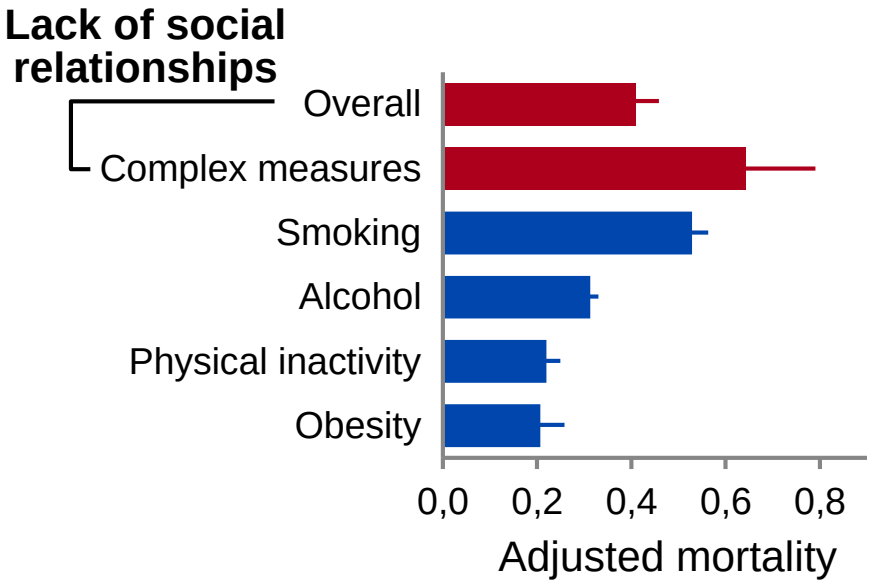
Rozanski et al: JAMA Network Open 2(9):e1912200, 2019

Loneliness, Social Isolation, and Cardiovascular Health

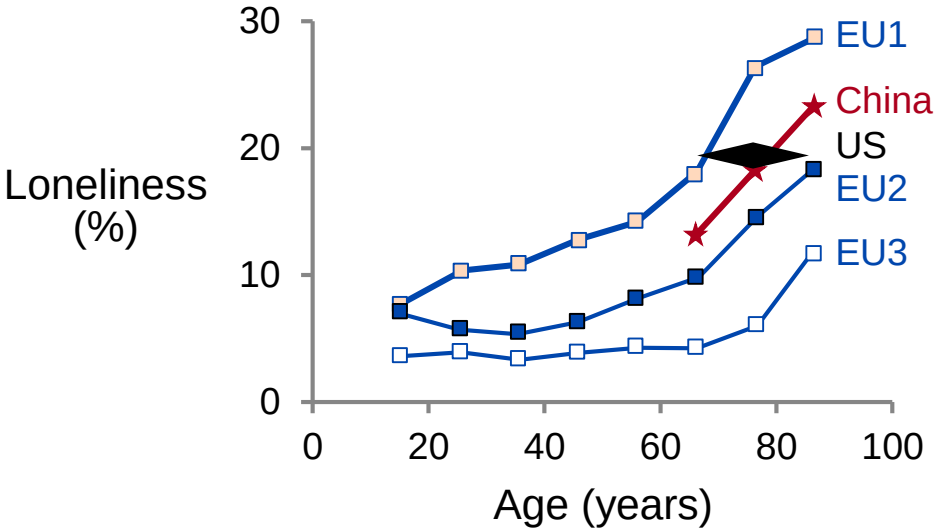
Ning Xia[1] and Huige Li[1–3]



Impact of Social Support on Mortality



Prevalence of Loneliness



Xia et al: Antioxidants & Redox Signaling; Volume 28, Number 9, 2018

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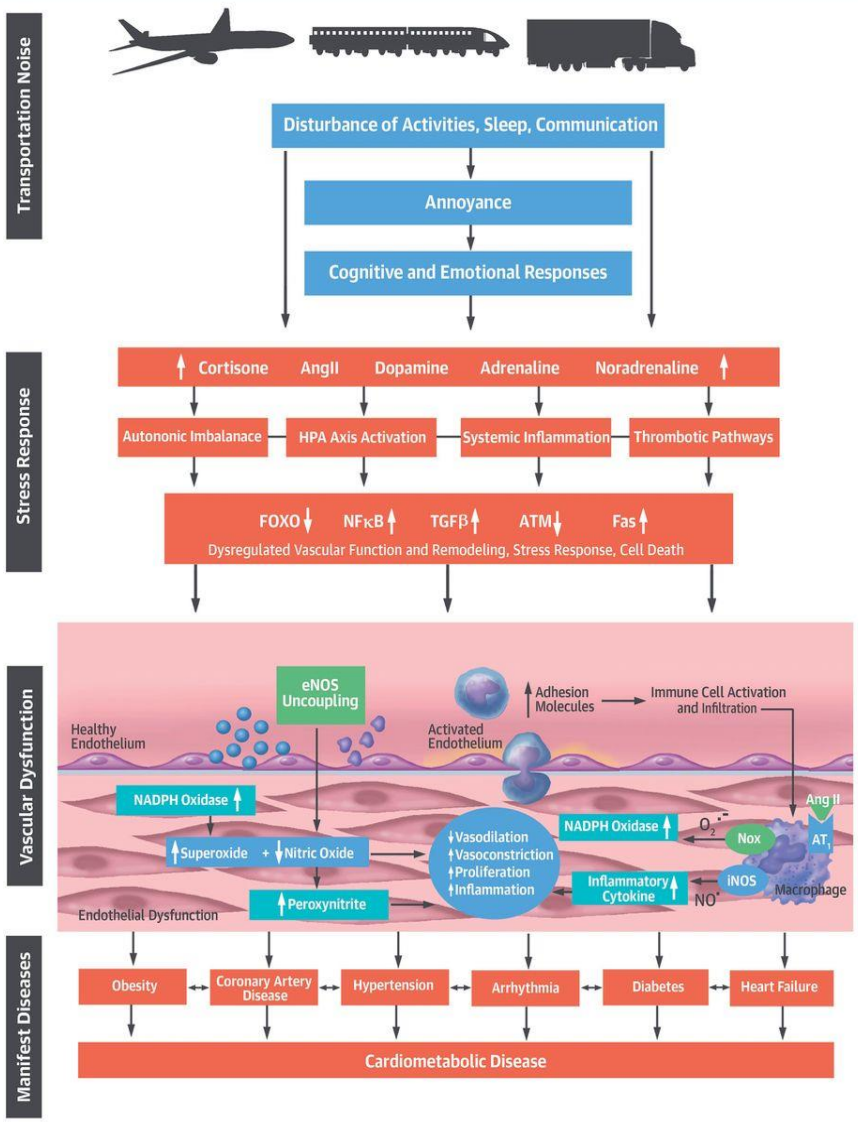
CENTRAL ILLUSTRATION: Proposed Pathophysiological Mechanisms of Noise-Induced Cardiometabolic Disease

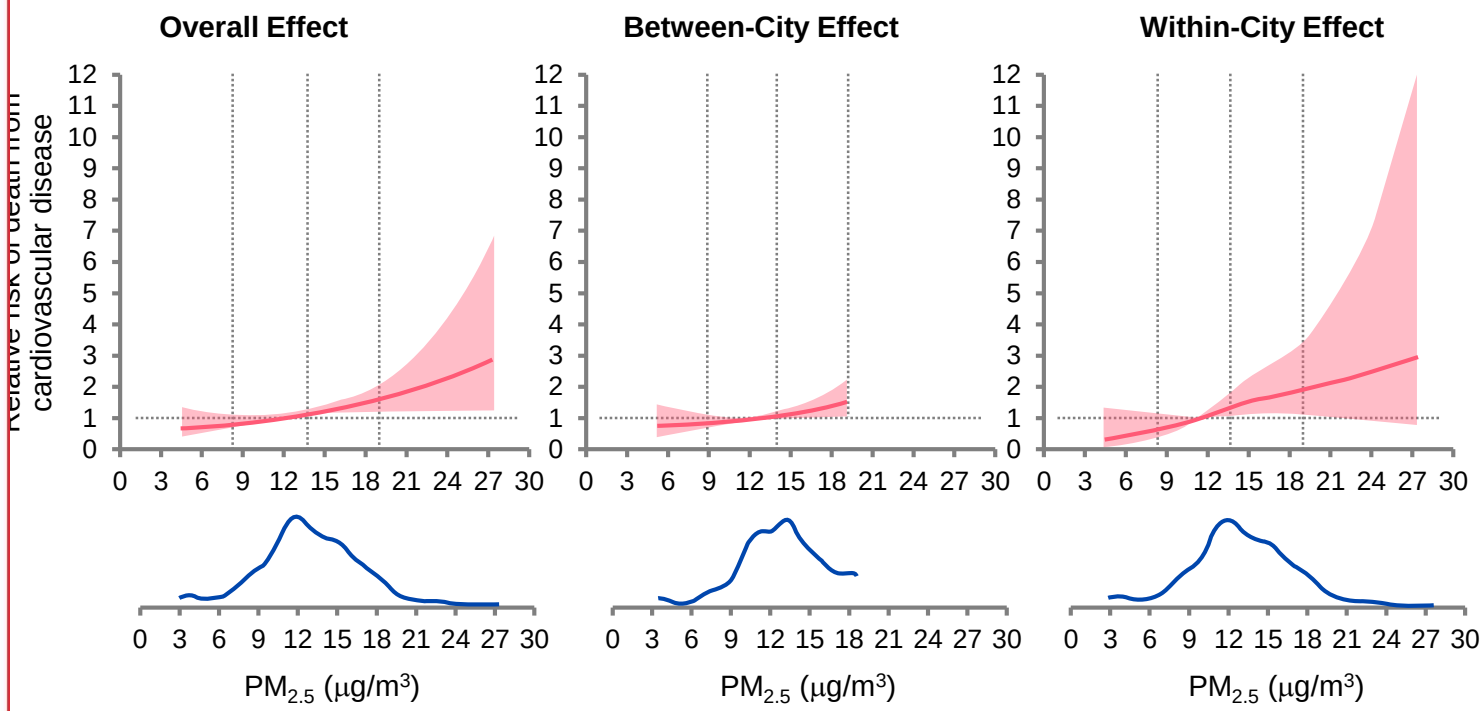


Münzel, T. et al. J Am Coll Cardiol. 2018;71(6):688-97.

Long-Term Exposure to Air Pollution and Incidence of Cardiovascular Events in Women

Kristin A. Miller, M.S., David S. Siscovick, M.D., M.P.H., Lianne Sheppard, Ph.D., Kristen Shepherd, M.S., Jeffrey H. Sullivan, M.D., M.H.S., Garnet L. Anderson, Ph.D., and Joel D. Kaufman, M.D., M.P.H.

We studied 65,893 postmenopausal women without previous cardiovascular disease in 36 U.S. metropolitan areas from 1994 to 1998, with a median follow-up of 6 years. We assessed the women's exposure to air pollutants



Miller et al: N Engl J Med 356:447, 2007

Traditional risk factors and Atherosclerosis

Smoking

Hypertension

Hypercholesterolemia

Age

Diabetes

Enviromental

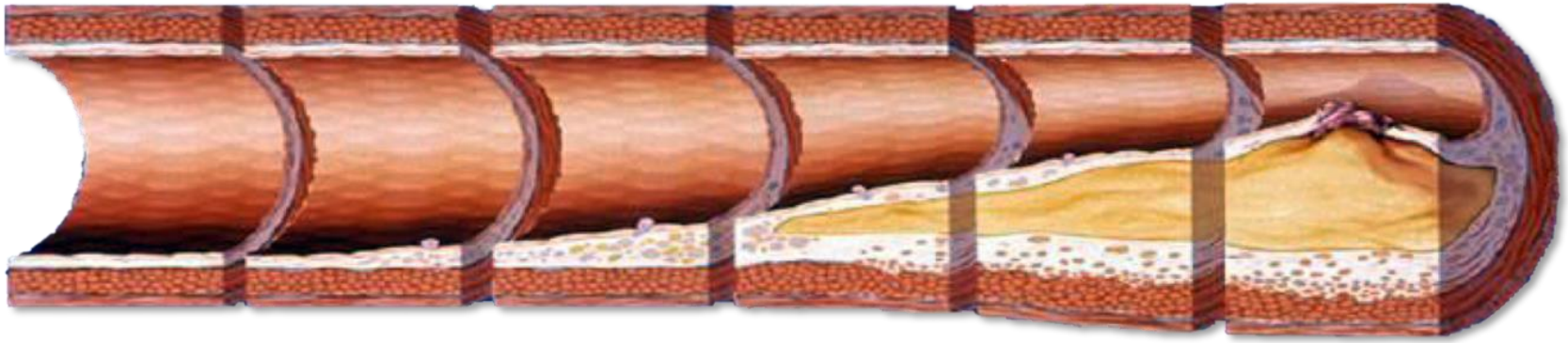
Vascular injury

Inflammation

Mental stress

Inflammation & oxidative stress

Endothelial dysfunction: The risk of the risk factors



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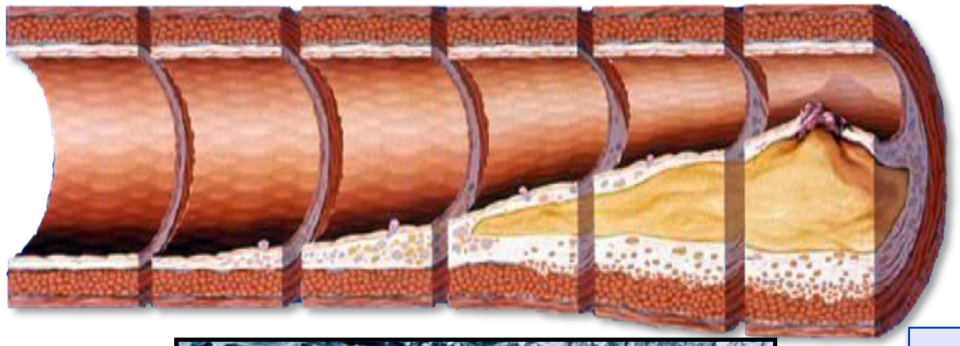
Non traditional (risk factors for CAD The) assessment of CAD risk



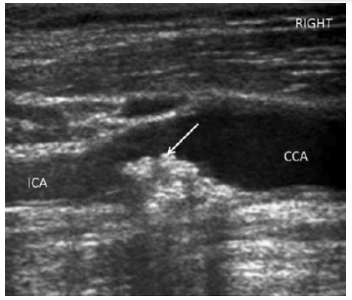
Vascular injury

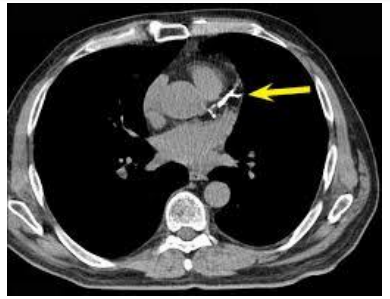
Assessment of the the disease process

Traditional and non traditional risk factors

Biomarkers of the disease
Inflammation &oxidative stress

Imaging assessment of the disease process

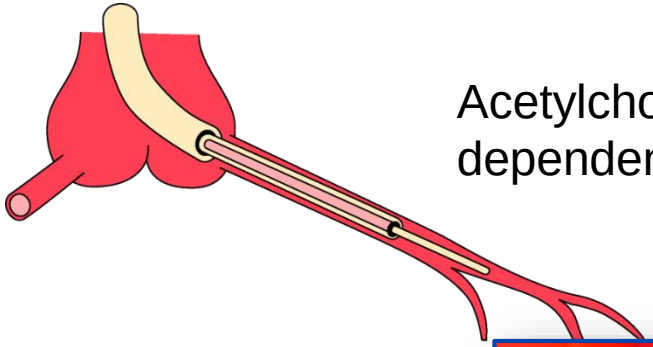




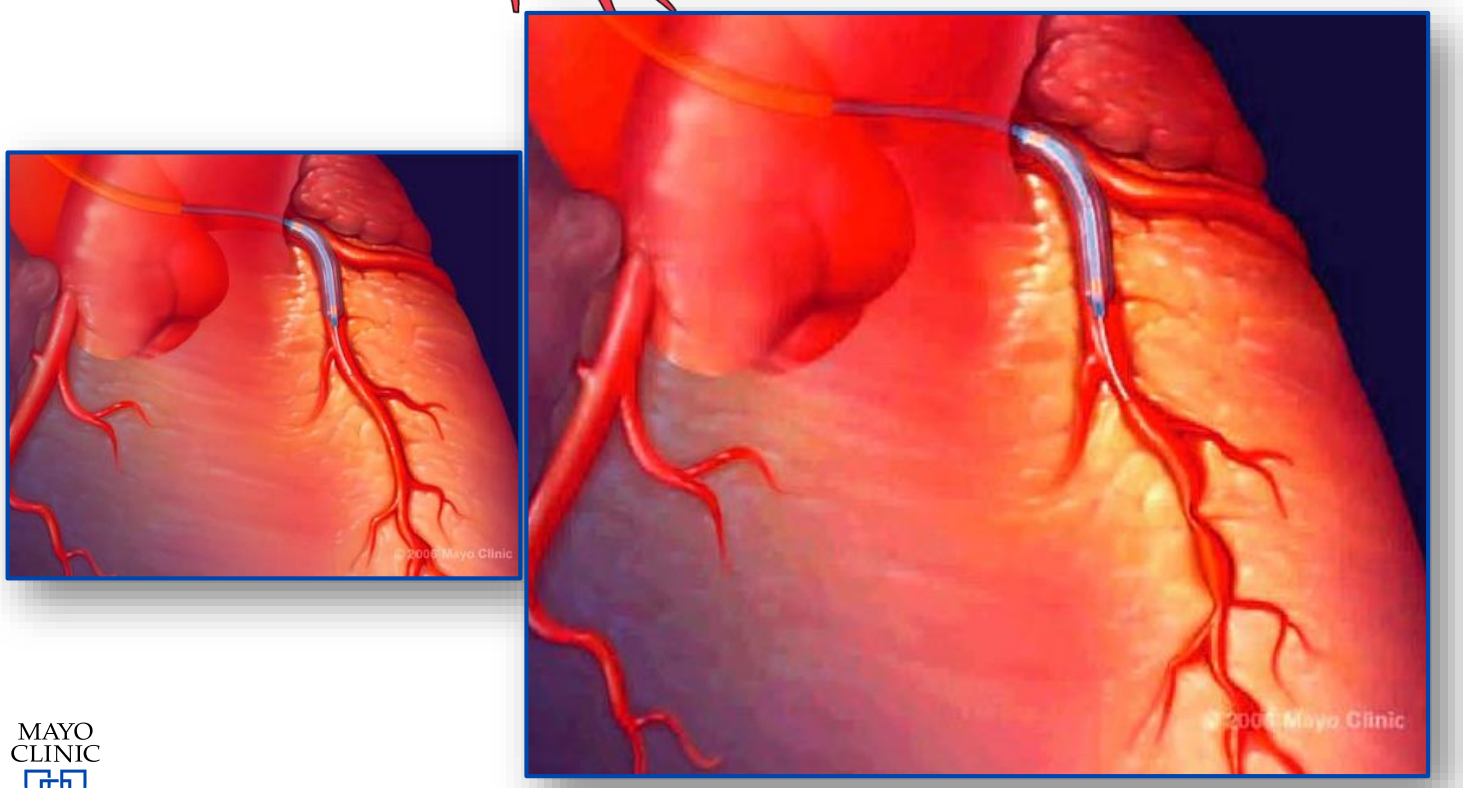
reversibility
Radiation
Accuracy
cost

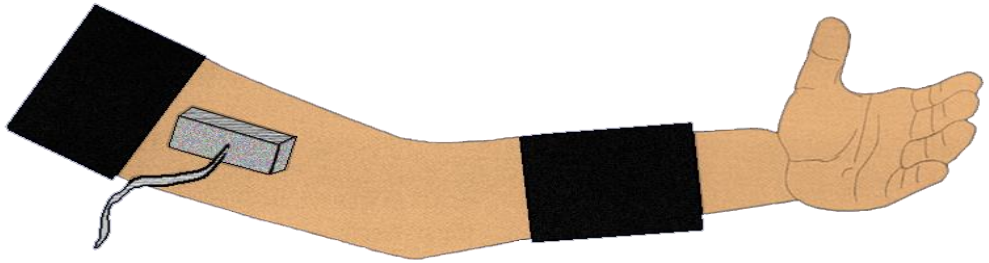
Functional assessment of the disease process

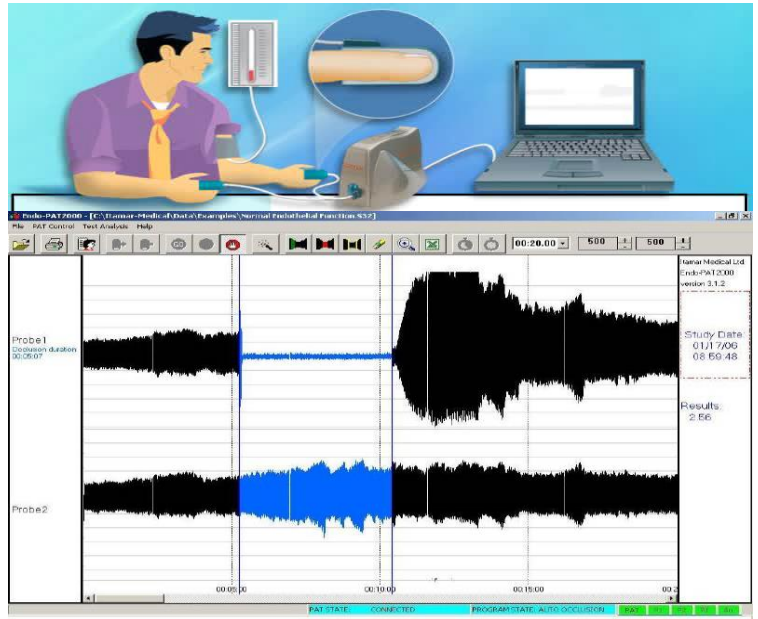
Assessment of Vascular Function:

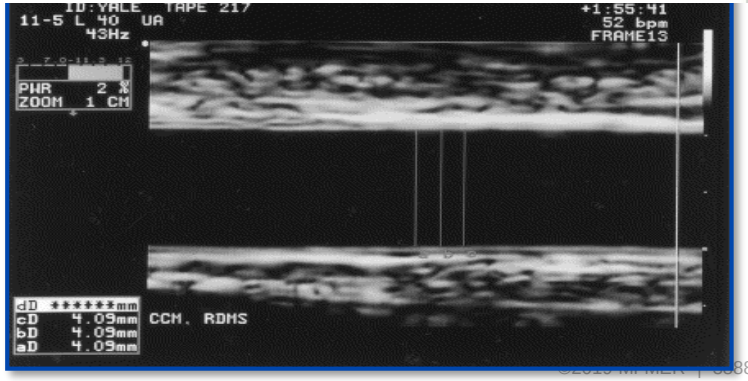


Acetylcholine (endothelium dependent vasodilator)









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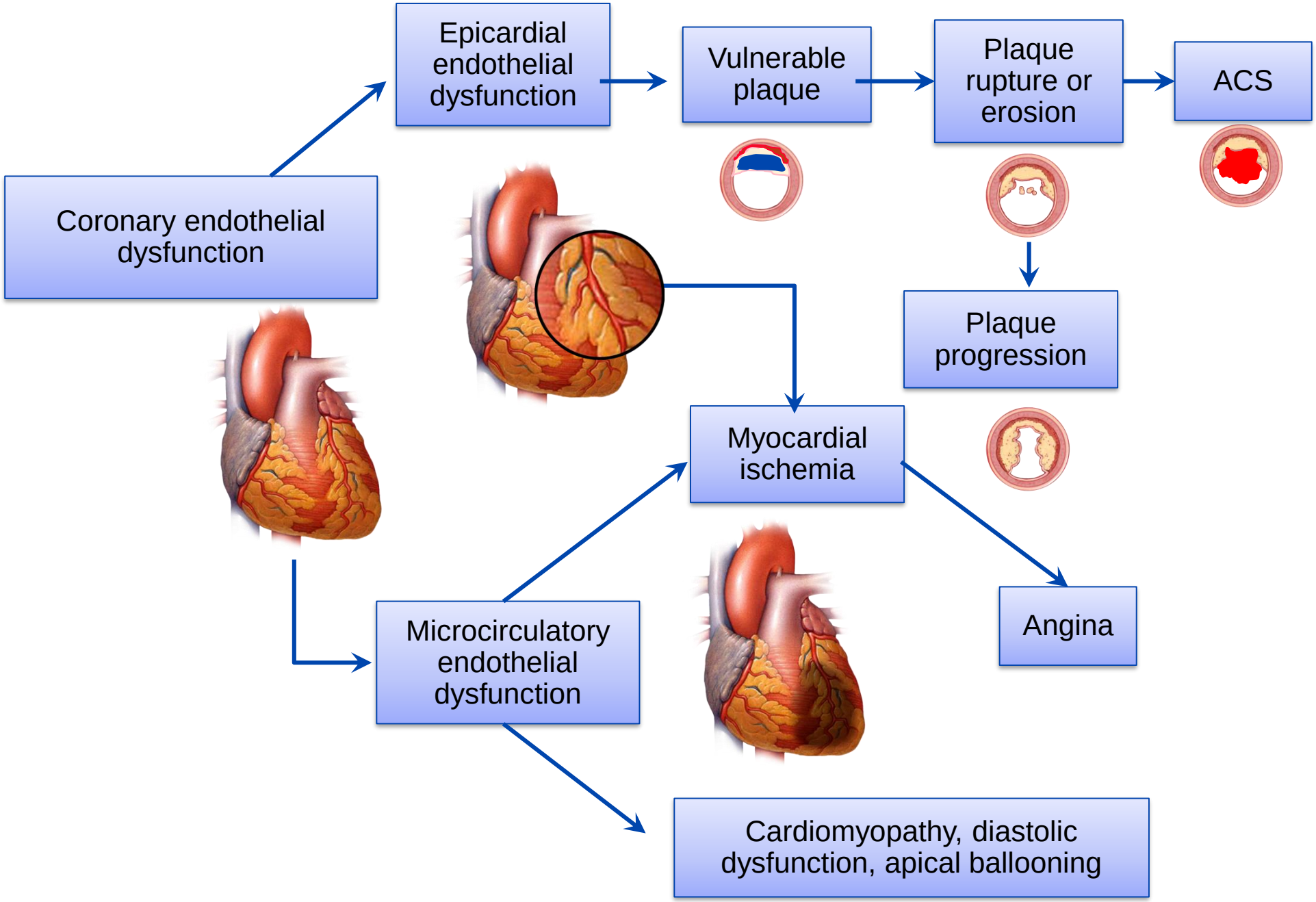

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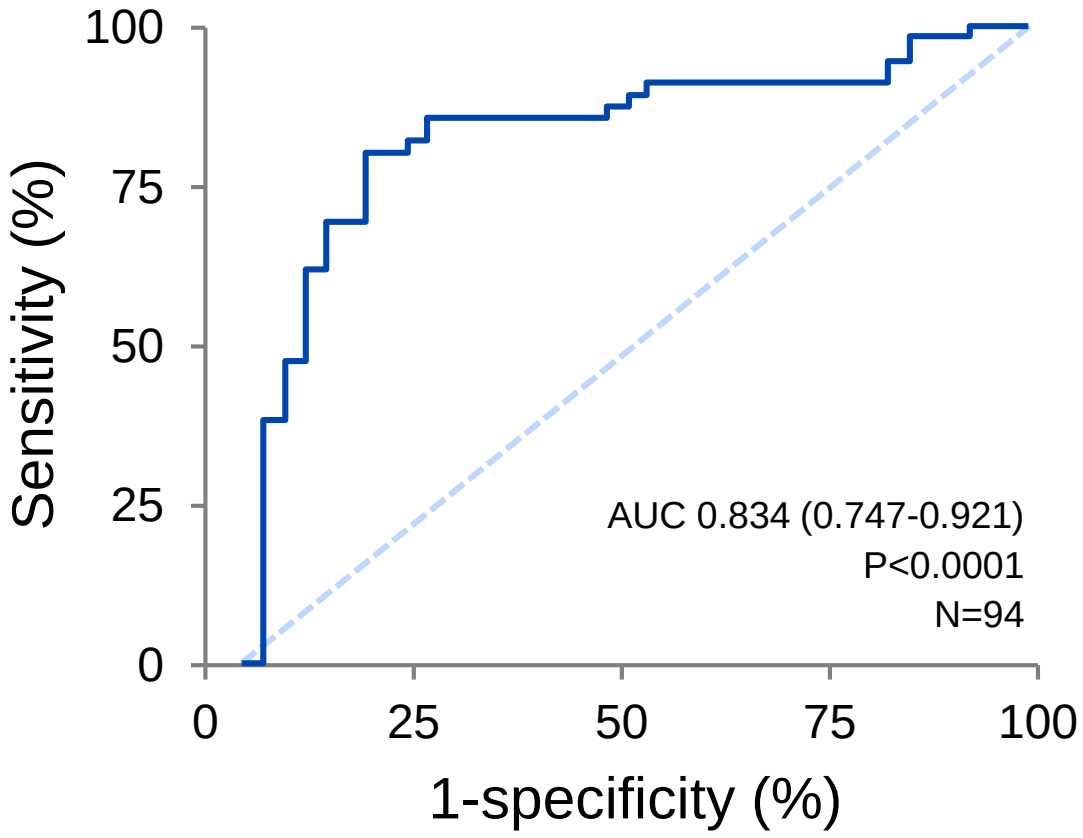
ISSN 0735-1097/04/$30.00
doi:10.1016/j.jacc.2004.08.062

Coronary Artery Disease

Noninvasive Identification of Patients With Early Coronary Atherosclerosis by Assessment of Digital Reactive Hyperemia

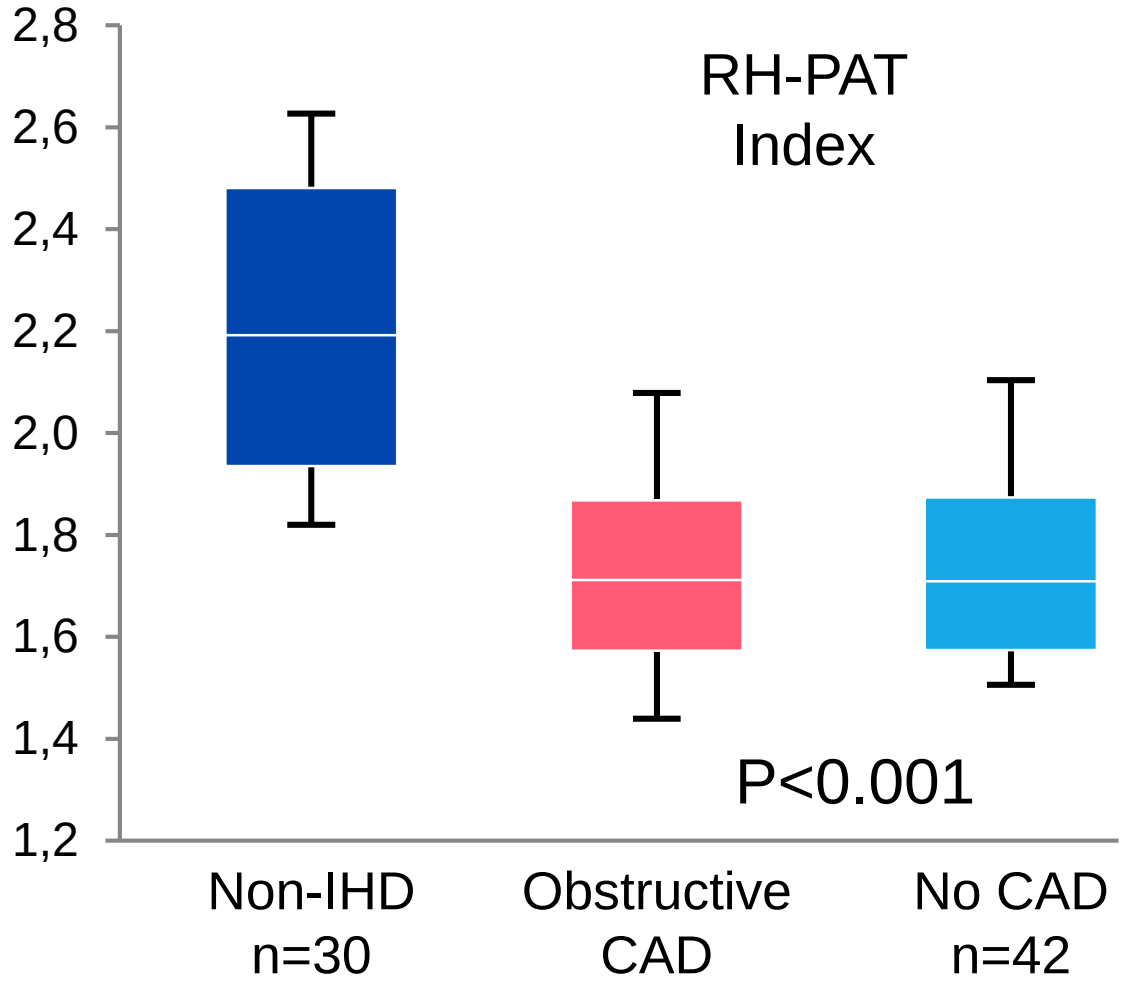
Piero O. Bonetti, MD,* Geralyn M. Pumper, RN,* Stuart T. Higano, MD, FACC,*
David R. Holmes, JR, MD, FACC,* Jeffrey T. Kuvin, MD, FACC,† Amir Lerman, MD, FACC*
Rochester, Minnesota; and Boston, Massachusetts



Bonetti & Lerman: JACC, 2004

Digital Assessment of Endothelial Function and Ischemic Heart Disease in Women

Yasushi Matsuzawa, MD,* Seigo Sugiyama, MD, PHD,* Koichi Sugamura, MD, PHD,*
Toshimitsu Nozaki, MD,* Keisuke Ohba, MD,* Masaaki Konishi, MD,* Junichi Matsubara, MD,*
Hitoshi Sumida, MD, PHD,* Koichi Kaikita, MD, PHD,* Sunao Kojima, MD, PHD,*
Yasuhiro Nagayoshi, MD, PHD,* Megumi Yamamuro, MD, PHD,* Yasuhiro Izumiya, MD, PHD,*
Satomi Iwashita, MT,* Kunihiko Matsui, MD, PHD,† Hideaki Jinnouchi, MD, PHD,‡
Kazuo Kimura, MD, PHD,§ Satoshi Umemura, MD, PHD,‖ Hisao Ogawa, MD, PHD*
Kumamoto and Yokohama, Japan



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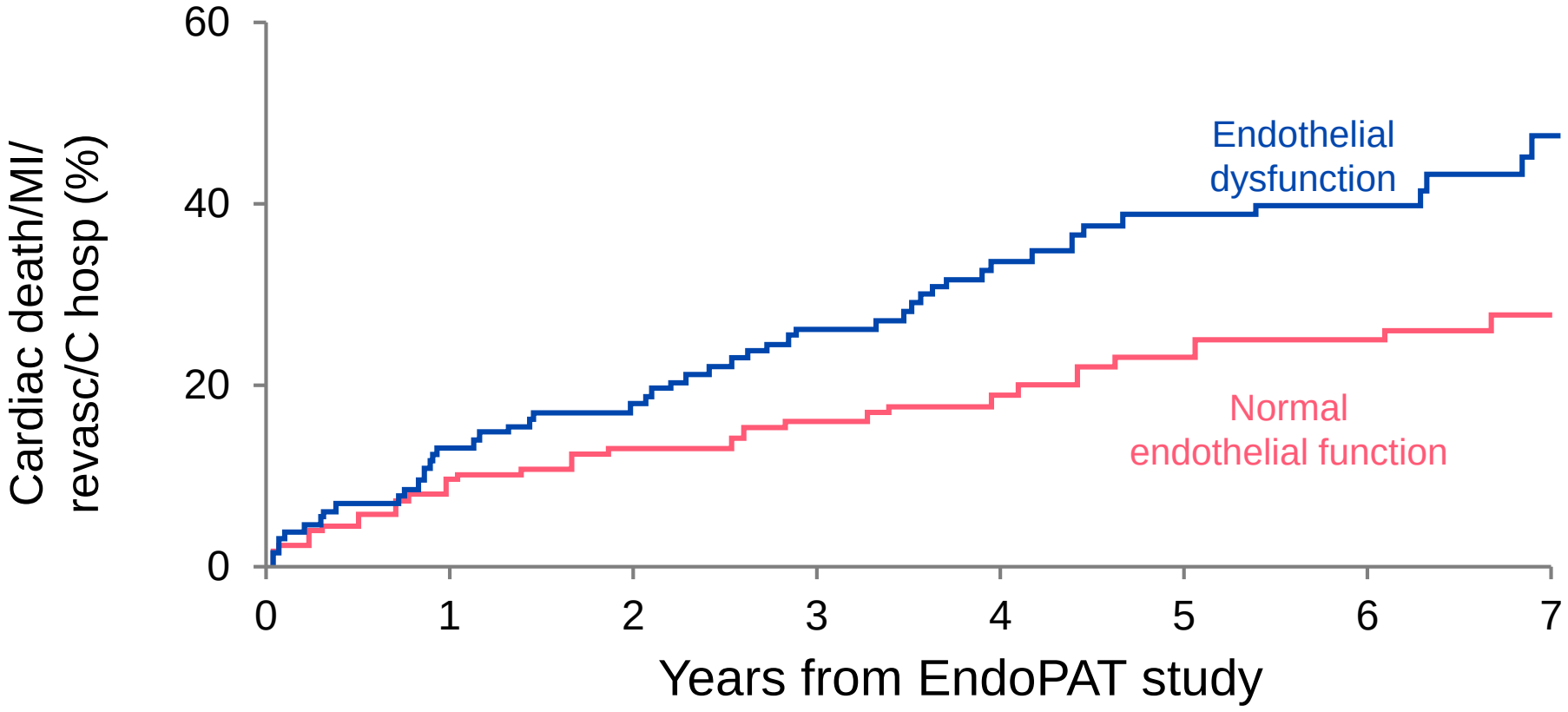
Cardiac Events in Patients With Low Framingham Score & Abnormal Peripheral Endothelial Function



Rubinshtein and Lerman: Euro Heart J, 2010

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ORIGINAL RESEARCH

American Heart Association | American Stroke Association

Prognostic Value of Flow-Mediated Vasodilation in Brachial Artery and Fingertip Artery for Cardiovascular Events: A Systematic Review and Meta-Analysis

Yasushi Matsuzawa, MD, PhD; Taek-Geun Kwon, MD, PhD; Ryan J. Lennon, MS; Lilach O. Lerman, MD, PhD; Amir Lerman, MD

Background—Endothelial dysfunction plays a pivotal role in cardiovascular disease progression, and is associated with adverse events. The purpose of this systematic review and meta-analysis was to investigate the prognostic magnitude of noninvasive peripheral endothelial function tests, brachial artery flow-mediated dilation (FMD), and reactive hyperemia—peripheral arterial tonometry (RH-PAT) for future cardiovascular events.

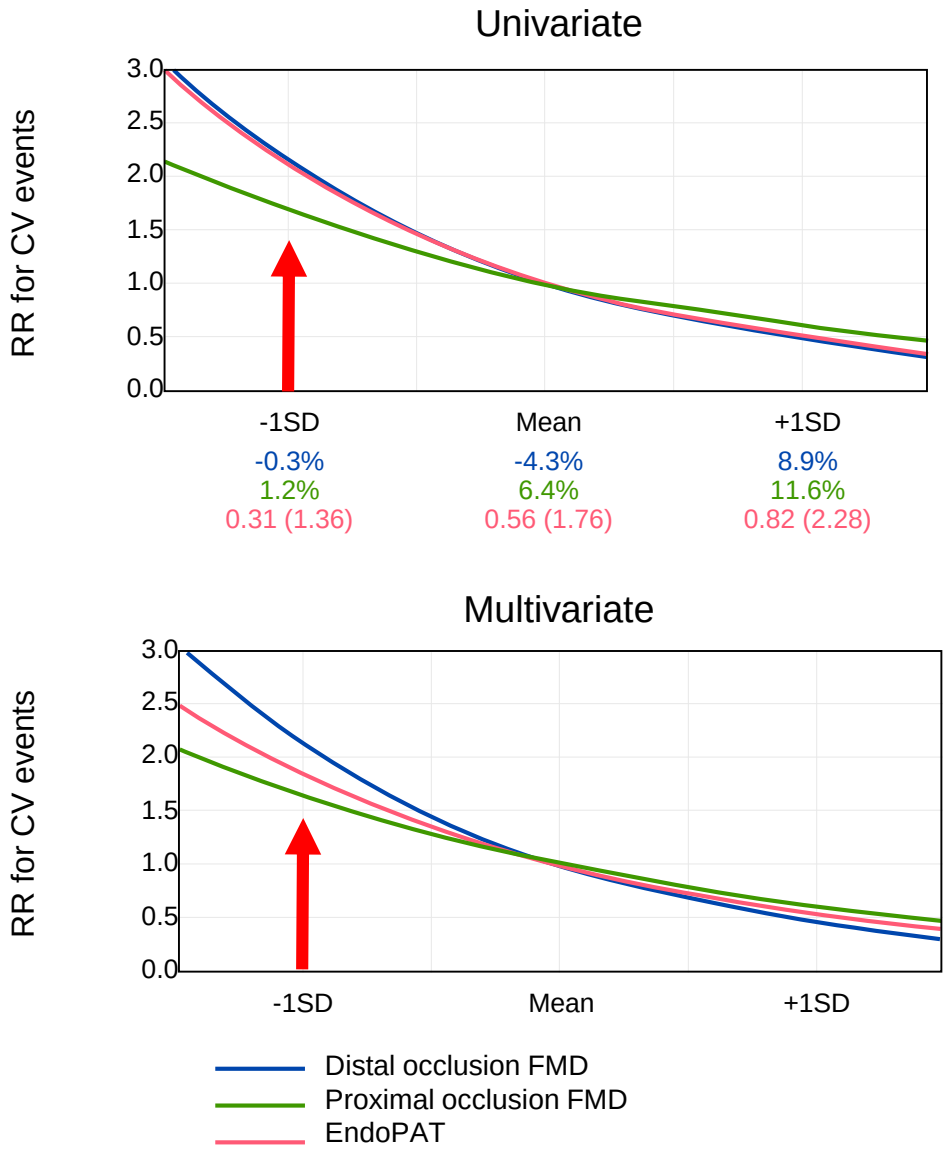
- Thirty-five FMD studies of 17 280 participants and 6 RH-PAT studies of 602 participants were included in the meta-analysis.
- The magnitude of the prognostic value in cardiovascular disease subjects was comparable between these 2 methods

Mayo Clinic, Rochester, MN.

during cardiac catheterization. More recently, several nonin-

A 1 SD worsening in endothelial function was associated with double cardiovascular risk.

Relative Risk for FMD and Endo PAT



JAMA Cardiology | Original Investigation

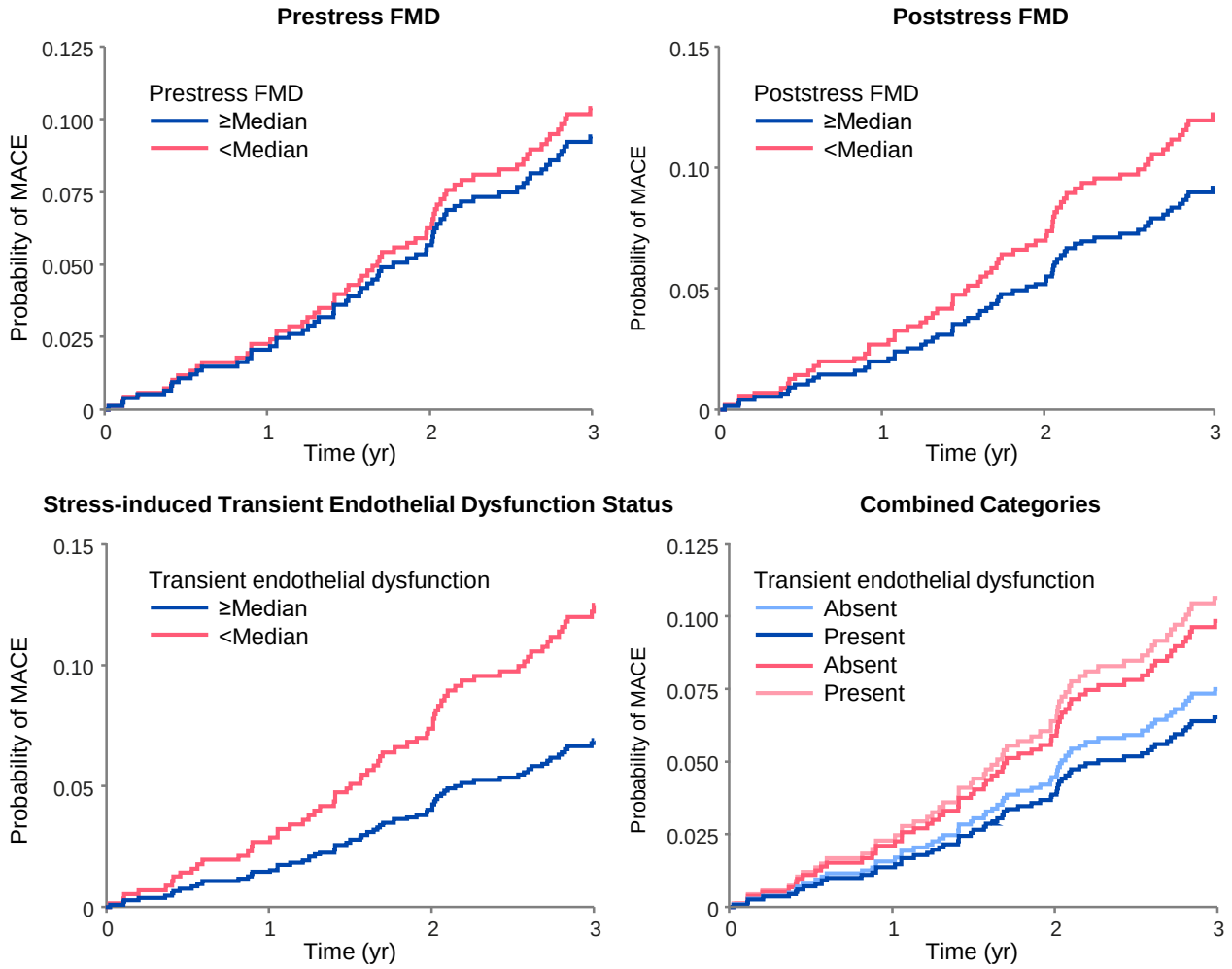
Association of Transient Endothelial Dysfunction Induced by Mental Stress With Major Adverse Cardiovascular Events in Men and Women With Coronary Artery Disease

Bruno B. Lima, MD, PhD; Muhammad Hammadah, MD; Jeong Hwan Kim, MD; Irina Uphoff, MD; Amit Shah, MD; Oleksiy Levantsevych, MD; Zakaria Almuwaqqat, MD; Kasra Moazzami, MD; Samaah Sullivan, PhD; Laura Ward, MPH; Michael Kutner, PhD; Yi-An Ko, PhD; David S Sheps, MD, MSPH; J. Douglas Bremner, MD; Arshed A. Quyyumi, MD; Viola Vaccarino, MD, PhD

OBJECTIVE To determine the association between mental stress-induced impairment in endothelium-dependent relaxation as

EXPOSURES Study participants were subjected to a laboratory mental stress task (public speaking).

Adjusted Cumulative Incidence of Major Adverse Cardiovascular Events (MACEs) According to Flow-Mediated Vasodilation (FMD) Levels



Lima B. et al: JAMA Cardiol E1, 2019

MAYO CLINIC

Can We use Endothelial Function to Individualize Therapy?

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PII S0735-1097(02)01976-9

Women and Cardiovascular Disease

Prognostic Role of Reversible Endothelial Dysfunction in Hypertensive Postmenopausal Women

Maria G. Modena, MD, FESC, FACC, Lorenzo Bonetti, MD, Francesca Coppi, MD, Francesca Bursi, MD, Rosario Rossi, MD

Modena, Italy

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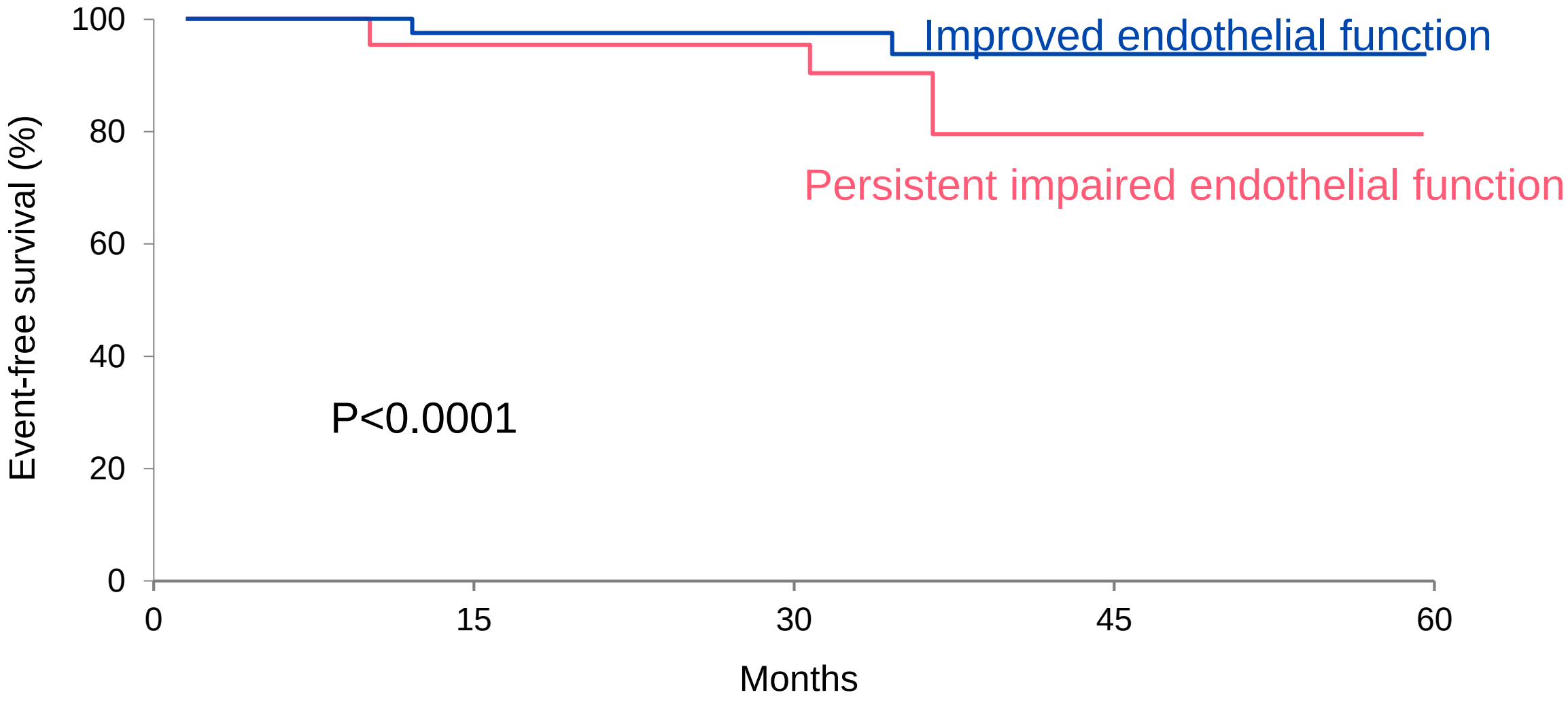
Persistent Impairment of Endothelial Vasomotor Function Has a Negative Impact on Outcome in Patients With Coronary Artery Disease

Yoshinobu Kitta, MD, PHD, Jyun-ei Obata, MD, PHD, Takamitsu Nakamura, MD, Mitsumasa Hirano, MD, Yasushi Kodama, MD, Daisuke Fujioka, MD, PHD, Yukio Saito, MD, Ken-ichi Kawabata, MD, PHD, Keita Sano, MD, Tsuyoshi Kobayashi, MD, Toshiaki Yano, MD, Kazuto Nakamura, MD, PHD, Kiyotaka Kugiyama, MD, PHD

Yamanashi, Japan

MAYO CLINIC

Event-Free Rate According to Persistent Endothelial Dysfunction in Patients With Mild CAD



Modena et al: JACC 40, 2002

MAYO CLINIC

Laughing your way to lower blood pressure and less stress

May 15, 2008 | Michael O'Riordan

ASH news New Orleans, LA - Laughter is the best medicine, a cliché to be sure, but a new study has shown that laughter yoga, a blend of playful laughter exercises coupled with gentle breathing and stretching, can significantly lower systolic and diastolic blood-pressure levels, as well as bring about significant reductions in the stress hormone cortisol [1].

Dr Madan Kataria

"Laughter yoga is a concept where anybody can laugh for no reason at all," Dr Madan Kataria, lead investigator of the study and founder of the Laughter Yoga school. "You don't need any jokes, any humor, or any comedy. You don't even need to be happy. What we do is laugh in a group and initiate laughter as a form of bodily exercise, but when we have eye contact with others, this laughter becomes real and contagious."

This laughter, explained Kataria, when combined with yoga breathing to bring more oxygen to the body and brain, results in significant biological and physiological changes, such as the reductions in blood-pressure and stress levels.

Speaking with heartwire here at the American Society of Hypertension 2008 Annual Meeting, Kataria said the idea of laughter yoga began in 1995 with just five participants in Mumbai, India. Now there are more than 6000 laughter clubs in 60 countries, and the present study was designed to show that real health benefits could be obtained from this simple form of exercise.

Pet Ownership, but Not ACE Inhibitor Therapy, Blunts Home Blood Pressure Responses to Mental Stress

Karen Allen, Barbara E. Shykoff, Joseph L. Izzo, Jr

Abstract—In the present study, we evaluated the effect of a nonevaluative social support intervention (pet ownership) on blood pressure response to mental stress before and during ACE inhibitor therapy. Forty-eight hypertensive individuals participated in an experiment at home and in the physician's office. Participants were randomized to an experimental group with assignment of pet ownership in addition to lisinopril (20 mg/d) or to a control group with only lisinopril (20

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Wine, Nicotine, and Cardiovascular Disease

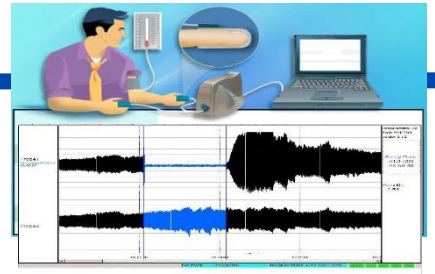
Red Wine Increases the Expression of Human Endothelial Nitric Oxide Synthase

A Mechanism That May Contribute to its Beneficial Cardiovascular Effects

Thomas Wallerath, PHD, Daniela Poleo, Huige Li, MD, PHD, Ulrich Förstermann, MD, PHD
Mainz, Germany

Smoking | Hypertension | Hypercholesterolemia | Obesity | Diabetes

Normal endothelial Function



Endothelial Dysfunction

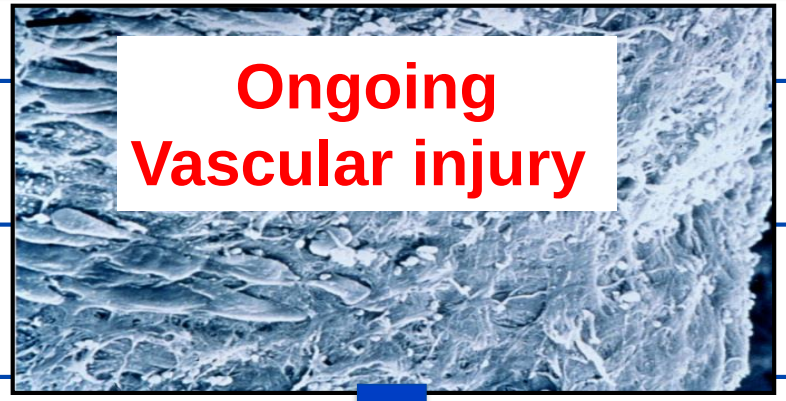
Continue current management

Ongoing CV risk and Events

Hypothyroidism

Sleep Apnea

Metabolic syndrome



Inflammation

Mental stress

Arrhythmias
A Fib

Modify current management

MAYO CLINIC

Gender Differences on Impact of Heavy Snowfalls and SCD–Olmsted County

Gerber. JACC, 2006

MAYO CLINIC