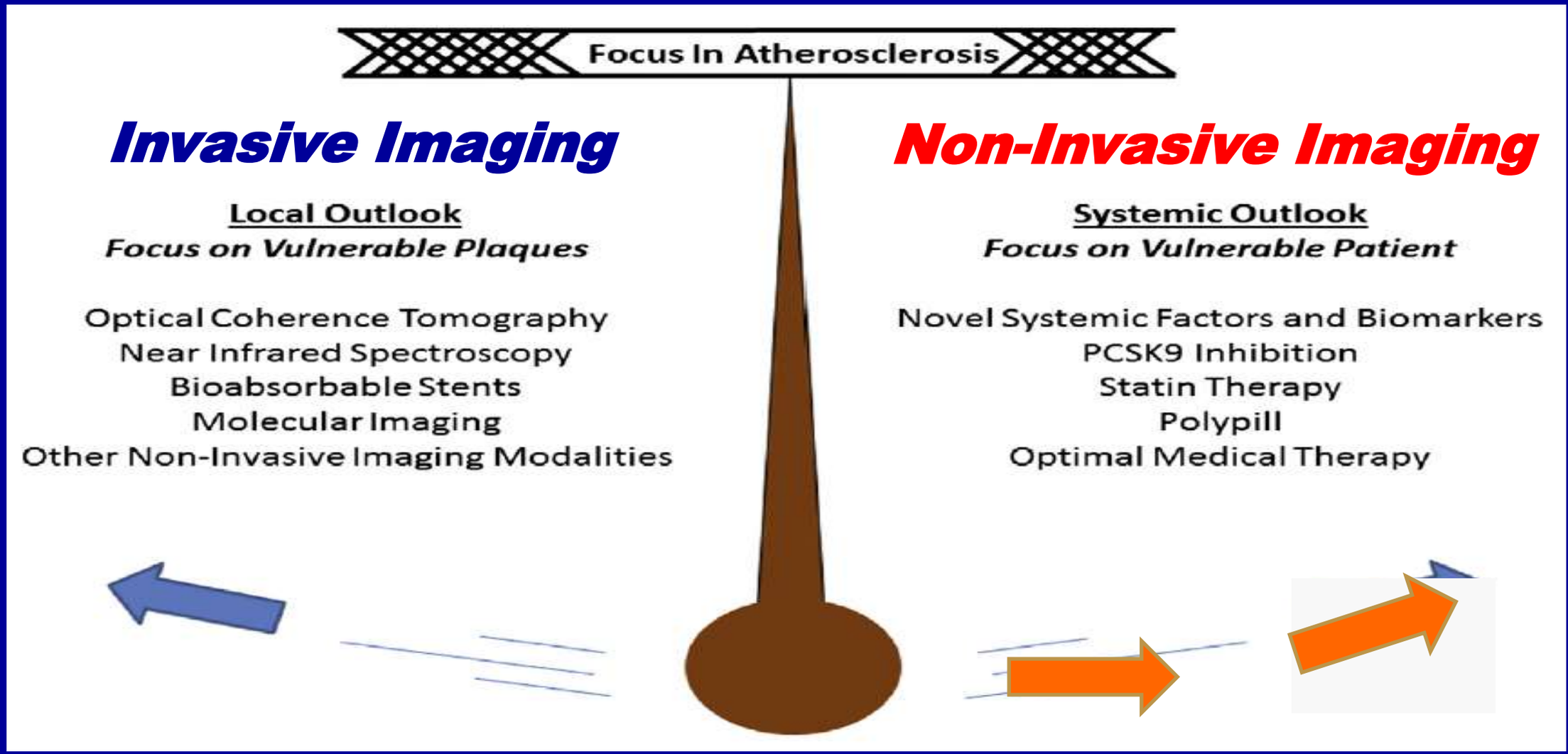
Subclinical Cardiovascular Disease
Integration of the Heart & Brain

Motivating Frontiers in CV Imaging

Seoul, April 29, 2015

No Disclosures

Atheroscler, 1990-2000 | 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

A Transition From Disease to Health
Heart – Brain Integration
Imaging / Omics / Regeneration / Life Style

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Science, Transatlantic Round Trip

1).MSSM

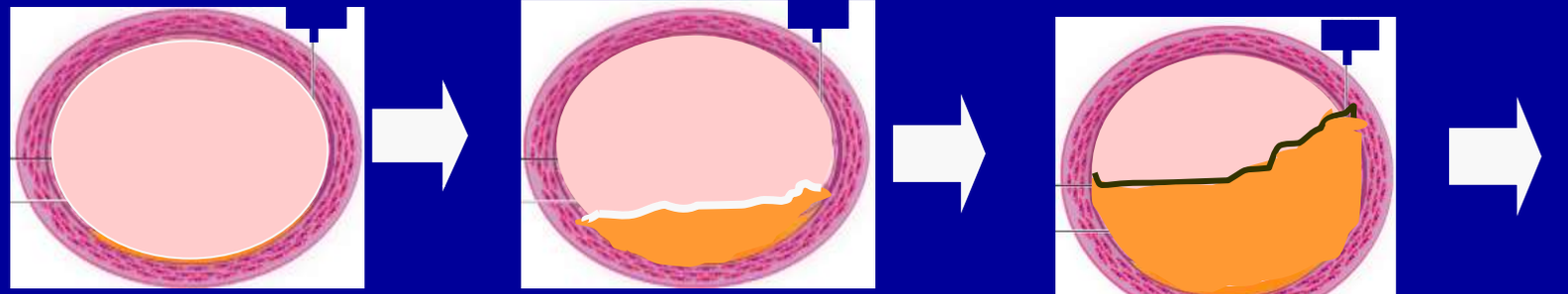
2). CNIC

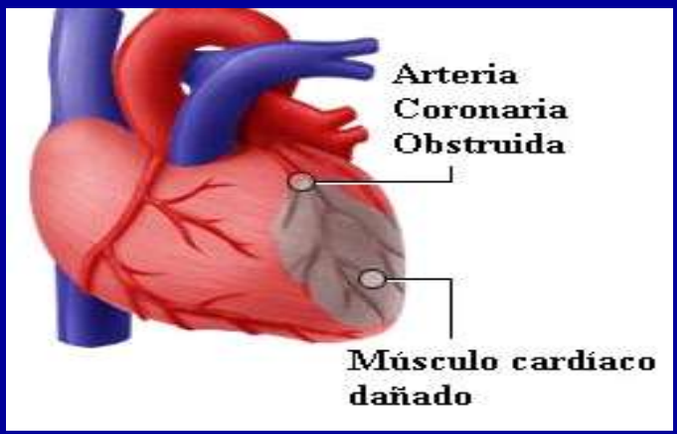
PESA & AWHS
40-54y, N= 4,060 , FU 0,3,6 y

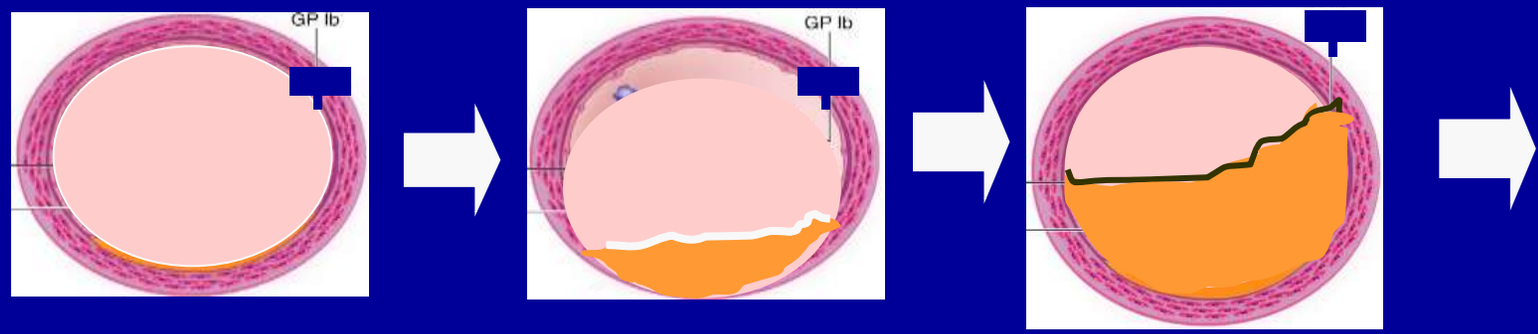
HRP > 55y,
N=5808 FU3y

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

1. Predict. Events (a-c)
2. Economics ?





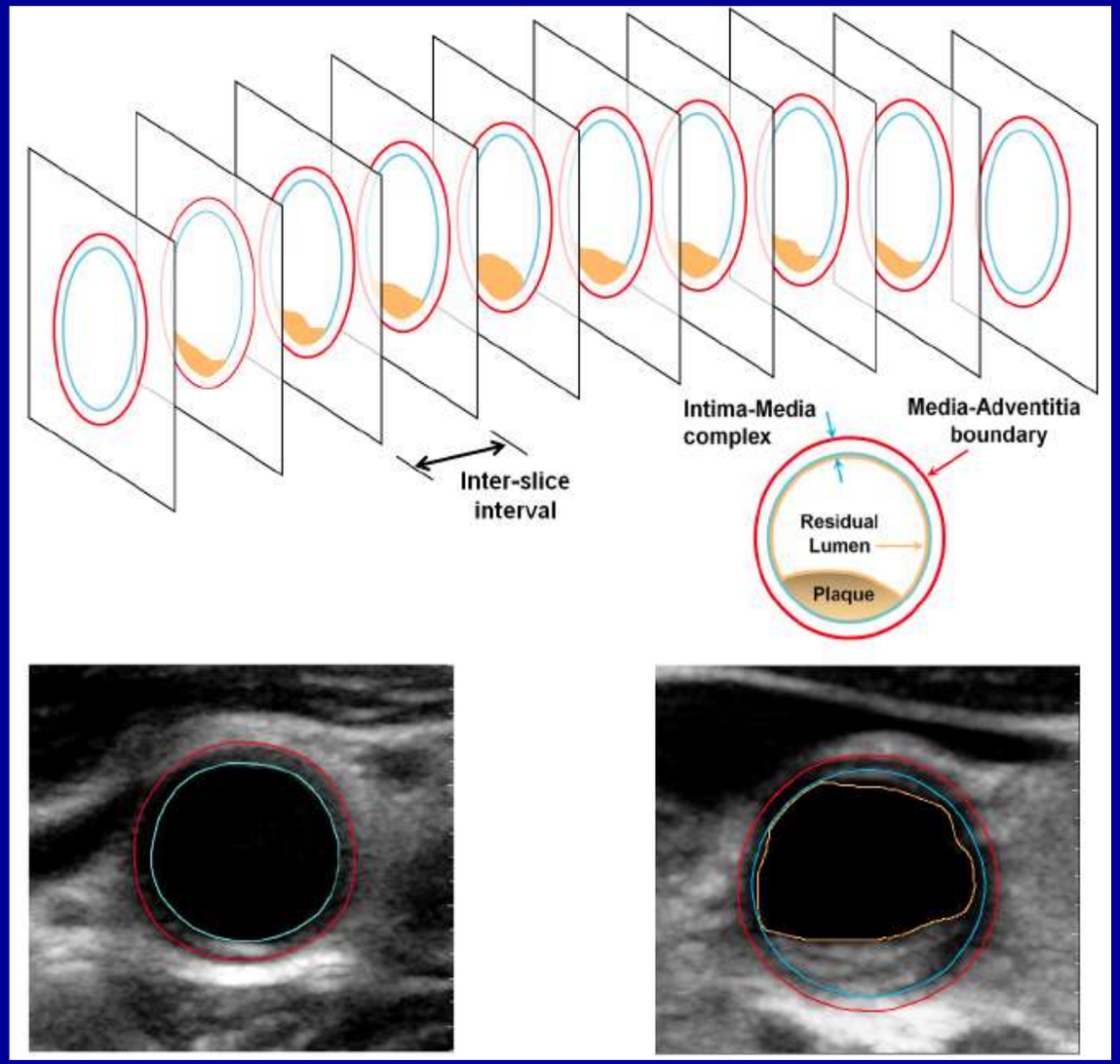


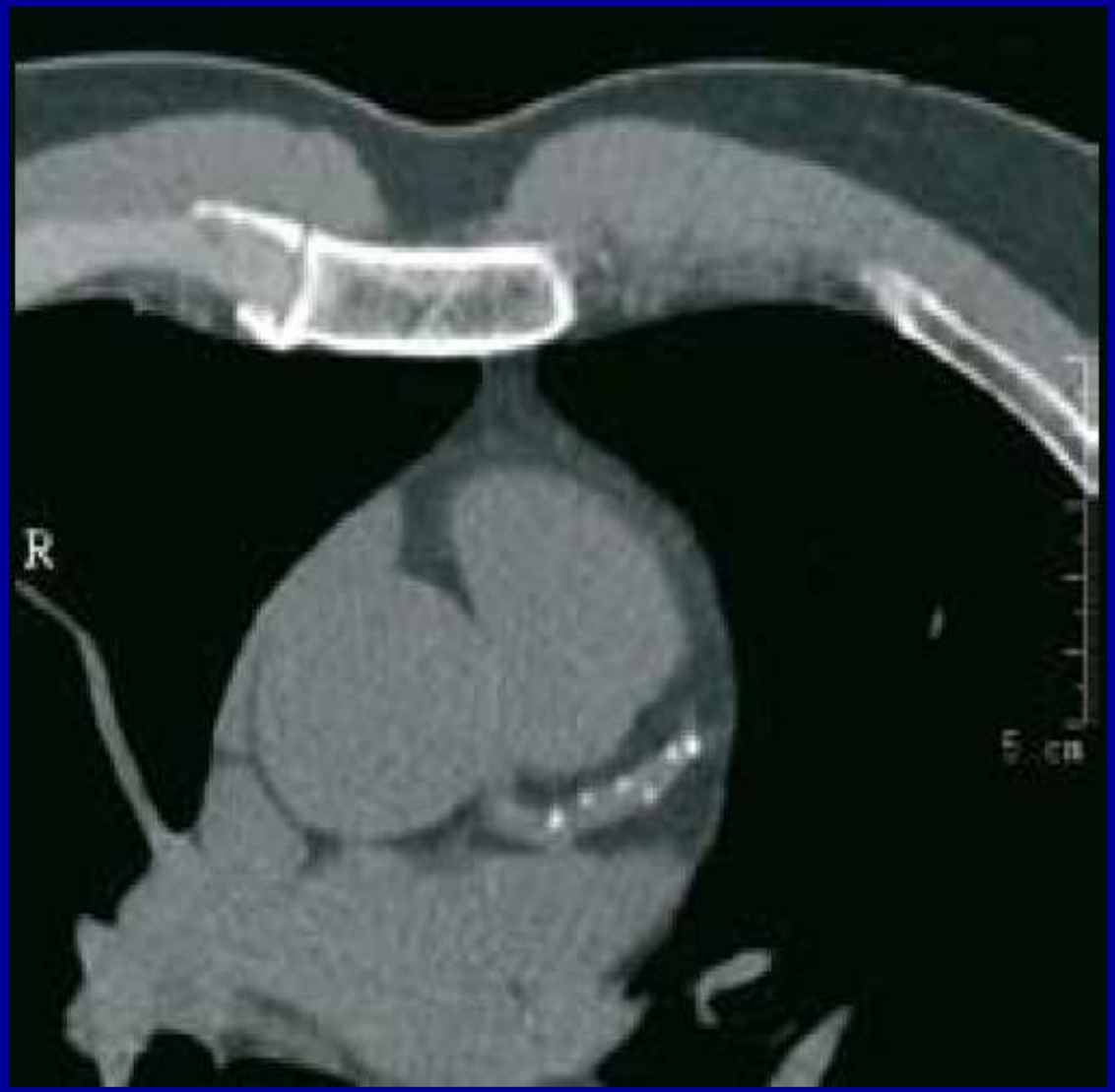
3. Omics (Framingham) - **4.** Telomeres (S.blot, qPCR, Fresh)

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

Plaque Burden (N=5808)

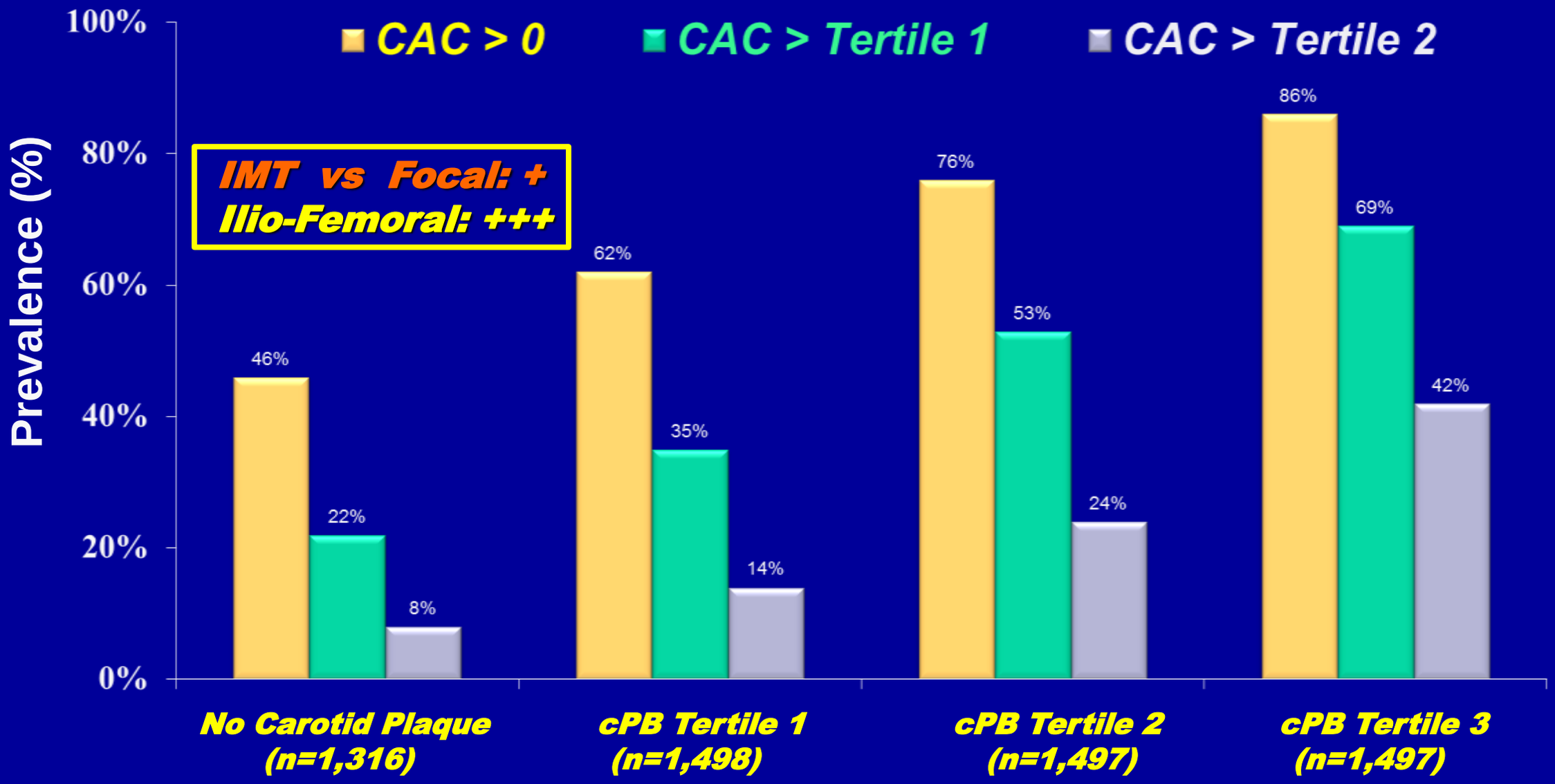
Carotid 3D-US, Coronary Calcification





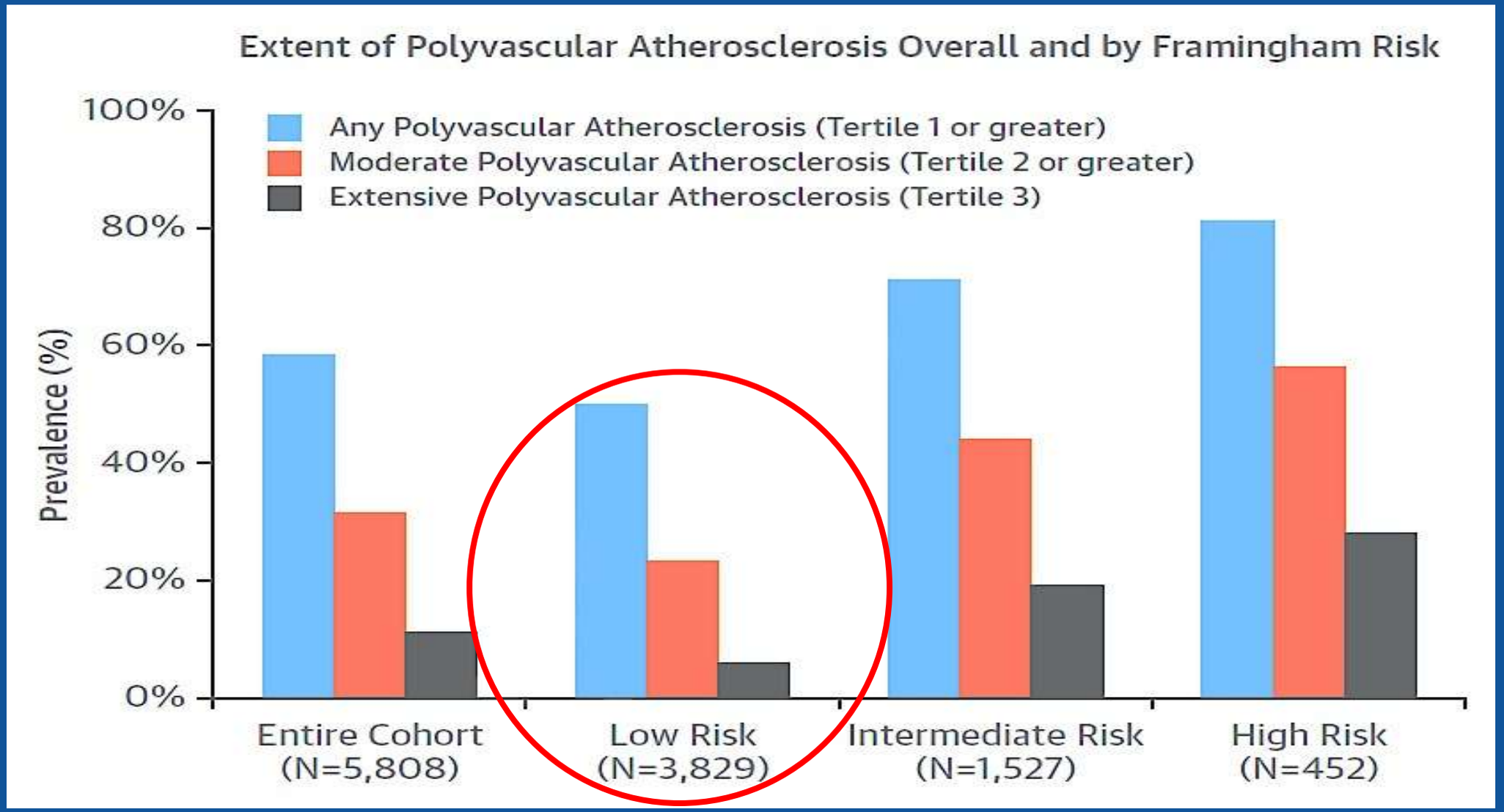
H Sillesen, P Muntendam, E Falk, V Fuster et.al JACC Imag. 2012;7:681.

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



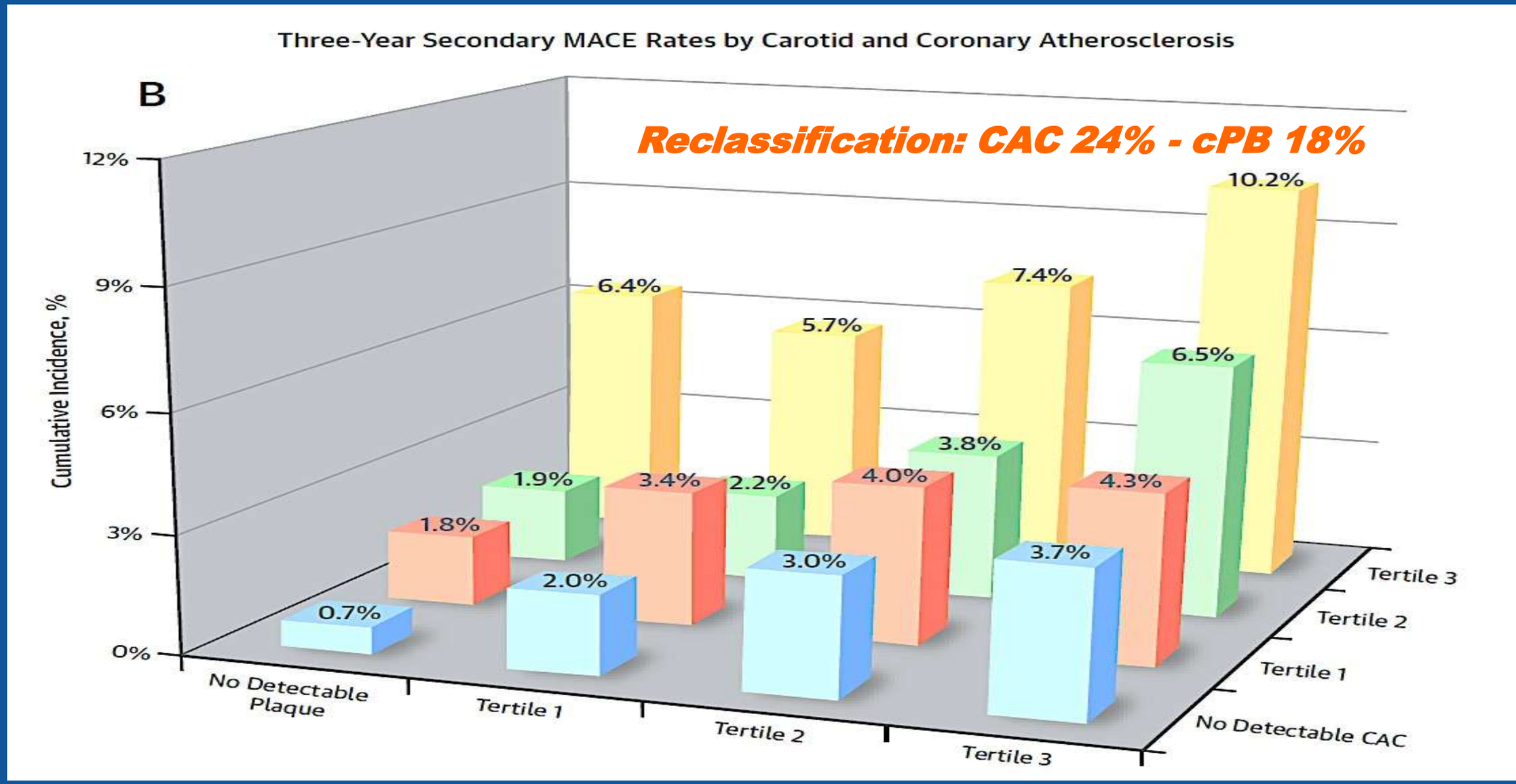
U Baber, R Mehran, V Fuster, et al. J. Am. Coll. Card. 2015; 65: 1065

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



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

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



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Science, Transatlantic Round Trip

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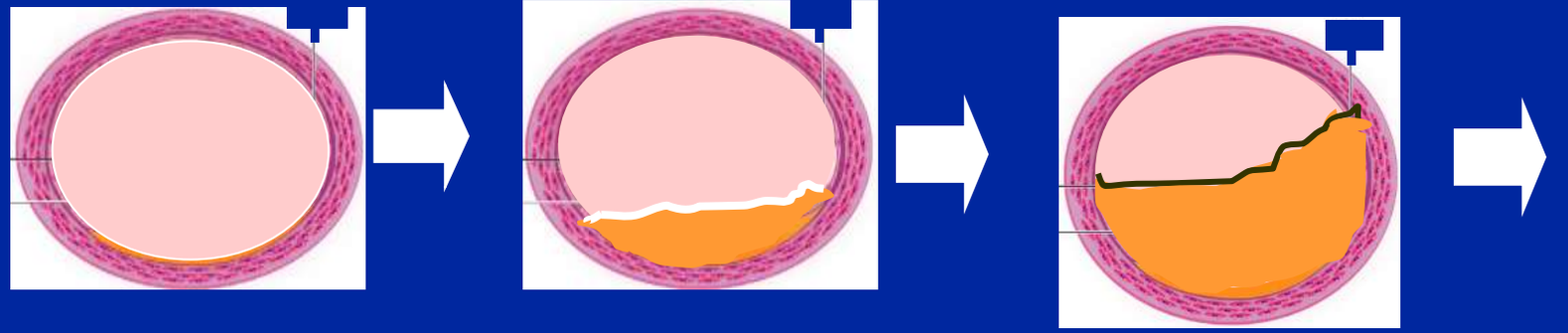
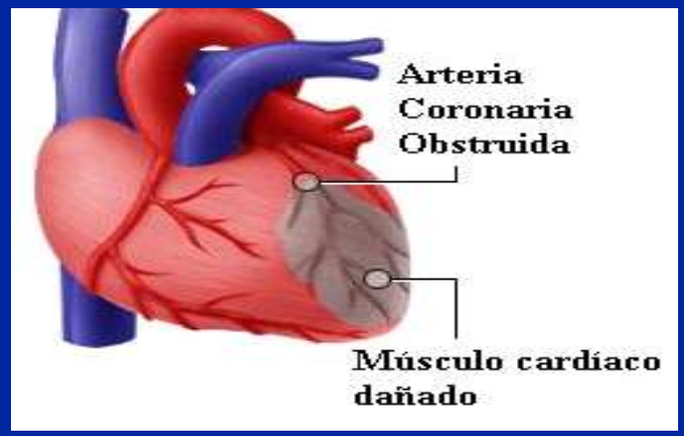
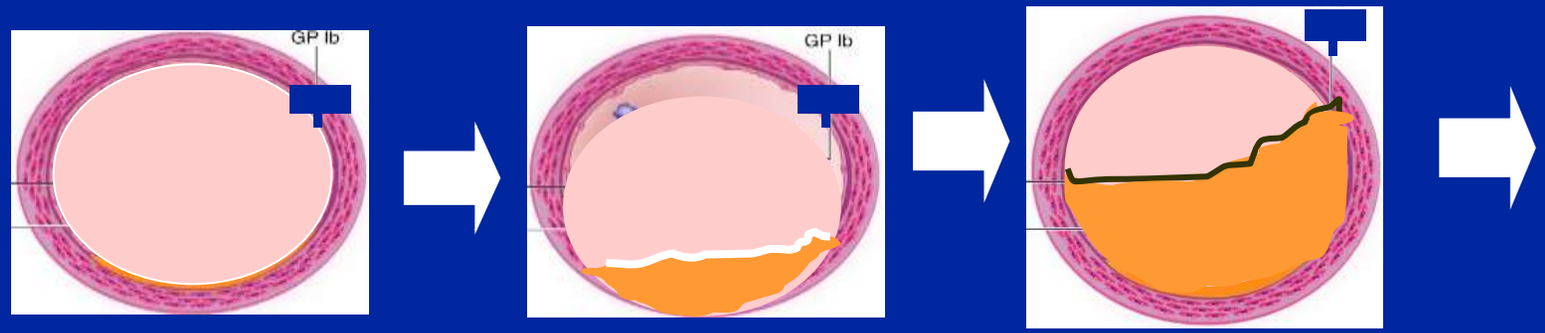


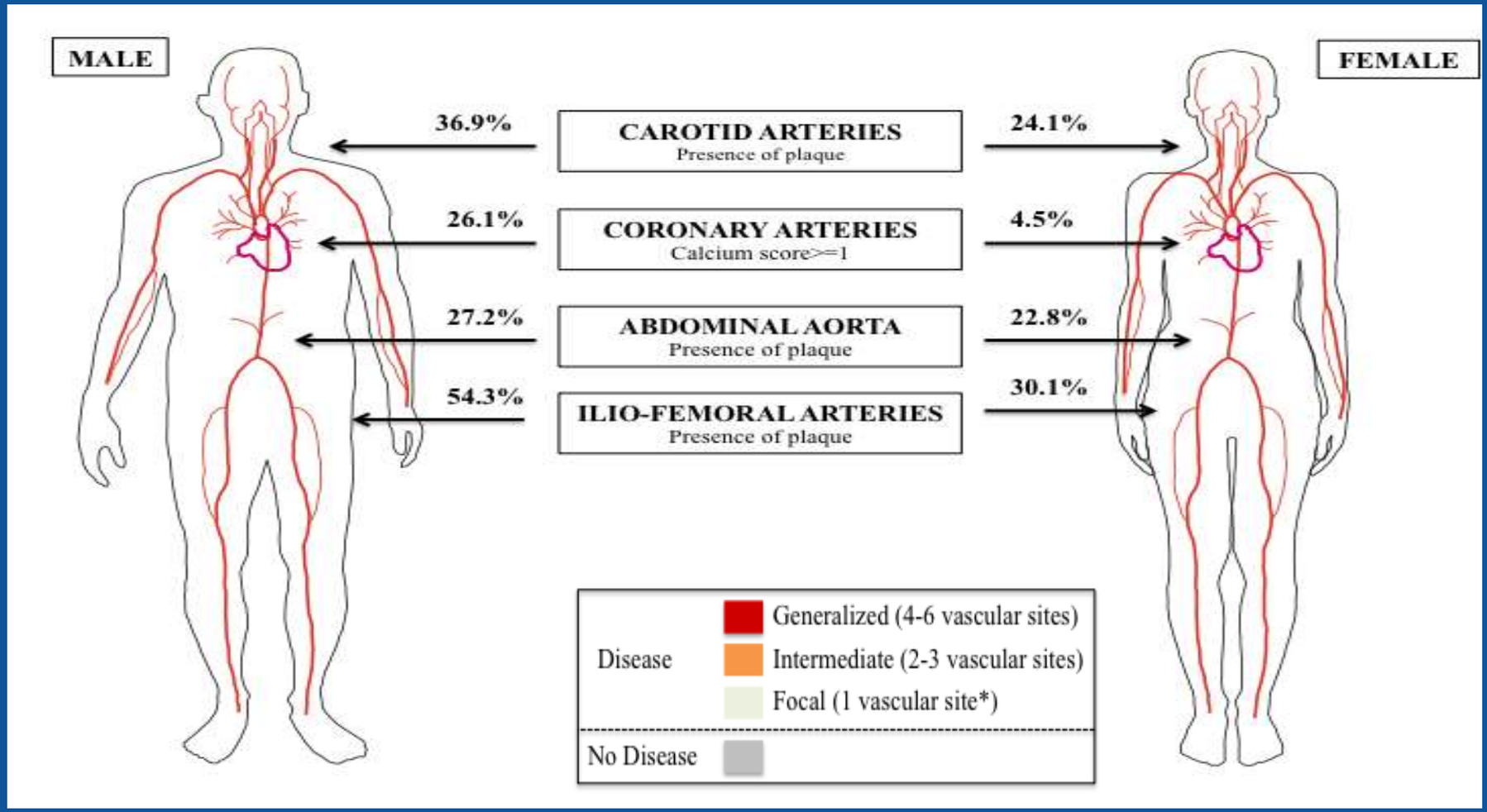




3. Omics (Framing.) **4.Telomeres (S.blot, qPCR, Fresh)**

PESA (L Fernandez-Friera, V Fuster et.al) Circ 2015 ,April 20

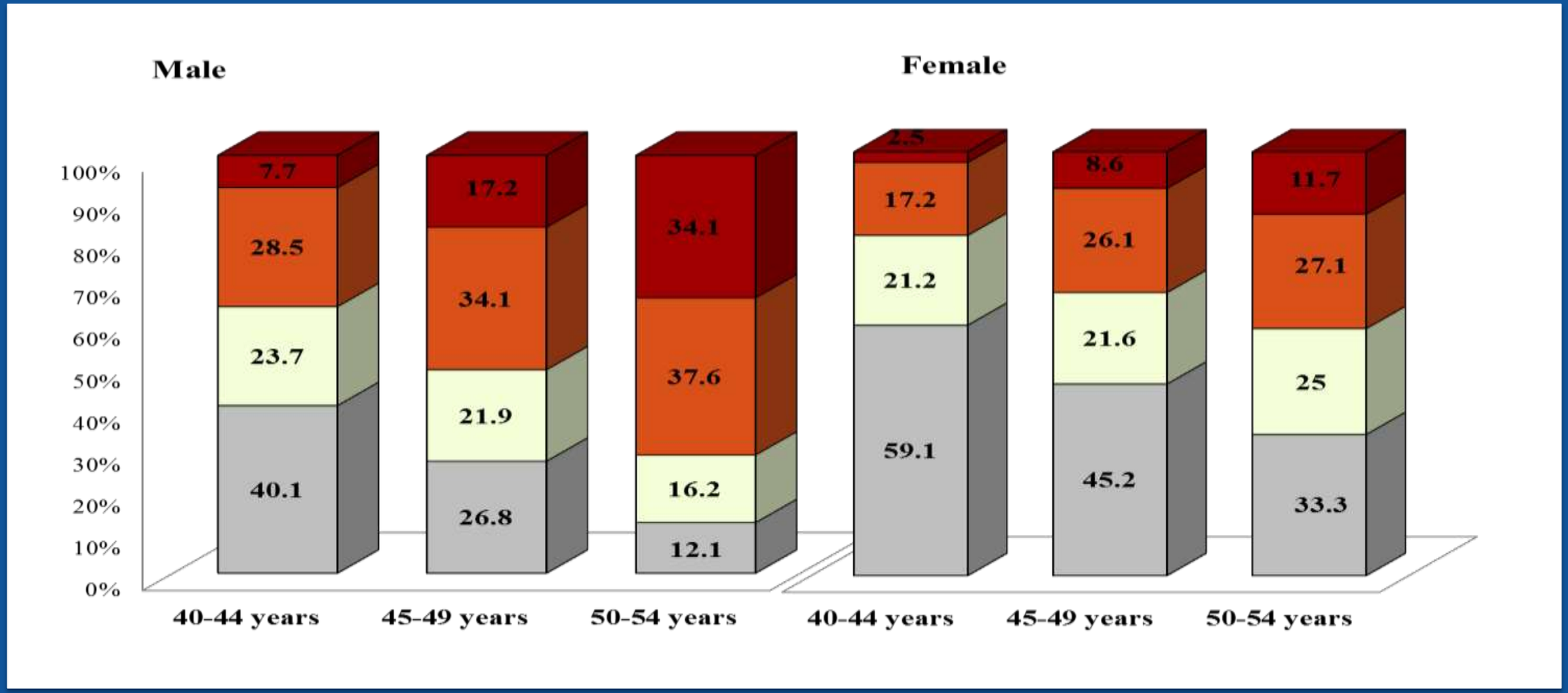
Sub-Clinical Atherosclerosis (n=4060)
By Vascular Territory



Ilio-femoral More Sensitive Than Carotid

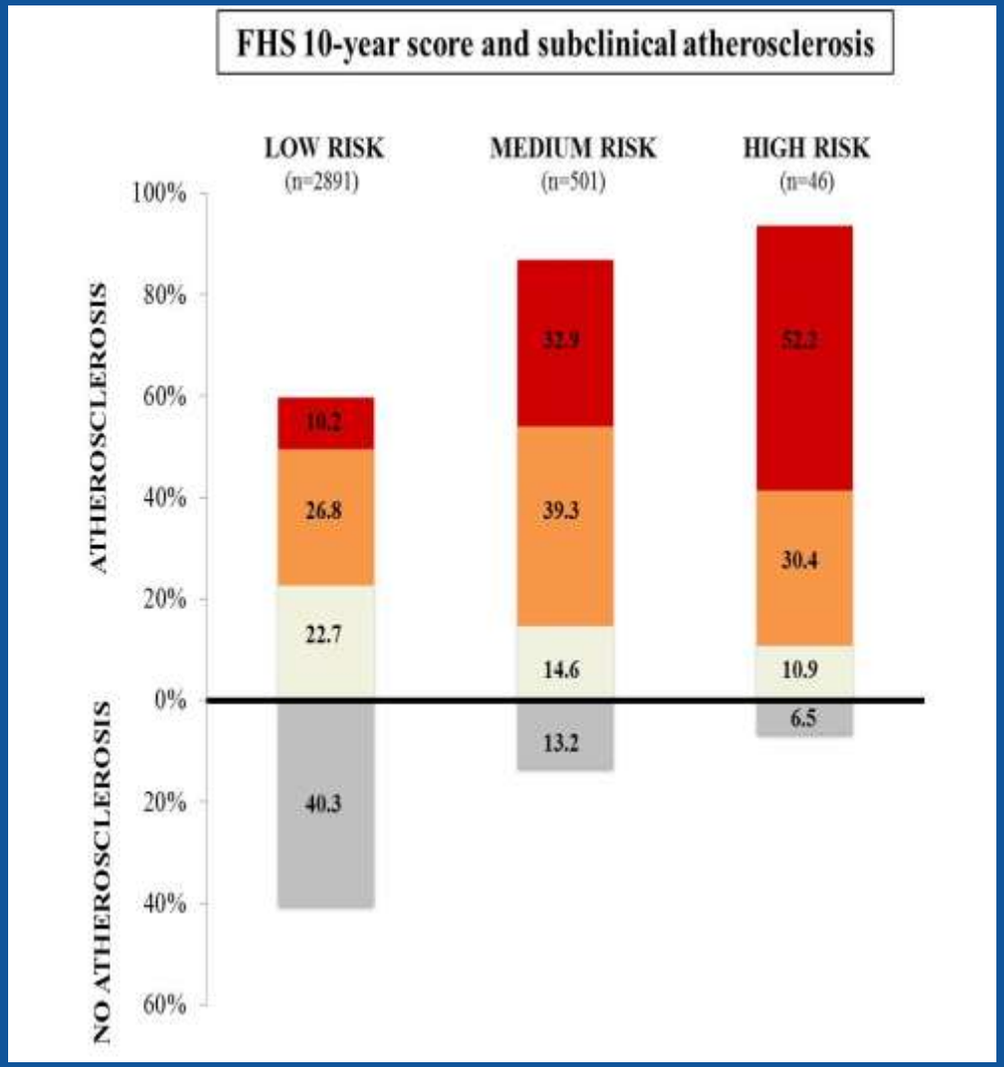
PESA (L Fernandez-Friera, V Fuster et.al) Circ 2015 ,April 20

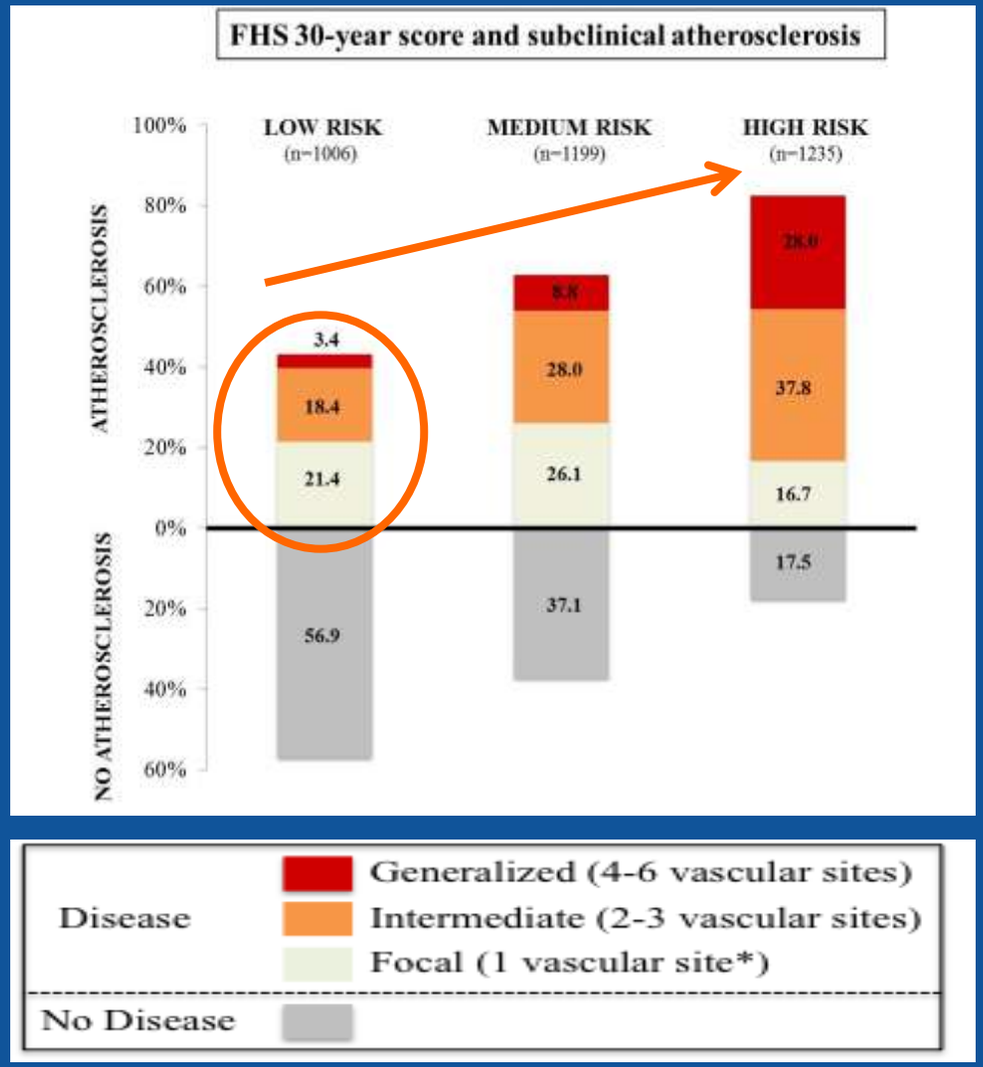
a). Distribution Of The Systemic Extent Of Subclinical Atherosclerosis



PESA (L Fernandez-Friera, V Fuster et.al) Circ 2015 ,April 20

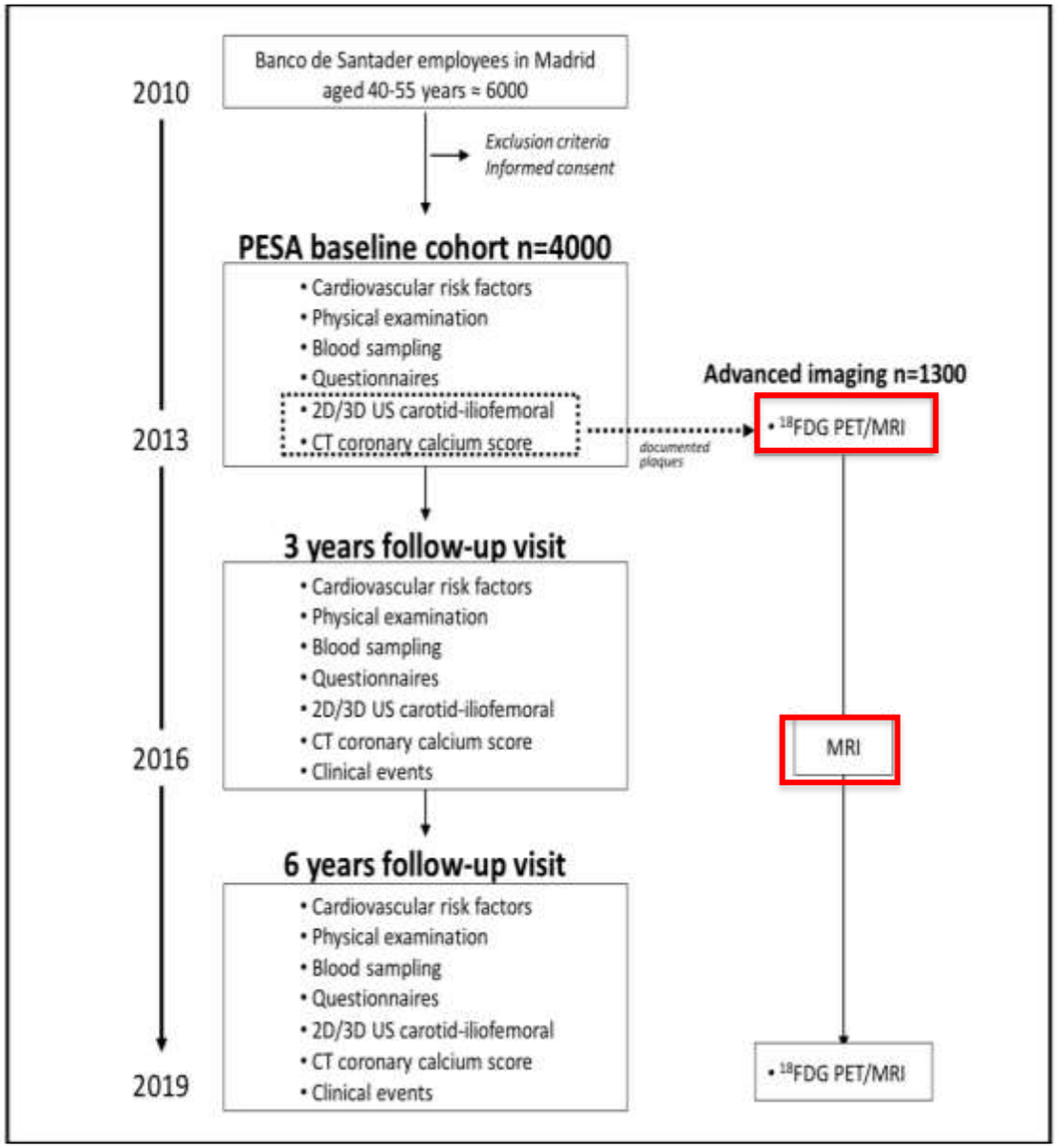
b). Subclinical Atherosclerosis (Imaging)
Relation To Framingham Risk Score





PESA (L Fernandez-Friera, V Fuster et. al.) 2015 (subm.)

c) 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)

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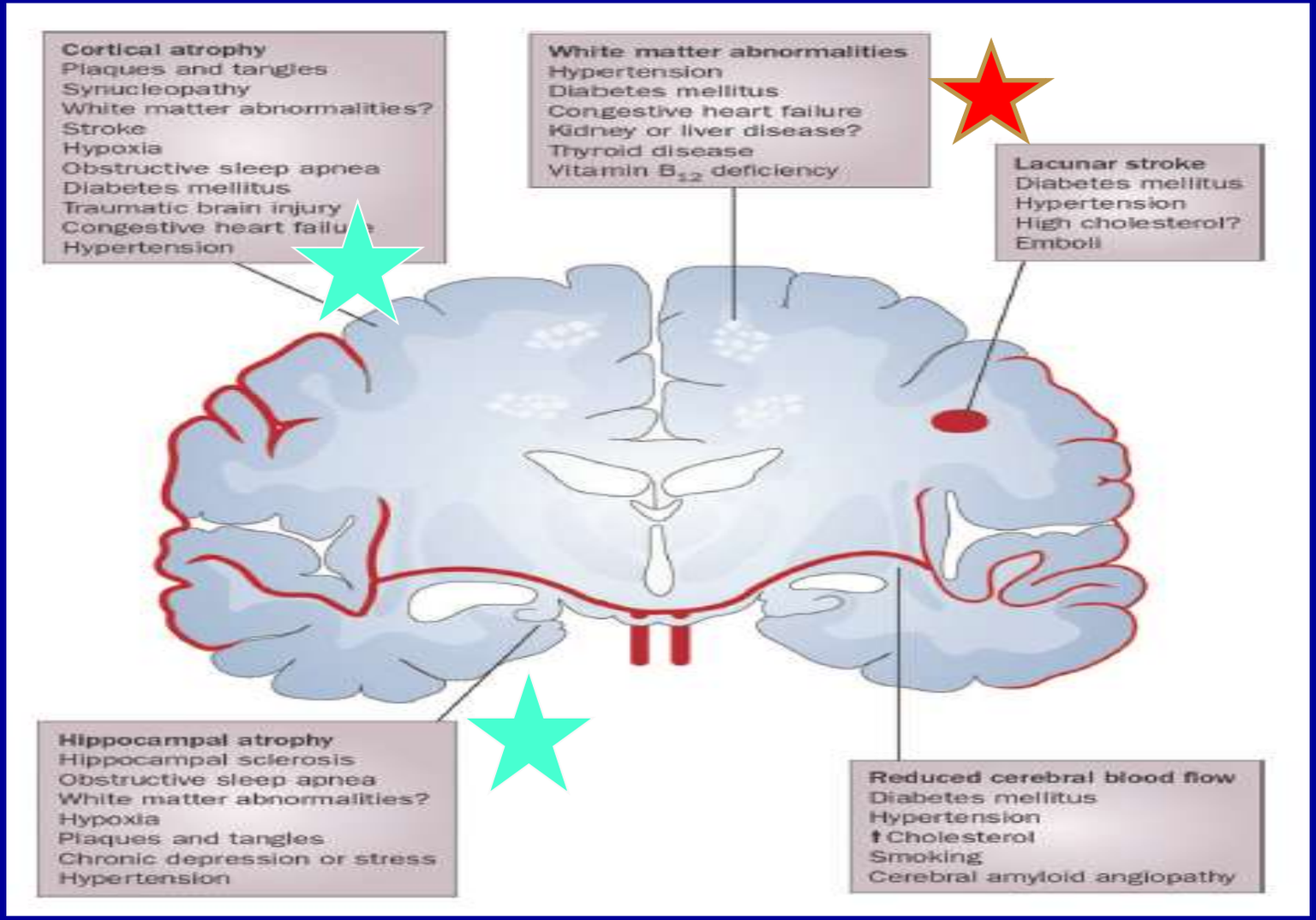
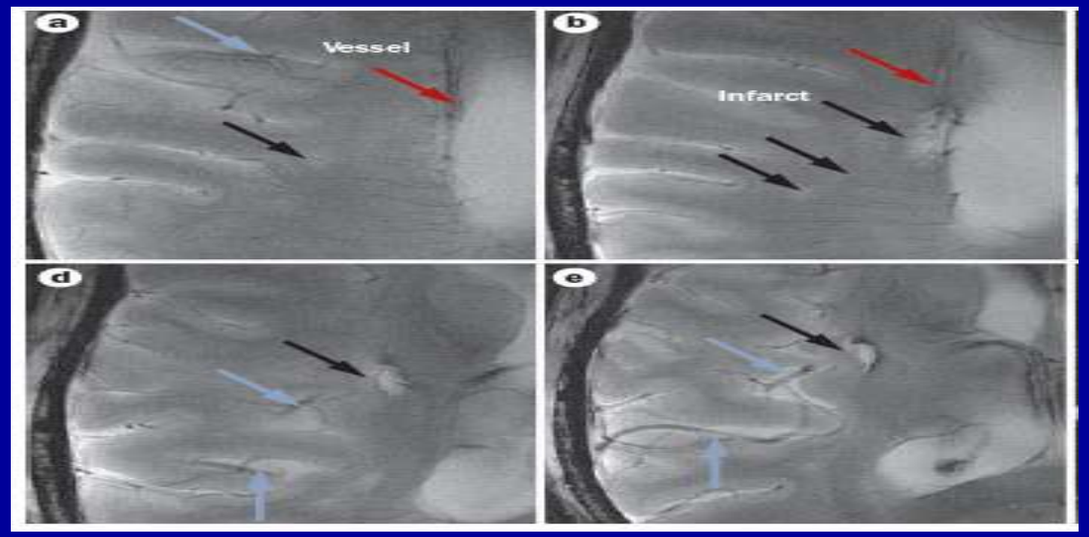
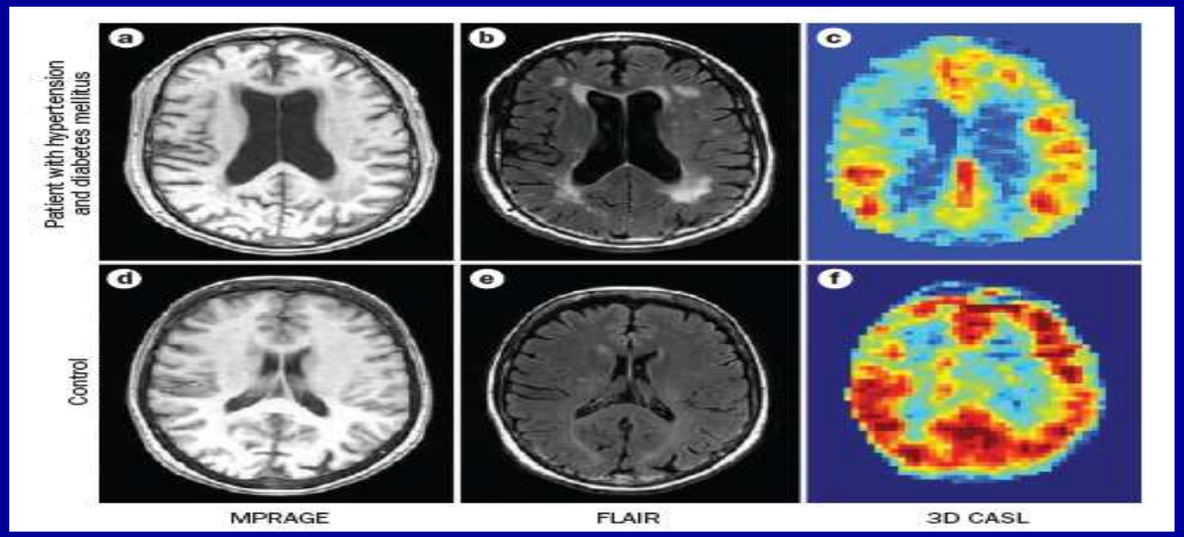
1). Risk Factors of CV Disease
White Matter & Lacunar Lesions (DBD)



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

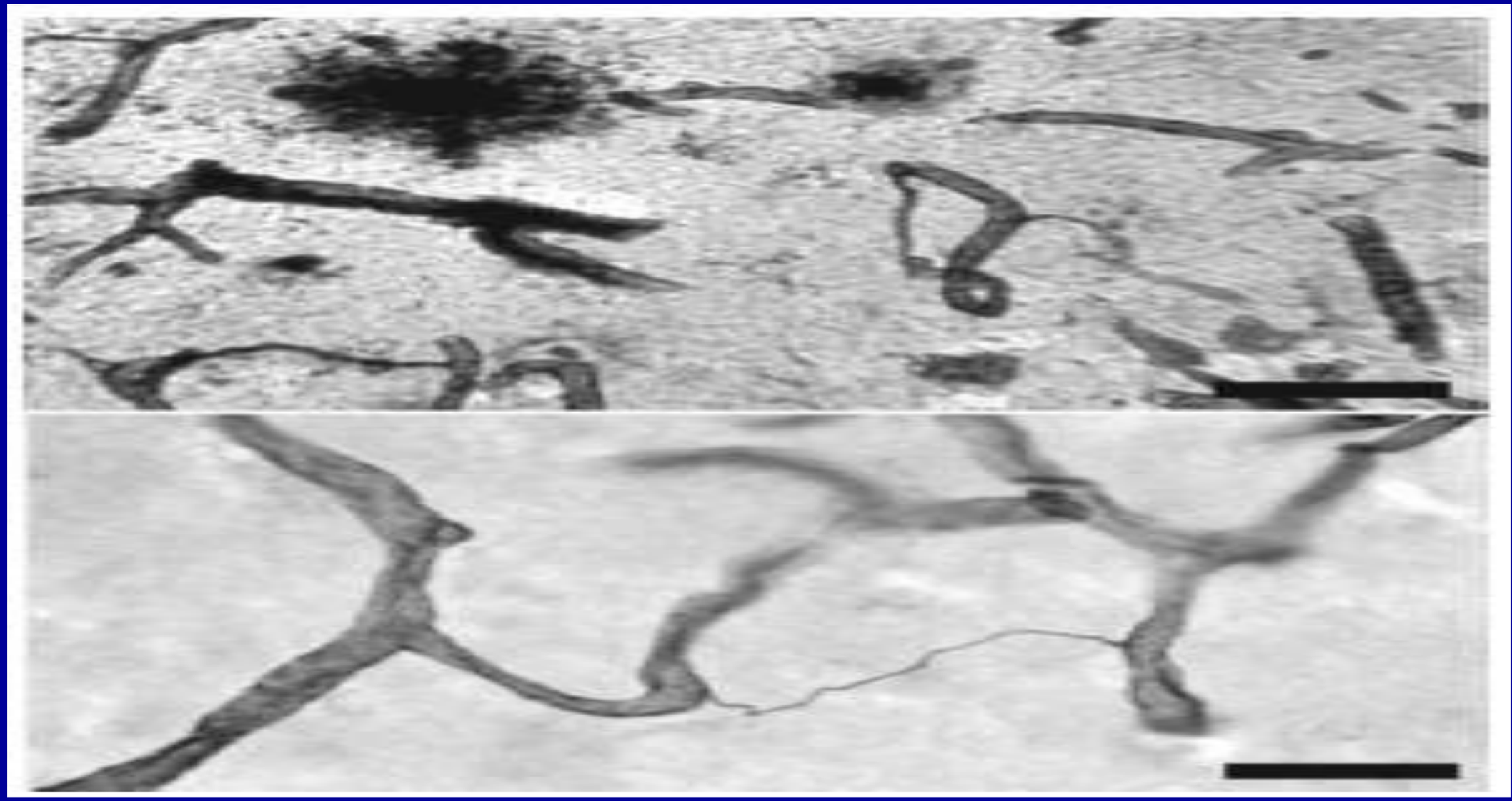
DBD/AD - CVRFs, Lacunar Les., < Cognitive
MRI – Perfusion





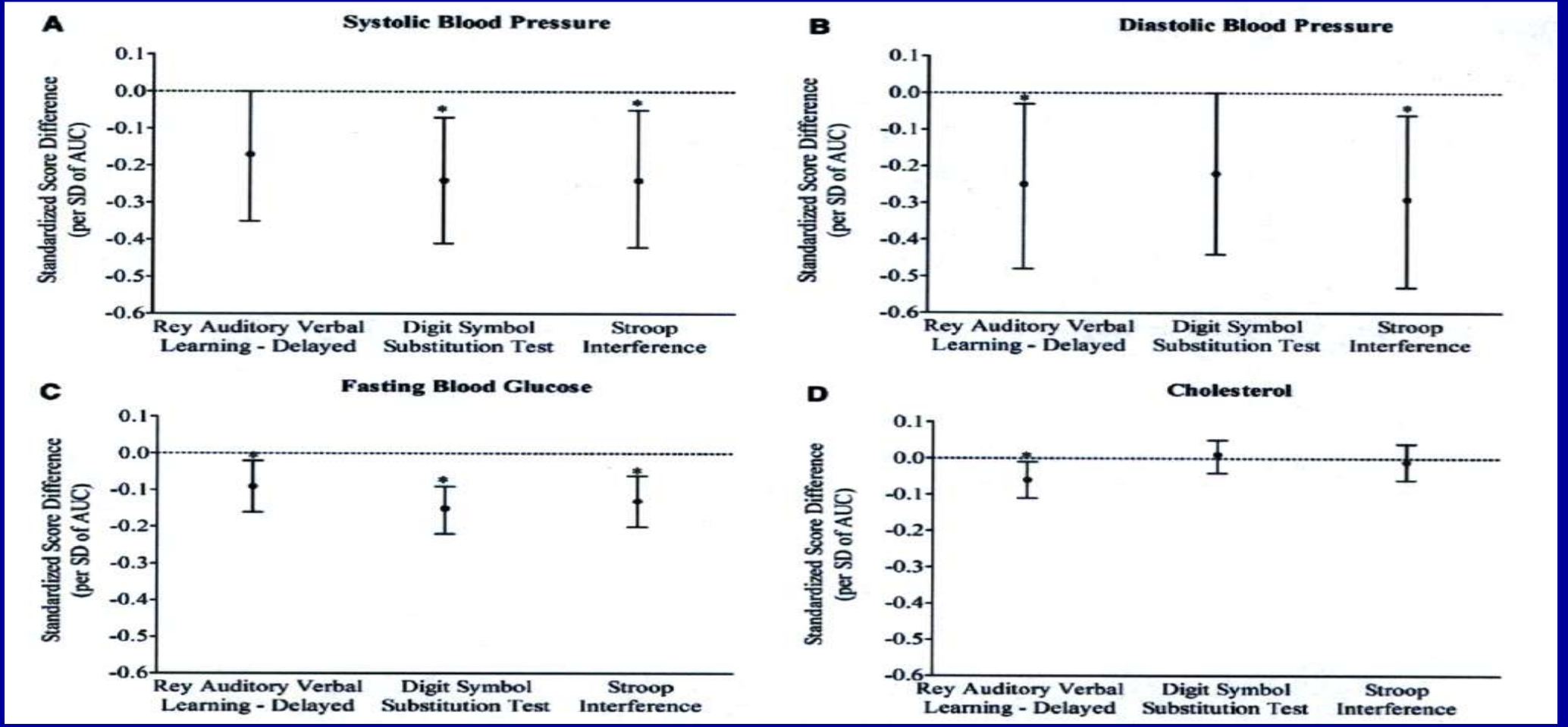
1. V Novak, I Hajjar. Nat. Rev. Cardiol. 2010;7:686(HMS)
2. HW Querfurth, FM LaFerla. NEJM 2010; 362:329
   Ischemia affects 60 to 90% of patients with Alzheimer's – RFs ?
3. WB White et al.Circ 2011;124:2312 (Farmington,Yale)
4. AHA/ASA, Stroke 2011; 42:2672
5. WHO - Dementia report 2012
6. JB Toledo et al. Brain July 10, 2013 – Autopsy (n=6000)
7. C Russo, RL Sacco et.al. Circ. 2013;128:1105
8. CARDIA (K Yaffe et al) Circ. 2014; 129 (In Press)
9. JI Friedman, ZA Fayad, J Narula, V Fuster - 2015 (In Press)
10. N Mattsson et al. Brain 2014;137:150 – 11. P Vemuri et.al. Brain. 2015
12. ARIC (DS Knopman et. al.) Stroke. 2015;46:433

1,2. Alzheimer's - Vascular - RFs ?



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

8,9. Early Adult to Midlife (N=3381,FU 25 yrs)
CV Risk Factors and Cognitive Function



Adjusted For Age, Sex, Race And Education

8. *CARDIA (K Yaffe, et al.) Circ 2015 (Birmingham, Chicago, Minneapolis, Oakland)*
9. *JI Friedman, ZA Fayad, J Narula, V Fuster - 2015 (In Press) – MRI: WMH, BF – BP, Diabetes*

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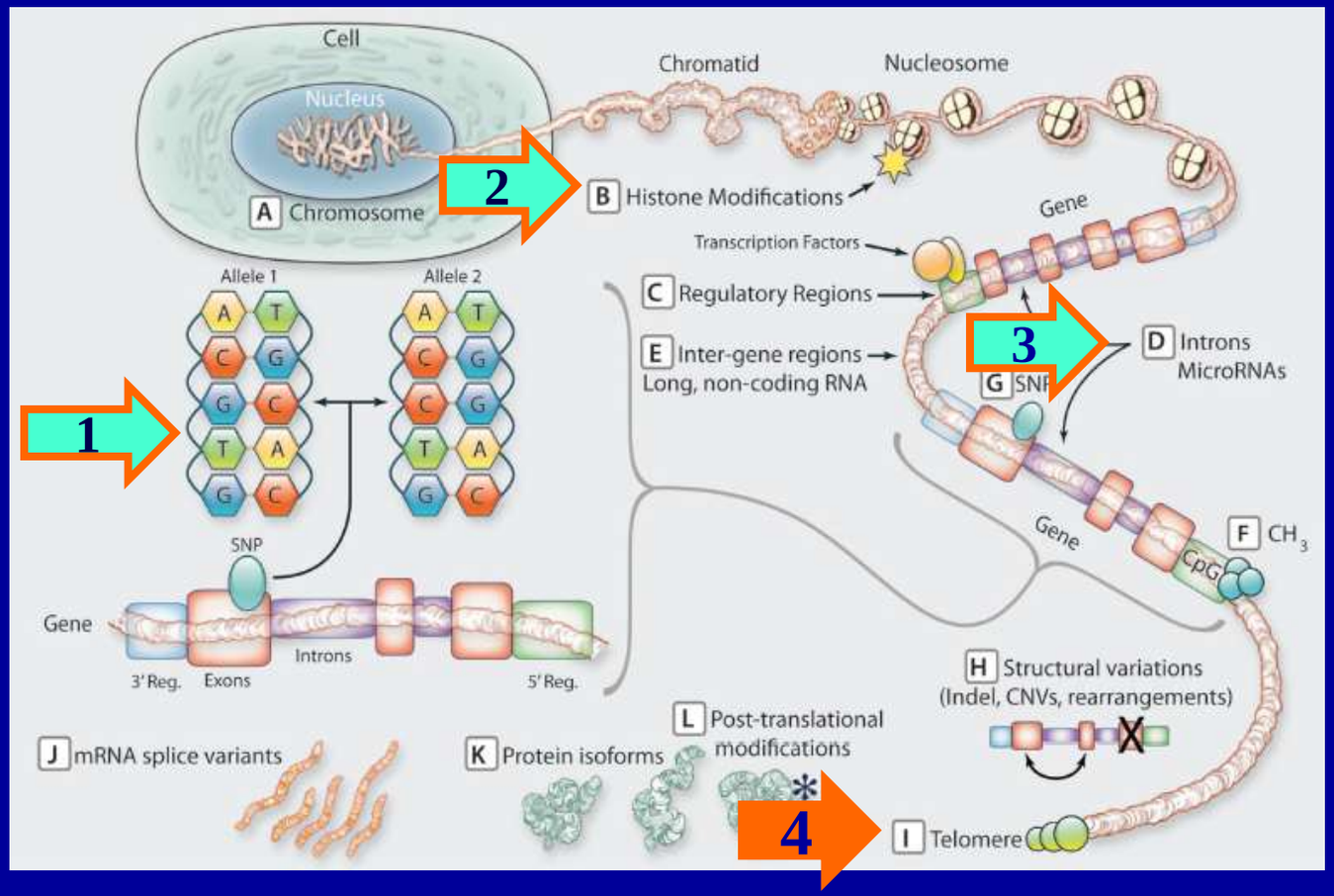
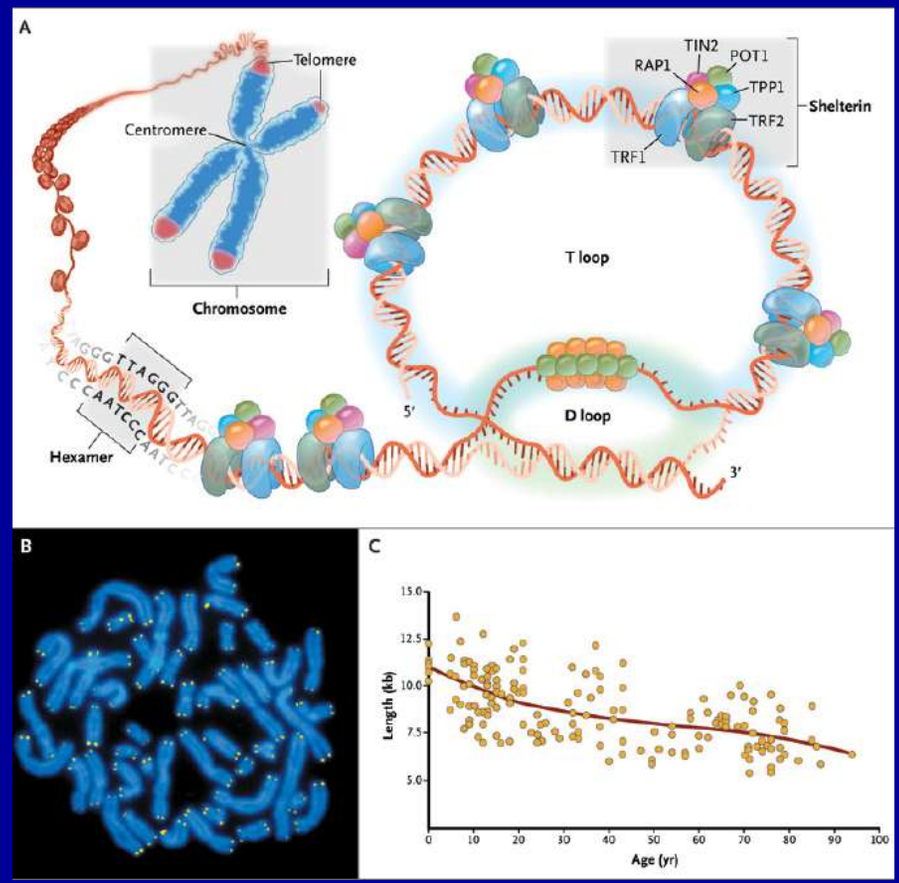
2). Aging / Frailty
Oxidative Stress on Telomere



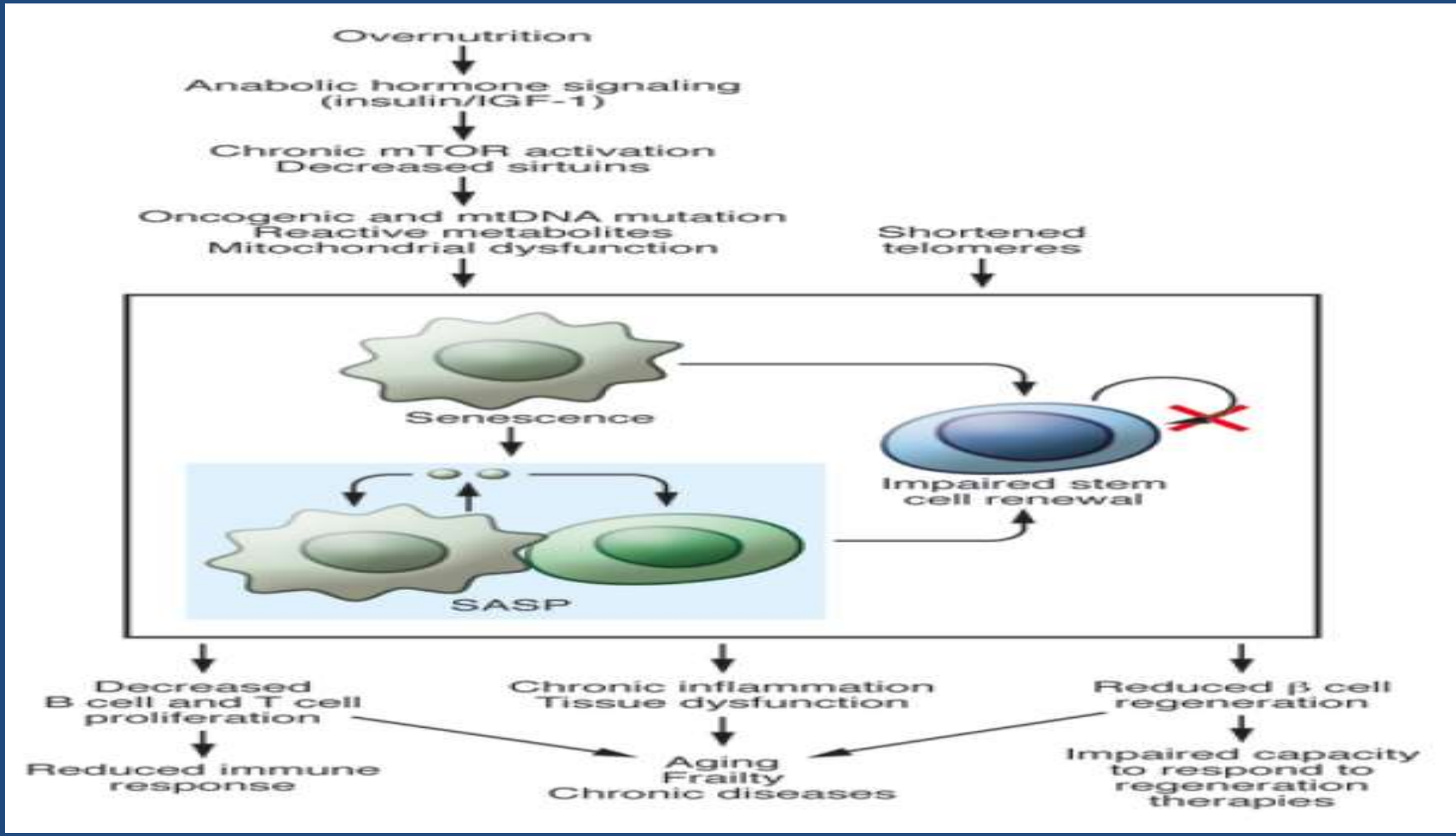


B Niemann et. al. JACC 2011; 57: 577.

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

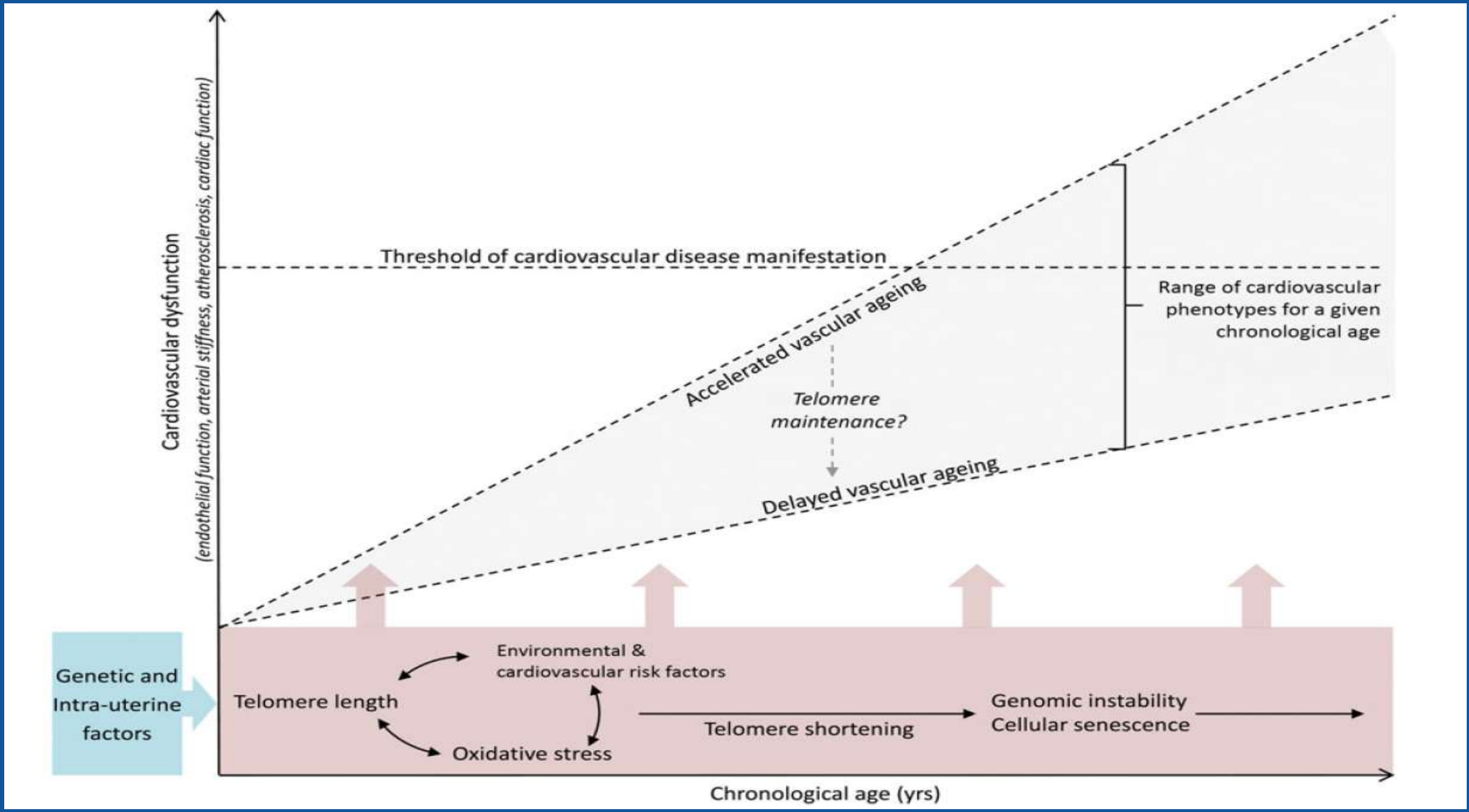
- Smoking
- Obesity
- Sedentary lifestyle

Inhibition of Telomere Shortening

- Healthy lifestyle

F Fyhrquist et al. Nat Rev Card. 2013; 10:274
PESA (V Andres, V Fuster et al) 2015

Telomere Length, Oxidative Stress & Risk Factors Resulting In Accelerated CV Ageing



M Muller et. al. Eur Heart J. 2014;35:3245

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