Estratificación del riesgo cardiovascular

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Conflictos de interés

- Conferencista: Astra Zeneca, Abbott Nutrición, Novartis, Novo Nordisk, Merck Sharp & Dohme, Roche, Glaxo SmithKline, Sanofi Aventis, Bayer, Pfizer
- Advisory Board: Novartis Oncology, Sanofi Aventis, Astra Zeneca, Novo Nordisk, Stendhal, Pfizer
- Investigación clínica: Astra Zeneca, Novartis Pharma Logistics Inc., Merck Sharp & Dohme, Glaxo SmithKline, Organon, Boehringer Ingelheim, Roche, Novo Nordisk, Novartis Oncology

Agenda

- Por qué estratificar el riesgo?
- Identificando grupos de algo y bajo riesgo
- Riesgo intermedio, cómo evaluarlos?
- Cuál escala de riesgo utilizar?

Introducción

- La enfermedad cardiovascular es la primera causa de muerte (no violenta) en la población occidental incluyendo Costa Rica
- Siempre se ha dicho que la prevención debe iniciar desde la infancia, pero esto no implica necesariamente fármacos
- Evidentemente el riesgo cardiovascular difere entre individuos
- La decisión de dar tratamiento se basa en un balance riesgo beneficio

Intervención farmacológia

- Pros
  - Prevención de eventos cardiovasculares
  - Prevención de demencia vascular?
  - Reducción de mortalidad total (especialmente con estatinas)
- Contras
  - Costo
  - Adherencia (incluyendo otros fármacos)
  - Interacciones medicamentosas
  - Efectos adversos
  - Mitos de los pacientes

Pacientes de alto riesgo

Alto riesgo

- Este es un grupo más fácil de identificar
- Pacientes que han tenido eventos cardiovasculares previos

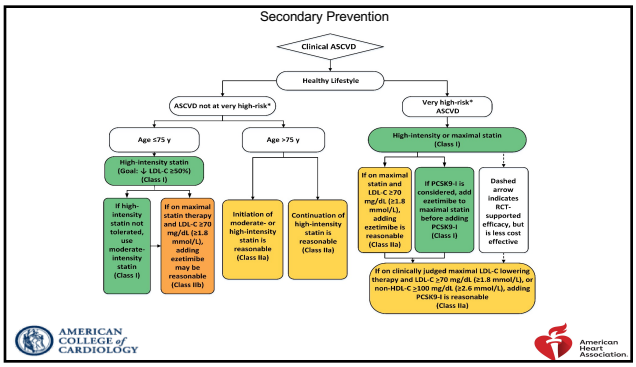

Table 4. Very High-Risk* of Future ASCVD Events

Major ASCVD Events
Recent ACS (within the past 12 mo)
History of MI (other than recent ACS event listed above)
History of ischemic stroke
Symptomatic peripheral arterial disease (history of claudication with ABI <0.85, or previous revascularization or amputation)

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Table 4 continued

High-Risk Conditions
Age ≥65 y
Heterozygous familial hypercholesterolemia
History of prior coronary artery bypass surgery or percutaneous coronary intervention outside of the major ASCVD event(s)
Diabetes mellitus
Hypertension
CKD (eGFR 15-59 mL/min/1.73 m²)
Current smoking
Persistently elevated LDL-C (LDL-C ≥100 mg/dL [≥2.6 mmol/L]) despite maximally tolerated statin therapy and ezetimibe
History of congestive HF

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Fig. 2. Treatment of T2DM for Primary Prevention of CVD

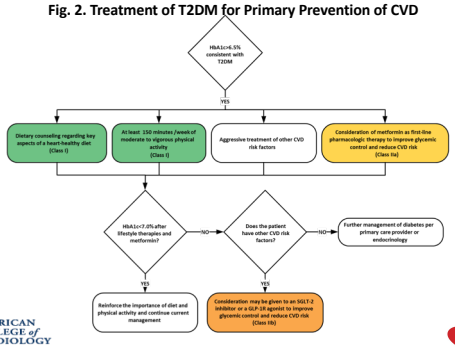

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Fig. 3.

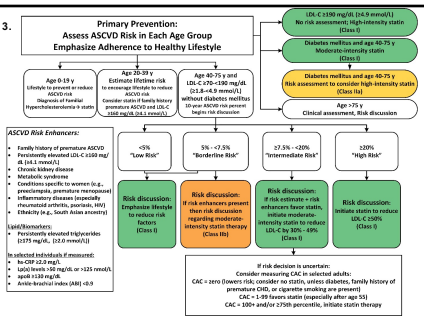

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Table 5. Diabetes-Specific Risk Enhancers That Are Independent of Other Risk Factors in Diabetes Mellitus

Risk Enhancers in Diabetic Patients
• Long duration (≥10 years for T2DM (S4.3-36) or ≥20 years for type 1 diabetes mellitus (S4.3-16)) • Albuminuria ≥30 mcg albumin/mg creatinine (S4.3-37) • eGFR <60 mL/min/1.73 m² (S4.3-37) • Retinopathy (S4.3-38) • Neuropathy (S4.3-39) • ABI <0.9 (S4.3-40, S4.3-41)

ABI indicates ankle-brachial index; eGFR, estimated glomerular filtration rate; and T2DM, type 2 diabetes mellitus.

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Diabetes Mellitus in Adults

Recommendations for Patients With Diabetes Mellitus		
COR	LOE	Recommendations
I	A	In adults 40 to 75 years of age with diabetes mellitus, regardless of estimated 10-year ASCVD risk, moderate-intensity statin therapy is indicated.
IIa	B-NR	In adults 40 to 75 years of age with diabetes mellitus and an LDL-C level of 70 to 189 mg/dL (1.7 to 4.8 mmol/L), it is reasonable to assess the 10-year risk of a first ASCVD event by using the race and sex-specific PCE to help stratify ASCVD risk.

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Diabetes Mellitus in Adults

Recommendations for Patients With Diabetes Mellitus		
COR	LOE	Recommendations
IIa	B-R	In adults with diabetes mellitus who have multiple ASCVD risk factors, it is reasonable to prescribe high-intensity statin therapy with the aim to reduce LDL-C levels by 50% or more.
IIa	B-NR	In adults older than 75 years of age with diabetes mellitus and who are already on statin therapy, it is reasonable to continue statin therapy.
IIb	C-LD	In adults with diabetes mellitus and 10-year ASCVD risk of 20% or higher, it may be reasonable to add ezetimibe to maximally tolerated statin therapy to reduce LDL-C levels by 50% or more.

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Diabetes Mellitus in Adults

Recommendations for Patients With Diabetes Mellitus		
COR	LOE	Recommendations
IIb	C-LD	In adults older than 75 years with diabetes mellitus, it may be reasonable to initiate statin therapy after a clinician–patient discussion of potential benefits and risks.
IIb	C-LD	In adults 20 to 39 years of age with diabetes mellitus that is either of long duration (≥10 years of type 2 diabetes mellitus, ≥20 years of type 1 diabetes mellitus), albuminuria (≥30 mcg of albumin/mg creatinine), estimated glomerular filtration rate (eGFR) less than 60 mL/min/1.73 m^2, retinopathy, neuropathy, or ankle-brachial index (ABI; <0.9), it may be reasonable to initiate statin therapy.

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Table 5. Diabetes-Specific Risk Enhancers That Are Independent of Other Risk Factors in Diabetes Mellitus

Risk Enhancers
• Long duration (≥10 years for type 2 diabetes mellitus (S.4.3-20) or ≥20 years for type 1 diabetes mellitus)
• Albuminuria ≥30 mcg of albumin/mg creatinine
• eGFR <60 mL/min/1.73 m^2
• Retinopathy
• Neuropathy
• ABI <0.9

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El otro extremo… los de bajo riesgo

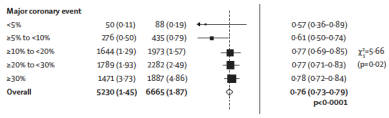
Bajo riesgo

- Aquí incluye por lo general pacientes menores de 40 años de edad sin factores de riesgo conocidos
- Incluyen niños en ausencia de historia familiar de eventos coronarios prematuros
- En mayores de 18 años se puede calcular el riesgo y repetir cada 3-5 años

El problema principal… los de riesgo intermedio

Hay un umbral donde la intervención no es efectiva?

Metanálisis CTT: eventos coronarios



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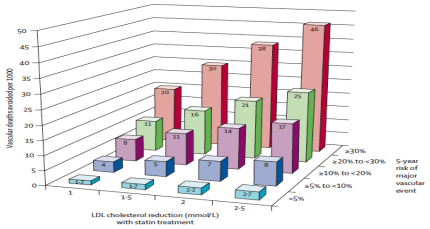
CTT. Lancet. 2012;May 17. Online.

Reducción de muerte cardiovascular según LDL y riesgo CV de base



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CTT. Lancet. 2012;May 17. Online.

Ejemplos de casos

Parámetro	Caso 1	Caso 2	Caso 3
Edad	45	55	65
Hipertensión (tx)	No	Si	Si
Presión	150/90	140/90	140/90
Tabaquismo	No	No	No
Colesterol total	235 mg/dl	235 mg/dl	235 mg/dl
HDL	35 mg/dl	35 mg/dl	35 mg/dl
Triglicéridos	185 mg/dl	185 mg/dl	185 mg/dl
LDL	163 mg/dl	163 mg/dl	163 mg/dl
Riesgo (calculado por Pooled Cohort Equation)			
RRA			
NNT			
NNH (NOD)			

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Ejemplos de casos

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Triglicéridos	185 mg/dl	185 mg/dl	185 mg/dl
LDL	163 mg/dl	163 mg/dl	163 mg/dl
Riesgo (calculado por Pooled Cohort Equation)	5.4%	12.4%	23%
RRA	1,62%	3.72%	6.9%
NNT	61.72	26.88	14.49
NNH (NOD)	255	255	255
NNH/NNT	4.13	9,51	17,59

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Poniéndolo en balance

Riesgos

- Es independiente del riesgo CV del paciente
- Algunos factores pueden aumentar el riesgo
  - Polifarmacia
  - Adultos mayores
  - Susceptibilidad genética

Beneficios

- Es dependiente del riesgo CV del paciente
- Si el paciente es de alto riesgo, no debe dejarse de lado el control de los otros factores de riesgo

Qué hacer en riesgo intermedio?

- Es tratar de encontrar el balance entre riesgo y beneficio
- Buscar aquel paciente que más se puede beneficiar
- La estrategia de dar tratamiento a todos no sería conveniente ya que el riesgo de eventos adversos podría ser mayor

Table 6. Risk-Enhancing Factors for Clinician–Patient Risk Discussion

Risk-Enhancing Factors
• **Family history of premature ASCVD** (males, age <55 y; females, age <65 y) • **Primary hypercholesterolemia** (LDL-C, 160–189 mg/dL [4.1–4.8 mmol/L); non–HDL-C 190–219 mg/dL [4.9–5.6 mmol/L])* • **Metabolic syndrome** (increased waist circumference, elevated triglycerides [>175 mg/dL], elevated blood pressure, elevated glucose, and low HDL-C [<40 mg/dL in men; <50 in women mg/dL] are factors; tally of 3 makes the diagnosis) • **Chronic kidney disease** (eGFR 15–59 mL/min/1.73 m^2 with or without albuminuria; not treated with dialysis or kidney transplantation) • **Chronic inflammatory conditions** such as psoriasis, RA, or HIV/AIDS • **History of premature menopause (before age 40 y) and history of pregnancy-associated conditions that increase later ASCVD risk such as preeclampsia** • **High-risk race/ethnicities** (e.g., South Asian ancestry)

Table 6 continued

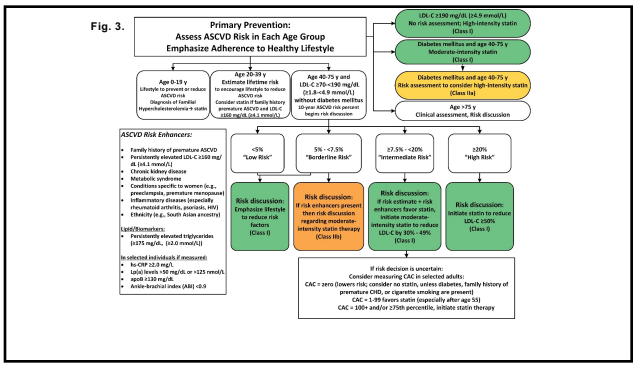
Risk-Enhancing Factors

• **Lipid/biomarkers**: Associated with increased ASCVD risk
  ○ Persistently* elevated, primary hypertriglyceridemia (≥175 mg/dL);
  ○ If measured:
  ▪ **Elevated high-sensitivity C-reactive protein** (≥2.0 mg/L)
  ▪ **Elevated Lp(a):** A relative indication for its measurement is family history of premature ASCVD. An Lp(a) ≥50 mg/dL or ≥125 nmol/L constitutes a risk-enhancing factor especially at higher levels of Lp(a).
  ▪ **Elevated apoB** ≥130 mg/dL: A relative indication for its measurement would be triglyceride ≥200 mg/dL. A level ≥130 mg/dL corresponds to an LDL-C >160 mg/dL and constitutes a risk-enhancing factor
  ▪ **ABI** <0.9

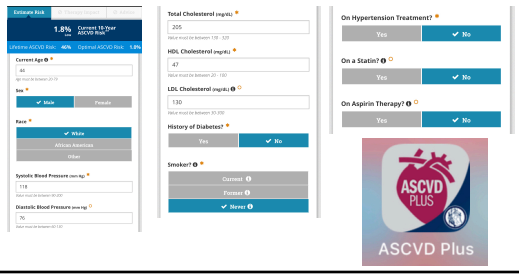
Calculadoras de riesgo

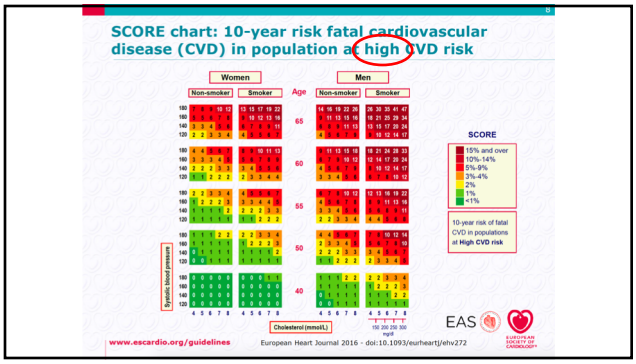
- Sirven para identificar aquel paciente que sea de un riesgo mayor
- Es un parámetro más objetivo que el “ojo clínico”
- Múltiples calculadoras de riesgo
- Variaciones según cada país y factores de riesgo incluidos
- Por lo tanto… Cuál usar?

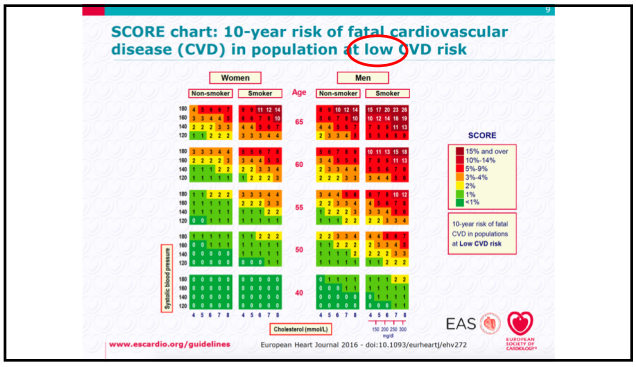
	Framinghan	Reynolds	ACC/AHA 2013	QRISK3	ERS-RA	RISK
Edad	✓	✓	✓	✓	✓	✓
Género	✓	✓	✓	✓	✓	✓
CT	✓	✓	✓	✓	✓	✓
HDL	✓	✓	✓	✓		✓
PAS	✓	✓	✓	✓		✓
Tx HTA	✓		✓	✓	✓	
DM			✓	✓	✓	
Tabaquismo	✓	✓	✓	✓	✓	✓
AHF		✓		✓		
hSPCR		✓				
Otros				AR, LES, FA, enfermedad mental, etnicidad, ERC, GC, IMC, DE, deprivación social	CDA, disabilidad, duración enfermedad, GC	País de alto o bajo riesgo
Predicción	Riesgo 10 años de EAC, ictus, EAP, FC, muerte cardíaca	Riesgo 10 años IAM, ictus, revascularíza-ción coronaria, muerte CV	Riesgo 10 años de IAM o ictus, muerte coronaria	Riesgo 10 años IAM, angina e ictus, ICT y muerte coronaria	Riesgo 10 años de IAM, ictus, muerte cardiovascular	Riesgo a 10 años de muerte cardiovsascular
Cortes	Alto >20%	No hay corte definido	Alto >20%%	Alto >20%		Alto >5%



Pooled cohort equation/ACC AHA 2013







Estrategias de intervención

Riesgo cardiovascular (SCORE)	Niveles de LDL colesterol				
	<70 mg/dl	70 a <100 mg/dl	100 a <155 mg/dl	155 a <190 mg/dl	≥190 mg/dl
<1%	Modificación de estilos de vida	Modificación de estilos de vida	Modificación de estilos de vida	Modificación de estilos de vida	Modificación de estilos de vida, considerer fármacos si no se controla
≥1% a <5%	Modificación de estilos de vida	Modificación de estilos de vida	Modificación de estilos de vida, considerer fármacos si no se controla	Modificación de estilos de vida, considerer fármacos si no se controla	Modificación de estilos de vida, considerer fármacos si no se controla
≥5% a <10% o alto riesgo	Modificación de estilos de vida	Modificación de estilos de vida, considerer fármacos si no se controla	Modificación de estilos de vida y fármacos para la mayoría	Modificación de estilos de vida y fármacos para la mayoría	Modificación de estilos de vida y fármacos para la mayoría
≥10% o muy alto riesgo	Modificación de estilos de vida, considerer fármacos si no se controla	Modificación de estilos de vida y fármacos para la mayoría	Modificación de estilos de vida y fármacos para la mayoría	Modificación de estilos de vida y fármacos para la mayoría	Modificación de estilos de vida y fármacos para la mayoría

Catapano AL. Eur Heart J. 2016;37(39):2999

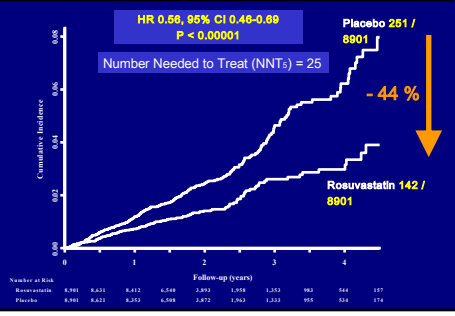
Inclusión por factores de riesgo

- QRISK3:
  - ACFA
  - Deprivación social, estrato socioeconómico: por Código postal del Reino Unido
  - IMC
  - Enfermedad renal crónica
  - Grupo étnico

JUPITER – Achieved LDL, Achieved hsCRP Analysis
Baseline Clinical Characteristics (N=15,548)

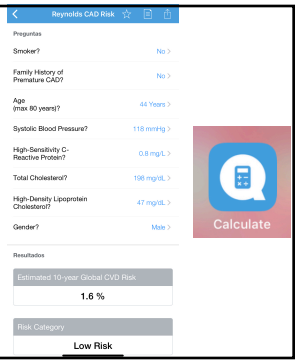
	Placebo	Rosuvastatin			
		LDL≥70	LDL<70	hsCRP≥2	hsCRP<2
Age, (years)	66	65	66	66	66
BMI, (kg/m2)	28.4	27.8	28.5	29.0	27.7
Blood pressure					
Systolic	134	134	135	135	134
Diastolic	80	80	80	80	80
Smoker, (%)	15.6	17.9	14.5	17.2	13.3
Fam His, (%)	11.8	11.3	11.7	11.0	12.4
Met Syn, (%)	41.5	38.3	42.2	43.5	37.8
hsCRP, mg/L	4.2	4.2	4.2	5.4	3.2
LDLC, mg/dL	108	112	106	108	109
HDLC, mg/dL	49	50	49	49	49
TG, mg/dL	118	115	119	120	116
ApoB:ApoA	0.7	0.7	0.7	0.7	0.7
HbA1c	5.7	5.7	5.7	5.7	5.7

JUPITER
Primary Trial Endpoint : MI, Stroke, UA/Revascularization, CV Death



Factores de riesgo

- Cómo incorporar hsPCR en nuestra práctica?
- La única calculadora de riesgo es Reynolds Risk Score
- Usa el cohort Framinghan y le agrega hsPCR



Limitantes de todas las calculadoras

- El problema fundamental es la población incluida en los diferentes cohortes de donde se calibran las diferentes calculadoras de riesgo
- Múltiples ejemplos donde el grupo étnico modifica el resultado
- RISK: países de alto y bajo riesgo
- QRISK3: etnicidad y por país de origen

Table 10 continued

	Racial/Ethnic Groupings			
	Asian Americans*	**Hispanic/Latino Americans†**	**Blacks**	**Comments**
Risk Decisions				
PCE	No separate PCE is available; use PCE for whites. PCE may underestimate ASCVD risk in South Asians. PCE may overestimate risk in East Asians.	**No separate PCE is available; use PCE for non-Hispanic whites. If African-American ancestry is also present, then use PCE for blacks.**	Use PCE for blacks.	Country-specific race/ethnicity, along with socioeconomic status, may affect estimation of risk by PCE.
CAC score	In terms of CAC burden, South Asian men were similar to non-Hispanic white men, but higher CAC when than blacks, Latinos, and Chinese Americans. South Asian women had similar CAC scores to whites and other racial/ethnic women, although CAC burden higher in older age.	**CAC predicts similarly in whites and in those who identify as Hispanic/Latino.**	In MESA, CAC score was highest in white and Hispanic men, with blacks having significantly lower prevalence and severity of CAC.	Risk factor differences in MESA between ethnicities did not fully explain variability in CAC. However, CAC predicted ASCVD events over and above traditional risk factors in all ethnicities.

Qué hacemos en Costa Rica?

- De hecho… sí hay una calculadora de riesgo calibrado para Costa Rica!
- Se calibró con los datos del Instituto Nacional de Estadística y Censos
- www.globorisk.org

Globorisk is the first cardiovascular disease risk score that predicts risk of heart attack or stroke in healthy individuals (those who have not yet had a heart attack or stroke) for all countries in the world. It uses information on a person's country of residence, age, sex, smoking, diabetes, blood pressure and cholesterol to predict the chance that they would have a heart attack or stroke in the next 10 years. If the person does not have a recent diabetes or cholesterol test, they can use the office-based version of Globorisk which is based on body weight and height instead.

Lancet Diabetes Endocrinol. 2017 March ; 5(3): 196–213. doi:10.1016/S2213-8587(17)30015-3.

Laboratory-based and office-based risk scores and charts to predict 10-year risk of cardiovascular disease in 182 countries: a pooled analysis of prospective cohorts and health surveys

Peter Ueda, Mark Woodward, Yuan Lu, Kaveh Hajifathalian, Rihab Al-Wotayan[*], Carlos A Aguilar-Salinas[*], Alireza Ahmadvand[*], Fereidoun Azizi[*], James Bentham[*], Renata Cifkova[*], Mariachiara Di Cesare[*], Louise Eriksen[*], Farshad Farzadfar[*], Trevor S Ferguson[*], Nayu Ikeda[*], Davood Khalili[*], Young-Ho Khang[*], Vera Lanska[*], Luz León-Muñoz[*], Dianna J Magliano[*], Paula Margozzini[*], Kelias P Msyamboza[*], Gerald Mutungi[*], Kyungwon Oh[*], Sophal Oum[*], Fernando Rodriguez-Artalejo[*], Rosalba Rojas-Martinez[*], Gonzalo Valdivia[*], Rainford Wilks[*], Jonathan E Shaw[*], Gretchen A Stevens[*], Janne S Tolstrup[*], Bin Zhou[*], Joshua A Salomon, Majid Ezzati, and Goodarz Danaei

LAB RISK CALCULATOR

Use this calculator if you know your serum cholesterol value and if you know whether you have diabetes.

OFFICE RISK CALCULATOR

Use this calculator if you do not know your serum cholesterol value or do not know if you have diabetes.

DOWNLOAD RISK CHARTS

Use this link to download lab-based or office-based risk charts for your country of interest.

Calculadora basado en laboratorios

Country
COSTA RICA

Gender
MALE

Your age?
40-44

Do you smoke?
NO

Do you have diabetes?
NO

Your systolic blood pressure (mmHg) 140

Your total cholesterol (mmol/L) 90

3%

YOUR PREDICTED RISK

This value shows the chance that you will have a heart attack or stroke in the next 10 years

Calculadora basado en la oficina

Country
COSTA RICA

Your Height (cm) 172

Your Weight (kg) 83

Gender
MALE

Your age?
40-44

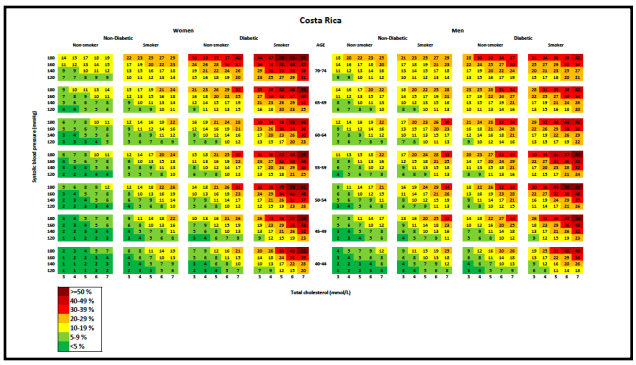
Do you smoke?
NO

Your systolic blood pressure (mmHg) 140

2%

YOUR PREDICTED RISK

This value shows the chance that you will have a heart attack or stroke in the next 10 years

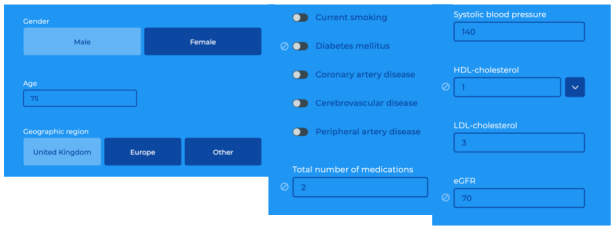


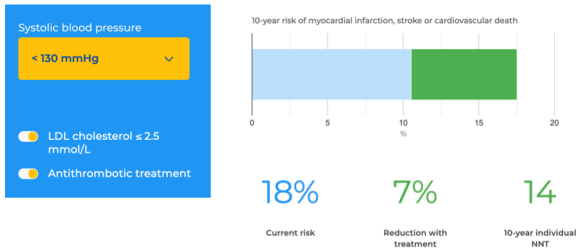
Otras poblaciones

Adultos mayores

Elderly Risk Score

- >70 años en prevención primaria o secundaria
- Riesgo de IAM, ictus o muerte vascular (MACE) en los siguientes 10 años
- Calculado usando el PROSPER y validado en los cohorts de SMART y ASCOT
- Para la región geográfica de ”otros” se usa los datos de Europa del norte y del este



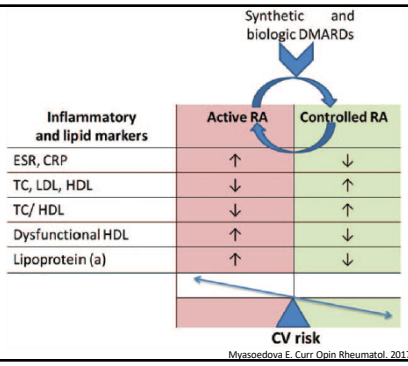


Pacientes reumatológicos

Recomendaciones EULAR 2016

Recommendations			
1. Disease activity should be controlled optimally in order to lower CVD risk in all patients with RA, AS or PsA	2b-3	B	9.1 (1.3)
2. CVD risk assessment is recommended for all patients with RA, AS or PsA at least once every 5 years and should be reconsidered following major changes in antirheumatic therapy	3–4	C	8.8 (1.1)
3. CVD risk estimation for patients with RA, AS or PsA should be performed according to national guidelines and the SCORE CVD risk prediction model should be used if no national guideline is available	3–4	C–D	8.7 (2.1)
4. TC and HDLc should be used in CVD risk assessment in RA, AS and PsA and lipids should ideally be measured when disease activity is stable or in remission. Non-fasting lipids measurements are also perfectly acceptable	3	C	8.8 (1.2)
5. CVD risk prediction models should be adapted for patients with RA by a 1.5 multiplication factor, if this is not already included in the model	3–4	C	7.5 (2.2)
6. Screening for asymptomatic atherosclerotic plaques by use of carotid ultrasound may be considered as part of the CVD risk evaluation in patients with RA	3–4	C–D	5.7 (3.9)
7. Lifestyle recommendations should emphasise the benefits of a healthy diet, regular exercise and smoking cessation for all patients	3	C	9.8 (0.3)
8. CVD risk management should be carried out according to national guidelines in RA, AS or PsA, antihypertensives and statins may be used as in the general population	3–4	C–D	9.2 (1.3)
9. Prescription of NSAIDs in RA and PsA should be with caution, especially for patients with documented CVD or in the presence of CVD risk factors	2a-3	C	8.9 (2.1)
10. Corticosteroids: for prolonged treatment, the glucocorticoid dosage should be kept to a minimum and a glucocorticoid taper should be attempted in case of remission or low disease activity; the reasons to continue glucocorticoid therapy should be regularly checked	3–4	C	9.5 (0.7)

Agca R. Ann Rheum Dis. 2017;76:17-28



Myasoedova E. Curr Opin Rheumatol. 2017;29:277

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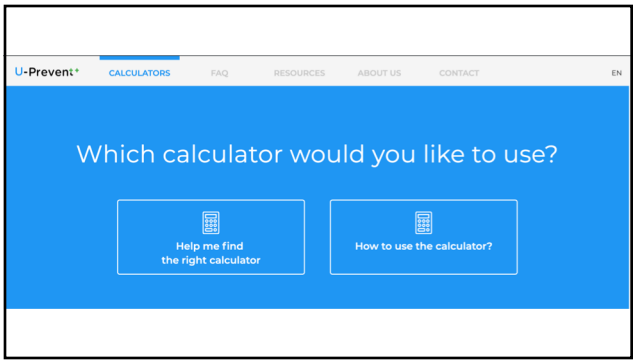

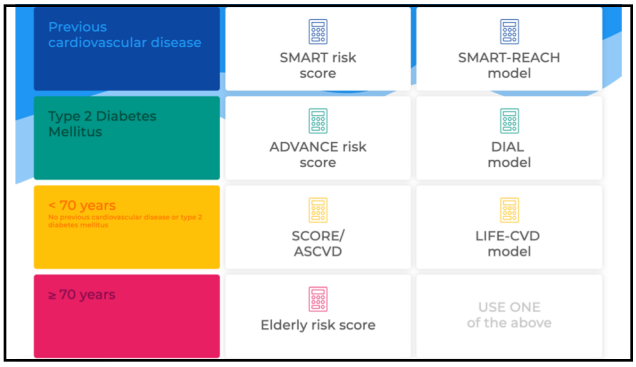

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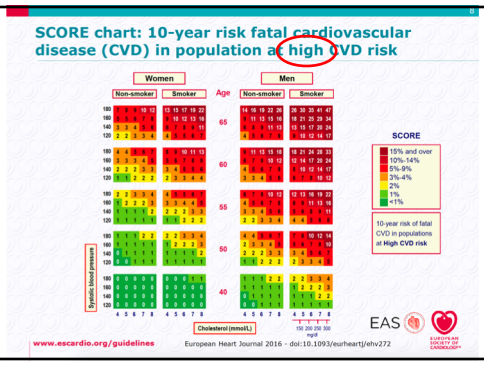
Consideraciones

- El riesgo es dinámico y va a ir cambiando con el tiempo
- Desde aparición de nuevos factores de riesgo hasta envejecimiento
- Debe calcularse periódicamente para ajustar el tratamiento
- Debe tomarse en cuenta que los valores que ingresa uno a las calculadoras de riesgo no está hecho para que sea bajo tratamiento

Otros usos

- Calculadoras de riesgo como herramienta educativa
- Calcular el riesgo a largo plazo
- Cuál es la edad cardiovascular?
- Cómo me comparo con alguien de la población general?
- Esto puede motivar a mayor adherencia a tratamiento por parte de paciente
- Explicar que en prevención primaria el objetivo es que la persona siga estando asintomática, no esperar a manifestaciones de enfermedad cardiovascular para intervenir



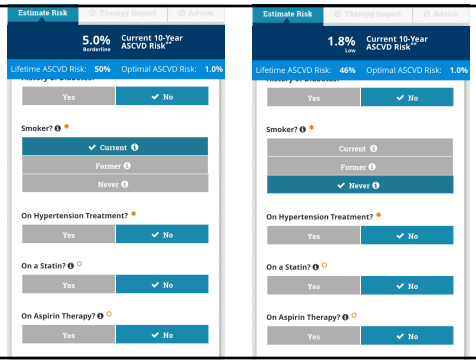
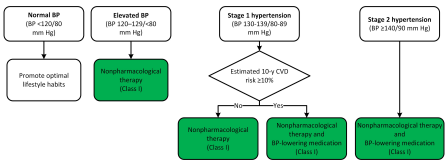


Figure 4. BP Thresholds and Recommendations for Treatment



BP indicates blood pressure; and CVD, cardiovascular disease.

Conclusiones

- La estratificación de riesgo sirve para seleccionar aquellos pacientes que tienen mayor riesgo de eventos cardiovasculares y que se beneficiarían más del tratamiento
- El reto principal lo confiere los de riesgo intermedio
- Calcular el riesgo cardiovascular
- Usar herramientas complementarias (hsPCR, CAC, otros biomarcadores)
- La intervención es multifactorial, no sólo lípidos sino también estilos de vida, control de HTA, control de DM

Preguntas…

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Puede descargar la presentación en:

www.EndoDrChen.com