SEEN
Sociedad Española de Endocrinología y Nutrición

28 y 29 de Septiembre de 2018

DEBATE: EVALUACIÓN DEL RCV

A favor incorporación estudios de imagen

J. Escalada

Dpto. Endocrinología y Nutrición

Clínica Universidad de Navarra

ciberobn isciii

IdiSNA
INSTITUTO DE INVESTIGACIÓN SANITARIA DE NAVARRA

Clínica Universidad de Navarra

EVALUACIÓN DEL RIESGO CARDIOVASCULAR

CON estudios de imagen

Evaluación clínica sola

CONFLICTOS DE INTERÉS

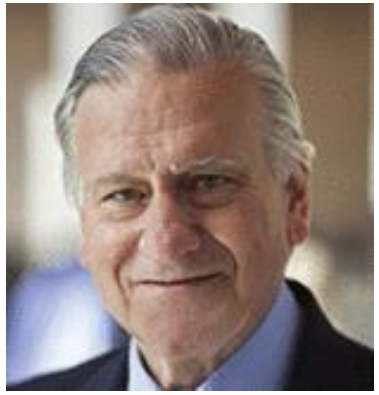
- Nada que declarar en relación al tema

PREGUNTAS A LA AUDIENCIA

- ¿Cuántos de uds USAN pruebas de imagen en valoración del RCV?

- ¿Quiénes CREEN que las pruebas de imagen pueden ser útiles en la valoración del RCV?

POSICIONAMIENTO



Rev Esp Cardiol Supl. 2008;8:35C-44C

"La enfermedad cardiovascular es la principal causa de mortalidad y morbilidad en los países desarrollados. La diabetes mellitus es un factor de riesgo importante para la enfermedad cardiovascular, que contribuye a producir sus devastadoras consecuencias económicas.

...**Las exploraciones de imagen cardiovasculares no invasivas recientemente aparecidas son un instrumento preciso para evaluar la carga de aterosclerosis**."

2014

J. of Cardiovasc. Trans. Res. (2014) 7:623–634
DOI 10.1007/s12265-014-9582-4

Imaging Subclinical Atherosclerosis: Is It Ready for Prime Time? A Review

Leticia Fernández-Friera · Borja Ibáñez · Valentín Fuster

2008

ACTUALIZACIÓN EN DIABETES Y ENFERMEDAD CARDIOVASCULAR

Diabetes y enfermedad cardiovascular

Valentín Fuster y Borja Ibáñez

Rev Esp Cardiol Supl. 2008;8:35C-44C

2017

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
VOL. 70, NO. 3, 2017

ISSN 0735-1097/$36.00
PUBLISHED BY ELSEVIER
http://dx.doi.org/10.1016/j.jacc.2017.05.033

ORIGINAL INVESTIGATIONS

Subclinical Atherosclerosis Burden by 3D Ultrasound in Mid-Life

The PESA Study

Beatriz López-Melgar, MD, PhD,[a,b] Leticia Fernández-Friera, MD, PhD,[a,b,c] Belén Oliva, MSc,[a] José Manuel García-Ruiz, MD,[a,c,d] José Luis Peñalvo, PhD,[a,e] Sandra Gómez-Talavera, MD,[a,f] Javier Sánchez-González, PhD,[g] José María Mendiguren, MD,[h] Borja Ibáñez, MD, PhD,[a,c,f] Antonio Fernández-Ortiz, MD, PhD,[a,c,i] Javier Sanz, MD,[a,j] Valentín Fuster, MD, PhD[a,j]

Risk stratification in asymptomatic subjects

"All adults should undergo an office-based assessment as the initial step to identify those at higher risk for a coronary event"

JAMA®

Online article and related content current as of October 10, 2010.

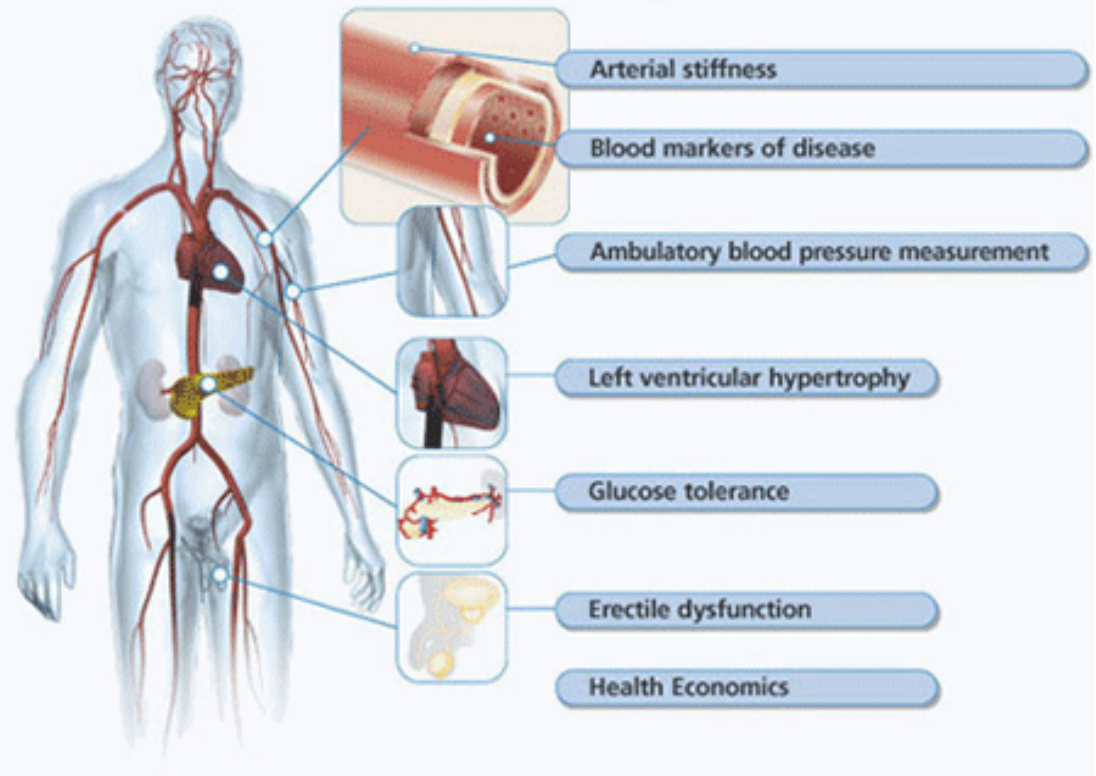
Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III)

Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults

JAMA. 2001;285(19):2486-2497 (doi:10.1001/jama.285.19.2486)

The intermediate risk cohort

- La mayoría de los eventos ocurre en esta población
- Tratar a TODAS las personas de “riesgo intermedio” es COSTE-INEFICIENTE
- **Un “ajuste” en la estratificación del riesgo** puede ser beneficioso
  - Muchos no tienen arteriosclerosis (cambio a “riesgo bajo”)
  - Hay un % de verdadero “alto riesgo”, y que se beneficiarían de un plan terapéutico dirigido a reducer su riesgo CV



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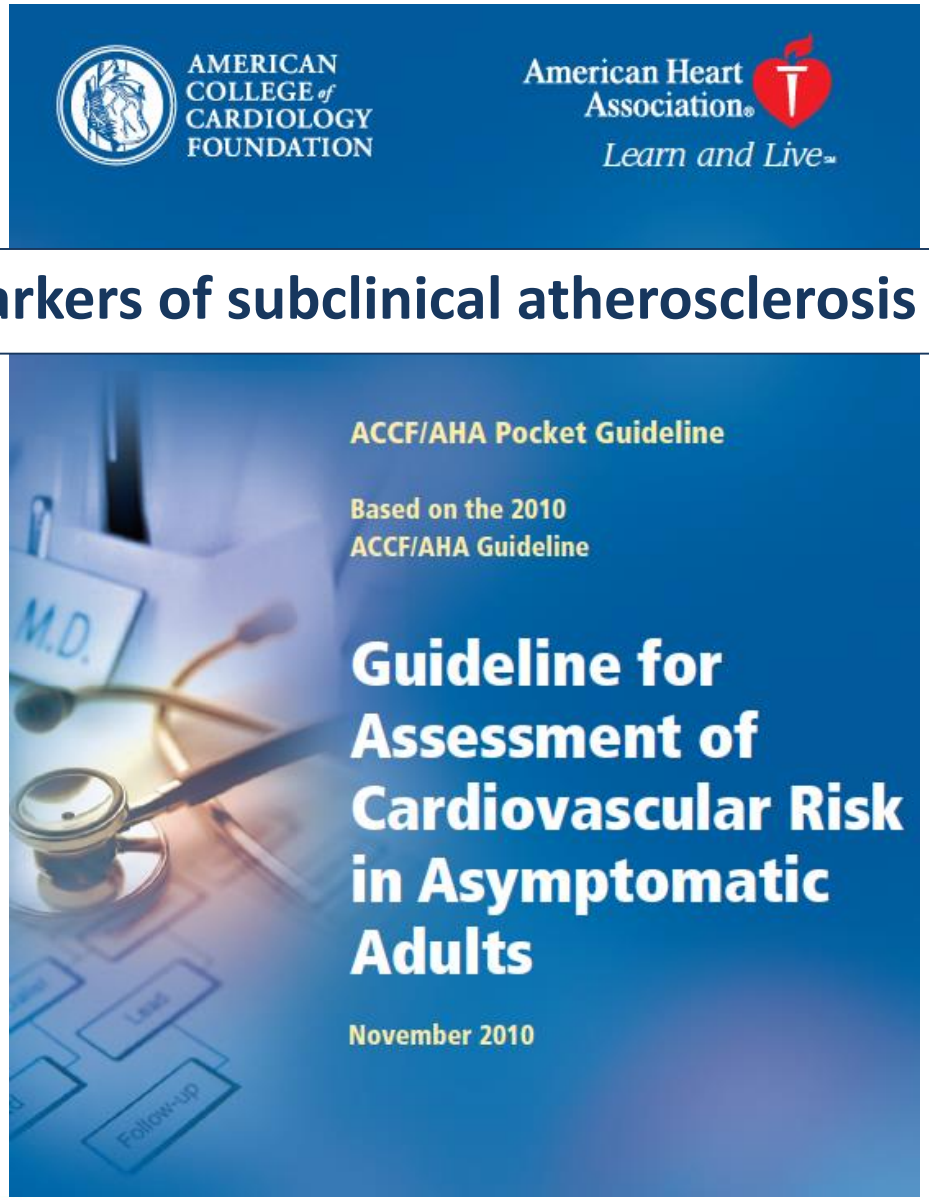
Markers of subclinical atherosclerosis



http://www.acc.org

Risk Stratification and Genomics

- Global Risk Scoring
- Family History Genotypes

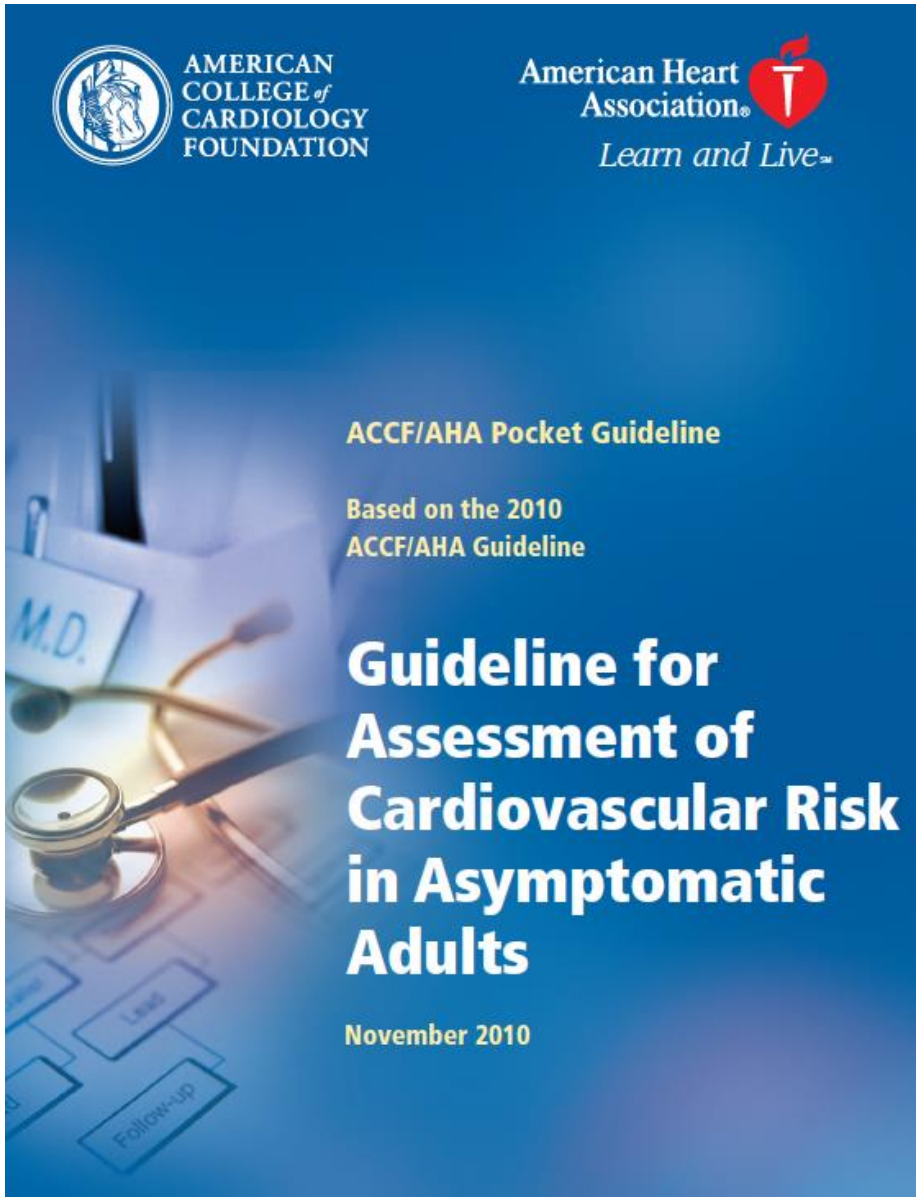
Lipoproteins and Circulating Blood Markers

- Lipoprotein and Apolipoprotein Assessments
- Natriuretic Peptides
- C-Reactive Protein
- Hemoglobin A1C
- Lipoprotein-Associated Phospholipase A2

Microalbuminuria

Cardiac and Vascular Tests

- Resting Electrocardiogram
- Transthoracic Echocardiography
- Carotid Intima-Media Thickness
- Brachial/Peripheral Flow-Mediated Dilation
- Specific Measures of Arterial Stiffness
- Ankle-Brachial Index
- Exercise Electrocardiography
- Stress Echocardiography
- Myocardial Perfusion Imaging
- Calcium Scoring Methods
- Coronary Computed Tomography Angiography
- Magnetic Resonance Imaging of Plaque



http://www.acc.org

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- **Calcium Scoring Methods**

- Coronary Computed Tomography Angiography
- Magnetic Resonance Imaging of Plaque

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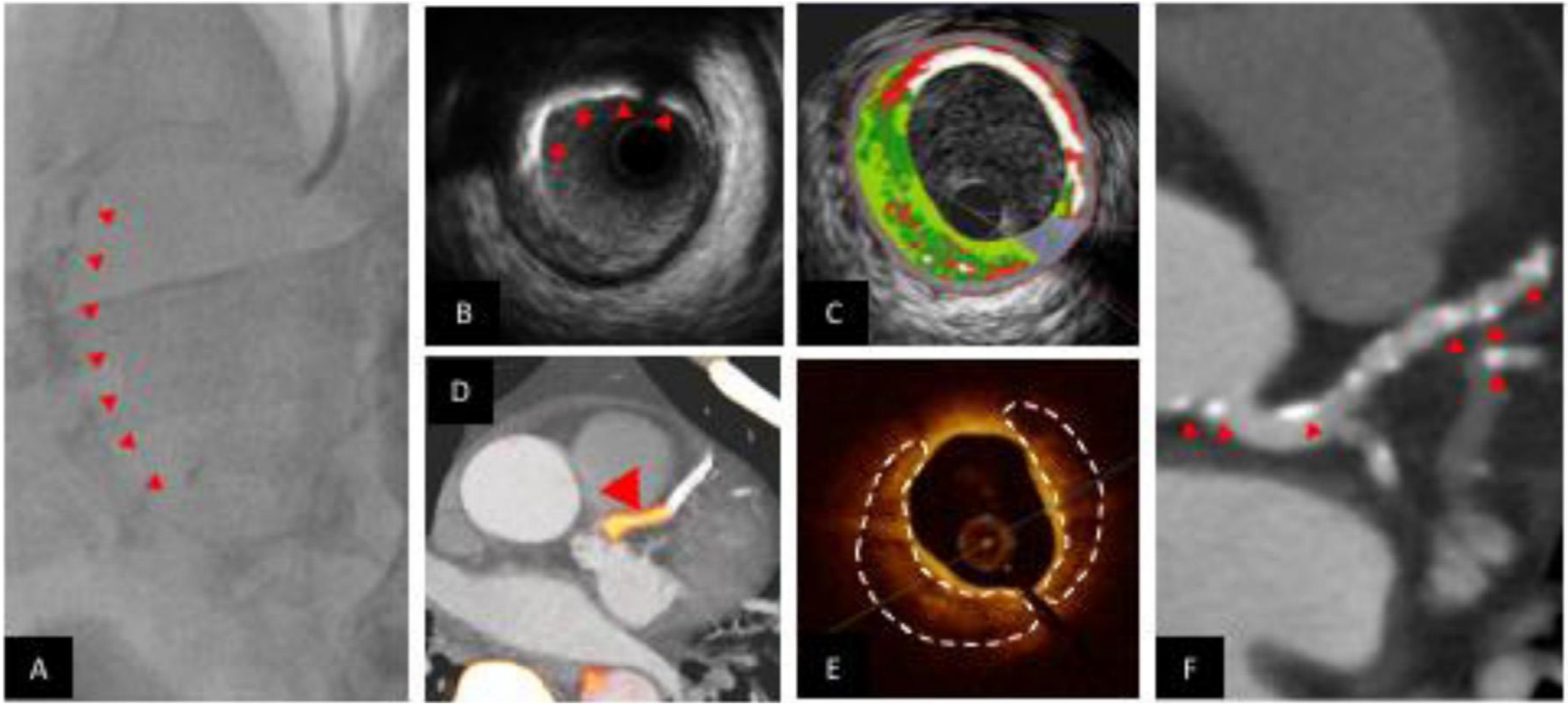
A
B
C
D
E
F

Los estudios de imagen (CAC) ayudan en la evaluación del riesgo cardiovascular

ARGUMENTACIÓN

ARGUMENTACIÓN. AGENDA

- Escenario: Casos clínicos

- Evidencia: ECAs, papers, guías clínicas

DM2

Tabaco

HTA

Ant.
Fam.

CASOS CLÍNICOS

54 años

- HTA (Telmisartan 40 mg/día)
- DISLIPEMIA
- NO FUMADOR
- ACTIVO (deporte)

→

- GLU 106 mg/dL; HbA1c 5,7%
- CT 230; TG 81; HDL 45; LDL 162
- RCV 10 años: 2%
- ASCVD risk: 7,9%

No hª familiar de ECV precoz, IMC 25,7 Kg/m2

¿?

59 años

- DM2 5 años (Met+iDPP4)
- EXFUMADOR
- DISLIPEMIA (Simva 20 mg/día)
- ACTIVO (deporte)

→

- HbA1c 6,7%
- CT 159; TG 51; HDL 58; LDL 91
- RCV 10 años: 9,7%
- ASCVD risk: 10,3%

No HTA, no hª familiar de ECV precoz, IMC 25,6 Kg/m2

Coronary artery calcification - CAC

- **The presence of calcium in coronary arteries is pathognomonic of atherosclerosis**

- As demonstrated both by histopathology and intravascular ultrasound, there is close correlation between the atherosclerotic plaque burden and the extent of coronary calcium

- The total coronary calcium score measured represents an anatomic measure of overall cardiac plaque burden

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Calcium scoring interpretation

Table 1. Guidelines for interpretation of coronary artery calcium score in asymptomatic patients (from [17])

Calcium score	Plaque burden	Probability of significant CAD	Implication for CV risk	Recommendation
0	No identifiable plaques	Very low	Very low	Reassure patient
1–10	Minimal identifiable plaque burden	Very unlikely	Low	Discuss guidelines for primary prevention of CAD
11–100	Mild atherosclerotic plaque	Mild or minimal coronary stenosis likely	Moderate	Counsel risk factor modification, daily ASS
101–400	Moderate atherosclerotic plaque	CAD highly likely	Moderately high	Institute risk factor modification, exercise testing
>400	Extensive atherosclerotic plaque burden	High likelihood of significant coronary stenosis	High	Aggressive risk factor modification, exercise or pharmacological stress test

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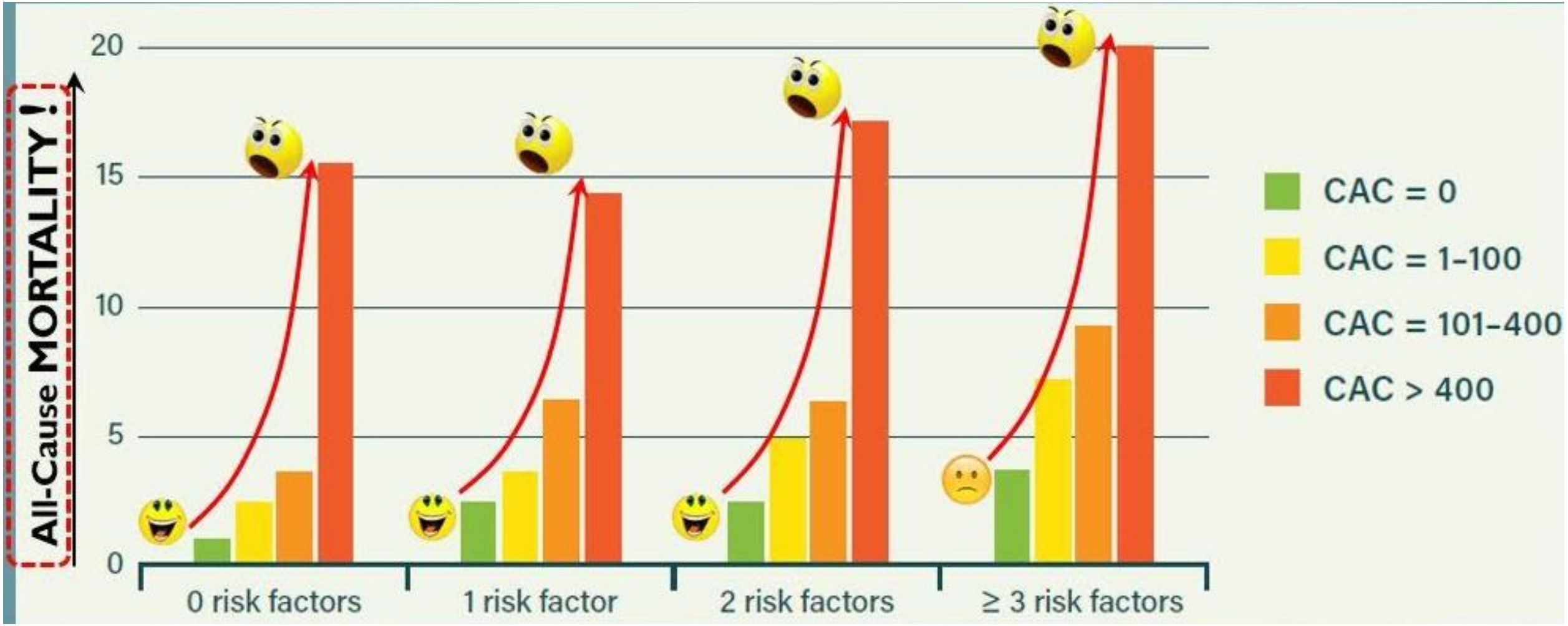
Rumberger J. Mayo Clin Proc 1999; 74:243-252

Calcio coronario



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Circ Cardiovasc Imaging 2012;5:467-473

CAC: Pronóstico como prevención primaria

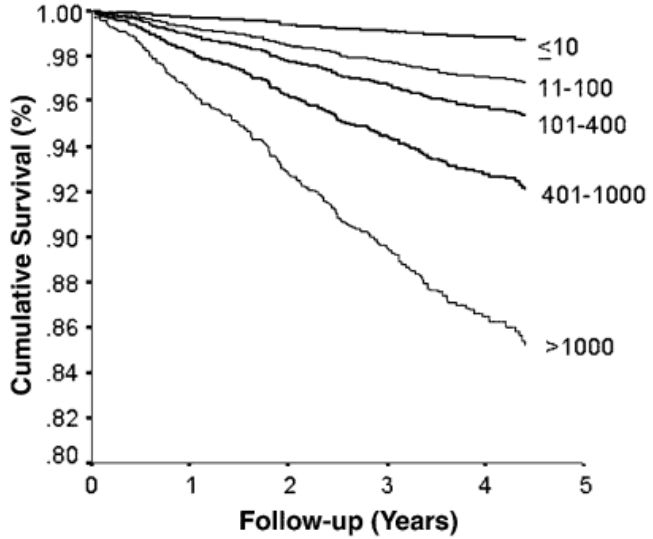
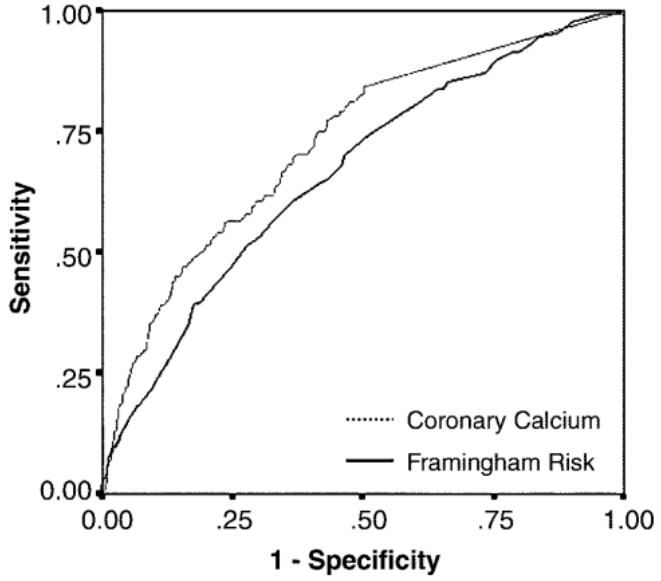


Figure 1. Graph shows unadjusted all-cause survival according to calcium score subsets. Survival rate is proportionally worse as the baseline calcium score increases.



- In 10,377 asymptomatic patients with a 5-year follow-up after an initial electron-beam CT evaluation
- **All-cause mortality** increased proportional to coronary calcium, which was an **independent predictor** of risk after adjusting for all of the Framingham risk factors ($p < 0.001$)
- Superiority of coronary calcium to conventional Framingham risk factor assessment was demonstrated by a significantly greater area under the ROC curves (0.73 versus 0.67, $p < 0.001$)
- **Incremental value of coronary calcium to Framingham risk** was also established by a significant increase of the area under the ROC curves, from 0.72 for Framing ham risk to 0.78 with the addition of coronary calcium ($p < 0.001$)

Shaw LJ. Radiology 2003;28:826–833.

JAMA Cardiology

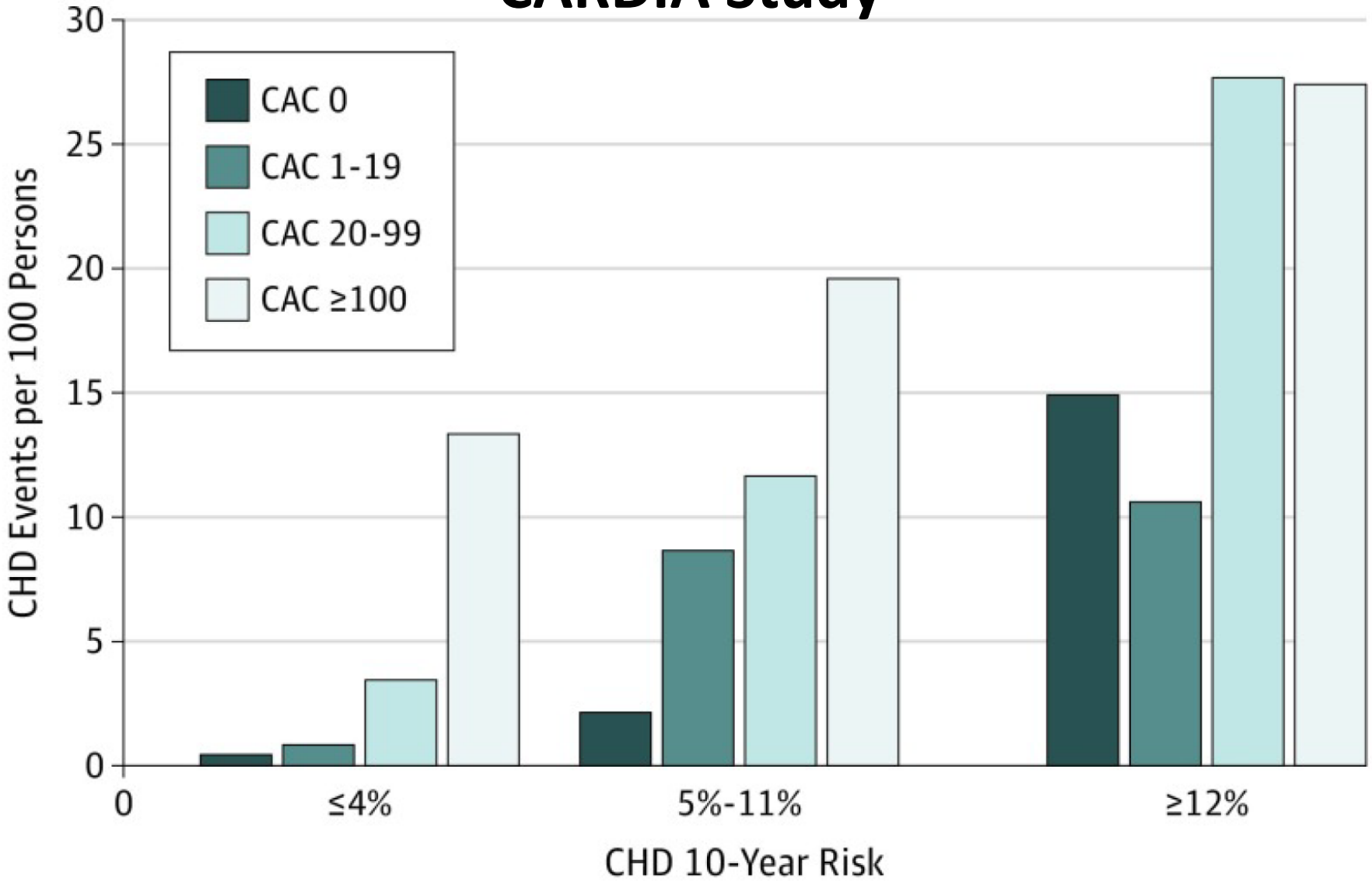
View Article

JAMA Cardiol. 2017 Apr; 2(4): 391–399.
Published online 2017 Apr 19. Prepublished online 2017 Feb 8.
doi: 10.1001/jamacardio.2016.5493

PMCID: PMC5397328
NIHMSID: NIHMS854043
PMID: 28196265

Association of Coronary Artery Calcium in Adults Aged 32 to 46 Years With Incident Coronary Heart Disease and Death

CARDIA Study



JAMA Cardiol. 2017 Apr; 2(4): 391-399

ESC
European Society of Cardiology

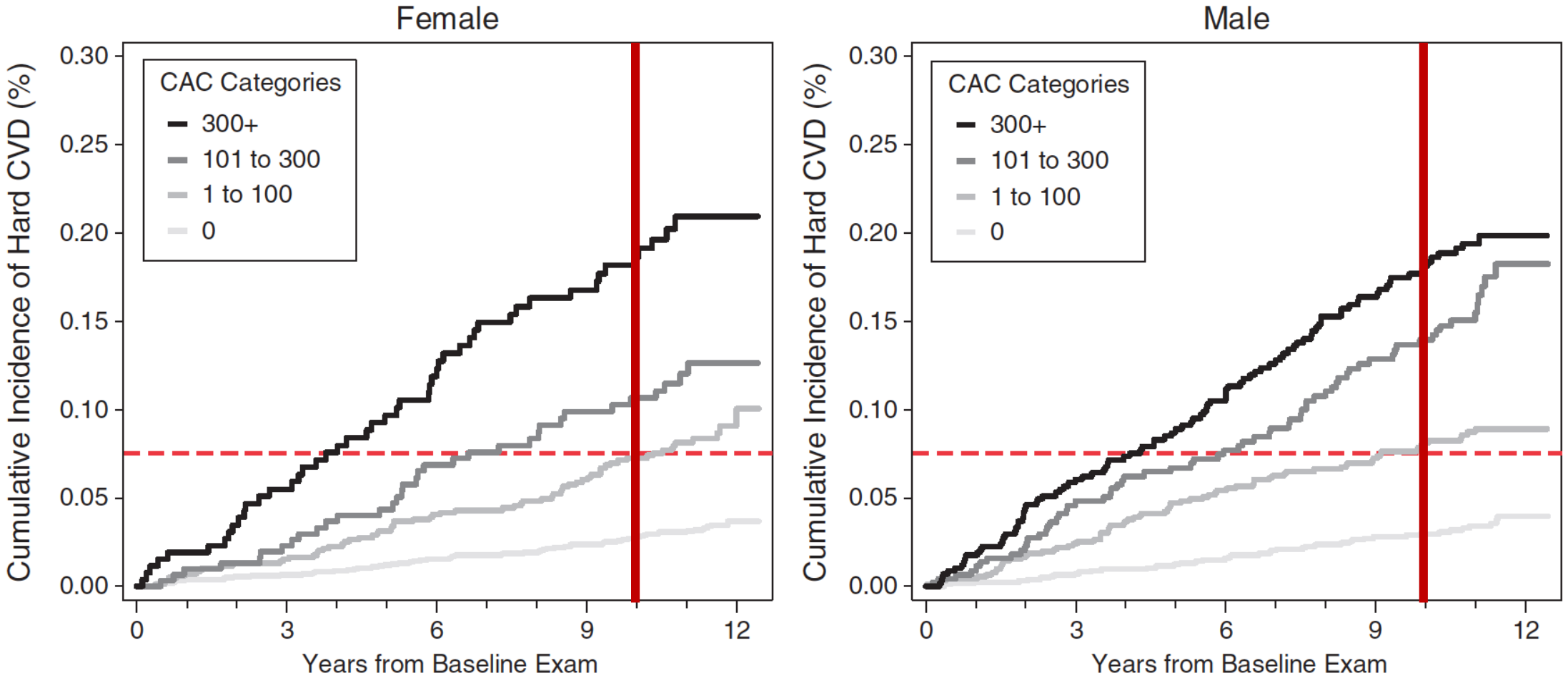
European Heart Journal (2018) **0**, 1–10
doi:10.1093/eurheartj/ehy217

CLINICAL RESEARCH
Prevention and epidemiology

Ten-year association of coronary artery calcium with atherosclerotic cardiovascular disease (ASCVD) events: the multi-ethnic study of atherosclerosis (MESA)

Matthew J. Budoff[1]*, Rebekah Young[2], Gregory Burke[3], J. Jeffrey Carr[4], Robert C. Detrano[5], Aaron R. Folsom[6], Richard Kronmal[2], Joao A.C. Lima[7], Kiang J. Liu[8], Robyn L. McClelland[2], Erin Michos[7], Wendy S. Post[7], Steven Shea[9], Karol E. Watson[10], and Nathan D. Wong[5]

- 6814 participants (51% women), aged 45–84 years, free of clinical CVD at baseline
- Relationship between CAC and incident ASCVD
- F-U: 11.1 years
- 500 incident ASCVD (7.4%) events



N=6,783. Red dashed line shows 7.5% risk.

CENTRAL ILLUSTRATION **Proposed Decision-Making Approach to Selective Use of Coronary Artery Calcium Measurement for Risk Prediction**

Using 10-year ASCVD risk estimate plus coronary artery calcium (CAC) score to guide statin therapy				
Patient's 10-year atherosclerotic cardiovascular disease (ASCVD) risk estimate:	<5%	5-7.5%	>7.5-20%	>20%
Consulting ASCVD risk estimate alone	Statin not recommended	Consider for statin	Recommend statin	Recommend statin

Greenland, P. et al. J Am Coll Cardiol. 2018;72(4):434-47.

Table 4 Risk of atherosclerotic cardiovascular disease associated with coronary artery calcium by age categories, sex, and race or ethnicity

Subset	HR (95% CI)	*P*-value
Age category		
45–54	1.20 (1.11–1.29)	<0.001
55–64	1.16 (1.10–1.22)	<0.001
65–74	1.13 (1.08–1.18)	<0.001
75–84	1.12 (1.06–1.17)	<0.001
Sex		
Male	1.14 (1.10–1.18)	<0.001
Female	1.13 (1.08–1.17)	<0.001
Race or ethnicity		
White	1.13 (1.08–1.18)	<0.001
Chinese	1.16 (1.05–1.28)	0.003
Black	1.13 (1.08–1.18)	<0.001
Hispanic	1.14 (1.09–1.20)	<0.001
Lipid-lowering medication at baseline		
No	1.14 (1.10–1.17)	<0.001
Yes	1.14 (1.10–1.17)	<0.001
Overall	1.14 (1.10–1.17)	<0.001

European Heart Journal (2018) 0, 1–10

ESC
European Society of Cardiology

European Heart Journal - Cardiovascular Imaging (2018) **19**, 838–846
doi:10.1093/ehjci/jey014

REVIEW

Non-invasive screening for coronary artery disease in asymptomatic diabetic patients: a systematic review and meta-analysis of randomised controlled trials

Olivier F. Clerc, Tobias A. Fuchs, Julia Stehli, Dominik C. Benz, Christoph Gräni, Michael Messerli, Andreas A. Giannopoulos, Ronny R. Buechel, Thomas F. Lüscher, Aju P. Pazhenkottil, Philipp A. Kaufmann, and Oliver Gaemperli*

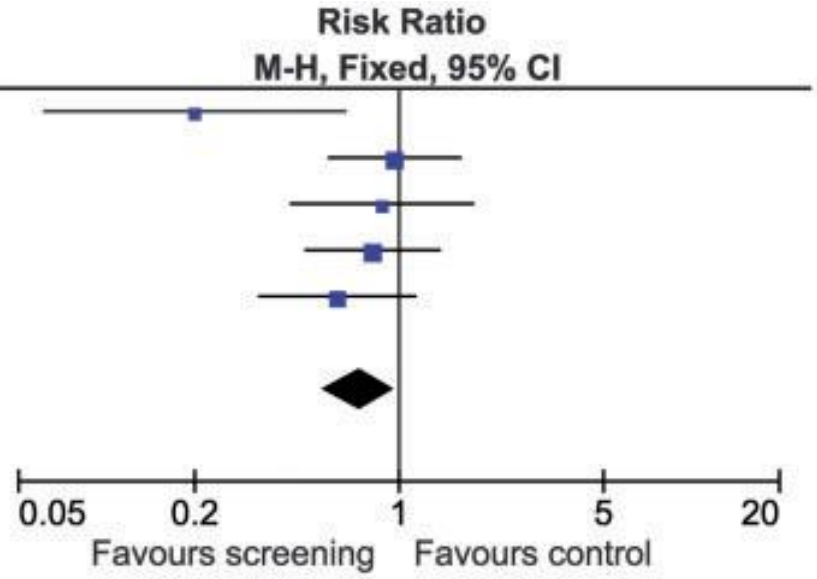
Los resultados arrojados mostraron que el screening no invasivo de enfermedad coronaria en pacientes diabéticos asintomáticos mostraba una reducción estadísticamente significativa de cualquier evento en un 27%

number needed to screen 56

Study or Subgroup	Screening Events	Screening Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI	Year
Faglia *et al.*	3	71	15	71	13.7%	0.20 [0.06, 0.66]	2005
DIAD	26	561	27	562	24.7%	0.96 [0.57, 1.63]	2009
DYNAMIT	13	306	15	309	13.7%	0.88 [0.42, 1.81]	2011
FACTOR-64	23	452	28	447	25.8%	0.81 [0.48, 1.39]	2014
DADDY-D	15	262	24	258	22.1%	0.62 [0.33, 1.15]	2015
Total (95% CI)		**1652**		**1647**	**100.0%**	**0.73 [0.55, 0.97]**	
Total events	80		109				

Heterogeneity: Chi² = 6.27, df = 4 (*P* = 0.18); I² = 36%

Test for overall effect: Z = 2.19 (*P* = 0.03)



"…the benefit of a screening strategy in this study can be compared with the effect of statin use for primary prevention of coronary heart disease events (-27%, number needed to treat 78)"

European Heart Journal - Cardiovascular Imaging (2018) 19, 838–846

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL. 72, NO. 4, 2018

PUBLISHED BY ELSEVIER

THE PRESENT AND FUTURE

JACC STATE-OF-THE-ART REVIEW

Coronary Calcium Score and Cardiovascular Risk

Philip Greenland, MD,[a] Michael J. Blaha, MD, MPH,[b] Matthew J. Budoff, MD,[c] Raimund Erbel, MD,[d] Karol E. Watson, MD, PhD[e]

TABLE 2 Summary of 4 Major Guidelines and Expert Consensus Documents on Use of Coronary Artery Calcium for Risk Assessment in Asymptomatic Patients

Guideline/Statement	Summary of CT Recommendations
2013 ACC/AHA risk assessment guideline	If, after quantitative risk assessment using traditional risk factors, a risk-based treatment decision is uncertain, CAC score may be considered to inform treatment decision making. Class IIb, Level of Evidence: B (7).
2016 European guidelines on CVD prevention	CAC scoring may be considered as a risk modifier in CV risk assessment. Class IIb, Level of Evidence: B (8).
2017 expert consensus from the Society of Cardiovascular Computed Tomography	It is appropriate to perform CAC testing in the context of shared decision making for asymptomatic individuals without clinical ASCVD who are 40–75 years of age in the 5%–20% ten-year ASCVD risk group and selectively in the <5% ASCVD risk group, such as those with a family history of premature CAD (91).
2018 U.S. Preventive Services Task Force draft guideline on nontraditional risk factors	In asymptomatic adults, the current evidence is insufficient to assess the balance of benefits and harms of adding CAC score to traditional risk assessment for CVD prevention. Class I (123).

ACC = American College of Cardiology; AHA = American Heart Association; ASCVD = atherosclerotic cardiovascular disease; other abbreviations as in Table 1.

ACC/AHA 2013: CAC score may be considered to inform treatment decisión making (IIb, B)

European guidelines (CVD prevention) 2016: CAC scoring may be considered as a risk modifier in CV risk assessment (IIb, B)

SCCT 2017: CAC for asymptomatic individuals without clinical ASCVD who are 40-75 years of age in the 5-20% ten-year ASCVD risk group

US Preventive Services Task Force 2018: In asymptomatic adults, the current evidence is insufficient to assess the balance of benefits and harms of adding CAC score to traditional risk assessment for CVD prevention (Class I)

J Am Coll Cardiol. 2018;72(4):434–47

“Cost-effectiveness analyses (9–14) have concluded that CAC testing is cost effective in asymptomatic populations.”

Using 10-year ASCVD risk estimate plus coronary artery calcium (CAC) score to guide statin therapy

Patient's 10-year atherosclerotic cardiovascular disease (ASCVD) risk estimate:	<5%	5-7.5%	>7.5-20%	>20%
Consulting ASCVD risk estimate alone	Statin not recommended	Consider for statin	Recommend statin	Recommend statin
Consulting ASCVD risk estimate + CAC				
If CAC score =0	Statin not recommended	Statin not recommended	Statin not recommended	Recommend statin
If CAC score >0	Statin not recommended	Consider for statin	Recommend statin	Recommend statin
Does CAC score modify treatment plan?	✗ CAC not effective for this population	✓ CAC can reclassify risk up or down	✓ CAC can reclassify risk up or down	✗ CAC not effective for this population

Greenland, P. et al. J Am Coll Cardiol. 2018;72(4):434-47.

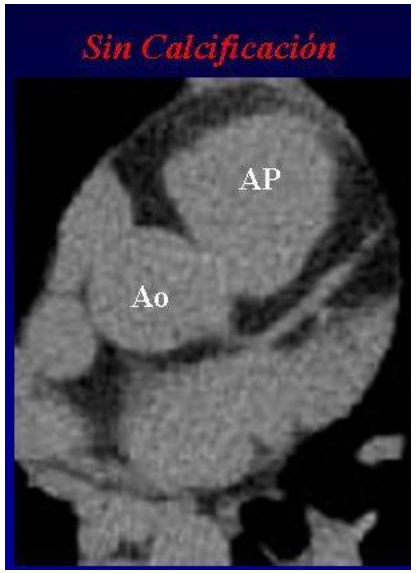
CASO CLÍNICO

54 años

- HTA (Telmisartan 40 mg/día)
- DISLIPEMIA
- NO FUMADOR
- ACTIVO (deporte)

- GLU 106 mg/dL; HbA1c 5,7%
- CT 230; TG 81; HDL 45; LDL 162
- RCV 10 años: 2%
- ASCVD risk: 7,9%

No hª familiar de ECV precoz, IMC 25,7 Kg/m2



0

- MESA CHD Estimator Risk: 3%
- Edad vascular: 39 años

NO HIPOLIPEMIANTE

https://www.mesa-nhlbi.org/MESACHDRisk/MesaRiskScore/RiskScore.aspx

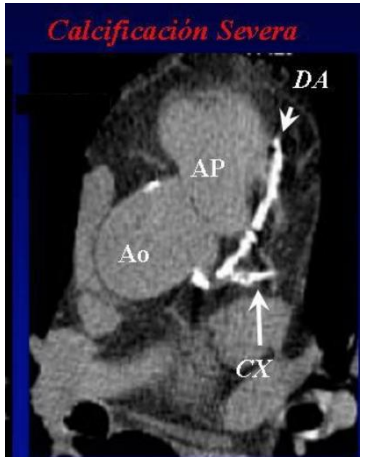
CASO CLÍNICO

59 años

- DM2 5 años (Met+iDPP4)
- EXFUMADOR
- DISLIPEMIA (Prava 20 mg/día)
- ACTIVO (deporte)

- HbA1c 6,7%
- CT 159; TG 51; HDL 58; LDL 91
- RCV 10 años: 9,7%
- ASCVD risk: 10,3%

No HTA, no hª familiar de ECV precoz, alb/creat < 30



435,4

- MESA CHD Estimator Risk: 20%
- Edad vascular: 83 años

Rosuvastatina 20 mg/día

+

AAS 100 mg/día

CT 129; TG 61; HDL 59; LDL 58

https://www.mesa-nhlbi.org/MESACHDRisk/MesaRiskScore/RiskScore.aspx

https://www.mesa-nhlbi.org/MESACHDRisk/MesaRiskScore/RiskScore.aspx

The Multi-Ethnic Study of Atherosclerosis

MESA 10-Year CHD Risk with Coronary Artery Calcification

Back to CAC Tools

1. Gender Male ○ Female ○

2. Age (45-85 years) _____ Years

3. Coronary Artery Calcification _____ Agatston

4. Race/Ethnicity **Choose One**

- Caucasian ○
- Chinese ○
- African American ○
- Hispanic ○

5. Diabetes Yes ○ No ○

6. Currently Smoke Yes ○ No ○

7. Family History of Heart Attack Yes ○ No ○
(History in parents, siblings, or children)

8. Total Cholesterol _____ mg/dL or _____ mmol/L

9. HDL Cholesterol _____ mg/dL or _____ mmol/L

10. Systolic Blood Pressure _____ mmHg or _____ kPa

11. Lipid Lowering Medication Yes ○ No ○

12. Hypertension Medication Yes ○ No ○

Calculate 10-year CHD risk

RÉPLICA y CONCLUSIONES

“En medicina cardiovascular, hay que estratificar el riesgo”

“Los estudios en Medicina tienen sentido si sirven para tomar decisiones terapéuticas”

“Estoy EN CONTRA de los estudios de imagen en la valoración del riesgo CV”

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY

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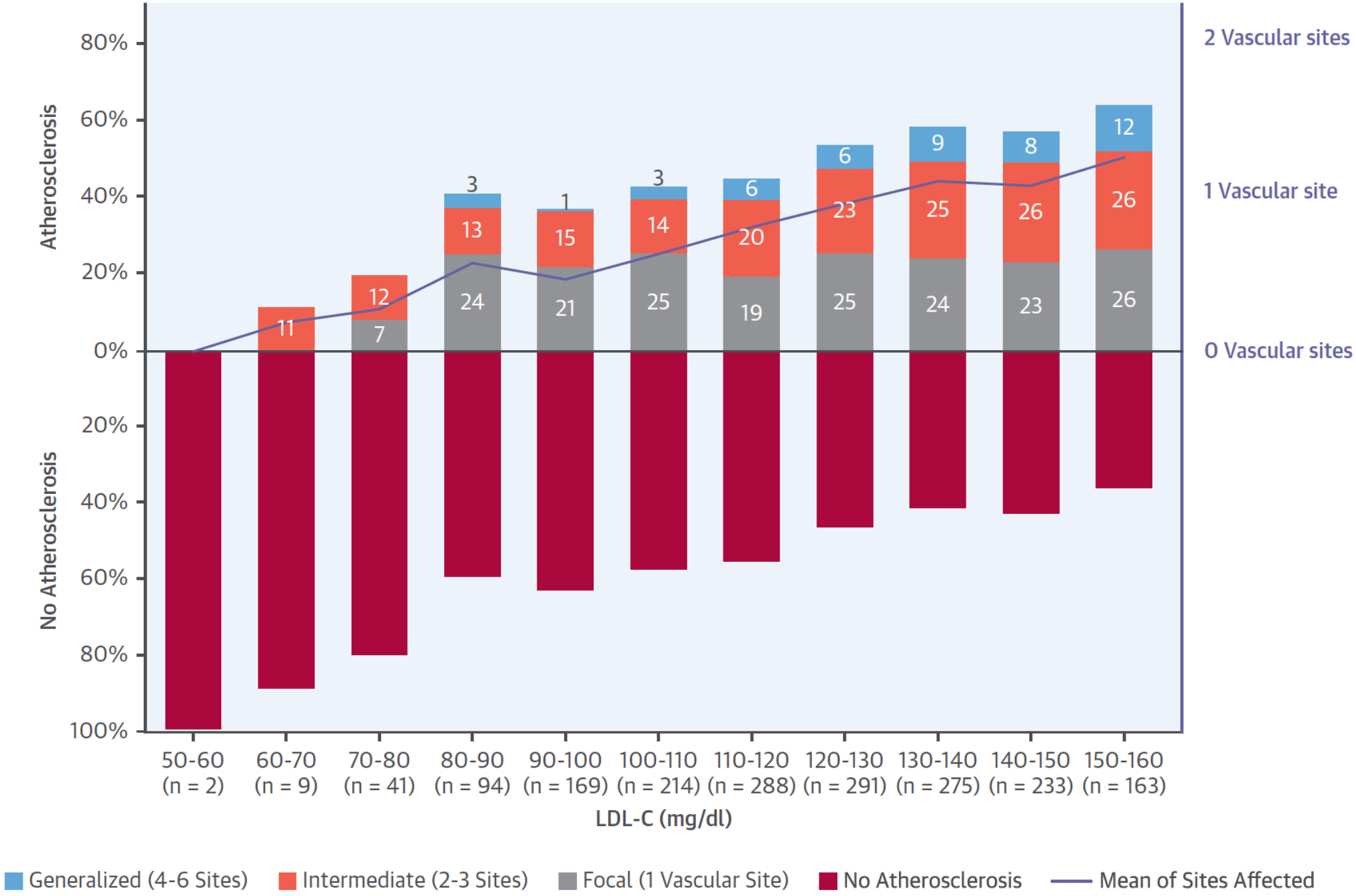
https://doi.org/10.1016/j.jacc.2017.10

Normal LDL-Cholesterol Levels Are Associated With Subclinical Atherosclerosis in the Absence of Risk Factors

Leticia Fernández-Friera, MD, PHD,[a,b,c] Valentín Fuster, MD, PHD,[a,d] Beatriz López-Melgar, MD, PHD,[a,b] Belén Oliva, MSC,[a] José M. García-Ruiz, MD,[a,c,e] José Mendiguren, MD,[f] Héctor Bueno, MD, PHD,[a,g] Stuart Pocock, MSC, PHD,[a,h] Borja Ibáñez, MD, PHD,[a,c,i] Antonio Fernández-Ortiz, MD, PHD,[a,c,j] Javier Sanz, MD[a,c]



Fernández-Friera, L. et al. J Am Coll Cardiol. 2017;70(24):2979–91.

Limitations of traditional risk screening methods

Framingham Risk Score

SCORE

PROCAM

REYNOLDS

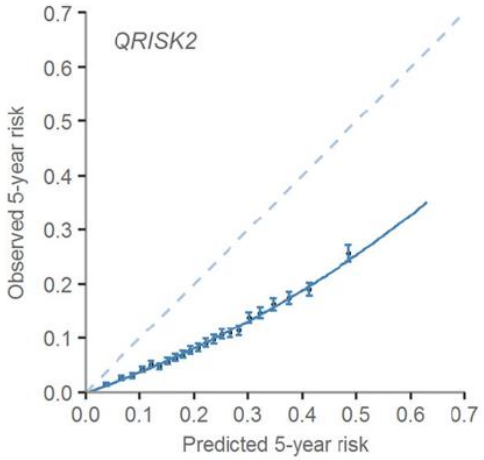
Otros…

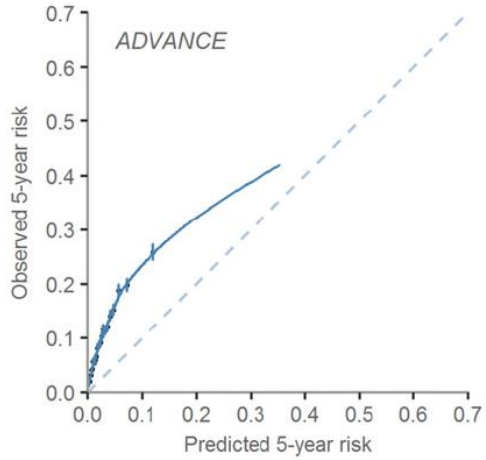
- Conventional office-based risk screening methods only **predict 60% - 65%** of cardiovascular risk
- The shortcomings of this approach are often highlighted by major cardiac events occurring in presumably **low-risk individuals**
- A relatively high proportion of previously **asymptomatic** patients will present with an acute coronary event as the initial manifestation of coronary artery disease (CAD)

Performance of Cardiovascular Disease Risk Scores in People Diagnosed With Type 2 Diabetes: External Validation Using Data From the National Scottish Diabetes Register

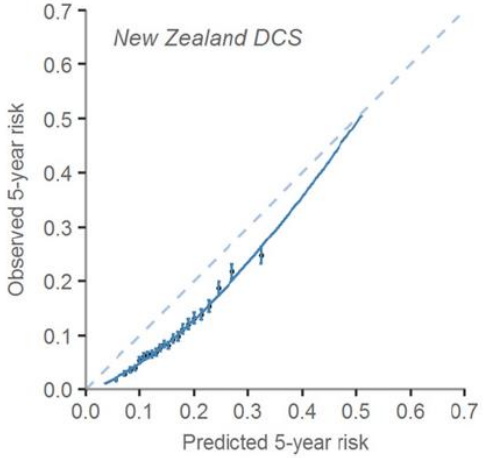
Stephanie H. Read,[1] Merel van Diepen,[2] Helen M. Colhoun,[3] Nynke Halbesma,[1] Robert S. Lindsay,[4] John A. McKnight,[5] David A. McAllister,[6] Ewan R. Pearson,[7] John R. Petrie,[4] Sam Philip,[8] Naveed Sattar,[4] Mark Woodward,[9,10,11] and Sarah H. Wild,[1] on behalf of the Scottish Diabetes Research Network Epidemiology Group

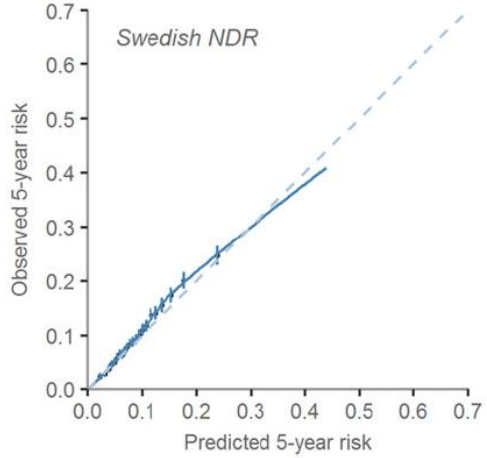
Diabetes Care 2018;41:2010–2018 | https://doi.org/10.2337/dc18-0578





None of the risk scores performed well among people with newly diagnosed type 2 diabetes.





Diabetes Care 2018;41:2010–2018

Risk stratification in asymptomatic subjects

"All adults should undergo an office-based assessment as the initial step to identify those at higher risk for a coronary event"

JAMA®

Online article and related content current as of October 10, 2010.

Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III)

Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults

JAMA. 2001;285(19):2486-2497 (doi:10.1001/jama.285.19.2486)

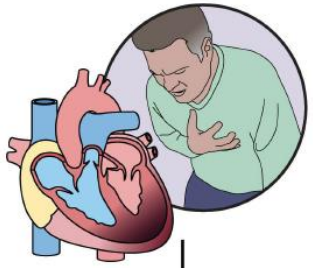
CONCLUSIONES

- Los “scores” actuales son IMPRECISOS
- Numerosos estudios sugieren que las herramientas de precisión CV deberían incluir ESTUDIOS DE IMAGEN (CAC)

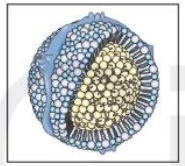
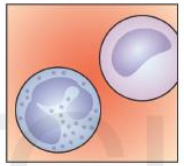
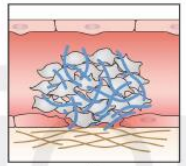
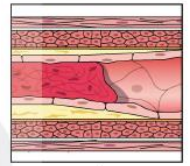
CONCLUSIONES

- CAC cumple los requisitos: muchos estudios de seguimiento a largo plazo muestran que CAC supera al score de riesgo ASCVD y otros marcadores de riesgo en la predicción de eventos cardíacos futuros
- “Zero CAC warranty”: el conocer que un paciente tiene un CAC score de “0” puede ser muy útil
- Motivador para estilos de vida: los pacientes que saben que tienen “calcio” en sus arterias coronarias pueden tener mayor motivación para hacer cambios de estilos de vida saludables
- La decisión final es más precisa con CAC

A Conceptual Framework for Addressing Residual Atherosclerotic Cardiovascular Disease Risk in the Era of Precision Medicine



Lifestyle interventions, guideline-directed medical therapy

	Lipoproteins	Inflammation	Metabolism	Platelets	Coagulation
Residual risk target					
Residual risk-lowering therapies	Ezetimibe PCSK9 inhibitor *Omega-3 fatty acids*	Canakinumab *Methotrexate* *Colchicine*	SGLT2 inhibitor GLP-1 agonist	Extended DAPT Low dose ticagrelor	Low dose rivaroxaban
Precision medicine toolbox	Standard lipids (e.g., LDL, HDL, TG), advanced lipid testing, Lp(a), HDL efflux capacity, genetic risk scores, atherosclerosis imaging	hs-CRP; biomarkers of inflammation, T cell and immune dysregulation, and clonal hematopoiesis; systemic inflammatory disease (e.g., psoriasis)	Prevalent type 2 DM, Hb A1c, HOMA-IR, BMI, visceral adiposity, liver fat	Antiplatelet risk scores (e.g., DAPT, PARIS, PRECISE-DAPT), platelet function testing, pharmacogenomics	PVD, prior VTE, thrombophilia, bleeding risk scores, coagulation biomarkers

Atherosclerosis imaging

Circulation. 2018 Jun 12;137(24):2551-2553

PREGUNTAS A LA AUDIENCIA

- ¿Quiénes CREEN que las pruebas de imagen pueden ser útiles en la valoración del RCV? (en determinados perfiles de riesgo CV: RIESGO INTERMEDIO)

fescalada@unav.es
@fjavesc

Clínica Universidad de Navarra

Hotel NH Nacional (Paseo del Prado, 48)

SALÓN PICASSO

28 y 29 de Septiembre de 2018

Organiza

FSEEN

Con la colaboración de

AMGEN

DEBATE: EVALUACIÓN DEL RCV

A favor evaluación clínica sola

Antonio Pérez

A favor incorporación estudios de imagen

Javier Escalada

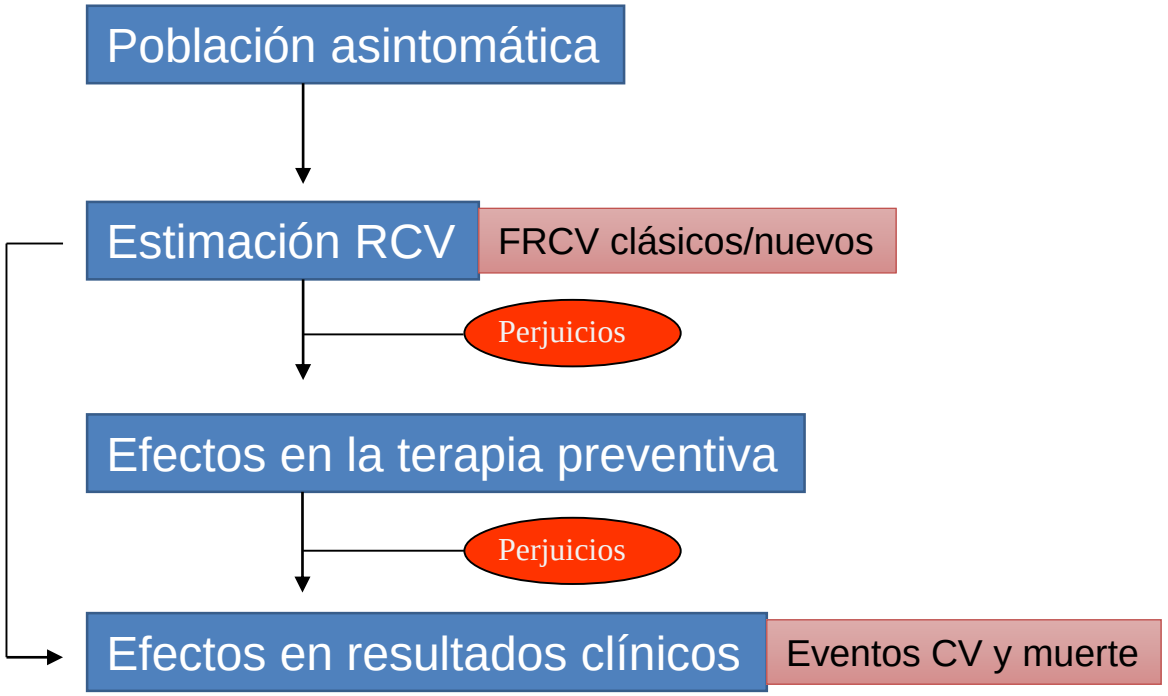
¿Incorporación estudios de imagen en la evaluación del RCV?

La respuesta sólidamente cimentada en la evidencia es un rotundo “NO”

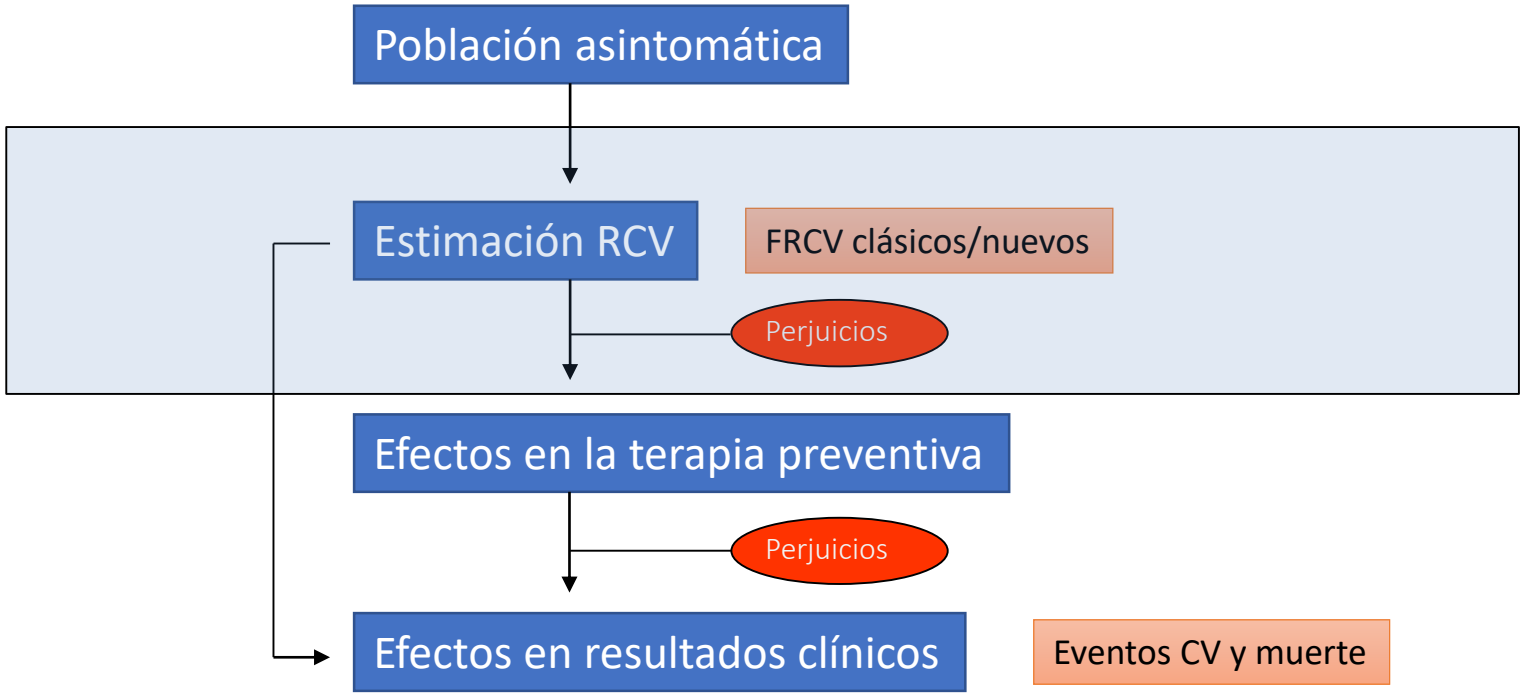
Dr. Antonio Pérez
Servicio de Endocrinología

¿Incorporación estudios de imagen en la evaluación del RCV?

No: argumentos



Evaluación de la estrategia de prevención



Screening for Atherosclerosis

Risk Factors vs Disease

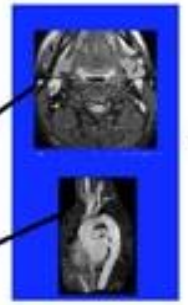
Numerous Risk Factors

- High LDL
- Low HDL
- High BP
- Diabetes
- Smoking
- CRP
- Metabolic Syn
- Lp(a)
- Homocysteine
- Dense LDL
- Lp-PLA2
- ApoB/ApoA
- Family History
- Sedentary Life
- Obesity
- Stress
- ...
- ?

Over 200 risk factors have been reported.

Examples of Arterial Structure Tests

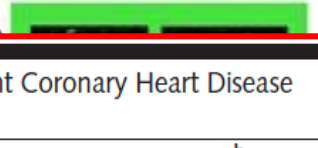
Carotid IMT and Plaque Measured by Ultrasound



Aortic and Carotid Plaque Detected by MRI

Coronary Calcium Score Measured by CT

Ankle Brachial Index



Brachial Vasoreactivity Measured by Ultrasound

Compliance
Radial Tonometry

Examples of Arterial Function Tests

ctivity
Measured by Fingertip Tonometry

Table 2. Association of Several Novel Risk Markers With Incident Coronary Heart Disease (No. of Events = 94)[a]

	Univariable		Multivariable[b]	
Marker	HR (95% CI)[c]	*P* Value	HR (95%CI)[c]	*P* Value
ABI	0.78 (0.66-0.93)	.005	0.79 (0.66-0.95)	.01
Brachial FMD	0.82 (0.66-1.03)	.09	0.93 (0.74-1.16)	.52
CAC[d]	2.72 (2.09-3.55)	<.001	2.60 (1.94-3.50)	<.001
Carotid IMT	1.33 (1.12-1.59)	.001	1.17 (0.95-1.45)	.13
Family history	2.39 (1.54-3.70)	<.001	2.18 (1.38-3.42)	.001
High-sensitivity CRP[d]	1.26 (1.01-1.57)	.05	1.28 (1.00-1.64)	.05

JAMA. 2012;308(8):788-795J

Utility of Nontraditional Risk Markers in Atherosclerotic Cardiovascular Disease Risk Assessment

Joseph Yeboah, MD, MS,* Rebekah Young, PhD,† Robyn L. McClelland, PhD,† Joseph C. Delaney, PhD,† J Am Coll Cardiol. 2016;67(2):139-147.

5185 sujetos sin estatinas de los incluidos en estudio MESA seguidos 10 años

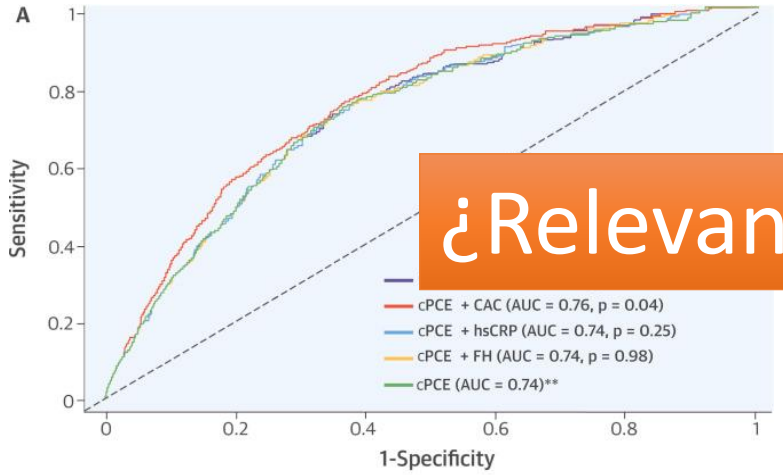
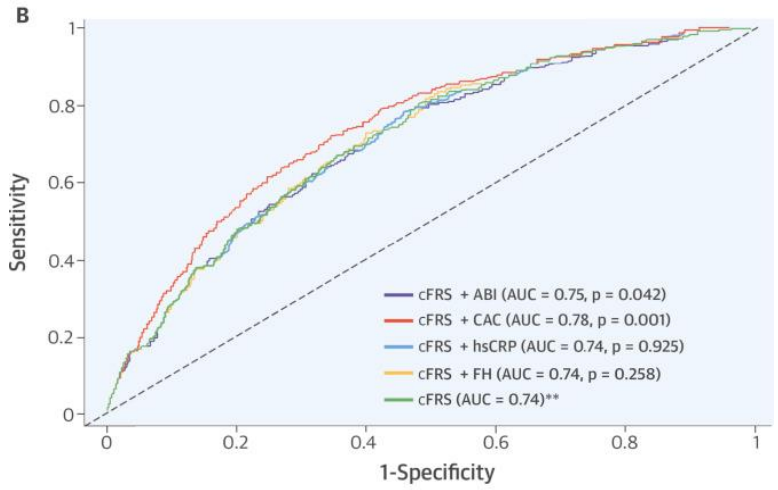


TABLE 3 NRI: Risk Markers Added to cPCE

	cPCE Alone <7.5%	cPCE Alone ≥7.5 %	Row Total	NRI (95% CI)
cPCE + CAC				
		19	126 (39.4)	0.178 (0.080 to 0.256)
		118	194 (60.6)	
		137 (42.8)		
Nonevent (n = 4,865)				
<7.5%	3,506	202	3,708 (76.2)	-0.059 (-0.075 to 0.030)
≥7.5%	496	661	1,157 (23.8)	
Column total	4,002 (82.3)	863 (17.7)		
Total NRI for CAC				0.119 (0.080 to 0.256)

¿Relevancia clínica?



La adición del CAC a los modelos de evaluación de riesgo de ECV:

-Limitada mejora en la discriminación

- cPCE vs cPCE +CAC: 0.74 vs 0.76

-Limitada mejora reclasificación (cPCE):

- Eventos NRI: 0.178
- No eventos NRI: –0.059

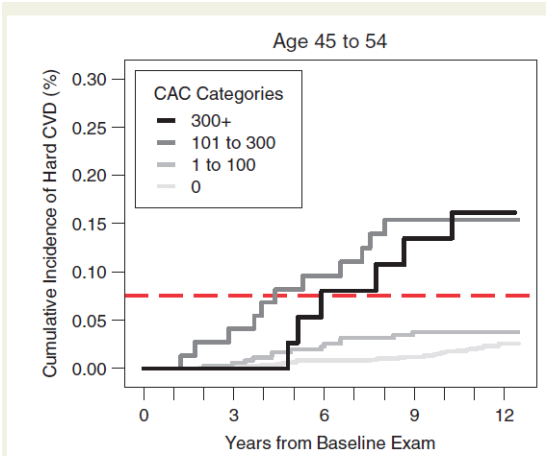
Ten-year association of coronary artery calcium with atherosclerotic cardiovascular disease (ASCVD) events: the multi-ethnic study of atherosclerosis (MESA)

Matthew J. Budoff[1]*, Rebekah Young[2], Gregory Burke[3], J. Jeffrey Carr[4],

European Heart Journal (2018) 0, 1–10 doi:10.1093/eurheartj/ehy217

Table 4 Risk of atherosclerotic cardiovascular disease associated with coronary artery calcium by age categories, sex, and race or ethnicity (CAP <0 vs >0)

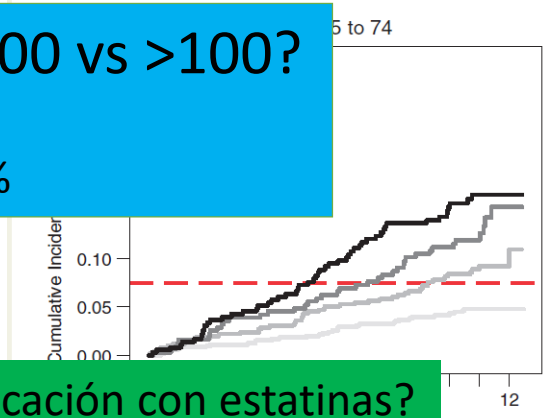
Subset	HR (95% CI)	*P*-value
Age category		
45–54	1.20 (1.11–1.29)	<0.001
55–64	1.16 (1.10–1.22)	<0.001
65–74	1.13 (1.08–1.18)	<0.001
75–84	1.12 (1.06–1.17)	<0.001
Sex		
Male		
Female		
Race or ethnicity		
White		
Chinese		
Black	1.13 (1.08–1.18)	<0.001
Hispanic	1.14 (1.09–1.20)	<0.001
Lipid-lowering medication at baseline		
No	1.14 (1.10–1.17)	<0.001
Yes	1.14 (1.10–1.17)	<0.001
Overall	1.14 (1.10–1.17)	<0.001



¿Utilizamos CAC < 0 vs >0 o <100 vs >100?

- CAC= 0 tienen riesgo <5%,
- CAC> 100 tienen un riesgo >7.5%

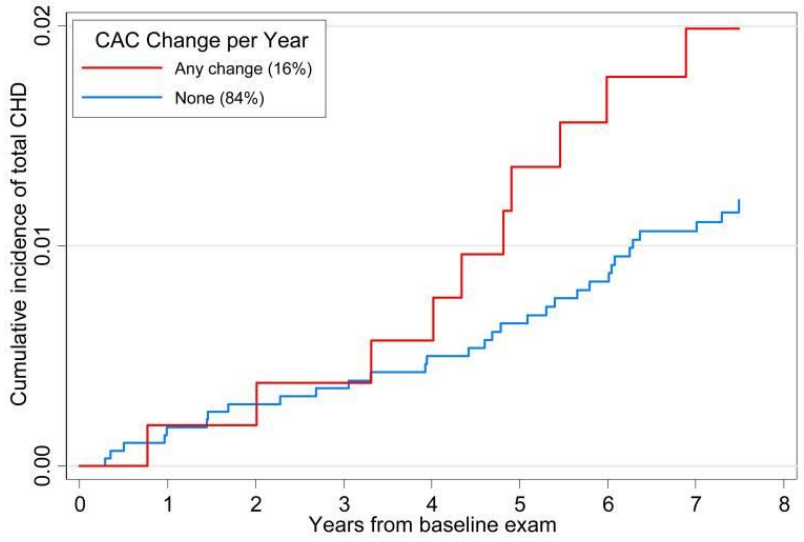
¿No modificación con estatinas?

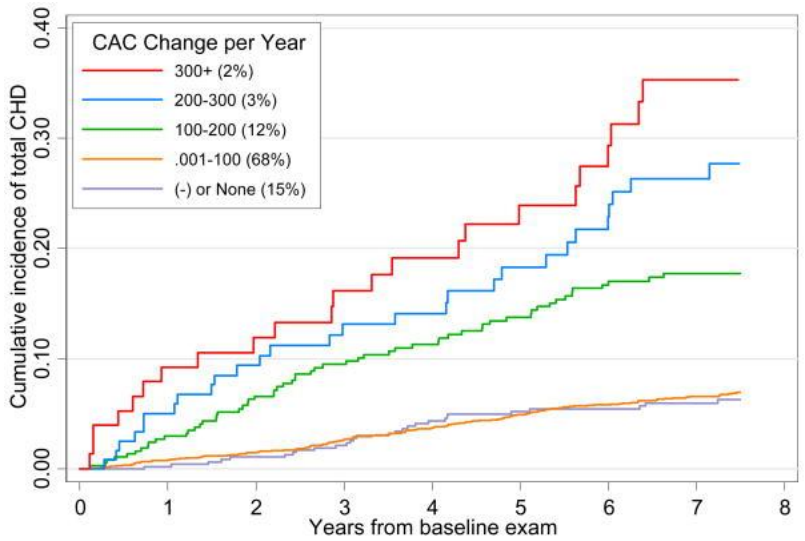


N=6,783. Red dashed line shows 7.5% risk.

Progression of Coronary Calcium and Incident Coronary Heart Disease Events: The Multi-Ethnic Study of Atherosclerosis

Dr. Matthew J. Budoff, MD, Dr. Rebekah Young, PhD, Mr. Victor A. Lopez, MS, Dr. Richard





¿Repetición CAC? ¿a qué intervalos?

J Am Coll Cardiol. 2013; 61: 1231–1239.

Prevalence of Significant Noncardiac Findings on Coronary Multidetector Computed Tomography Angiography in Asymptomatic Patients

Bachar N. Gil, MD,†‡ Kornowski Ran, MD,†‡§ Gaspar Tamar, MD,‡// Fuchs Shmuell, MD,†§ and Atar Eli, MD*†‡*

J Comput Assist Tomogr 2007;31:1Y4

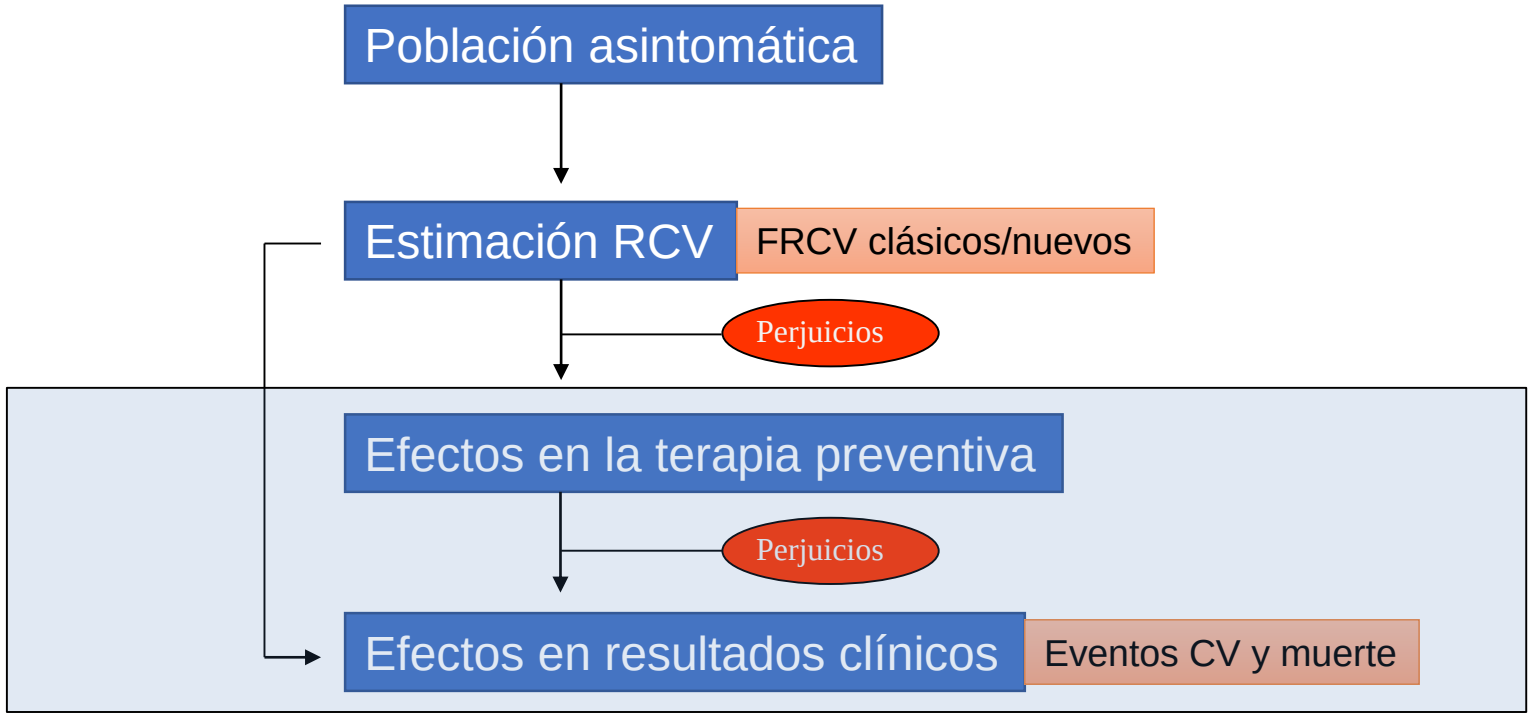
TABLE 2. Summary of Extracardiac Abnormalities in 258 Asymptomatic Patients

	No. Patients (%) (n = 258)
Lung abnormalities	91 (35.3%)
Emphysema and bulla	28
Interstitial lung disease	3
Pulmonary nodule <10 mm	49
Pulmonary mass >10 mm	3
Lung infiltrate	8
Pericardial abnormalities	10 (3.8%)
Vascular abnormalities	5 (1.9%)
Aneurysmal dilatation of ascending aorta	4
Ectasia of innominate artery	1
Enlarged mediastinal lymph node	4 (1.5%)
Esophageal wall thickening	1 (0.4%)
Retrosternal thymus	3 (1.1%)
Diaphragmatic hernia	6 (2.3%)
Liver abnormalities	12 (4.6%)
Multiple cysts	5
Calcified cyst	1
Liver mass	5
Fatty liver	1
Adrenal mass	8 (3.1%)
Thyroid abnormalities	8 (3.1%)
Bone abnormalities	3 (1.1%)

Incidentalomas en 56% pacientes
- -Mayoría sin significación clínica
- - Algunos tumores malignos

Exploraciones/procedimientos para seguimiento:
- - Caros
- - Invasivos/radiación adicional
- - Ansiedad del paciente.

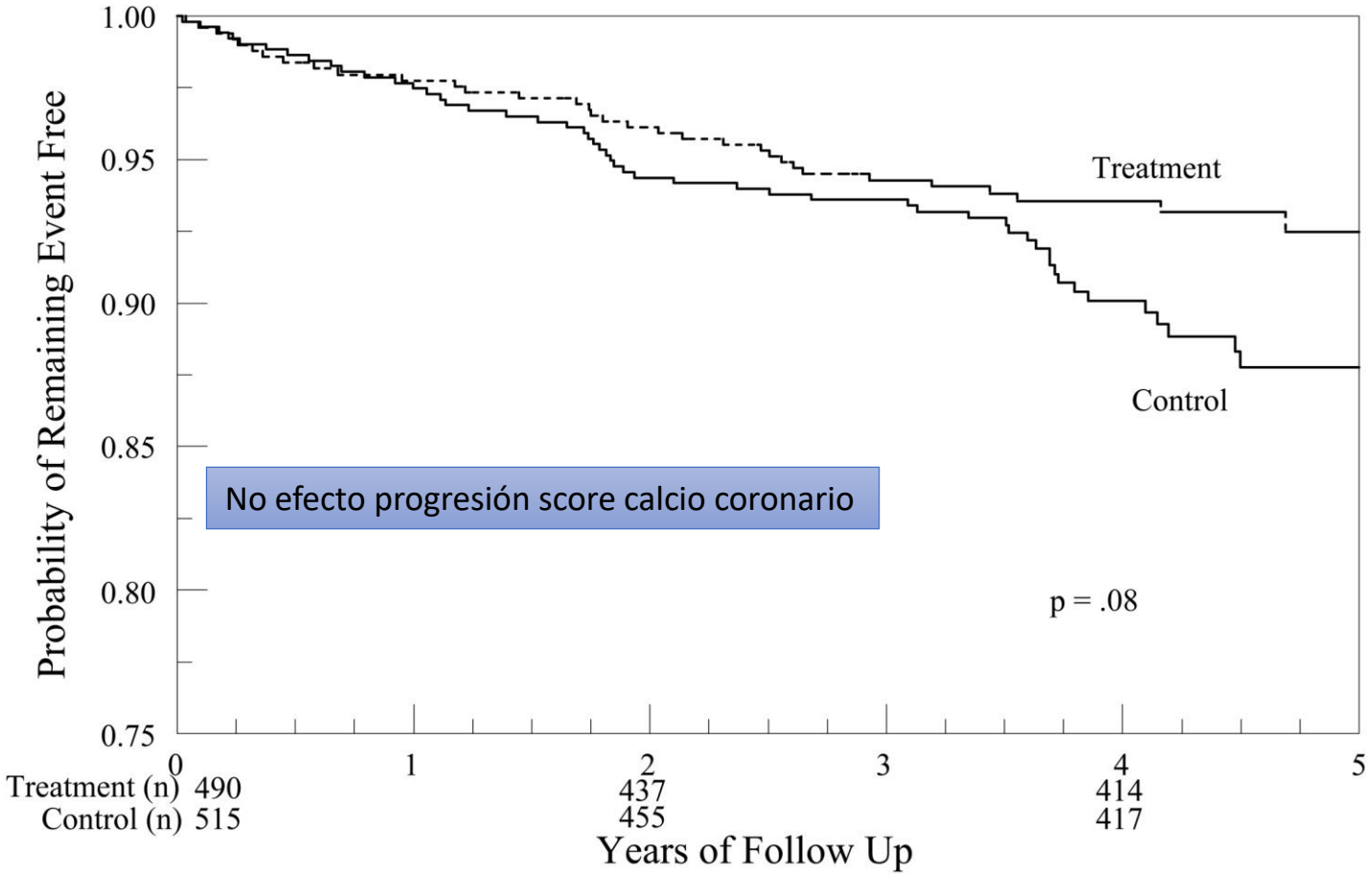
Evaluación de la estrategia de prevención



Treatment of Asymptomatic Adults With Elevated Coronary Calcium Scores With Atorvastatin, Vitamin C, and Vitamin E

The St. Francis Heart Study Randomized Clinical Trial

1005 sujetos 50-70 a sin ECV y CAC >p 80 por edad y sexo

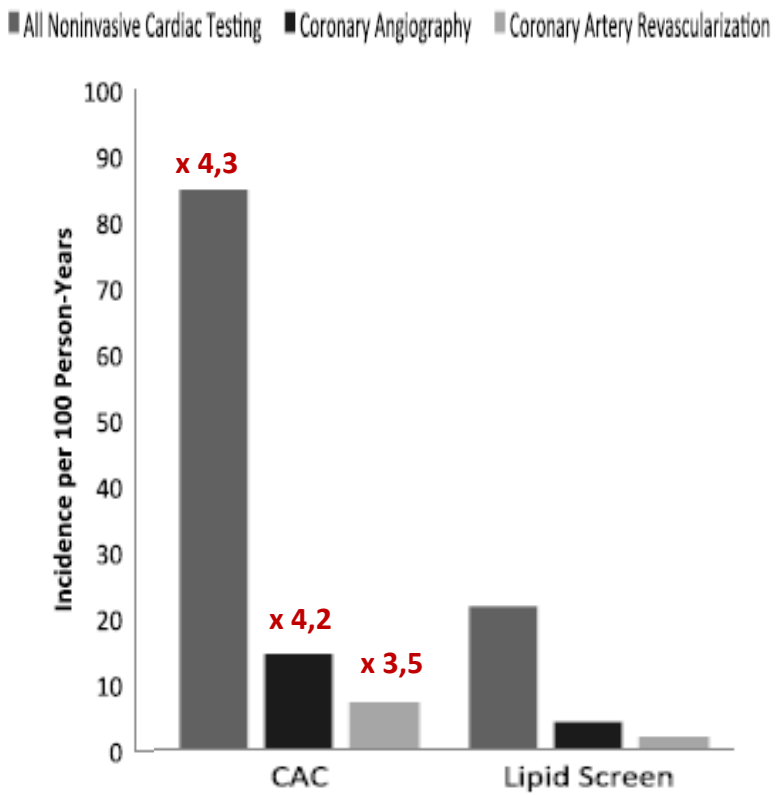


Arad Y,. J Am Coll Cardiol. 2005;46:166-72.

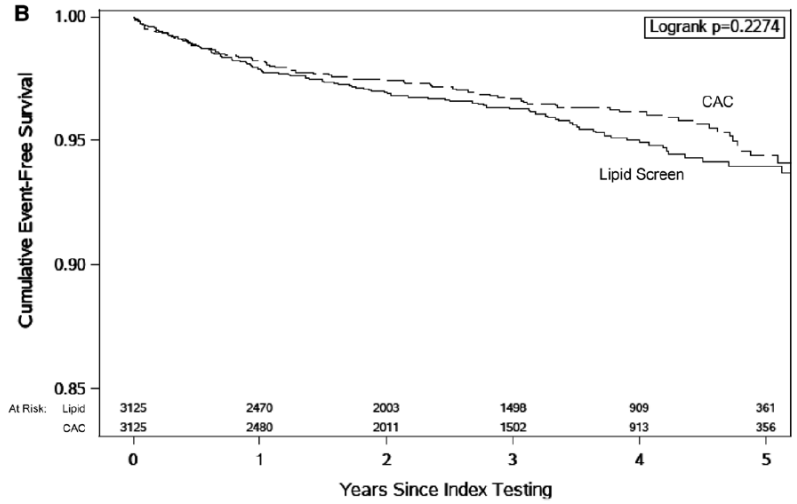
Outcomes After Coronary Artery Calcium and Other Cardiovascular Biomarker Testing Among Asymptomatic Medicare Beneficiaries

Jacqueline Baras Shreibati, MD, MS; Laurence C. Baker, PhD;
Michael V. McConnell, MD, MSEE; Mark A. Hlatky, MD

Procedimientos CV



Muerte, IAM, Ictus



Gasto relacionado con ECV en 3 años

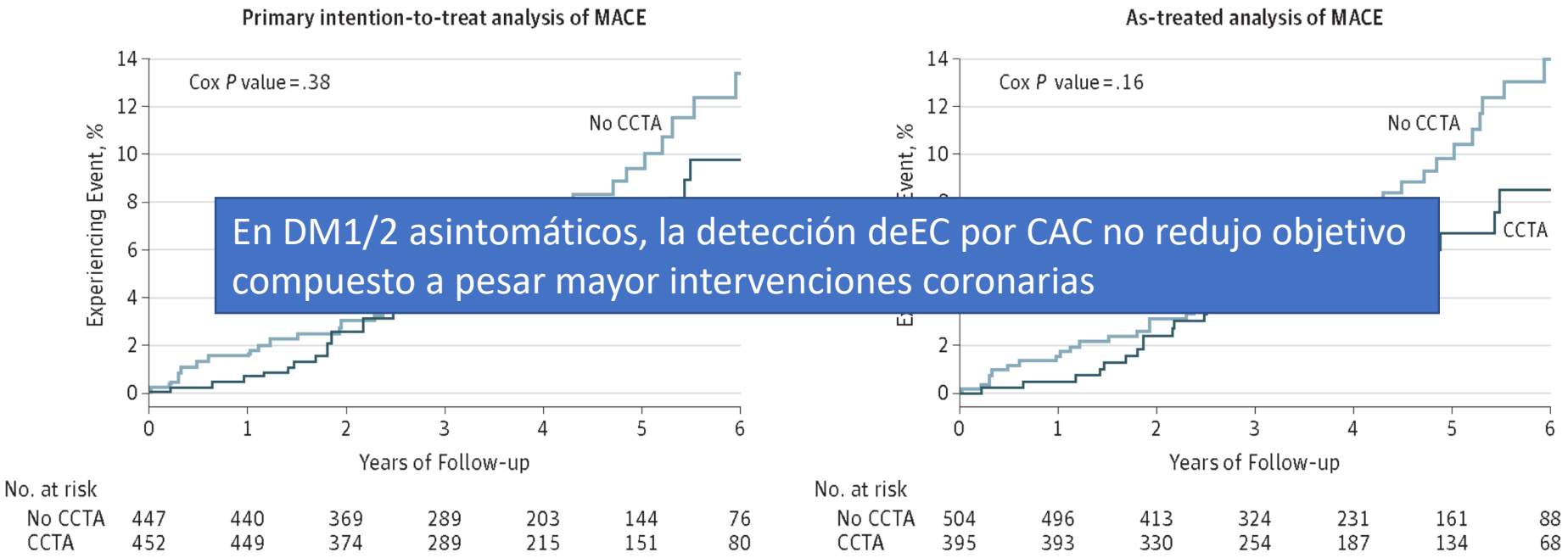
- CAC: 6525 $
- Detección de lípidos: 3073 $

Circ Cardiovasc Imaging. 2014;7(4):655-662.

Effect of Screening for Coronary Artery Disease Using CT Angiography on Mortality and Cardiac Events in High-Risk Patients With Diabetes

The FACTOR-64 Randomized Clinical Trial

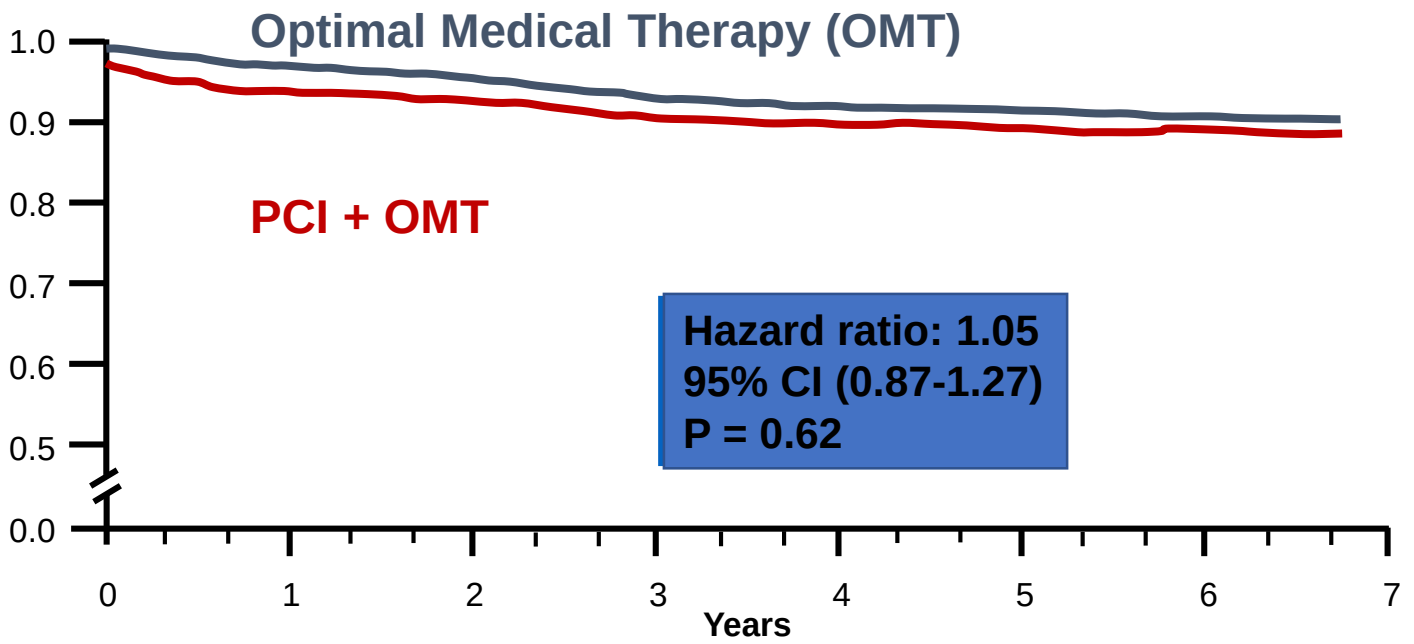
Primary Composite End Point (MACE; Death, Nonfatal Myocardial Infarction, or Hospitalization for Unstable Angina)



En DM1/2 asintomáticos, la detección deEC por CAC no redujo objetivo compuesto a pesar mayor intervenciones coronarias

Muhlestein JB. JAMA. 2014;312(21):2234-2243. doi:10.1001/jama.2014.15825

Survival Free of Death from Any Cause and Myocardial Infarction



Number at Risk

Medical Therapy	1138	1017	959	834	638	408	192	30
PCI	1149	1013	952	833	637	417	200	35

JAMA | US Preventive Services Task Force | RECOMMENDATION STATEMENT

Risk Assessment for Cardiovascular Disease With Nontraditional Risk Factors

US Preventive Services Task Force Recommendation Statement

- The USPSTF found adequate evidence that adding the ABI, hsCRP level, and CAC score to existing CVD risk assessment models results in small improvements in discrimination and risk reclassification
- The USPSTF found inadequate evidence to assess whether treatment decisions guided by the ABI, hsCRP level, or CAC score, in addition to risk factors in existing CVD risk assessment models, leads to reduced incidence of CVD events or mortality

CONCLUSIONS AND RECOMMENDATION The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of adding the ABI, hsCRP level, or CAC score to traditional risk assessment for CVD in asymptomatic adults to prevent CVD events. (I statement)

JAMA. doi:10.1001/jama.2018.8359. Published online July 10, 2018.

2016 European Guidelines on cardiovascular disease prevention in clinical practice

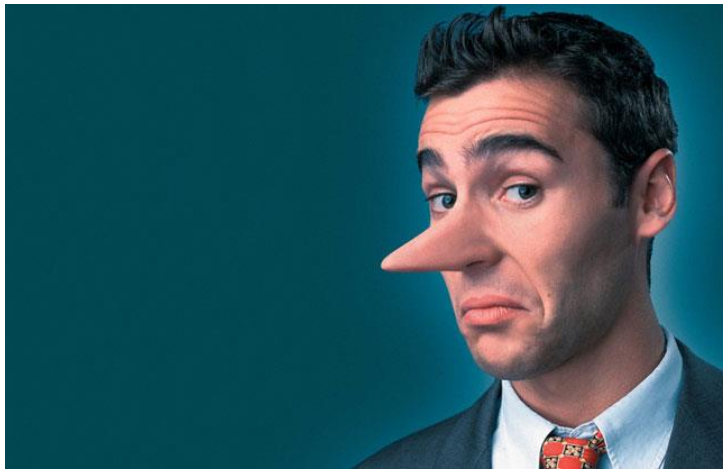
Class IIb	*Usefulness/efficacy is less well established by evidence/opinion.*	May be considered
Class III	Evidence or general agreement that the given treatment or procedure is not useful/effective, and in some cases may be harmful.	Is not recommended

Recommendations for imaging methods

Recommendations	Class[a]	Level[b]	Ref[c]
Coronary artery calcium scoring may be considered as a risk modifier in CV risk assessment.	IIb	B	120–125
Atherosclerotic plaque detection by carotid artery scanning may be considered as a risk modifier in CV risk assessment.	IIb	B	126–128
ABI may be considered as a risk modifier in CV risk assessment.	IIb	B	129–132
Carotid ultrasound IMT screening for CV risk assessment is not recommended.	III	A	128, 133

¿Sigue en sus trece Dr Escalada?

Lo nuevo, no es siempre lo mejor



Dr Escalada

"La verdad ... Es algo hermoso y terrible, y por lo tanto, debe tratarse con gran precaución".

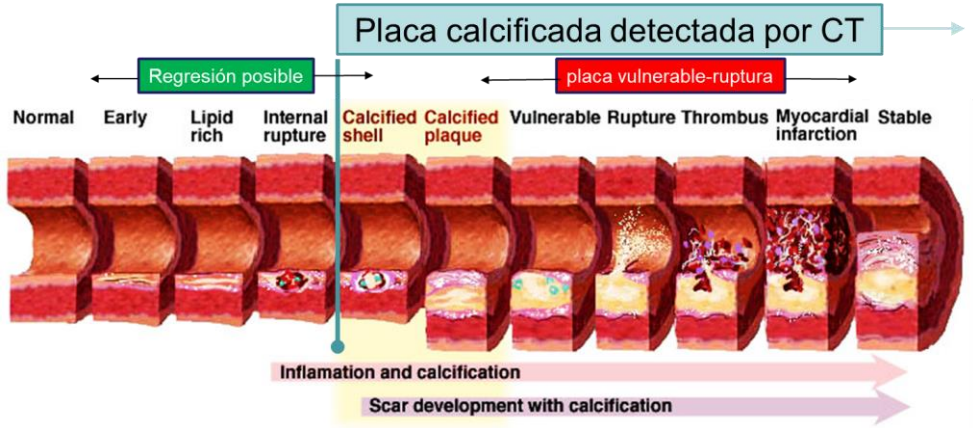
- J. K. Rowling, Harry Potter y la piedra del hechicero

¿Incorporación estudios de imagen en la evaluación del RCV?

Valor Añadido = Satisfacción necesidades / Recursos empleados

Incorporación estudios de imagen	
Estrategia NOVER (0-10)	
Necesidad?	9
Oportunidad?	9
Viabilidad?	4
Equidad?	5
Resultados?	-/??

La ↓riesgo ECV tras reclasificación con CAC/ABI aún no se ha demostrado.



¿Inicio tardío de la prevención?

Evaluación del RCV

¿Necesidad de nuevo enfoque ?

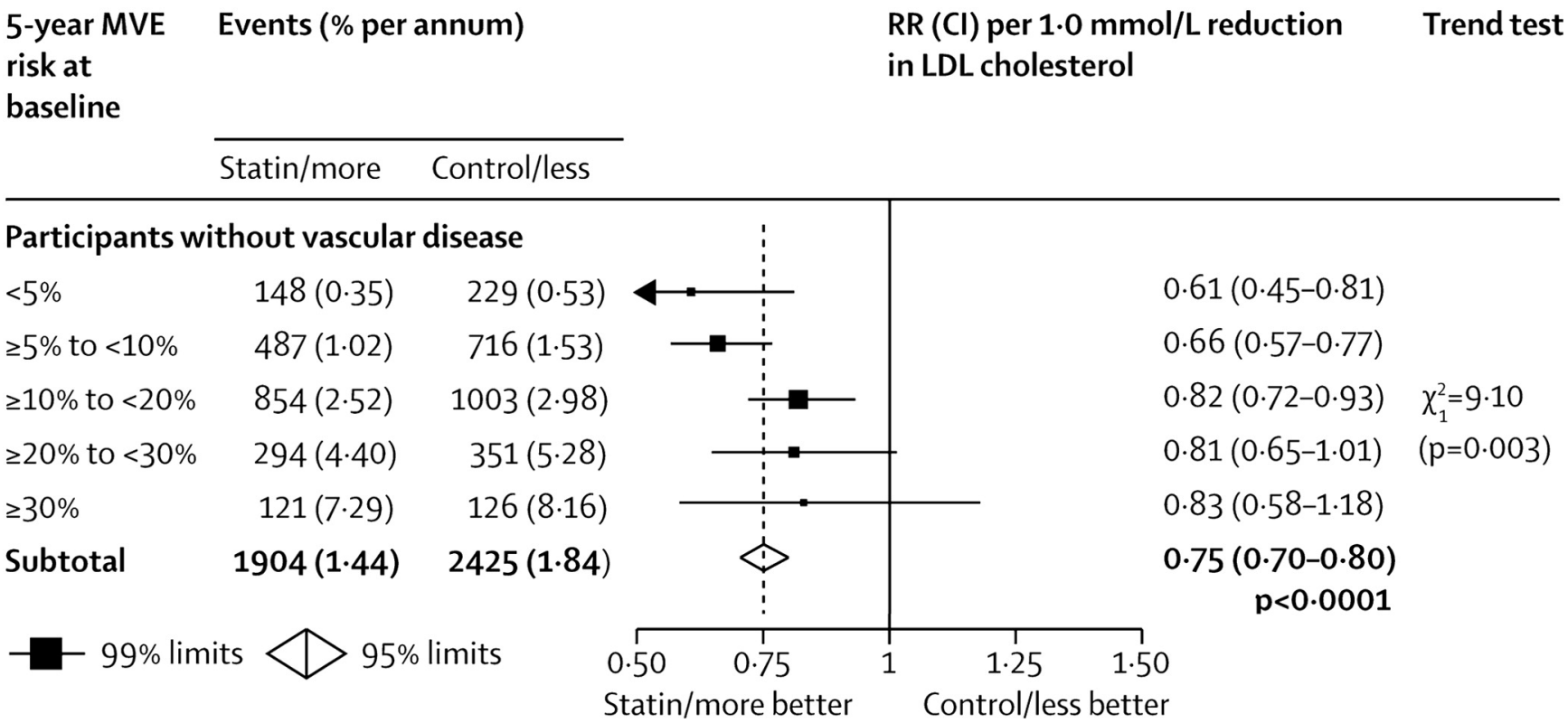
- La regresión y normalización de la función vascular puede ocurrir si la disminución del cLDL ocurre:

  -Temprano en el curso de la aterosclerosis

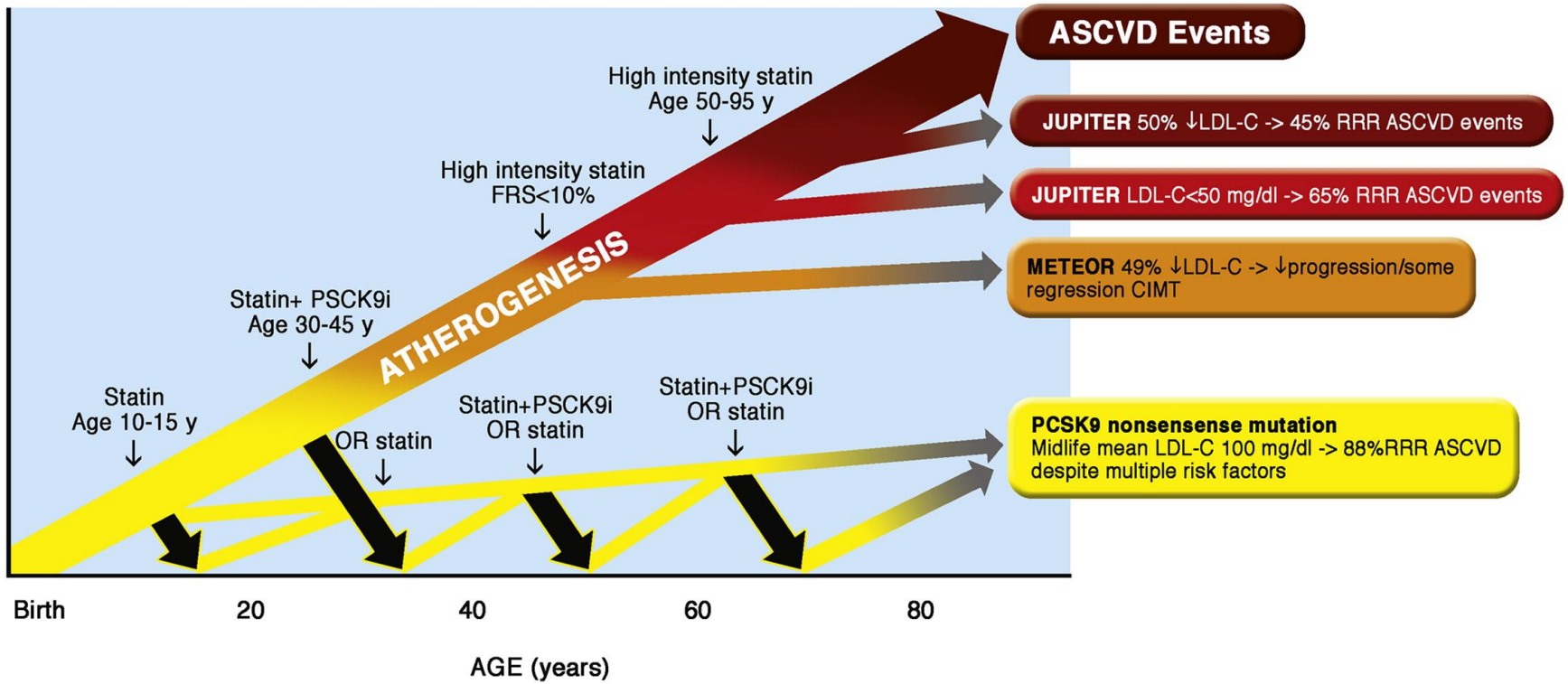
  -De forma muy agresiva en fases más tardías.

- ¿Riesgo clínico a corto plazo o a tiempo de vida?

Effects on Major Atherosclerotic Cardiovascular Disease Events per 1.0-mmol/l (39 mg/dl) Reduction in LDL-C

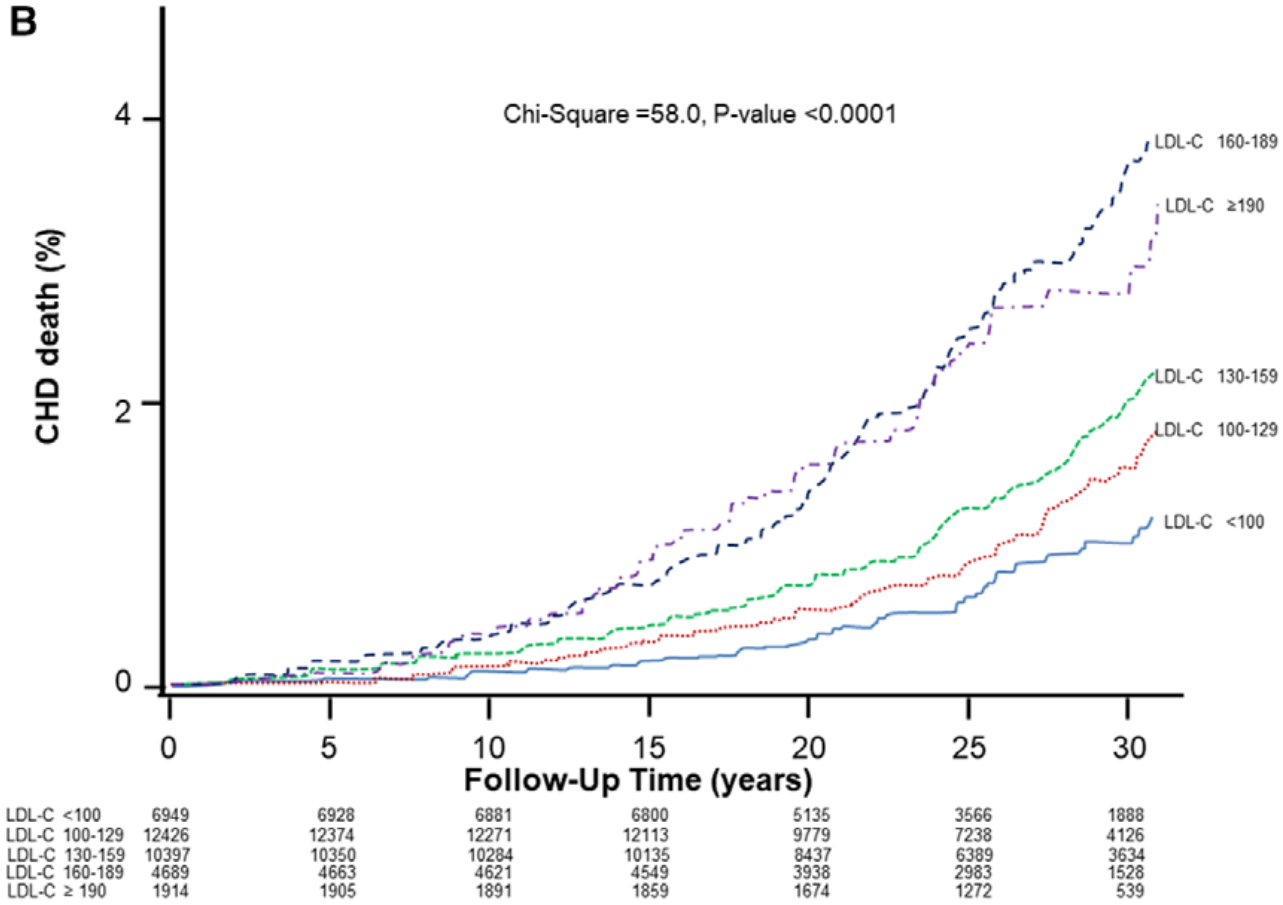


Conceptual Model for Resetting Vascular Age Clock Approach to the Primary Prevention of ASCVD



LDL-C Prognosis in Low-Risk Population

36 375 subjects of Cooper Clinic Longitudinal Study with 10-year estimated risk of CVD <7.5% followed for >2 decades (median of 26.8 years),

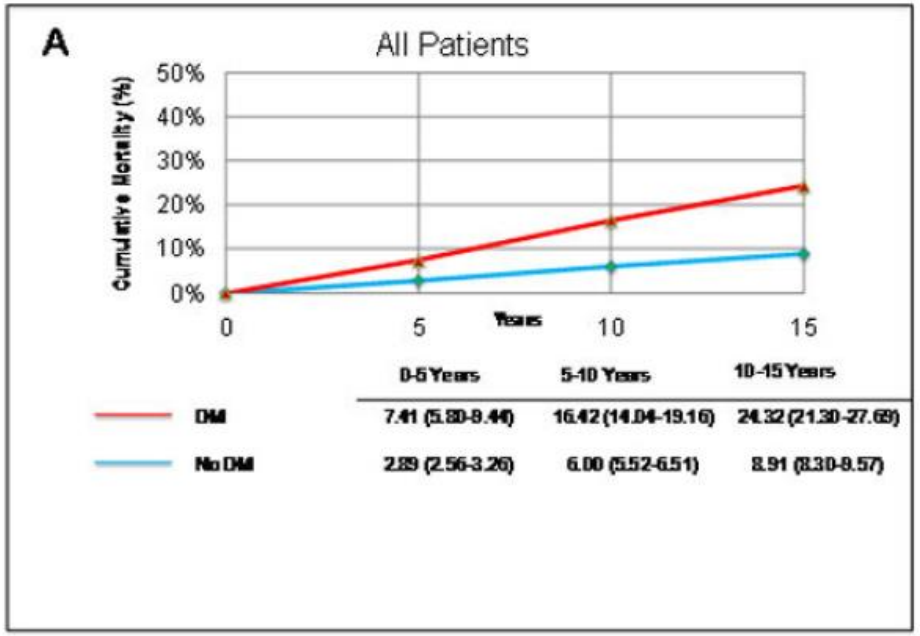


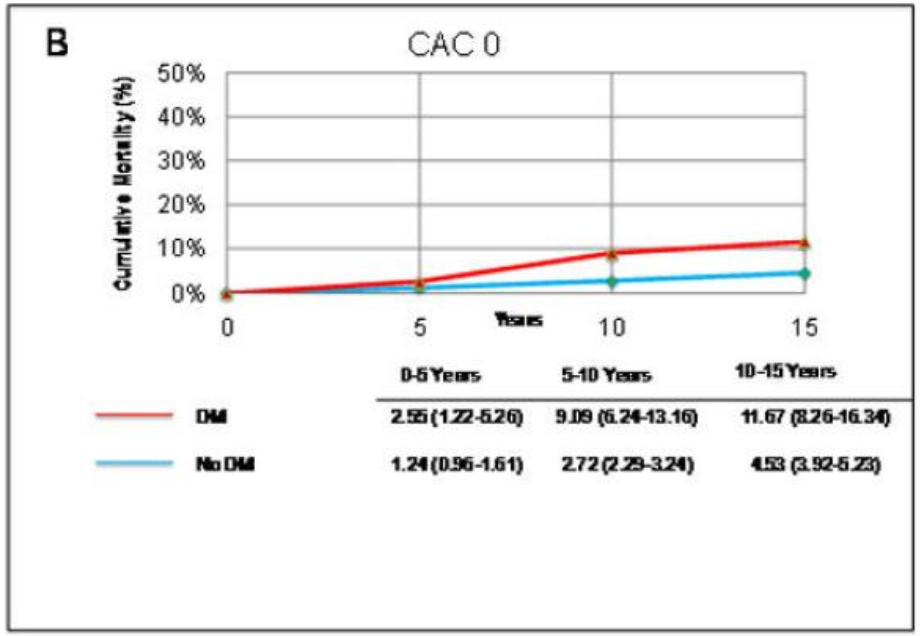
↑ 50-80% RR mortalidad CV

Circulation. 2018;138:00–00. DOI: 10.1161/CIRCULATIONAHA.118.034273

Absence of Coronary Artery Calcium Identifies Asymptomatic Diabetic Individuals at Low Near-Term But Not Long-Term Risk of Mortality: A 15-Year Follow-Up Study of 9715 Patients

Cumulative mortality rate over 15 years of follow-up among diabetic and non-diabetic individuals stratified by coronary artery calcification (CAC) score (A) CAC=0, (B) CAC 1–399, and (C) CAC ≥ 400.





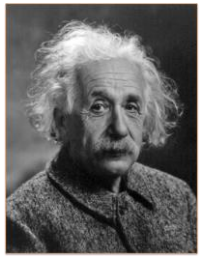
Circ Cardiovasc Imaging. 2016 Feb; 9(2): e003528.

La solución hoy

Pacientes jóvenes con riesgo bajo e intermedio

Yogi Berra

"Es difícil hacer predicciones, especialmente sobre el futuro"..



Albert Einstein

“Es una locura seguir haciendo lo mismo y esperar que las cosas cambien”

- Cálculo del RCV a 10 años + evaluación clínica
- Cálculo del RCV a 10 años +cálculo RCV de por vida
  - QRISK: Reino Unido)
  - American College of Cardiology/American Heart Association). Estados Unidos
  - IBERLIFERISK. España

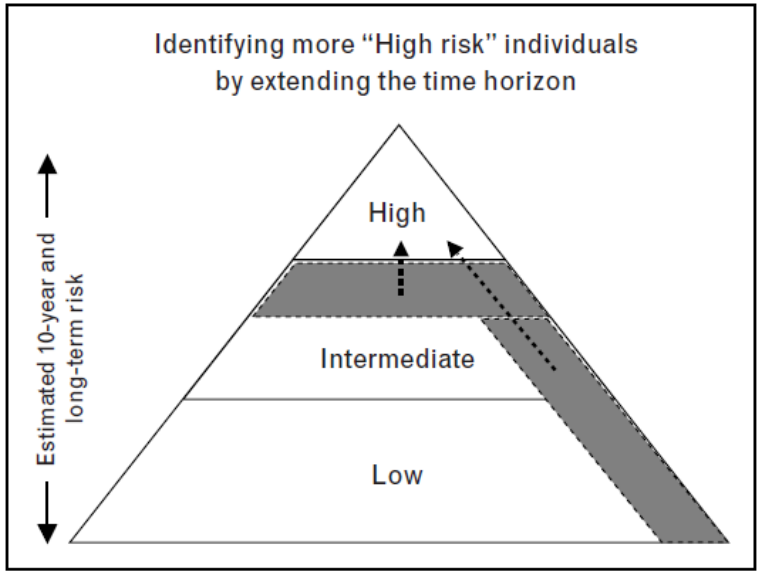
¿Riesgo a 10 años o de por vida?

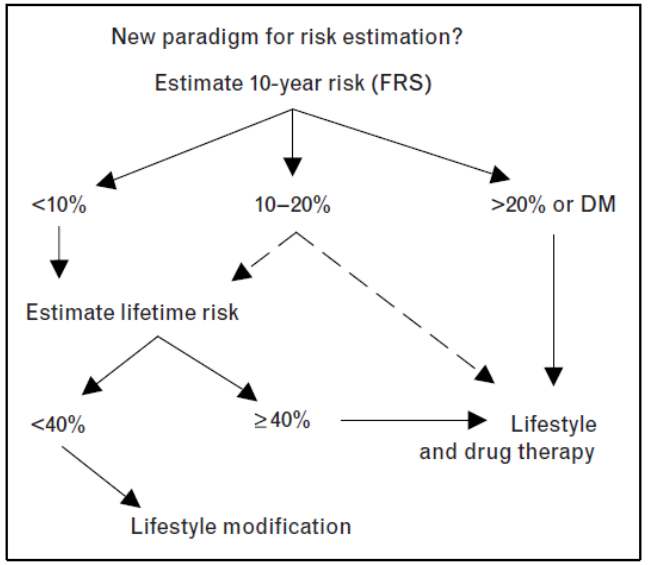
Enfoque basado en riesgo absoluto a 10 años (Dependencia cronológica de edad)

- No identificación Individuos jóvenes de alto riesgo
- Puede retrasar la intervención hasta edades más avanzadas

Enfoque basado en el riesgo de por vida

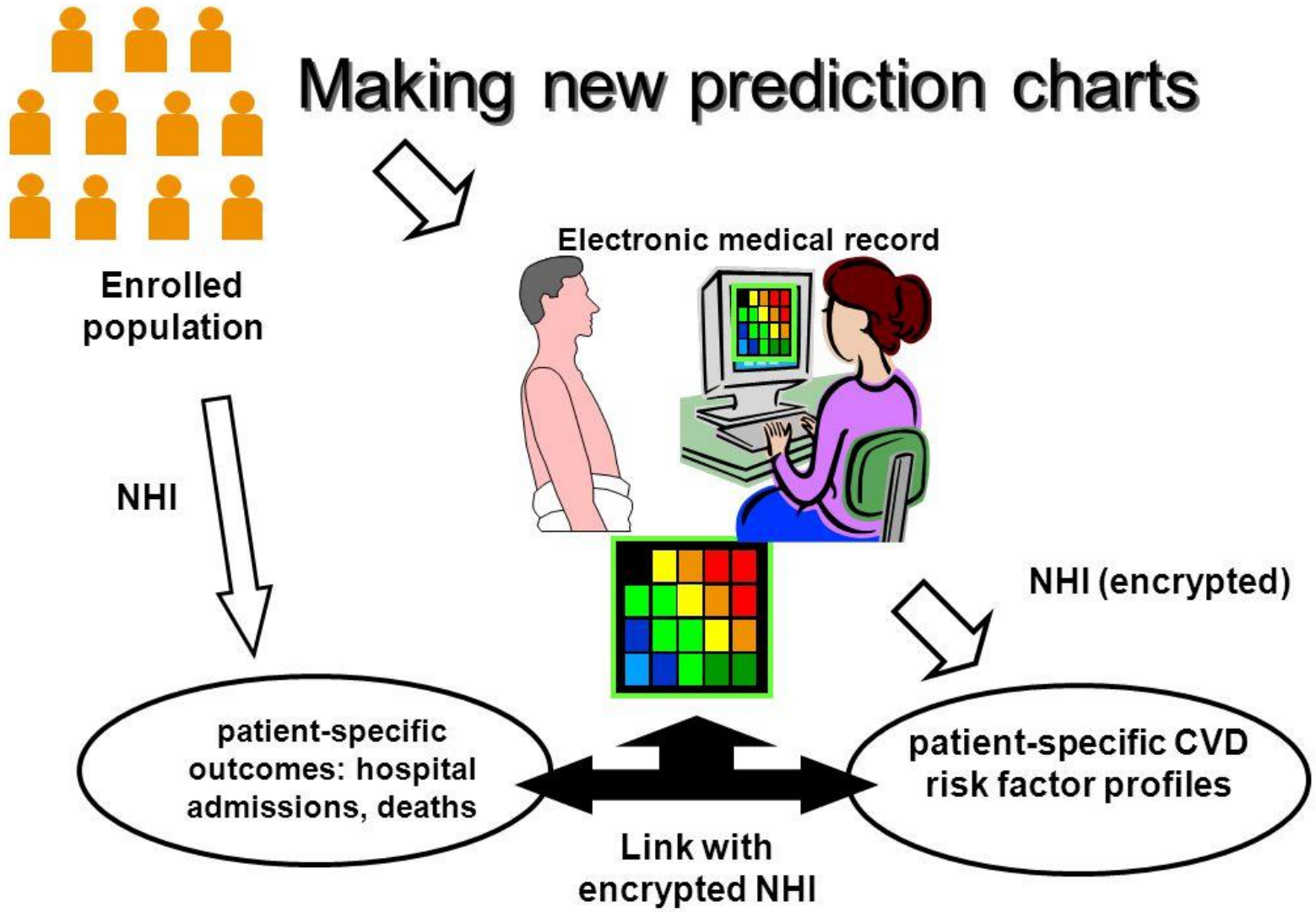
- "La intervención temprana paga dividendos a largo plazo"





Curr Opin Lipidol 2006;17:619–625

La solución mañana



El debate