

Our Physical & Mental Health Are Powered By Three Concepts



Youth

Motivation

Mid - Life

Life Style

Aging

Heart-Mind

A Transition From Disease to Health – 2010-2020

Cardiovascular & Mental



CAD – *Coronary Artery Disease*

HRP – *High Risk Plaque*

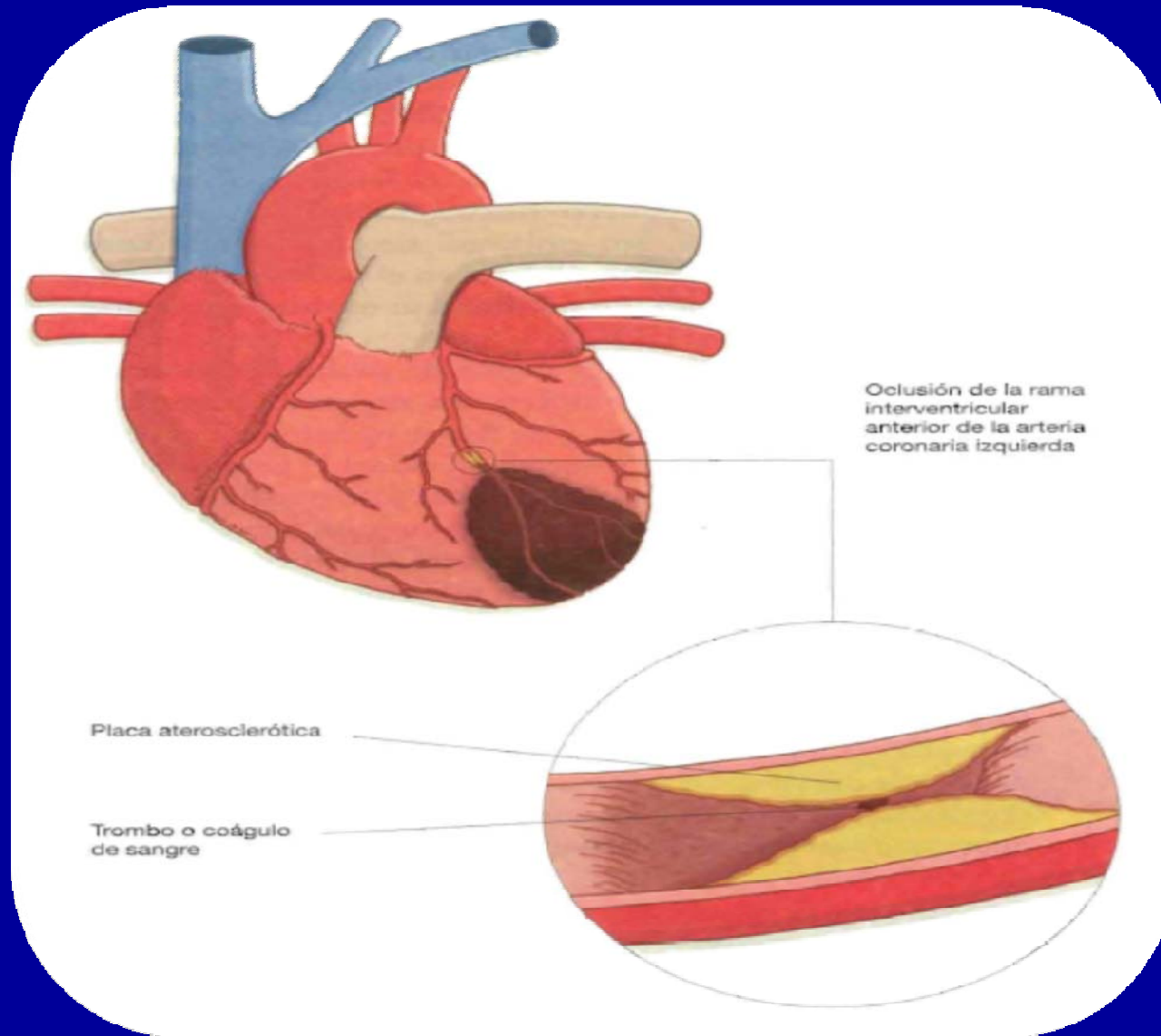
IOM – *Institute of Medicine*

CVD – *Cerebro Vascular Disease*

DBD – *Degenerative Brain Disease*

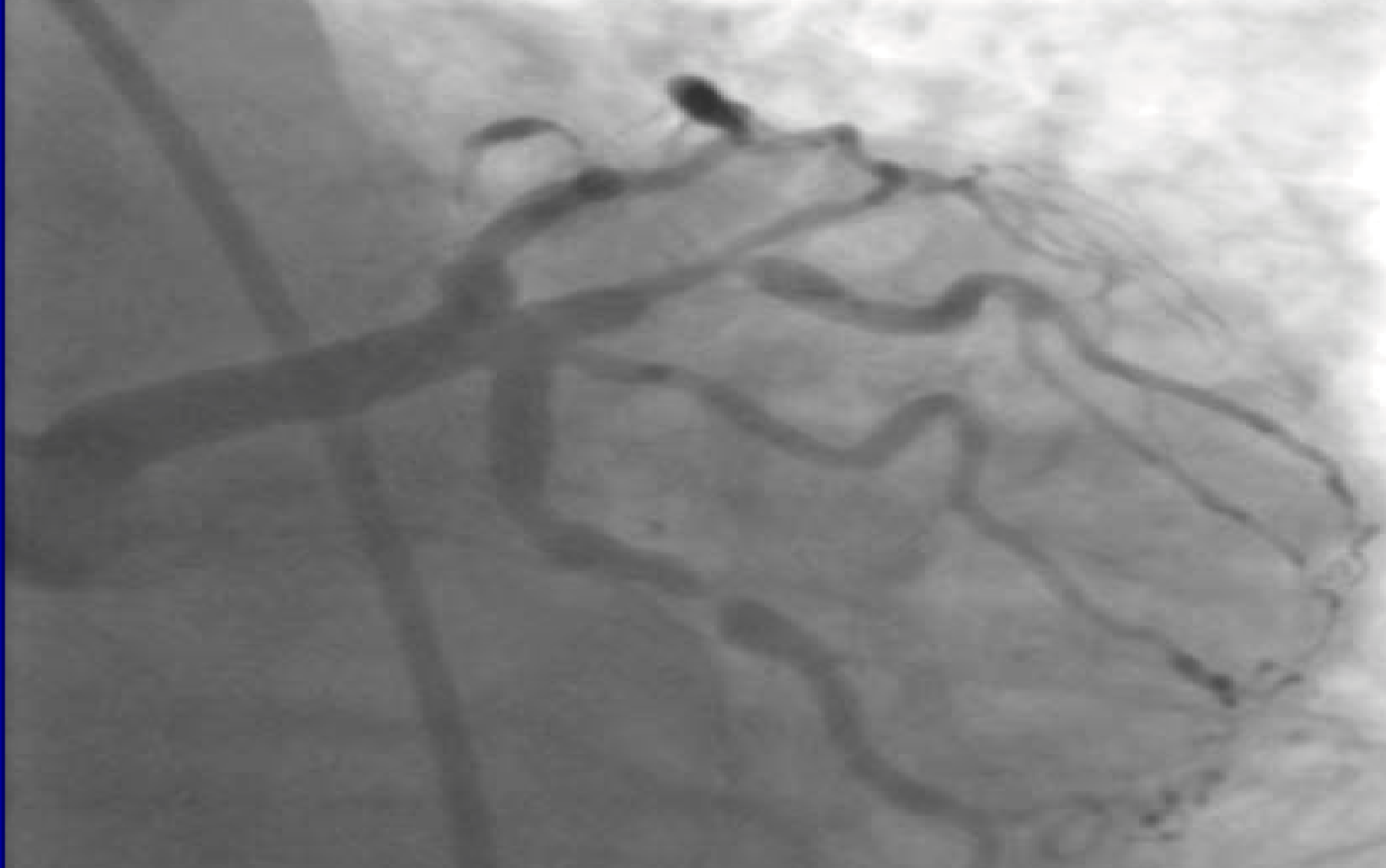
SHE – *Science Health & Education*

ANGINA , MYOCARDIAL INFARCTION

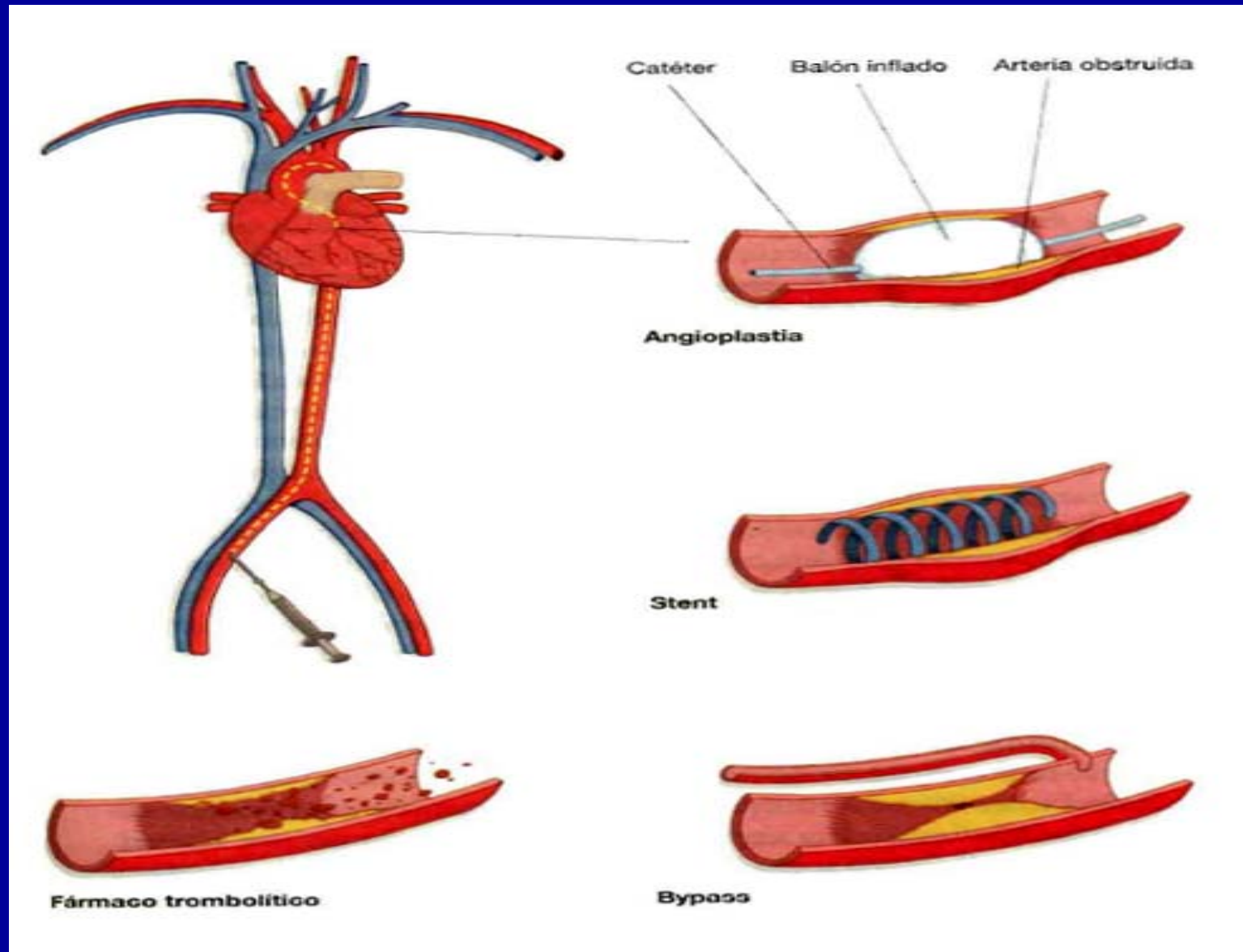


C=Clinical
B=Basic

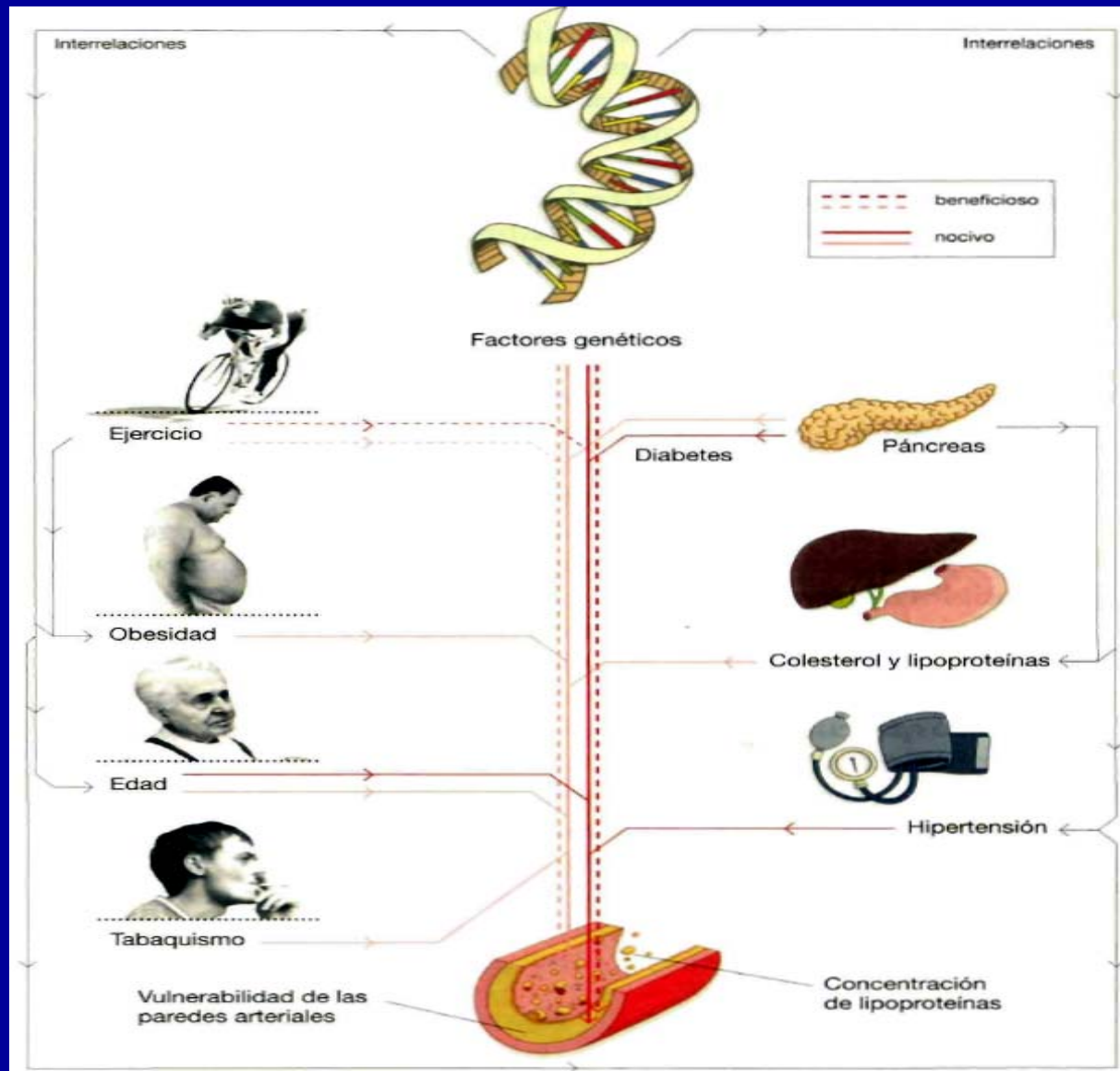
C) COMPLEX CORONARY ARTERY DISEASE



C) CORONARY INTERVENTION



C) MT - CARDIOVASCULAR RISK FACTORS (7)



>2RF = MI-Stroke

25% in 10 Yrs

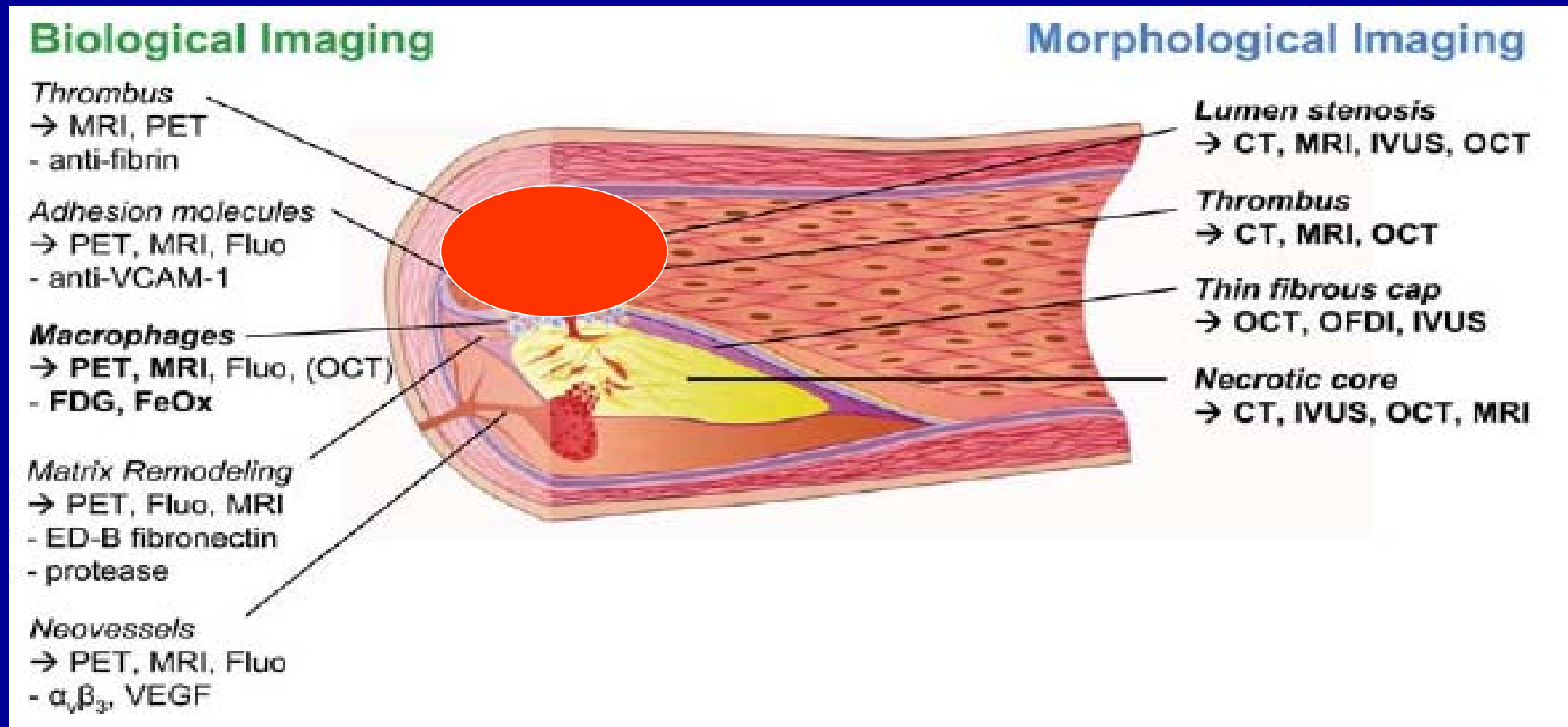
75% in 30 Yrs

C) Complex Coronary Artery Disease

Evidence Base Management - \$ 250 Million

<i>TRIAL</i>	<i>MVD</i>	<i>DM</i>	<i>INTERV.</i>	<i>MT.</i>	<i>EP.</i>	<i>Data</i>
<i>SYNTAX (FAME)</i>	+	-	++	-	++	<i>Revasc < CABG</i> <i>➤ Sx Sc. (Reg) < CABG</i> <i>DM – Int. Sx Sc. < CABG</i> <i>(Ischemic Score)</i>
<i>BARI (COURAGE)</i>	-	+	+	+	+/-	<i>INTERV. vs RX = EP</i> <i>Sx Sc < CABG,</i> <i>Revasc. Xover 42%</i> <i>(ischemic Score?)</i>
<i>FREEDOM</i>	+	+	++	+	+/-	<i>Largest DB DM</i> <i>FREEDOM Score (3)</i> <i>Rx Approach-Polypill</i> <i>Non Invasive Imaging</i>

B). Imaging the Atherothrombotic Process



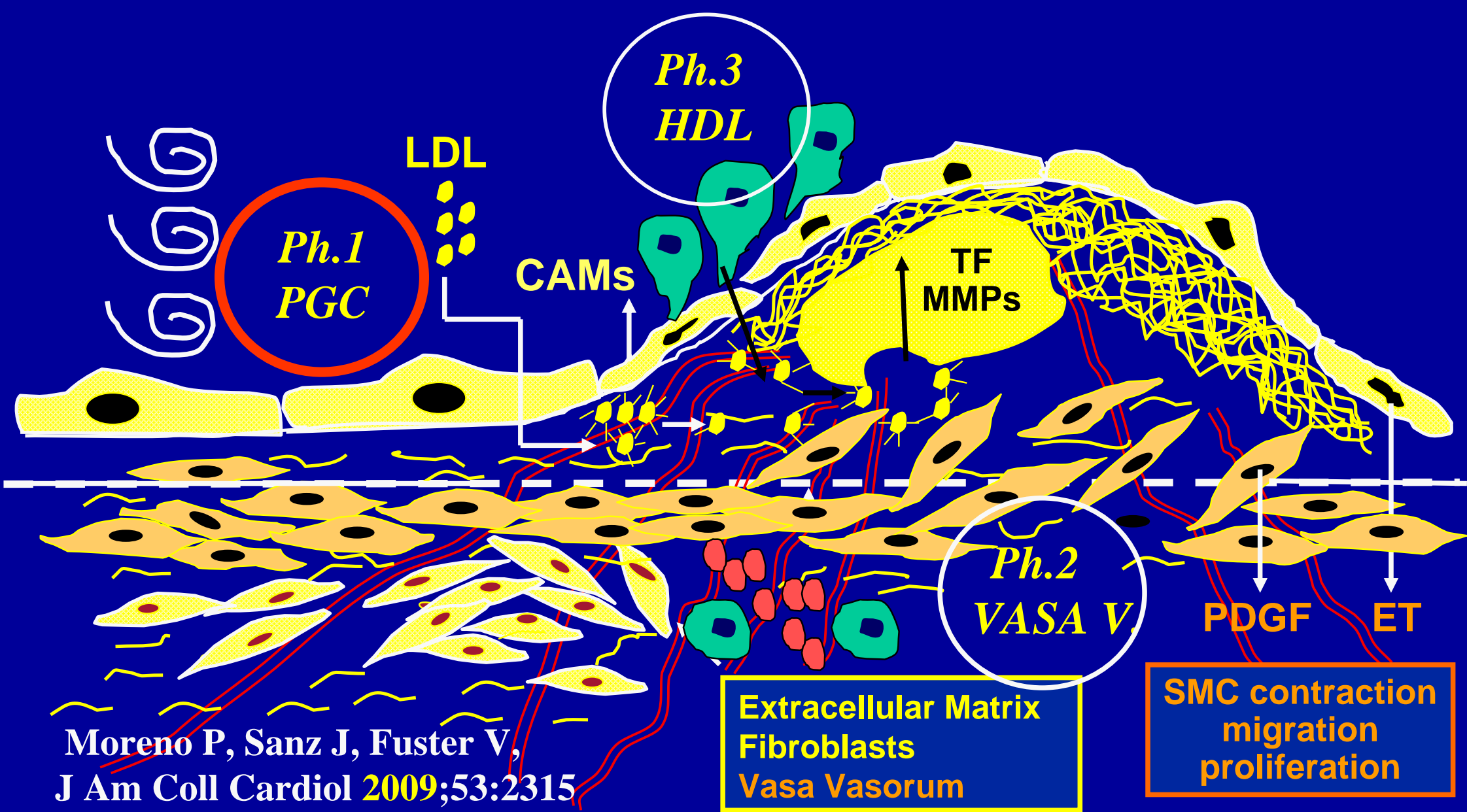
Choudhury R, Fuster V, Fayad ZA *Nature Rev. Drug Disc* **2004**;3:913.

Jaffer FA et al., *Circ* 2007; 116:1052 - Sanz J et al., *Nature* **2008**; 451:953.

Mulder WJM, Fayad ZA et al. et. al. *Nat CP Cardio. Med.* **2008**;5:s103.

CM Matter, M Nahrendorf et. al. *Eur Heart J.* **2009**;30:2566

HIGH RISK PLAQUE - < ACTIVE INFL.

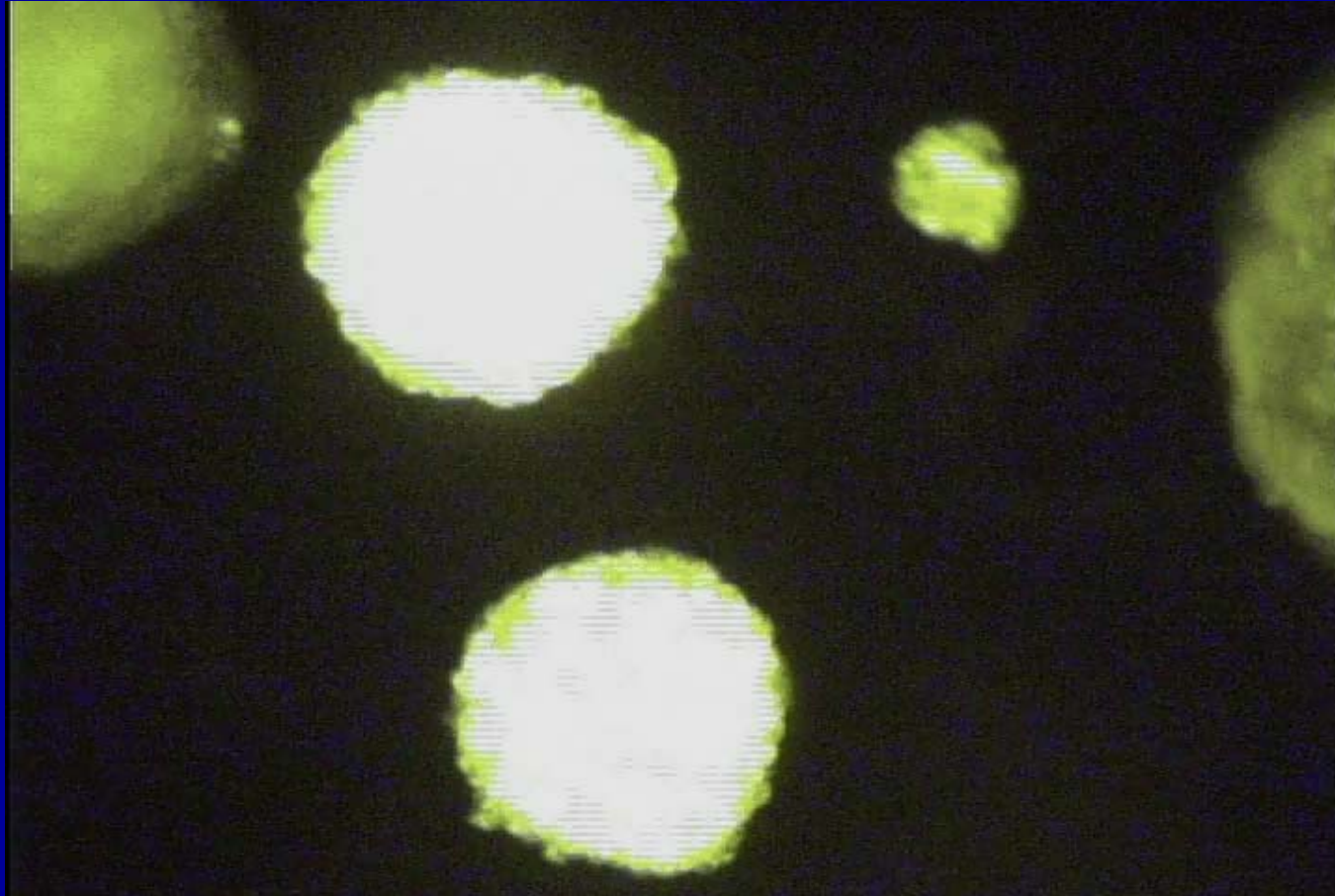


Moreno P, Sanz J, Fuster V,
J Am Coll Cardiol 2009;53:2315

Extracellular Matrix
Fibroblasts
Vasa Vasorum

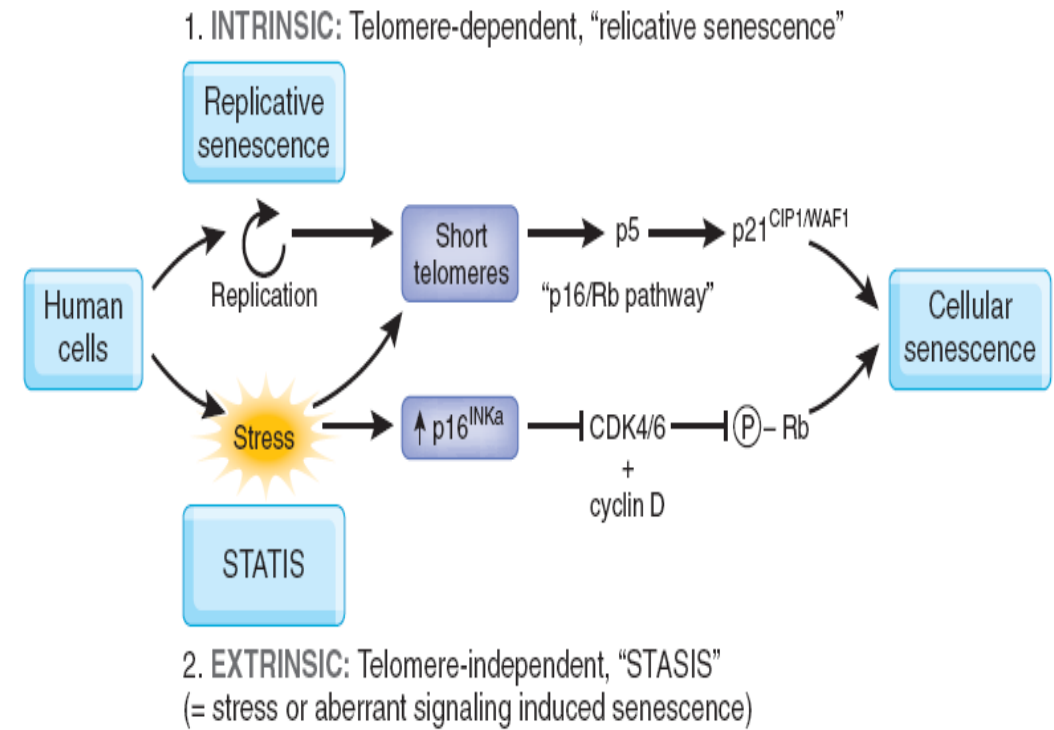
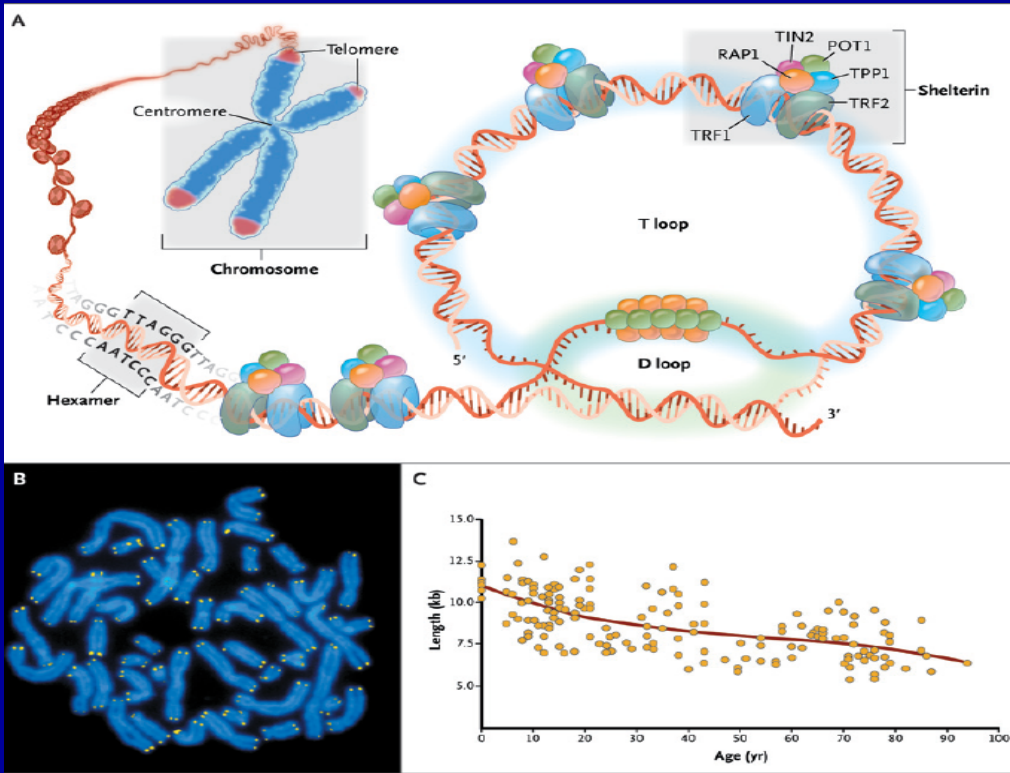
SMC contraction
migration
proliferation

Embryonic Stem Cell Derived, CV Progenitor Cells (FLK Positive Cells)



E Adler, ZA Fayad, S Kattman, G Keller et al **2010(Subm)**
K.A. Moore, I R Lemischka et. al. Science **2006**;311:1880.

Senescence-Associated Telomere Changes



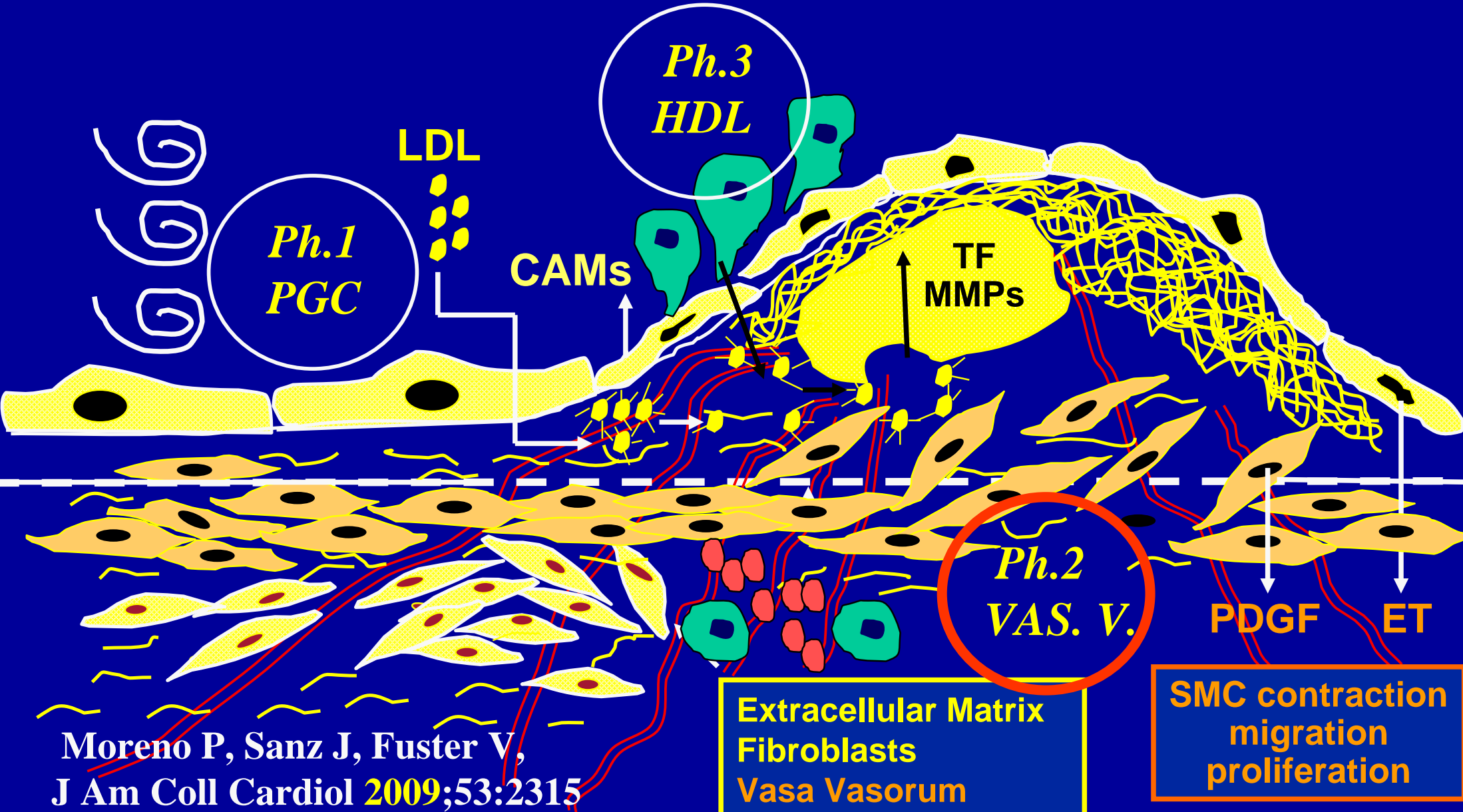
RT Calado et. al. *N Engl J Med.* **2009**;361:2353.

S. Anderson et.al. *J Am Soc Nephrol* **2009**;20:1199

M Mimeault et.al. *Ageing Res Rev.* **2009**;8:94-

Oxidative Stress - Aging, Cancer
Smoking ? Low Caloric diet ?, Exercise ?,

HIGH RISK PLAQUE - > ACTIVE INFL.



Moreno P, Sanz J, Fuster V,
J Am Coll Cardiol 2009;53:2315

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Fibroblasts
Vasa Vasorum

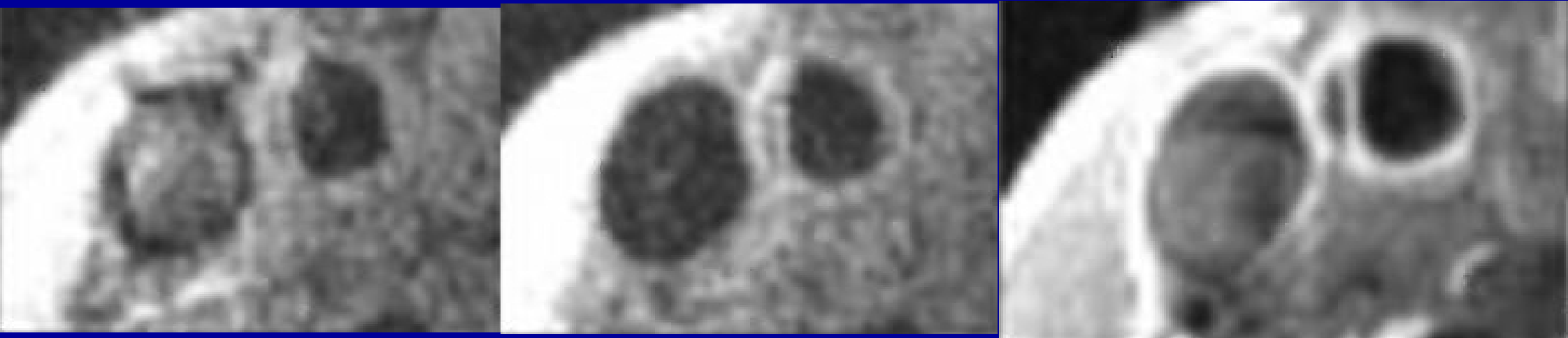
SMC contraction
migration
proliferation

Dynamic Contrast Enhanced (DCE) MRI (Gd)

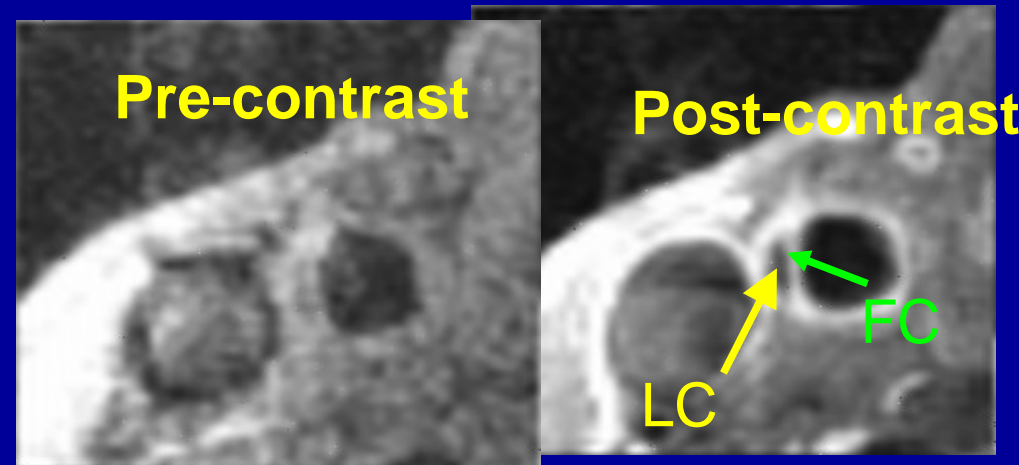
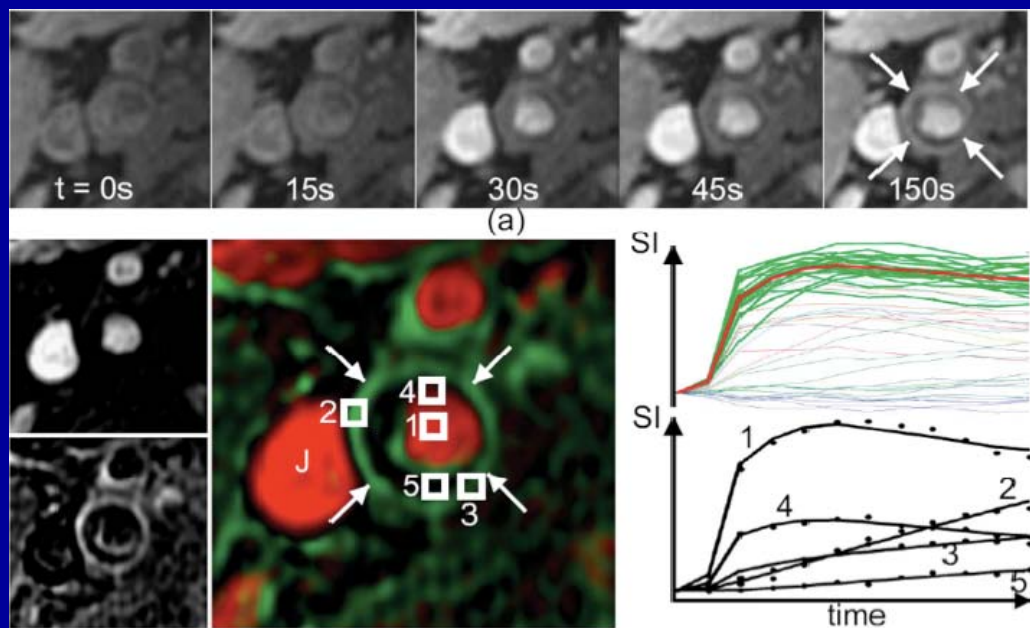
Pre-contrast

Post-contrast 2 min

Post-contrast 8 min



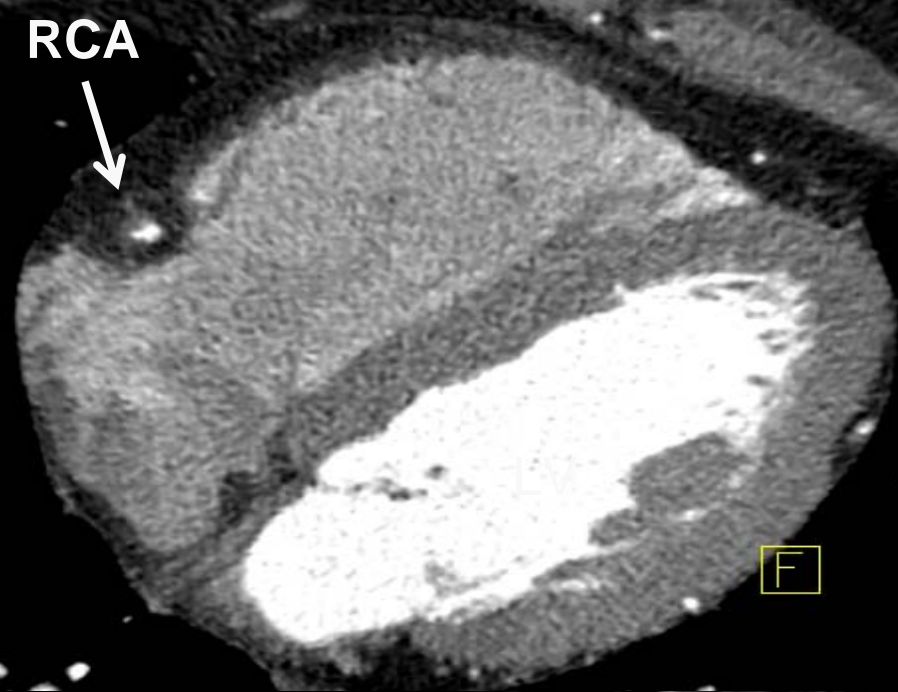
T1W



LC = lipid rich/necrotic core
FC = Fibrous cap

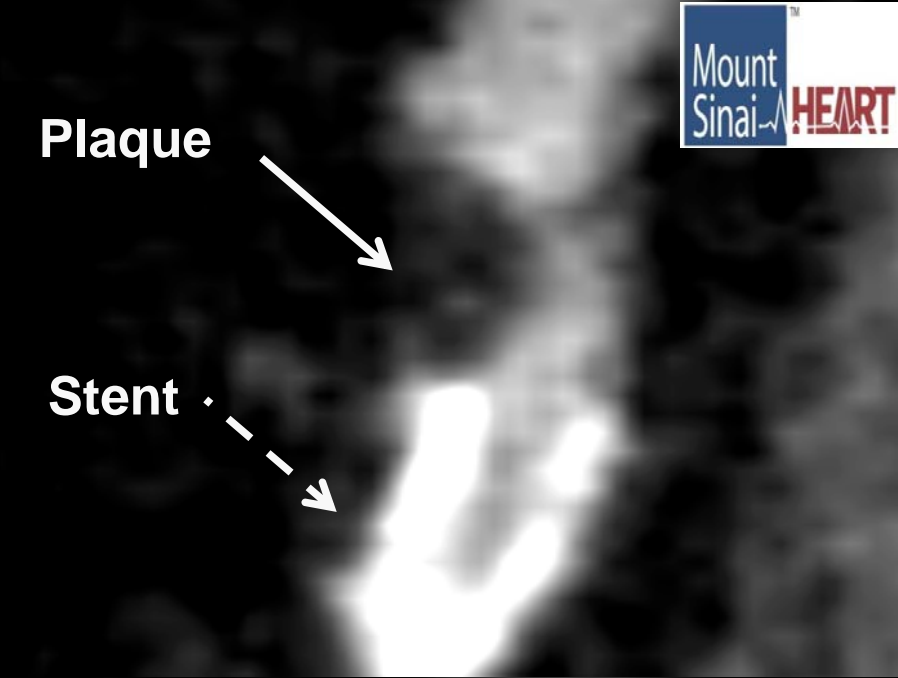
Coronary
FDG Uptake

CT
Angiogram

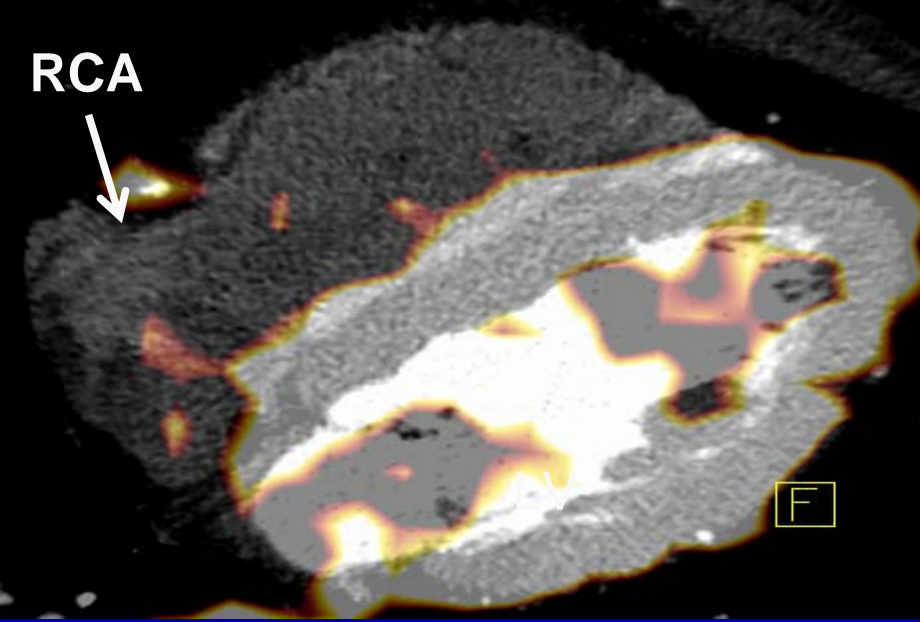


Plaque

Stent

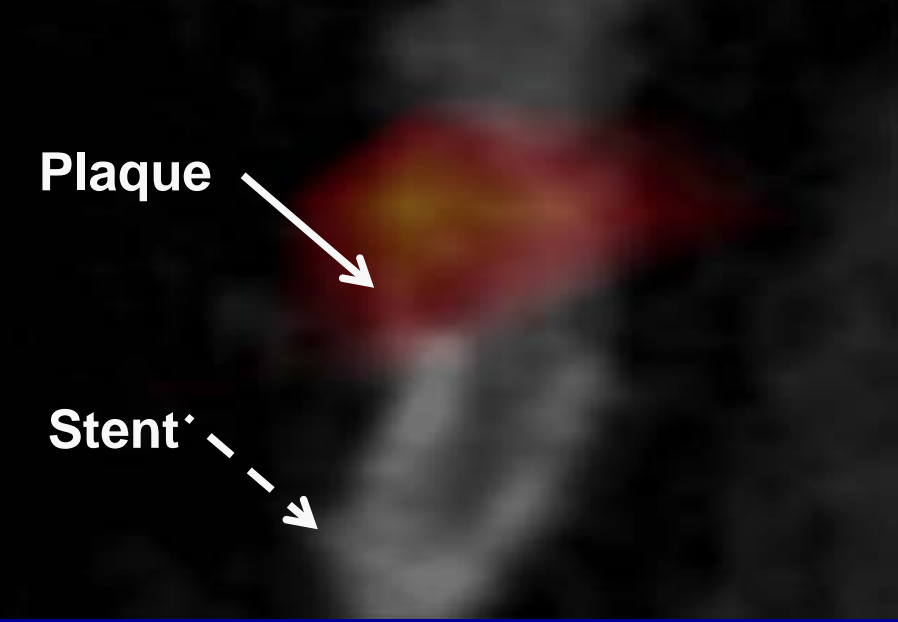


Fused
PET and CTA
Images

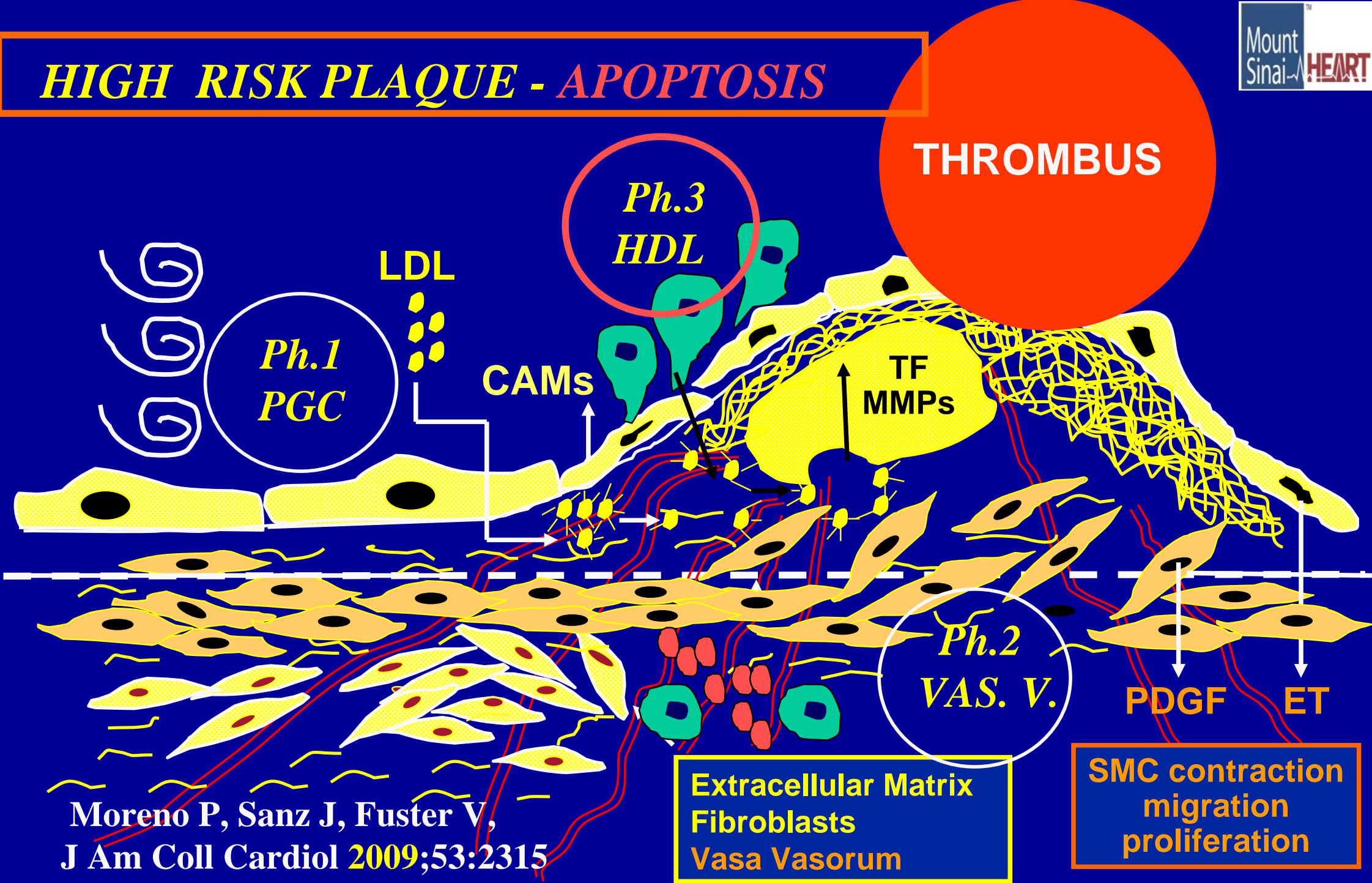


Plaque

Stent



HIGH RISK PLAQUE - APOPTOSIS

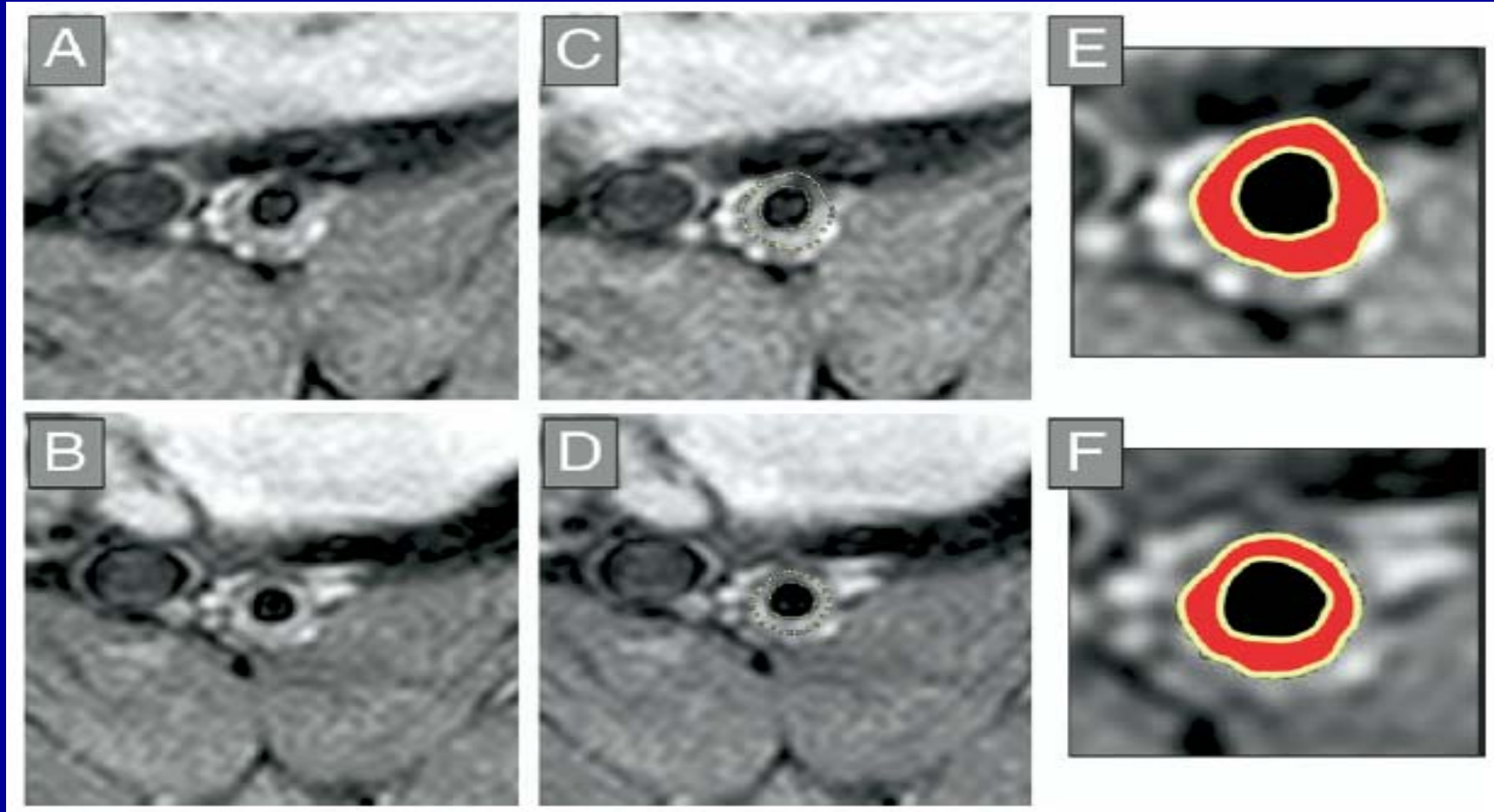


Moreno P, Sanz J, Fuster V,
J Am Coll Cardiol 2009;53:2315

Extracellular Matrix
Fibroblasts
Vasa Vasorum

SMC contraction
migration
proliferation

MRI - Atherosclerotic Plaque Regression & TF in Rabbits Recombinant ApoA-I_{Milano}



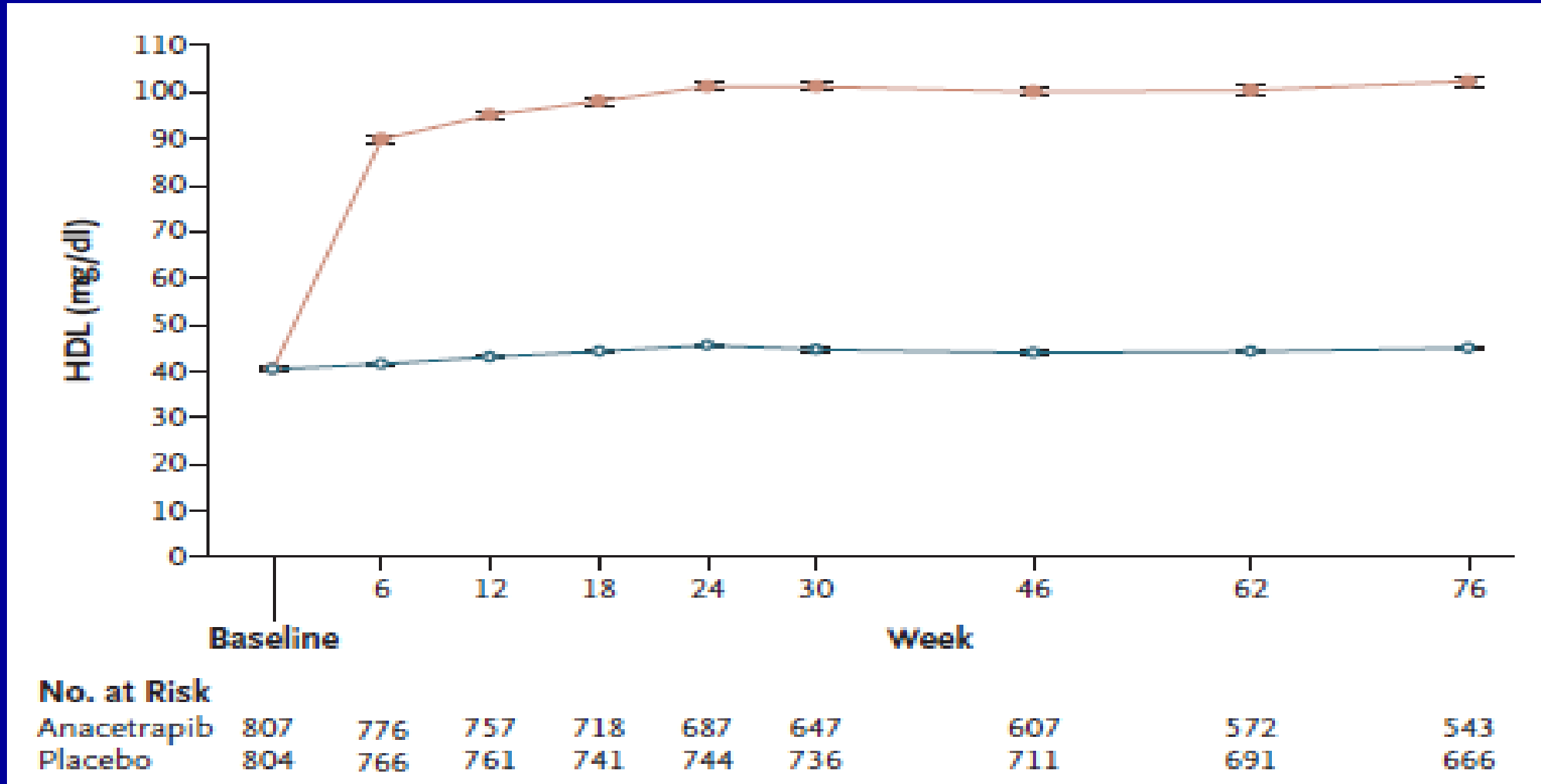
3) Reduction in gene & Protein Tissue Factor Expression

Ibanez B, Badimon JJ, Fuster V et. al. JACC 2008;51:1104.

1) Badimon JJ, Badimon L, Fuster V, JCI 1990; 85:1234 –Apo A1 Rabbits

2) Nissen SE JAMA 2003; 290:2292 – Apo A1 in Humans - IVUS

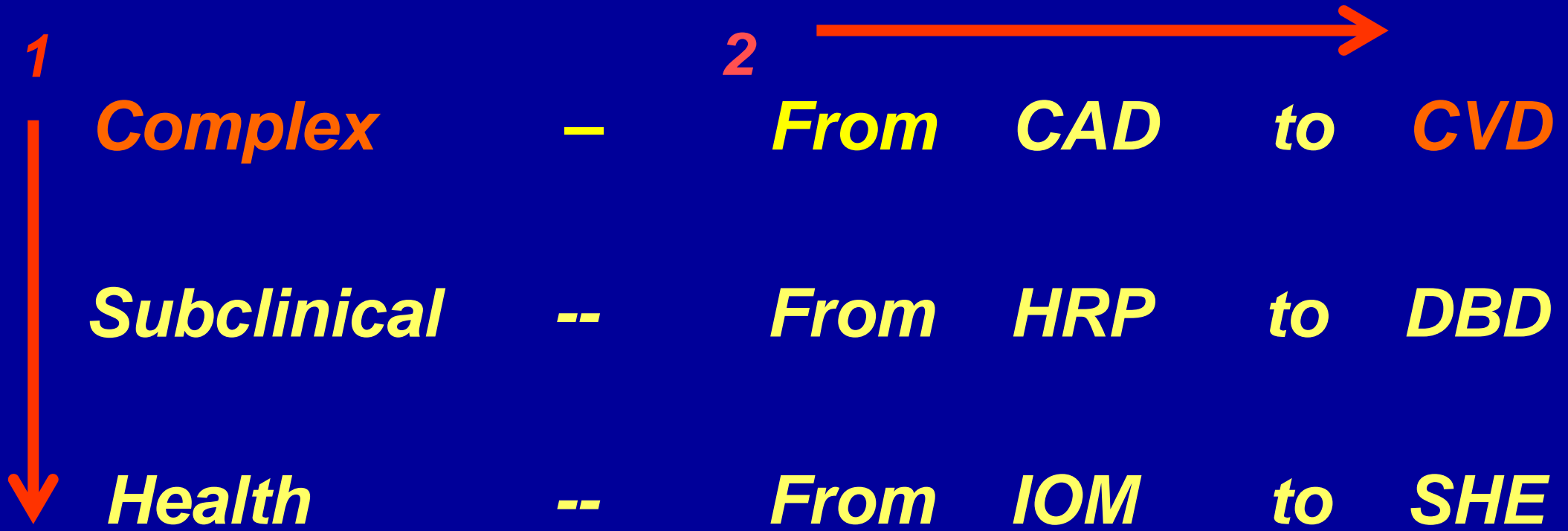
CETP Inhibition (Anacetrapib) Changes in Cholesterol Levels



DEFINE Investigators (CP Cannon et. al.) *N Engl J Med* 2010, Nov 17

A Transition From Disease to Health – 2010-2020

Cardiovascular & Mental



CAD – Coronary Artery Disease

HRP - High Risk Plaque

IOM – Institute of Medicine

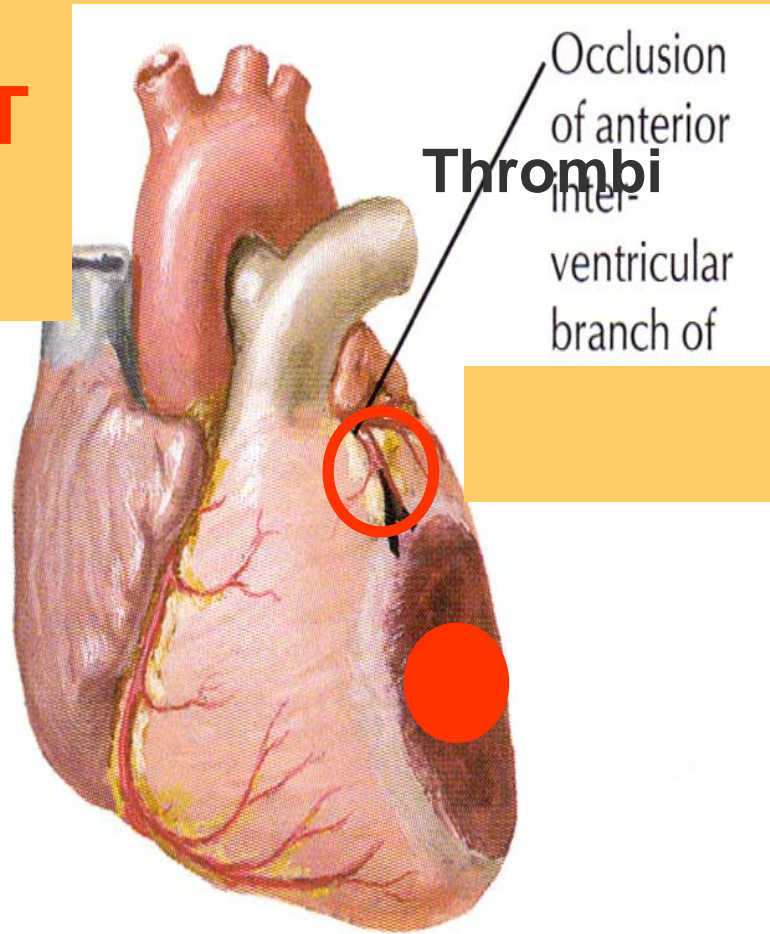
CVD – Cerebro Vascular Disease

DBD – Degenerative Brain Disease

SHE – Science Health & Education

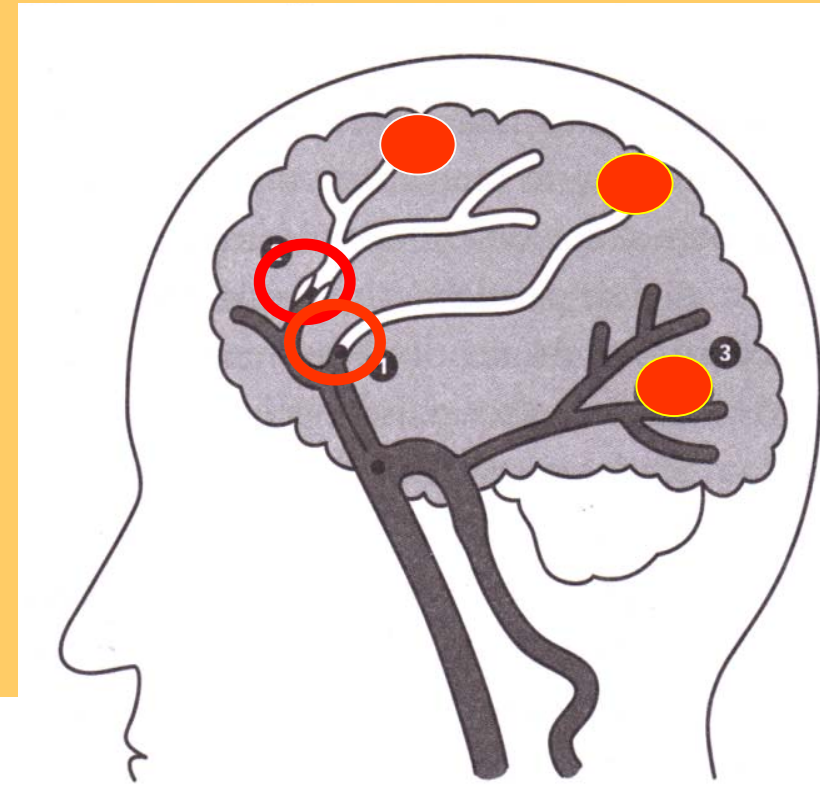
C) Cardiovascular(Cerebrovascular)

**HEART
MI**



**BRAIN -
STROKE**

- 1) Emboli
- 2)Thrombi
- 3)Hemorrh



Cardiovascular & Mental Health

C) SYMPTOMATIC CAROTID ENDARTER. VS STENTING – \$200 Million



CAS	CEA		RR (95% CI)
n/N	n/N		

All-cause death

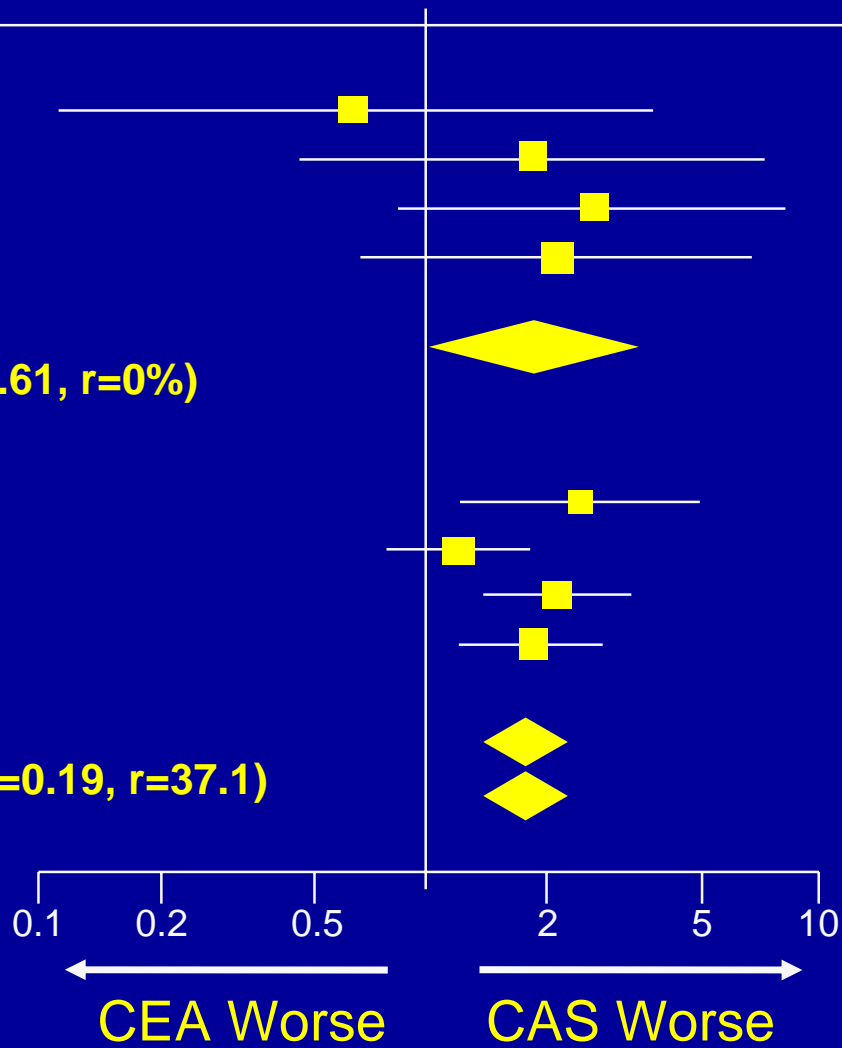
EVA-3S	2/260	3/257	0.66 (0.11-3.91)
SPACE	6/591	3/567	1.92 (0.48-7.64)
ICSS	11/828	4/821	2.73 (0.87-8.53)
CREST	9/1262	4/1140	2.21 (0.68-7.16)

Overall effect: $p=0.04$ (heterogeneity: $p=0.61, r=0\%$)

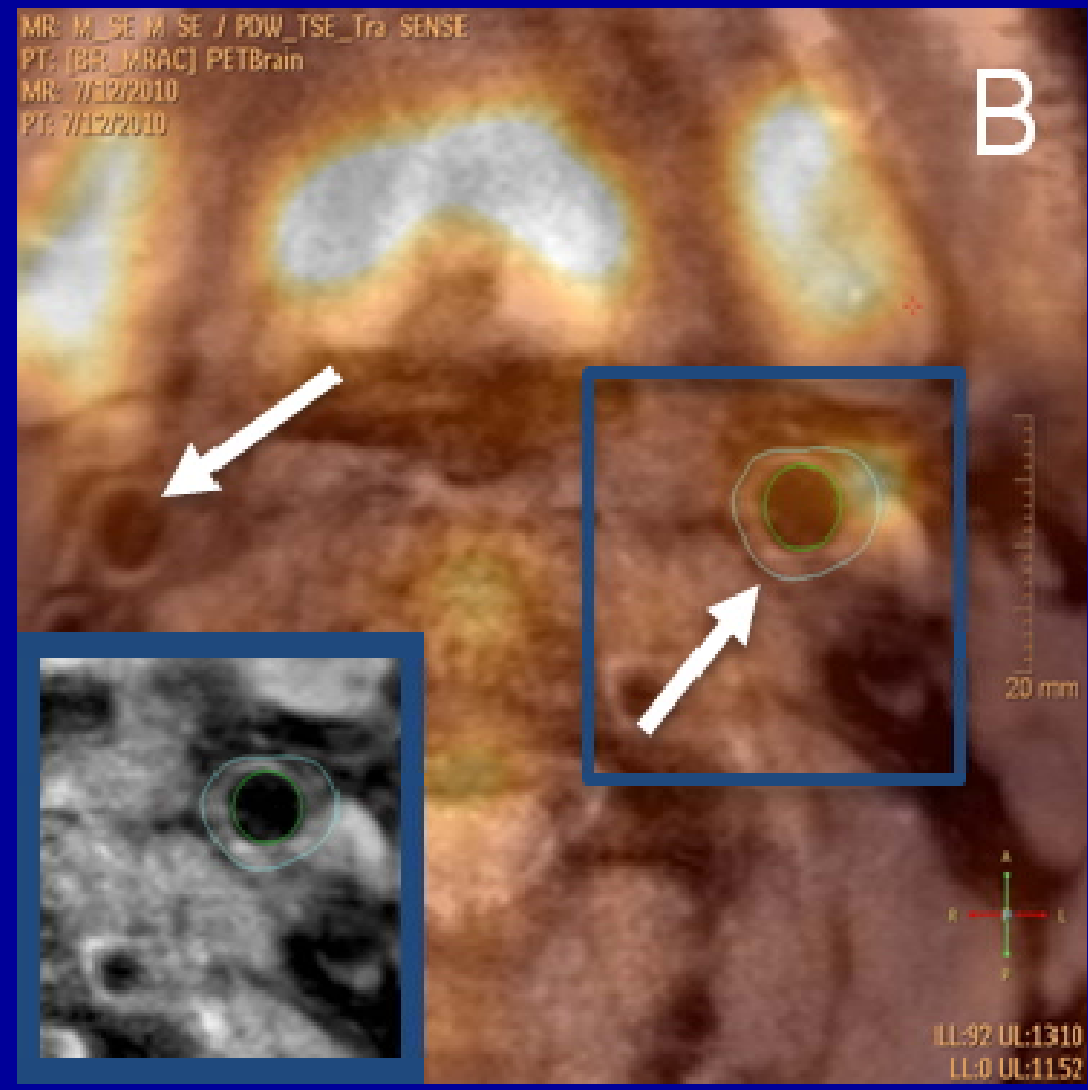
Any stroke or death

EVA-3S	25/260	10/257	2.47 (1.21-5.04)
SPACE	44/591	35/567	1.21 (0.79-1.85)
ICSS	61/828	28/821	2.16 (1.40-3.34)
CREST	55/1262	29/2340	1.86 (1.20-2.90)

Overall effect: $p<0.0001$ (heterogeneity: $p=0.19, r=37.1$)



B) Integration of Noninvasive Imaging PET/MR For Early Identification of CVD



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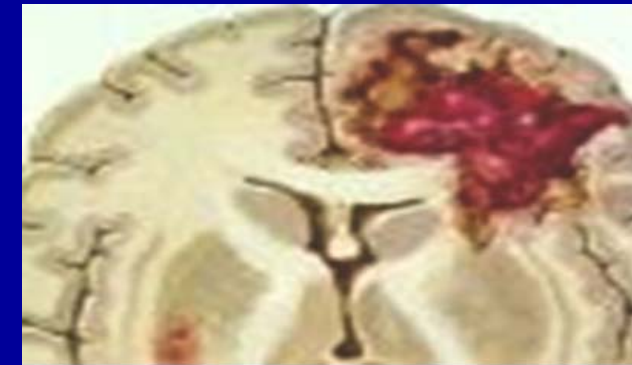
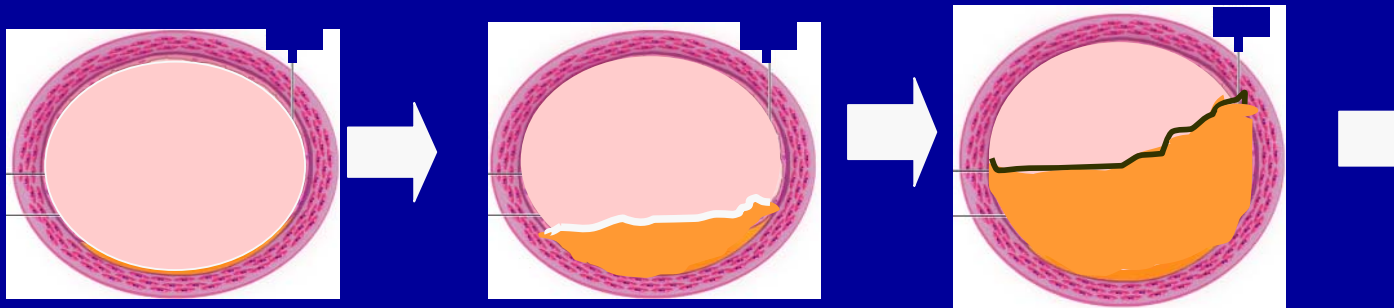
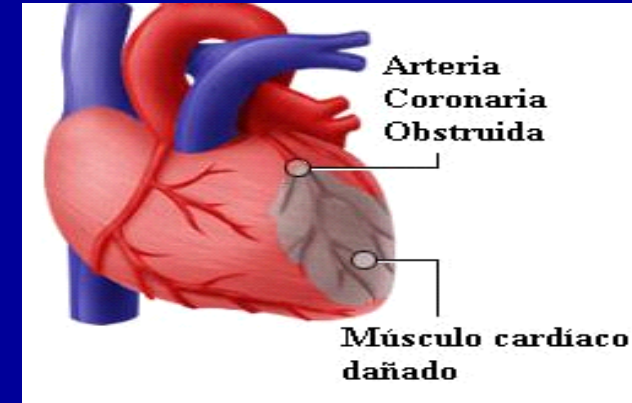
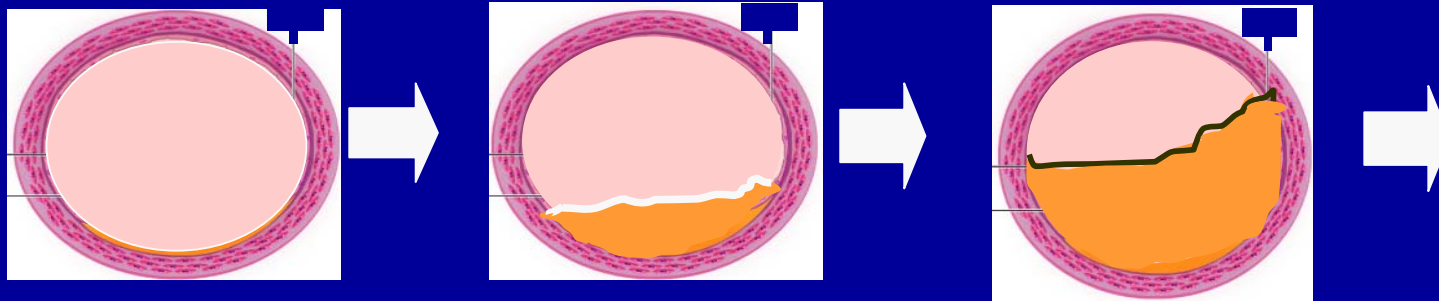
SHE – Science Health & Education

PESA
40-54y, n= 4,000 , FU 0,3,6 y

HRP > 55y,
N=7000 FU 3y

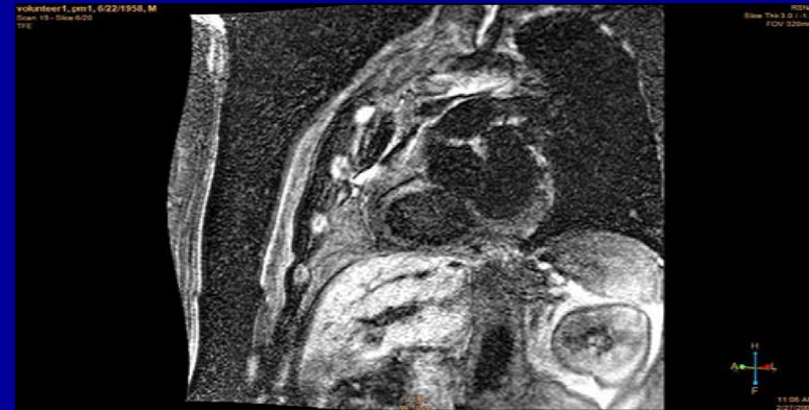
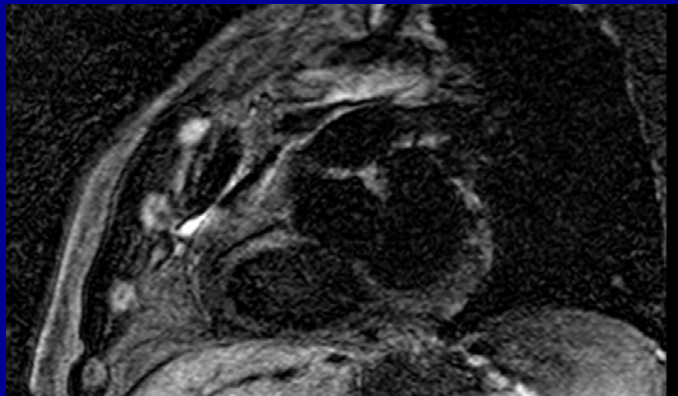
↓ → **Life Style ?**

↓ → **Predictive ?**



“Omics – Copenhagen Heart Study, Framingham,

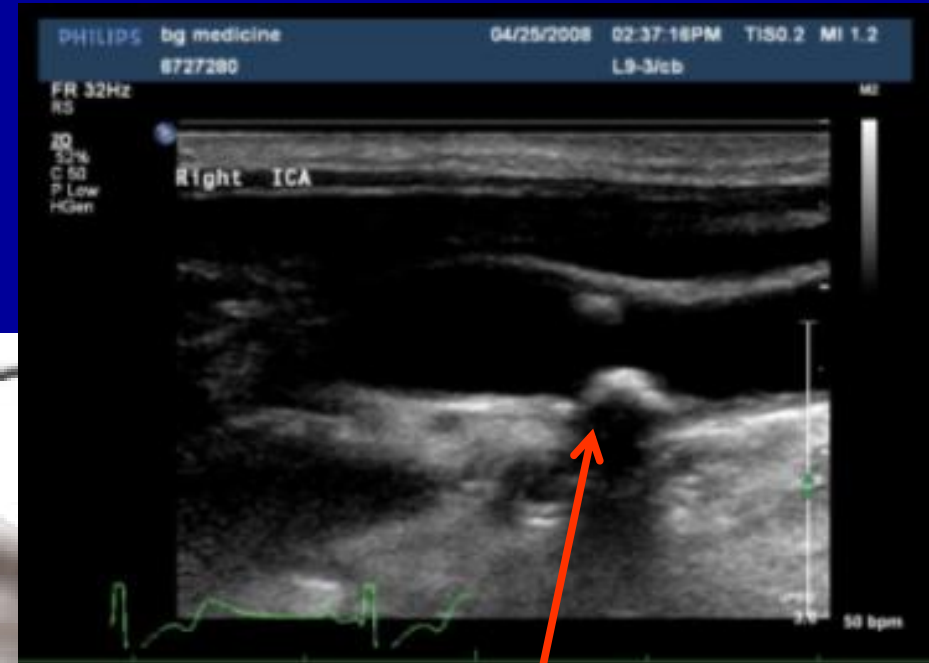
HRP - BioImage Study – Mobile Units



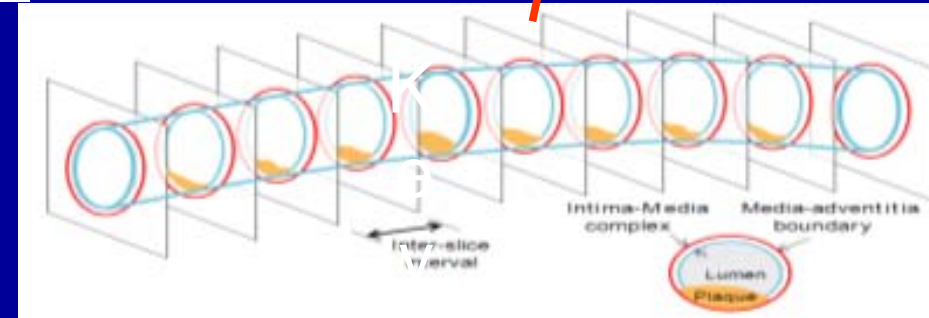
HRP - Biolmage Study –US Observations

Both conventional longitudinal scan and transverse (axial) sweep of carotids:

- “Manual 3D”: T.P Area
- 3D transducer: P Volume

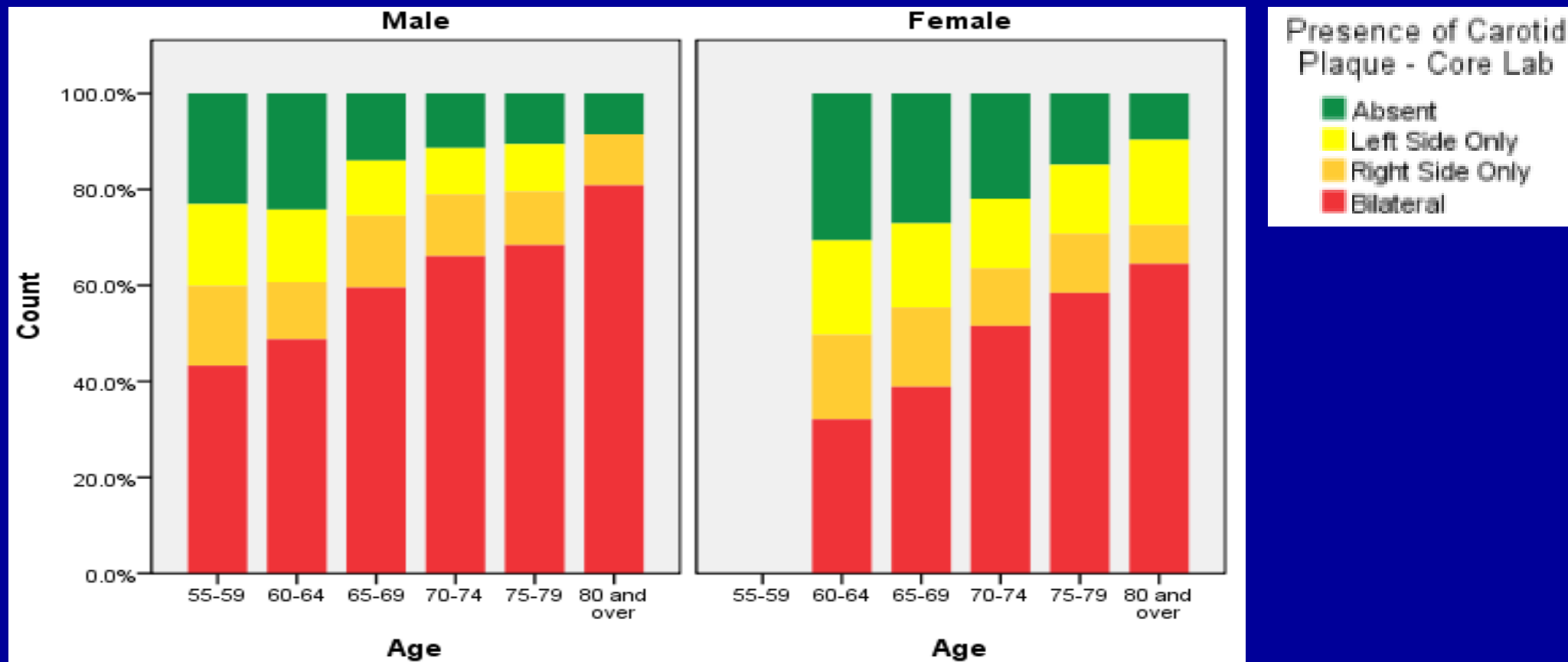


37% of subjects with plaques would have been missed in conventional longitudinal scans



Plaque Definition: focal structure encroaching into the arterial lumen of at least 0.50 mm or 50% of surrounding IMT value

HRP - Biolmage Study – Carotid Plaques & Age



Events 8 mo: 94 – 34 Heart Attacks -

- 1) Extensive Plaque Burden - 2) Bilateral Predictive (X2 FRS)**
- 3) No Change in Life Style? - 4) Economic ?**

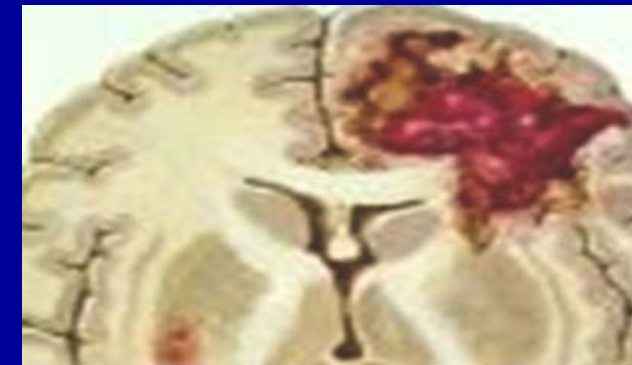
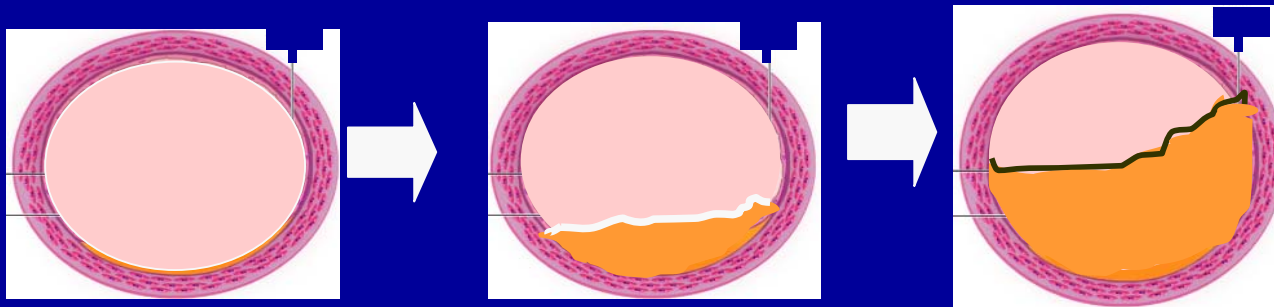
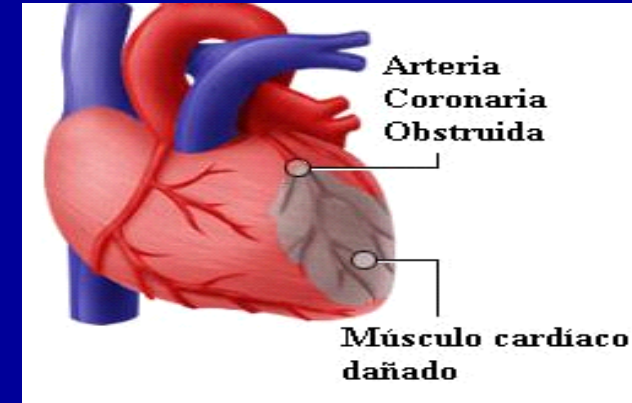
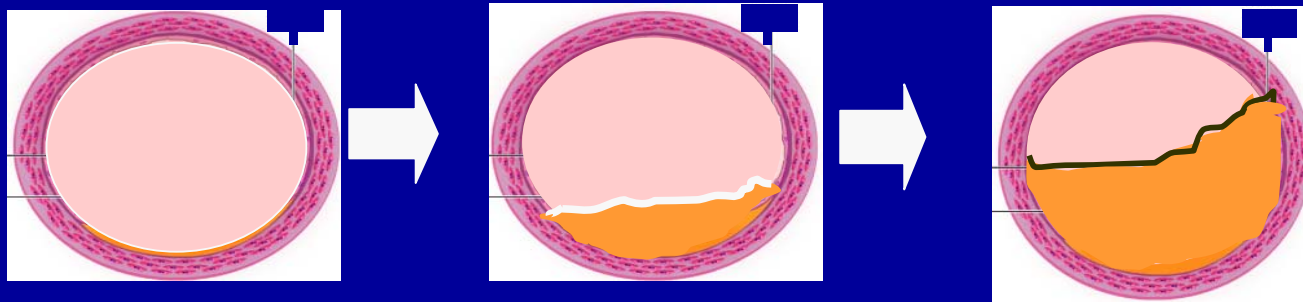
H Sillesen, V Fuster, E Falk, C McCall, P Muntendam AHA 2011

PESA
40-54y, n=4,000 FU 0,3,6 y

HRP > 55y,
N=7000 FU 3y

↓ → **Life Style ?**

↓ → **Predictive ?**



“Omics – Copenhagen Heart Study, Framingham,

PESA - CNIC Santander



40 personas

A Transition From Disease to Health – 2010-2020

Cardiovascular & Mental



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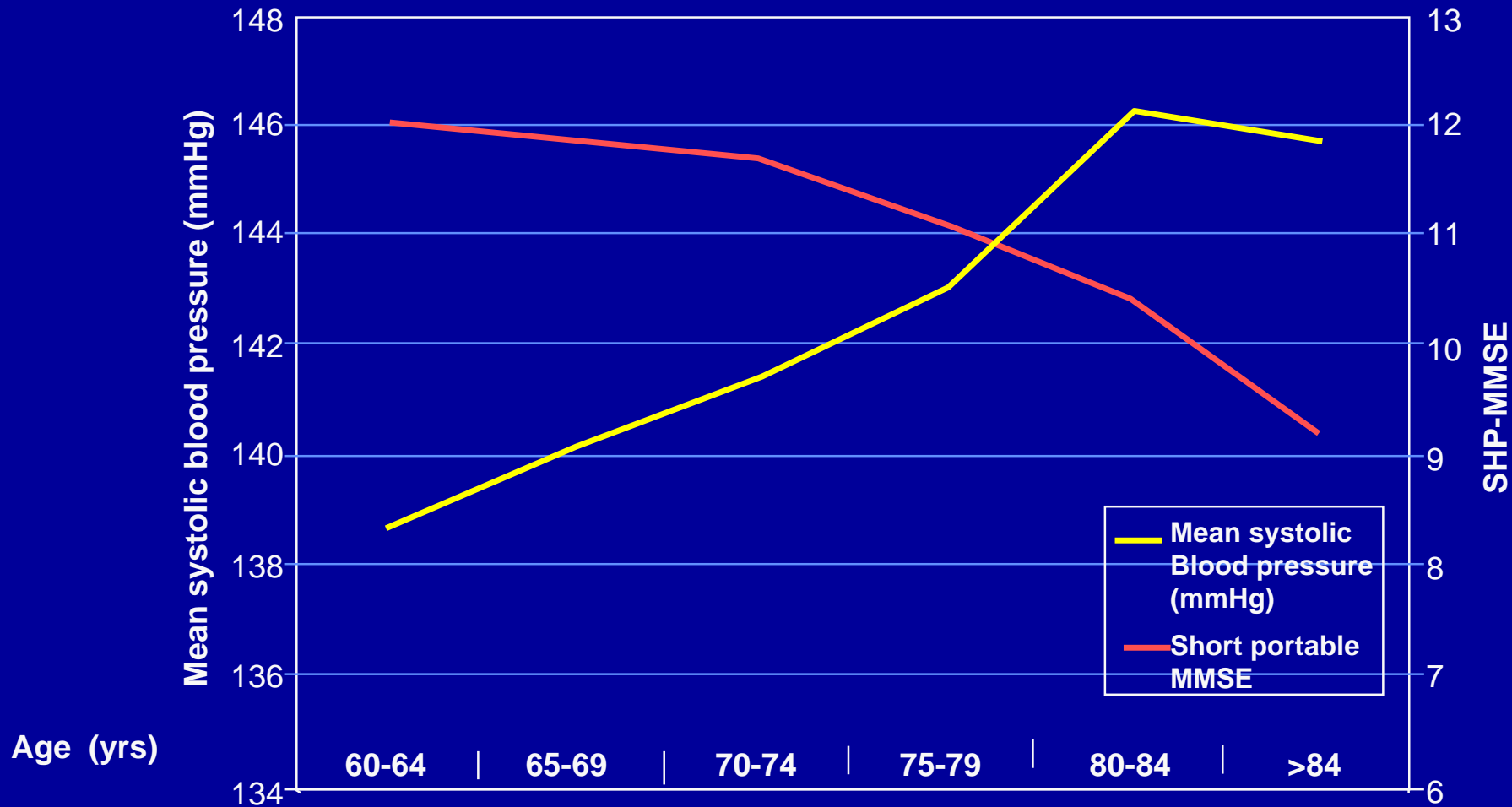
CVD – Cerebro Vascular Disease

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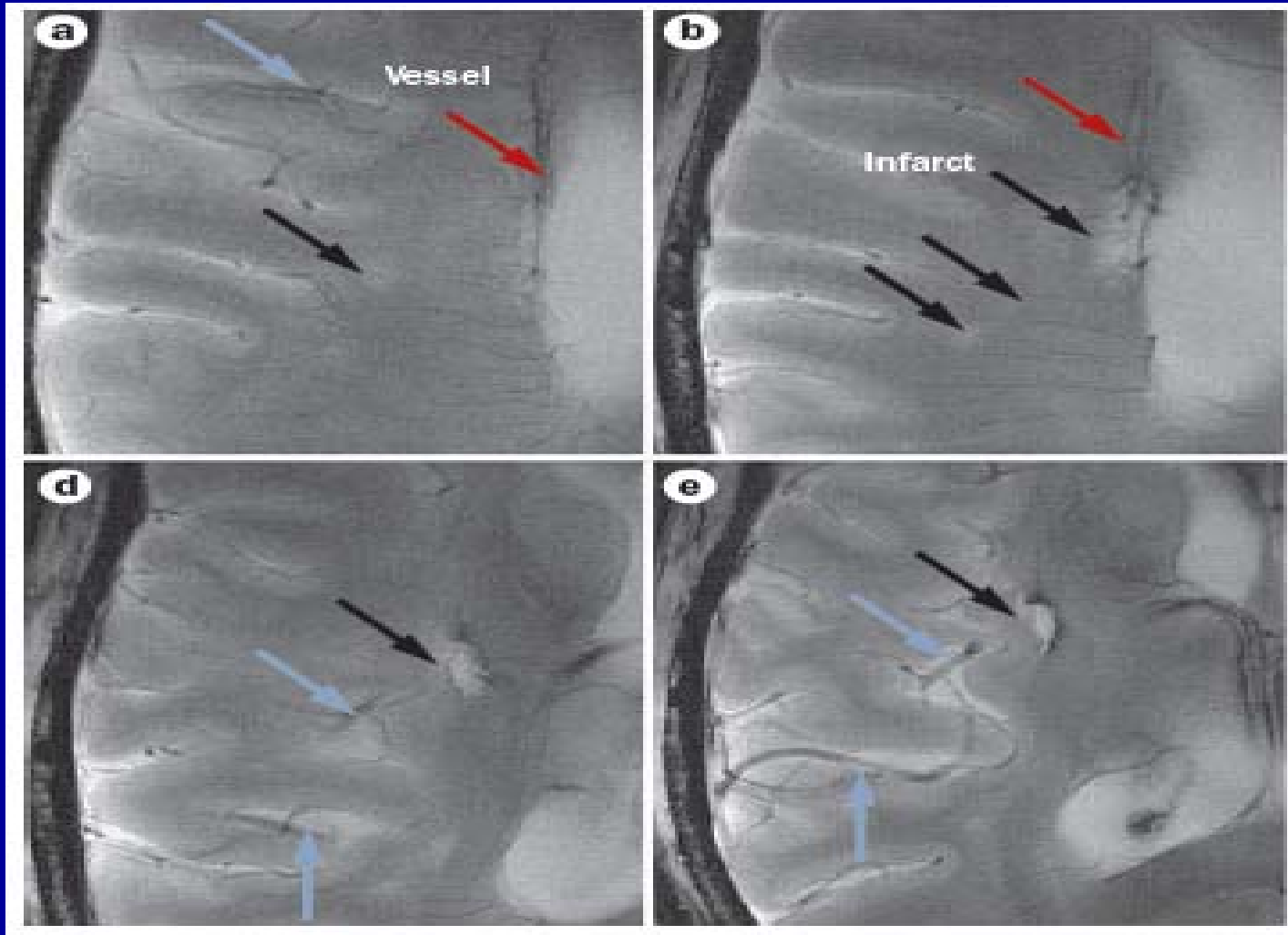
ADVANCED AGE, HYPERTENSION AND DEMENTIA

SBP AND SHORT PORTABLE MMSE SCORE BY INCREASING AGE GROUPS

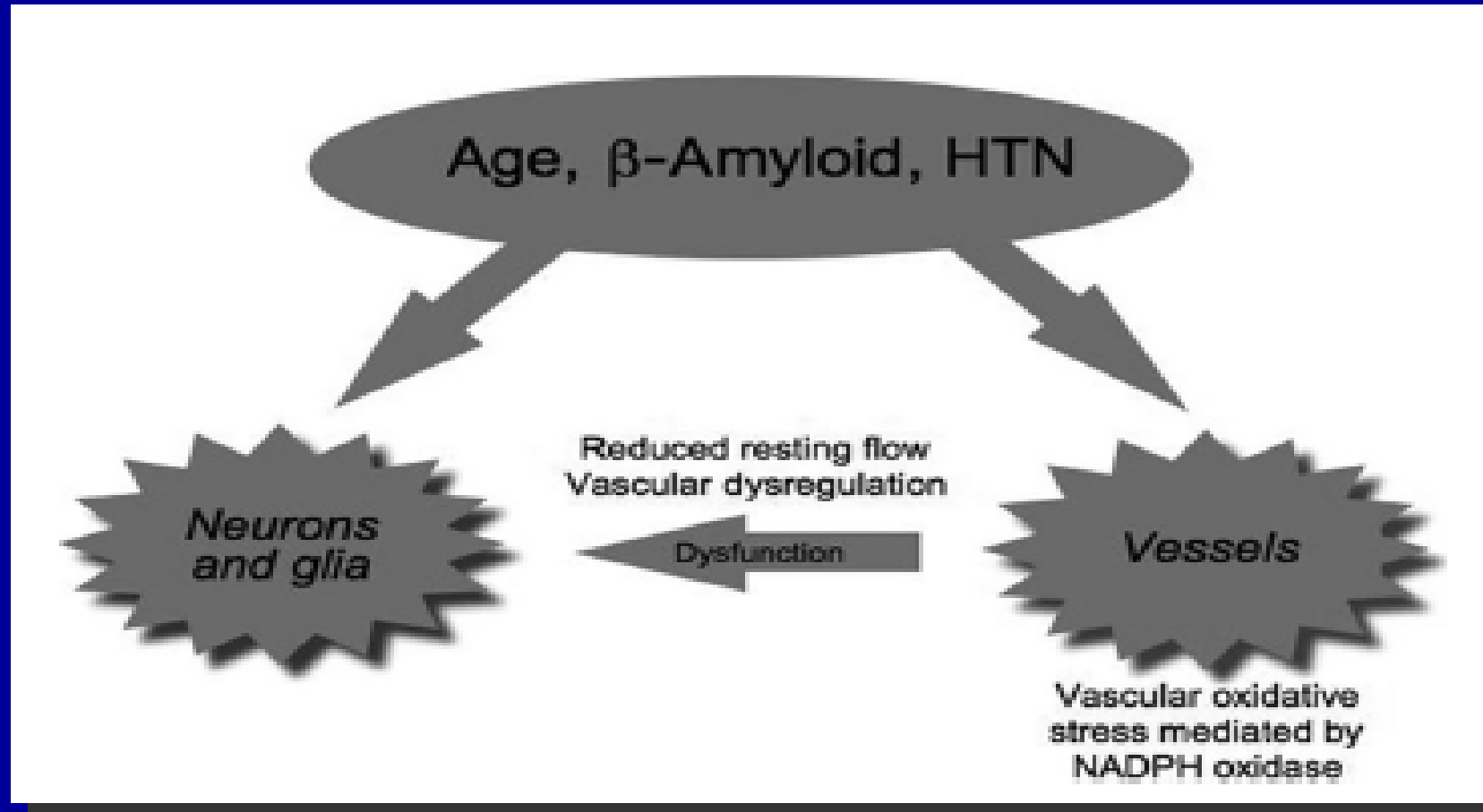


TO Obisecon. Clin Geriatr Med **2009**; 25:259 (NIH) – Age, BP, Cognitive Function
SP Kennelly, BA Lawlor, RA Kenny. Ageing Research Reviews **2009**; 8:61 - Review
HW Querfurth, FM LaFerla. NEJM **2010**; 362:329 - Imaging

High Resolution 8-T Gradient Gd-Enhanced Echography Slices



Mechanisms of Disease: Alzheimer's Disease



1. C. Iadecola et. al. *Stroke* **2009**;40[suppl 1]:S40.
2. HW Querfurth, FM LaFerla. *NEJM* **2010**; 362:329
Ischemia affects 60 to 90% of patients with Alzheimer's
3. Mount Sinai Journal of Medicine **2010**; 77:82-102
Hypertension, Hypotension, Cholesterol, Diabetes, Smoking

A Transition From Disease to Health – 2010-2020

Cardiovascular & Mental



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Promoting Cardiovascular Health

National Heart, Lung, and Blood Institute

**Institute of Medicine,
of The National Academy of Sciences**

Promoting
Cardiovascular Health
in the Developing World

**A Critical Challenge
to Achieve Global Health**

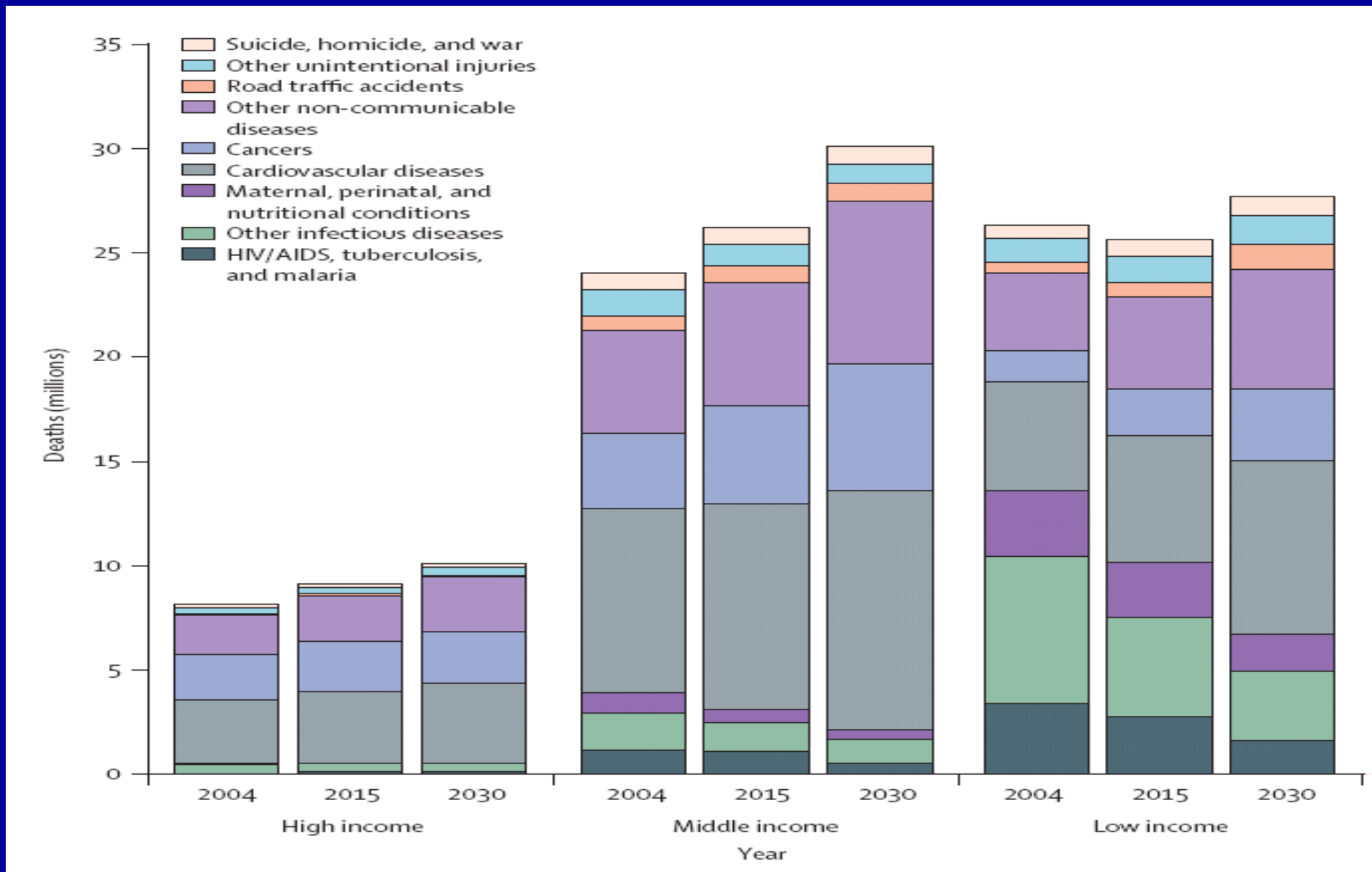
INSTITUTE OF MEDICINE
OF THE NATIONAL ACADEMIES

Report Brief, Report Summary, and Full
Prepublication Report can be
downloaded for free:

www.iom.edu/globalcvd

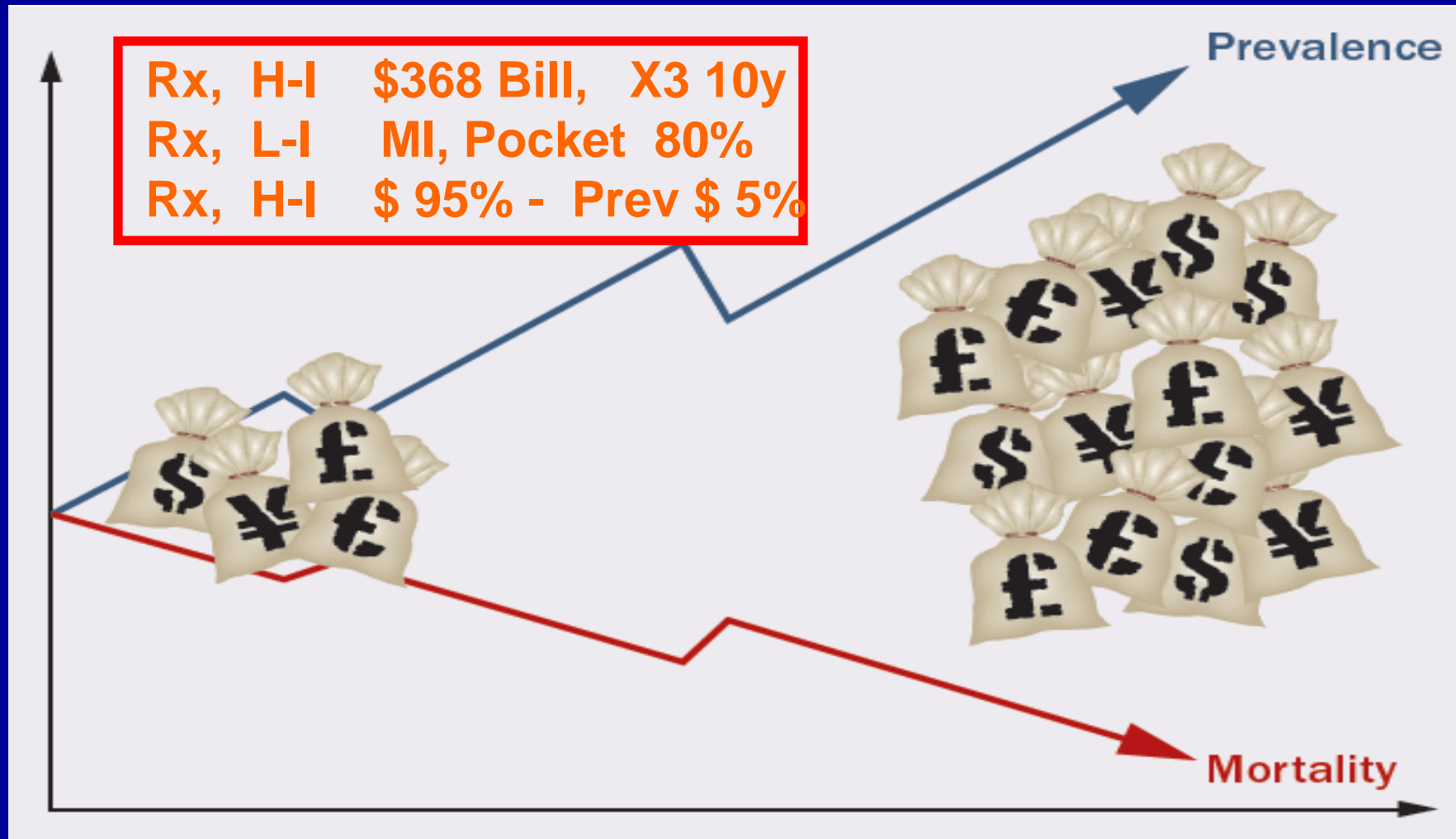
Chair – Valentin Fuster

K1 - HML). Projected Deaths by Cause, 2004, 2015, 2030



R. Beaglehole et. al. *Lancet* 2008;372:1988.

K2 - Prevalence of CVD is Increasing Treatment (Live Longer) and Technology (\$)



DETERMINANTS

Globalization

Demographic Change

Social Determinants

Health Inequities

Education

Cultural and Social Norms

Biological Risk

Behavioral Risk

K3

POLICY APPROACHES (Global; National; Local)

Financial

Legal

Regulatory

Trade

Environment To Enable Individuals To Make and Maintain Healthy Choices

WIDER SOCIETY

INDIVIDUAL

FAMILY

NEIGHBORHOOD, COMMUNITY

Preventive, Diagnostic, Therapeutic, Rehabilitative Services

Enhancement of Knowledge, Motivation, and Skills of Individuals

Media

Community Interventions

Settings Based

HEALTH COMMUNICATION

Health Workforce

Drugs & Technologies

Quality of Care

Access to Care

Systems Infrastructure

HEALTH CARE DELIVERY

A1- WE KNOW THE RISK FRS CONTRIBUTING TO CVD

Consumption

*Foods/
Calories
Fats/oils
Salt
Tobacco*

Activity

Work
School
Leisure

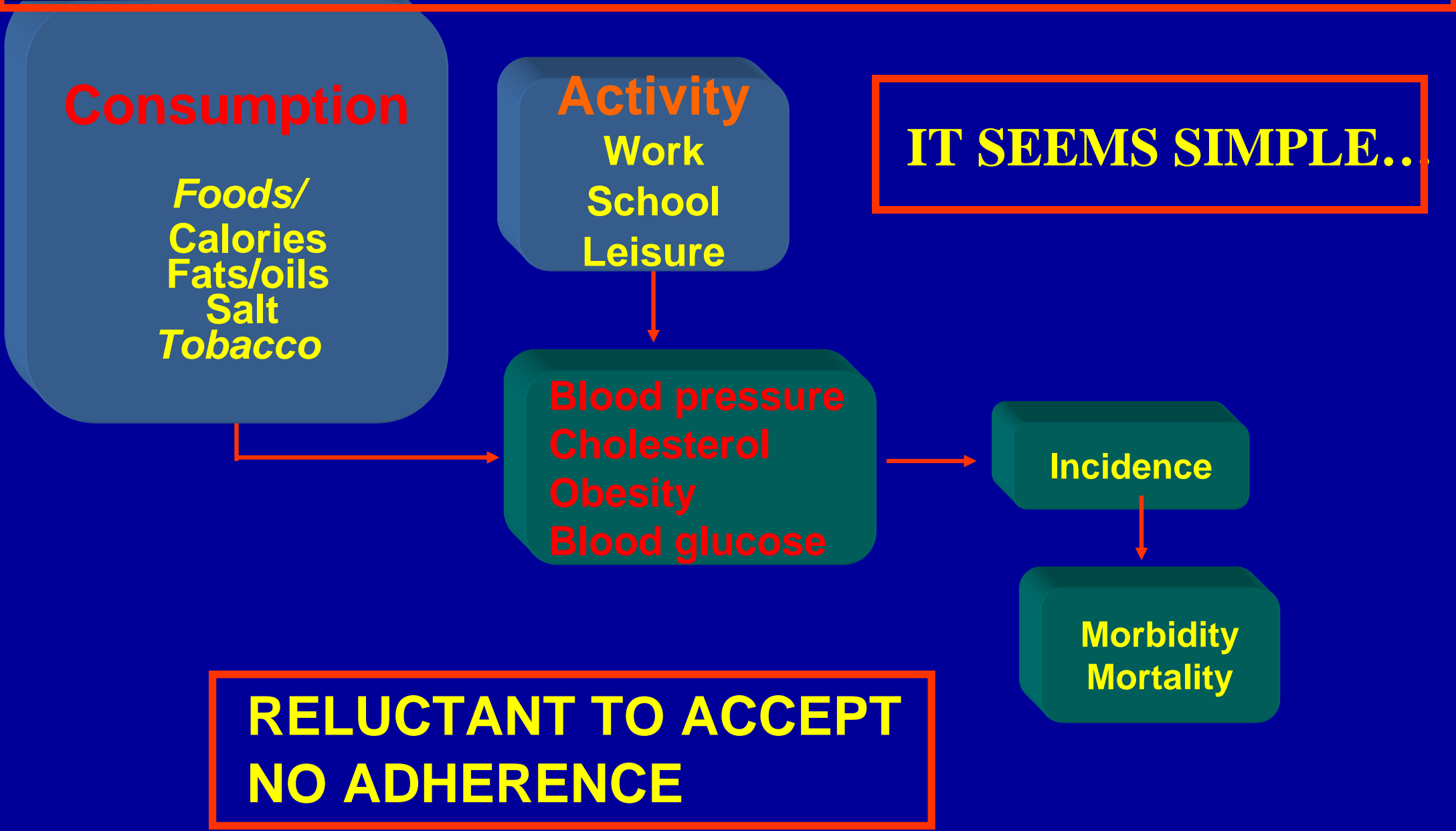
IT SEEMS SIMPLE..

Blood pressure
Cholesterol
Obesity
Blood glucose

Incidence

Morbidity
Mortality

RELUCTANT TO ACCEPT
NO ADHERENCE



A2 - Sharing for Action: Essential Functions

	Stakeholder Group	Funding	Advocacy	Leadership	Policy	Implementation	Capacity Building	Research	Monitoring and Evaluation
International	WHO		✓	✓	✓				✓
	World Bank	✓		✓	✓		✓	✓	
	WEF			✓	✓				
	FAO		✓	✓	✓		✓		✓
	UNICEF		✓	✓	✓				✓
	UNGASS			✓					
	International Aid Agencies	✓		✓	✓	✓	✓	✓	
	Global Health Research Initiatives			✓			✓	✓	✓
	U.S. Government	✓		✓	✓	✓	✓	✓	✓
	International NGOs		✓	✓		✓	✓	✓	
	Private Donors	✓							
	Industry	✓	✓	✓		✓	✓	✓	
	PPPs				✓				✓
Regional	UN / WHO Regional Offices		✓	✓	✓	✓	✓	✓	✓
	Regional Development Banks	✓		✓	✓		✓		
	Regional NGOs		✓	✓		✓	✓	✓	
National/Subnational	National Governments	✓		✓	✓	✓	✓		✓
	Ministries of Health	✓	✓	✓	✓	✓	✓		✓
	National Research Institutes/ MRCs	✓		✓			✓	✓	
	Local Governments	✓		✓	✓	✓	✓		✓
	Local NGOs		✓	✓		✓	✓	✓	
	Local Academia			✓		✓	✓	✓	✓
	Local donors	✓							

A3 -Transition From Disease to Health – 2010-2020

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A3



**Foundation
for Science, Health
and Education**

SHE - Global Demonstration Projects

A. Children (3-6yrs) – Sesame Street

B. Adults Cultural Groups - GHP

C. Adults Regulations & Law – NY

D. Millenium Project – Infrastructure

E. Polypill – Adherence & Economy

F. Youth – It is Never too Early



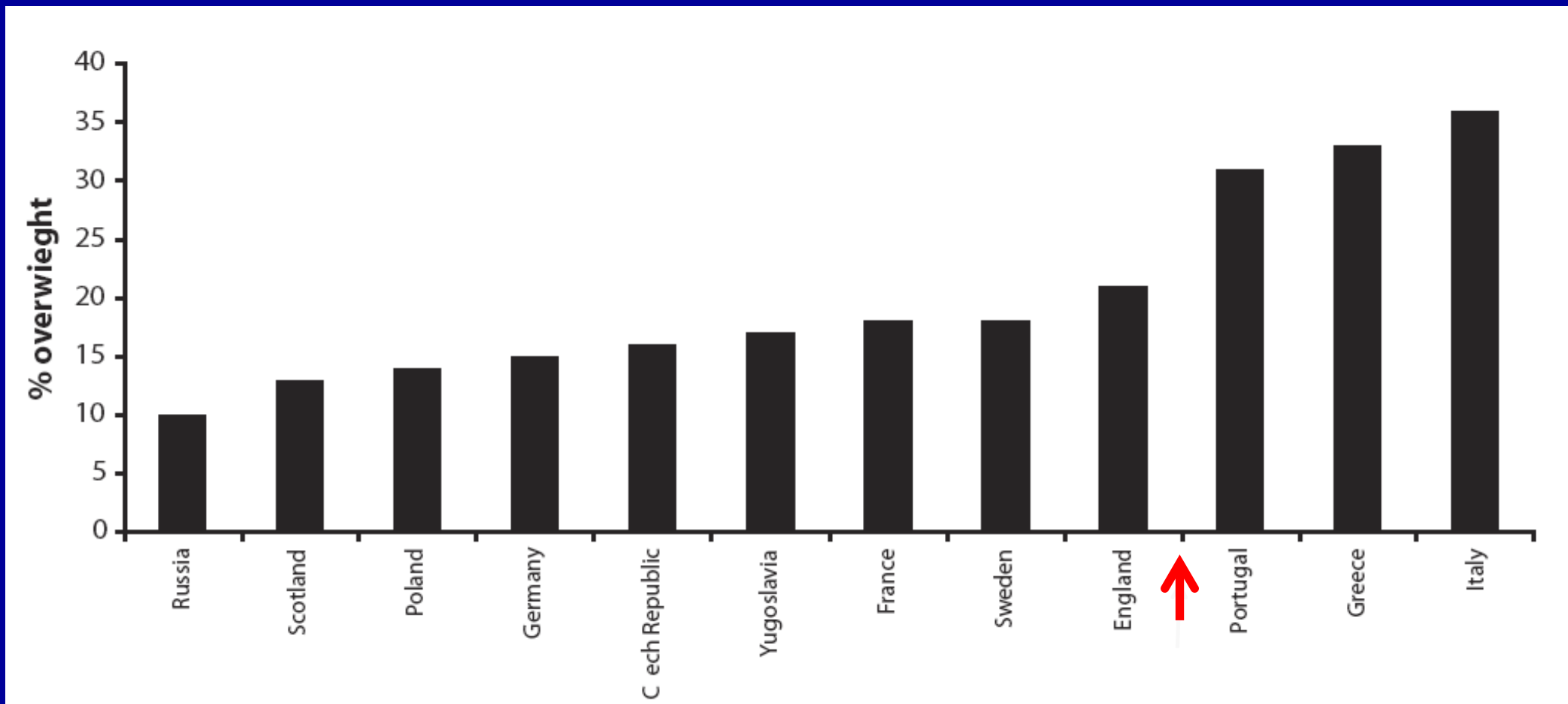
Innovation

***A1 -The Early Relationship Between Parent , Child
& Environment are Crucial to Later Development***



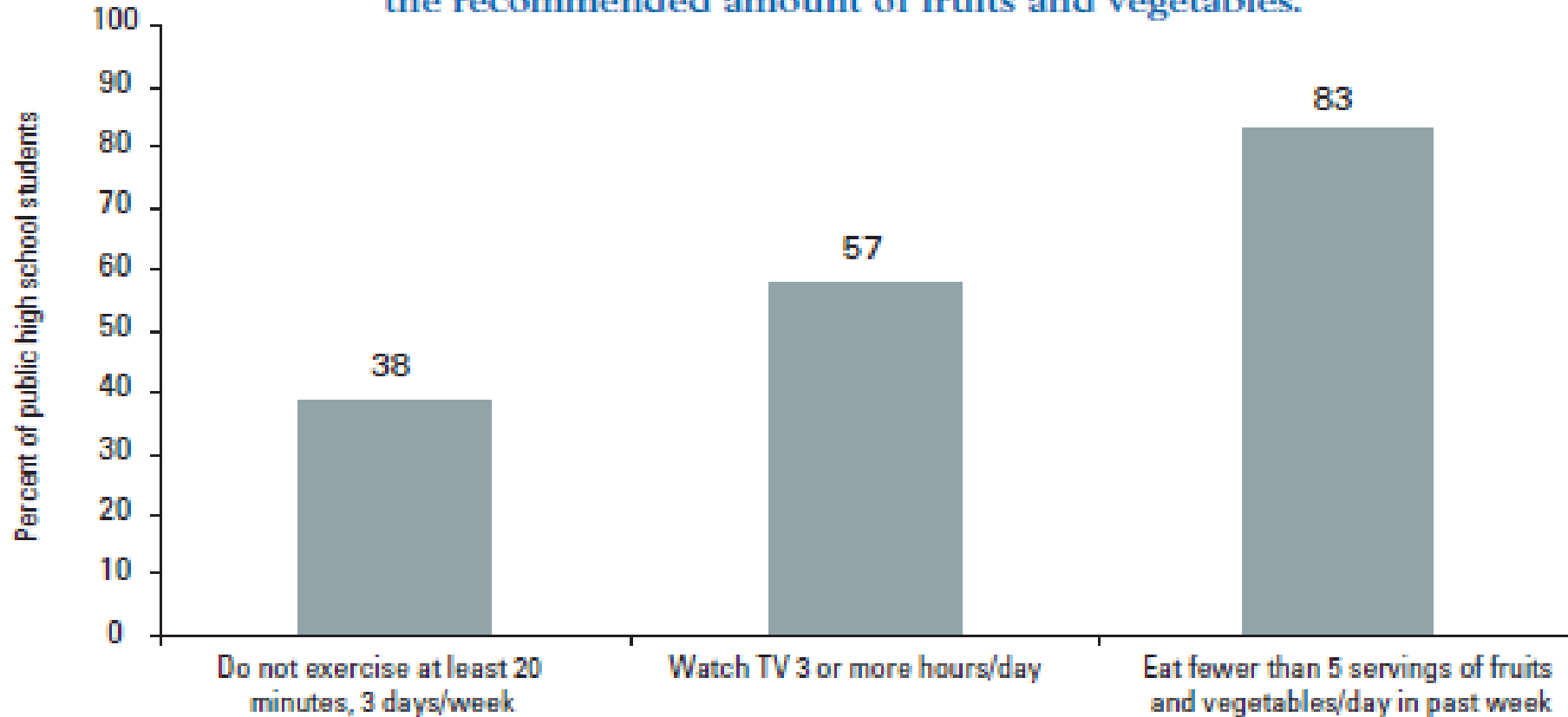
M Kringelbach. Nature. 2010;467:918.

A2 - Overweight % in Children Aged 4-11 years,



**European Cardiovascular Disease Statistics
British Heart Foundation, February 2005.
European Heart Network, February 2005.**

Many adolescents do not get enough exercise, more than half watch too much TV, and most consume less than the recommended amount of fruits and vegetables.



Matte et. al., Obesity in East and Central Harlem: A look across generations. New York, NY: New York City Department of Health and Mental Hygiene, 2007.

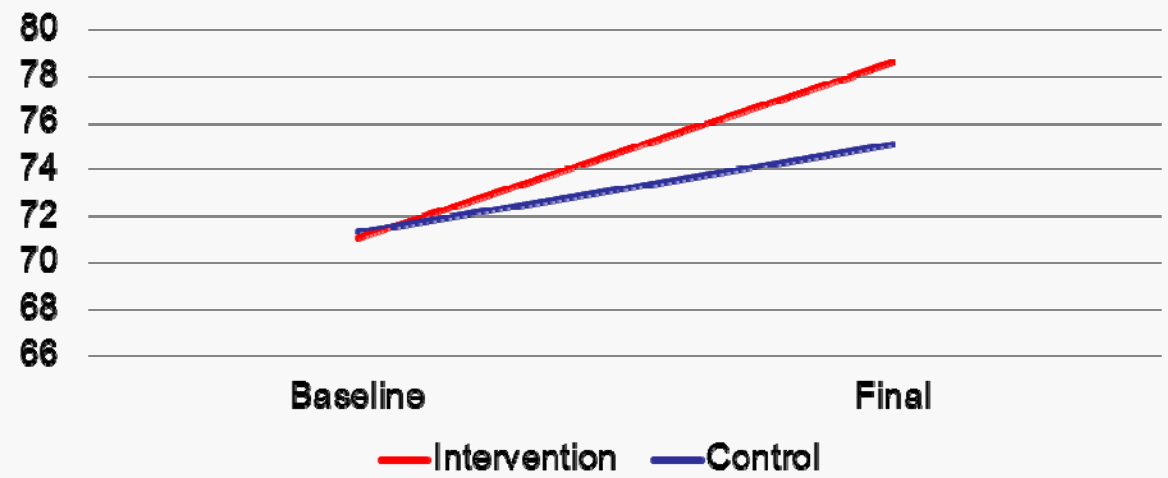
A. Bogota (n=6000), Madrid, Cardona (n=1200) Health, Drugs, Tolerance



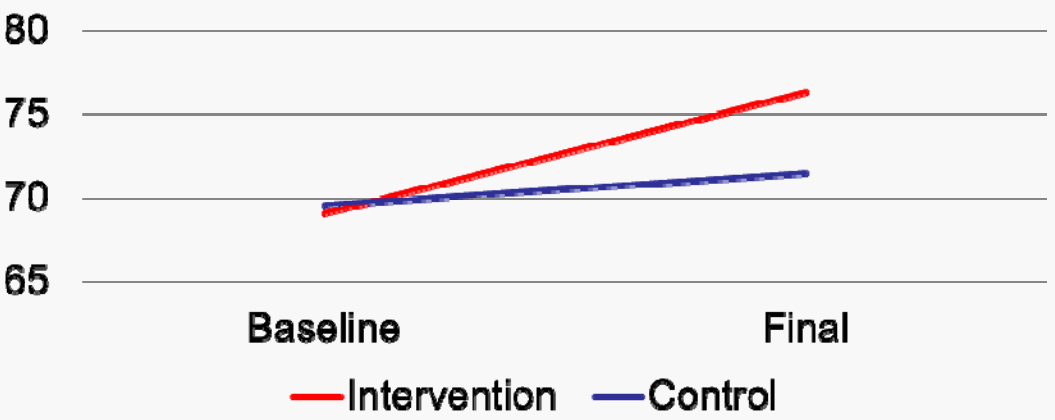
Randomized Study: End Points 1 Year – 20 Years

IMPACT OF THE HEALTHY HABITS INTERVENTION IN USAQUEN

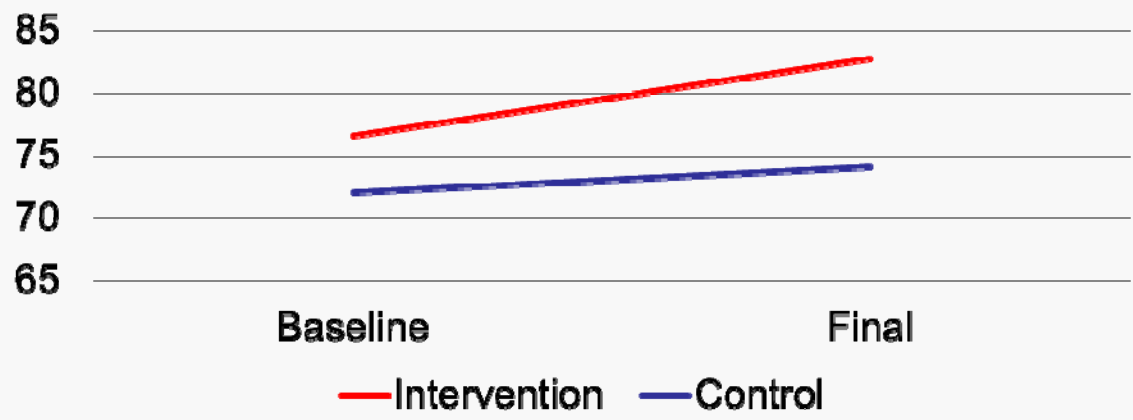
Changes in knowledge, attitudes and habits in **Children**



Changes in knowledge, attitudes and habits in **Parents**



Changes in knowledge, attitudes and habits in **Teachers**



Project Expansion Through Partners

Partner	Beneficiarie		Cover	Printed		Costs			
	Childr	Teach.		Full	Childr	Kits	Train.	Follow-up	Assess
MSI-Cimientos/ USAID	6755	805	Cesar Guajira Magdalena Norte de Santander	800	6500	MSI-C	MSI-C Sicol	MSI-C	MSI-C
Fundación Éxito	14000	25x	Antioquia Cesar Bogotá Huila Meta Nariño Risaralda Santander Tolima Valle del Cauca	1000	14000	FE	FE Sicol	FE	FE Sicol
Fundación Antonio Puerto	650	38	Boyacá	40	200	Sicol	FAP Sicol	FAP	FAP

SHE - 20 Schools in Madrid and Cataluña



International Foundation for Science, Health and Education (SHE)



Programa de Salud Integral



ACQUISITION OF HEALTHY FOOD HABITS



PHYSICAL ACTIVITY



KNOWLEDGE OF HOW YOUR BODY AND HEART WORKS



ACQUISITION OF PREVENTIVE HABITS TO AVOID ADDICTIONS

EDUCATIVE GOAL: HEALTHY HABITS FOR CHILDREN BETWEEN 3 AND 16 YEARS

SHE – Progress & Dissemination



International Foundation for Science, Health and Education (SHE)

EDUCATIONAL BOOKS

CHILDREN



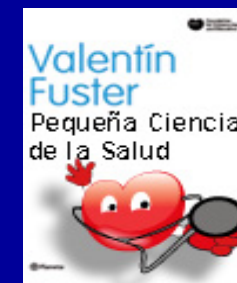
3-6



5-8



9-14



GENERAL PUBLIC



SHE - Global Demonstration Projects

A. Children (3-6yrs) – Sesame Street

B. Adults Cultural Groups – GHP

C. Adults Regulations & Law – NY

D. Millenium Project – Infrastructure

E. Polypill – Adherence & Economy

F. Youth – It is Never too Early

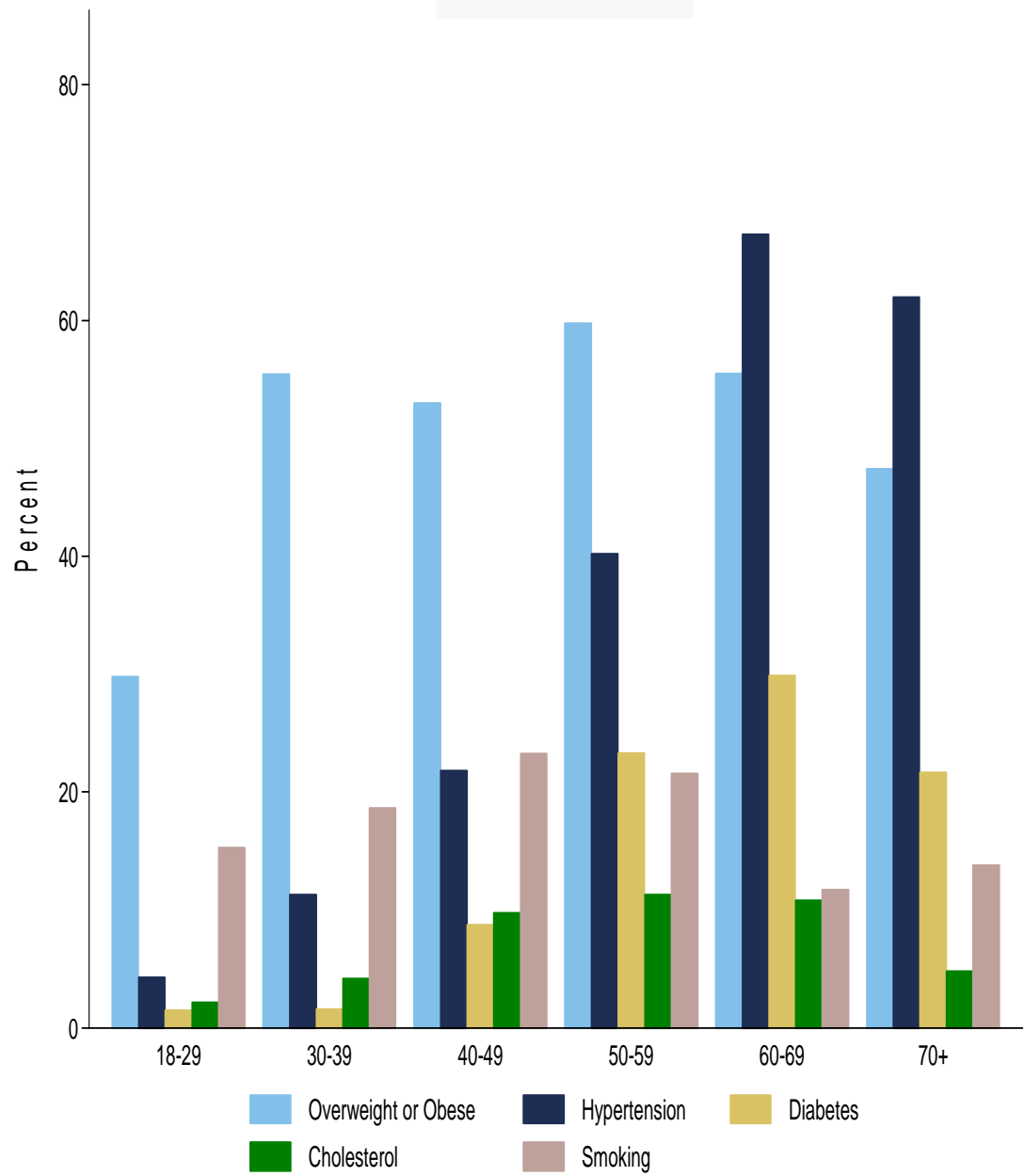


Customer Relationships

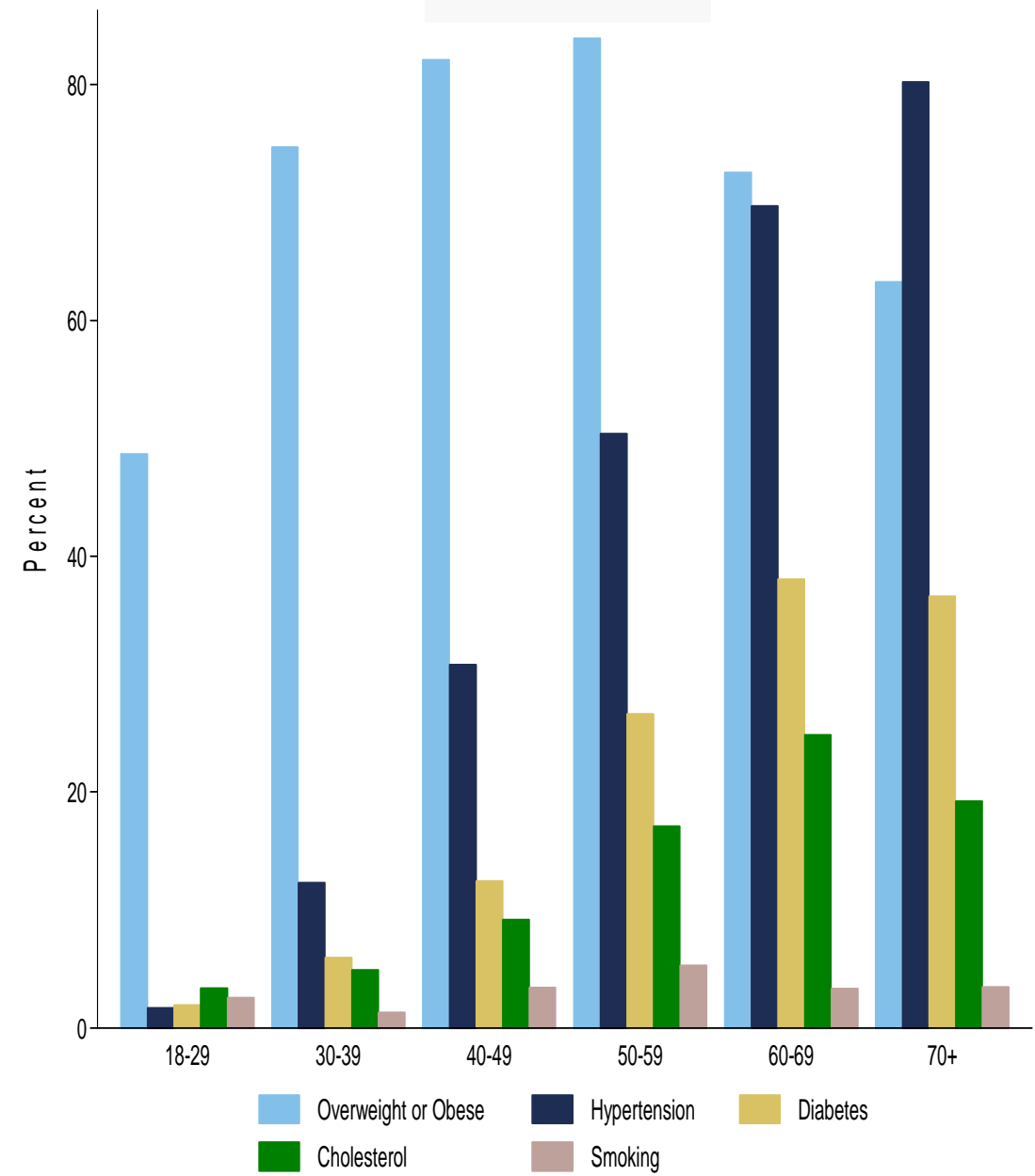
B. GHP – Background (LMIC) and Observational Objectives



RISK FACTORS: MAN



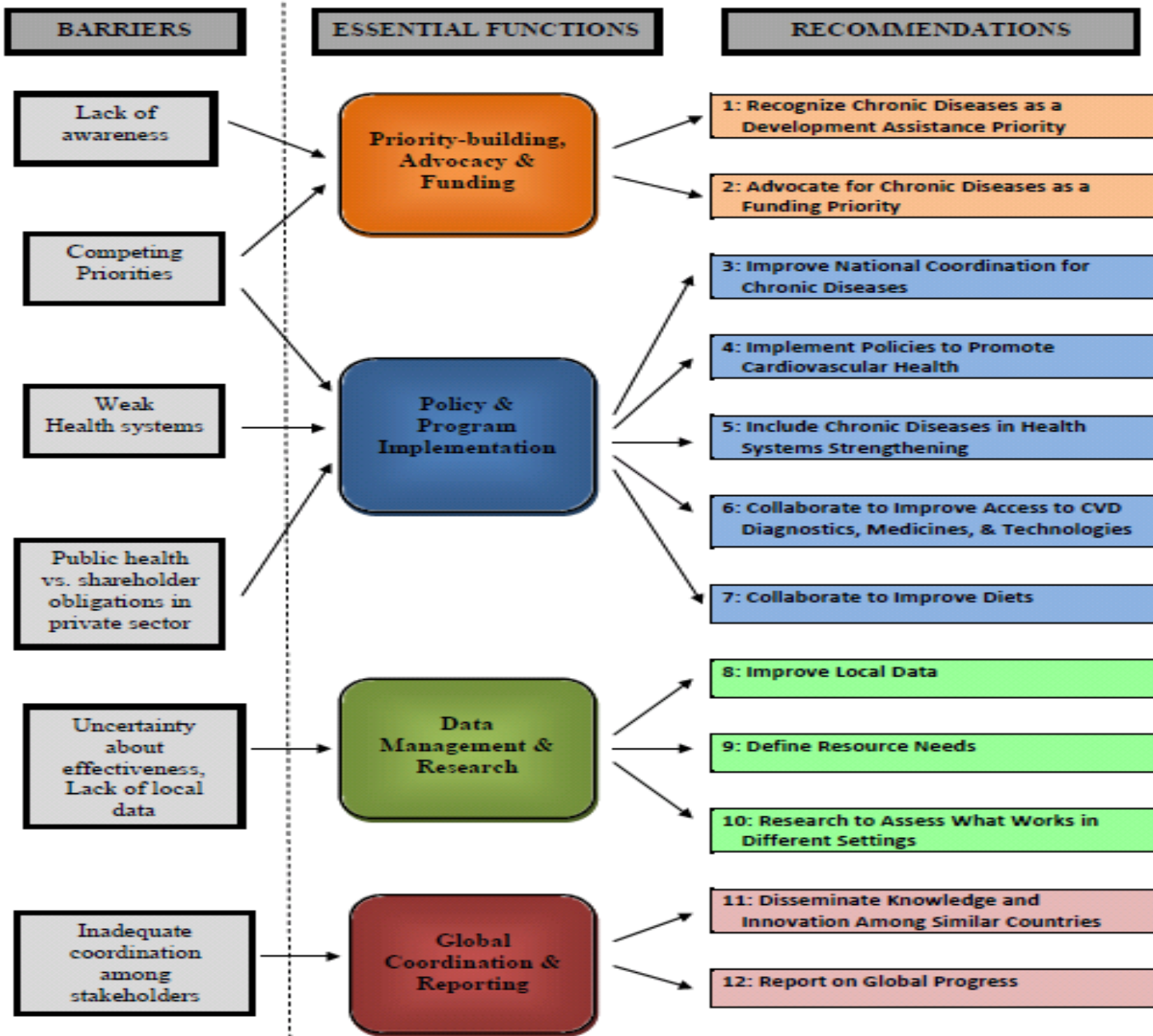
RISK FACTORS: WOMAN



1) *GHP INCENTIVE GROUP APPROACHES*

- **Blood Pressure**
 - **Physical Activity**
 - **Weight / Diet**
-

2) IOM CHALLENGE 12 RECOMMENDATIONS



MHG - MS/AHA

MS/AHA - MHG

GG COMMISSION

MHG POLICY (Salt, BP,)

MHG HEALTH SERVICES

MHG CLINICAL SERVICES

MS/AHA MHG (Food Industry)

MS/AHA

MHG

MS/AHA

MHG - PAHO

MHG - MS/AHA

SHE - Global Demonstration Projects

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C. Adults Regulations & Law – NY

D. Millenium Project – Infrastructure

E. Polypill – Adherence & Economy

F. Youth – It is Never too Early



Leadership

C. The Epidemic of CVD & The Law



Hypertension ?

SHE - Global Demonstration Projects

A. Children (3-6yrs) – Sesame Street

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C. Adults Regulations & Law – NY

D. Millenium Project – Infrastructure

E. Polypill – Adherence & Economy

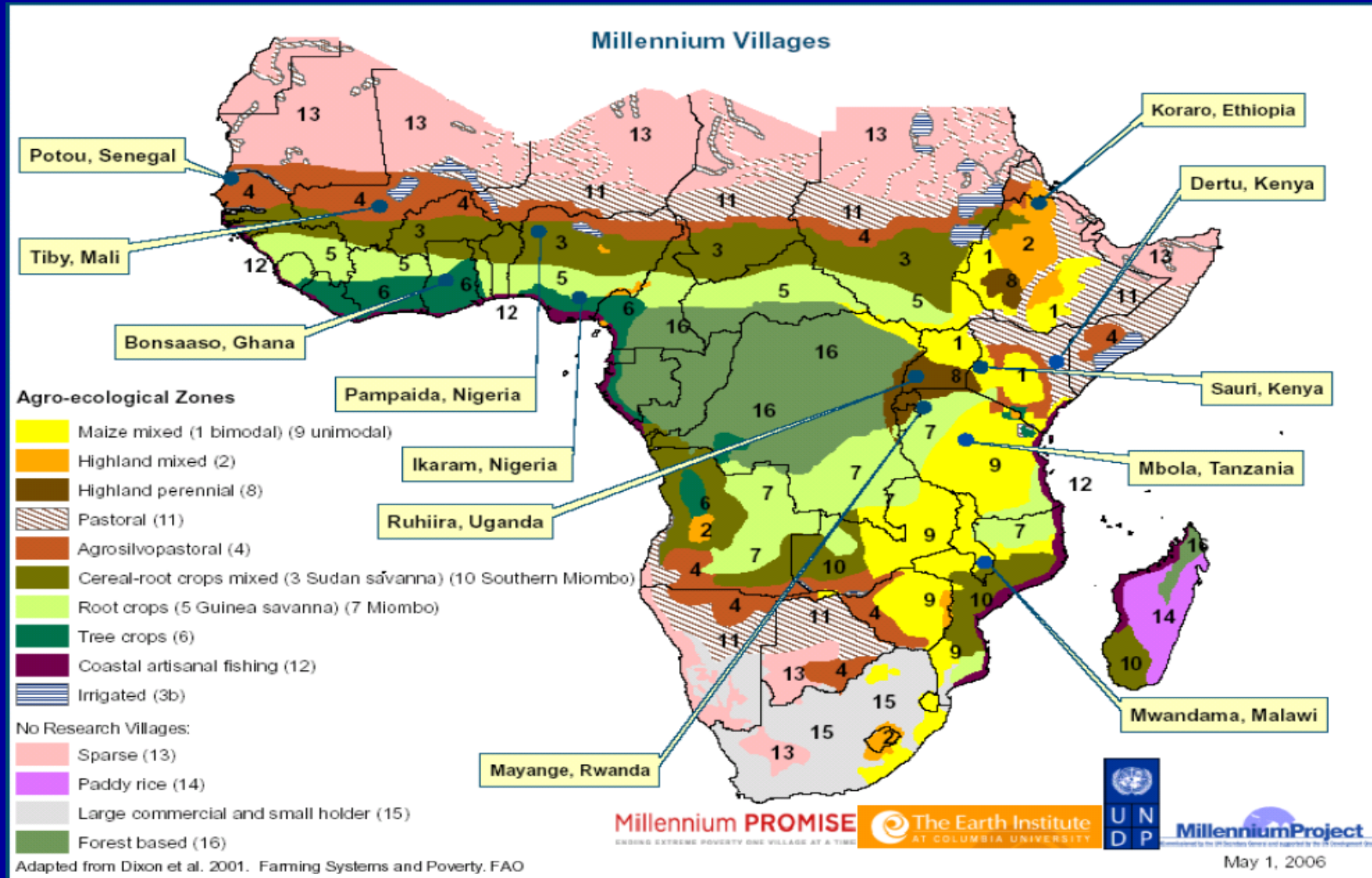
F. Youth – It is Never too Early



Emerging Markets

D. Africa's Ecological Zones & Initial 12 MV Sites

UN & Earth Institute, NY



SHE - Global Demonstration Projects

A. Children (3-6yrs) – Sesame Street

B. Adults Cultural Groups – GHP

C. Adults Regulations & Law – NY

D. Millenium Project – Infrastructure

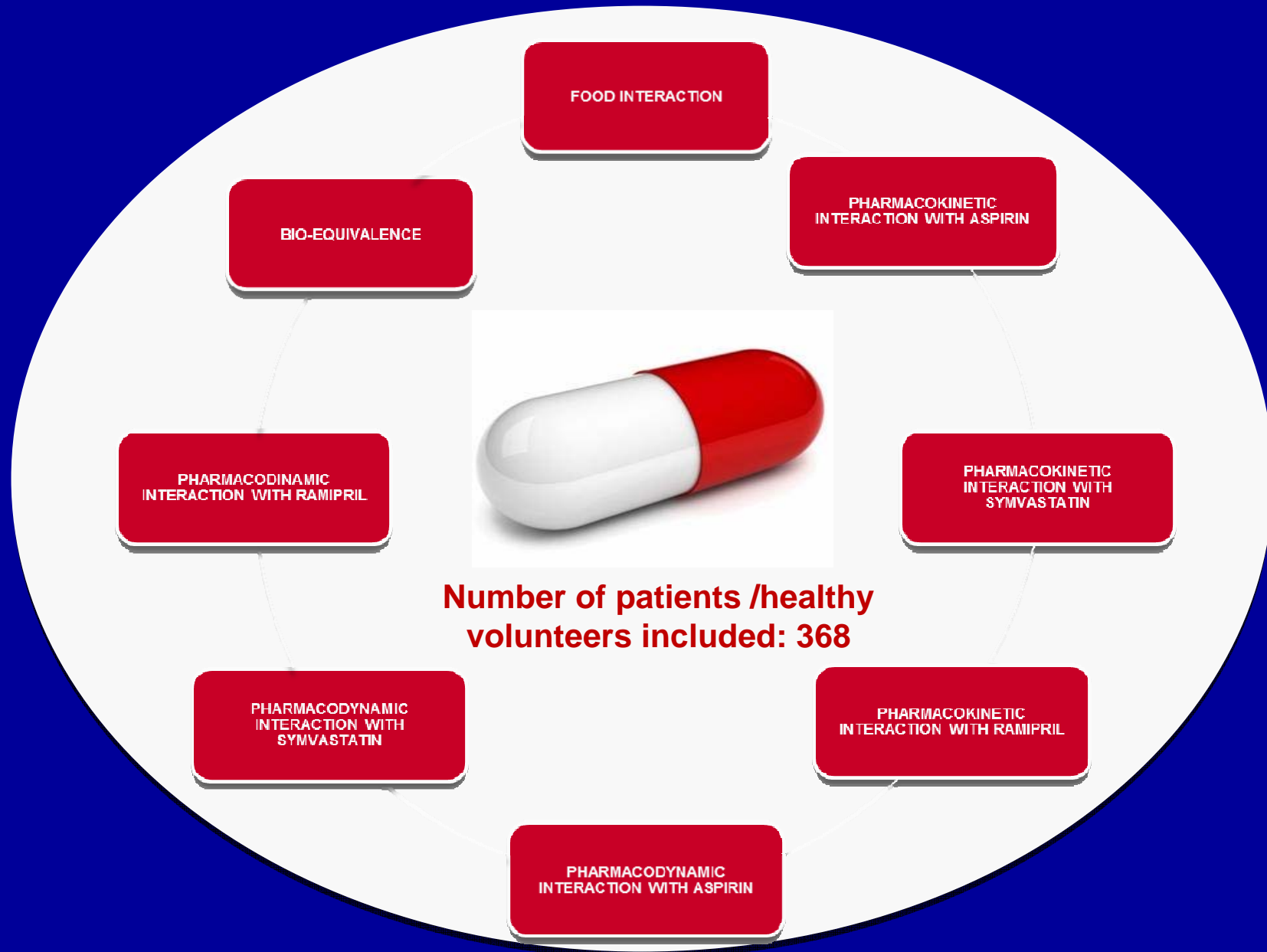
E. Polypill – Adherence & Economy

F. Youth – It is Never too Early



Sustainability

E. Polypill CNIC-Ferrer: Adherence - Economics



SHE - Global Demonstration Projects

A. Children (3-8yrs) – Sesame Street

B. Adults Cultural Groups – GHP

C. Adults Regulations & Law – NY

D. Millenium Project – Infrastructure

E. Polypill – Adherence & Economy

F. Youth – It is Never too Early



Everyday People

F - Creativity - Responsibility - Youth –(CRY)

SPANISH YOUTH 2010

*Survey by Foundation SM
3513 young Ages 15-24 y*

HEALTH IN SPAIN 2010

*European Survey (EES09)
22188 over age 16 y*

ALCOHOL & DRUGS IN SPAIN 2010

*House Survey (EDADES)
Large population over Age 16 y*

INNOVATION AND BUSINESS 2010

*Survey by McKinsey's
50 Business People*

F - Creativity - Responsibility - Youth – (“CRY”)

**3. LOW IN
EDUCATION
4.5 % PIB**

**1. LOW IN
CONFIDENCE
65%**

**SPANISH
YOUTH
2011**

**2. LOW IN
FUTURE
Pesimistic 62%**

F1. The Future of Well Being Promotion of Mental Health

- *Time to Reflect* *Calmer* *(Stress)*
 - *Talent to Discover* *Fulfilled* *(Neurosis)*
 - *Transmit Positive* *Happiness* *(Hostage)*
 - *Tutoring the Young* *Responsible* *(Future)*
-

F - Creativity - Responsibility - Youth – (“CRY”)

**3. LOW IN
EDUCATION
4.5 % PIB**

**1. LOW IN
CONFIDENCE
65%**

**SPANISH
YOUTH
2011**

**2. LOW IN
FUTURE
Pesimistic 62%**

F2. Lifetime Happiness

- 1. “Happiness comes from our own attitude. If your mental attitude is correct, even in a hostile atmosphere, you feel happy.” (Dalai Lama)*
- 2. “Success is getting what you want. Happiness is accepting what you get.” (Dale Carnegie)*
- 3. “Happiness is the key to success. If you love what you are doing, you will be successful”. (Albert Schweitzer)*
- 4. “Happiness is when what you think, you say, and you do are in harmony”. (M. Gandhi)*
- 5. “Happiness for a lifetime – help someone else”*

F - Creativity - Responsibility - Youth – (“CRY”)

**3. LOW IN
EDUCATION
4.5 % PIB**

**1. LOW IN
CONFIDENCE
65%**

**SPANISH
YOUTH
2011**

**2. LOW IN
FUTURE
Pesimistic 62%**

F3. Pro CNIC Board of Trustee Funding – 38%

Fundación **pro**cnic



Intramural Education (12)
Extramural Grants (2- 4 x year)
Equipment (Imaging etc)

SCIENCE July 8, 2005 & Sept 1, 2006

THE LANCET Aug 19, 2006



- 1.- César Alierta
Telefónica
- 2.- Ignacio Polanco
Grupo Prisa
- 3.- Emilio Botín
Fundación Marcelino Botín
- 4.- José Manuel Entrecanales
Acciona, Pro CNIC F. Pres.
- 5.- Valentín Fuster
CNIC Scientific President
- 6.- Isidro Fainé
La Caixa
- 7.- Francisco González
BBVA
- 8.- Luis Suárez de Lezo
Repsol YPF
- 9.- Ignacio Garralda
F. I. Médica Mutua Madrileña
- 10.- Carlos Martínez Echevarría
Fundación Ramón Areces
- 11.- Salvador Gabarró
Gas Natural
- 12.- Luis de Carlos
Uría Menéndez
- 13.- Rodolfo Martín Villa
Fundación Endesa
- 14.- Miquel Roca
Fundación Abertis
- 15.- Pablo Isla
Inditex

F3. CNIC (Spain) - Discovering / Tutoring



2007, 2008, 2009, 2010

A Transition From Disease to Health – 2010-2020

Cardiovascular & Mental



CAD – *Coron. Art. Dis.-Myocard.*

HRP - *High Risk Plaque*

IOM – *Institute of Medicine*

CVD – *Cerebro Vascular Disease*

DBD – *Degenerative Brain Disease*

SHE – *Science Health & Education*

Our Physical & Mental Health Are Powered By Three Concepts



Youth

Motivation

Mid - Life

Life Style

Aging

Heart-Mind