Evaluación y manejo del paciente con riesgo intermedio cardiovascular

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Conflictos de interés

- Conferencista: Astra Zeneca, Abbott Nutrición, Novartis Oncology, Novo Nordisk, Merck Sharp & Dohme, Roche, Glaxo SmithKline, Sanofi Aventis, Bayer, Pfizer, Novartis
- 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

Agenda

- Identificación del paciente en riesgo intermedio
- Cálculo de riesgo y sus limitantes
- Cómo calcular el riesgo para la región?
- Cómo tratar al paciente en riesgo intermedio?

Evaluación de riesgo

Pacientes de alto riesgo

Alto riesgo

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

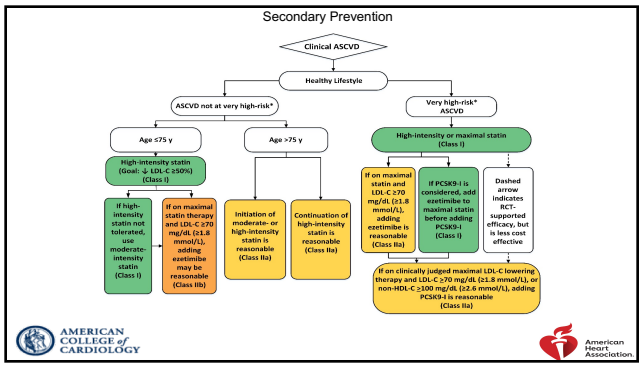

Table 4. Very High-Risk* of Future ASCVD Events

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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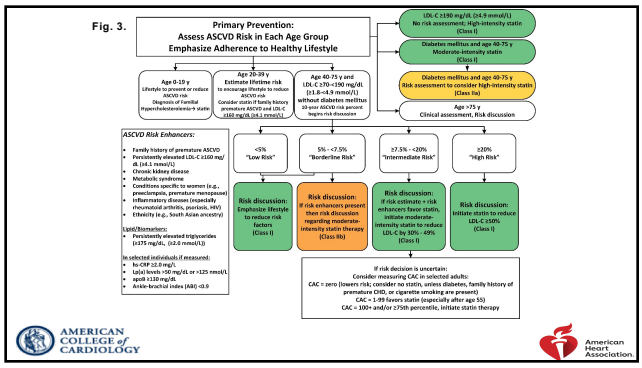

Table 5. Diabetes-Specific Risk Enhancers That Are Independent of Other Risk Factors in Diabetes Mellitus

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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El otro extremo… los de bajo riesgo

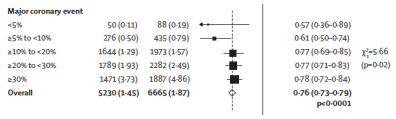
Bajo riesgo

- 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
- En este contexto lo importante es reforzar estilos de vida saludables
  - Mantener peso normal
  - Evitar tabaquismo
  - Actividad física
  - Aumento de consumo de fibra

El problema principal… los de riesgo intermedio

Hay un umbral donde la intervención no es efectiva?

Metanálisis CTT: eventos coronarios



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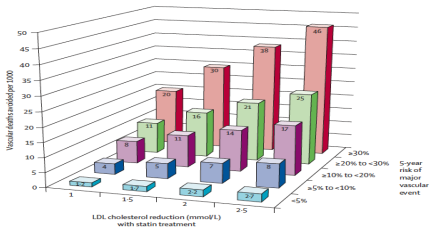
CTT. Lancet. 2012;May 17. Online.

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)	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 cardiaca	Riesgo 10 años IAM, ictus, revascularizacion 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 cardiovascular
Cortes	Alto >20%	No hay corte definido	Alto >20%%	Alto >20%		Alto >5%

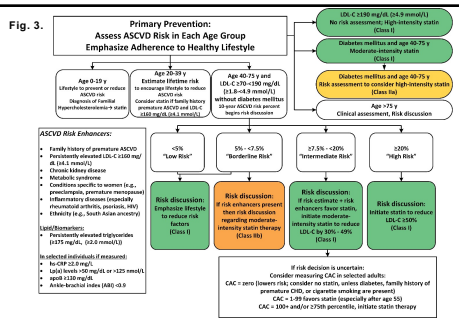
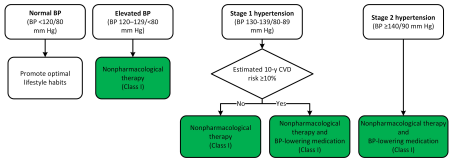
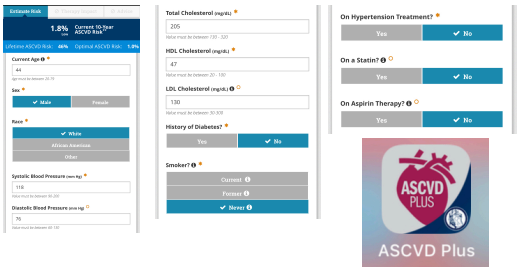


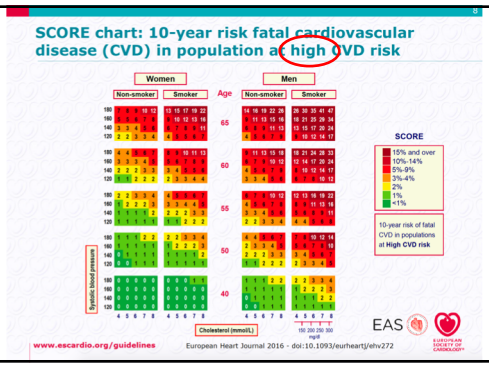
Figure 4. BP Thresholds and Recommendations for Treatment

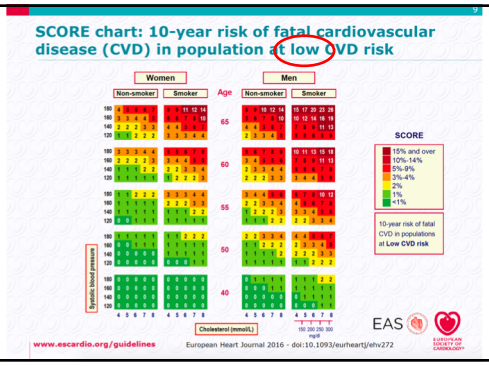


BP indicates blood pressure; and CVD, cardiovascular disease.

Pooled cohort equation/ACC AHA 2013





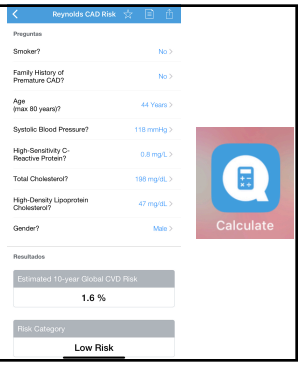


Inclusión por factores de riesgo

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

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

Qué hacemos en Centro América?

- De hecho… sí hay una calculadora de riesgo calibrado para los diferentes países de Centro América!
- Se calibró con los datos del Instituto Nacional de Estadística y Censos (al menos en Costa Rica)
- 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 Rodríguez-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) 5

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

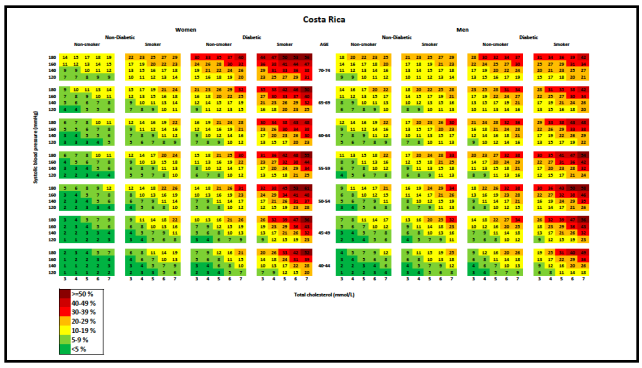
Do you smoke?
NO

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

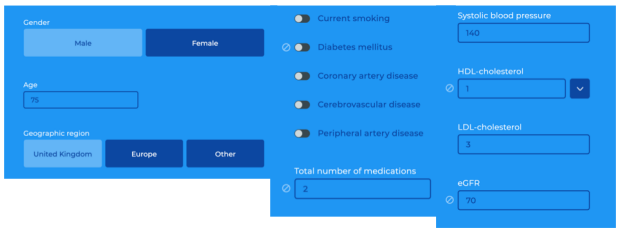


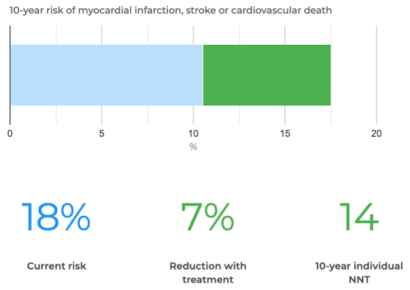
Otras poblaciones

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



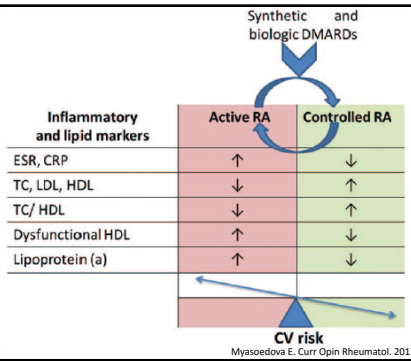


Pacientes reumatológicos

Recomendaciones EULAR 2016

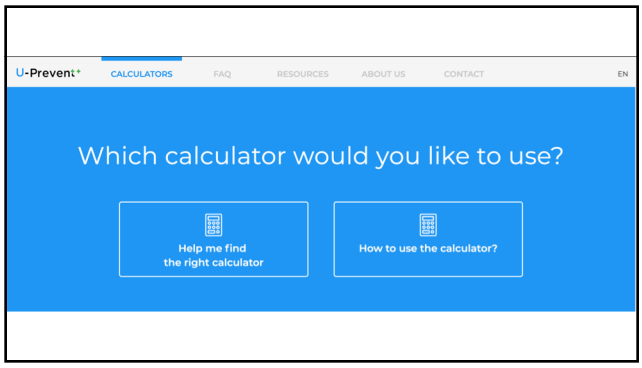
Recommendations			
1. Disease activity should be controlled optimally in order to lower CVD risk in all patients with RA, AS or PsA	2b-3	B	9.1 (1.3)
2. CVD risk assessment is recommended for all patients with RA, AS or PsA at least once every 5 years and should be reconsidered following major changes 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)

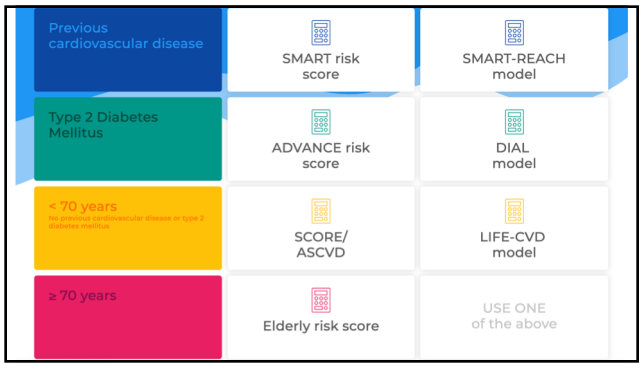
Agca R. Ann Rheum Dis. 2017;76:17-28

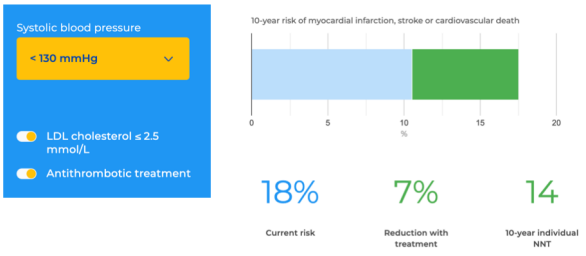


Myasoedova E. Curr Opin Rheumatol. 2017;29:277

U-prevent


U-Prevent+
CALCULATORS
FAQ
RESOURCES
ABOUT US
CONTACT
EN
Which calculator would you like to use?
Help me find the right calculator
How to use the calculator?


Previous cardiovascular disease
SMART risk score
SMART-REACH model
Type 2 Diabetes Mellitus
ADVANCE risk score
DIAL model
< 70 years
No previous cardiovascular disease or type 2 diabetes mellitus
SCORE/ ASCVD
LIFE-CVD model
≥ 70 years
Elderly risk score
USE ONE of the above



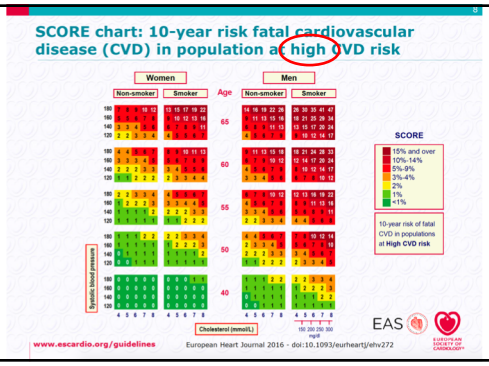
www.u-prevent.com

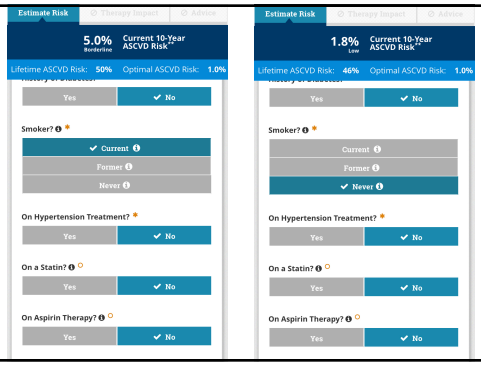
Consideraciones

- 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





Cuándo puede una herramienta reducir el riesgo de una persona?

Primary Prevention Adults 40 to 75 Years of Age With LDL-C Levels 70 to 189 mg/dL (1.7–4.8 mmol/L)

Primary Prevention Recommendations for Adults 40 to 75 Years of Age With LDL Levels 70 to 189 mg/dL (1.7–4.8 mmol/L)		
COR	LOE	Recommendations
IIa	B-NR	In intermediate-risk adults or selected borderline-risk adults in whom a CAC score is measured for the purpose of making a treatment decision, AND • If the coronary calcium score is zero, it is reasonable to withhold statin therapy and reassess in 5 to 10 years, as long as higher risk conditions are absent (diabetes mellitus, family history of premature CHD, cigarette smoking); • If CAC score is 1 to 99, it is reasonable to initiate statin therapy for patients ≥55 years of age; • If CAC score is 100 or higher or in the 75th percentile or higher, it is reasonable to initiate statin therapy.

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American Heart Association.

Cuál es la evidencia que tratar pacientes en riesgo intermedio funciona?

HOPE3

- Pacientes sin eventos cardiovasculares previos
- Hombres >55 años y mujeres >65 años, con al menos un factor de riesgo adicional, ó mujeres >60 años con 2 ó más factores de riesgo:
  - Relación cintura cadera >0.85 en mujeres ó >0.90 en hombres
  - Tabaquismo activo o en los últimos 5 años
  - HDL bajo (<38.8 mg/dl en hombres ó <50 mg/dl en mujeres)
  - Disglicemia (prediabetes ó DM tratado con sólo dieta)
  - Disfunción renal temprana (microalbuminuria, AEC <60 cc/min ó creatinina >1.4 mg/dl)
  - Historia familiar de enfermedad cardiovascular prematura en familiares de primer grado (hombres < 55 años y mujeres <65 años)

HOPE3

- Paciente prototipo:
  - Hombres, de 65 años de edad
  - Con obesidad central
  - 28% tabaquismo
  - 37% HDL bajo
  - 37% con HTA
  - PA 132/81 mm Hg
  - LDL 127, HDL 44.7, triglicéridos 128 mg/dl
  - hsPCR 2.1 mg/L

Hope-3

Unique Aspects of HOPE-3

PHRI

- BP lowering trial with wide range of BP entry criteria
- Cholesterol lowering treatment based on risk opposed to baseline LDL or HDL measurement
- Diverse population

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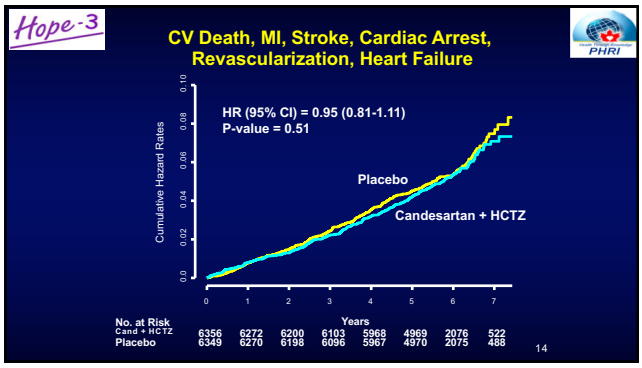
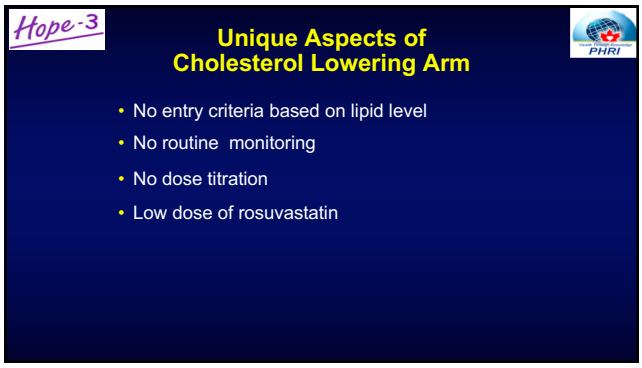
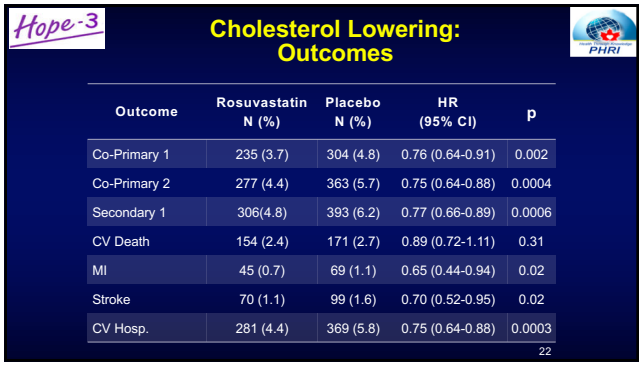
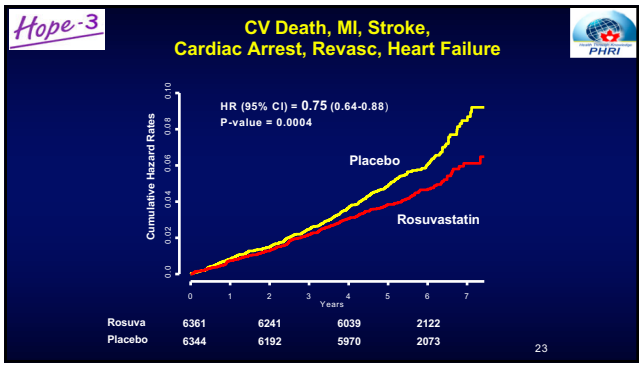
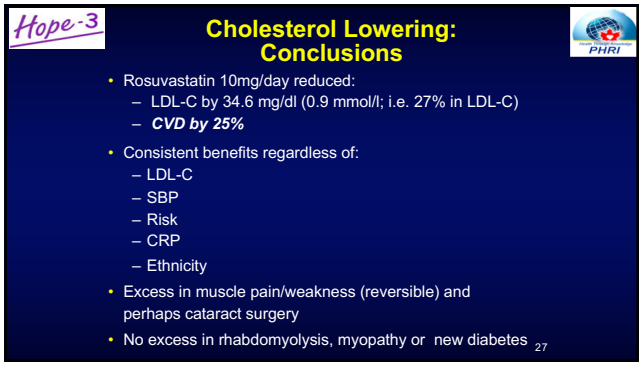


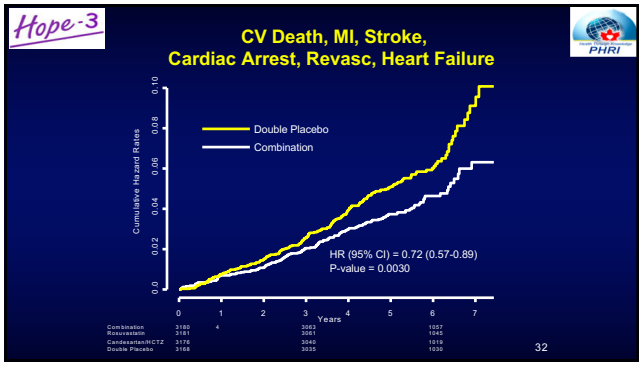


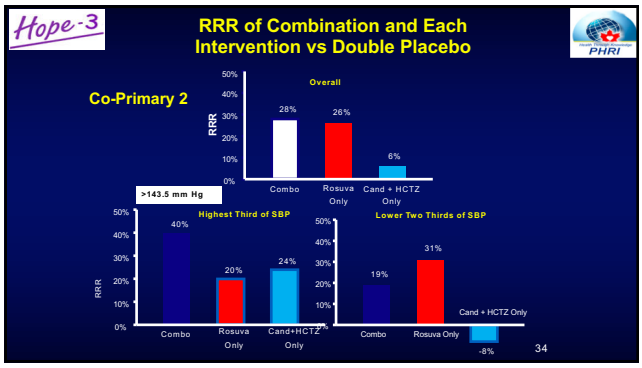


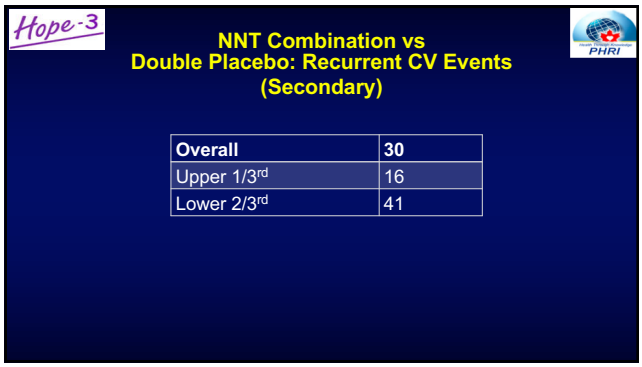
Outcome	Rosuvastatin N (%)	Placebo N (%)	HR (95% CI)	p
Co-Primary 1	235 (3.7)	304 (4.8)	0.76 (0.64-0.91)	0.002
Co-Primary 2	277 (4.4)	363 (5.7)	0.75 (0.64-0.88)	0.0004
Secondary 1	306(4.8)	393 (6.2)	0.77 (0.66-0.89)	0.0006
CV Death	154 (2.4)	171 (2.7)	0.89 (0.72-1.11)	0.31
MI	45 (0.7)	69 (1.1)	0.65 (0.44-0.94)	0.02
Stroke	70 (1.1)	99 (1.6)	0.70 (0.52-0.95)	0.02
CV Hosp.	281 (4.4)	369 (5.8)	0.75 (0.64-0.88)	0.0003


Hope-3
CV Death, MI, Stroke,
Cardiac Arrest, Revasc, Heart Failure
PHRI
HR (95% CI) = 0.75 (0.64-0.88)
P-value = 0.0004
Placebo
Rosuvastatin
Cumulative Hazard Rates
0.0
0.02
0.04
0.06
0.08
0.10
0
1
2
3
4
5
6
7
Years
Rosuva 6361 6241 6039 2122
Placebo 6344 6192 5970 2073
23


Hope-3
Cholesterol Lowering:
Conclusions
PHRI
• Rosuvastatin 10mg/day reduced:
– LDL-C by 34.6 mg/dl (0.9 mmol/l; i.e. 27% in LDL-C)
– CVD by 25%
• Consistent benefits regardless of:
– LDL-C
– SBP
– Risk
– CRP
– Ethnicity
• Excess in muscle pain/weakness (reversible) and perhaps cataract surgery
• No excess in rhabdomyolysis, myopathy or new diabetes
27


Hope-3
CV Death, MI, Stroke,
Cardiac Arrest, Revasc, Heart Failure
PHRI
Double Placebo
Combination
Cumulative Hazard Rates
0.0
0.02
0.04
0.06
0.08
0.10
HR (95% CI) = 0.72 (0.57-0.89)
P-value = 0.0030
0
1
2
3
4
5
6
7
Years
Combination 3180 4 3063 1057
Rosuvastatin 3181 3061 1045
Candesartan/HCTZ 3176 3040 1019
Double Placebo 3168 3035 1030
32





Overall	**30**
Upper 1/3rd	16
Lower 2/3rd	41

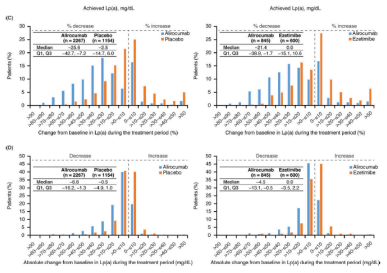
Tratamiento por risk enhancers

Table 6 continued

Risk-Enhancing Factors
• **Lipid/biomarkers**: Associated with increased ASCVD risk o Persistently* elevated, primary hypertriglyceridemia (≥175 mg/dL); o 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

Lp(a)

Alirocumab y Lp(a)



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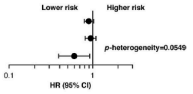
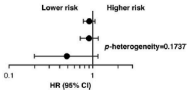
Alirocumab y Lp(a)

Population	n	HR (95% CI) per 35% reduction	*p*-value
All	4738	0.89 (0.79–1.01)	0.0780
Baseline Lp(a) <50 mg/dL	3199	0.94 (0.81–1.09)	0.3837
Baseline Lp(a) ≥50 mg/dL	1539	0.60 (0.39–0.92)	0.0201



Population	n	HR (95% CI) per 1 SD lower	*p*-value
All	4738	0.91 (0.77–1.07)	0.2387
Baseline Lp(a) <50 mg/dL	3199	0.91 (0.71–1.17)	0.4604
Baseline Lp(a) ≥50 mg/dL	1539	0.49 (0.20–1.16)	0.1026



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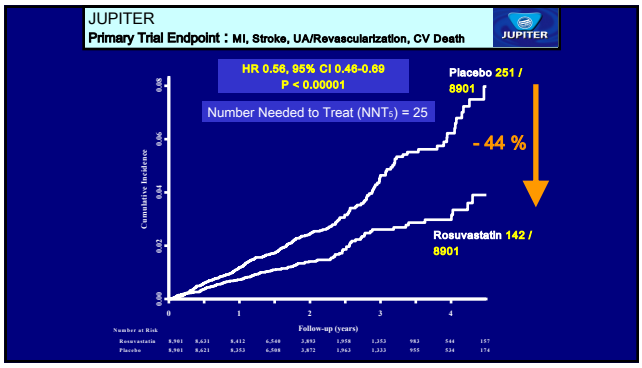
PCR ultrasensible

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



Conclusiones

- Se debe estratificar el riesgo para encontrar el balance riesgo/beneficio de la intervención
- Esta estratificación nos permite identificar quién se beneficia de tratamiento hipolipemiante y antihipertensivo
- Los pacientes en riesgo intermedio usualmente son aquellos que además de la edad tienen un factor de riesgo adicional
- Todas las calculadoras de riesgo tiene sus limitantes
- Globorisk es una calculadora de riesgo validado para la región
- Las estatinas son efectivas en pacientes con riesgo intermedio, los antihipertensivos sólo si el paciente tiene HTA

Preguntas…

chenku2409@gmail.com

Puede descargar la presentación en:

www.EndoDrChen.com