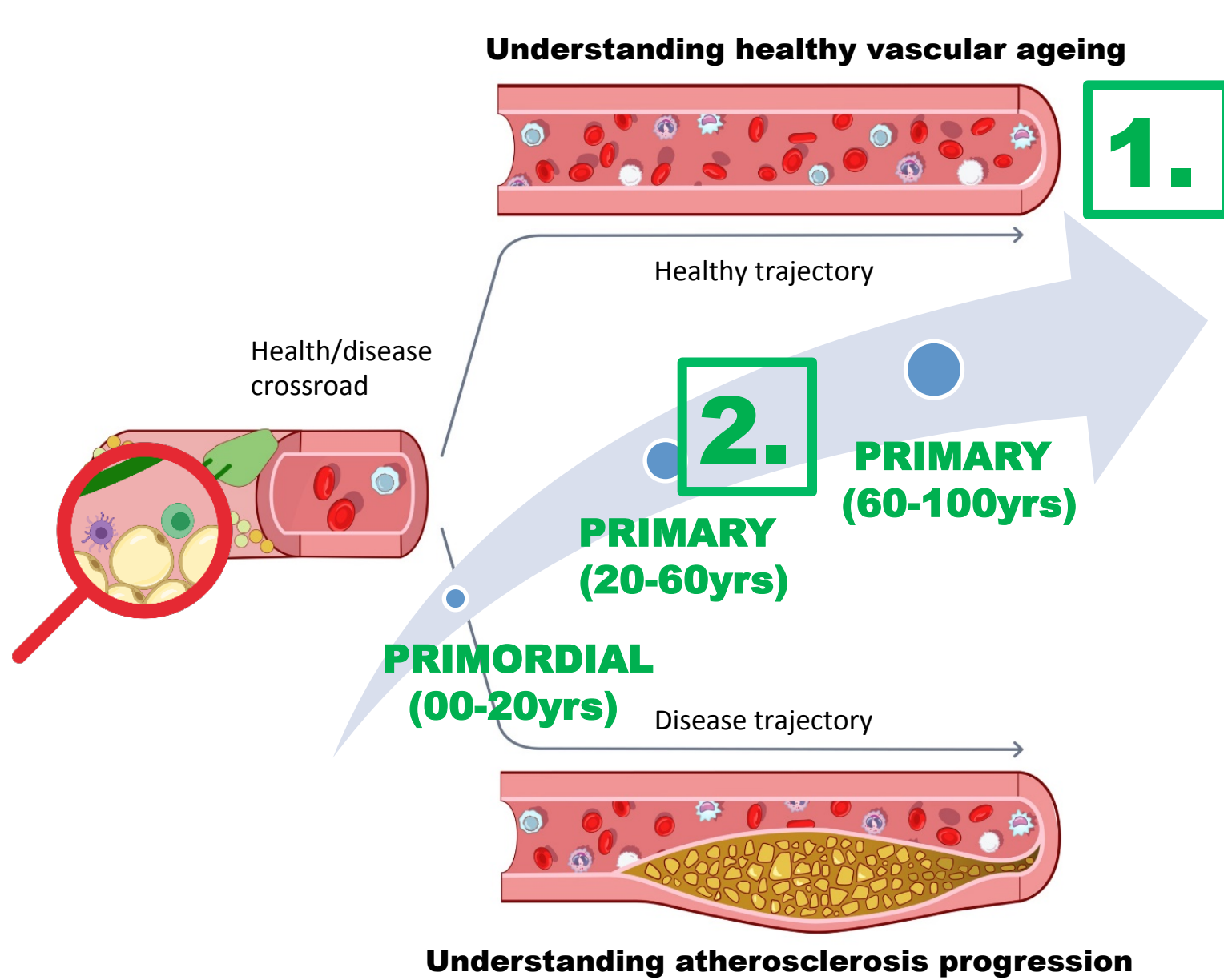


# ***Cardiovascular Health 2023 - 2030***

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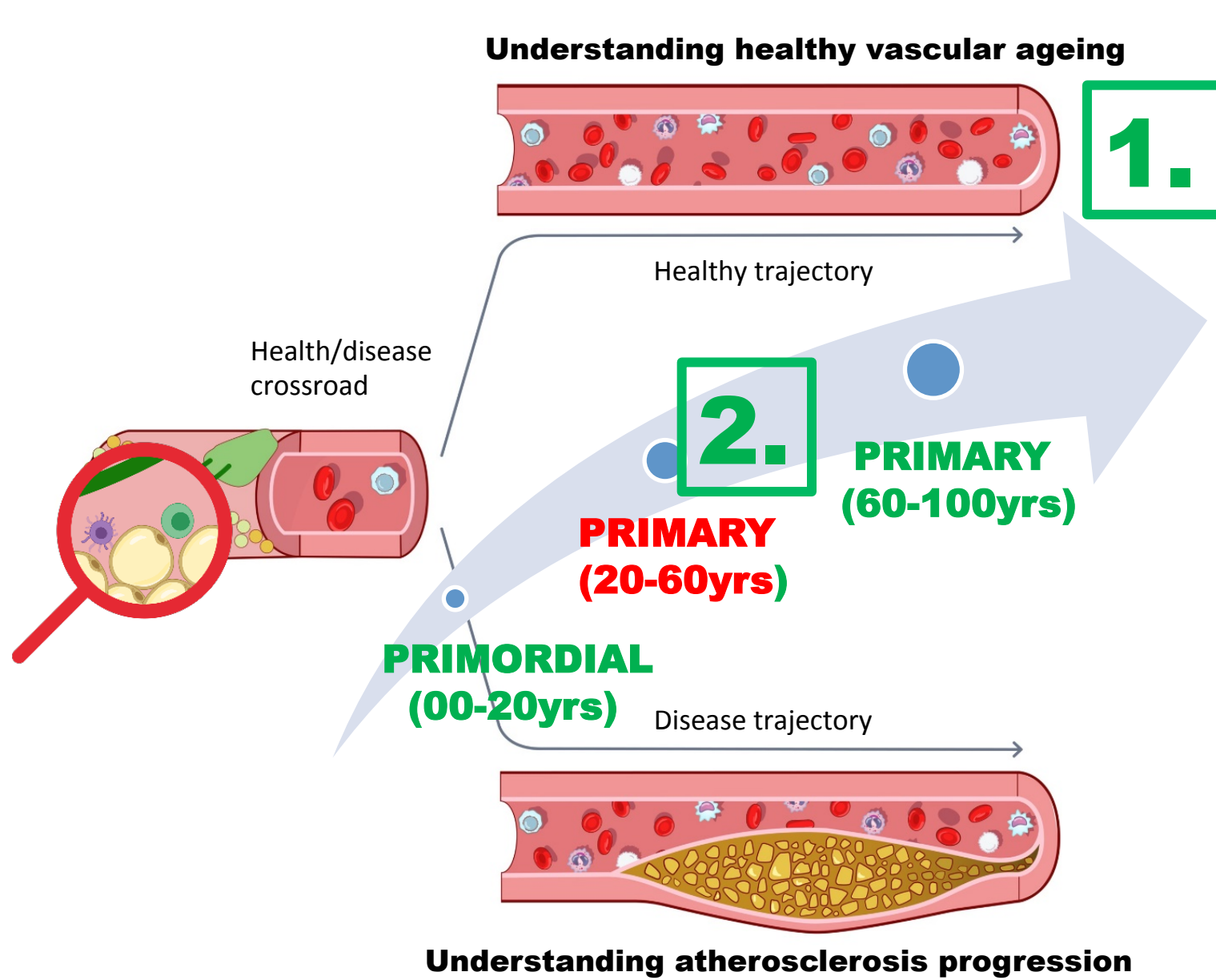
***Throughout Lifespan - 3 Ages  
9 Findings - 3 Trials***

# ***Innovation in CV Health Age Dependent – New Technology***



***V Fuster, F Swirski, ZA Fayad, Science/AAAS, 2021; P 12***  
***M Merad et al. Science/AAAS, 2021; P 21***

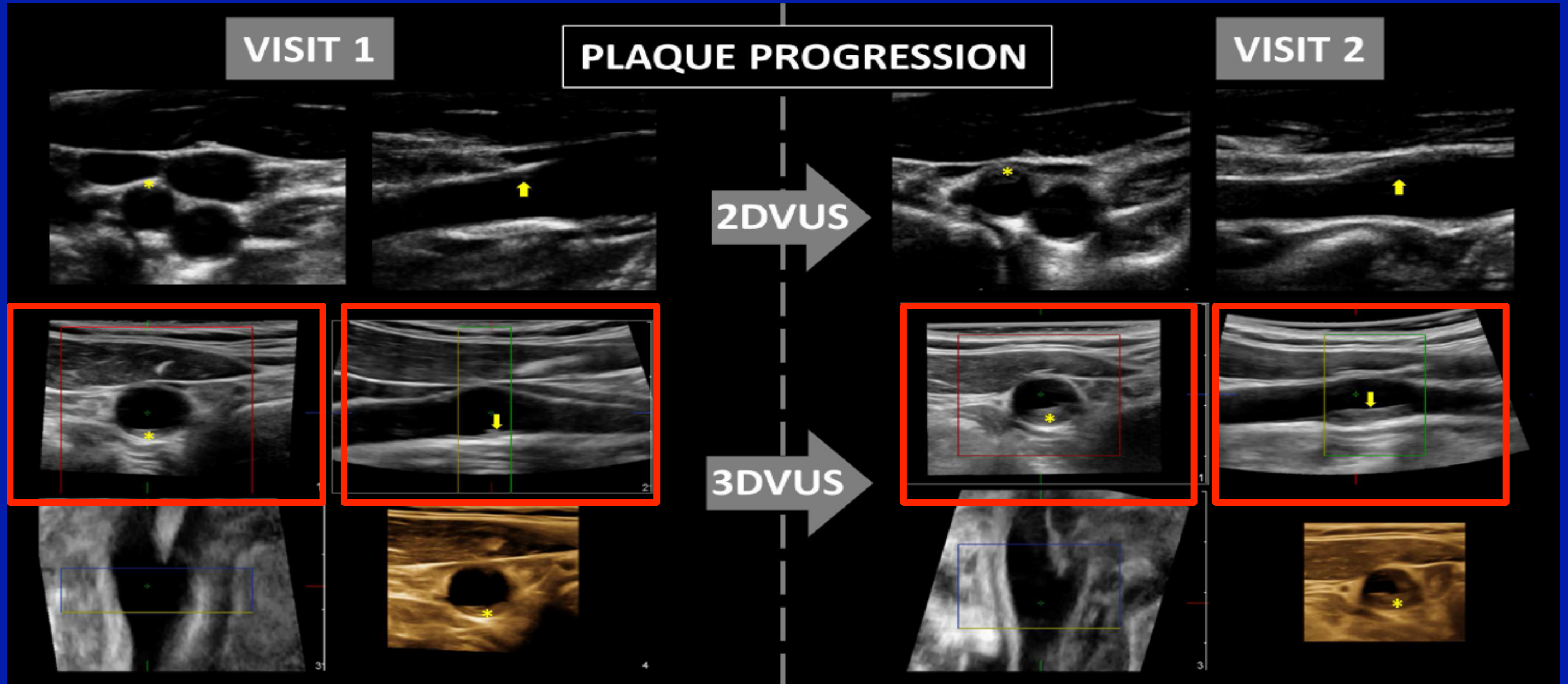
# ***Innovation in CV Health*** ***Age Dependent – New Technology***



***V Fuster, F Swirski, ZA Fayad, Science/AAAS, 2021; P 12***  
***M Merad et al. Science/AAAS, 2021; P 21***

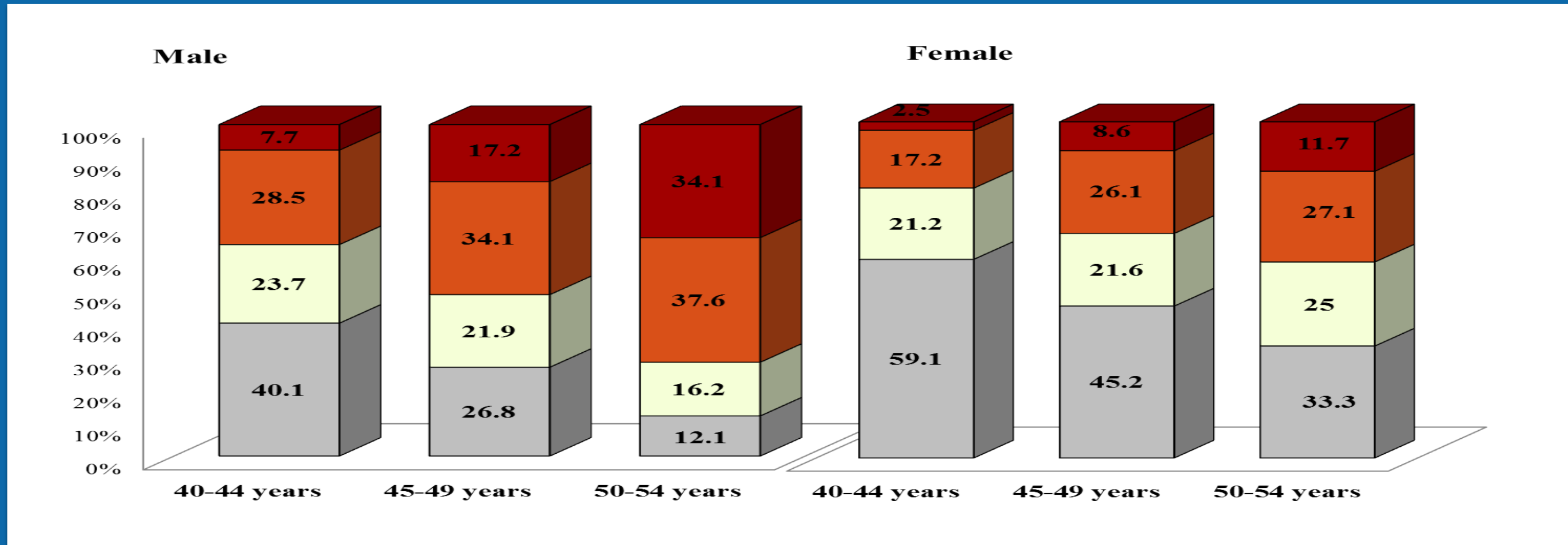
# 1) Subclinical Atherosclerosis – 2D/3D US & CT

## PESA - N=4184 – Age 40-55 yrs

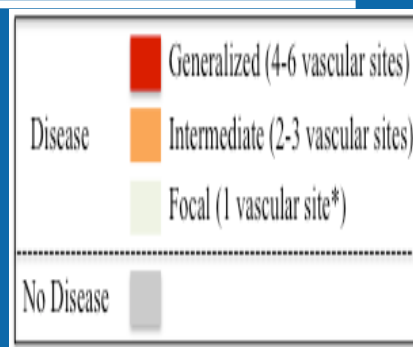


# Burden Subclinical Atherosclerosis – 2D/3D US & CT

## N=4184 – Age 40-55 yrs

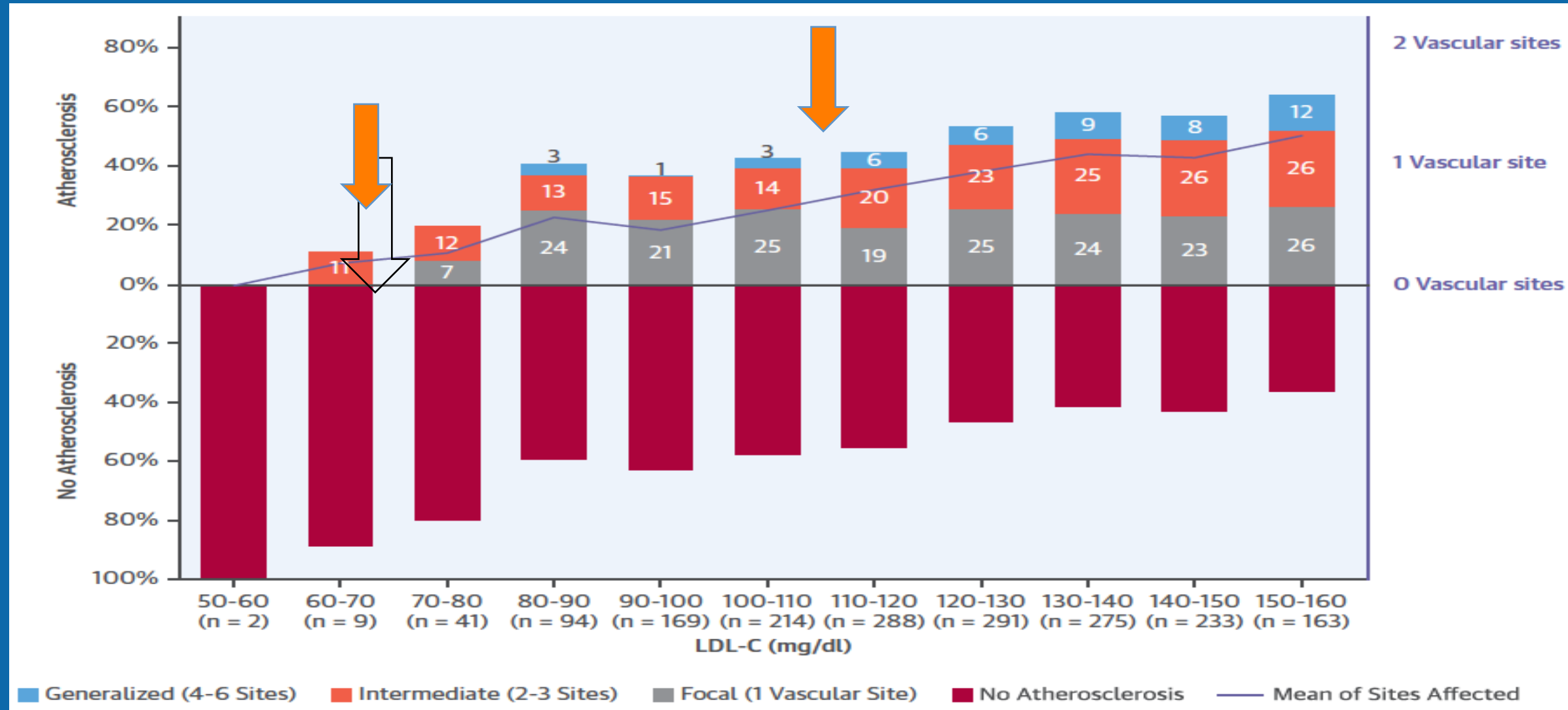


**PESA, Circulation 2015;131:2104 – High Incidence Early in life**  
**J Am Coll Cardiol 2020; 75: 1617 – High Progression Rate, 33%**  
**Submitted 2023 – Progression Associated to Risk Fr Profile**



## 2). LDL-Cholesterol - LEVELS

### Subclinical Atherosclerosis



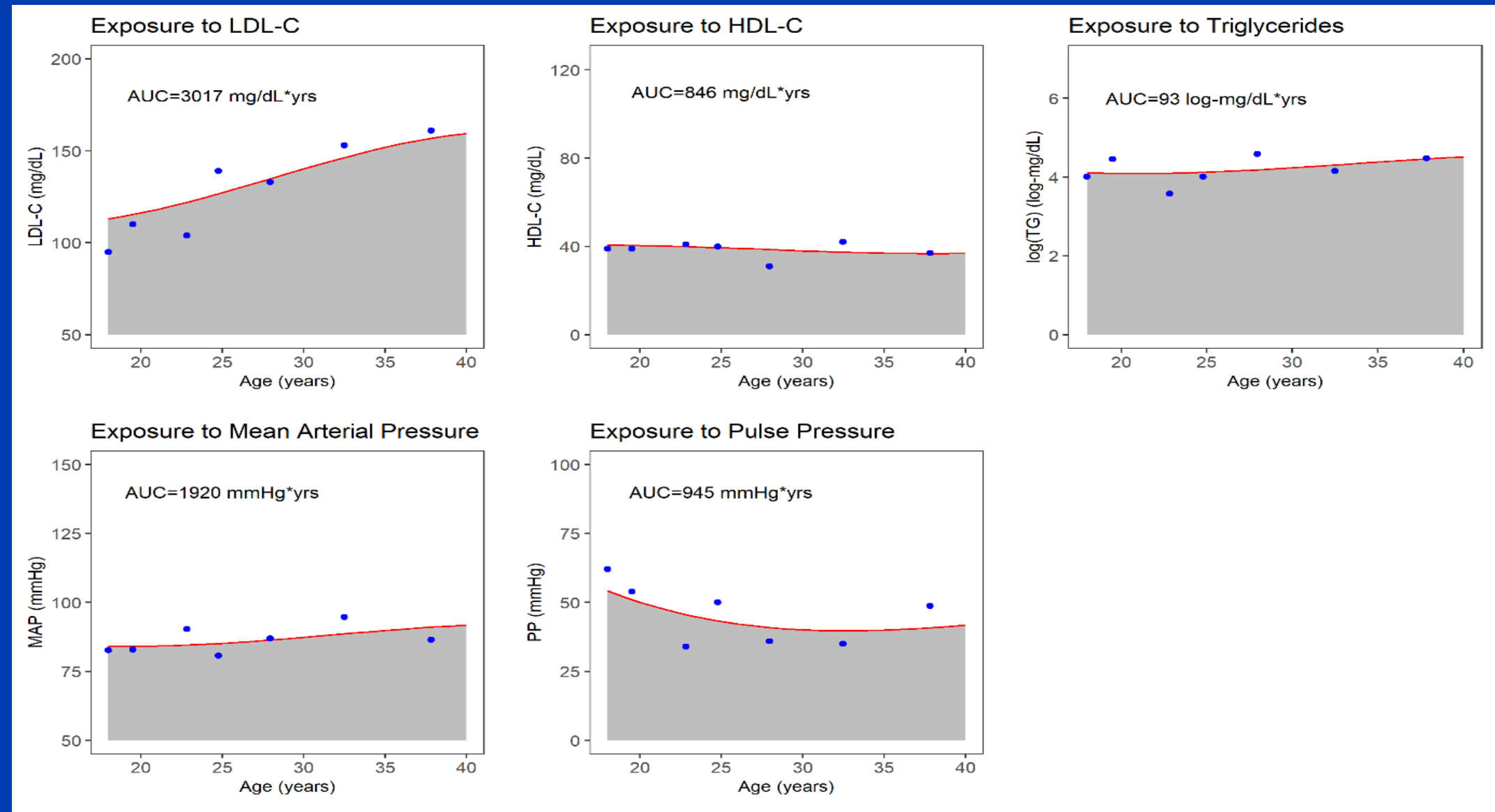
L Fernández-Friera, B Ibanez, V Fuster et. al. *J Am Coll Cardiol* 2017;70:2979

X Rossello, B Ibanez, V Fuster et. al. *J Am Coll Cardiol* 2021; 77: 2777 – HgbA1c

S Raposeiras-Roubin, B Ibanez, V Fuster et. al. *J Am Coll Cardiol* 2021;77:30 - TGC

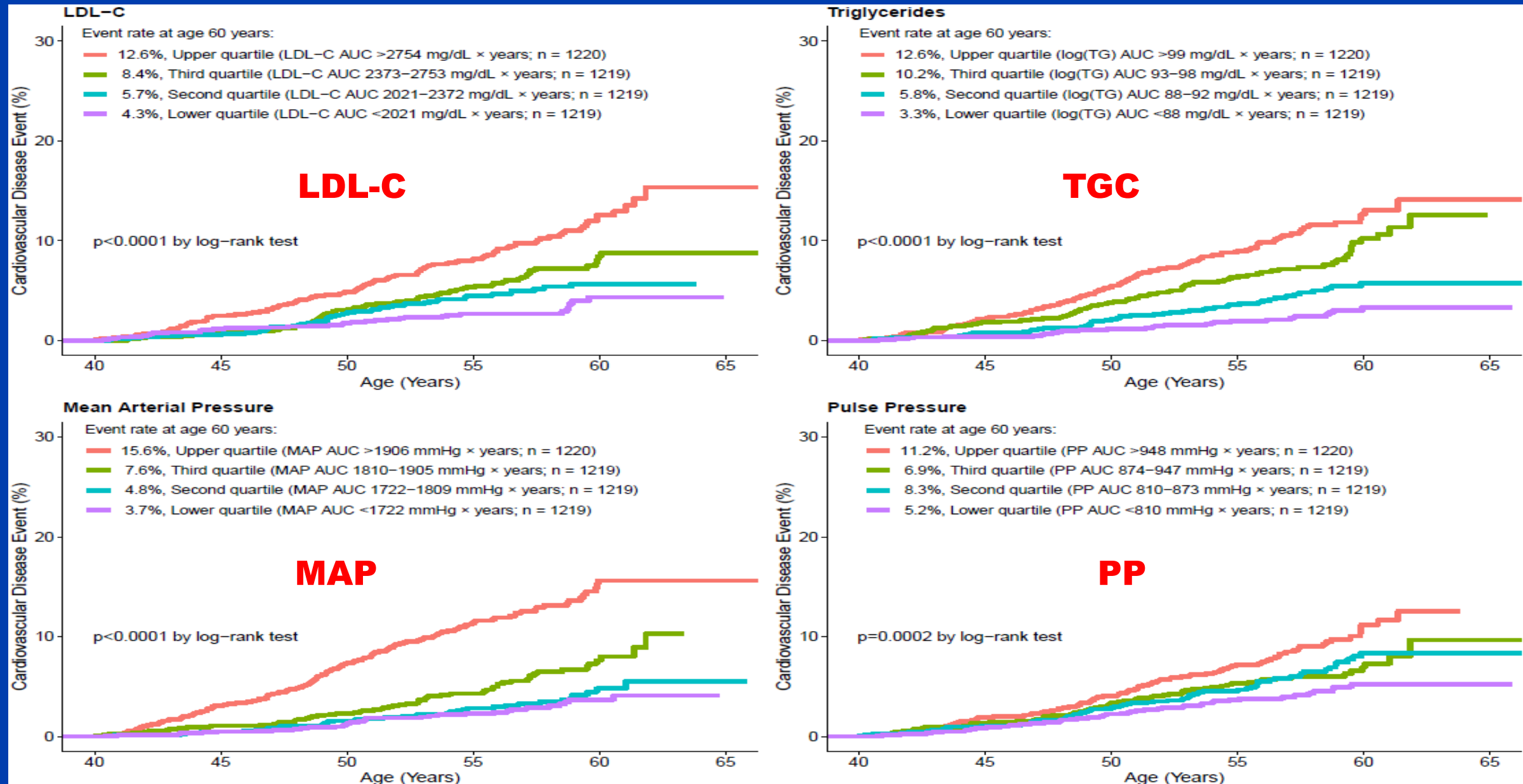
# 3). **CARDIA - Cumulative RF Exposure Age 20-40**

## **Event Rates Later In Life**



*MJ Domanski, V Fuster et. al. J Am Coll Cardiol 2020;76:1507*  
*MJ Domanski, JP Reis, DM Lloyd-Jones, V Fuster, et. al. 2023 (In Press)*

# CARDIA Study – 20-40 Yrs - Event Rates Later In Life Course & Cumulative Exposure to Multiple Risk Factors



MJ Domanski, JP Reis, DM Lloyd-Jones, V Fuster, et. al. 2023 (In Press)



# 1). *Primary Preventive Coronary Artery Disease Trial (PRE-CAD)*

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- 20 - 39 years
- LDL-C >70 mg/dl

**Baseline assessment atherosclerotic plaque burden (PESA score)**

**Standard of care**

**Active treatment**

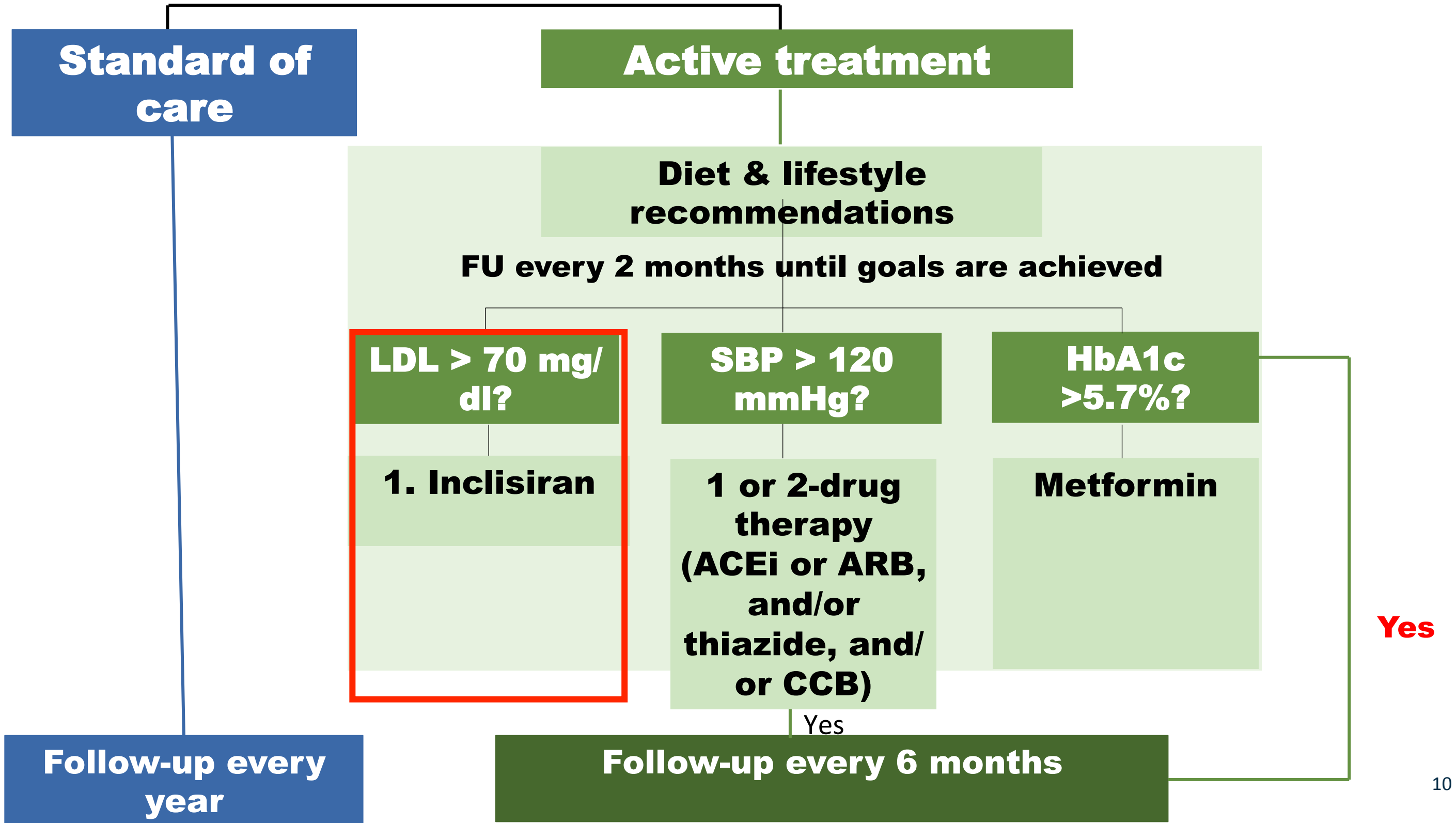
**LDL-C < 70 mg/dl  
SBP <120  
HbA1c <5.7**

**5-year post-randomization FU assessment (PESA score)**

**Primary Endpoint:** change in atherosclerotic plaque burden from baseline (PESA score)

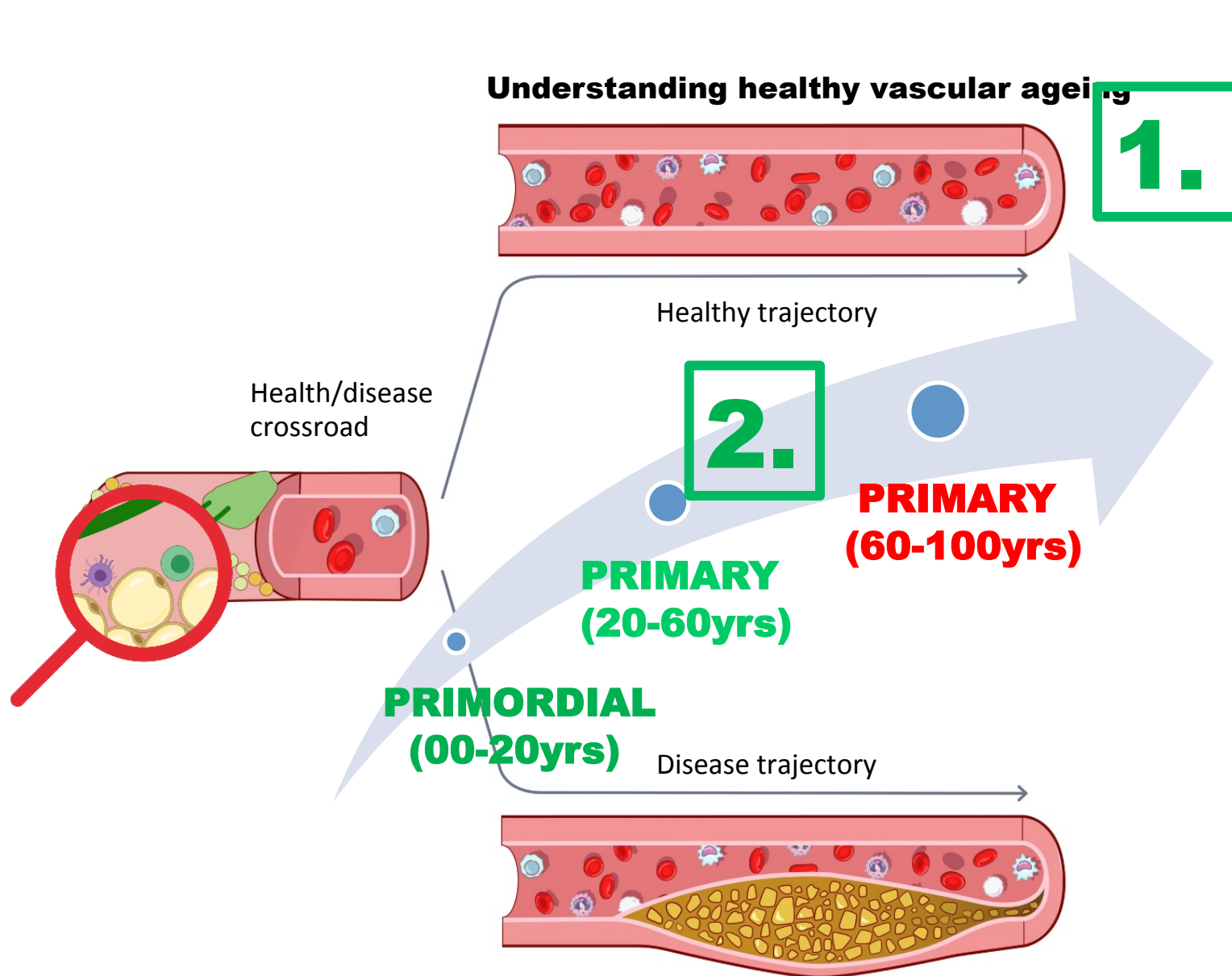
**Secondary Endpoints:** incident CV disease (MI, stroke,

# Randomization 1:1



# Innovation in CV Health

## Age Dependent – New Technology



Understanding atherosclerosis progression

**V Fuster, F Swirski, ZA Fayad, Science/AAAS, 2021; P 12**

**M Merad et al. Science/AAAS, 2021; P 21**



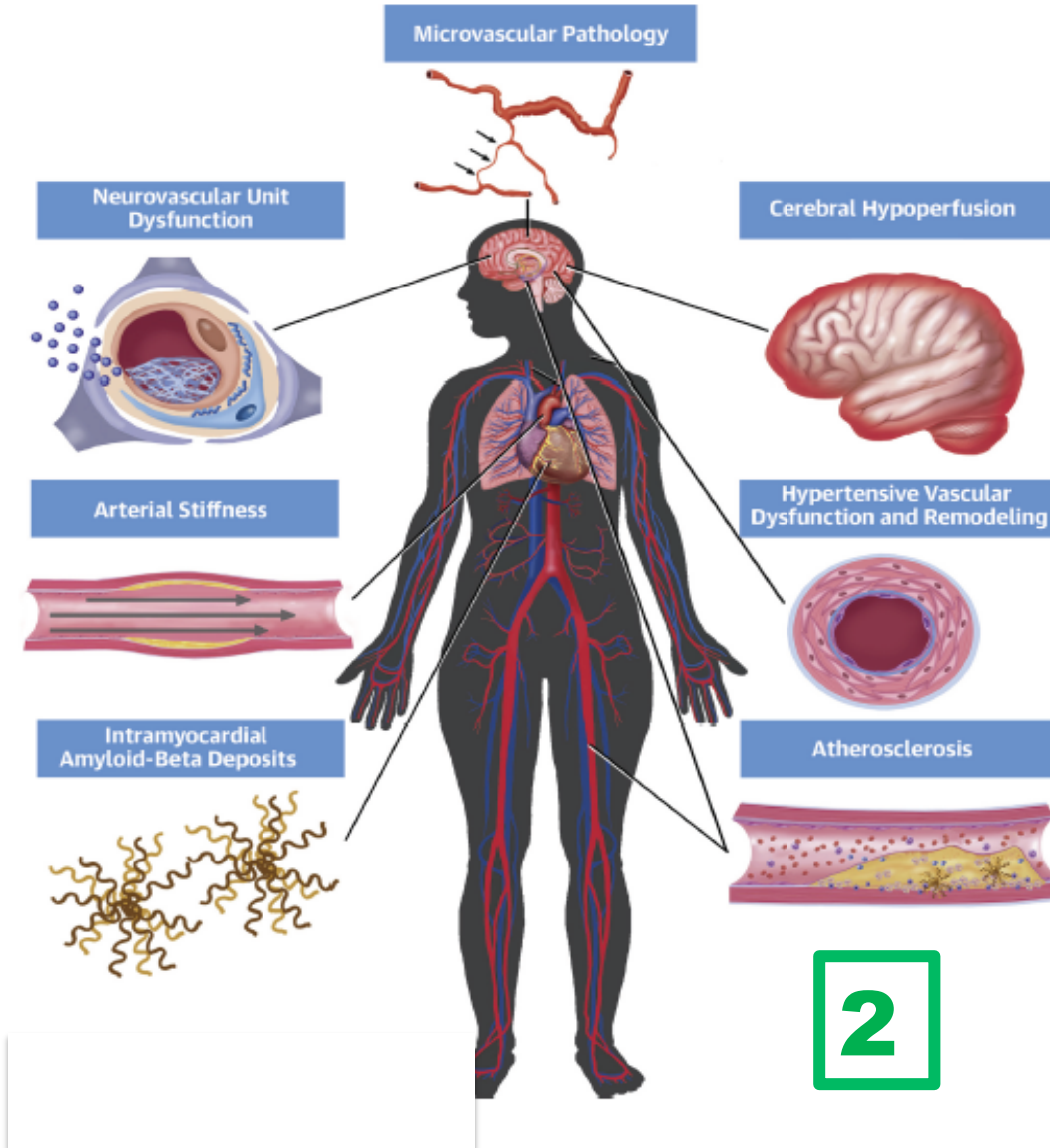
Dr. Alois Alzheimer

1

**Auguste D. autopsy (1<sup>st</sup> patient with AD)**

*During the morning exitus letalis; cause of death: septicaemia due to decubitus; anatomical diagnosis: moderate hydrocephalus (external internal); cerebral atrophy; arteriosclerosis of the small cerebral blood vessels; ? ; pneumonia of both inferior lobes; nephritis.*

**CENTRAL ILLUSTRATION Alzheimer's Disease-Associated Vascular Alterations Inside and Outside the Brain**



2

**Cortes-Candell M et al JACC. 2020  
Fuster V et al JACC 2021**

		No Association	Insufficient Evidence	Conflicting Evidence	Established Evidence	Vascular dementia	Post-stroke dementia	Dementia unspecified	Alzheimer's dementia
Non-modifiable risk factors	age								
	sex								
	genetic factors (ApoE)								
Lifestyle factors	education								
	smoking								
	diet								
	homocysteine								
	physical activity								
	obesity, BMI								
	cognitive activity								
Physiological risk factors	mid-life hypertension								
	late-life hypertension								
	hyperglycemia, diabetes								
	lipids, dyslipidemia								
	Inflammation								
	frailty								
	stroke								
Concomitant clinical vascular disease	coronary artery disease								
	atrial fibrillation								
	peripheral arterial disease								
	chronic kidney disease								
	low cardiac output								
	depression								

**Iadecola C et al. JACC. 2019**

3

# **TANSNIP - H2H – 2020 - 2023**

## **Vascular Cognitive Dysfunction**

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**1.**

**LVD -RF  
&  
Microvasc.  
Disease  
Brain**

**2.**

**Microvasc.  
Disease  
Brain  
&  
Metab/Str.**

**3.**

**Brain  
Struct/Met.  
&  
Cognitive  
Dysfunct.**

**Alzheimer's  
Microvasc.  
&  
Thrombotic**

**Tristao-Pereira C, Fuster V, Cortés-Canteli M. Subm. Lancet 2023**



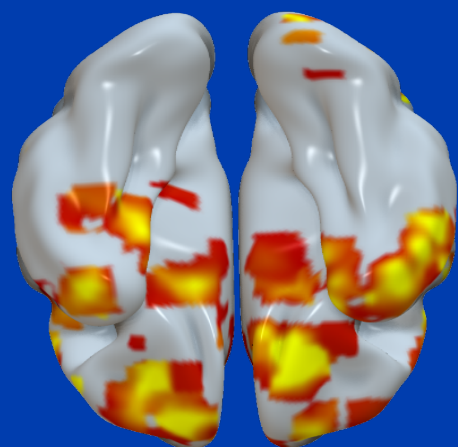
**Statistical  
Parametric  
Mapping  
ASL-MRI (H2H  
Spanish Cohort)  
N=96 (59 women)  
Age= 64-82 years  
(mean=72.4)**

# 1). Cerebral Blood Flow

**Carotid Plaque Volume (Ind  
RF) vs CBF (p<0.05)**

**High carotid plaque volume  
is associated with brain  
hypoperfusion**

**Covariates: age+sex**



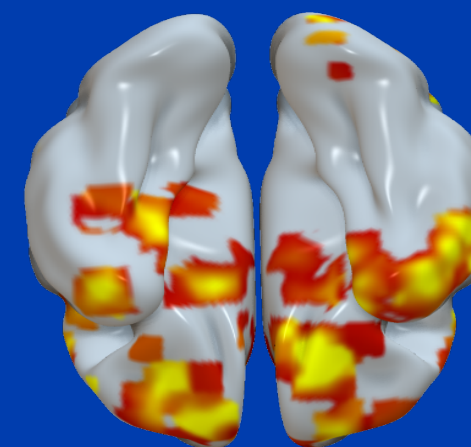
**These regions:  $0.001 < p < 0.004$**

**Precentral gyrus, Inferior Middle/Superior temporal gyrus, Brainstem/Parahippocampal gyrus, Superior parietal lobule, Orbital gyrus, Supramarginal gyrus/Postcentral**

**Carotid Plaque Volume (Ind RF)  
vs CBF (p<0.05)**

**High carotid plaque volume is  
associated with brain  
hypoperfusion**

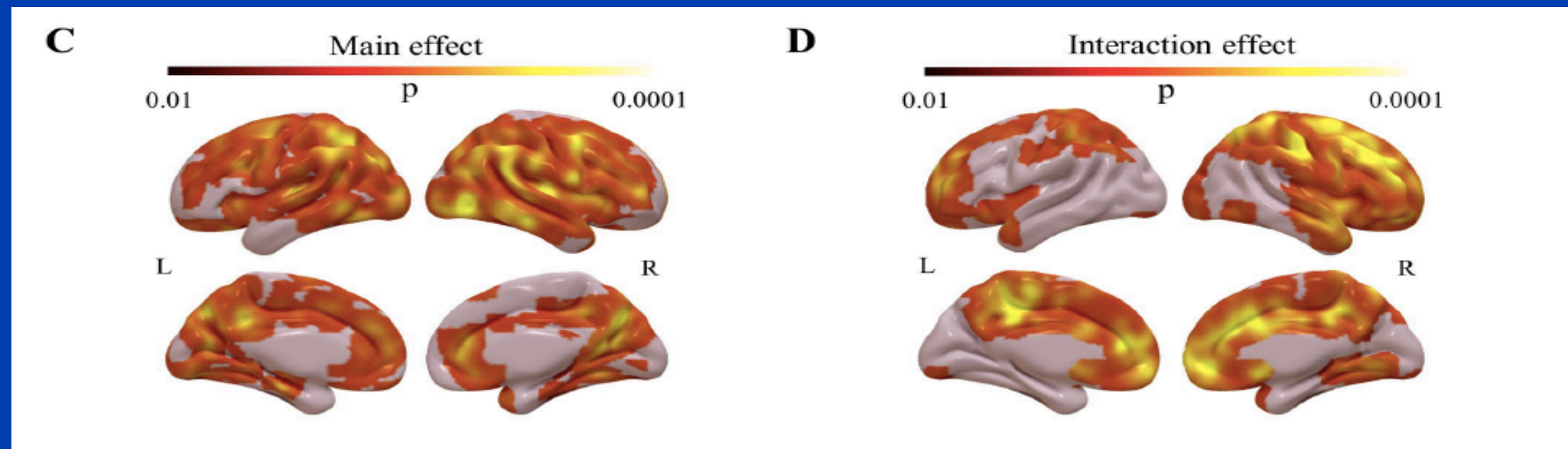
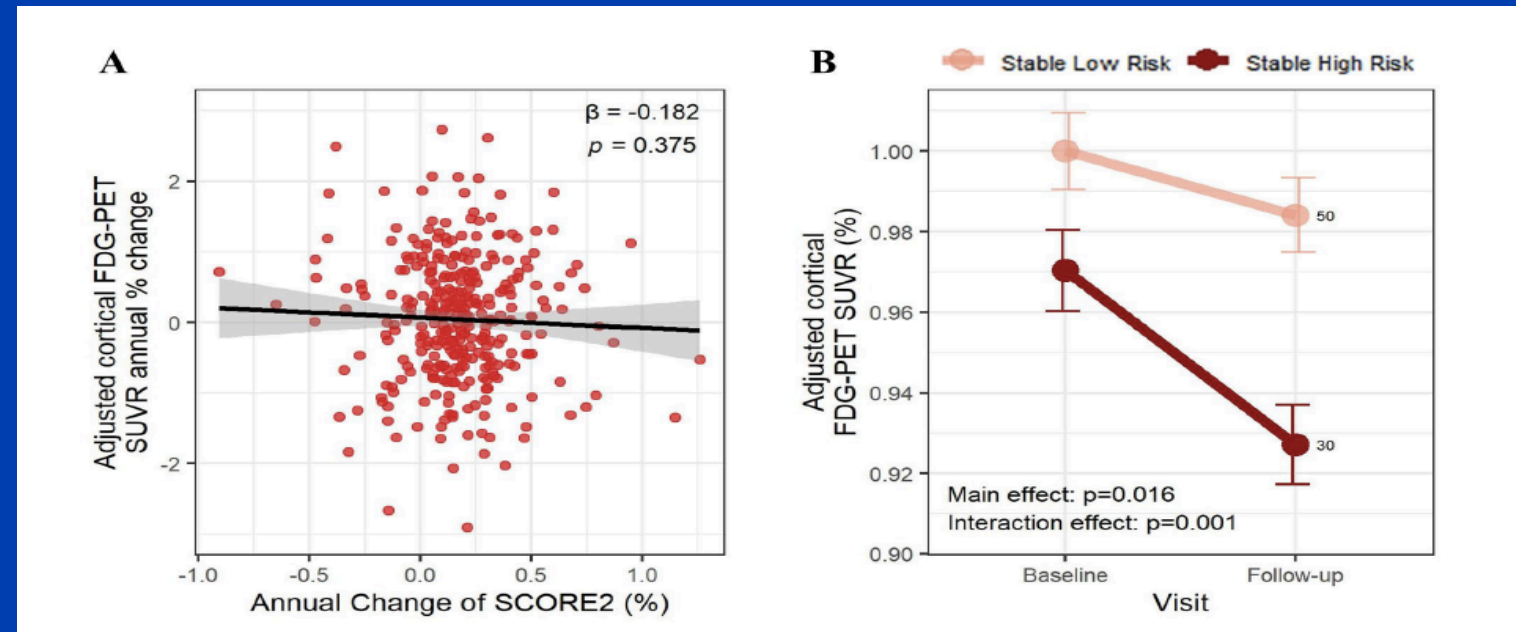
**Covariates: age+sex+MOCA**



**These regions:  $0.001 < p < 0.004$**

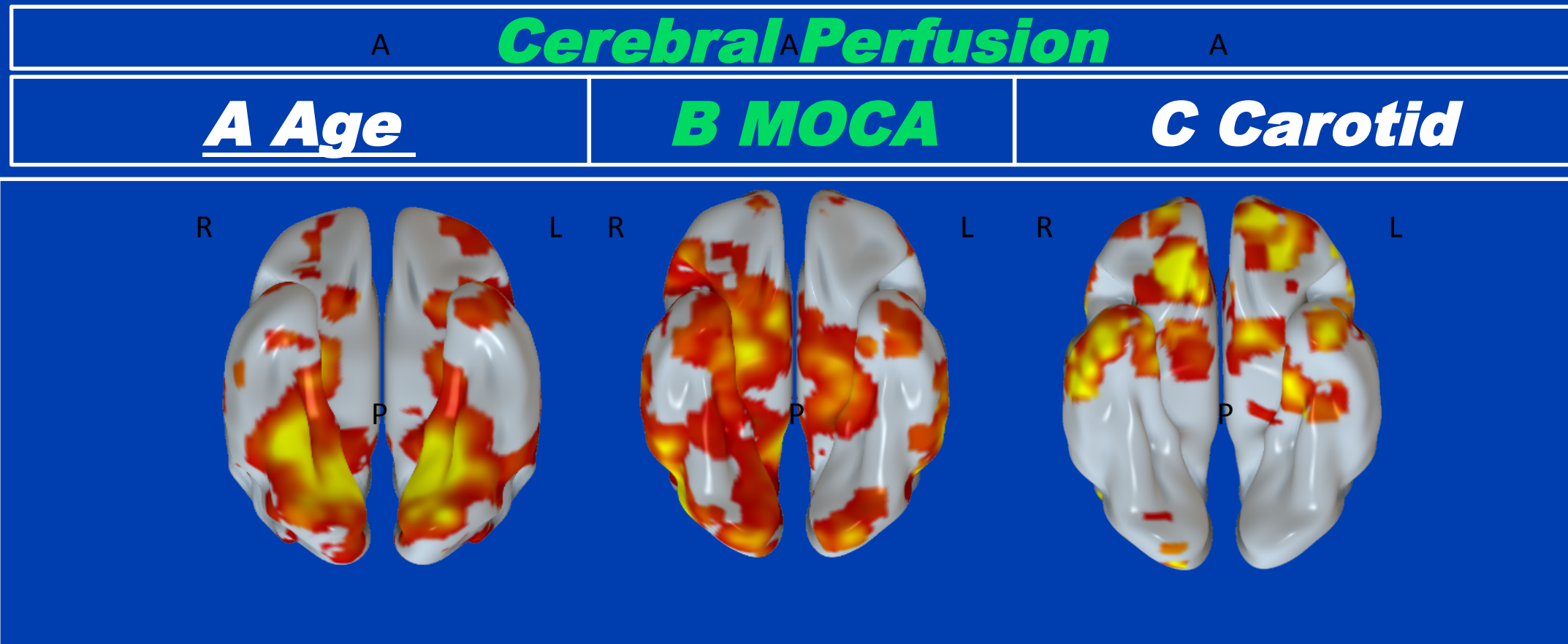
**Precentral gyrus, Inferior Middle/Superior temporal gyrus, Brainstem/Parahippocampal gyrus, Superior parietal lobule, Orbital gyrus, Supramarginal gyrus/Postcentral**

## 2). High SCORE2 Over Time (N=370) Greater Decline In Brain Glucose Uptake



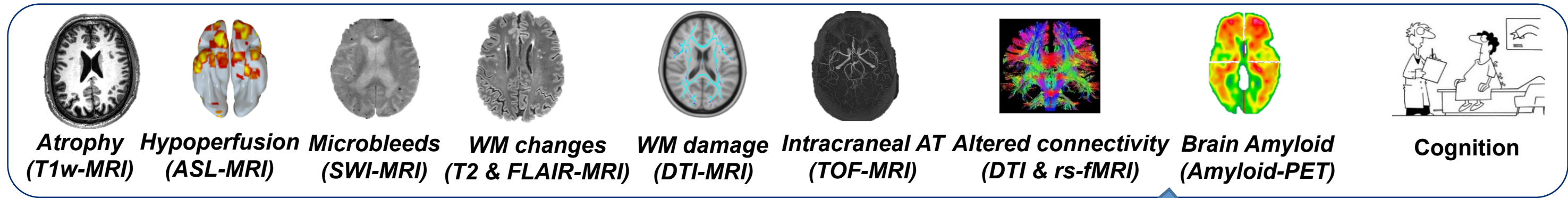
# 3). Cerebral Hypoperfusion Detected By Arterial Spin Labeling – MRI (Ind. Metab)

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# 2) Prospective Heart-Brain-Axis 2022 - 2030 (CNIC / MSH)



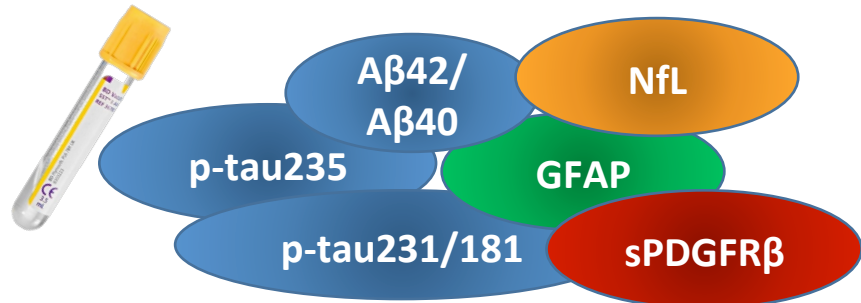
## FINAL GOAL

**Understanding the most possible causal path by which atherosclerosis contributes to Alzheimer's disease in preclinical stages**

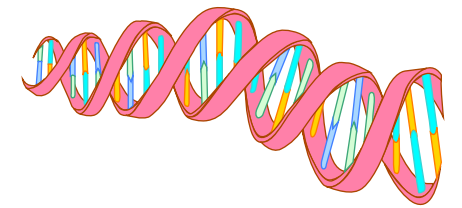
## Causal Inference



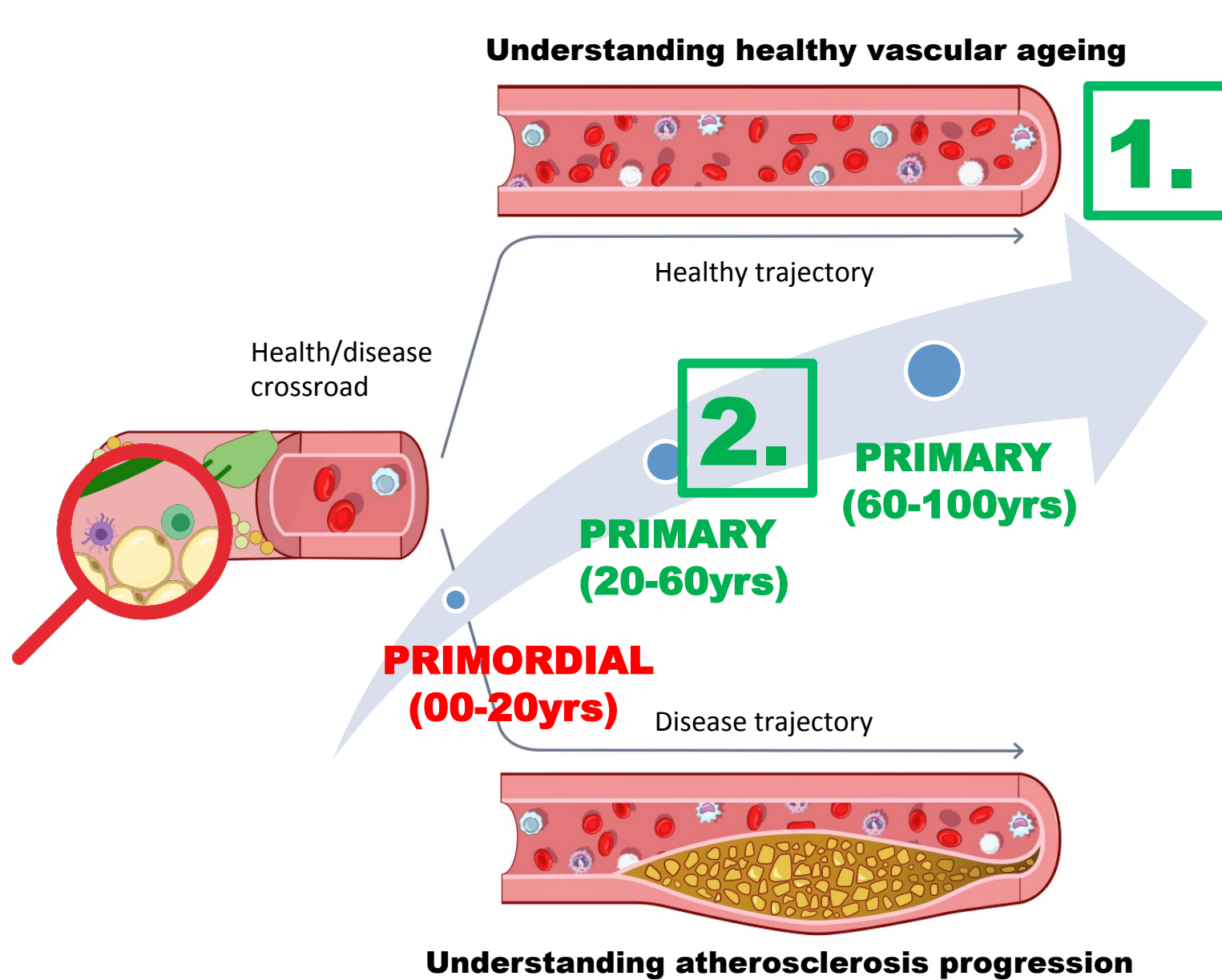
## Blood-based AD biomarkers



## SNPs Arrays

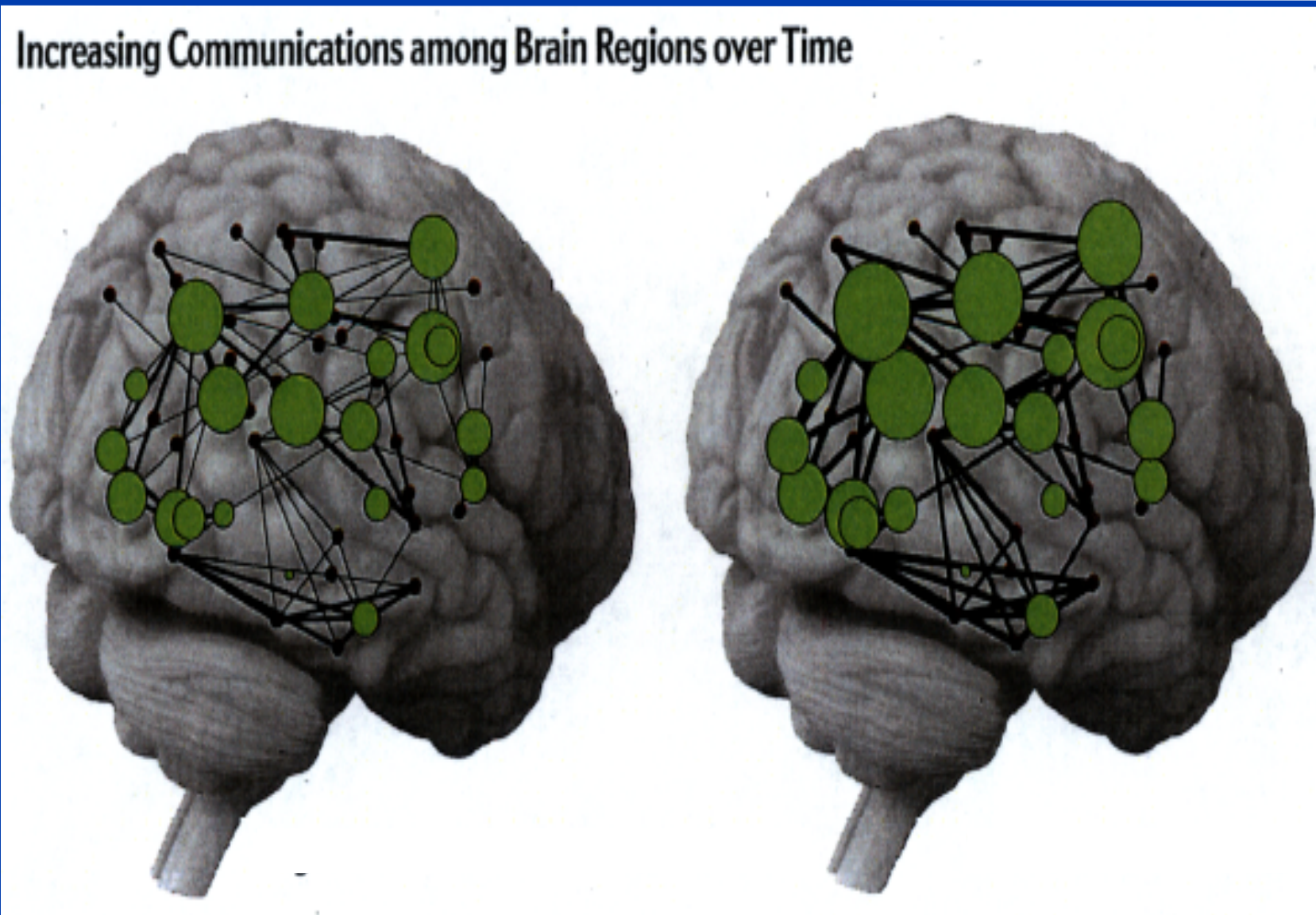


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***V Fuster, F Swirski, ZA Fayad, Science/AAAS, 2021; P 12***  
***M Merad et al. Science/AAAS, 2021; P 21***

# Three Children Programs



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

*G Santos-Beneit, V Fuster et al J.Am.Coll.Card.* **2022**;79:283

# 1). Bogota, Madrid, Harlem NY – 5,000



HOW YOUR BODY  
& HEART WORK



HEALTHY FOOD  
HABITS



PHYSICAL  
ACTIVITY



EMOTIONAL  
HABITS TO AVOID  
ADDICTIONS

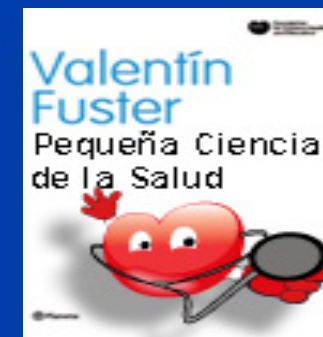
EDUCATIVE GOAL: HEALTHY HABITS FOR CHILDREN BETWEEN 3 & 5 YRS

CHILDREN

3-5



6-8

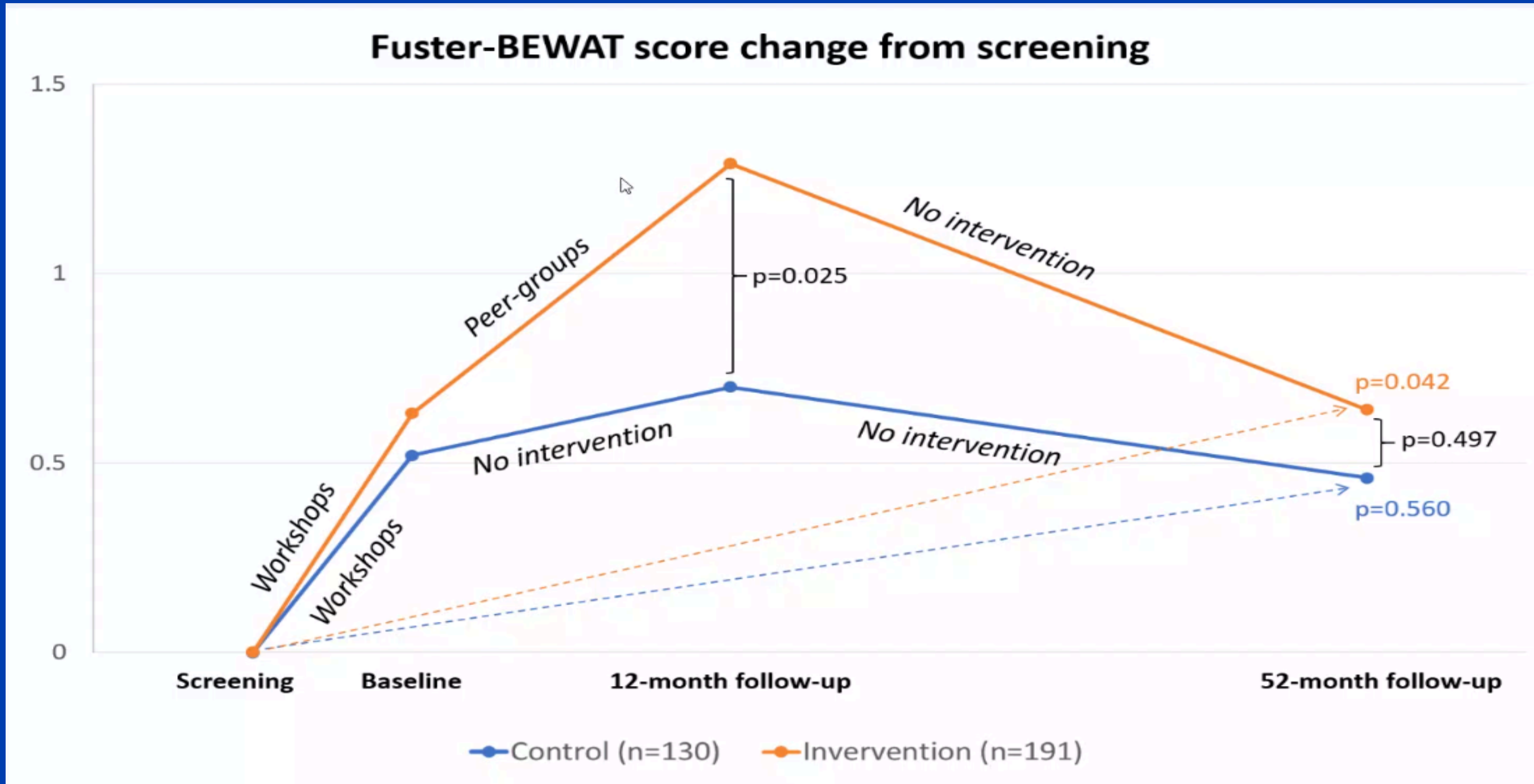


9-14



*The Amer J of Med 2012; 126, 27 - The Amer J of Med 2013;126:1122*  
*J. Amer. Coll. Card. 2015; 66: 1525 - J. Amer. Coll. Card. 2018;72:3310*  
*Am. Heart J. 2019; 210: 9 - Am. Heart J. 2019;215:27 – Nutrients 2019;11:2297 -*  
*J. Am. Coll. Card. 2019; ; 73:211 J. Am. Coll. Card. 2020; 75: 42 – J.Am.Coll.Card. 2022*

# Sustainability & Environment

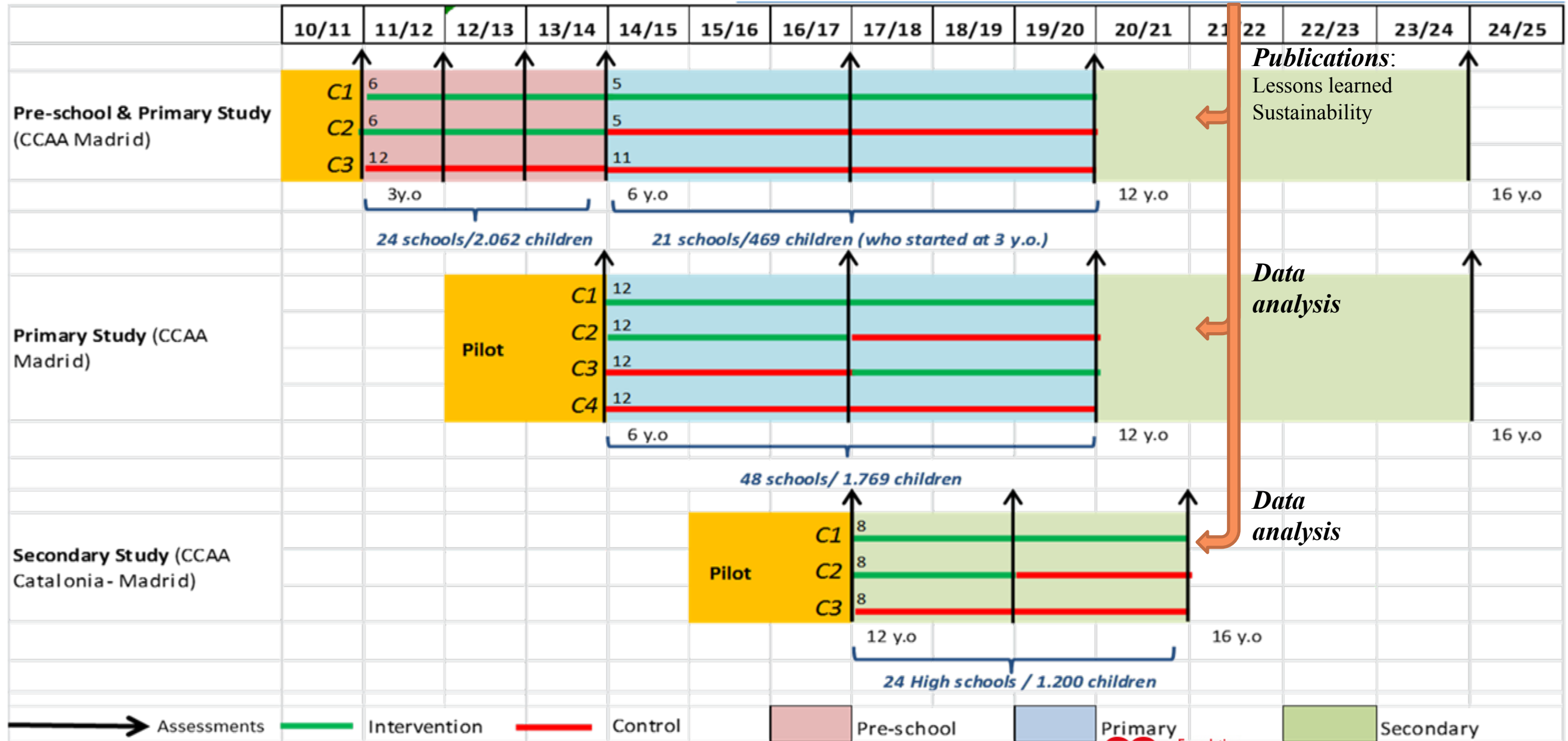


**Fernández-Jiménez R, V. Fuster et al. 2022 (Subm) Children**

**Fernández-Jiménez R, Alvira JM, Fuster V, et al. 2022 (Subm) Group Therapy**

**García-Lunar I, Fuster V, et al. Eur. J. Card. 2022; July 23 - Individual**

# 2) Sustainability - SHE Program - N=50,000



**Publications:**  
Lessons learned  
Sustainability

**Data analysis**

**Data analysis**

Assessments  
 Intervention  
 Control  
 Pre-school  
 Primary  
 Secondary



Foundation for Science, Health and Education  
**SI!** Salud Integral



Fundación "la Caixa"

# **3). Environment: Family University of Health**

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## **4 Objectives / 24 Actions**

**1. Knowledge of How Body and Heart Work**

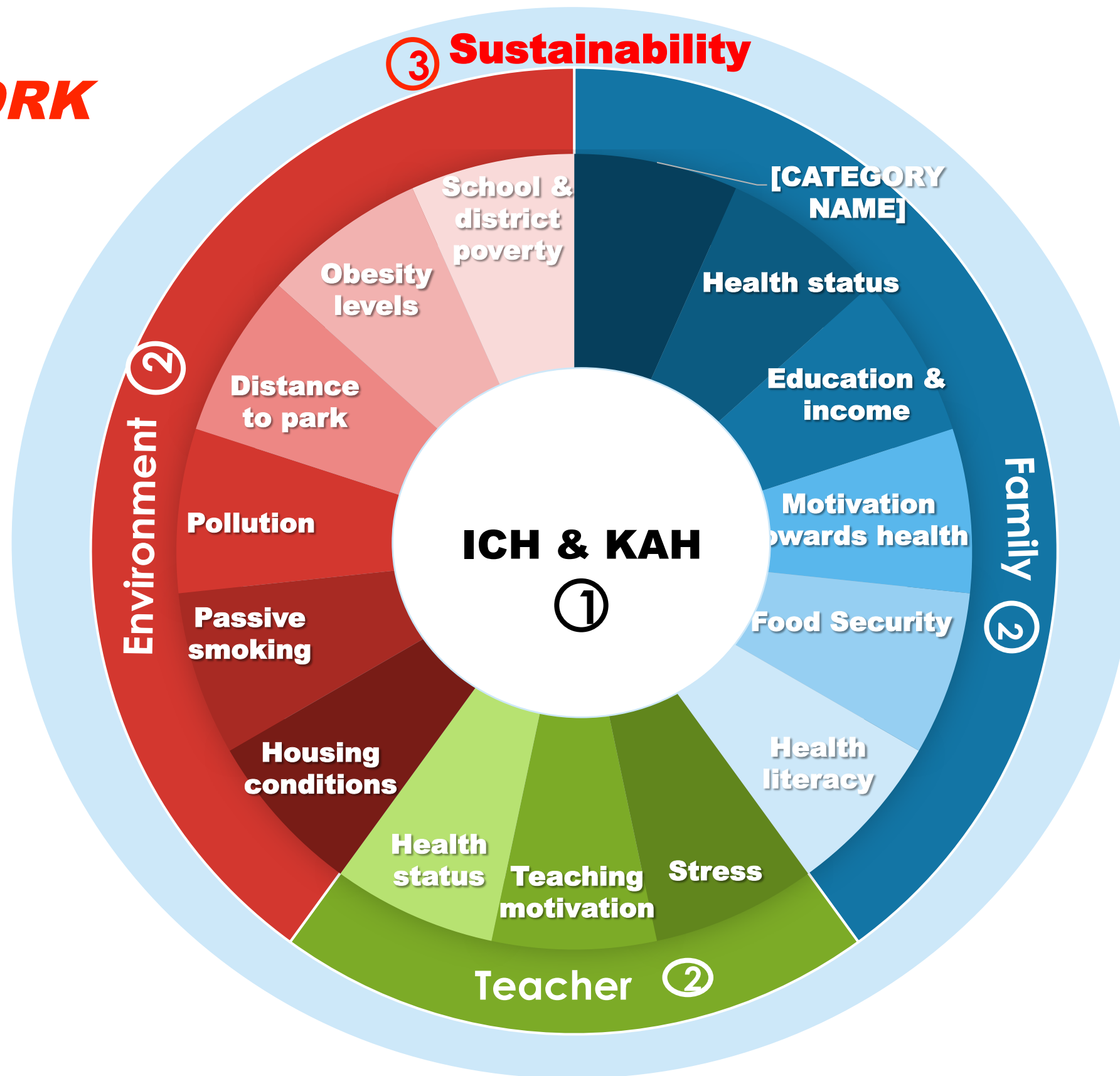
**2. Promote Physical Activity**

**3. Acquisition of Healthy Food Habits**

**4. Encourage better management of emotions**

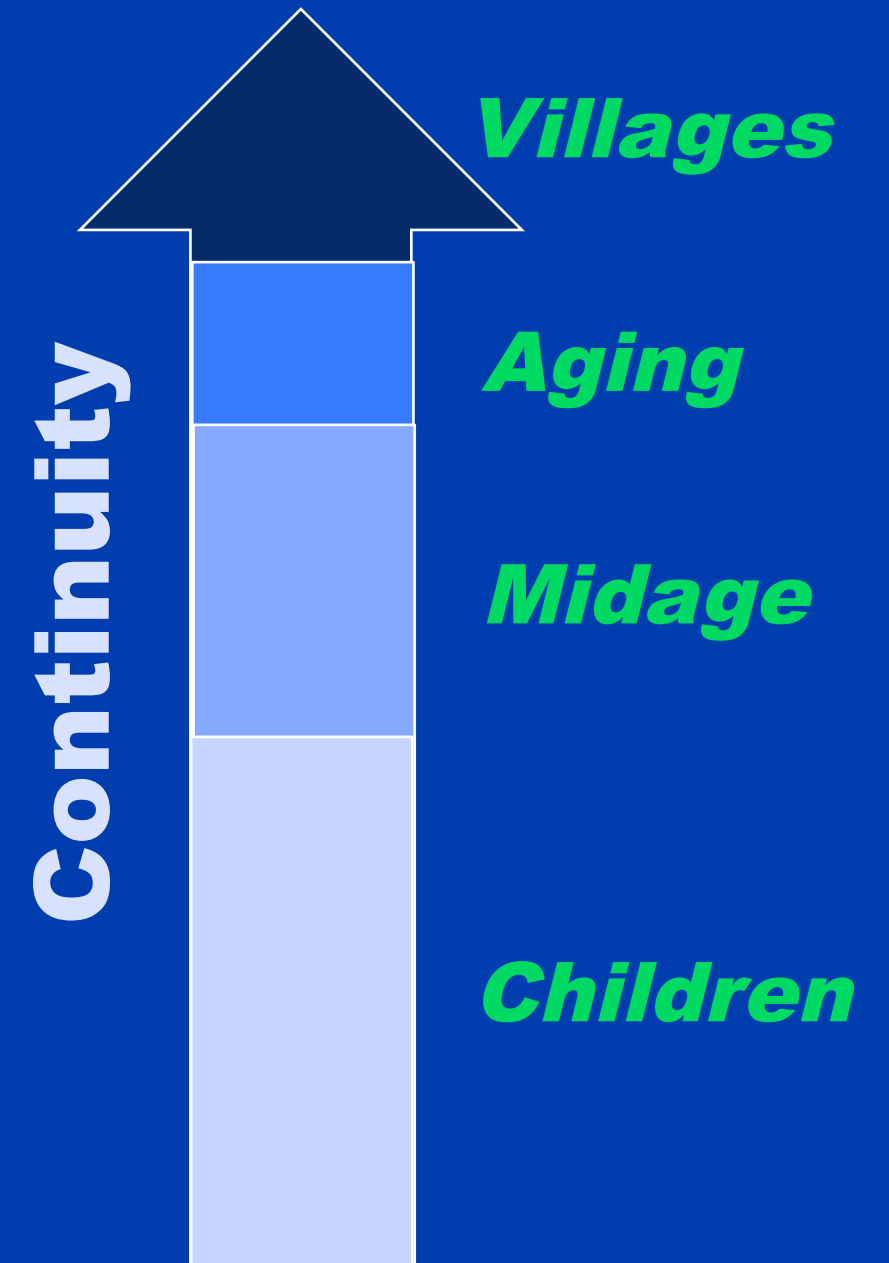
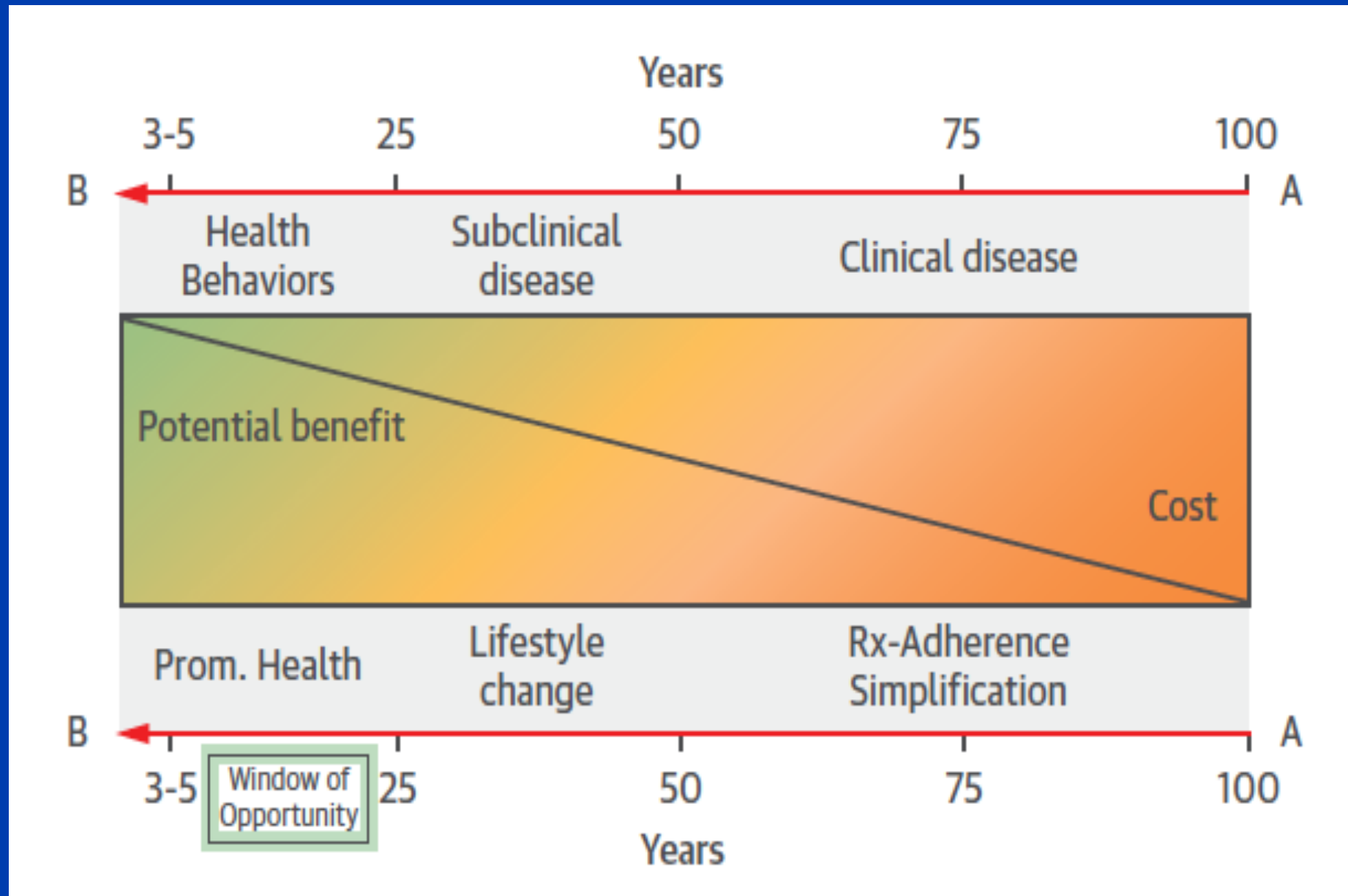


# 3) NEW YORK MADRID





# Scientific & Economic Bases of Health



**60 -100 - 20-40 - 3-20 -Yrs**

# ***Cardiovascular Health 2023 - 2030***

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***Throughout Lifespan - 3 Ages  
9 Findings - 3 Trials***