

Cardiovascular Risk and Cognition

Ralph L. Sacco, MS MD FAAN FAHA

Olemberg Family Chair in Neurological Disorders

**Miller Professor of Neurology, Public Health Sciences,
Human Genetics, & Neurosurgery**

Executive Director, Evelyn McKnight Brain Institute

Miller School of Medicine, University of Miami

Jackson Memorial Hospital

**Supported by grants R37 NS 29993, U54 NS 081763, R01 NS 240807, R01 42912,
047655, DE 13094, Evelyn McKnight Brain Institute**

**Consultant: Boehringer Ingelheim (RESPECT),
UCSF (SOCRATES DSMB), DCRI (EUCLID DSMB)**



Cardiovascular Risk and Cognition

- **Vascular Disease and Cognition**
- **Findings from NOMAS**
 - GQRS and Successful Cognitive Aging
 - Metabolic Syndrome and Cognition
 - AHA Ideal CV Health and Cognitive Decline
- **Heart function and Brain Aging**
 - Cardiac Index
 - LV Ejection Fraction
 - Global longitudinal Strain and LV Systolic Dysfunction

Relationships between Vascular and Neurodegenerative Processes in Cognitive Impairment and Dementia

- It is accepted that many traditional risk factors for stroke are also risk markers for AD and VCI
- There may be a convergence of pathogenic mechanisms in vascular and neurodegenerative processes which cause cognitive impairment
- Epidemiologic studies also point to linkages between traditional CV risk factors and AD risk

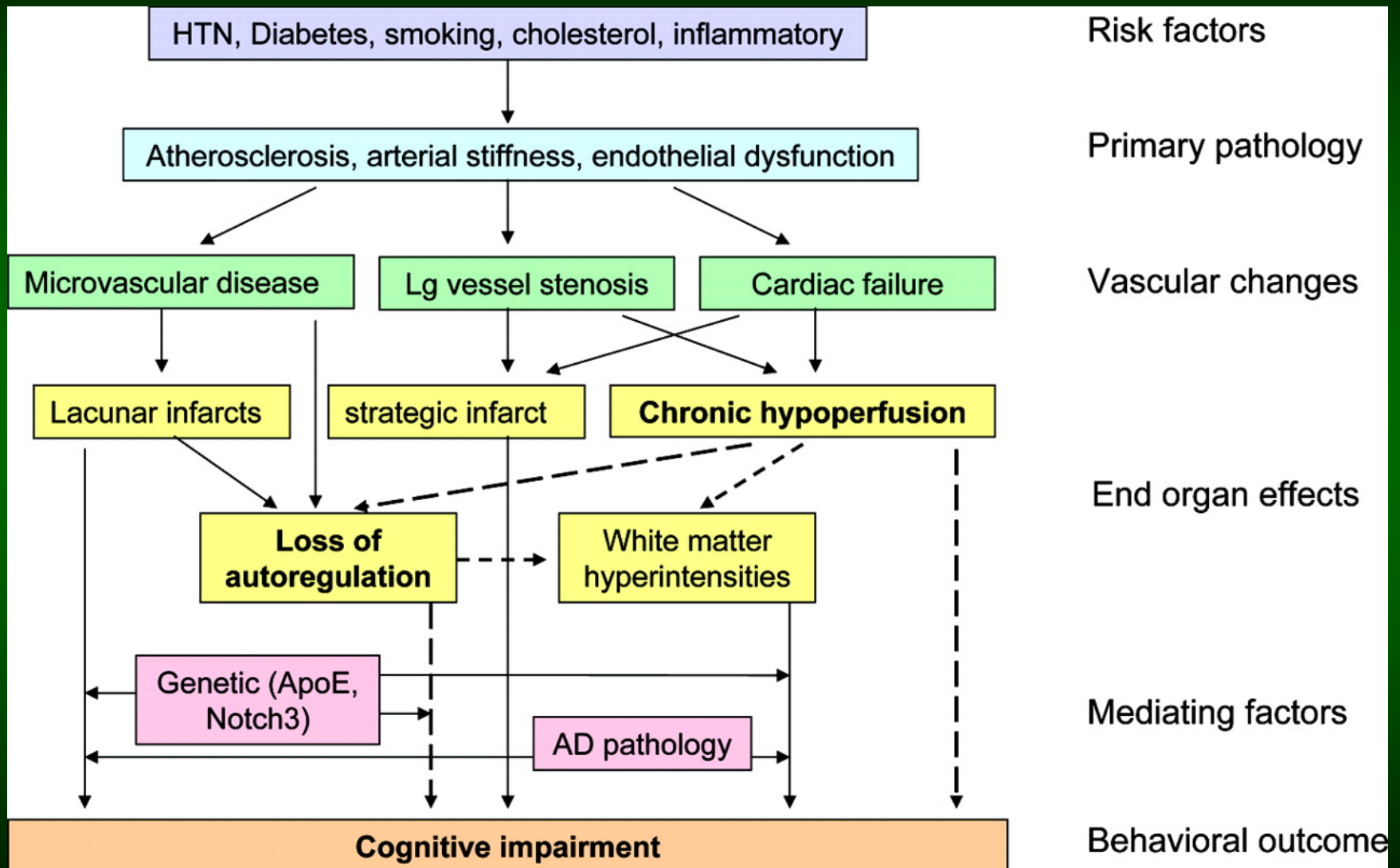
Vascular Contributions to Cognitive Impairment and Dementia : A Statement for Healthcare Professionals From the American Heart Association/American Stroke Association

Philip B. Gorelick, Angelo Scuteri, Sandra E. Black, Charles DeCarli, Steven M. Greenberg, Costantino Iadecola, Lenore J. Launer, Stephane Laurent, Oscar L. Lopez, David Nyenhuis, Ronald C. Petersen, Julie A. Schneider, Christophe Tzourio, Donna K. Arnett, David A. Bennett, Helena C. Chui, Randall T. Higashida, Ruth Lindquist, Peter M. Nilsson, Gustavo C. Roman, Frank W. Sellke and Sudha Seshadri

Stroke published online July 21, 2011

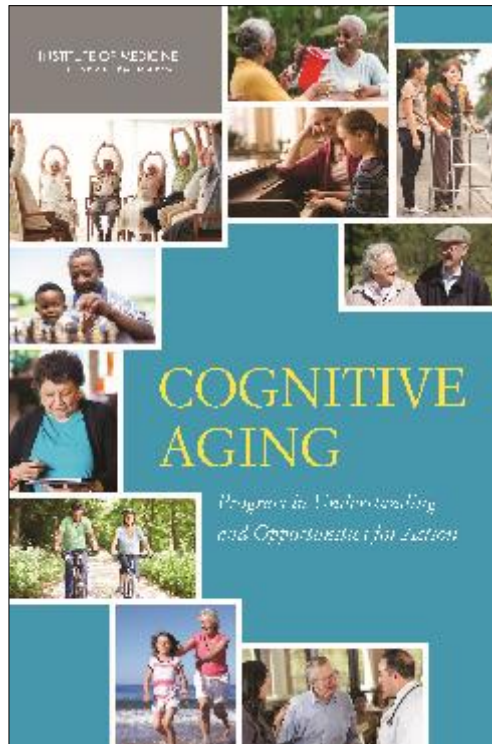
Gorelick et al. Vascular Contributions to Cognitive Impairment and Dementia. AHA/ASA Scientific Statement. *Stroke*; 2011

Model for the Pathophysiology of VCI



Cognitive Aging: Progress in Understanding and Opportunities for Action

[www/iom.edu/cognitiveaging](http://www.iom.edu/cognitiveaging)



Suggested citation: IOM (Institute of Medicine). 2015. *Cognitive aging: Progress in understanding and opportunities for action*. Washington, DC: The National Academies Press.

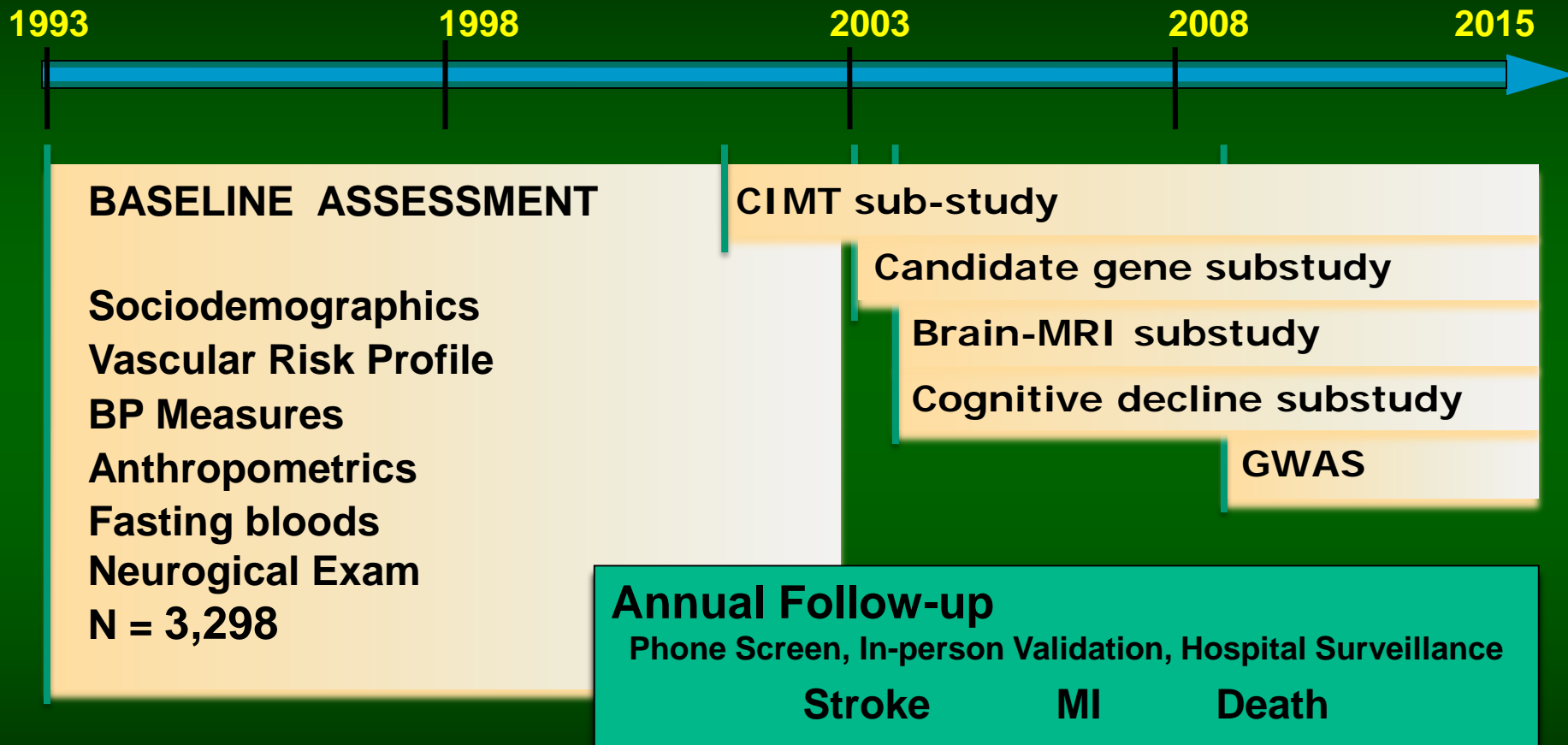
INSTITUTE OF MEDICINE
OF THE NATIONAL ACADEMIES

IOM Report Cognitive Aging

- 1. Increase Research and Tools for Assessing Cognitive Aging and Cognitive Trajectories**
- 2. Collect and Disseminate Population-based data on Cognitive Aging**
 - high-risk populations, longitudinal assessments, diverse populations
- 3. Take Actions to Reduce Risks of Cognitive Decline with Age**
 - Physically active
 - Reduce and manage CV disease risk factors
- 4. Increase Research on Risk and Protective Factors and Interventions**

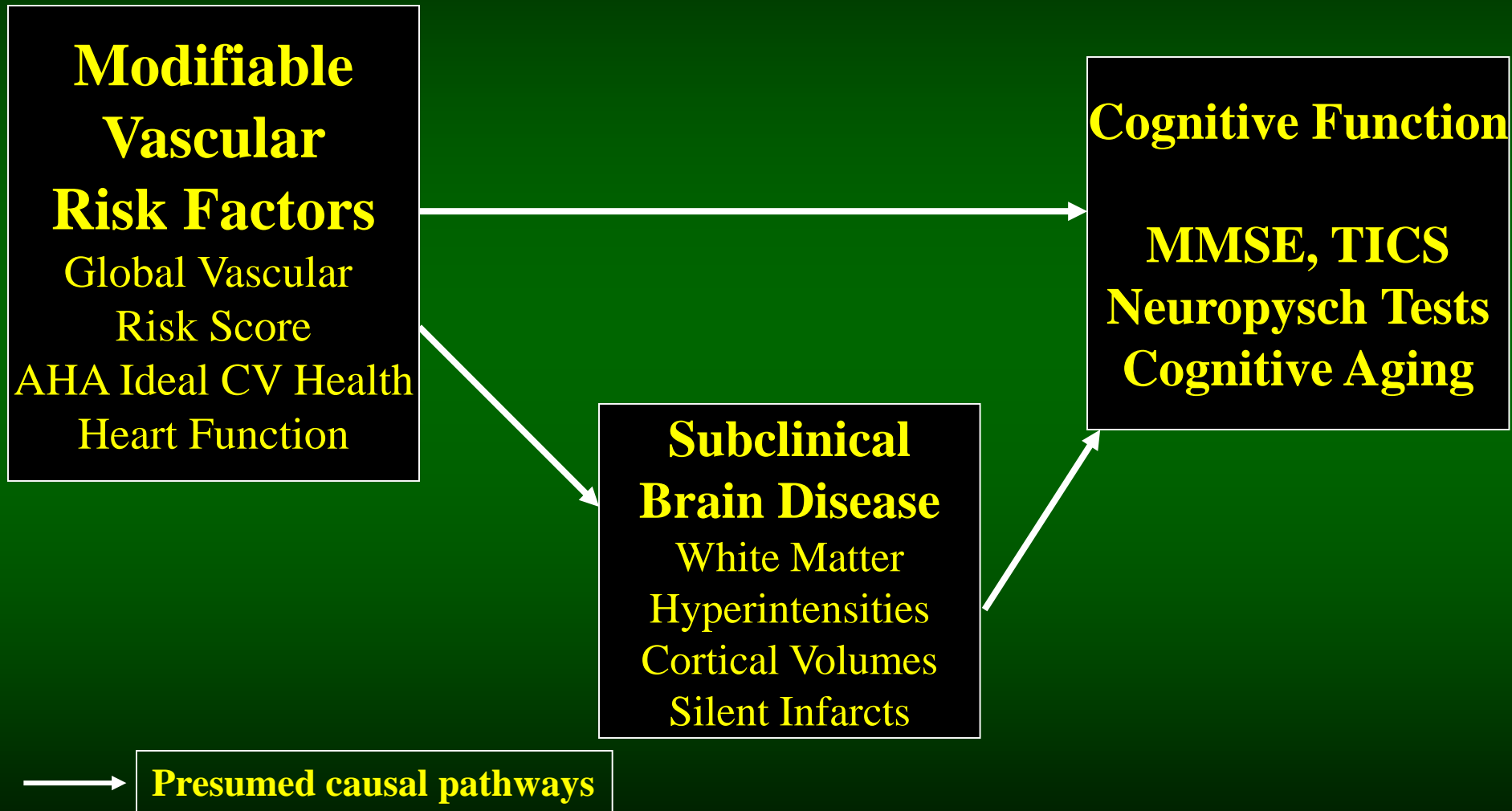
NORTHERN MANHATTAN STUDY

Prospective Cohort



Funding: NINDS R37 NS 29993 (Sacco), R01 NS 40807 (Sacco), R01 HL 108623 (Wright), K24 (Rundek), R01 NS 047655 (Rundek), R01 NS 36286 (Di Tullio), R01 DE 013094 (Desvarieux), Evelyn McKnight Brain Institute

Northern Manhattan Study



Association Between Northern Manhattan Study Global Vascular Risk Score and Successful Aging

Jessica R. L. Warsch, MD, PhD,^{*} Tatjana Rundek, MD, PhD,^{*} Myunghee C. Paik, PhD,[†]
Mitchell S. V. Elkind, MD, MS,^{‡§} Ralph L. Sacco, MD, MS,^{*||} and Clinton B. Wright, MD, MS^{*||}
J Am Geriatr Soc 61:519–524, 2013

Physical activity and cognition in the Northern Manhattan Study

Joshua Z Willey, MD, MS, Yeseon Park Moon, MS, Rachel Ruder, BA, Yuen K Cheung, PhD,
Ralph L. Sacco, MD, MS, Mitchell S.V. Elkind, MD, MS, and Clinton B. Wright, MD, MS

McKnight Brain Institute, University of Miami, Miami, FL *Neuroepidemiology*. 2014

CKD Associates with Cognitive Decline

J Am Soc Nephrol 20: 2427–2432, 2009.

Minesh Khatri,^{*} Thomas Nickolas,[†] Yeseon P. Moon,[‡] Myunghee C. Paik,[‡] Tatjana Rundek,[§]
Mitchell S. V. Elkind,^{||} Ralph L. Sacco,[§] and Clinton B. Wright[§] *J Am Soc Nephrol* 20: 2427–2432, 2009.

Modeling Metabolic Syndrome and Its Association with Cognition: The Northern Manhattan Study

Journal of the International Neuropsychological Society (2014), 20, 951–960.

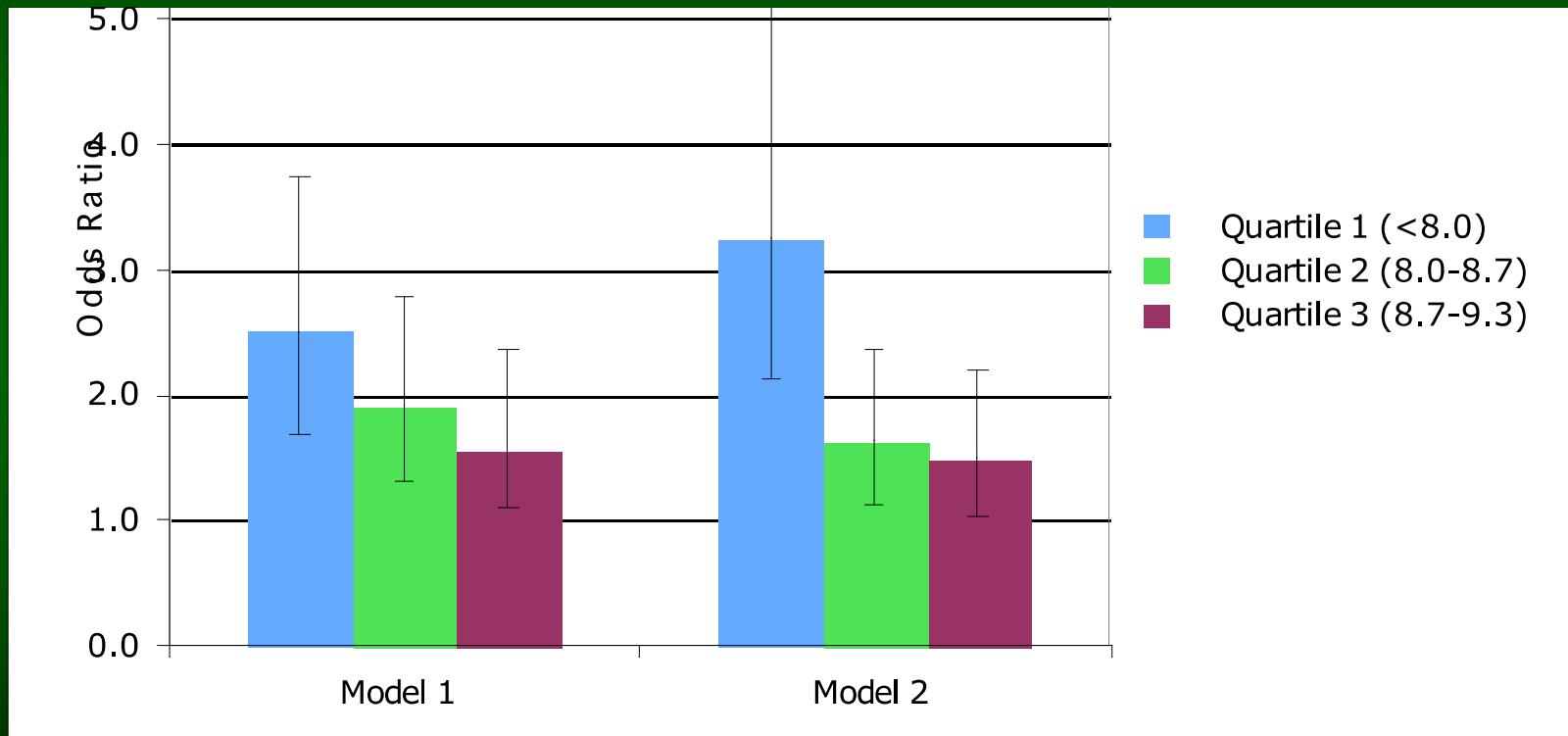
Bonnie E. Levin,^{1,2} Maria M. Llabre,² Chuanhui Dong,¹ Mitchell S.V. Elkind,³ Yaakov Stern,⁴ Tatjana Rundek,^{1,5}
Ralph L. Sacco,^{1,5,6} AND Clinton B. Wright^{1,6}

¹Evelyn F. McKnight Brain Institute, Department of Neurology, University of Miami Leonard M. Miller School of Medicine, Miami, Florida

Association Between Northern Manhattan Study Global Vascular Risk Score and Successful Aging

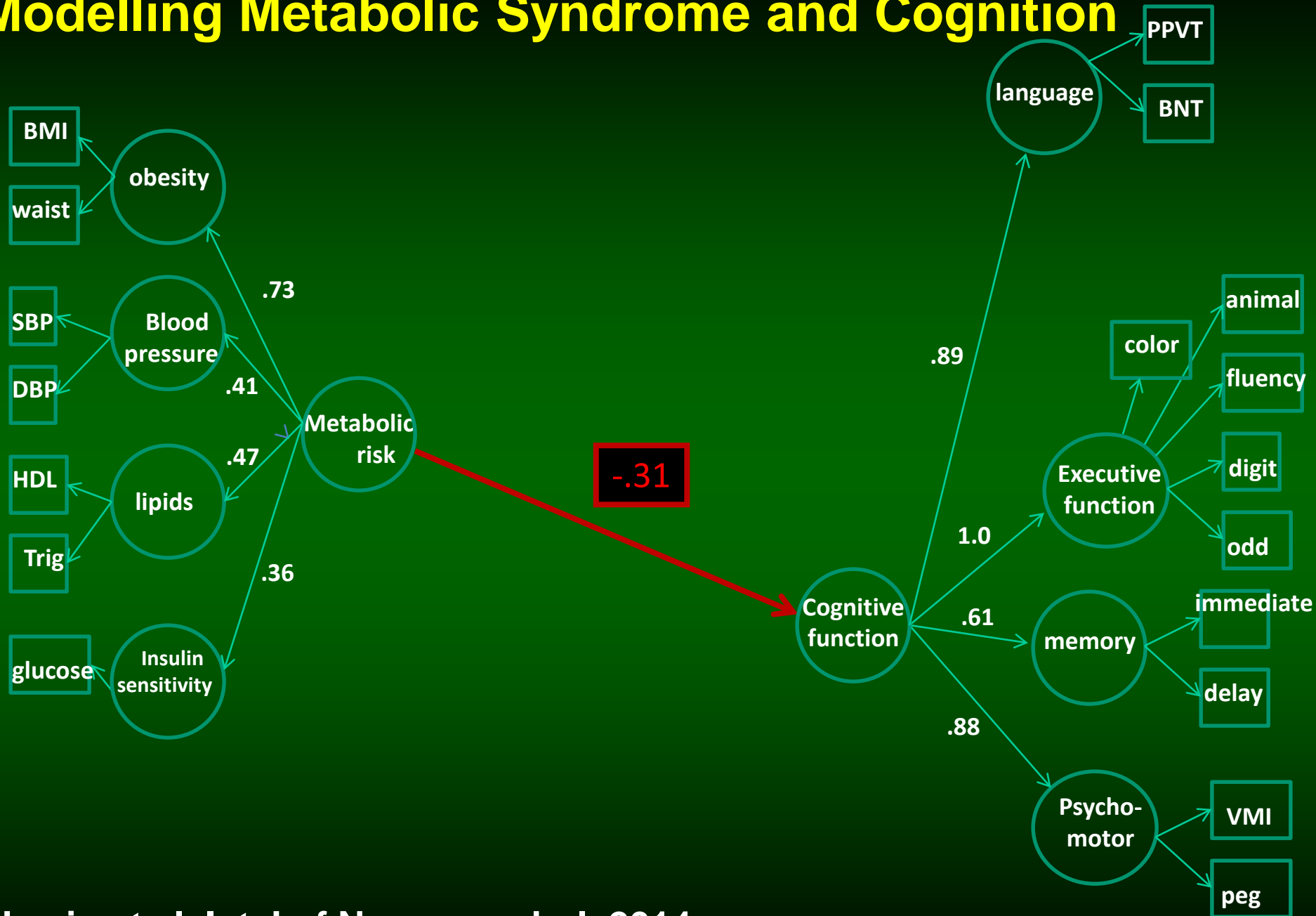
Jessica R. L. Warsch, MD, PhD,* Tatjana Rundek, MD, PhD,* Myunghee C. Paik, PhD,†
Mitchell S. V. Elkind, MD, MS,‡§ Ralph L. Sacco, MD, MS,*|| and Clinton B. Wright, MD, MS*||

J Am Geriatr Soc 61:519–524, 2013

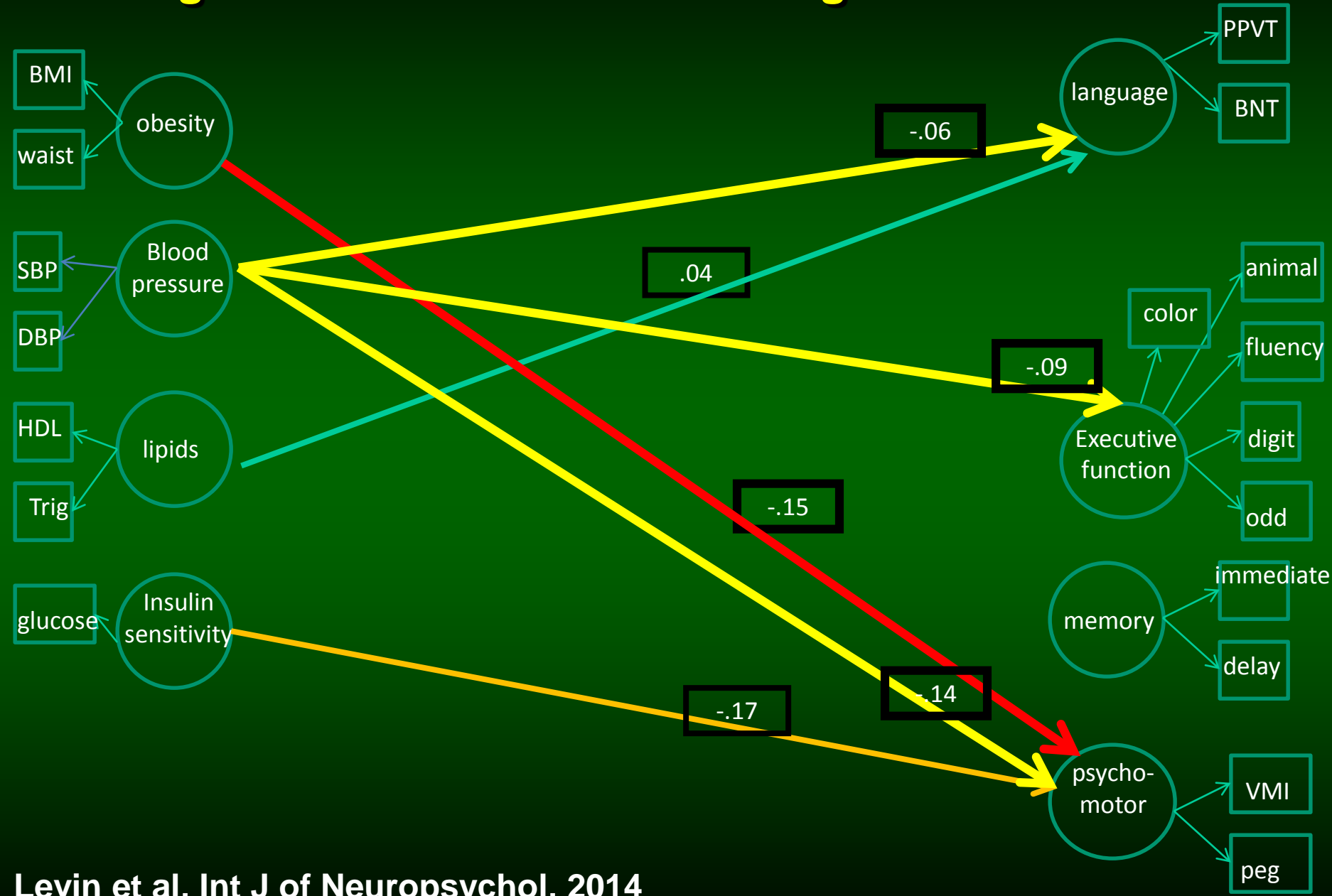


Odds ratio for Successful Aging without cognitive decline and better GVRS scores
Model 1 adjusted for length of time between baseline and follow-up cognitive testing only
Model 2 adjusted for years of education, health insurance status, and follow-up time.

Modelling Metabolic Syndrome and Cognition



Links between cardiometabolic risk factors and cognitive factors after controlling for covariates



Classification of Cardiovascular Health

Life's Simple 7

	Ideal	Intermediate	Poor
Smoking	Never or quit > 1 year	Quit < 1 year	Current
BMI	< 25 kg/m ²	25 - <30 kg/m ²	≥ 30 kg/m ²
Physical activity	≥ 75 min/wk vigorous or ≥ 150 min/wk moderate or equivalent combination	1-74 min/wk vigorous or 1-149 min/wk moderate or equivalent combination	No moderate or vigorous activity
Diet	4-5 healthy components	2-3 healthy components	0-1 healthy components
Blood pressure	Untreated & SBP < 120 & DBP < 80 mmHg	Treated to <120/<80 or 120-139/80-89 mmHg	SBP ≥ 140 mmHg or DBP ≥ 90 mmHg
Fasting glucose	Untreated & < 100 mg/dL	Treated to <100 mg/dL or 100-125 mg/dL	>125mg/dL
Total cholesterol	Untreated & < 200 mg/dL	Treated to < 200 mg/dL or 200-239 mg/dL	≥ 240 mg/dL

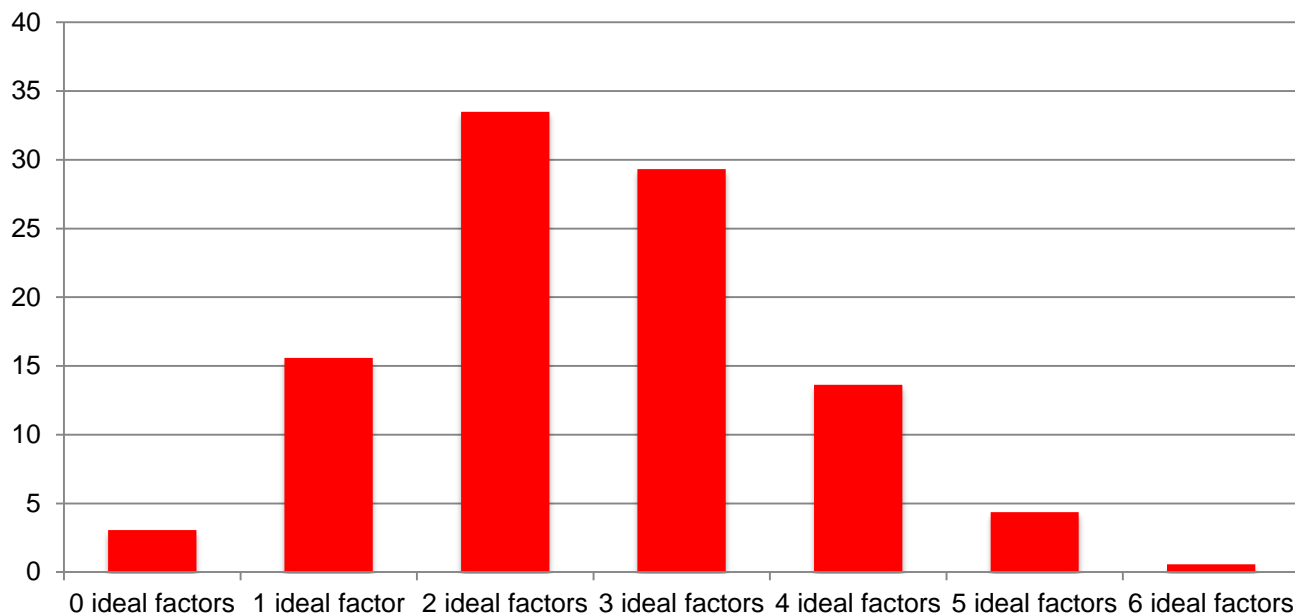
Ideal Cardiovascular Health

- **Strong relationship with stroke, MI, and vascular death in NOMAS**
- **Ideal CV Health factors may also impact cognitive or brain health.**
- **We examined the relationship between the number of ideal CV health metrics with**
 - **Mini-Mental State Exam**
 - **Domains of cognitive performance (language, memory, executive function, processing speed)**
 - **Cognitive Decline**

Northern Manhattan Study

MRI Subcohort

- 1033 with baseline cognitive data with 722 with follow-up cognitive data
 - Mean age at baseline = 64 ± 8
 - Mean age at first cognitive assessment = 72 ± 8
 - 39% Male; 65% Hispanic, 16% NH-White, 19% NH-Black



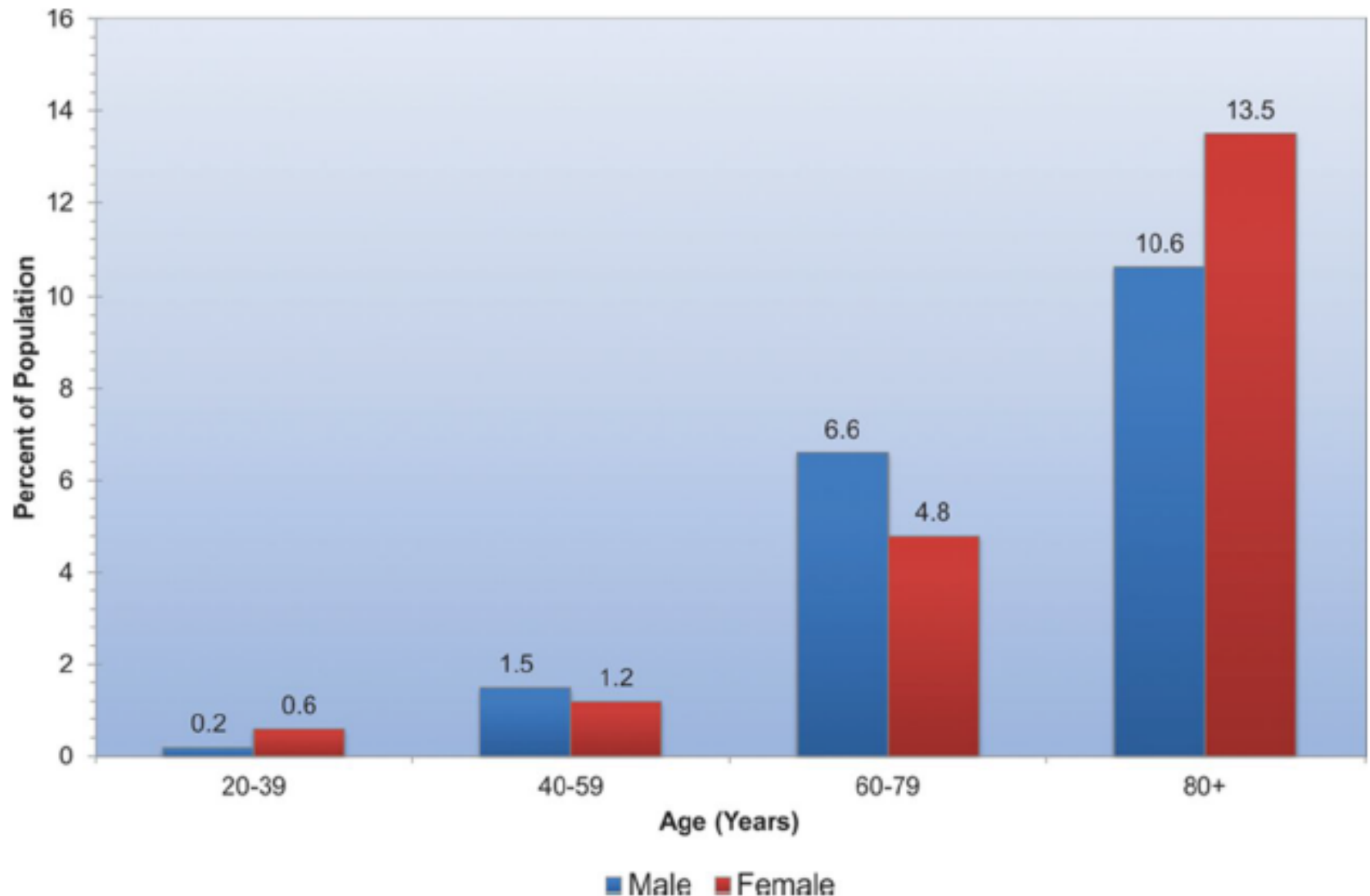
Cognitive Assessment

- **Cognitive domain Z scores derived from factor analysis of neuropsychological battery**
 - **Episodic Memory**
 - **Semantic Memory**
 - **Executive function**
 - **Processing speed**
- **Z scores for change in performance incorporate age, education, time between assessments**

What is the risk of brain aging and cognitive impairment in LV dysfunction or heart failure?



Prevalence of heart failure by sex and age



National Health and Nutrition Examination Survey: 2009–2012.

Cardiac Index Is Associated With Brain Aging

The Framingham Heart Study

Circulation. 2010;122:690-697.

Angela L. Jefferson, PhD; Jayandra J. Himali, MS; Alexa S. Beiser, PhD; Rhoda Au, PhD; Joseph M. Massaro, PhD; Sudha Seshadri, MD; Philimon Gona, PhD; Carol J. Salton, BA; Charles DeCarli, MD; Christopher J. O'Donnell, MD, MPH; Emelia J. Benjamin, MD, ScM; Philip A. Wolf, MD; Warren J. Manning, MD

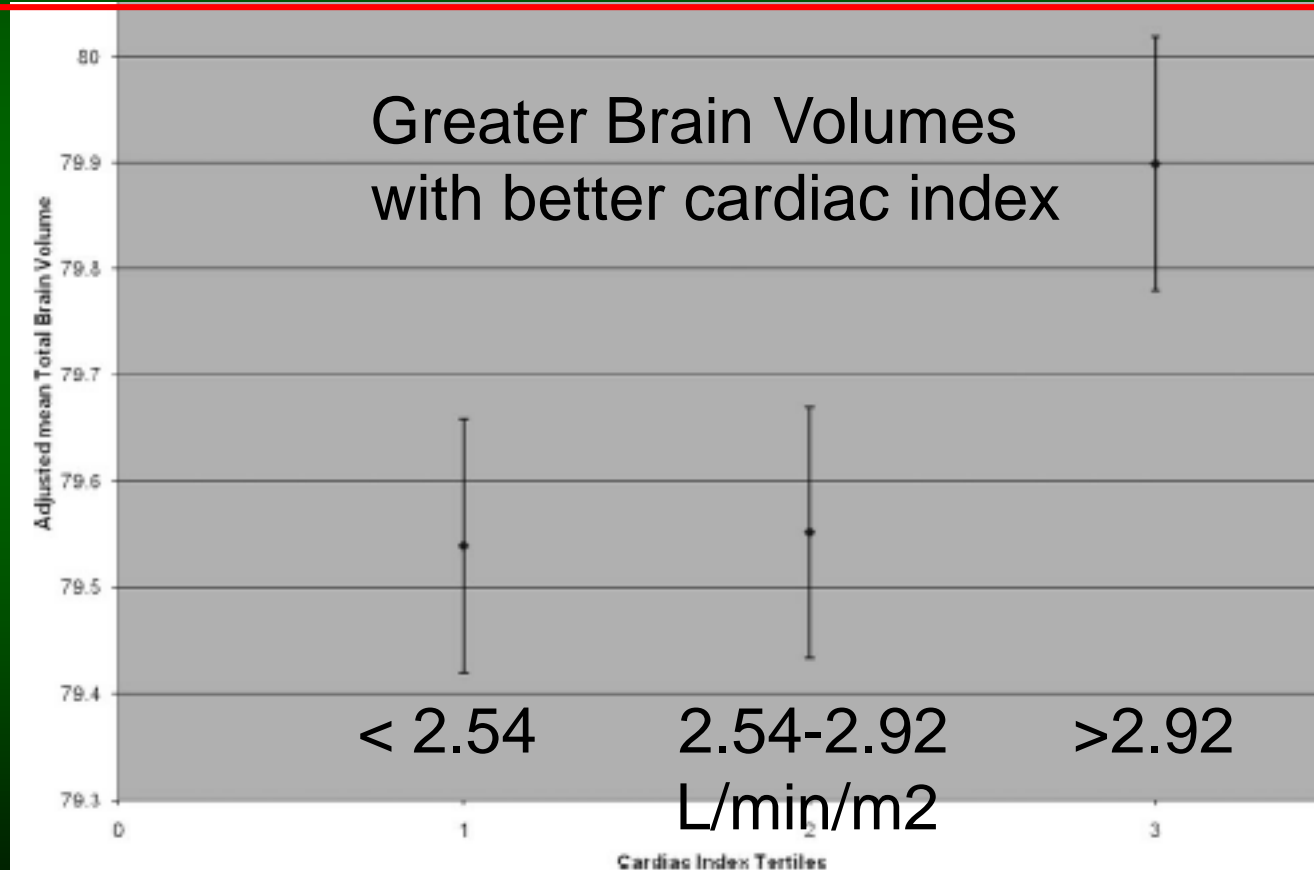


Figure. Mean total brain volume (with SE bars) adjusted for age, sex, systolic blood pressure, cigarette smoking status, diabetes mellitus, hypertension treatment, atrial fibrillation, and prevalent CVD is depicted by tertile of cardiac index. Tertile 3 is significantly different from tertiles 1 ($P=0.04$) and 2 ($P=0.04$).

Cardiac Index as a Correlate of Brain Volume

Separating the Wheat of Normal Aging From the Chaff of Vascular Cognitive Disorders

Clinton B. Wright, MD, MS; Ralph L. Sacco, MD, MS

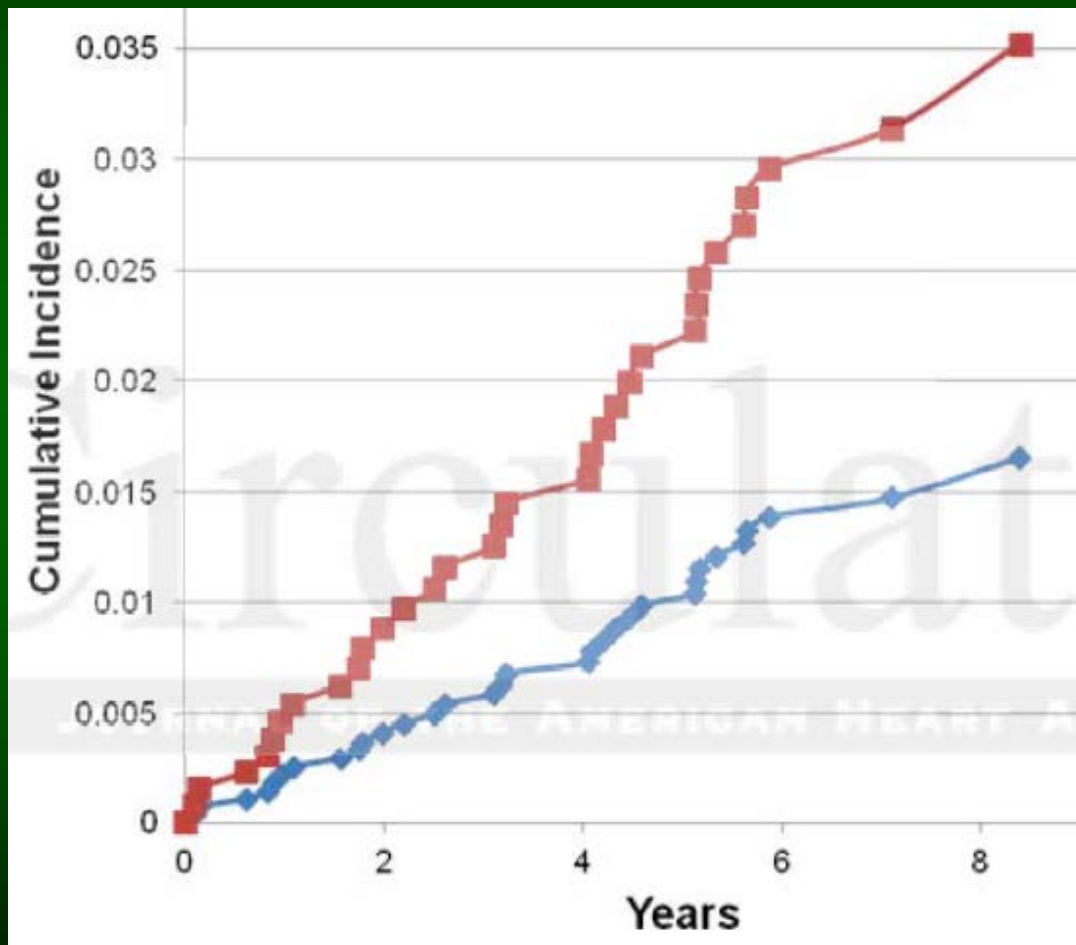
Circulation. 2010;122:676-678.

Patients with perfusion failure due to low systemic blood pressures, such as occurs in heart failure, can experience tissue injury and cognitive decline.^{12–15} Indeed, cognitive decline due to heart failure has generated great interest because it may be reversible, and it is of great importance to identify markers of cognitive dysfunction at the earliest stages if there is therapeutic potential. However, less is known about the relationship between subclinical reductions in cardiac function in normal populations.

Low Cardiac Index is Associated with Incident Dementia and Alzheimer's

Disease: The Framingham Heart Study

Jefferson et al. Circulation 2015



Impaired Cardiac
Index < 2.5 L/min/m²

Normal Cardiac
Index ≥ 2.5 L/min/m²

Subclinical Left Ventricular Dysfunction and Silent Cerebrovascular Disease

The Cardiovascular Abnormalities and Brain Lesions (CABL) Study

Cesare Russo, MD; Zhezhen Jin, PhD; Shunichi Homma, MD; Mitchell S.V. Elkind, MD, MS; Tatjana Rundek, MD, PhD; Mitsuhiro Yoshita, MD, PhD; Charles DeCarli, MD; Clinton B. Wright, MD, MS; Ralph L. Sacco, MD, MS, FAHA; Marco R. Di Tullio, MD

Russo C. et al. *Circulation* 2013 128(10):1105-11



European Journal of Heart Failure (2014) 16, 1301–1309
doi:10.1002/ejhf.154

Prevalence and prognostic value of subclinical left ventricular systolic dysfunction by global longitudinal strain in a community-based cohort

Cesare Russo^{1*}, Zhezhen Jin², Mitchell S.V. Elkind³, Tatjana Rundek^{4,5}, Shunichi Homma¹, Ralph L. Sacco^{4,5,6}, and Marco R. Di Tullio¹

Editorial

Enhancing Detection of Subclinical End-Organ Damage

Echocardiographic Left Ventricular Strain Holds Up a Mirror to the Brain

Jorge R. Kizer, MD, MSc

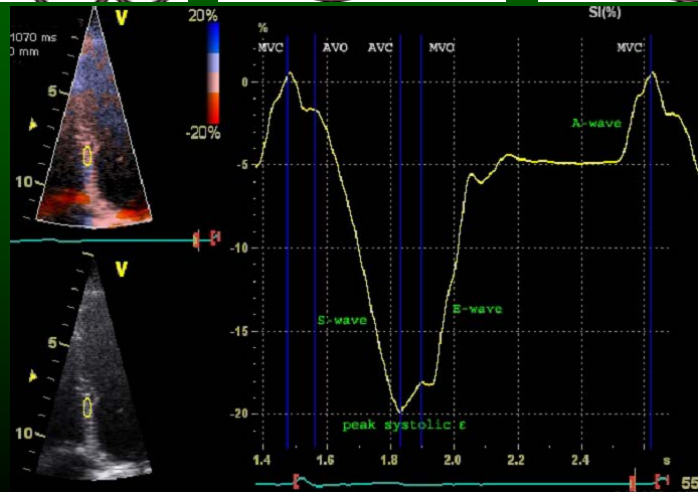
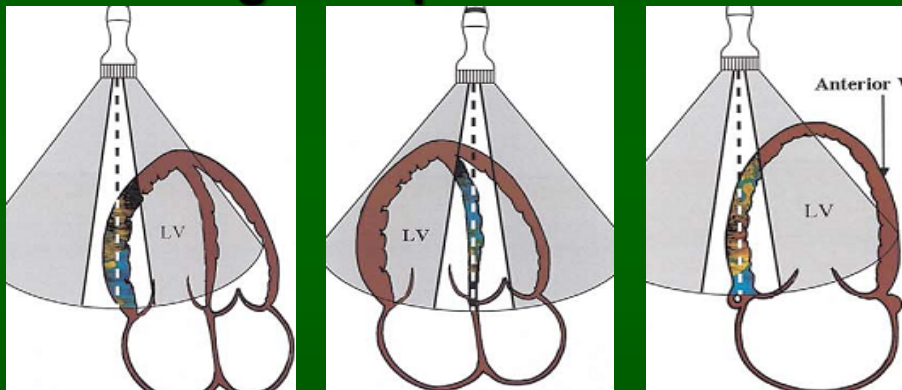
LVEF: Long-standing monarch of systolic dysfunction, buckling under the strain?

Emer Joyce*

Myocardial Strain Assessment

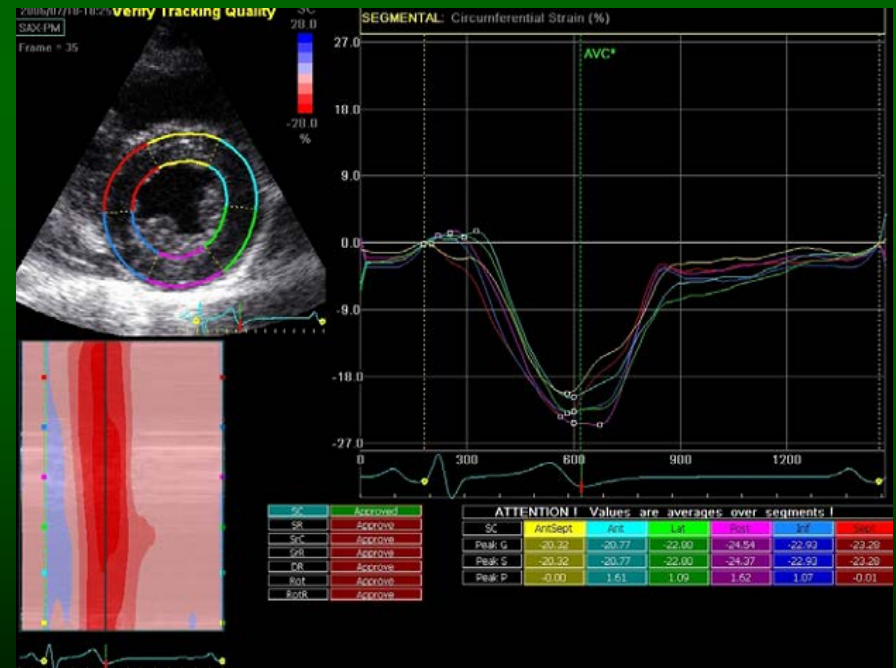
Tissue Doppler

- Angle-dependent
- Lower signal/noise ratio
- High temporal resolution

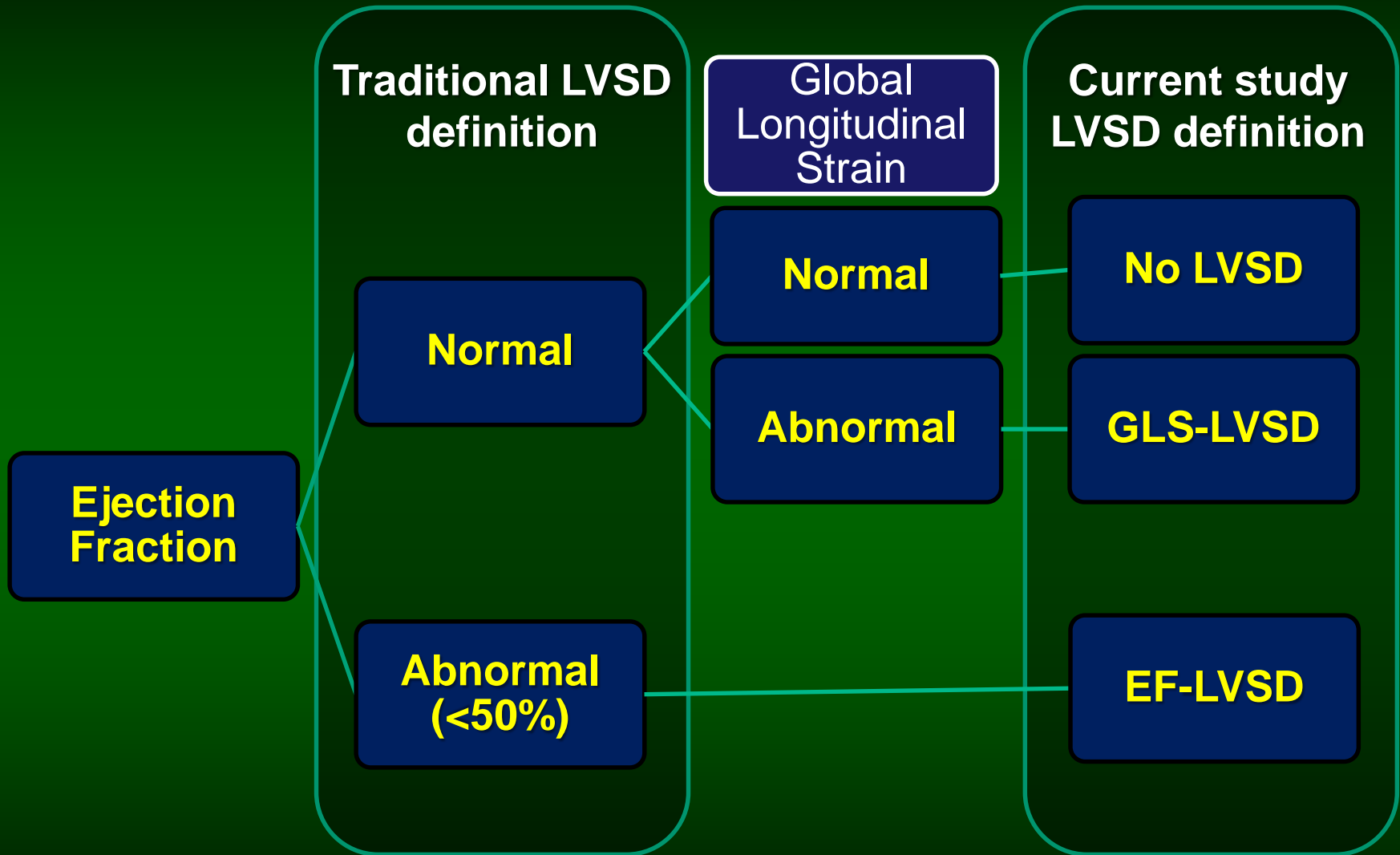


Speckle-tracking

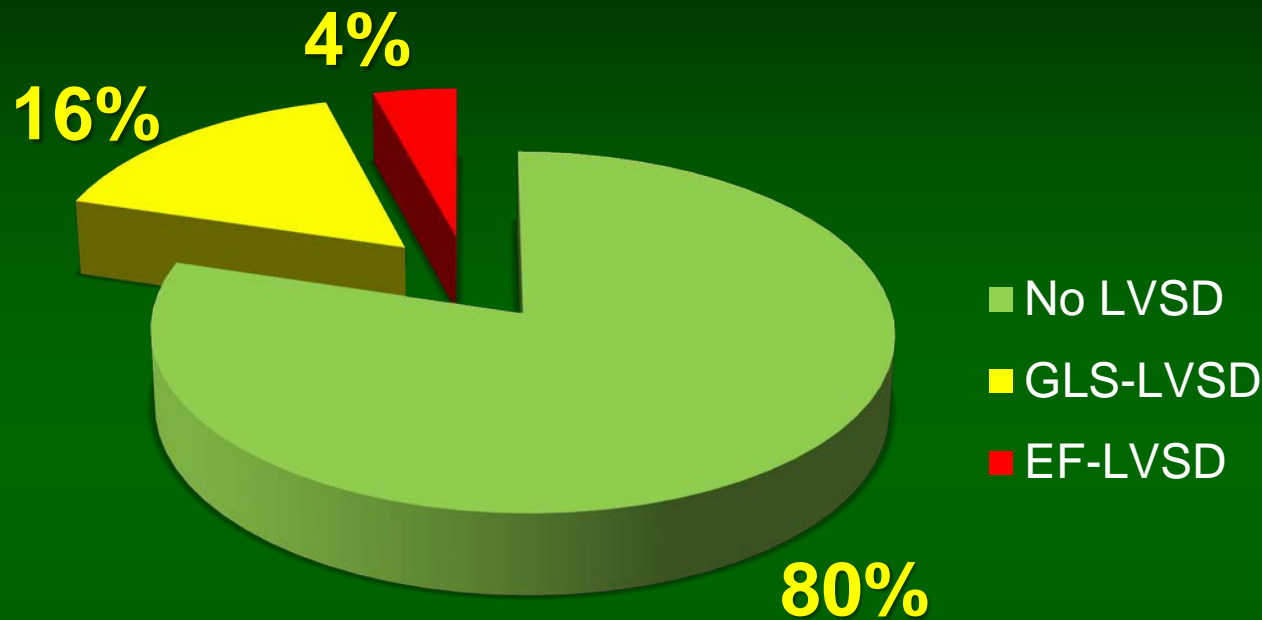
- Angle-independent
- Less noise
- Lower temporal resolution



Modified Definition of LV systolic dysfunction (LVSD) using Global Longitudinal Strain (GLS)



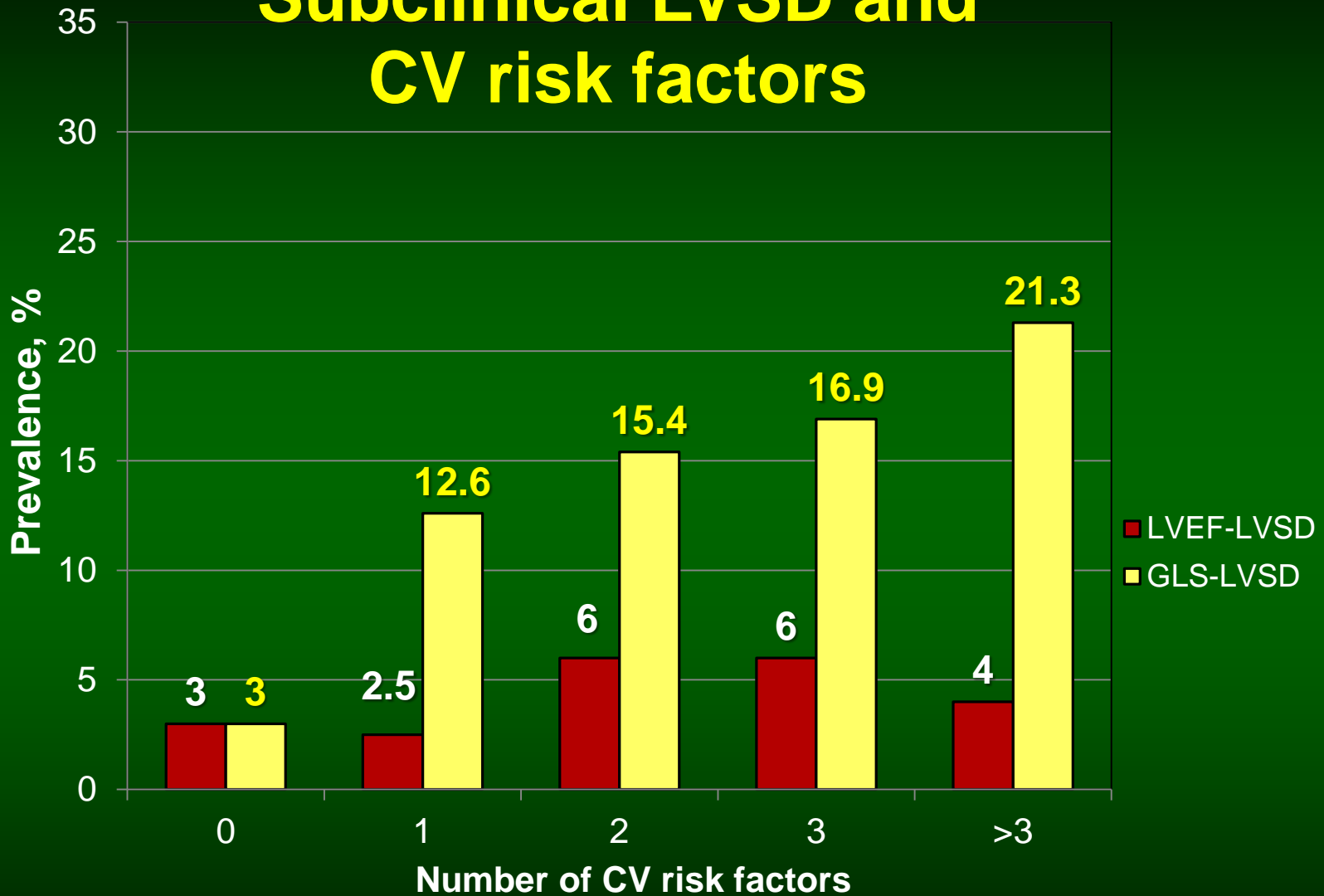
Prevalence of Subclinical Left Ventricular Systolic Dysfunction



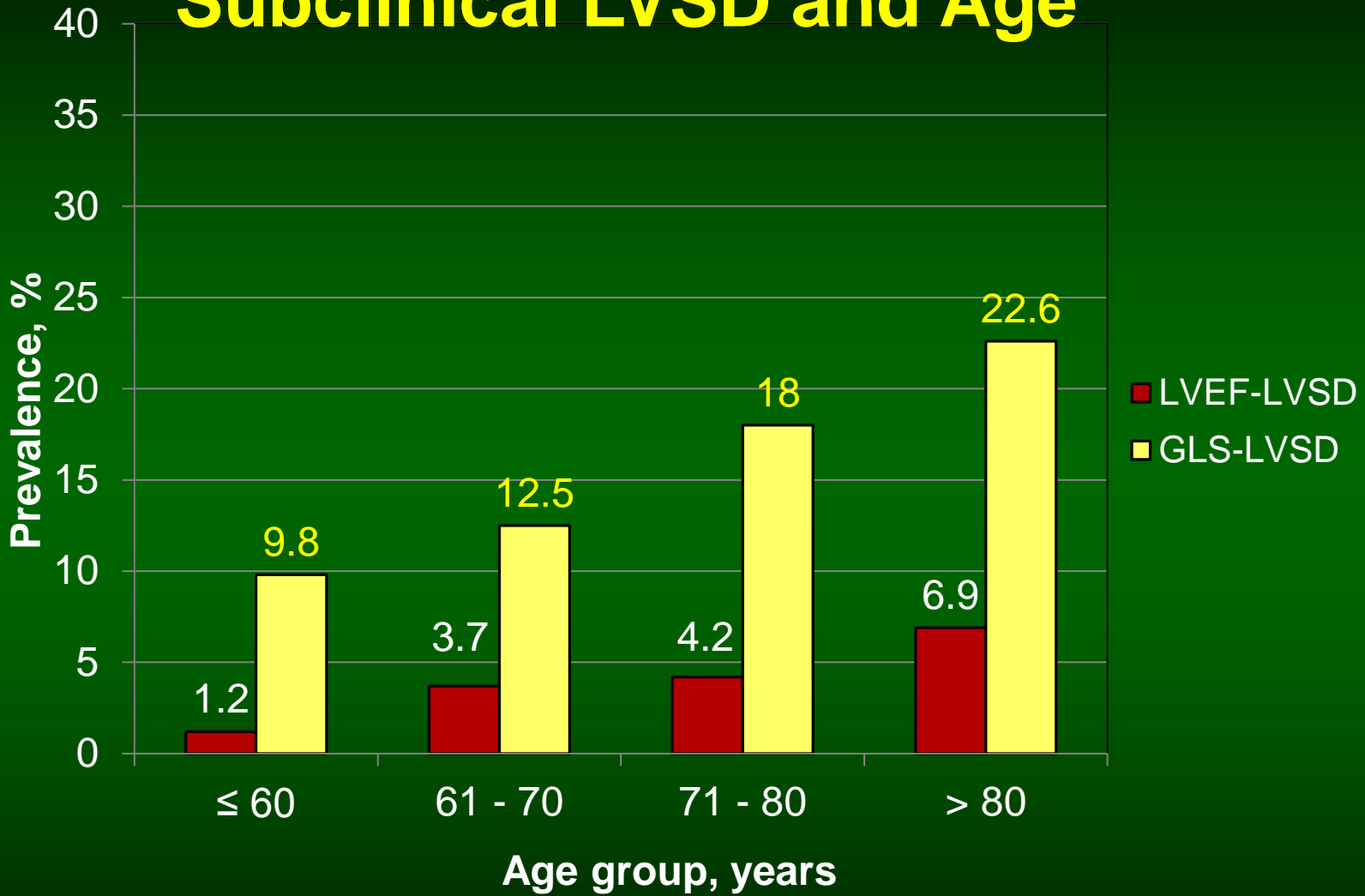
GLS-LVSD:

- Was present in 16% of study participants (114/708)
- Was 4 times more frequent than EF-LVSD (4%)

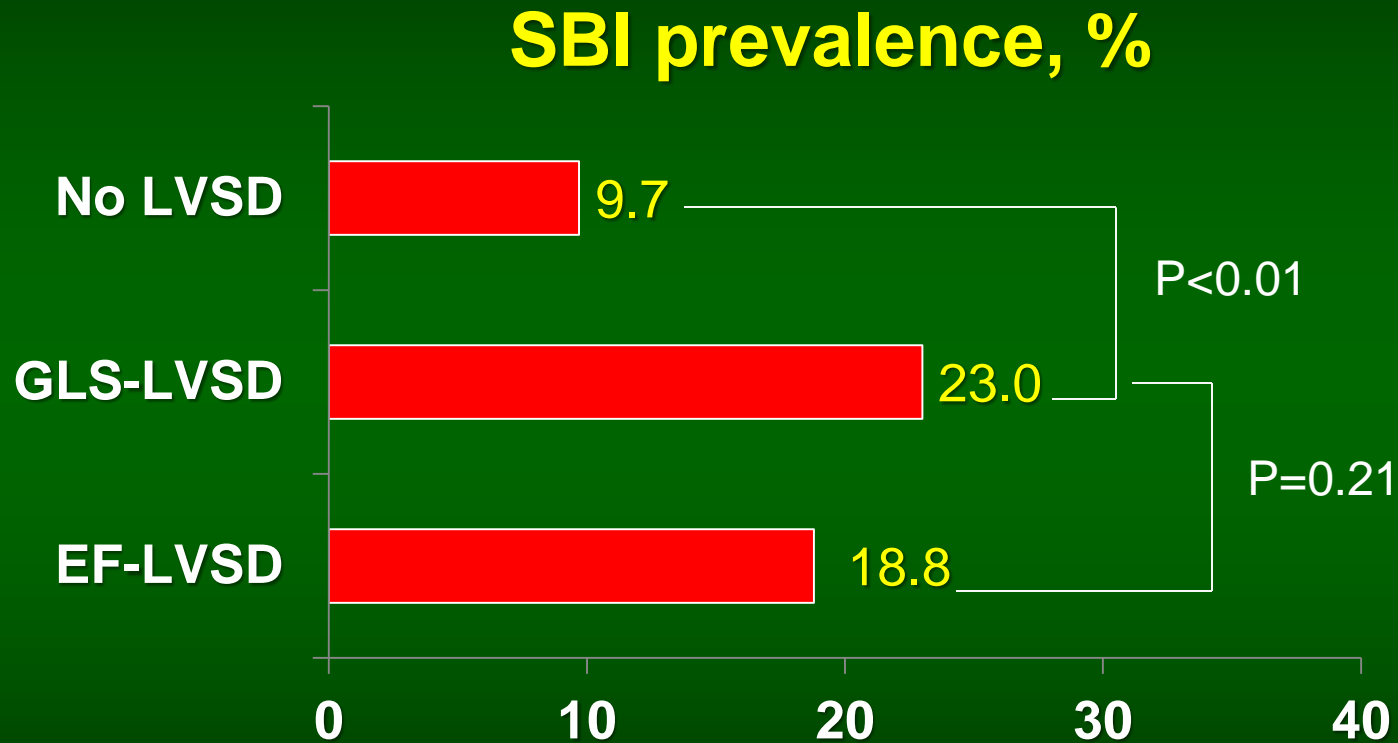
Subclinical LVSD and CV risk factors



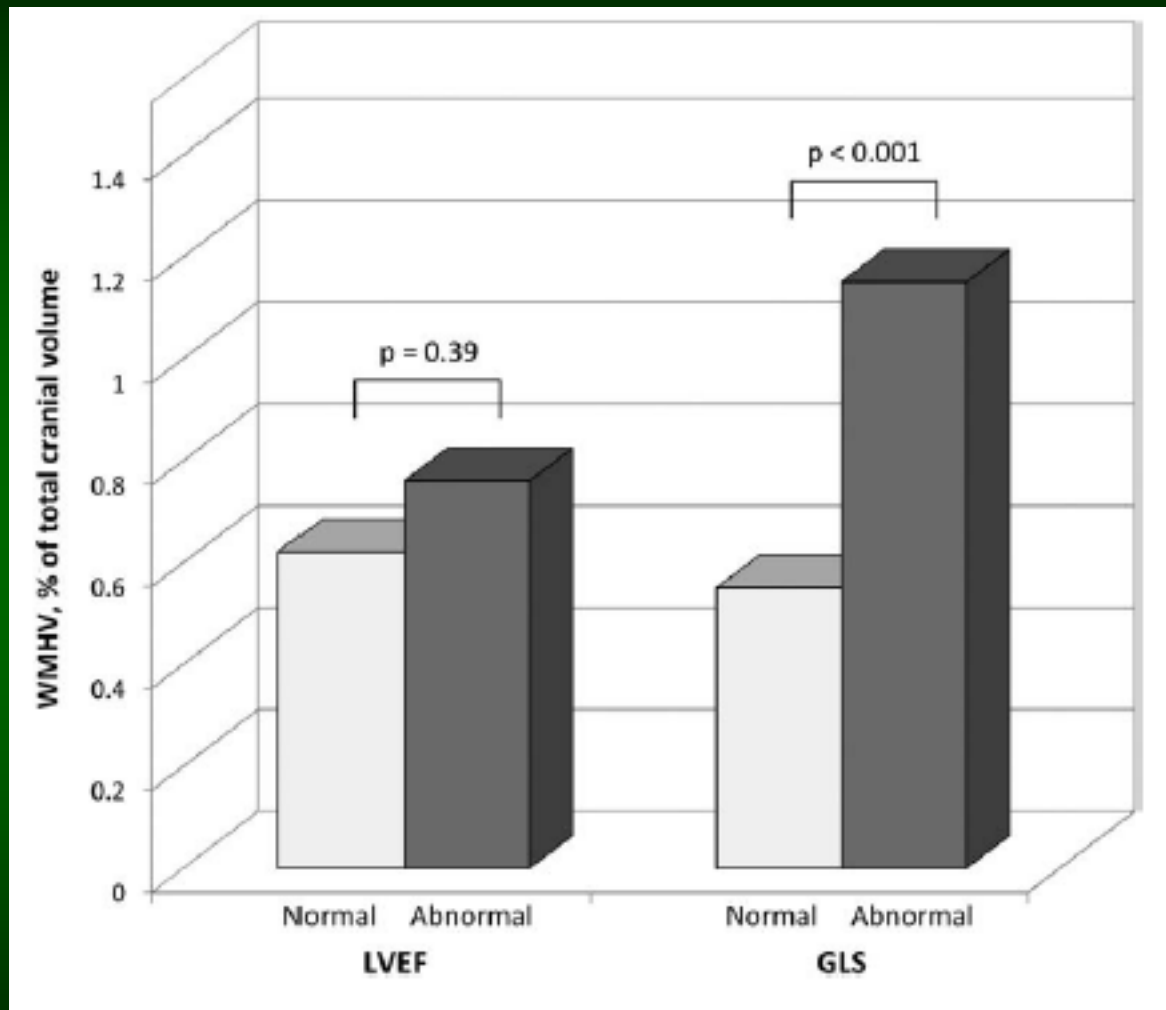
Subclinical LVSD and Age



LVSD and Silent brain infarcts (SBI)



LVSD and White Matter Hyperintensities



Cardiovascular Risk and Cognition

- **GQRS, Met Syndrome and ICVH scores are associated with cognitive performance and decline.**
- **The ICVH components driving the associations are BMI, smoking, diabetes, and SBP.**
- **A lower cardiac index is associated with brain imaging measures of aging and dementia**
- **Subclinical LV dysfunction is frequent and associated with WMHI and SBI**
- **Preventing and early treatment of heart failure may be important for reducing age-related cognitive decline**



COLUMBIA UNIVERSITY
MEDICAL CENTER

Discover. Educate. Care. Lead.



**Evelyn F. McKnight
Brain Institute**

**Mitch Elkind, MD
Bernadette Boden-Albala, DrPH**

**Tanja Rundek, MD PhD Clinton Wright, MD MS
Chuanhui Dong, MD PhD; Susan Blanton, PhD**



Funding: NINDS R37 NS 29993 (Sacco/Elkind), R01 NS 40807 (Sacco), R01 HL 108623 (Wright), K24 (Rundek), R01 NS 047655 (Rundek/Blanton), R01 NS 36286 (Di Tullio), R01 DE 013094 (Desvarieux), Evelyn McKnight Brain Institute

