

Promoting Cardiovascular Health A Scientific & Stratified Approach

Subclinical – Heart, Brain, Longevity

ACC-New York, Dec. 11, 2015

No Disclosures

NHLBI Strategic Visioning: Setting an Agenda for the NHLBI of 2025

Goal 1: Human Health	To expand knowledge of the molecular and physiological mechanisms governing the normal function of HLBS systems as essential elements for sustaining human health.
Goal 2: Human Disease	To extend our knowledge of the pathobiology of HLBS disorders and enable clinical investigations that advance the prediction, prevention, preemption, treatment, and cures of human diseases.
Goal 3: Translational Research	To facilitate innovation and accelerate research translation, knowledge dissemination, and implementation science that enhances public health.
Goal 4: Workforce and Resources	To develop and enable a diverse biomedical workforce equipped with the essential skills and research resources to pursue emerging opportunities in science.

*M Lauer, GH Gibbons et. al. JACC 2015; 65: 1130 - **Environment***

Integration of social science into research is crucial

Social scientists must be allowed a full, collaborative role if researchers are to understand and engage with issues that concern the public, says Ana Viseu.

FOR THE SOCIAL
SCIENCES TO MAKE
MEANINGFUL
CONTRIBUTIONS,
FUNDING
STRUCTURES MUST BE
RETHOUGHT.

*A Viseu. Nature **2015**;525:291*

Health - Scientific Translational Approach



Clinical to Health - Aging (A) to Birth (B)

Present



1. Health (QoL)

Early Economic Late Expensive

*Policy Mandatory (?)
Air Pollution & Noise*

2. Environment

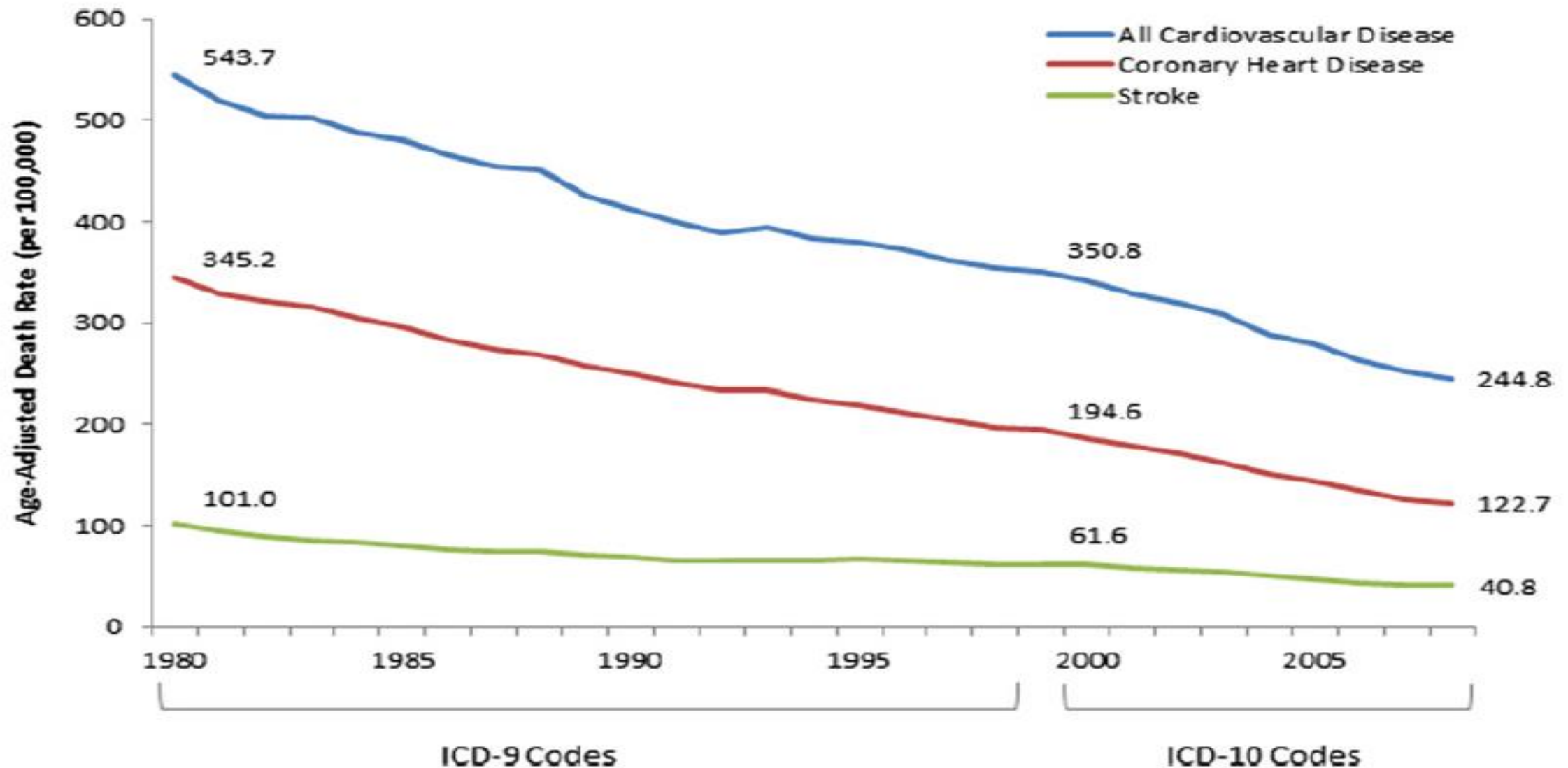
3. Science

Future

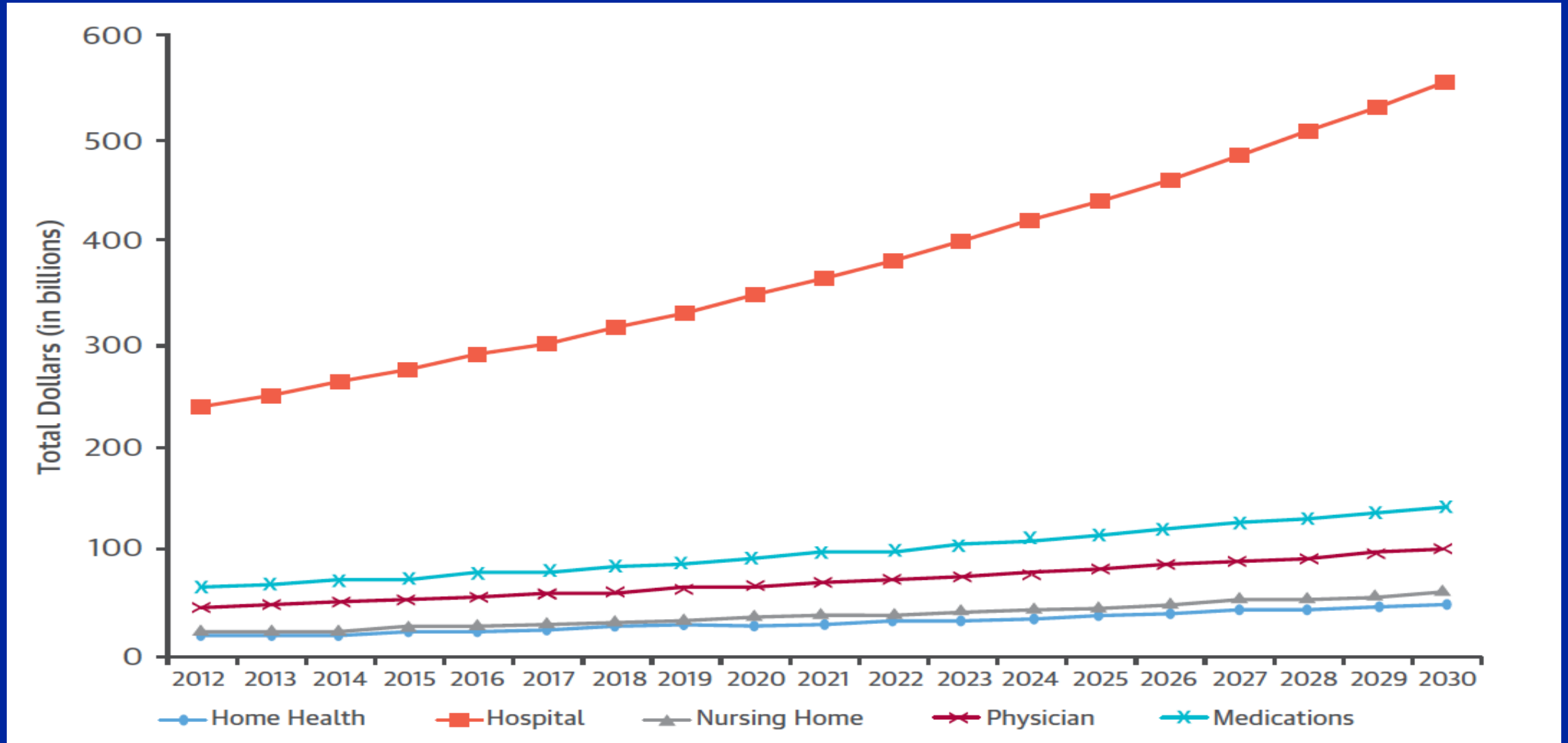
4. Education



1a. Age-Adjusted Deaths for CVD, CAD & Stroke US 1980 to 2008 – The 50% / 50%

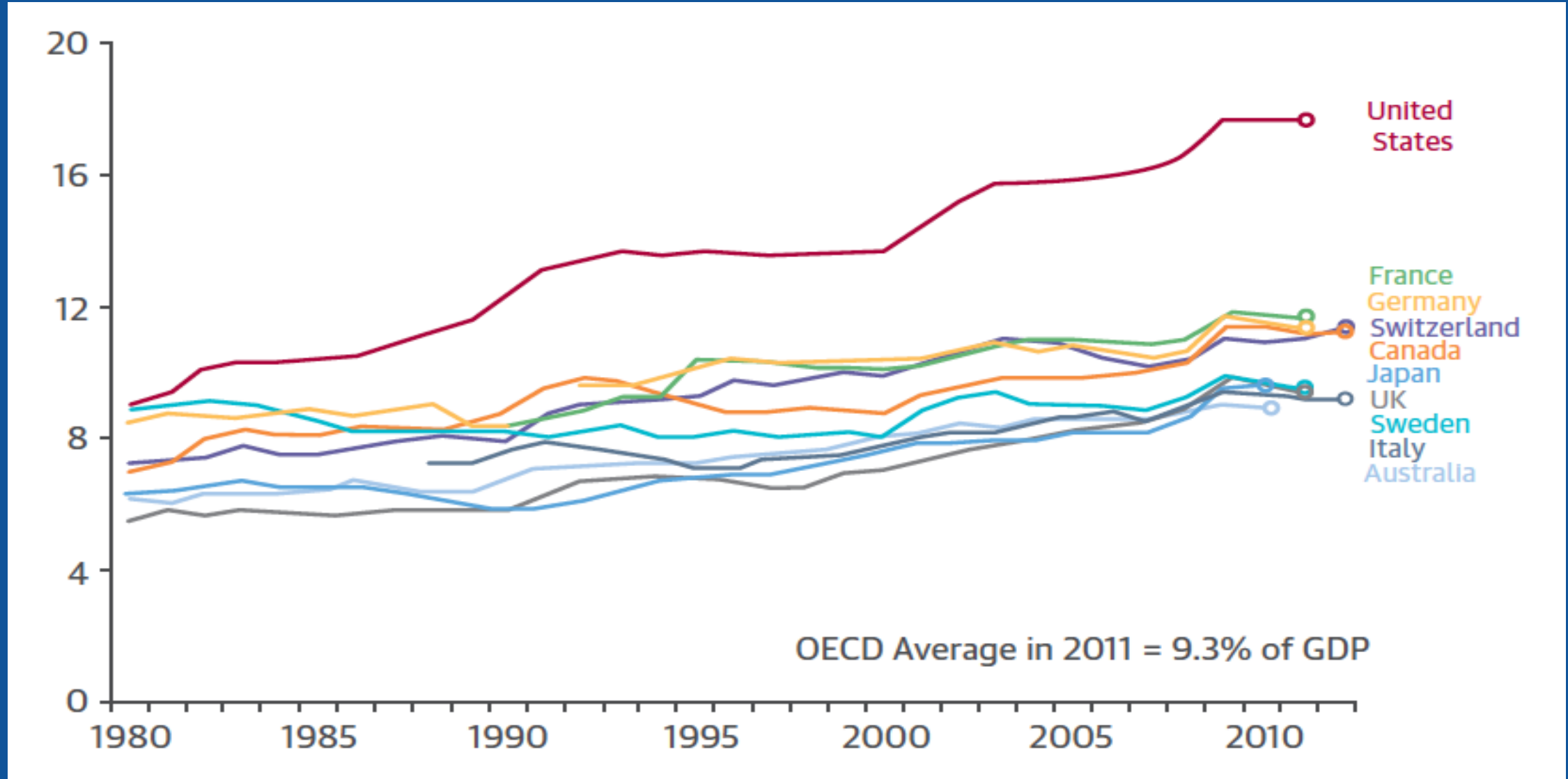


1b. Projected Direct Costs of Total CVD by Type of Cost (in Billions) - / 50%



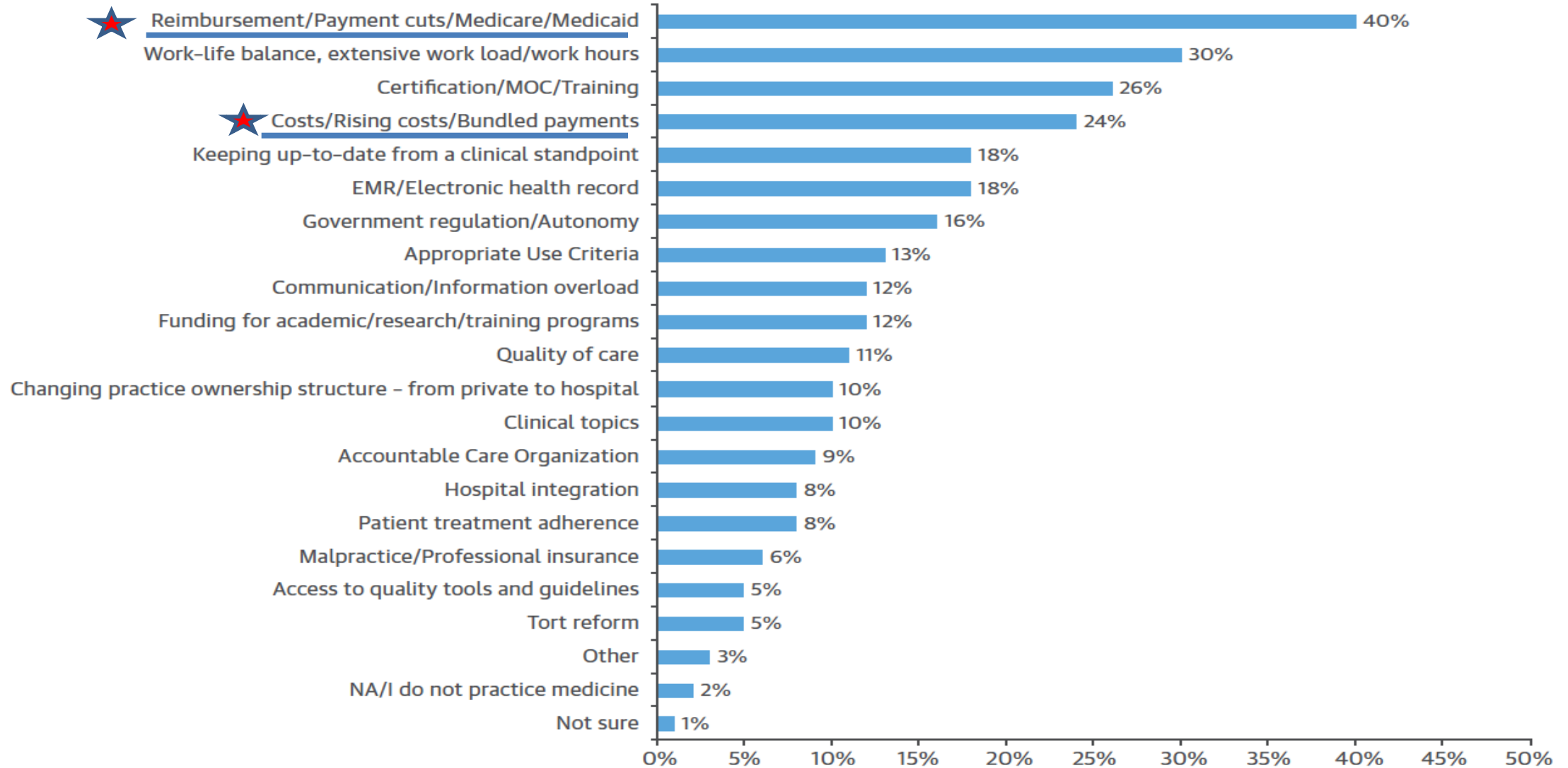
ACC BOT' ESGW Members (L Laslett et. al.) JACC **2015**; 66 (suppl D).

1b. Healthcare Spending As a % of GDP for OECD Countries



1b. Biggest Challenges in CV Medicine

■ Two fifths (40%) of members identify reimbursement as the biggest issue facing CV medicine. Work-life balance (30%), certification/MOC (26%), and costs/rising costs/bundled payments (24%) are also challenges.



Clinical to Health - Aging (A) to Birth (B)

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Prom. Health **Subcl. Disease** **Stable-Unst. Disease**

3. Science

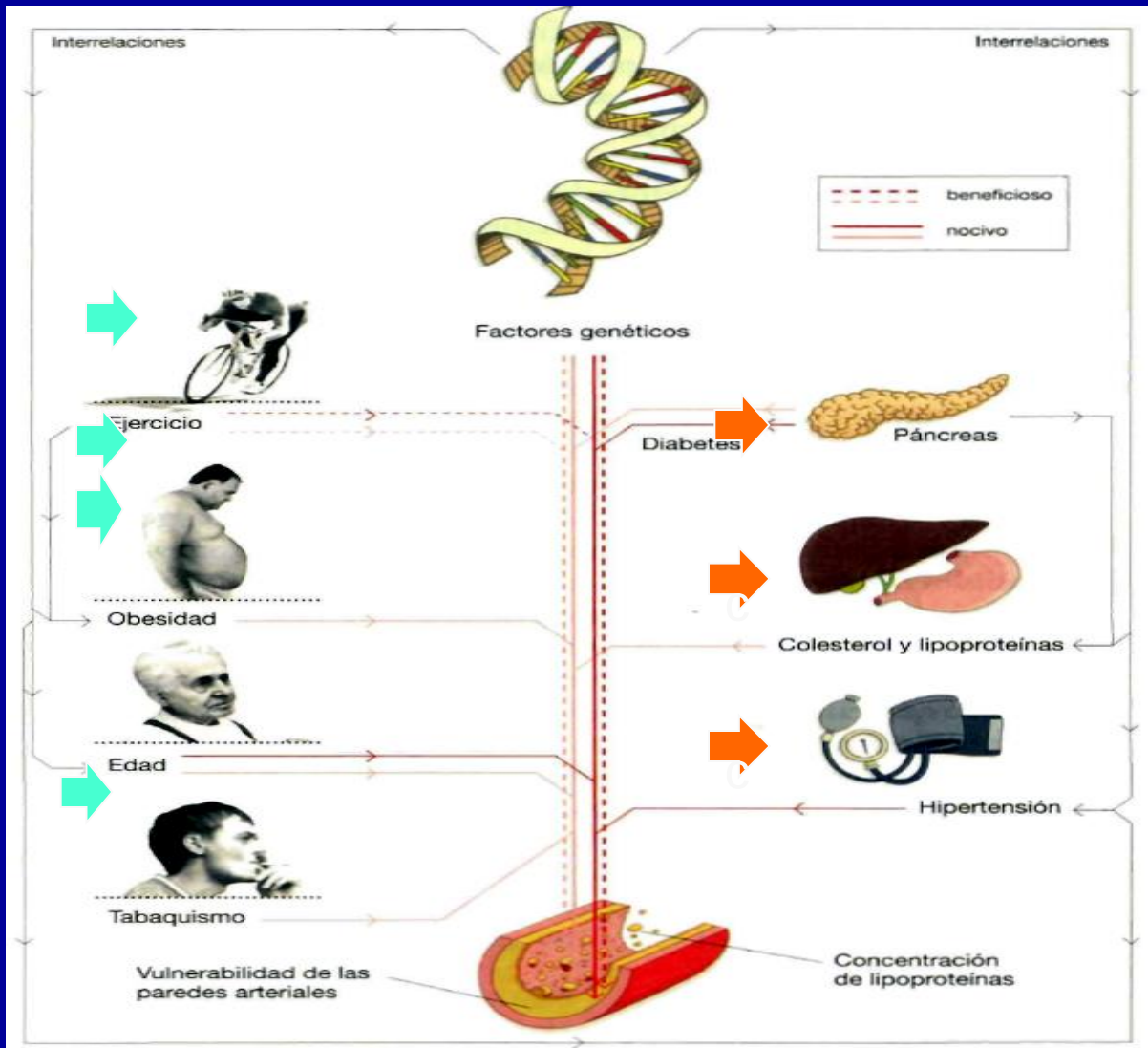
Future

4. Education



Window Behav. **Adherence**
Young Change **Simplicity**

2a. Modifiable CV Risk Factors (7) & Life Style



>2 Risk Factors

1. MI & 2. Stroke

25% in 10 Yrs

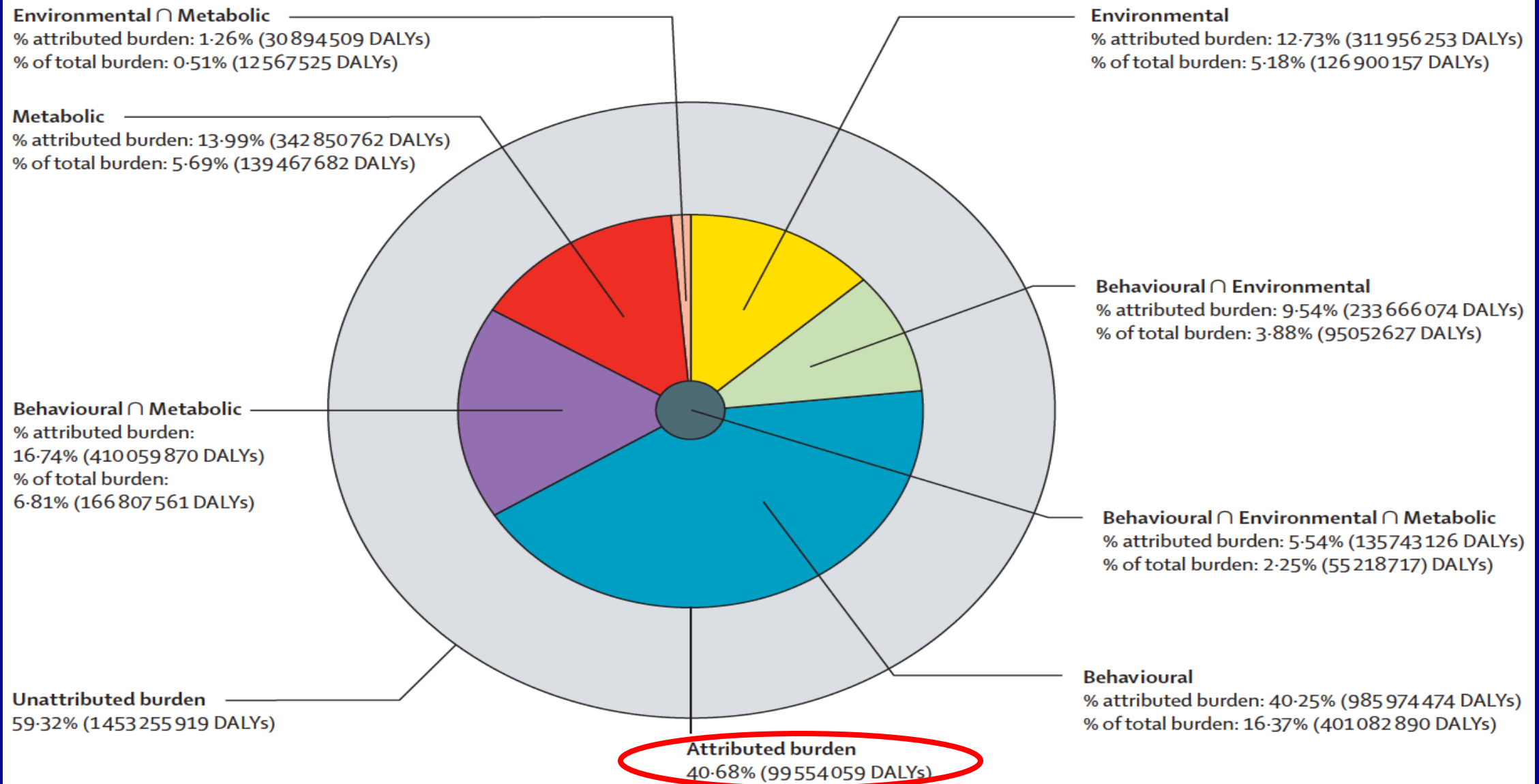
75% in 30 Yrs

3. DBD & 4. AD

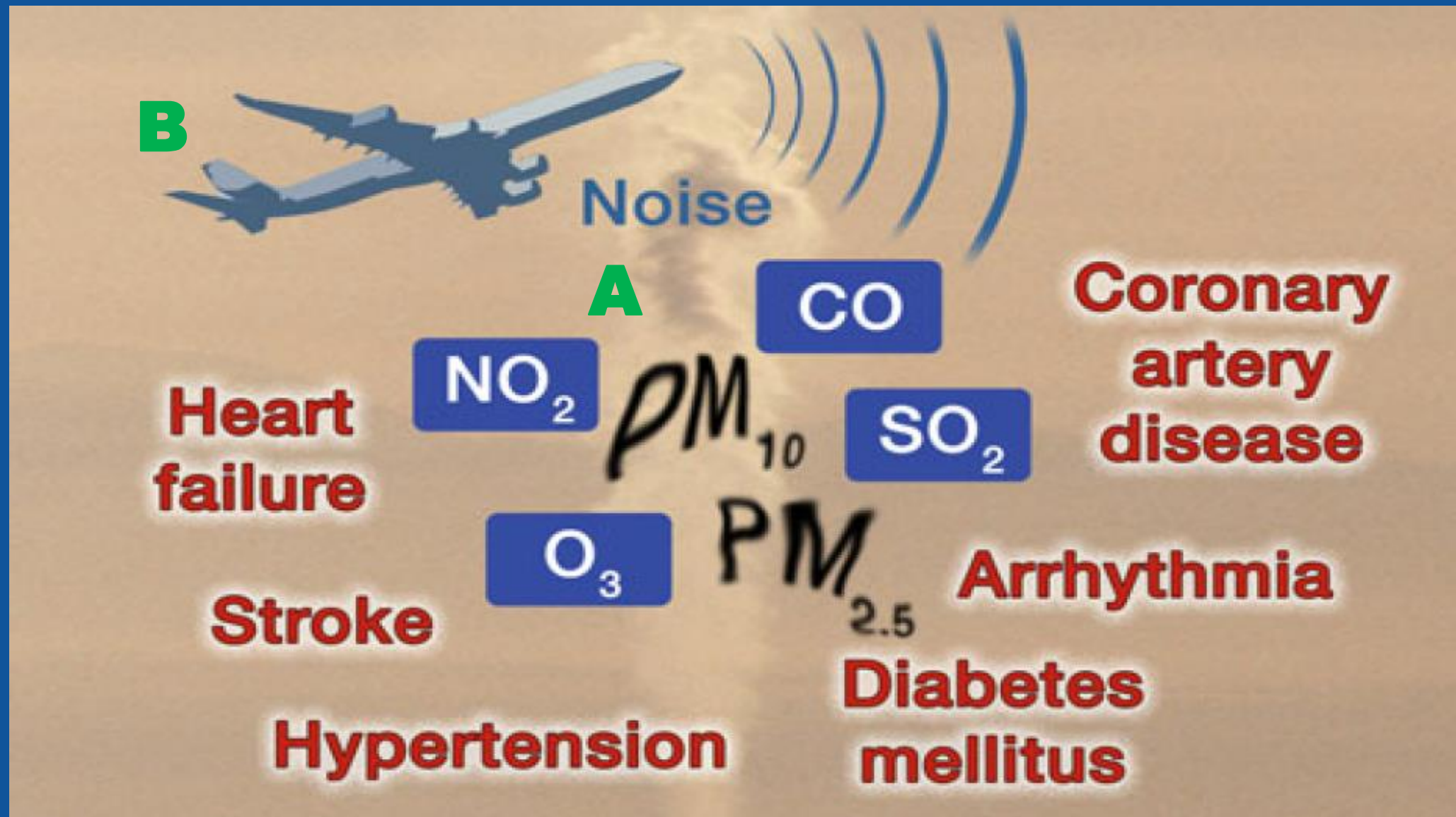
Quality

WHO - WHF - AHA: Death Reduction - 25% by 2025 ?????
NY - Bloomberg: Smoking Cessation - 2002-2010 Success

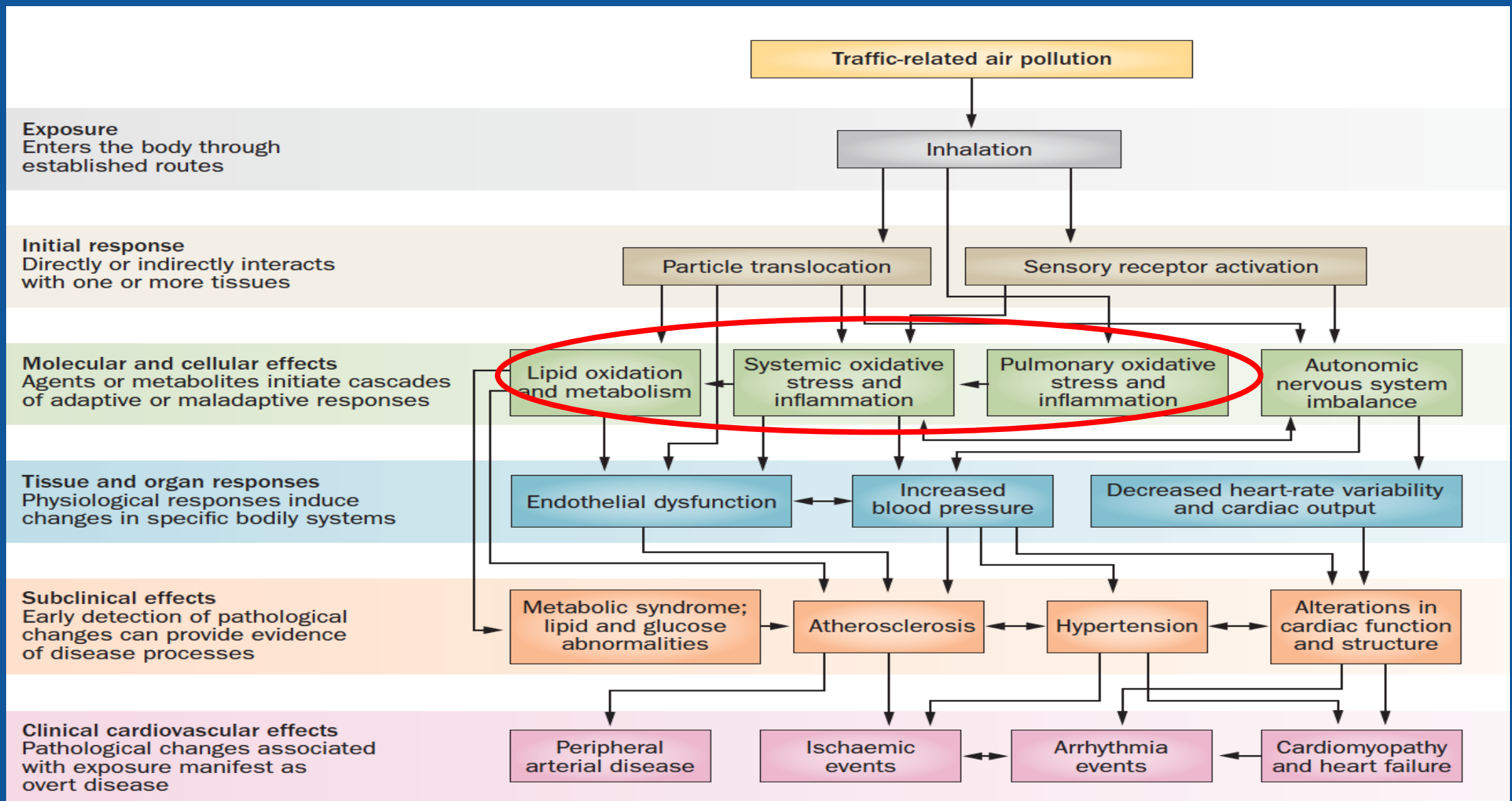
2a. % Of All-cause DALYs- Attributable Behaviour, Environment & Metabolic RFs - 2013



2b. Proposed Cardiovascular Side Effects Of Noise & Air Pollution - ROS



2b. CV Effects And Proposed Mechanisms To Chronic Environmental & Traffic-related Air Pollution



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The Three Challenges of Aging Quantity / Quality of Mental Life

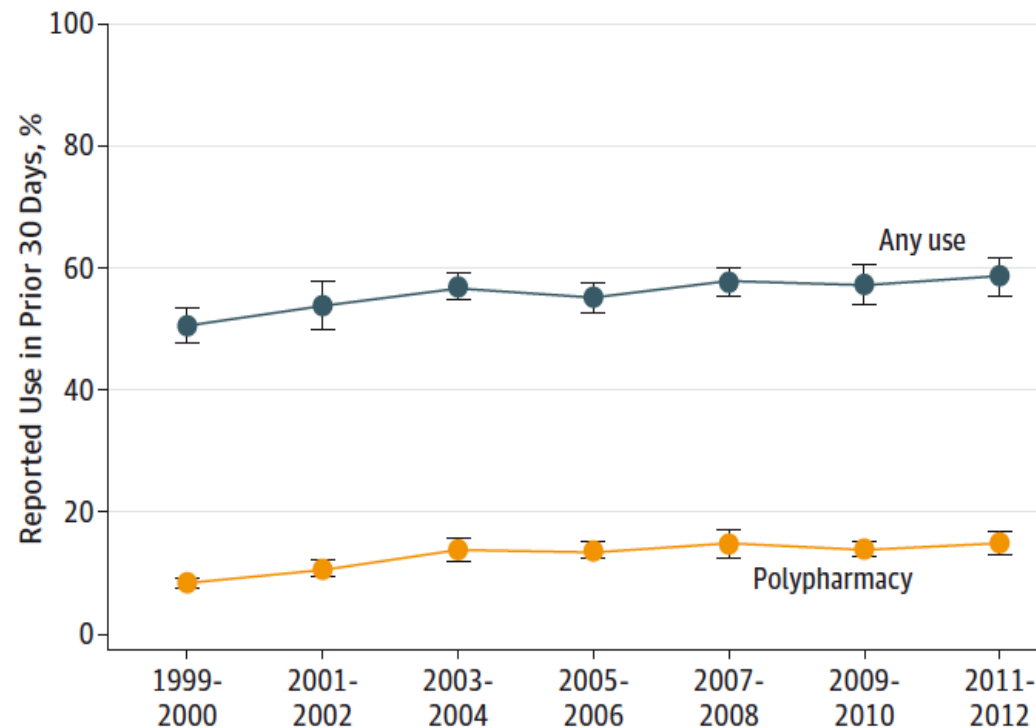
1. CV Drugs Overuse vs Underuse

2. Burden of Disease – QOML / Longevity

3. Wellbeing - Evaluative, Hedonic, Eudemonic

1. Prescription in Any Drug or of 5 or More Trends, Overall and by Age Group

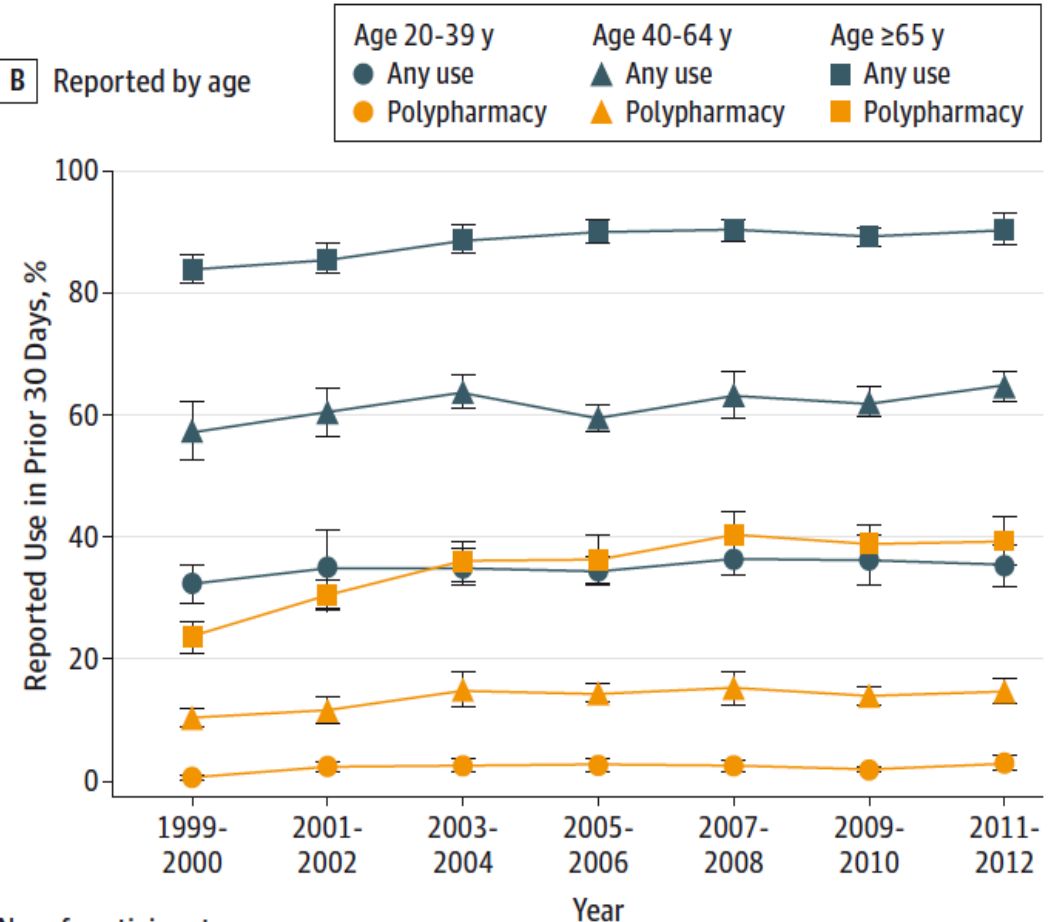
A All participants



No. of participants

Year	1999-2000	2001-2002	2003-2004	2005-2006	2007-2008	2009-2010	2011-2012
No. of participants	4861	5399	5029	4970	5930	6212	5558

B Reported by age



No. of participants

Age Group	20-39 y	40-64 y	≥65 y
No. of participants	1692	1787	1382
1999-2000	1692	1787	1382
2001-2002	1925	2022	1452
2003-2004	1737	1799	1493
2005-2006	1923	1864	1183
2007-2008	1910	2469	1551
2009-2010	2081	2611	1520
2011-2012	1957	2352	1249

The Three Challenges of Aging Quantity / Quality of Mental Life

1. CV Drugs Overuse vs Underuse

2. Burden of Disease – QOML / Longevity

3. Wellbeing - Evaluative, Hedonic, Eudemonic

1. CV Drugs – Underuse

Risk Factors - Proportion of Participants at Goal % – 1 year

Trials	L	SBP	DBP	Hb A1C	Meet Goals	
					Base	FU
BARI-2D	75	56	70	52	14	20
COURAGE	51	55	55	59	12	19
FREEDOM	55	63	53	55	12	20

Freedom, Bari-2D, Courage Investigators, JACC 2013;61:1607

PURE (S Yusuf et al.) Lancet 2011; Aug 28 - Poor Countries, 7% !!!

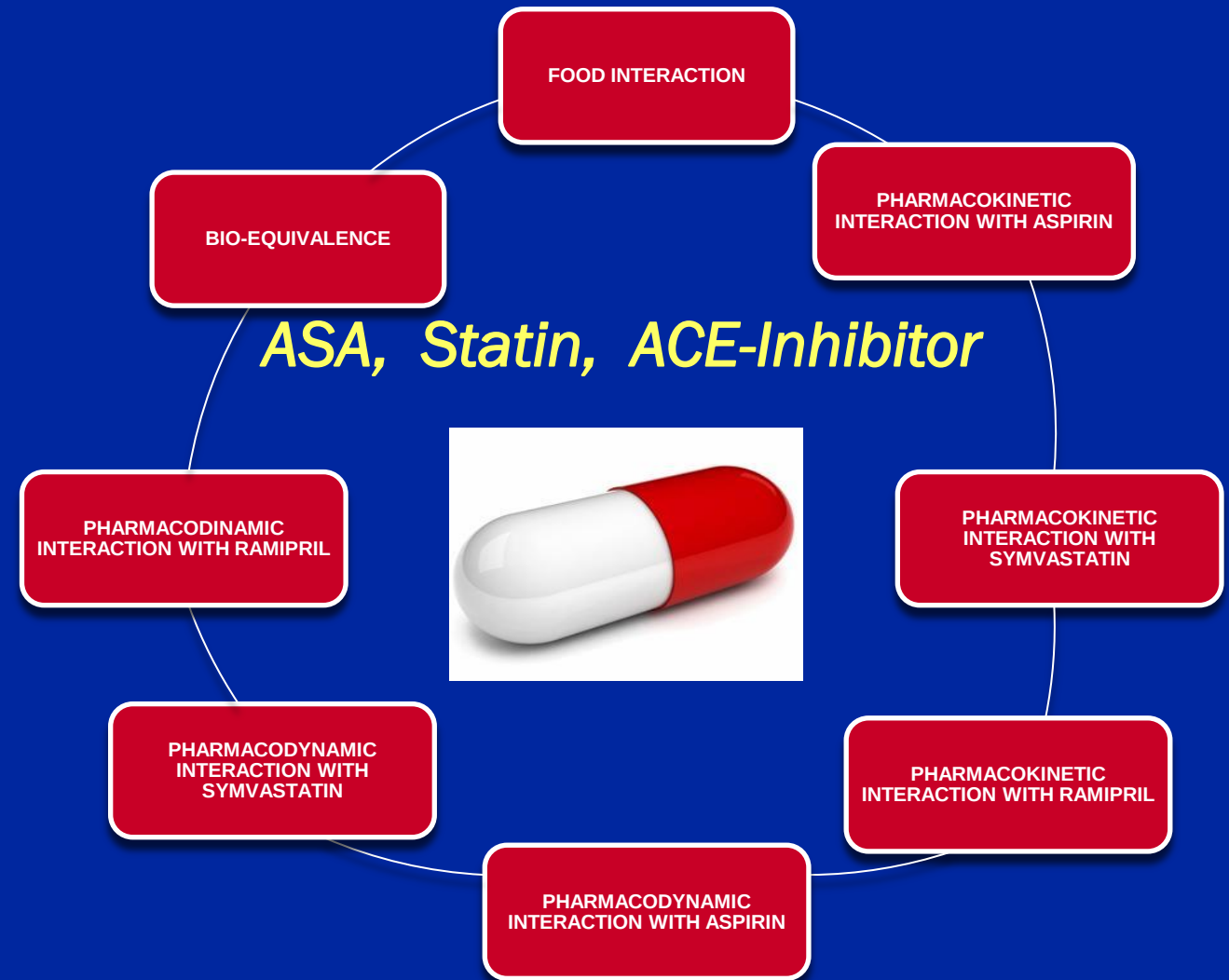
NHANES, AHA, NHLBI-JNC-7, NHLBI-NCEP – < Adherence

P Muntner, V Fuster et al., AHJ 2011; 161: 719 – 49 seconds !!!!

CV Drugs Underuse - Polypill, 2ary Prevention.

FOCUS 1 & 2
Argentina
Brazil
Paraguay
Italy
Spain

FREEDOM
AETNA-DIABETES
SECURE-EC 2015



Approved in 26 Countries

Am. H J 2011;162:811

Semin.Thor.Cardiov.Surg 2011;23:24

JACC, 2014; 64:2071

*** Valentín Fuster (inventor)**

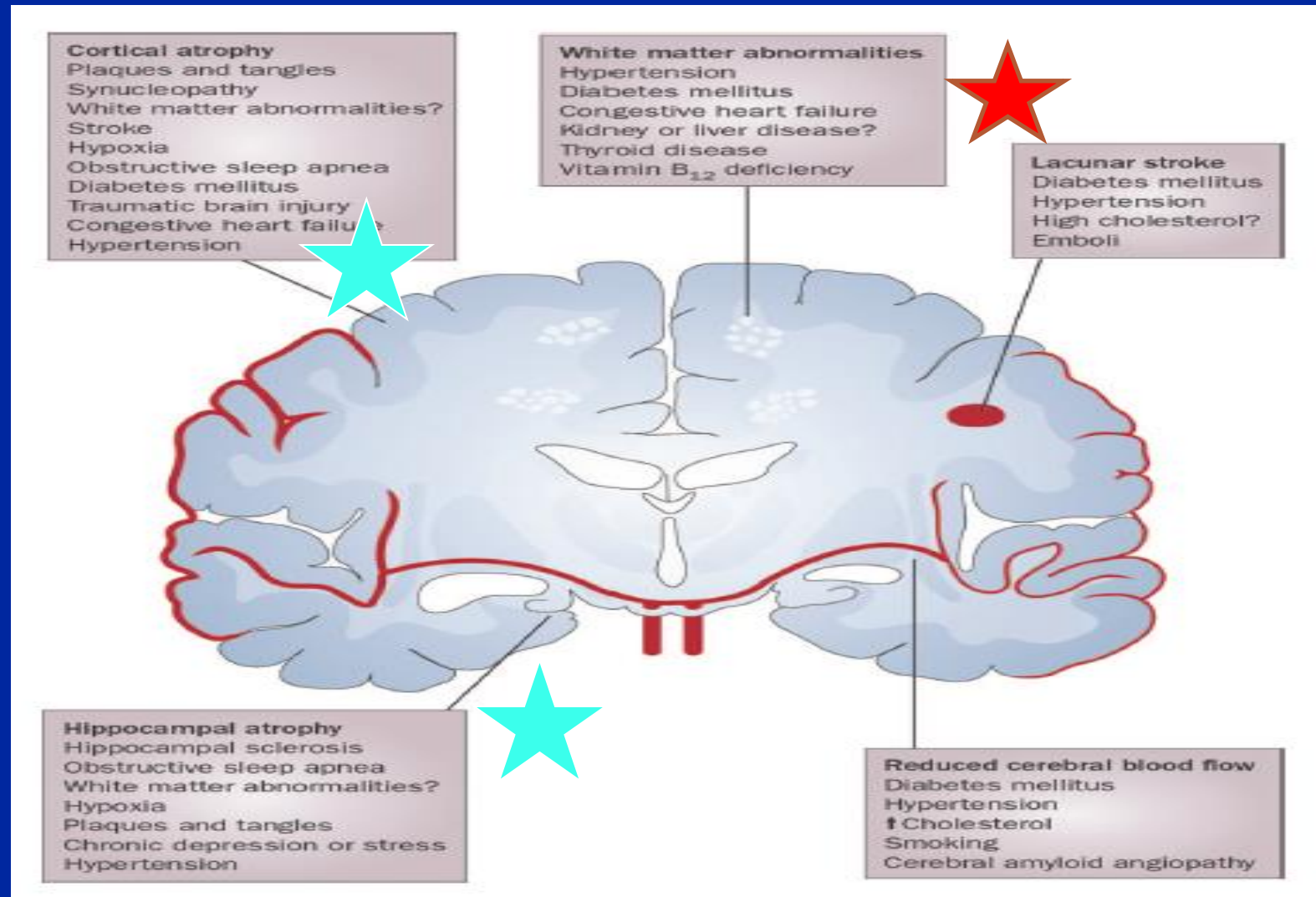
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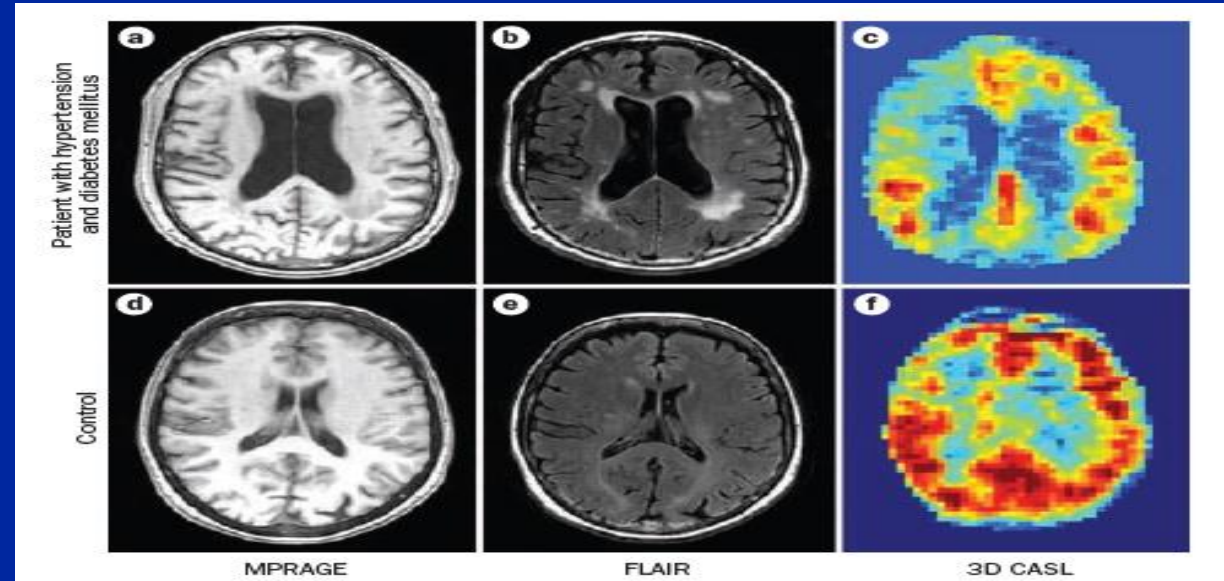
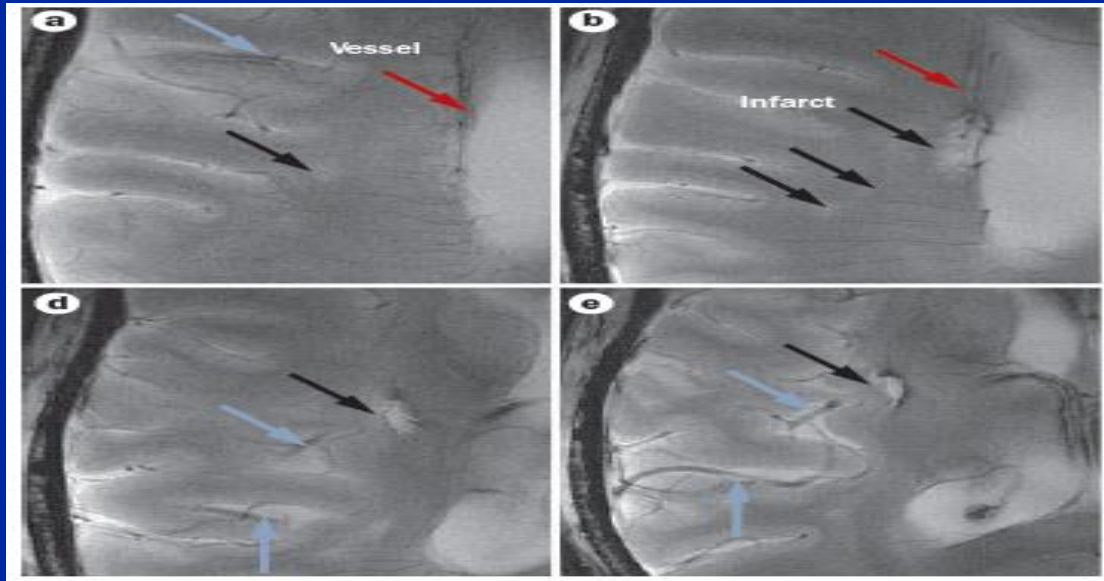
2. Risk Factors of CV Disease White Matter & Lacunar Lesions (DBD)



1B

MA Lim et. al. Clin Geriatr Med. 2009;25:191.
JC Kovacic, V Fuster et. al. Circulation. 2011;123:1900

DBD/AD - CVRFs, Lacunar Les., < Cognitive MRI – Perfusion



Ischemia affects 60 to 90% of patients with Alzheimer's

1. V Novak, I Hajjar. Nat. Rev. Cardiol. 2010; 7:686(HMS)

2. HW Querfurth, FM LaFerla. NEJM 2010; 362:329

Autopsy (n=6000)

3. JB Toledo et al. Brain July 10, 2013

CV Risk Factors, Cognitive Function, Imaging

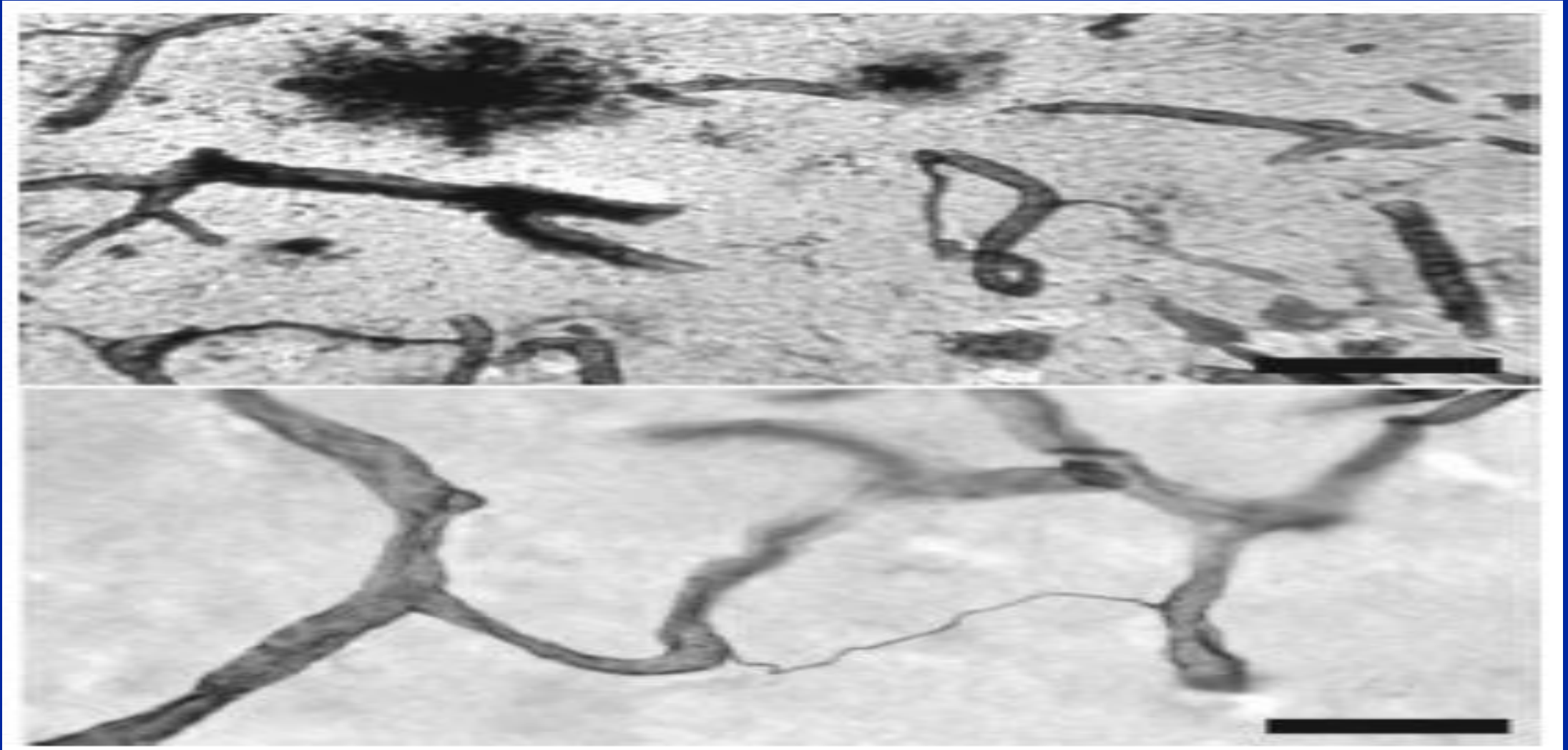
4. CARDIA (K Yaffe et al) Circ. 2015 (In Press)

5. JI Friedman, V Fuster et. al- JACC CV Imag. 2015 (In Press)

Intervention

6. FINGER (T Ngandu et al)., The Lancet 2015; 385:2255

A'sD Vascular – Amyloid, Ather ?

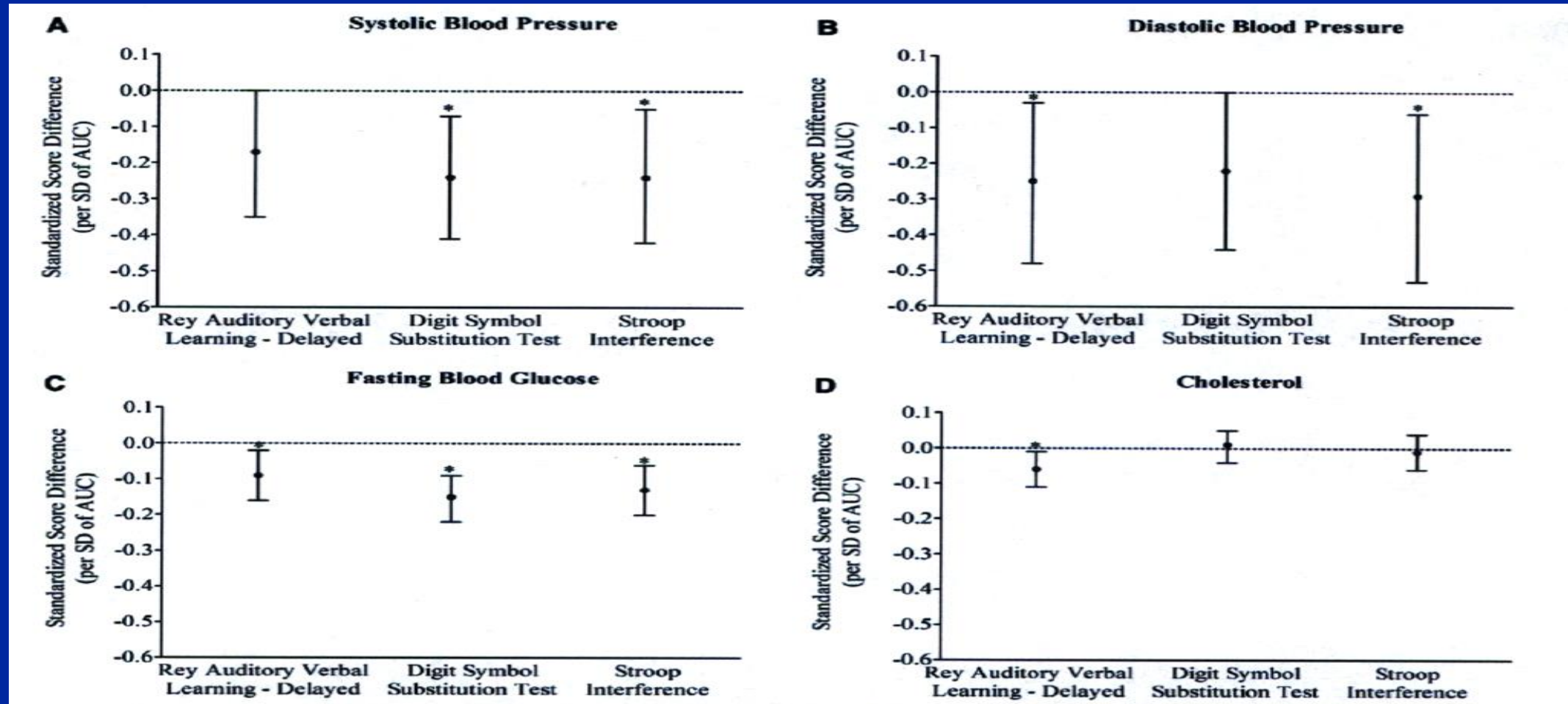


1. V Novak, I Hajjar. Nat. Rev. Cardiol. 2010;7:686

2. HW Querfurth, FM LaFerla. NEJM 2010; 362:329

Ischemia affects 60 to 90% of patients with Alzheimer's – RFs ?

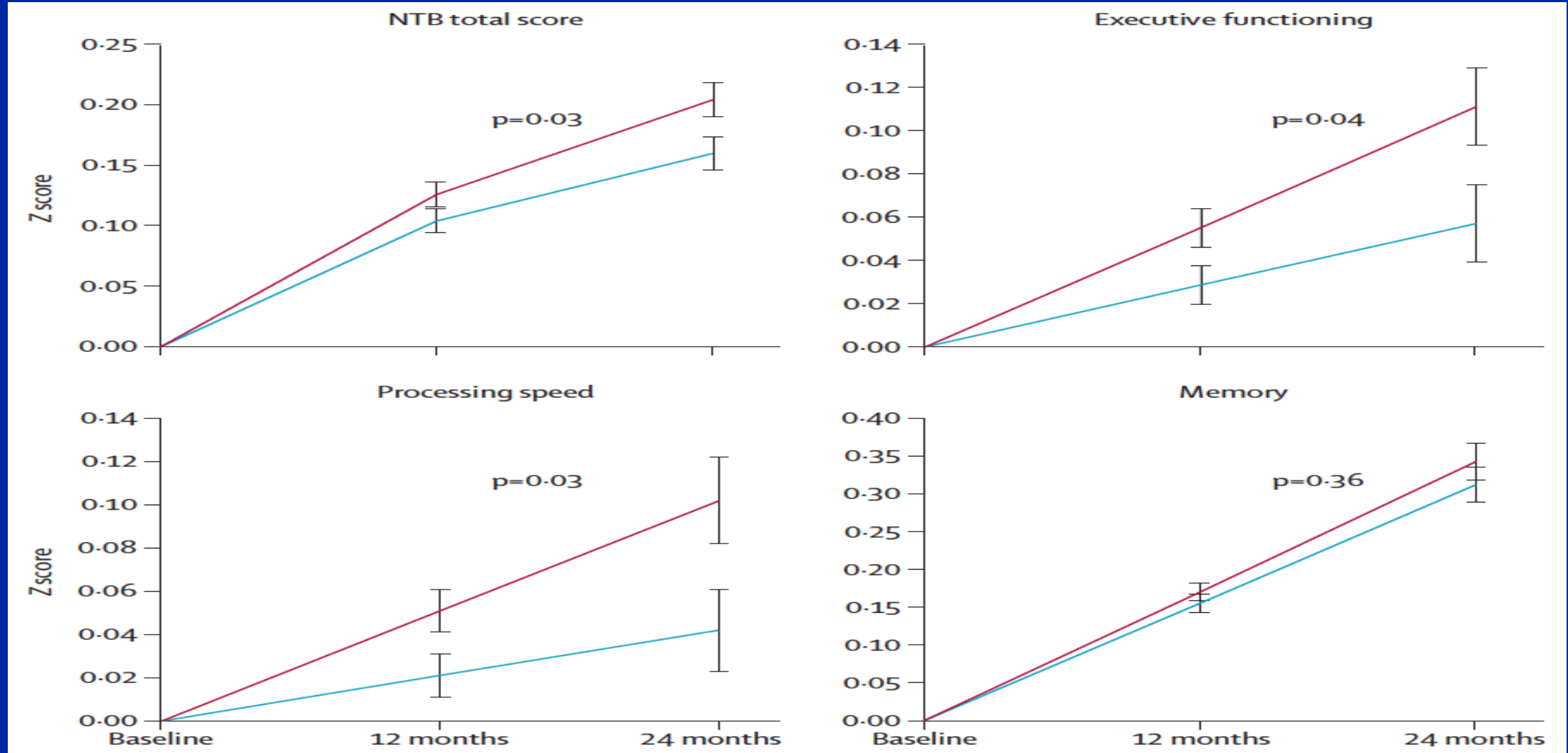
CV Risk Factors, Cognitive Function, Imaging **Early Adult to Midlife (N=3381, FU 25 yrs)**



Adjusted For Age, Sex, Race And Education

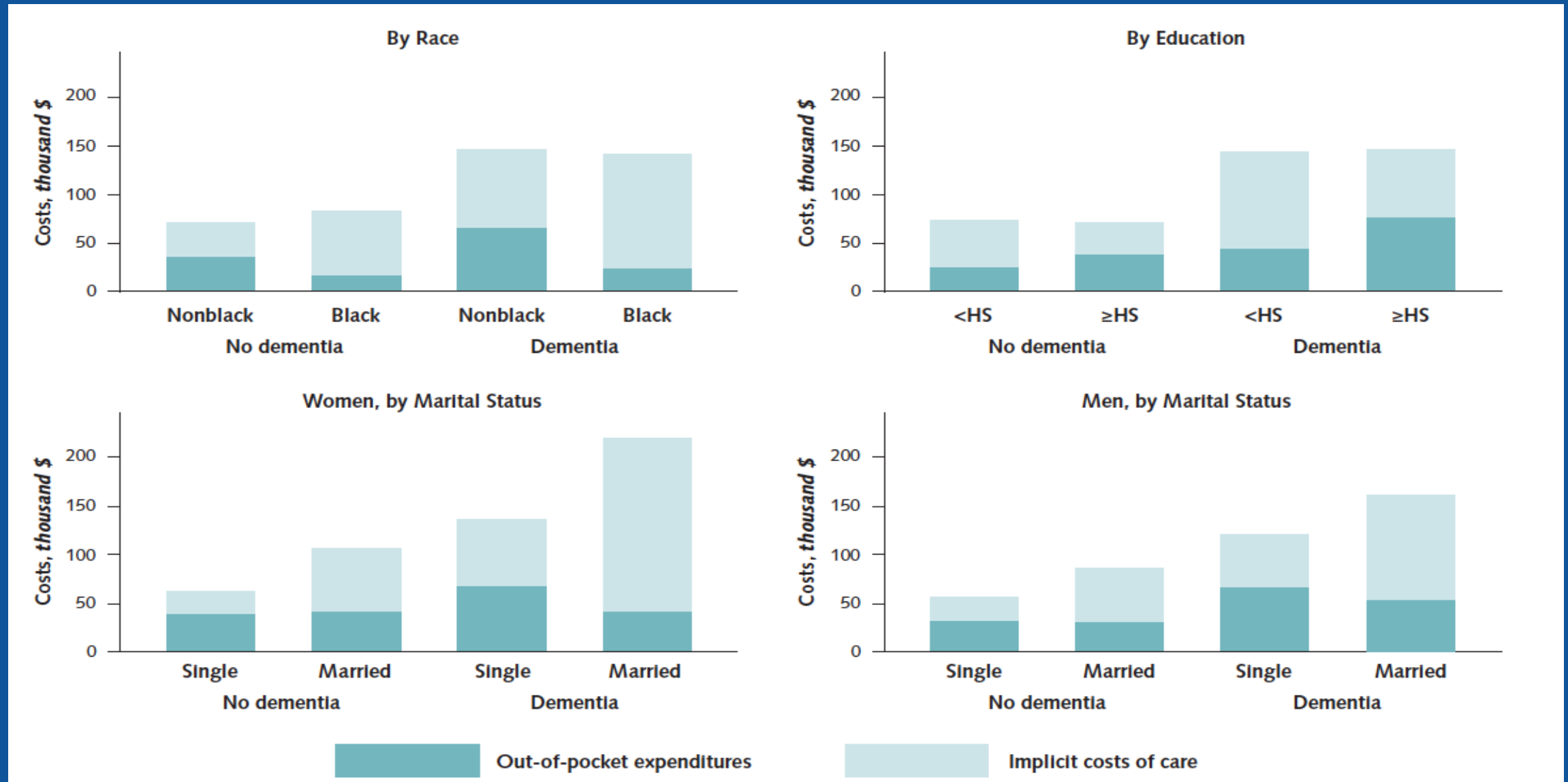
- 4. CARDIA (K Yaffe, et al.) Circ 2015– Cognitive – BP, Diabetes**
- 5. JI Friedman, V Fuster et. al– JACC CV Imag. 2015 – MRI /PET - BP, Diab., Smok.**

Change In Cognitive Performance During The 2 Year Intervention



6. FINGER (T Ngandu et al)., The Lancet 2015; 385:2255

The Burden of Health Care Costs for Patients With Dementia in the Last 5 Years of Life



B. Fibrinogen, Alzheimer's Disease (Mice)

In AD, Fibrinogen deposits with A β in the brain parenchyma and cerebral blood vessels. We found that A β and fibrin(ogen) interact, and their binding leads to increased **fibrinogen aggregation** and the formation of degradation-resistant **fibrin clots**, decreased cerebral blood flow **and eventual neurodegeneration**. Modest decrease in fibrinogen levels improves neuronal health. **Blocking the interaction** between fibrin(ogen) & A β **and/or antithrombotics** may become a **therapeutic target**.

M Cortes-Canteli et al. Neuron 2010. 66, 695-709

M Cortes-Canteli et al., J Alzheimer's Dis 2012; 32:599

M Cortes-Canteli et al., Neurobiology of Aging 2015:36:608

A. Imaging Study in Humans

The Three Challenges of Aging Quantity / Quality of Mental Life

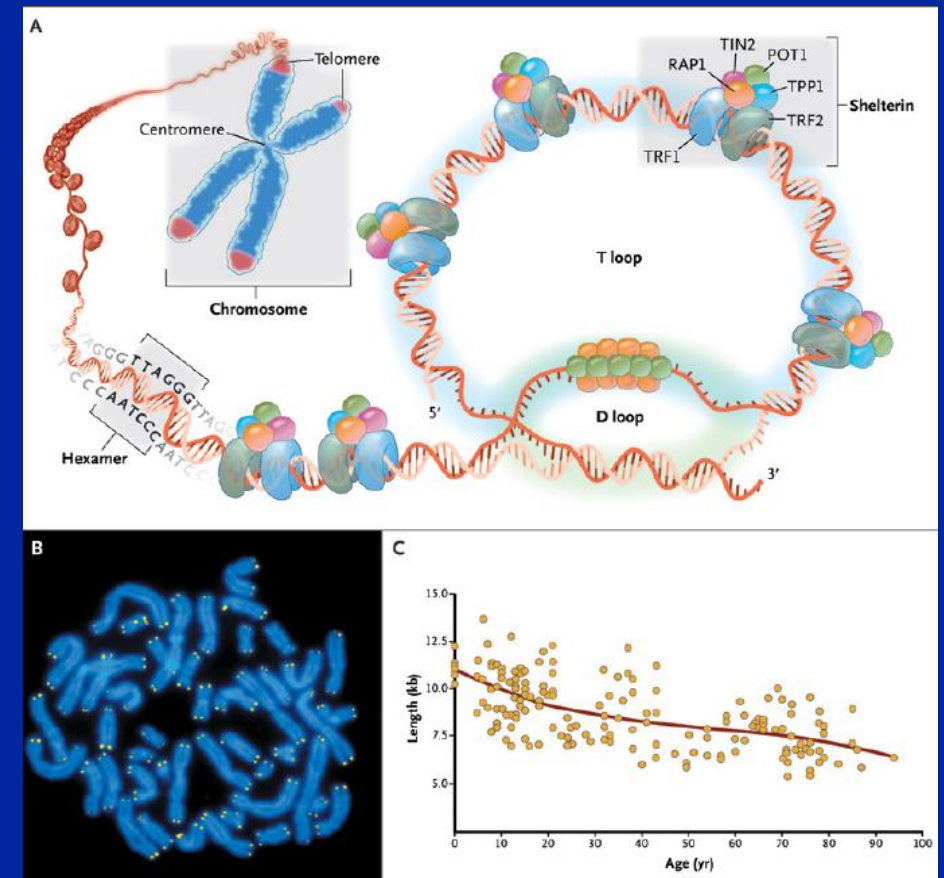
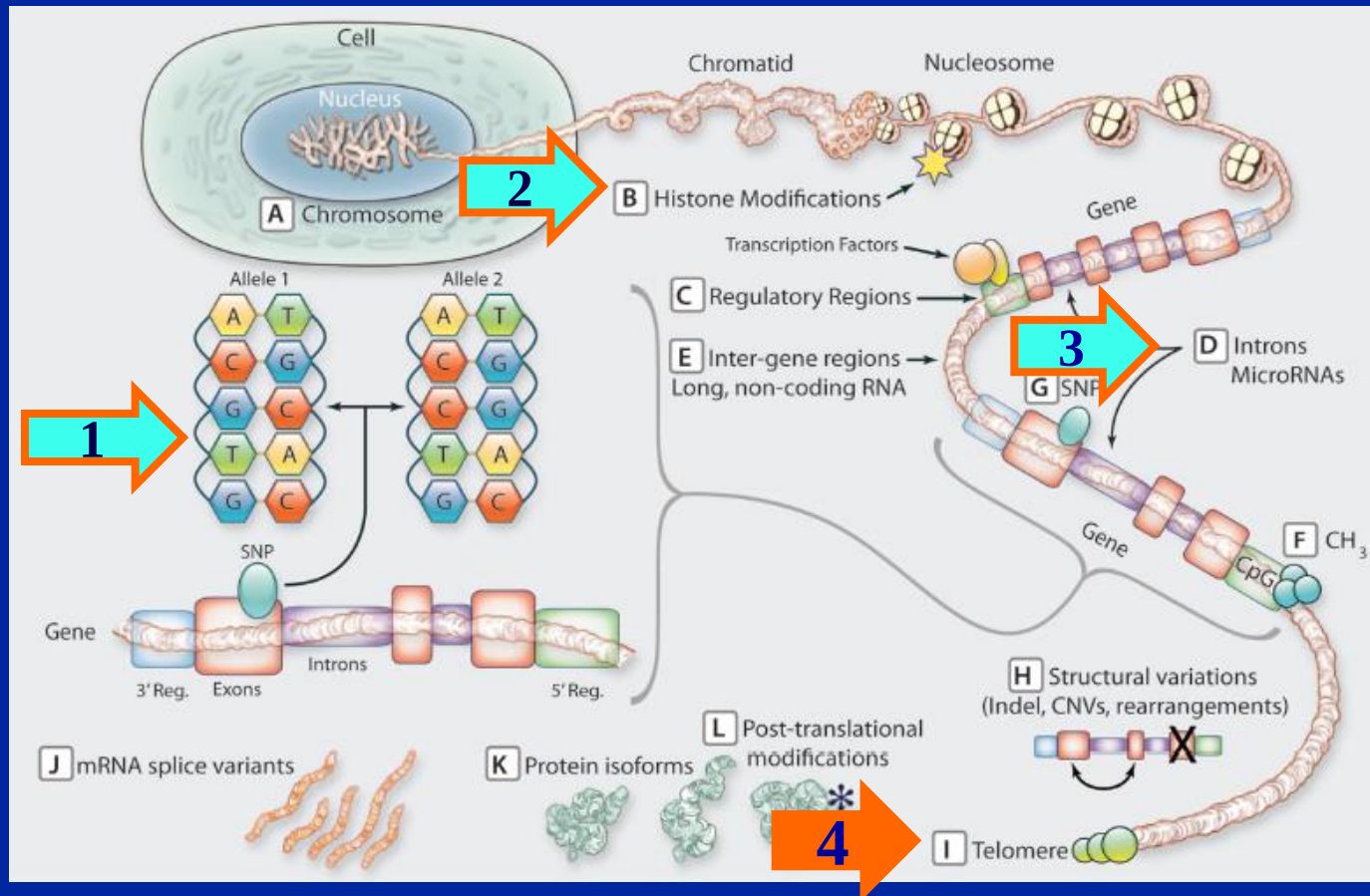
1. CV Drugs Overuse vs Underuse

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3. Wellbeing - Evaluative, Hedonic, Eudemonic

2. Aging / Frailty

Oxidative Stress on Telomere

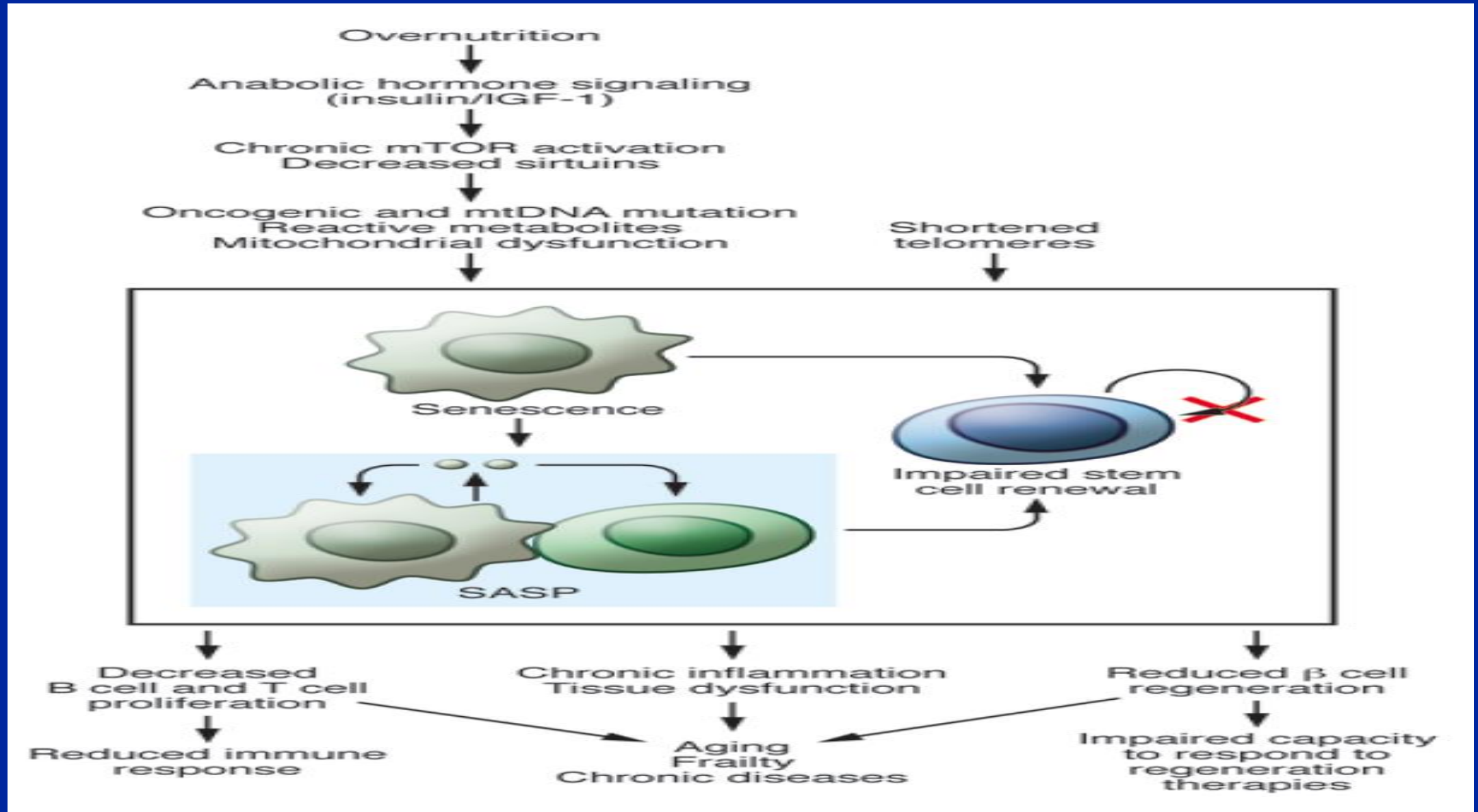


B Niemann et. al. JACC **2011**; 57: 577.

R Madonna, R De Caterina et. al EHJ **2011**;32:1190 (Houston &Chieti, Italy)

JC Kovacic, EG Nabel, V Fuster – Circ. **2011**;123:1650

Cell / Molecular Pathways & Aging



CB Newgard et. al. *J Clin Invest.* 2013;123:946

Oxidative Stress & Environment

Telomere Attrition & Shortening

- ***Smoking***
- ***Obesity***
- ***Sedentary lifestyle***

Inhibition Of Telomere Shortening

- ***Healthy lifestyle***

F Fyhrquist et al. Nat Rev Card. 2013; 10:274

PESA (*V Andres, V Fuster et al*) ***2015***

The Three Challenges of Aging Quantity / Quality of Mental Life

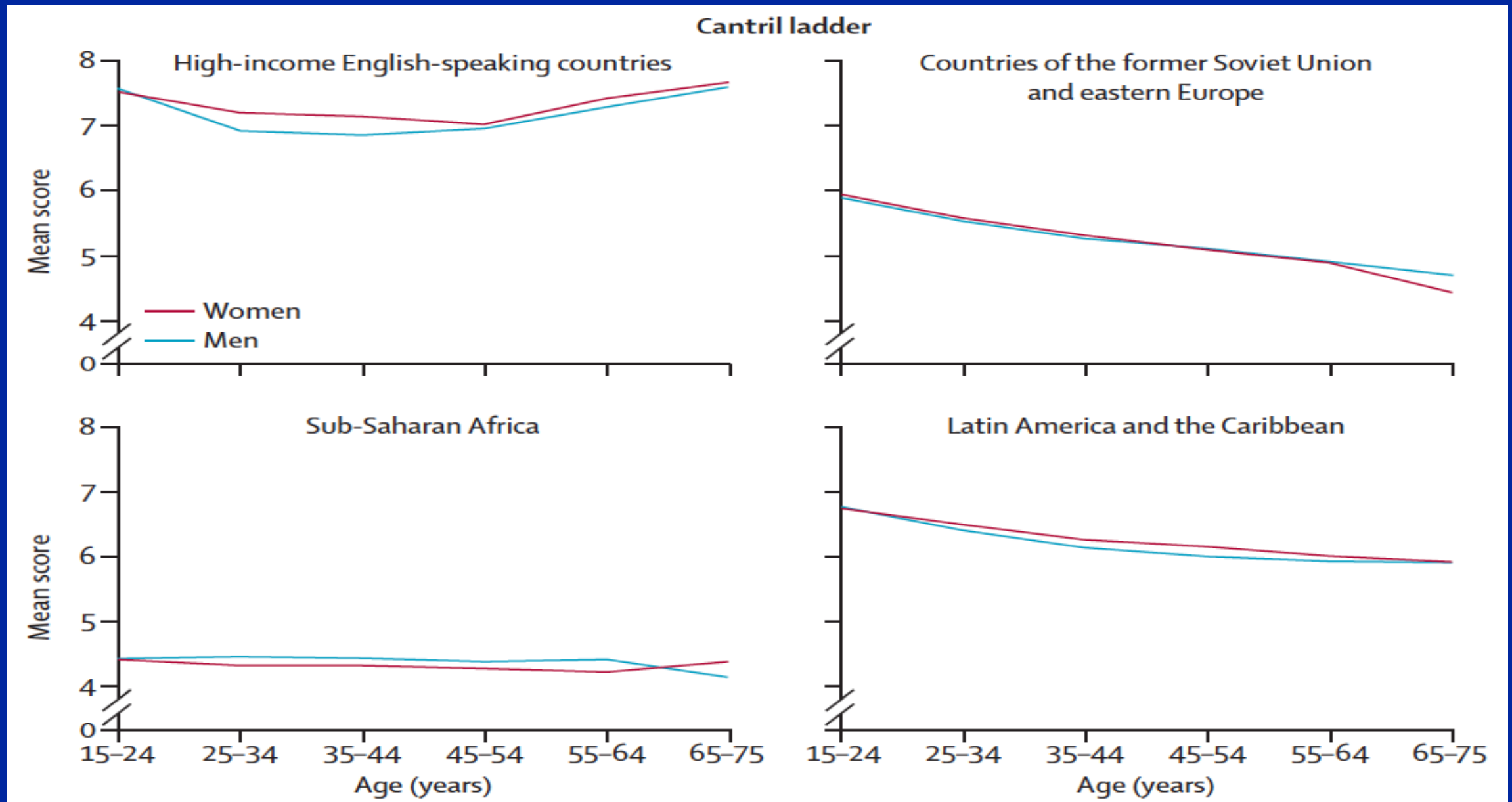
1. CV Drugs Overuse vs Underuse

2. Burden of Disease – QOML / Longevity

3. Wellbeing - Evaluative, Hedonic, Eudemonic

A Steptoe et al., Lancet 2015; 385:641

3. Wellbeing Evaluation & Age In Four Regions



A Steptoe et al., *Lancet* 2015; 385:641

Clinical to Health - Aging (A) to Birth (B)

Present

1. Health (QoL)

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Policy Mandatory (?)
Air Pollution & Noise

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Future

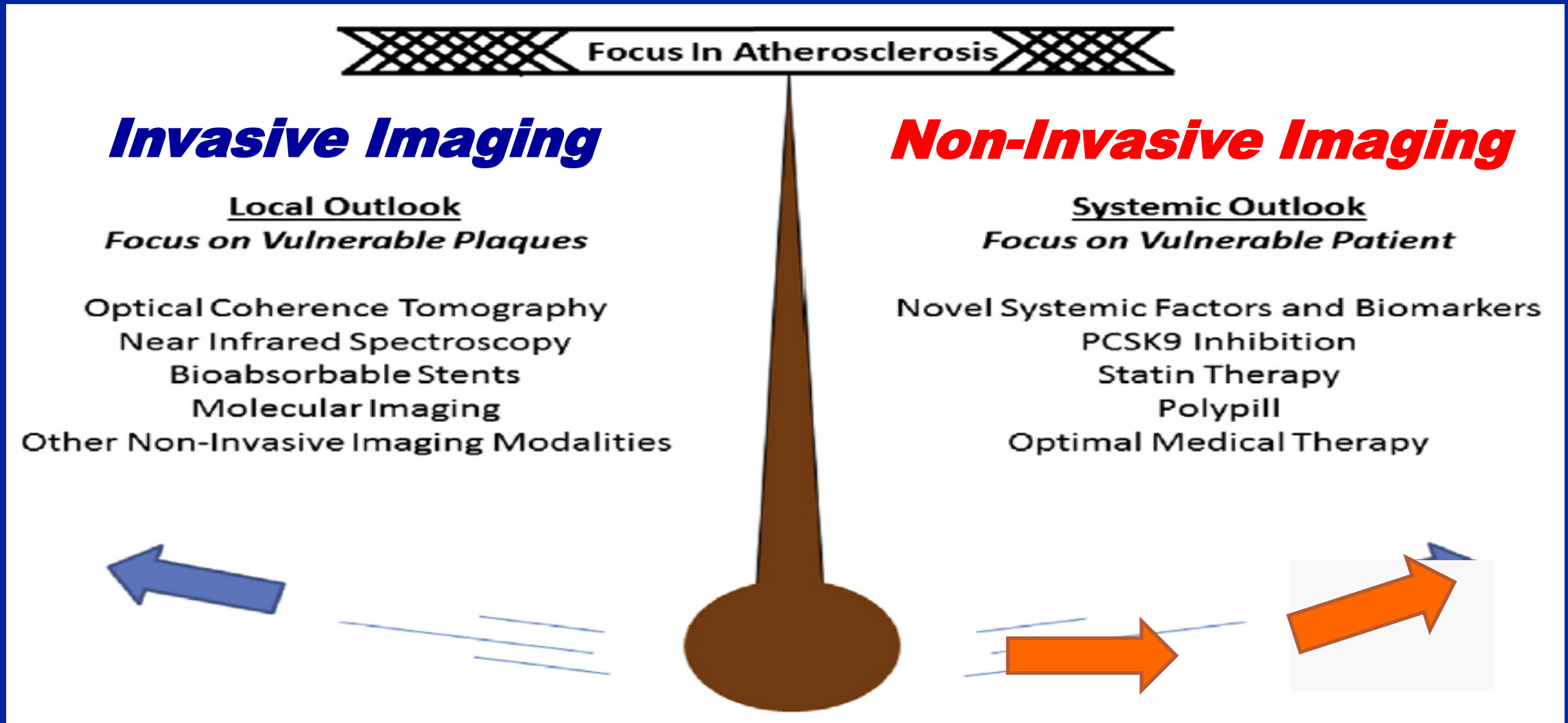
4. Education



Atheroscler,
1980-2000

VP/HRP
2000-2015

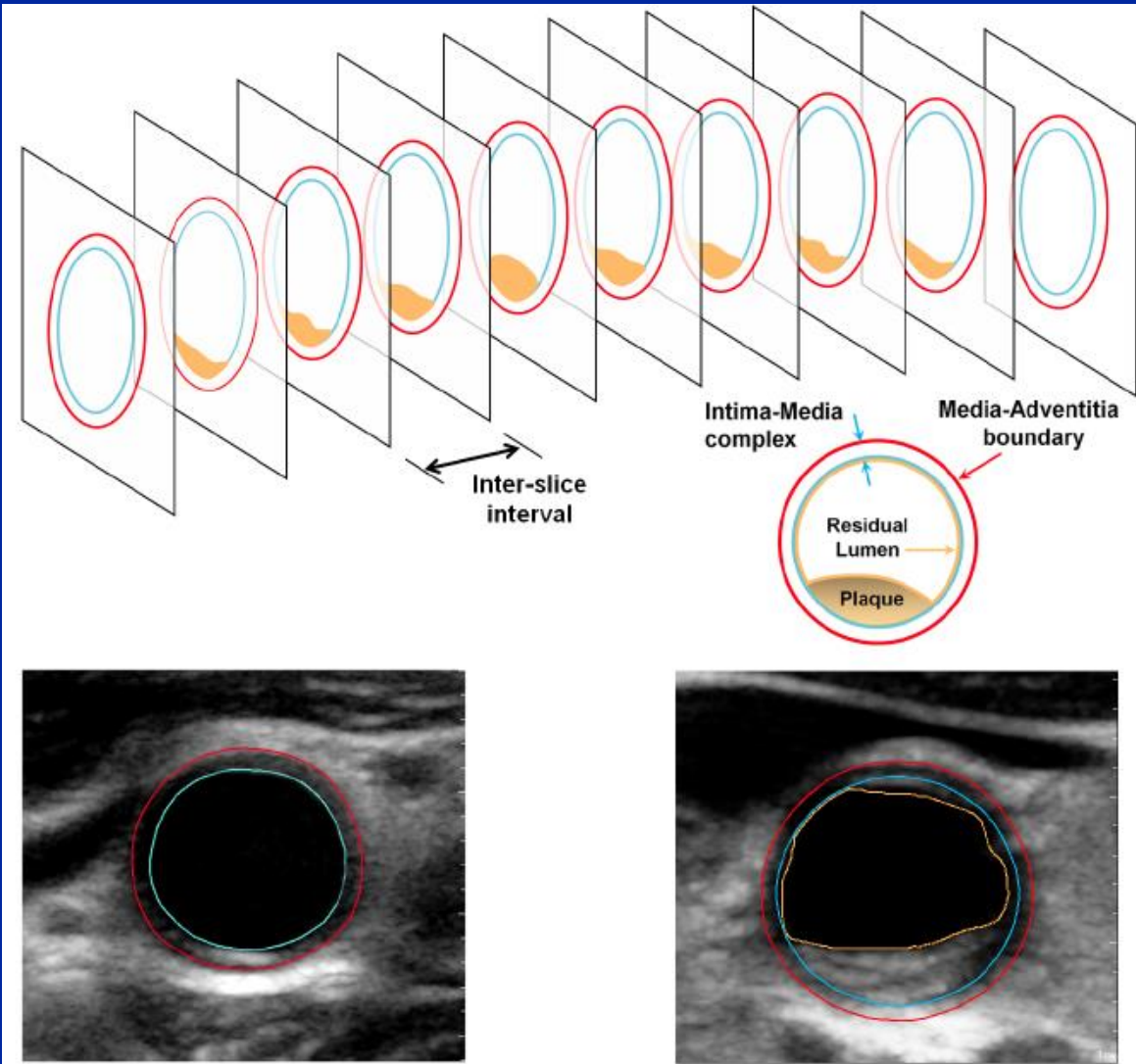
Burden Disease
2015-2020



MI Tomey, J Narula, J Kovacic, JACC 2014; 63: 1604 - **VF Modified**
A Arbab-Zadeh, V Fuster J. Am. Coll. Card. 2015; 65: 846

Plaque Burden (N=10,000)

Carotid 3D-US, Coronary Calcification



PI: Valentin Fuster, Mobile Units - AHJ 2010;160:49

H Sillesen, P Muntendam, E Falk, V Fuster et.al JACC Imag. 2012;7:681.

Science, Transatlantic Round Trip



1). MSSM



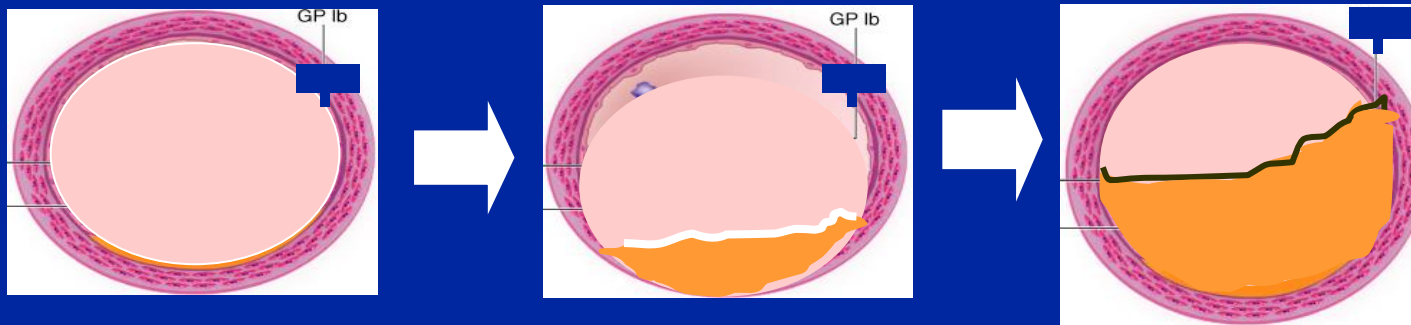
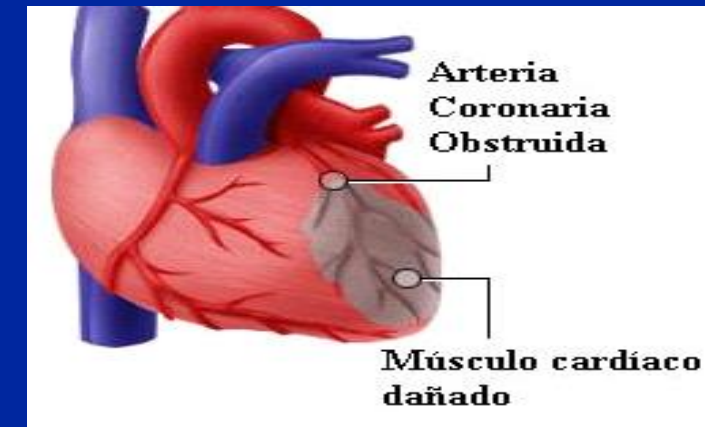
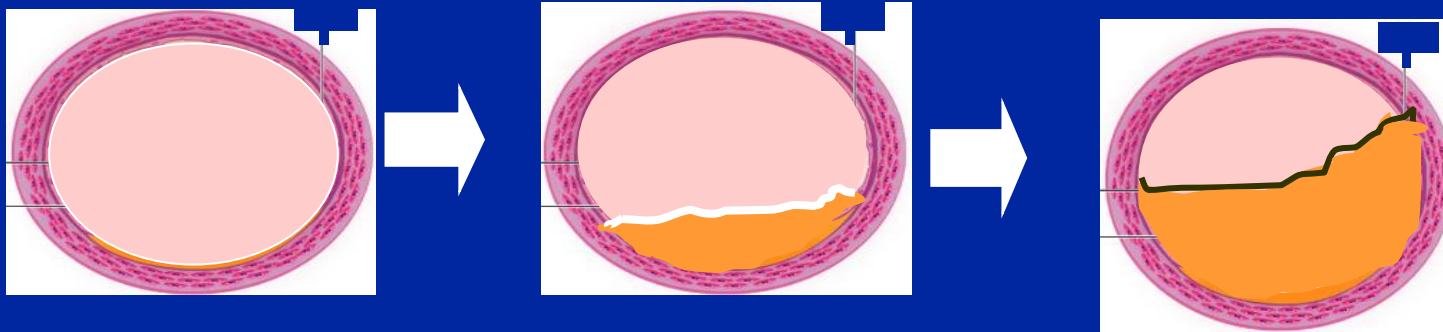
2). CNIC

PESA & AWHs
40-54y, N= 4,060 , FU 0,3,6 y

HRP > 55y,
N=5808 FU3y

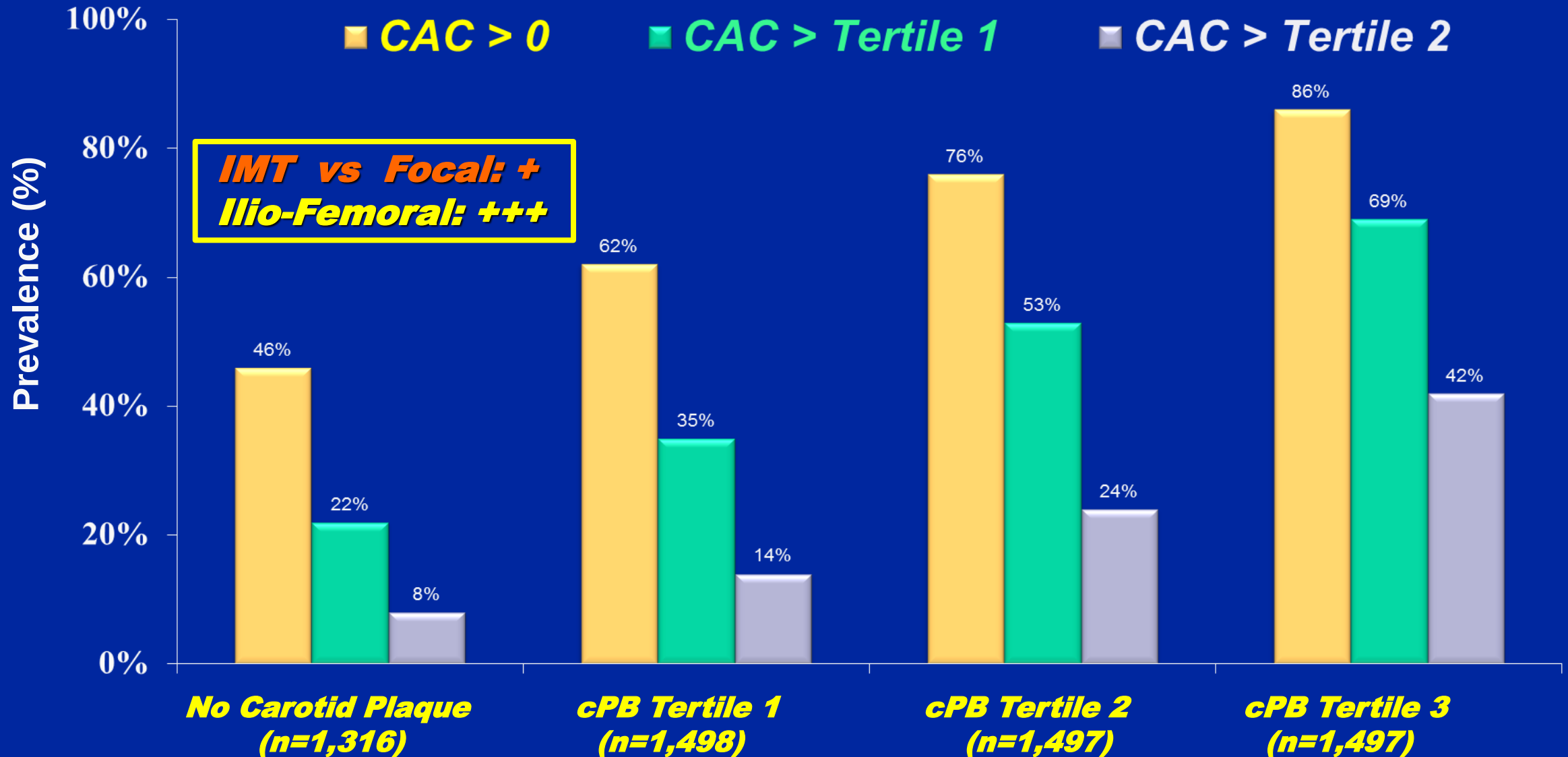
- 1. Predicting Progression (a-b)**
- 2. Three Life Style Approaches**

- ↓
- 1. Predict. Events (a-b)**
 - 2. Economics ?**

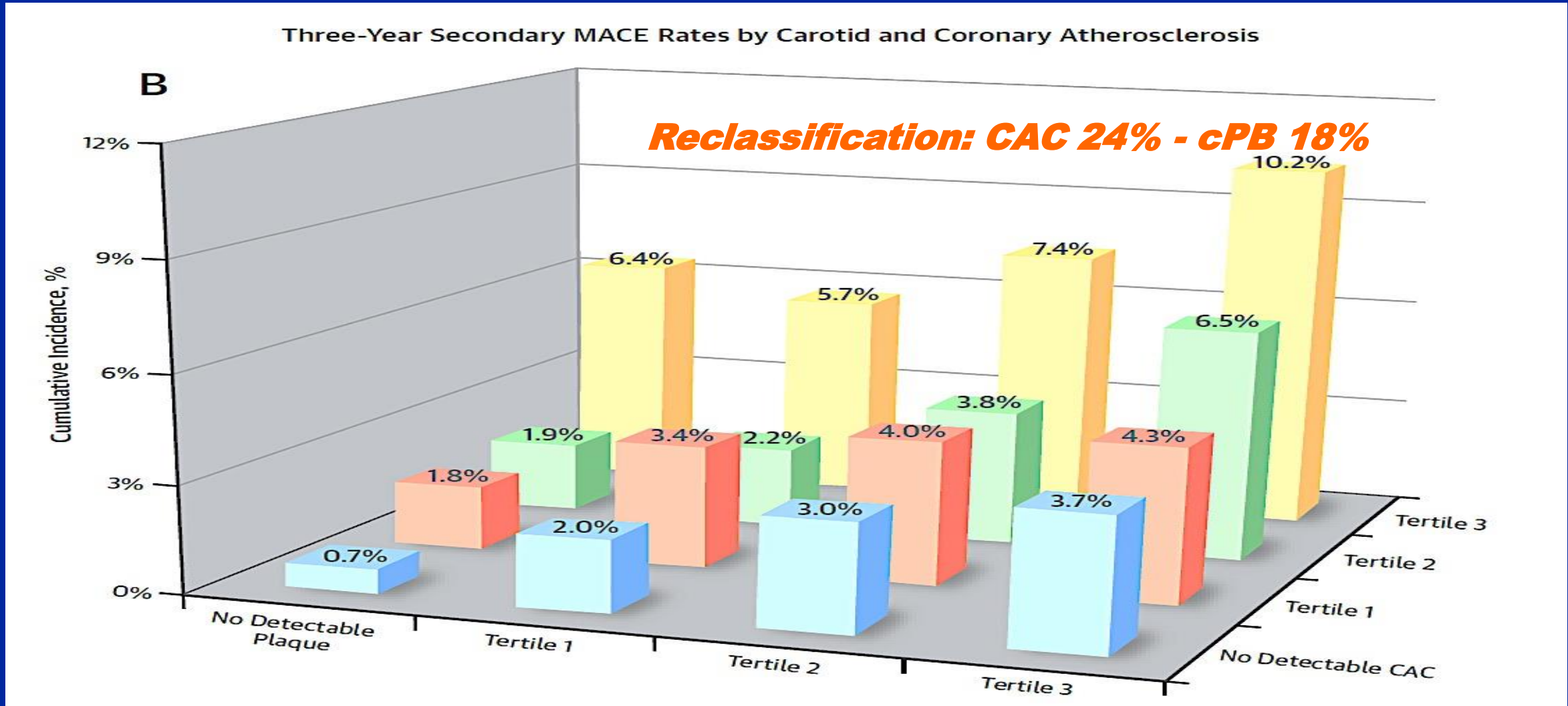


- 3. Omics (Framingham) - 4. Telomeres (S.blot, qPCR, Fresh)**

1a). Cross Interaction (n=5808) Between Carotid Plaque & CAC



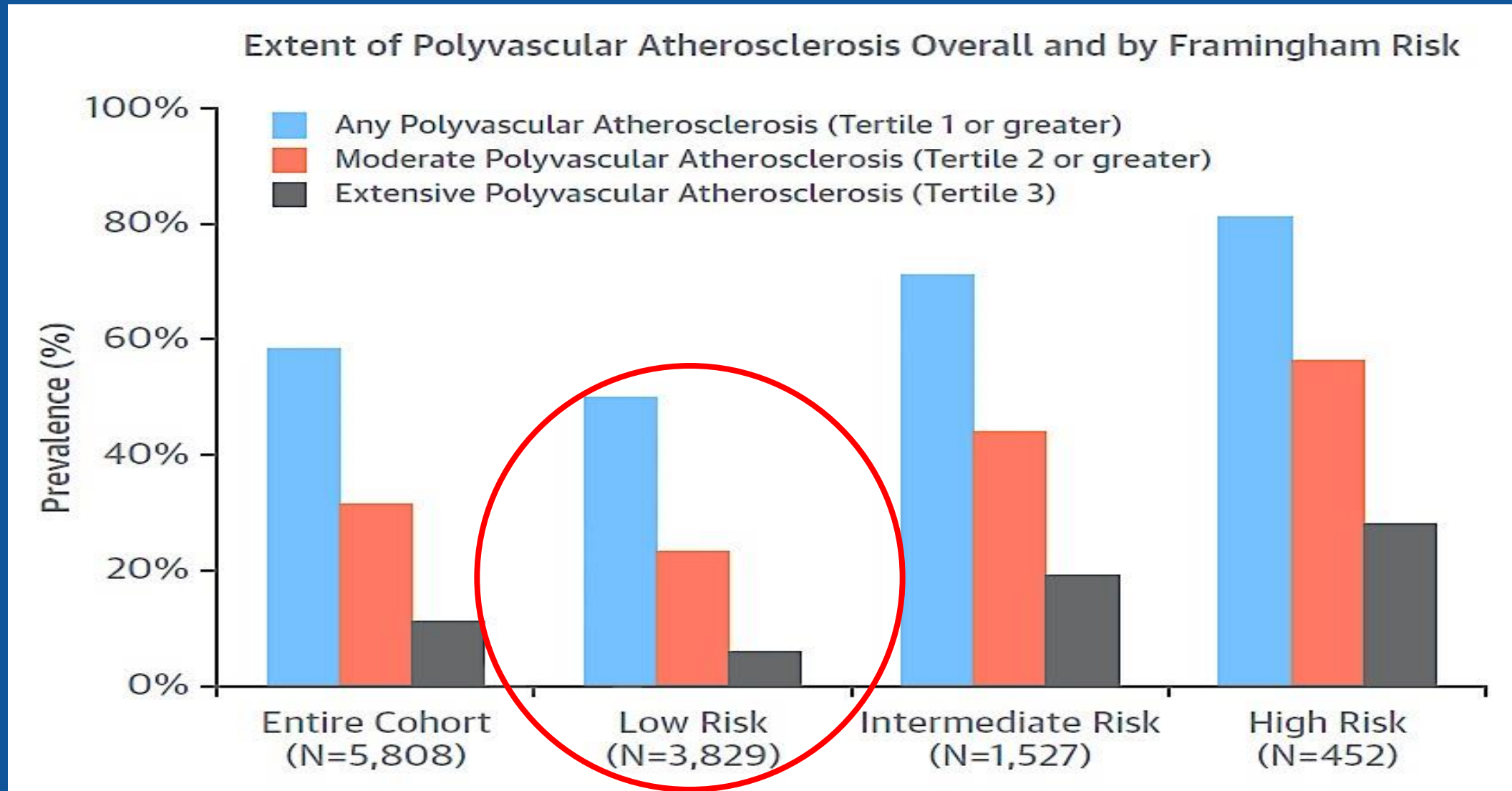
1b). Three Year All-Cause MACE Rates (N=216) by Carotid and Coronary Atherosclerosis



U Baber, R Mehran, V Fuster, et al. J. Am. Coll. Card. 2015; 65: 1065

Upcoming 8 Year Follow up

1c). Extent of Poly-Vascular Disease (N=5808) and by Framingham Risk Strata



U Baber, V Fuster et. al. J Am Coll Cardiol 2015 (In Press).

Science, Transatlantic Round Trip



1).MSSM



2).CNIC

TECHNOLOGY AND INFRASTRUCTURE

PRECLINICAL IMAGING FACILITIES

Nano PET



Operating Theater



Hemodynamic Laboratory



PET/CT



CARDIOVASCULAR IMAGING RESEARCH LABORATORY



ANIMAL MODELS



The CNIC is an international reference center in imaging technology

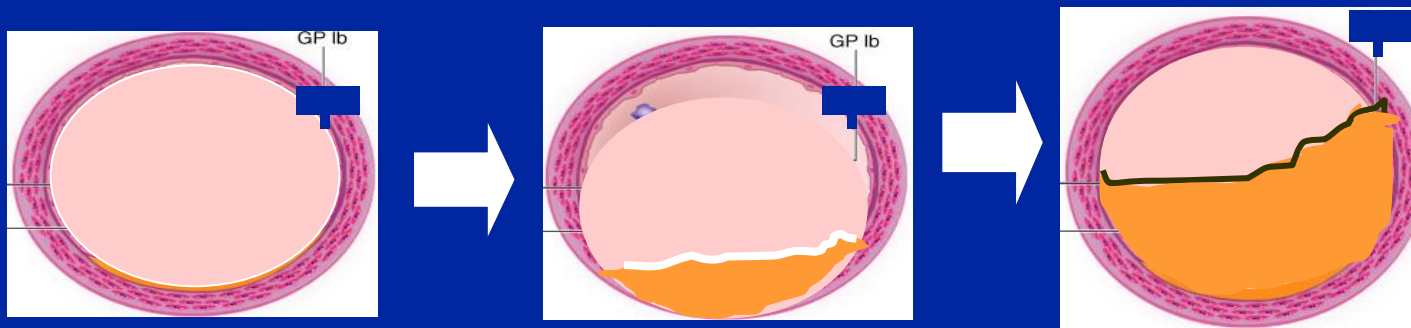
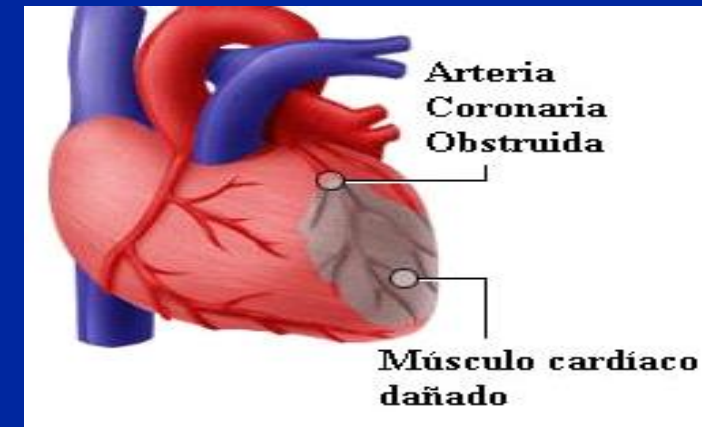
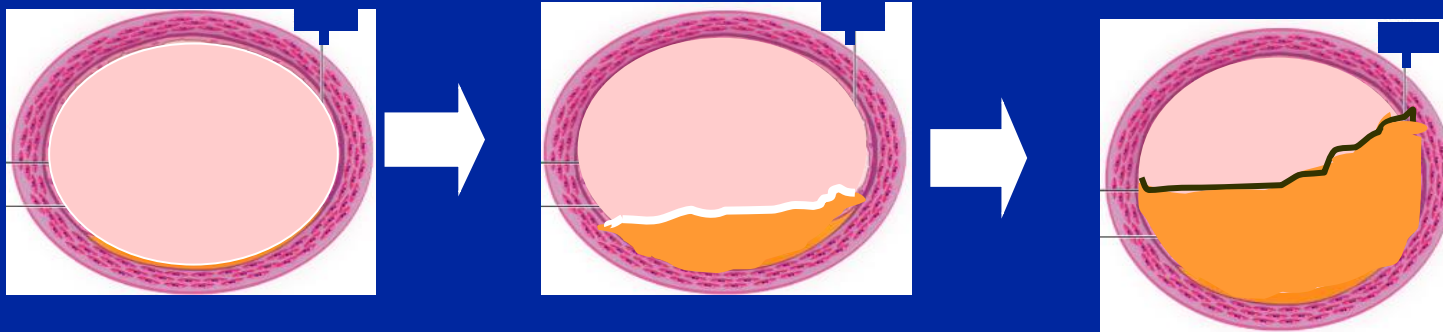
PESA & AWHHS
40-54y, N= 4,060 , FU 0,3,6 y

HRP > 55y,
N=5808 FU3y

- 1. Predicting Progression (a-b)**
- 2. Two Life Style Approaches**



- 1. Predict. Events (a-b)**
- 2. Economics ?**

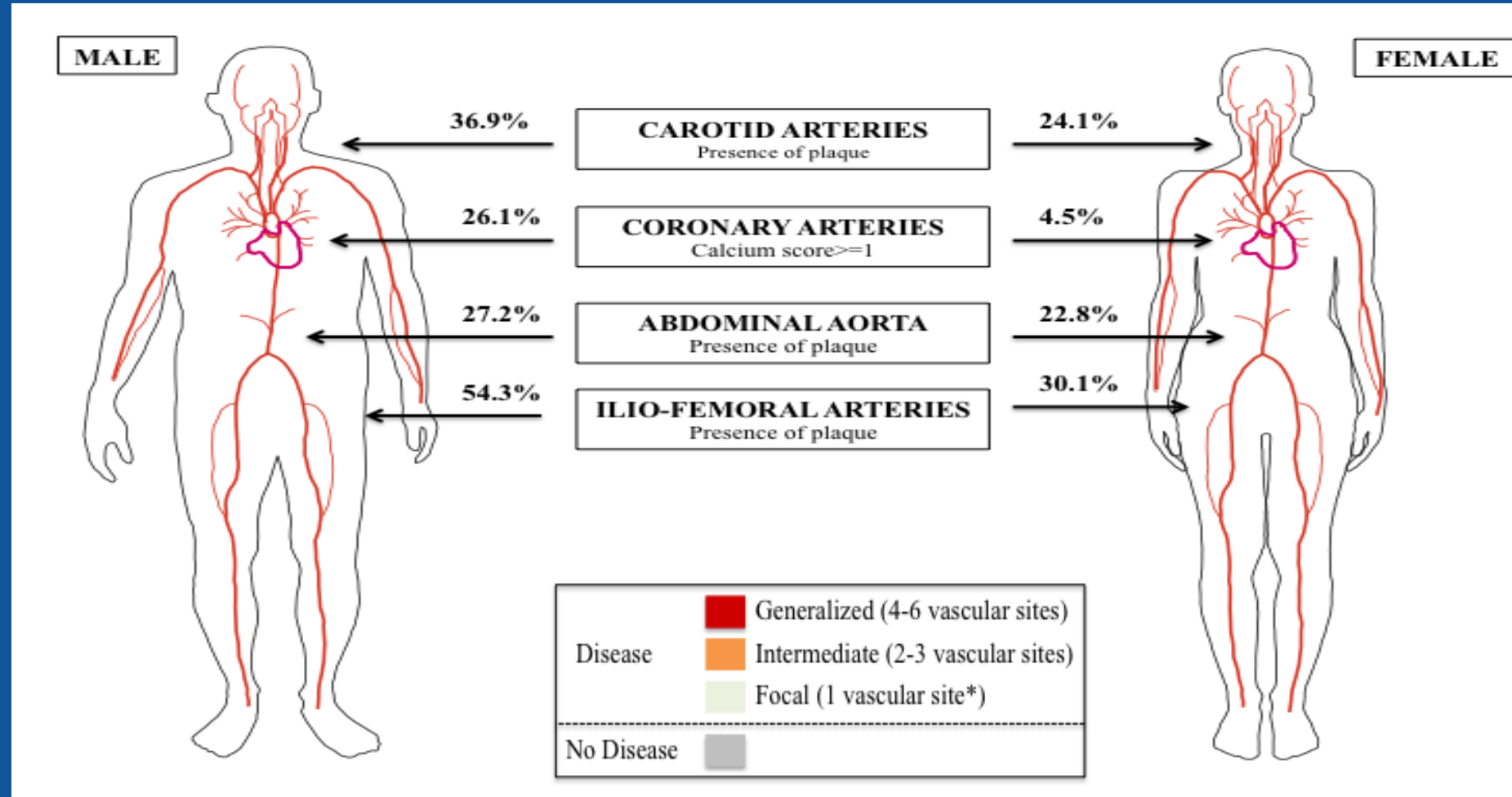


- 3. Omics (Framing.)**
- 4. Telomeres (S.blot, qPCR, Fresh)**

PESA (L Fernandez-Friera, A Fernandez-Ortiz, V Fuster et.al) Circ 2015, 4/20

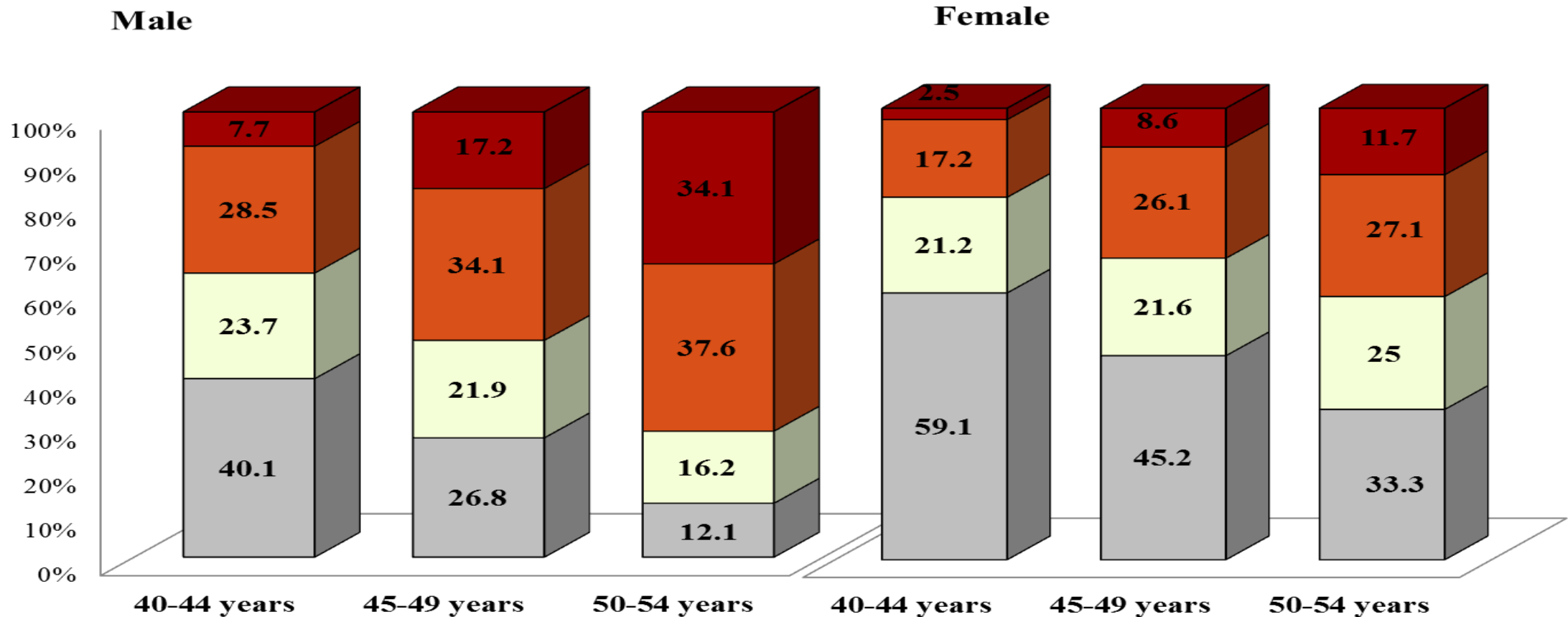
Sub-Clinical Atherosclerosis (n=4060)

Ilio-femoral More Sensitive Than Carotid (6 regions)

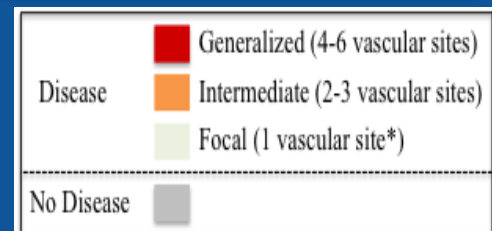


PESA (L Fernandez-Friera, A Fernandez-Ortiz, V Fuster et.al) Circ 2015, 4/20

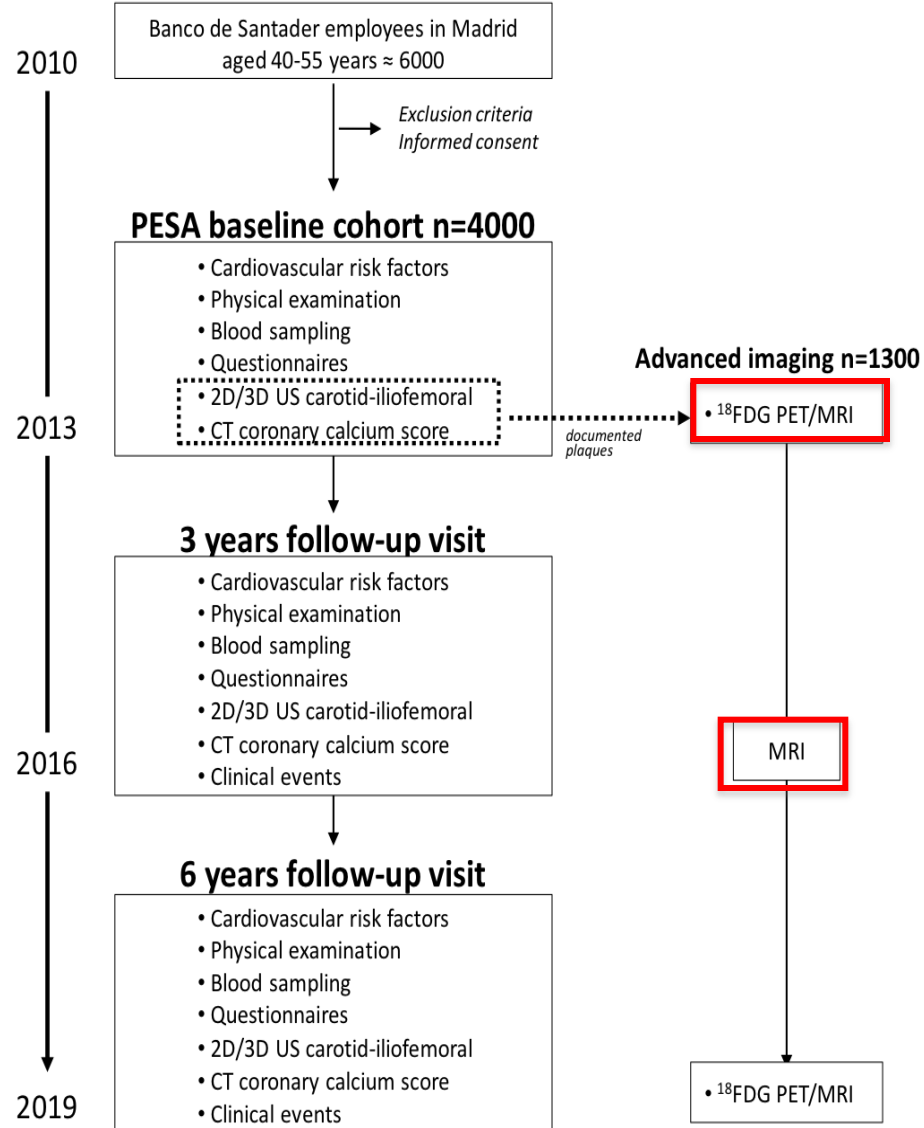
1a). *Distribution Of The Systemic Extent Of Subclinical Atherosclerosis*



PESA (L Fernandez-Friera, A Fernandez-Ortiz, V Fuster et.al)
Circulation 2015, 4/20



1b) PET / MRI Protocol



Study population

≈950 individuals who had baseline vascular PET/MRI and will returned for follow-up vascular MRI to CNIC

Imaging protocol

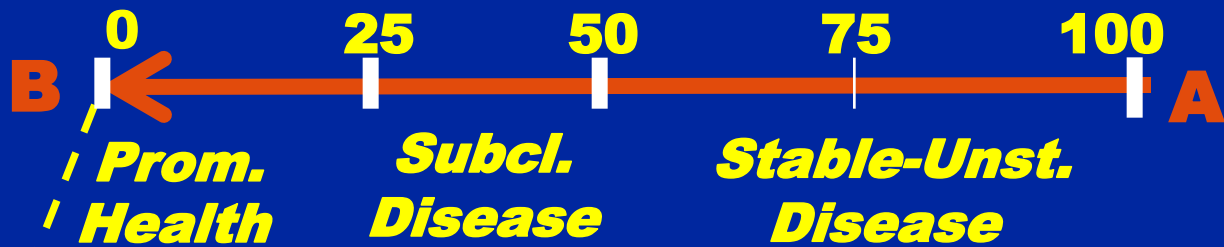
A cardiac MRI study, including cine (LV function and structure), T1- and T2-mapping (Inflammation and diffuse fibrosis) and LGE (scar)

Advantages / Requirements

- Instead of having a vascular PET (30 min), they will have a cardiac MRI (novel heart assessment in PESA)
- Fibrosis quantification: creatinin / Hb
- Additional Budget: contrast for 950 cardiac MRI: 46.400 € (personal included)

Clinical to Health - Aging (A) to Birth (B)

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1. Health (QoL)

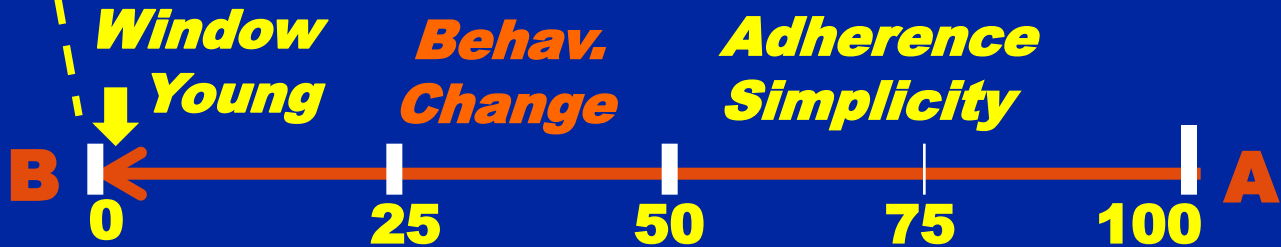


2. Environment

Science

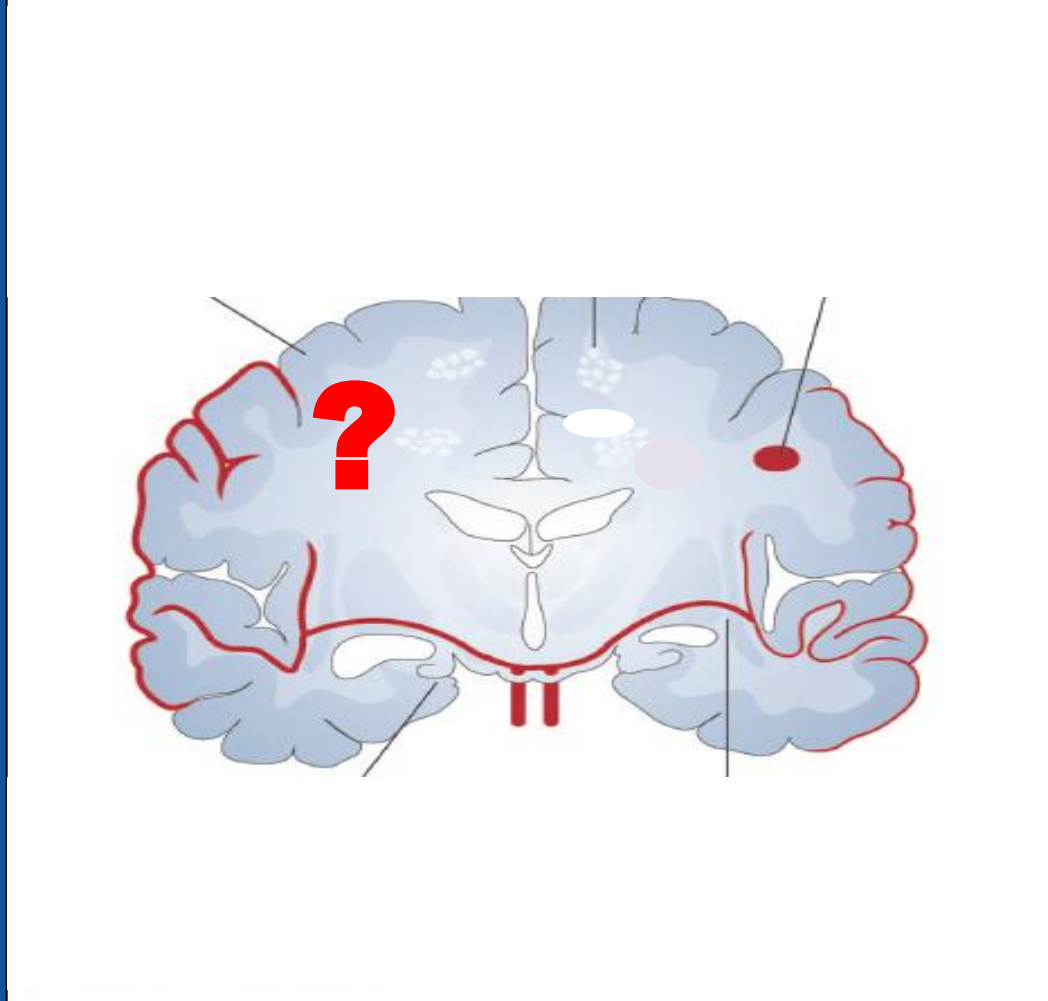
Future

Education



A Health Center In The Adult Brain (?)

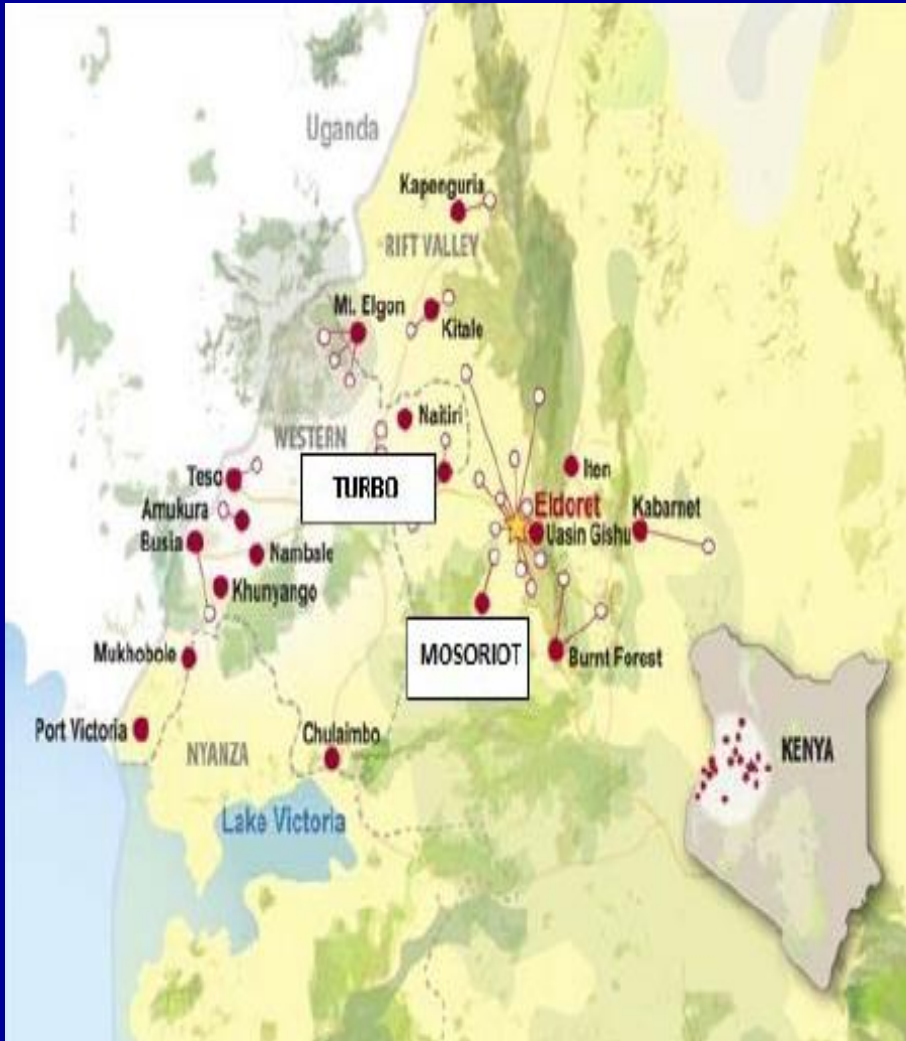
2B



To Stimulate / Motivate

1. AMPATH Centers In Kenya

BP Control / Non MD / High Technology



R Vedanthan, V Fuster, NHLBI / Kenya Model (2012-2016)

2. CARDONA INTEGRAL – “FIFTY-FIFTY”

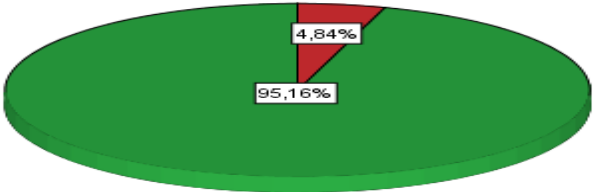
SMOKING	0	1 ¹	2	--	--	2
OVERWEIGHT	0	1 ²	2	--	--	2
SEDENTARISM	0	1 ³	2	--	--	2
HYPERTENSION	0	1 ⁴	2 [†]	--	--	2

TOTAL HABIT SCORE

—————→ 8



SIX MONTHS



95% of the people have improved in one or more of the habits or RF.

The Seven Community Study

N=552



E. Gomez, V Fuster et al 2015 (Subm)

Approach 3: Ongoing PESA Program, Madrid – AHA 2015

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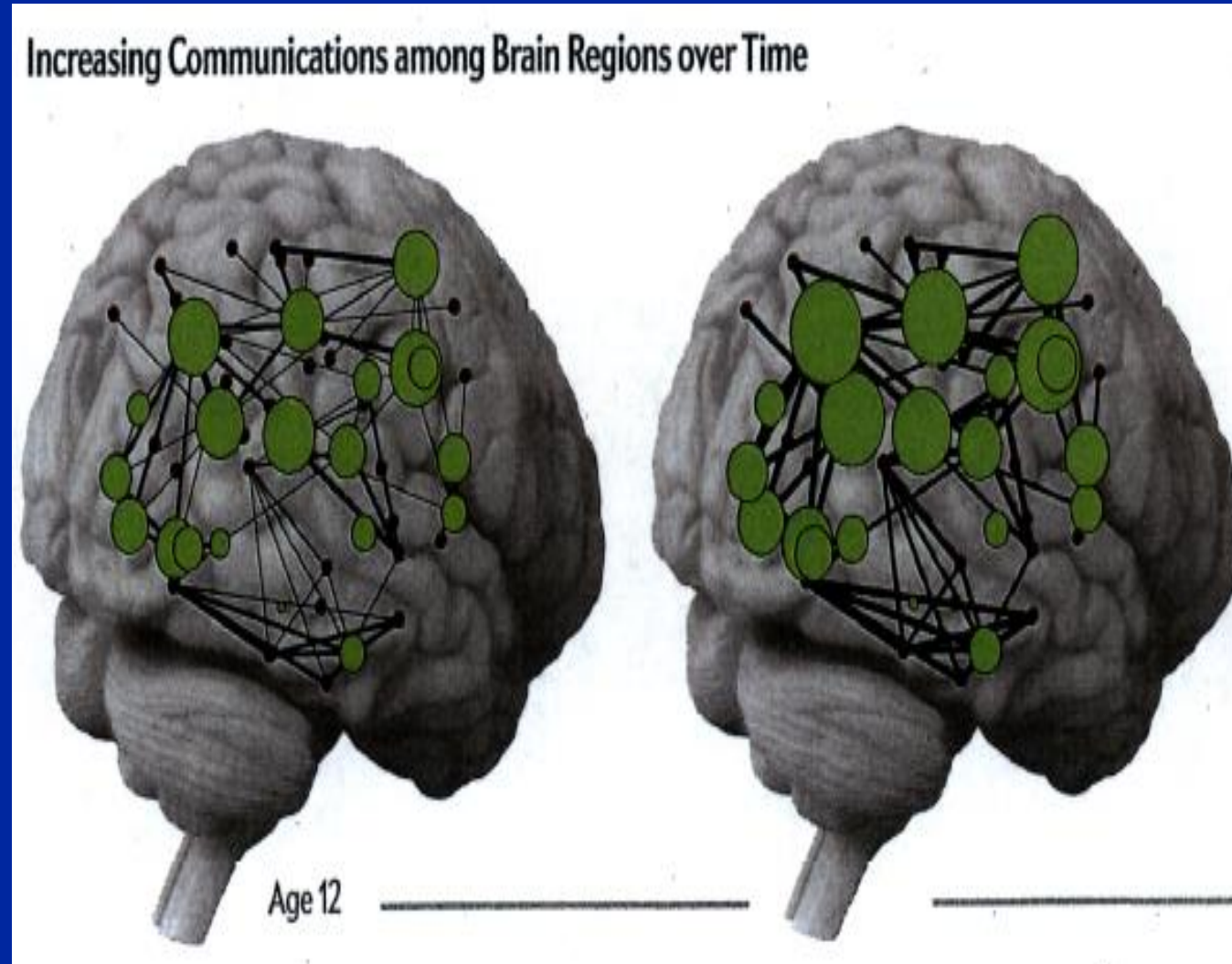
Future

4. Education



Child's Brain Development Less Networking Brings Attention

3B



JN Giedd. *Scientific American* 2015;312:32

Promoting Cardiovascular Health A Motivational & Stratified Approach

Subclinical – Heart, Brain, Longevity

ACC-New York, Dec. 11, 2015

No Disclosures