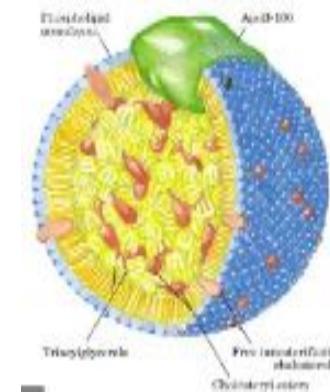


Más allá de Colesterol LDL



Christian Teijo Núñez

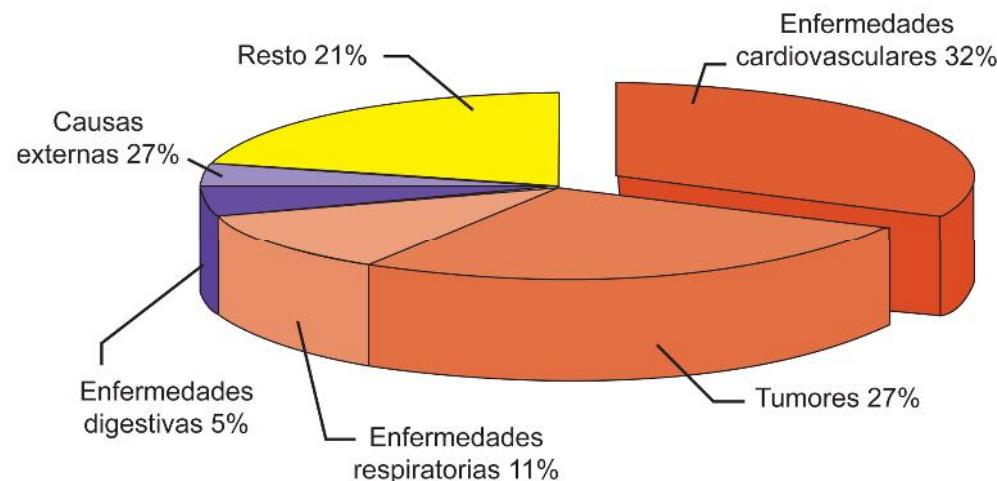
M. Interna (Ed. MONTE SAN ISIDRO - CAULE)

17/06/2022



Mortalidad cardiovascular en España

Las enfermedades cardiovasculares constituyen la primera causa de muerte en el conjunto de la población española:



INE, 2006



10 de noviembre de 2021

(Actualizada a las 13:30)

Defunciones según la Causa de Muerte
Año 2020

El 24,3% de las defunciones se debieron a enfermedades del sistema circulatorio y el 22,8% a tumores

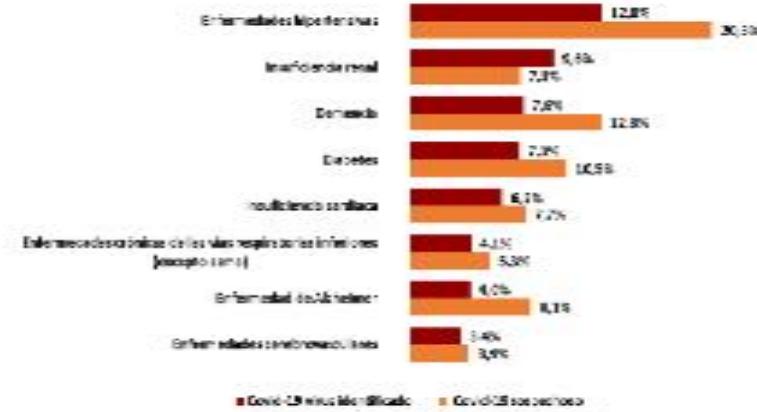
Las enfermedades infecciosas, que incluyen COVID-19 *virus identificado* y COVID-19 *sospechoso*, fueron la tercera causa de muerte (16,4% del total)¹

Defunciones por capítulos de la CIE-10. Año 2020

Valores absolutos y porcentajes

| Capítulos de la CIE-10 | Defunciones | % |
|--|-------------|-------|
| Total Defunciones | 493.776 | 100,0 |
| Enfermedades del sistema circulatorio | 119.853 | 24,3 |
| Tumores | 112.741 | 22,8 |
| Enfermedades infecciosas y parasitarias(1) | 80.796 | 16,4 |
| Enfermedades del sistema respiratorio | 42.423 | 8,6 |
| Enfermedades del sistema nervioso y de los órganos de los sentidos | 27.508 | 5,6 |

Comorbilidades más frecuentes en defunciones por COVID-19
Porcentajes



Causas de muerte más frecuentes con COVID-19 como comorbilidad

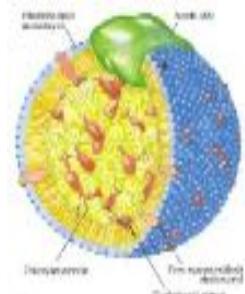
Historia del colesterol y la enfermedad cardiovascular

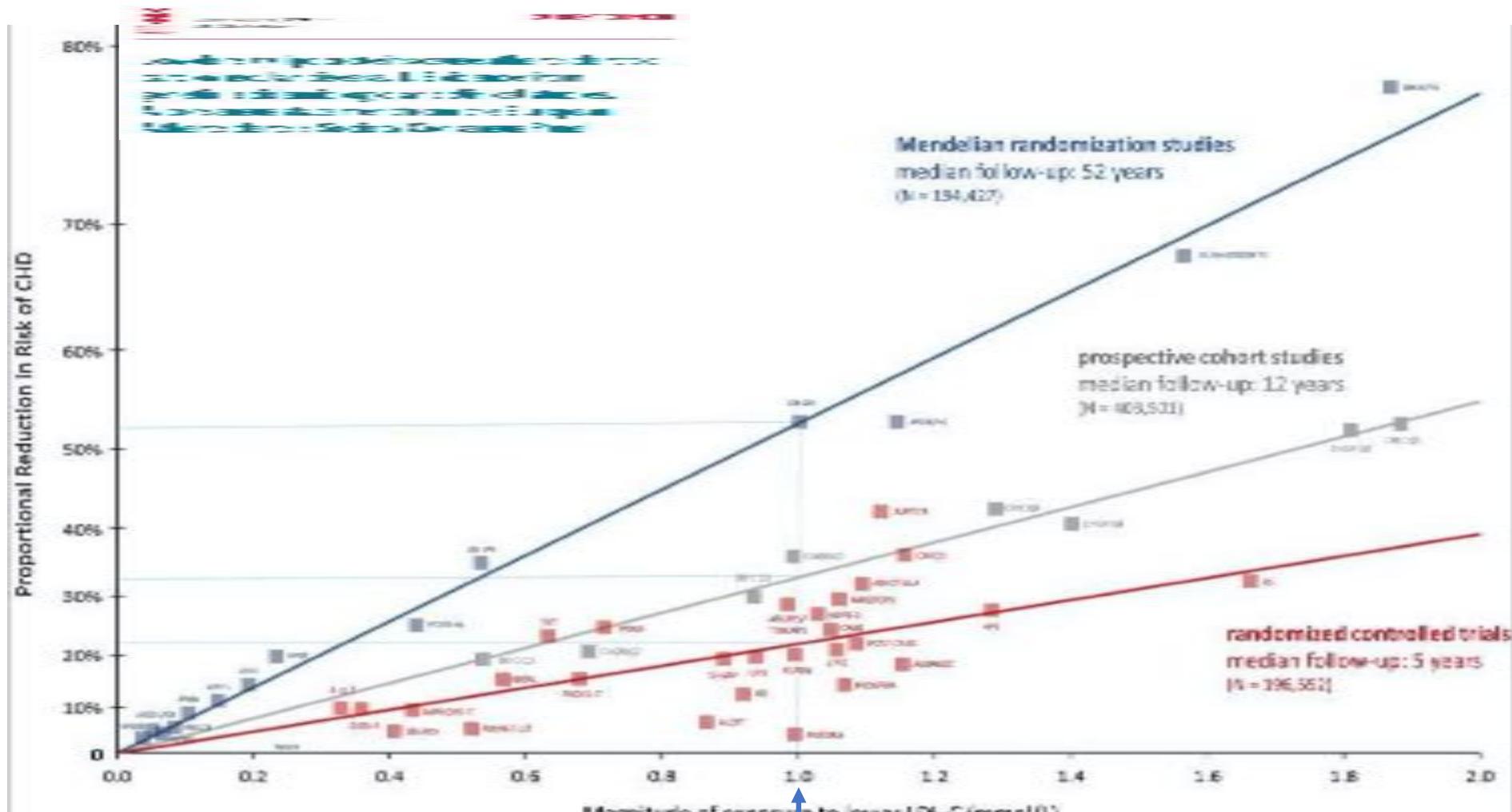
Primera mitad del siglo xx: la era del colesterol

- 1910 Las placas ateroescleróticas humanas contienen colesterol
- 1913 La dieta rica en colesterol causa aterosclerosis en conejos
- 1938 Se describe la hipercolesterolemia familiar
- 1950 Se dilucida la vía biosintética del colesterol
- 1951 Las dietas altas en grasas aumentan el colesterol plasmático en humanos
- 1953 Concepto de factor de riesgo

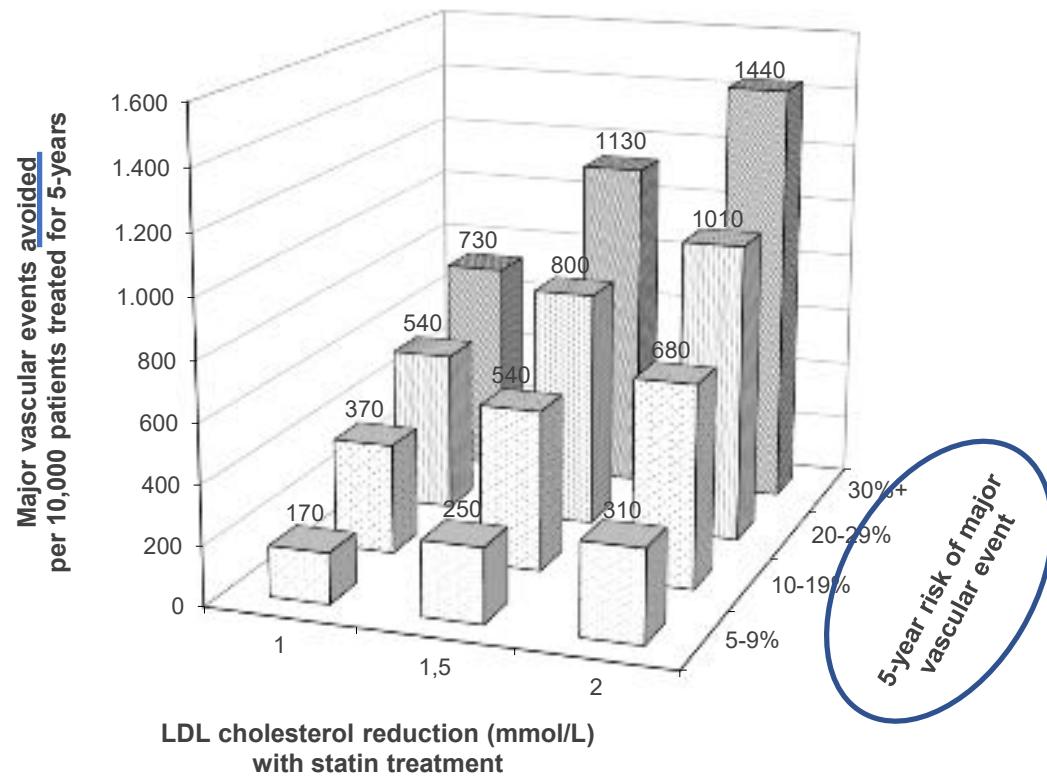
Segunda mitad del siglo xx: la era del LDL

- 1955 Se identifica el cLDL como factor de riesgo de enfermedad coronaria
- 1973 Descripción del receptor de las LDL
- 1976 Descubrimiento de los inhibidores de la HMG CoA reductasa (estatinas)
- 1984 La reducción del cLDL reduce la incidencia de enfermedad coronaria
- 1985 Recomendación de reducir el cLDL del National Cholesterol Education Program (NCEP)
- 1987 Primera estatina (lovastatina) aprobada para uso humano
- 1994 Las estatinas disminuyen los infartos de miocardio y prolongan la vida
- 2006 Se descubre la PCSK9: regulador de los receptores de las LDL





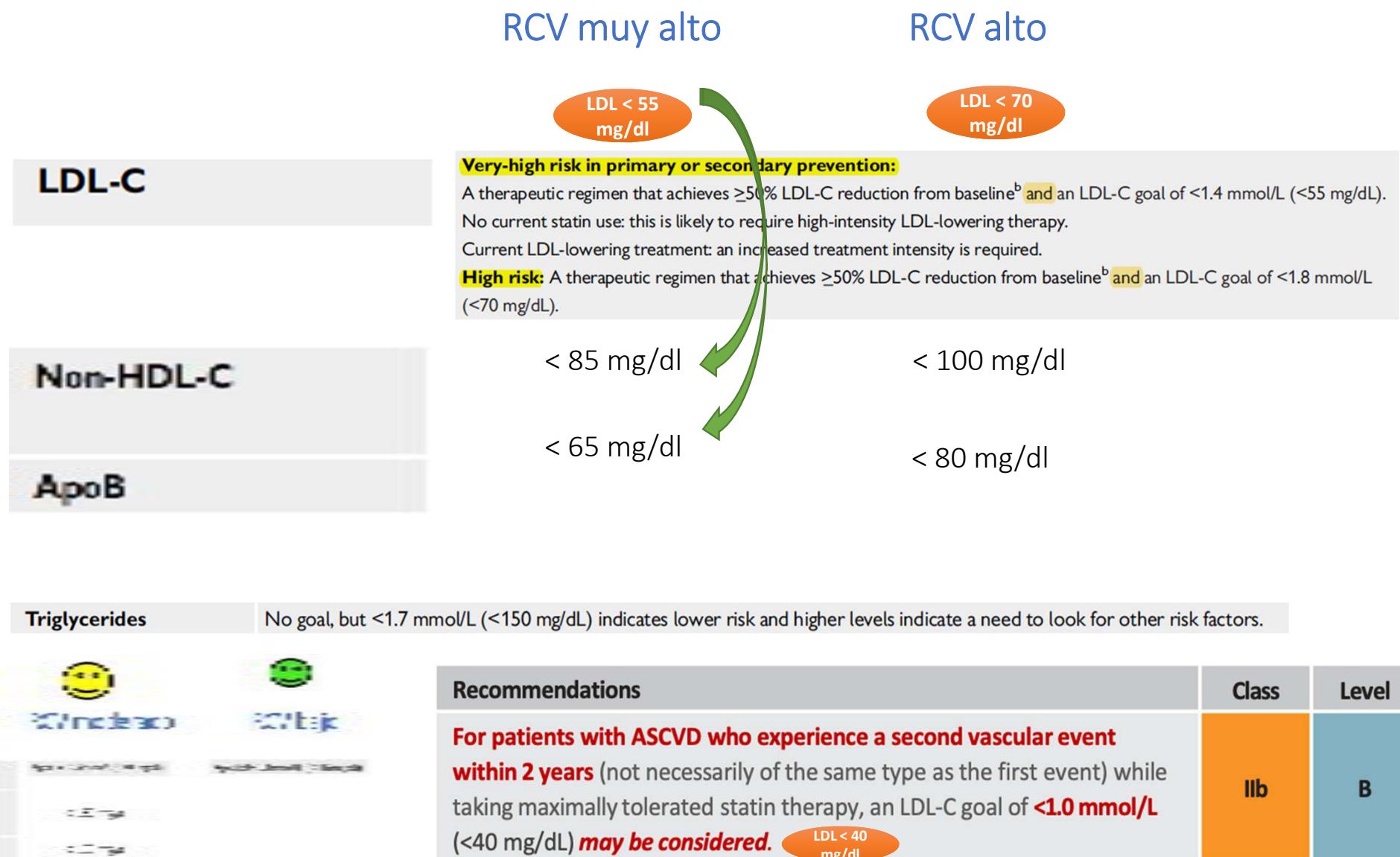
Absolute effect of statin therapy on MAJOR VASCULAR EVENTS



A consensus statement from the European Atherosclerosis Society Consensus Panel

Conclusion: Consistent evidence from numerous and multiple different types of clinical and genetic studies unequivocally establishes that LDL causes ASCVD

Colesterol LDL, cuanto más bajo y antes mejor
Estratificar y Tratar de inmediato

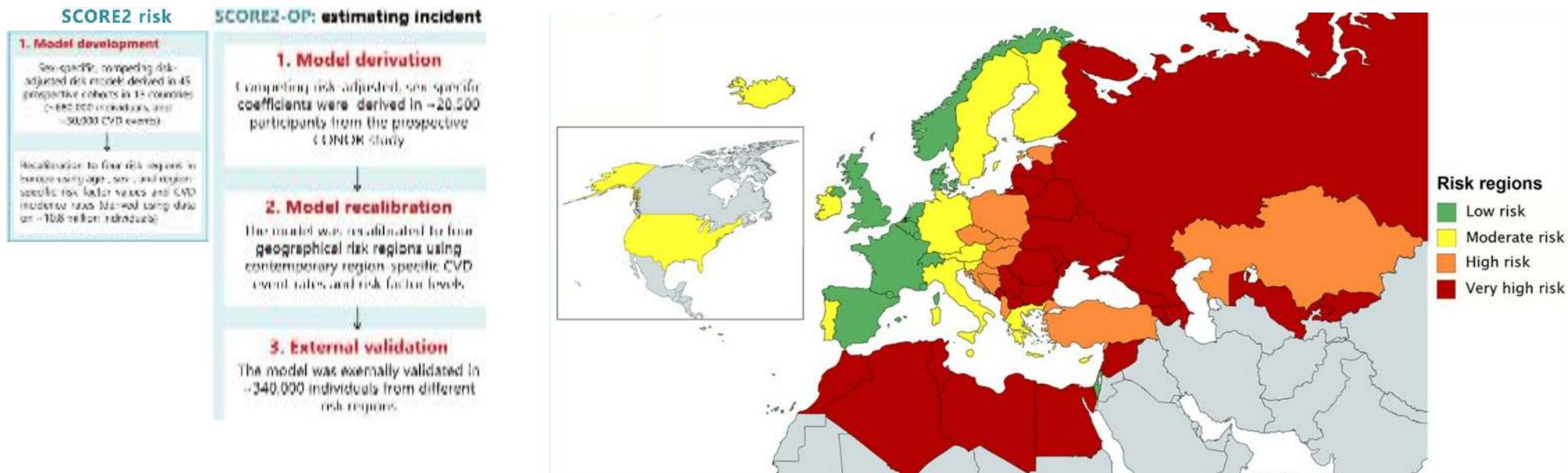


- SCORE: Riesgo a 10 años de evento cardiovascular “fatal”.



Systematic Coronary Risk Estimation 2 and Systematic Coronary Risk Estimation 2-Older Persons – SCORE 2 / SCORE OP (≥ 70 años)

.. Risk charts for fatal and non-fatal (myocardial infarction, stroke) cardiovascular disease.



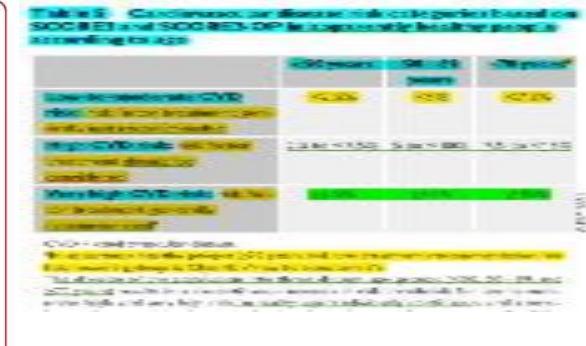
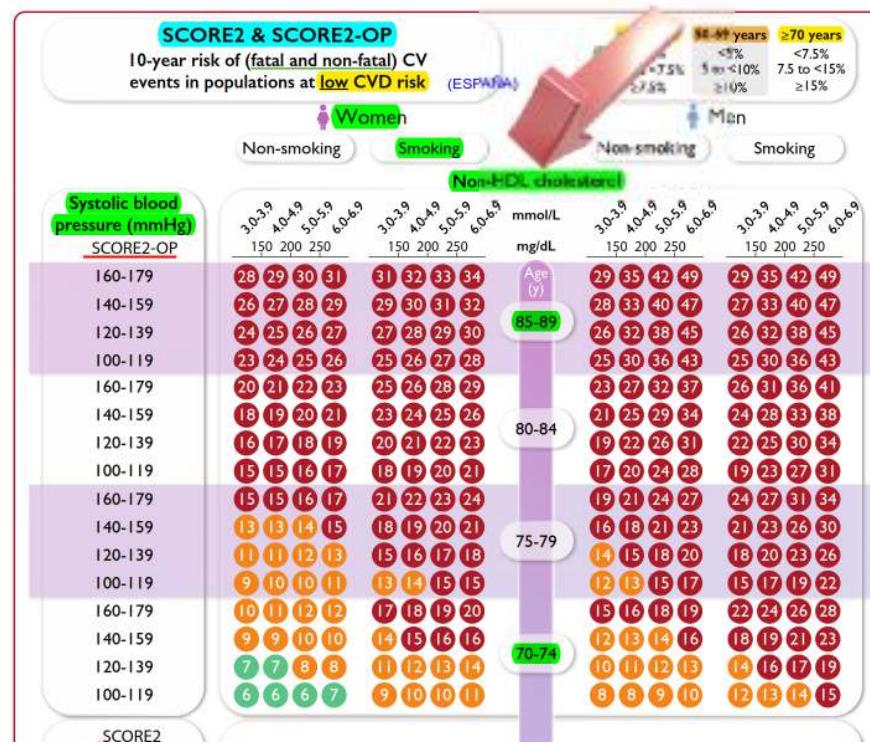
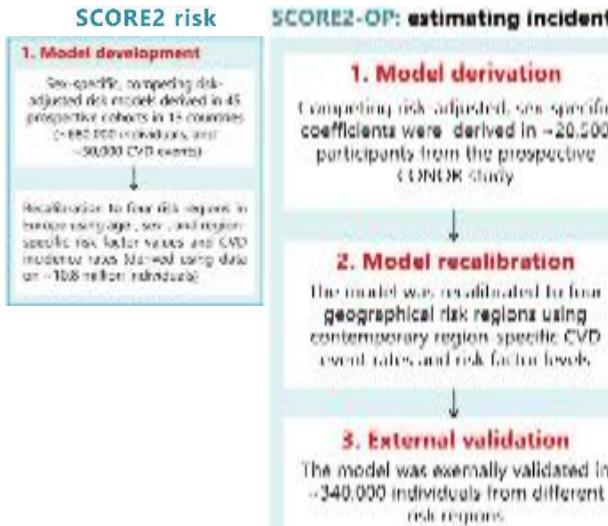
Diapositiva 11

CC1

CTN CTN; 30/05/2022

Systematic Coronary Risk Estimation 2 and Systematic Coronary Risk Estimation 2-Older Persons – SCORE 2 / SCORE OP (≥ 70 años)

.. Risk charts for fatal and non-fatal (myocardial infarction, stroke) cardiovascular disease.



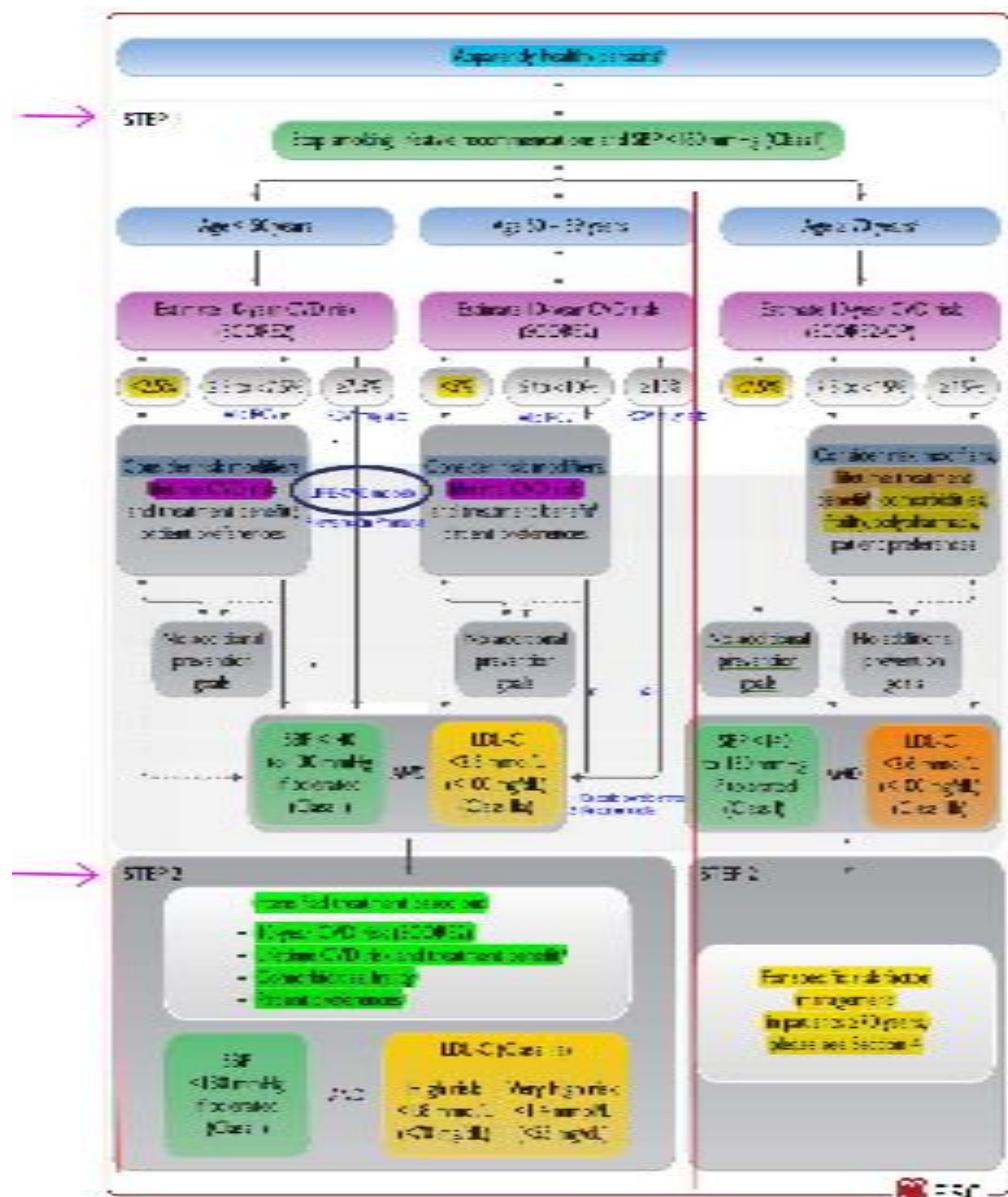
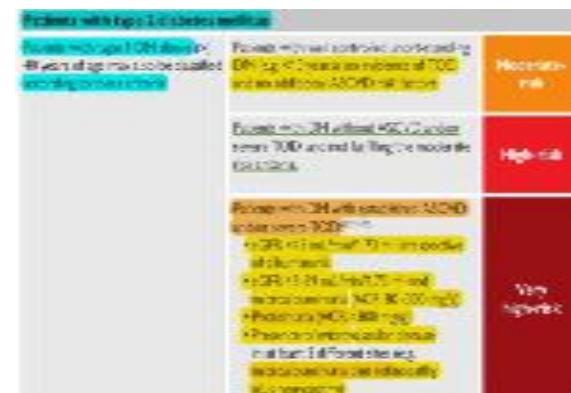
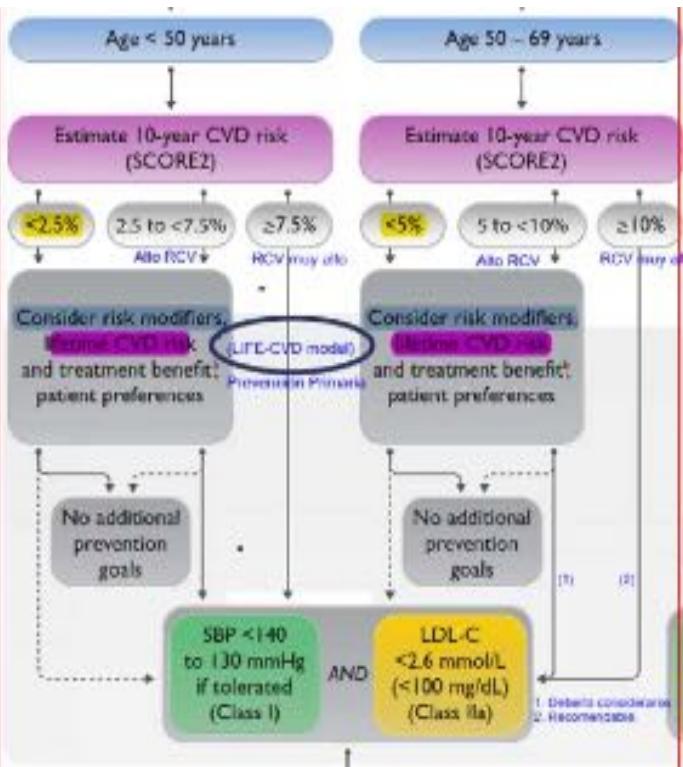


Figure 6. Flowchart of cardiovascular risk assessment and risk reduction treatment in apparently healthy persons.

2021 ESC/EAS Guidelines: Objetivo LDL en 2 pasos:

- Valorar modificadores de RCV.
- Valorar Riesgo/beneficio.
- Valorar comorbilidades.
- Valorar Beneficio tratamiento a lo largo de la vida.
- Valorar PASO DIRECTO a 2 → si Alto/ muy Alto RCV. ECV. DM Alto/muy Alto RCV.





- La concentración de cLDL recomendada es cLDL < 115 mg/dL

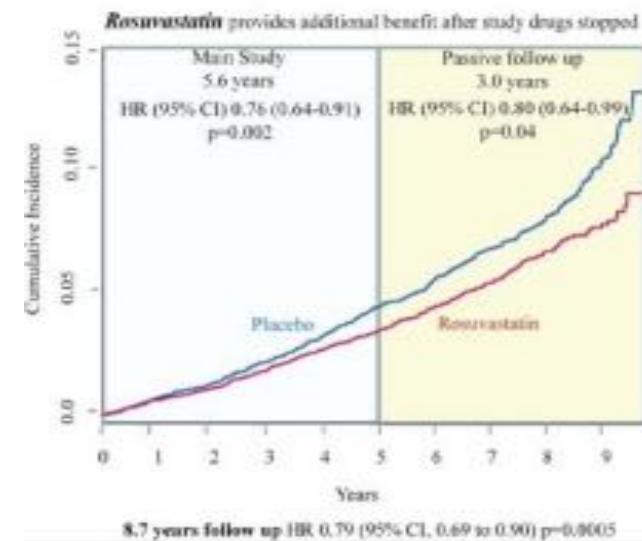
fuerza necesaria. La prescripción de fármacos para disminuir el colesterol no está universalmente indicada y deberá considerarse de forma individualizada si un paciente presenta dos de los siguientes factores: edad (hombres > 45 años; mujeres > 50 años); IMC > 30 kg/m²; tabaquismo; HTA; antecedentes familiares de ECVA precoz; dislipemia aterogénica; SM; o Lp(a) > 50 mg/dL.

Randomized Controlled Trial > Eur Heart J. 2021 Aug 17;42(31):2995-3007.
doi: 10.1093/eurheartj/ehab225.

Lowering cholesterol, blood pressure, or both to prevent cardiovascular events: results of 8.7 years of follow-up of Heart Outcomes Evaluation Prevention (HOPE)-3 study participants

12 705 participants at intermediate CV risk after 5.6 years.

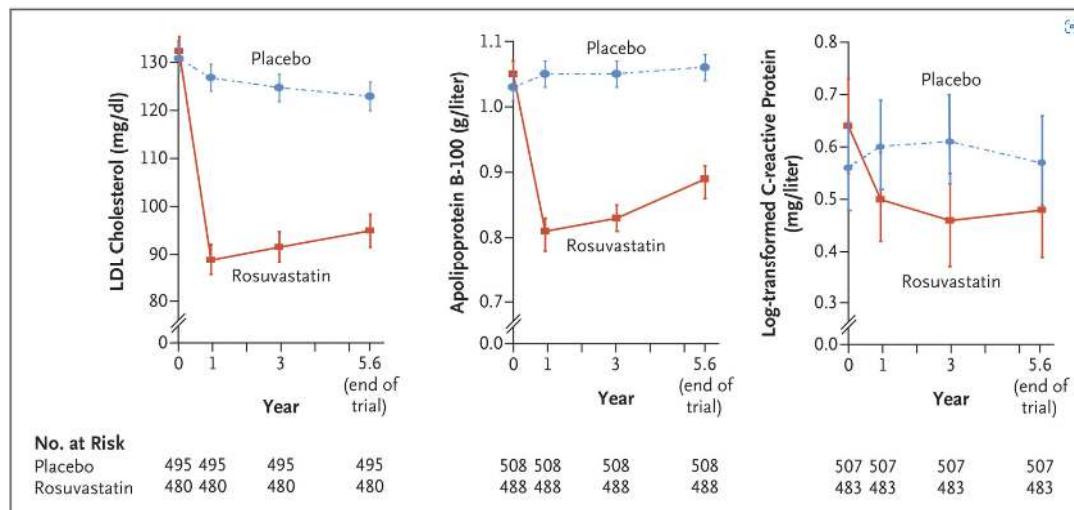
| Cardiovascular risk factors — no. (%) | | |
|--|-------------|-------------|
| Elevated waist-to-hip ratio | 5540 (87.1) | 5494 (86.6) |
| Recent or current smoking | 1740 (27.4) | 1784 (28.1) |
| Low HDL cholesterol level | 2344 (36.8) | 2244 (35.4) |
| Impaired fasting glucose or impaired glucose tolerance | 809 (12.7) | 807 (12.7) |
| Early diabetes mellitus | 374 (5.9) | 357 (5.6) |
| Family history of premature coronary heart disease | 1675 (26.3) | 1660 (26.2) |
| Early renal dysfunction | 169 (2.7) | 181 (2.9) |
| Hypertension | 2403 (37.8) | 2411 (38.0) |



Nivel medio del colesterol LDL fue 127,8 mg/dL.

Tabla 11 Indicaciones de tratamiento hipolipemiante según riesgo cardiovascular y concentración de cLDL

| Riesgo vascular | Colesterol LDL | | | | |
|-----------------|----------------|--|--|--|--|
| | 55-70 mg/dL | < 70 mg/dL | 70-115 mg/dL | 116-190 mg/dL | > 190 mg/dL |
| Bajo o moderado | | Recomendaciones de hábitos de vida. No precisa tratamiento | Recomendaciones de hábitos de vida. No precisa tratamiento | Modificación de hábitos de vida y alimentos funcionales. Valorar tratamiento hipolipemiante Objetivo cLDL < 115 mg/dL | Riesgo alto por definición Modificación de hábitos de vida y alimentos funcionales. Iniciar tratamiento hipolipemiante de alta intensidad Objetivo cLDL < 70 mg/dL |



N Engl J Med 2016; 374:2021-2031

U-Prevent: You are in control

Watch a video or jump right in

Start calculator



▶ Clinician video



▶ Patient video

We provide tools for personalized Vascular Medicine. Get more insights by calculating individual cardiovascular risk and the effect of preventive treatment.

SCORE2 and SCORE2-OP are integrated in U-Prevent menu

Dear visitor,

We have updated the U-Prevent site with a new calculator overview that integrates the recently published, [SCORE2](#) and the [SCORE2-OP](#) calculators. Using the updated calculators have been advised by the European Society of Cardiology (ESC) on 30.08.2021. The new guidelines are available via the [European Society of Cardiology website](#) and in the [European Heart Journal](#). Please refer to your local medical guidelines when using these or other guidelines.

The U-Prevent team.

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Agreed

No, I prefer not



Prediction of individualized lifetime benefit from cholesterol lowering, blood pressure lowering, antithrombotic therapy, and smoking cessation in apparently healthy people

The LIFE-CVD model can estimate therapy-benefit from CVD risk-modification in apparently healthy people



U-Prevent⁺

CALCULATORS



European Heart Journal (2020) **41**, 1190–1199

Select a calculator

Use the search bar or scroll down to find the calculator you're looking for.

Search or

Calculator type: Financial calculator

Personal calculator



Calculator

Business calculator



Calculator

Financial calculator



Calculator

Business calculator



Calculator

Accounting calculator
Financial calculator for accountants
and auditors



Calculator

Business calculator
Financial calculator for business
and finance professionals

Financial calculator based on European regulations

Accounting calculator
Financial calculator for accountants
and auditors



Calculator

Accounting calculator
Financial calculator for accountants
and auditors



Calculator

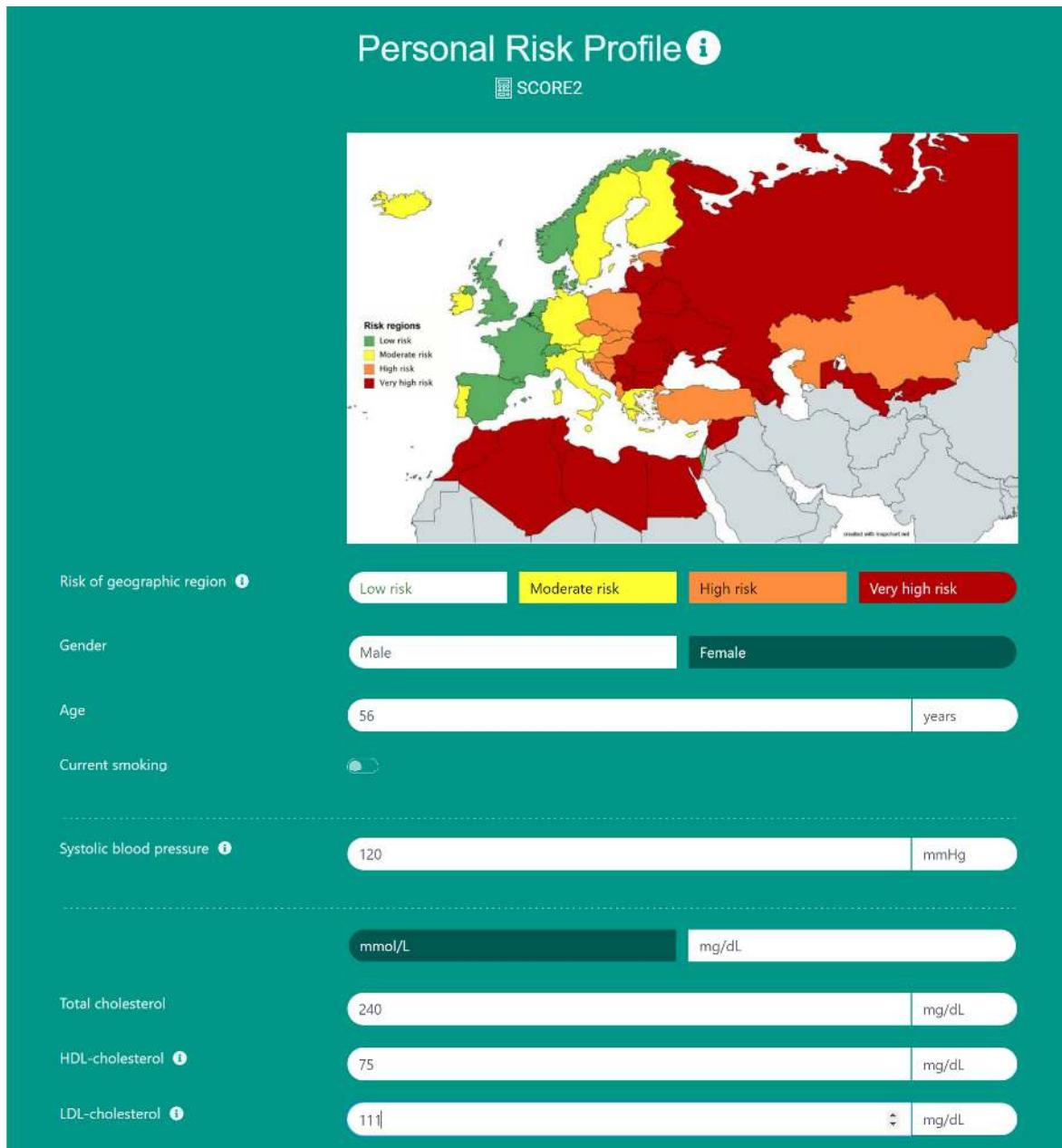


Junta de
Castilla y León



Sacyl





SCORE2

Personal Risk Profile i

Risk of geographic region

Gender

Age

Current smoking

Lo*

M*

56

years

Systolic blood pressure

120

mmHg

240

mg/dL

Total cholesterol

75

mg/dL

HDL-cholesterol

111

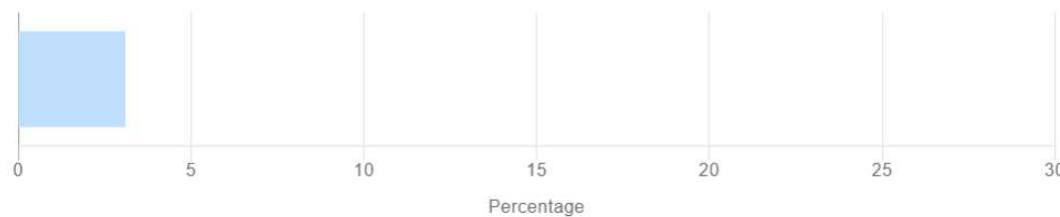
mg/dL

LDL-cholesterol

Adjust intake

10-years risk

Current 10-year risk of myocardial infarction, stroke
or cardiovascular death



3.1%

Current risk i

0.0%

Reduction with treatment i

Future treatment i

LDL-cholesterol

No treatment target

Systolic blood pressure

No treatment target

Antithrombotic treatment



Reset



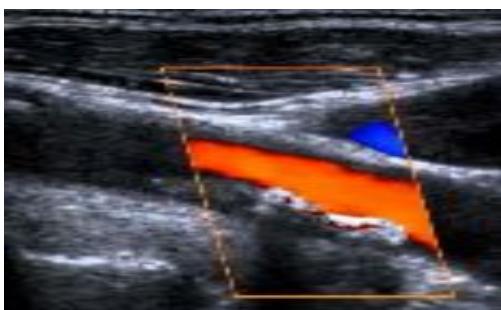
Estándares SEA 2022 para el control global del riesgo cardiovascular

| Método de diagnóstico | Indicación en el paciente de riesgo cardiovascular |
|-------------------------------|---|
| Angiografía o TAC coronario | - Riesgo cardiovascular elevado: Score > 10% - Estenosis > 50% de dos arterias epicárdicas - Angiografía: Score > 10% + 1 si se incluye la arteria coronaria descendente anterior izquierda (ACA) o la arteria coronaria descendente posterior (ACP). - TAC: Score > 10% + 1 si se incluye la arteria coronaria descendente anterior izquierda (ACA) o la arteria coronaria descendente posterior (ACP). |
| Ecografía carotídea o femoral | Riesgo alto: - Si el paciente tiene una estenosis > 50% de la arteria carótida interna (ACI) o la arteria femoral. |

⁴ Se considera ECVA o equivalente

- Mediante angiografía o TAC coronario (enfermedad multivaso con obstrucción > 50% de dos arterias epicárdicas)
- Mediante ecografía carotídea o femoral (estenosis > 50%).

Muy alto



Con LOD¹, EVS² u otros factores moduladores del riesgo³

Incrementar en un escalón la categoría obtenida con el SCORE

- LDL-Col - Paciente "X" = 79 mg/dl

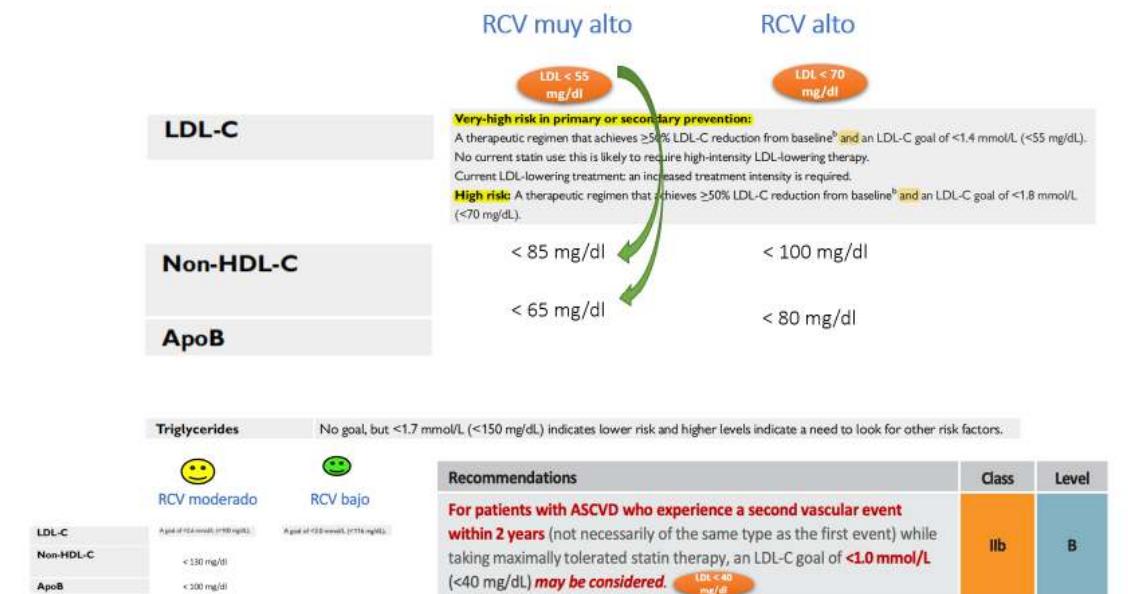
- PASO 2 - LDL-Col < 70 mg/dl ???

- Riesgo residual ???

Col NO HDL : Paciente "X" = 165 mg/dl

Apo B

Lp(a).



Lp(a) LDL particle with an Apo(a) y ApoB

Lipid analyses for CVD risk estimation

Lp(a) measurement should be considered at least once in each adult person's lifetime to identify those with very high inherited Lp(a) levels >180 mg/dL (>430 nmol/L) who may have a lifetime risk of ASCVD equivalent to the risk associated with heterozygous familial hypercholesterolaemia.

Table 6 Physical and chemical characteristics of human plasma lipoproteins

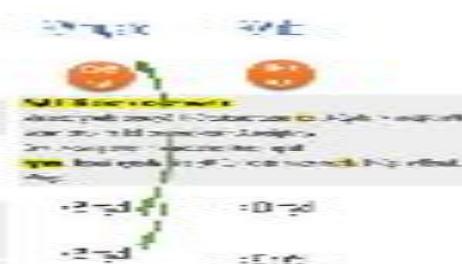
| | Density (g/mL) | Diameter (nm) | TGs (%) | Cholesteryl esters (%) | PLs (%) | Cholesterol (%) | Apolipoproteins | |
|--------------|----------------|---------------|---------|------------------------|---------|-----------------|-----------------|----------------|
| | | | | | | | Major | Others |
| Chylomicrons | <0.95 | 80–100 | 90–95 | 2–4 | 2–6 | 1 | ApoB-48 | ApoA-I, A-II |
| VLDL | 0.95–1.006 | 30–80 | 50–65 | 8–14 | 12–16 | 4–7 | ApoB-100 | ApoA-I, C-II |
| IDL | 1.006–1.019 | 25–30 | 25–40 | 20–35 | 16–24 | 7–11 | ApoB-100 | ApoC-II, C-III |
| LDL | 1.019–1.063 | 20–25 | 4–6 | 34–35 | 22–26 | 6–15 | ApoB-100 | |
| HDL | 1.063–1.210 | 8–13 | 7 | 10–20 | 55 | 5 | ApoA-I | ApoA-II, C-I |
| Lp(a) | 1.006–1.125 | 25–30 | 4–8 | 35–46 | 17–24 | 6–9 | Apo(a) | ApoB-100 |

2019

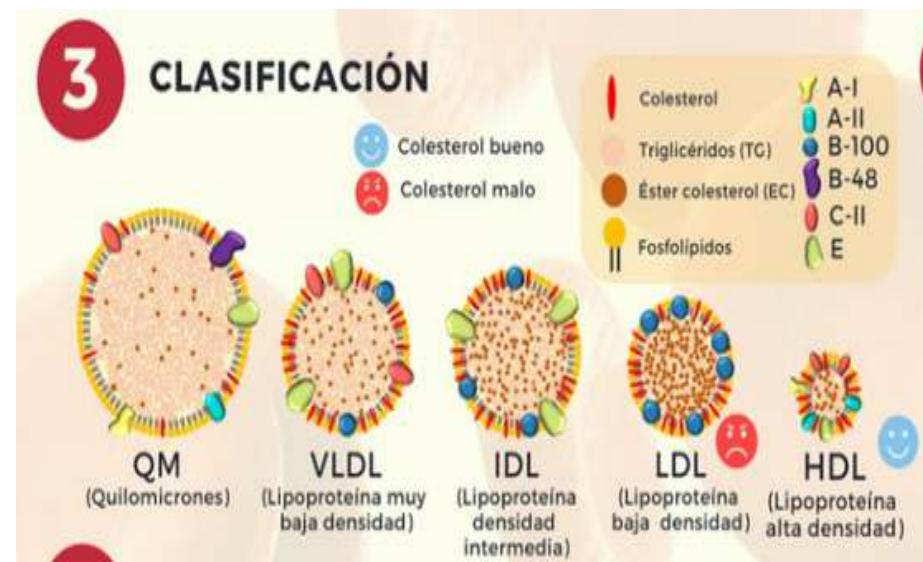
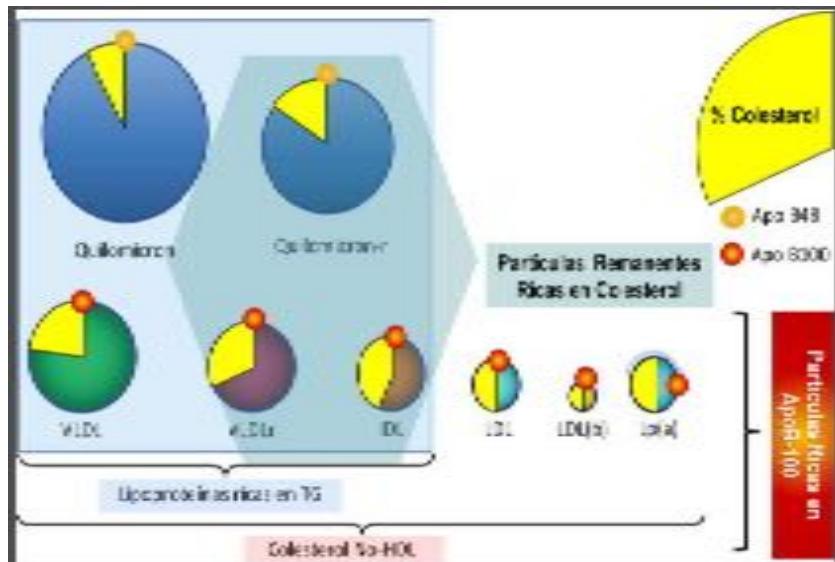
Lipid analyses for CVD risk estimation

ApoB analysis is recommended for risk assessment, particularly in people with high TG, DM, obesity or metabolic syndrome, or very low LDL-C. It can be used as an alternative to LDL-C, if available, as the primary measurement for screening, diagnosis, and management, and may be preferred over non-HDL-C in people with high TG, DM, obesity, or very low LDL-C.

- In general, LDL-C, non-HDL-C, and ApoB concentrations are very highly correlated (ASCVD risk)
- Si TG > 400 mg/dl → Col no HDL y ApoB



2021 ESC Guidelines on cardiovascular disease prevention in clinical practice



- Modificadores de Riesgo / Reclasificación

- Lp(a)

- 1 Vez en la vida

- Si $> 180 \text{ mg/dL}$. RCV moderado \rightarrow RCV Alto

| | | Continuous risk categories | |
|---|-----------|---|----------|
| Heterozygous inheritance | High-risk | Moderate-risk | Low-risk |
| Propensity of the following: Elevated ASCVD risk factors associated with Lp(a) levels. Elevated ASCVD risk factors include: ASCVD or atherosclerotic disease history, total cholesterol >200 mg/dL and either arterial blood pressure >140 mmHg, LDL-C >130 mg/dL, and triglycerides >150 mg/dL. Uniquely, however, Lp(a) may trigger the above findings that are known to be predictive of cardiovascular events, such as significant carotid artery stenosis, angioplasty or CTO lesions, and coronary disease with two major clinical events having $>50\%$ stenosis or thrombosis. | | <p>Non-smoker, elevated triglycerides, in particular TC $>400 \text{ mg/dL}$ or TG $>150 \text{ mg/dL}$ $>180 \text{ mg/dL}$ or BP $>130/85 \text{ mmHg}$ Previous CVD without other major risk factors Previous CHD without major risk factors, including 2 risk factors or another additional risk factor Moderate CVD ($>10\% 10\text{-year risk} \geq 7.5\%$) Calculated SCORE $>10\%$ and $<10\%$ for 10-year risk of fatal CVD.</p> | |
| Elevated Lp(a) levels and at least three major risk factors, or subclinical CVD ($>10\% 10\text{-year risk}$) Severe CVD ($>50\% >30\% \text{ lesions}$). Calculated SCORE $>10\%$ for 10-year risk of fatal CVD. Having CVD with another major risk factor. | | <p>Young patients ($<10\text{-year } 10\text{-year risk} <10\%$) no CHD or stroke $<10\text{-year risk}$ without other risk factors. Calculated SCORE $>1\%$ and $<10\%$ for 10-year risk of fatal CVD.</p> | |
| | | Lp(a) measurement should be considered at least once in each adult person's lifetime to identify those with very high Lp(a) levels $>180 \text{ mg/dL}$ ($>430 \text{ nmol/L}$) who may have a lifetime risk of ASCVD equivalent to the risk associated with heterozygous familial hypercholesterolemia. | |
| | | Lp(a) should be considered in selected patients with a family history of premature CVD, and for reclassification in people who are borderline between moderate and high-risk. | |

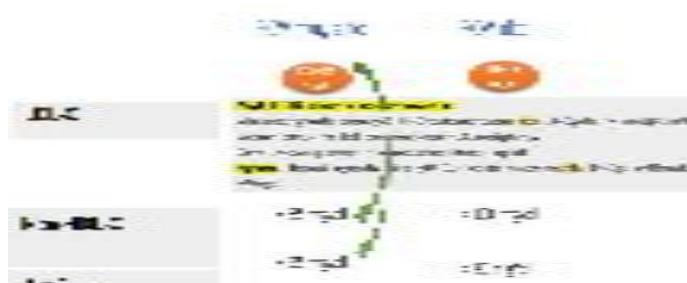
2021 ESC Guidelines on cardiovascular disease prevention in clinical practice

Table 10 Corresponding non-high-density lipoprotein cholesterol and apolipoprotein B levels for commonly used low-density lipoprotein cholesterol goals

| LDL-C | Non-HDL-C | Apolipoprotein B |
|------------------------|------------------------|------------------|
| 2.6 mmol/L (100 mg/dL) | 3.4 mmol/L (131 mg/dL) | 100 mg/dL |
| 1.8 mmol/L (70 mg/dL) | 2.6 mmol/L (100 mg/dL) | 80 mg/dL |
| 1.4 mmol/L (55 mg/dL) | 2.2 mmol/L (85 mg/dL) | 65 mg/dL |

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HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol.



2021 ESC Guidelines on cardiovascular disease prevention in clinical practice

"Simple division of the plasma TG by five does not give a very accurate estimate of VLDL-C."

- Friedewald



LDL-C can be measured directly, but in most studies and many laboratories, LDL-C is calculated using the Friedewald formula:

- In mmol/L: $\text{LDL-C} = \text{total cholesterol} - \text{HDL-C} - (0.45 \times \text{triglycerides})$
- In mg/dL: $\text{LDL-C} = \text{total cholesterol} - \text{HDL-C} - (0.2 \times \text{triglycerides})$

The calculation is only valid when the concentration of triglycerides is <4.5 mmol/L (~400 mg/dL), and not precise when LDL-C is very low [<<1.3 mmol/L (50 mg/dL)]. In patients with low LDL-C levels and/or hypertriglyceridaemia (>300 mg/dL), alternative formulae are available^{511,512} or LDL-C can be measured directly.



4.6.1.3 Non-high-density lipoprotein cholesterol

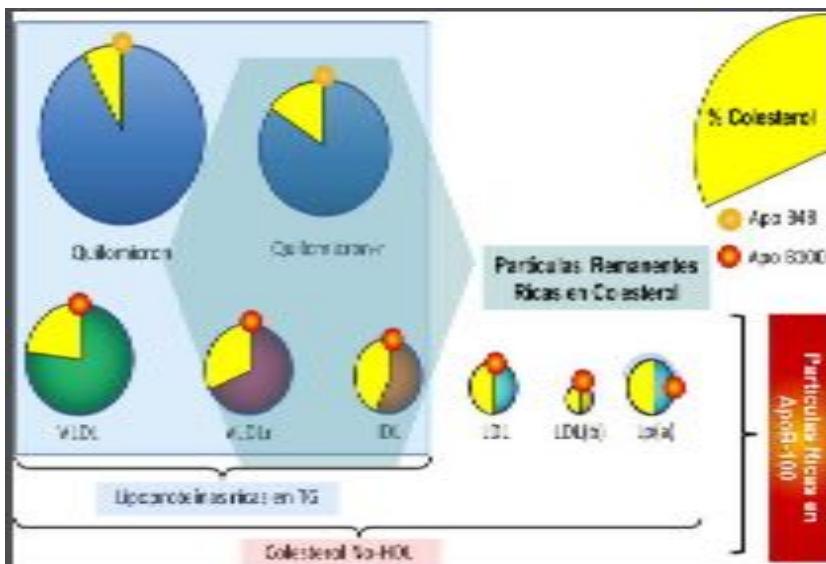
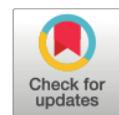
The non-HDL-C value is calculated by subtracting HDL-C from total cholesterol. Non-HDL-C, unlike LDL-C, does not require the triglyceride concentration to be <4.5 mmol/L (400 mg/dL). It also has an advantage in that it is accurate in a non-fasting setting, and may be more accurate in patients with DM. There is evidence for a role of non-HDL-C as a treatment target as it captures the information regarding all apoB-containing lipoproteins.⁵¹³ We suggest it as a reasonable alternative treatment goal for all patients, particularly for those with hypertriglyceridaemia or DM. How non-HDL-C levels correspond to commonly used LDL-C goals is shown in Table 10.

4.6.1.4 Apolipoprotein B

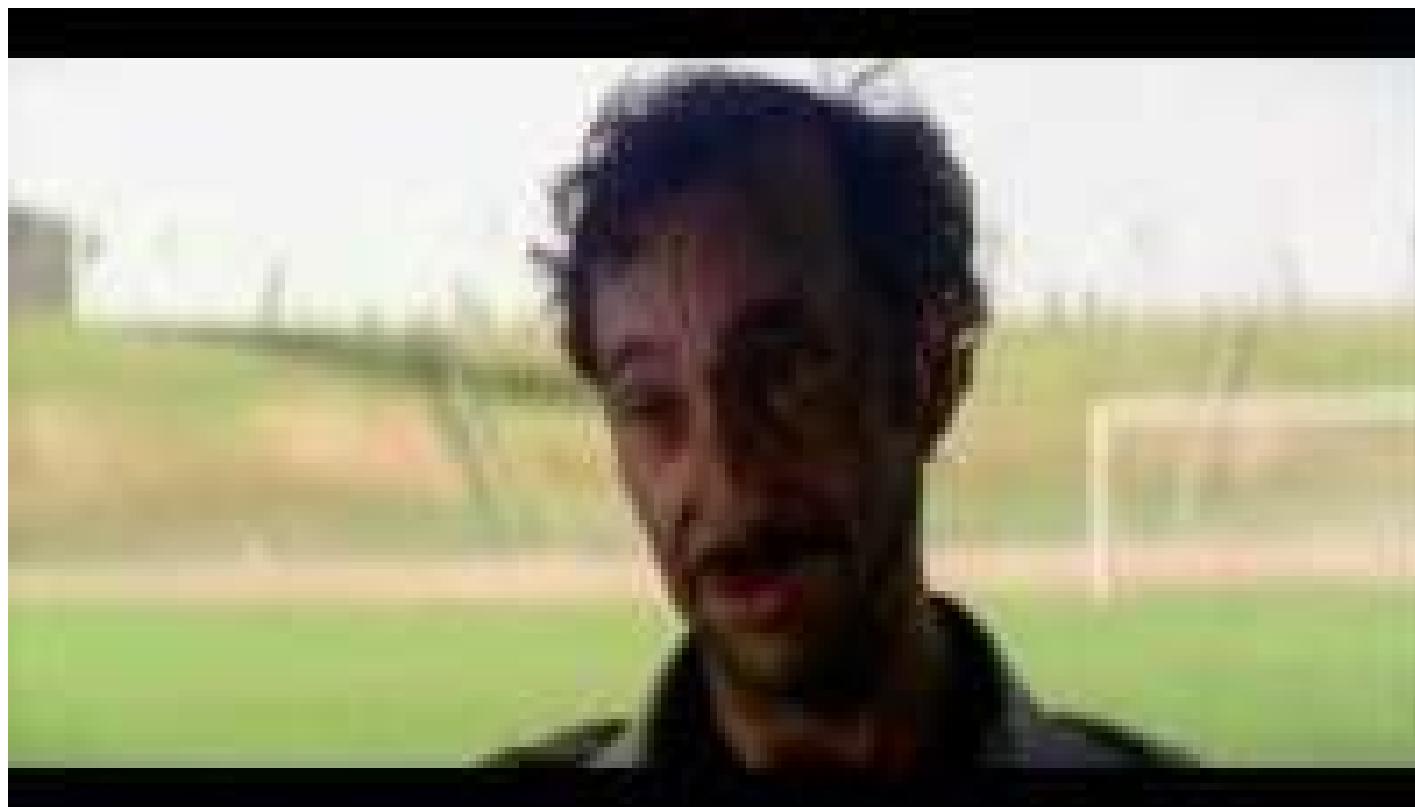
Apolipoprotein B provides a direct estimate of the total concentration of atherogenic lipid particles, particularly in patients with elevated triglycerides. However, on average, the information conferred by apolipoprotein B is similar to that of calculated LDL-C.⁵¹⁴

DOCUMENTO DE CONSENSO

Comentario del CEIPV a la actualización de las Guías Europeas de Prevención Vascular en la Práctica Clínica[☆]



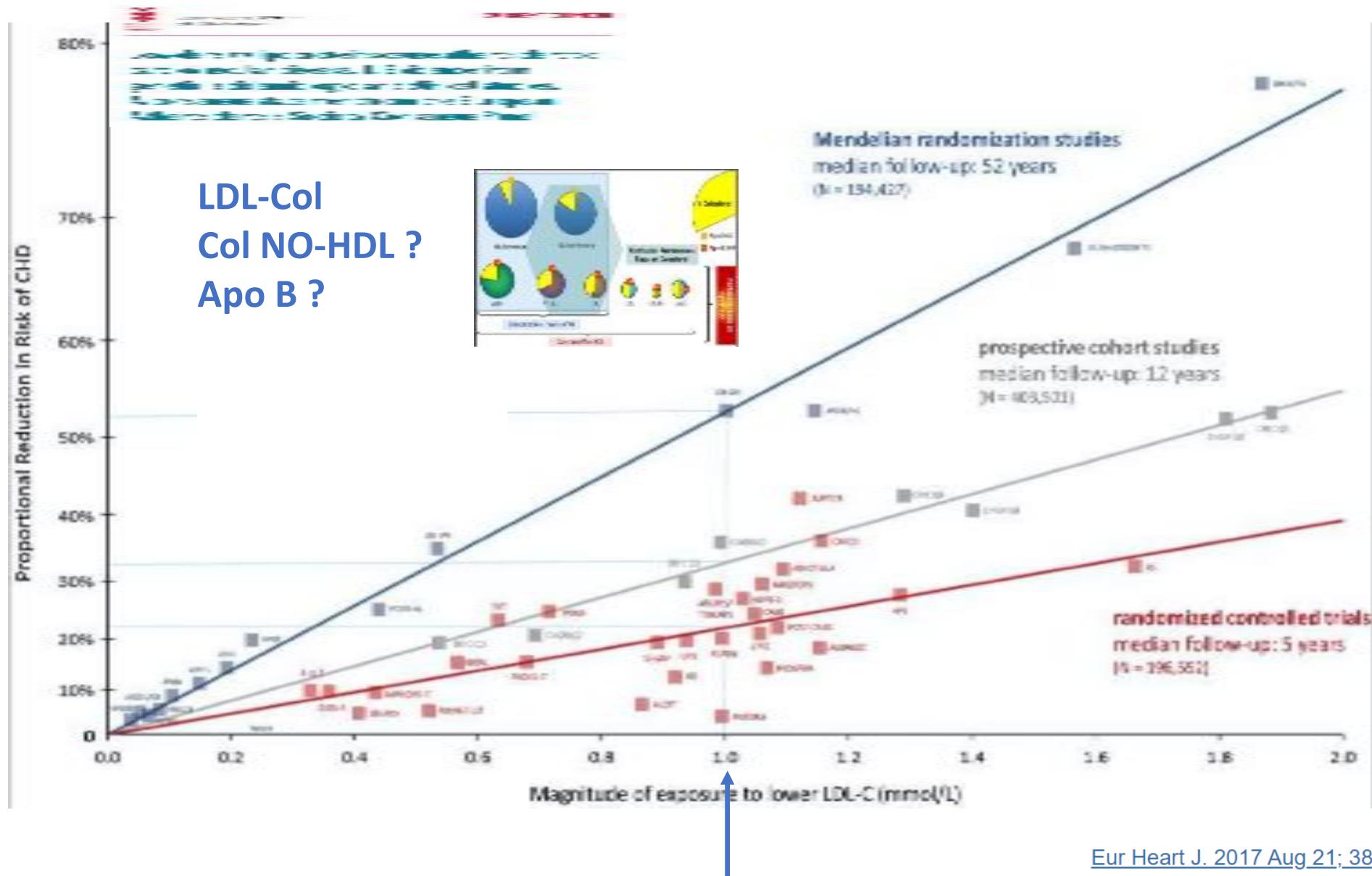
* La ApoB se recomienda como una alternativa ideal al cLDL, particularmente en personas con niveles altos de TG, DM, obesidad, síndrome metabólico o niveles muy bajos de cLDL. Se puede usar, si está disponible, como la medida principal para la detección, el diagnóstico y el tratamiento, y puede preferirse a los de C-no-HDL en estos grupos de pacientes, si bien su baja disponibilidad en nuestro medio, hace que el C-no-HDL sea la opción más operativa.



Residual Lipid Risk

— — —

Residual Lipid Risk



Discordance Between Standard Equations for Determination of LDL Cholesterol in Patients With Atherosclerosis



El siguiente artículo compara la estimación de los valores de LDL-c usando diferentes métodos, como son las **ecuaciones de Friedewald, Sampson y Martin/Hopkins**. A continuación, se exponen estas ecuaciones:

- Ecuación de Friedewald: $LDL-c = CT - HDL-c - (TG/5)$.
- Ecuación de Sampson: $LDL-c = CT/0,948 - HDL-c/0,971 - [TG/0,56 + (TG \times no HDL-c)/2,140 - (TG^2/16,100) - 9,44]$.
- Ecuación de Martin/Hopkins: integra un factor individualizado en el denominador, para tener en cuenta la heterogeneidad de la relación de TG y VLDL-c.

- 146.106 pacientes con enfermedad ateroesclerótica.
- Base de datos electrónica de pacientes de Estados Unidos con enfermedad cardiovascular ateroesclerótica y niveles de TG < 400 mg/dl.

- **2 categorías:**

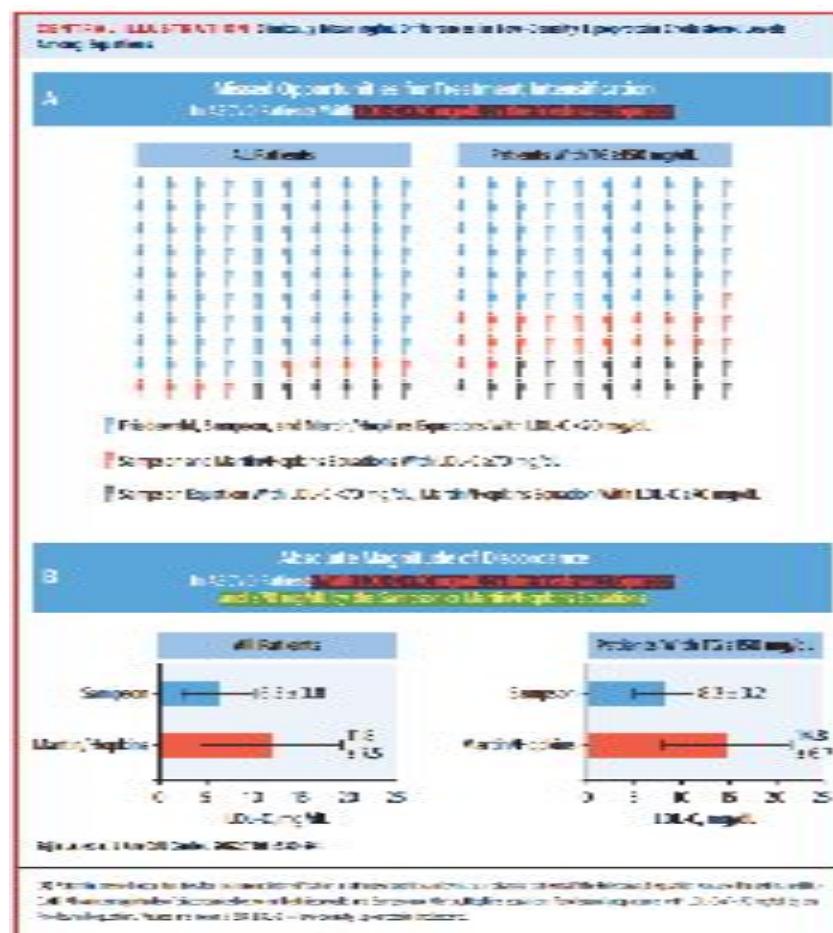
Concordantes si los niveles de LDL-c < 70 mg/dl entre las comparaciones en parejas de las distintas ecuaciones utilizadas.

Discordantes ...

- Para toda la cohorte, los pacientes con discordancia en las cifras de LDL-c presentaban más **D. mellitus** e **hipercolesterolemia familiar**, en puntos de corte más bajos para el **LDL-c (15% en < 70 mg/dl, 23% en < 55 mg/dl)** y en aquellos pacientes con **niveles altos de triglicéridos (> 150 mg/dl)**.



Discordance Between Standard Equations for Determination of LDL Cholesterol in Patients With Atherosclerosis



Discordance Between Standard Equations for Determination of LDL Cholesterol in Patients With Atherosclerosis



AHA/ACC 2018 Guidelines on Treatment of Blood Cholesterol Update

Guías de 2018 de la AHA/ACC se recomendaba el uso de la **ecuación de Martin/Hopkins (Recomendación IIa, nivel de evidencia C)** en pacientes con niveles de LDL-c <70 mg/dl para aumentar la precisión con respecto a la ecuación de Friedewald.

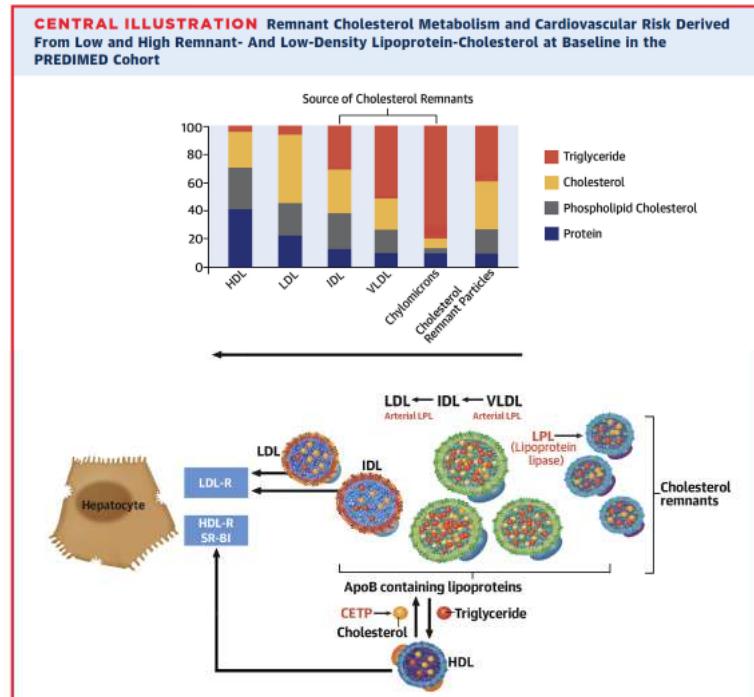
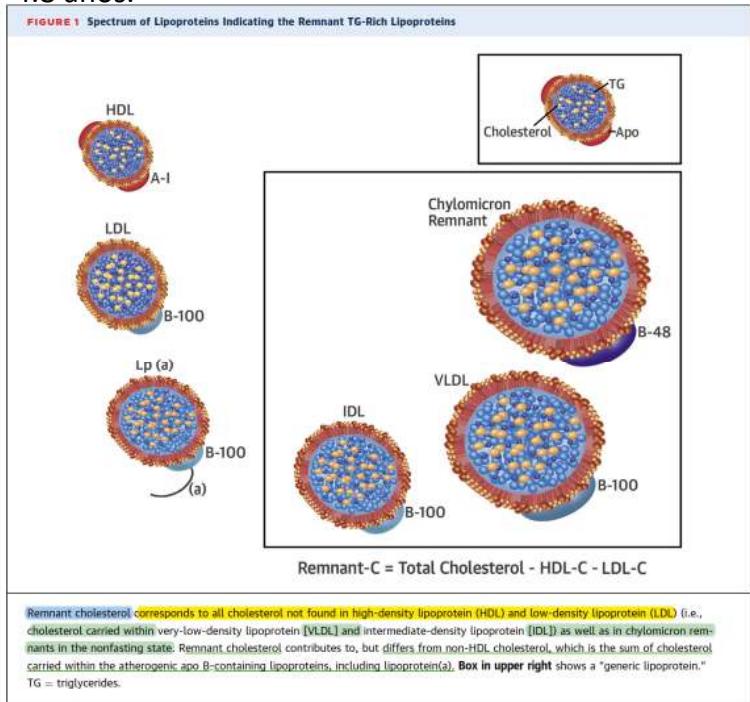


Remnant Cholesterol, Not LDL Cholesterol, Is Associated With Incident Cardiovascular Disease

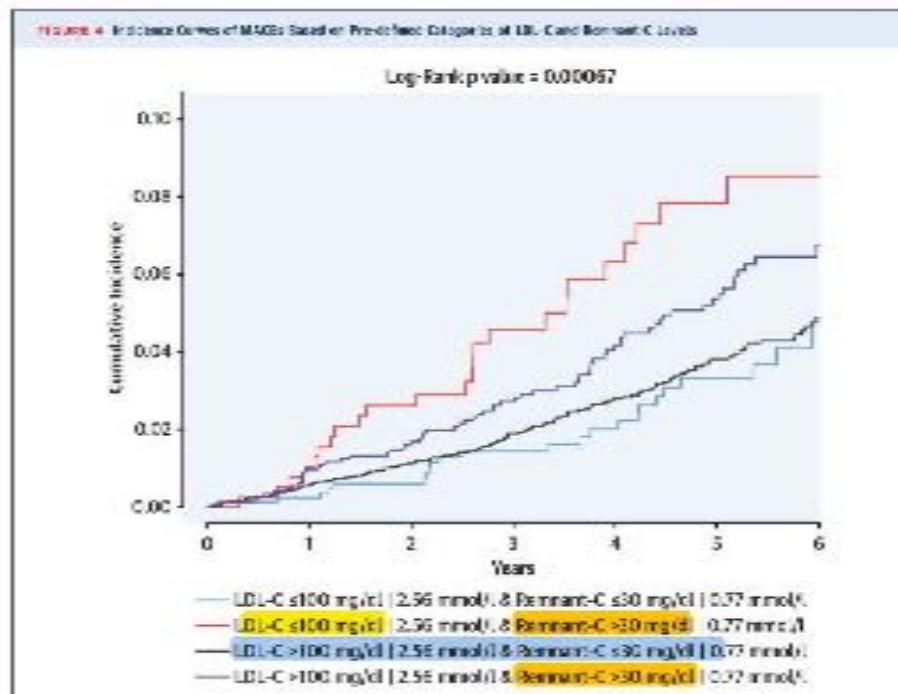
6901 pacientes, MACE 263.

Cohorte PREDIMED

4.8 años.



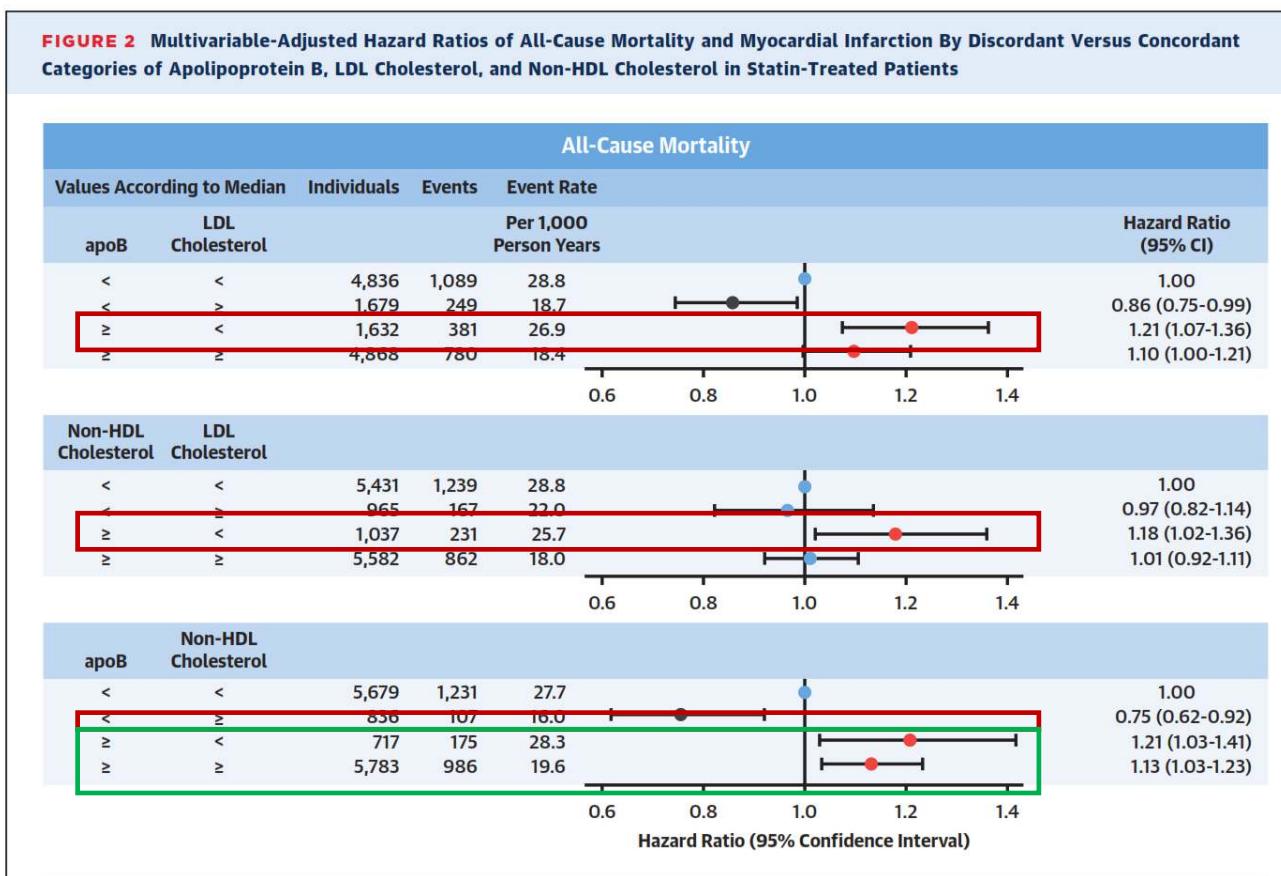
Remnant Cholesterol, Not LDL Cholesterol, Is Associated With Incident Cardiovascular Disease



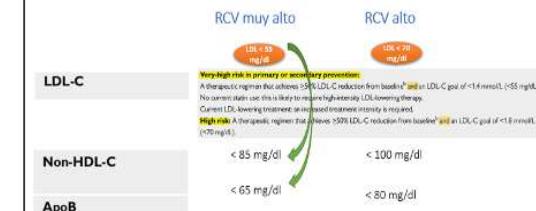
Apolipoprotein B and Non-HDL Cholesterol Better Reflect Residual Risk Than LDL Cholesterol in Statin-Treated Patients



FIGURE 2 Multivariable-Adjusted Hazard Ratios of All-Cause Mortality and Myocardial Infarction By Discordant Versus Concordant Categories of Apolipoprotein B, LDL Cholesterol, and Non-HDL Cholesterol in Statin-Treated Patients



| Median Values |
|--|
| ApoB 92 mg / dl |
| Non-HDL Cholesterol 3.1 mmol / l (120 mg / dl) |
| LDL Cholesterol 2.3 mmol / l (89 mg / dl) |



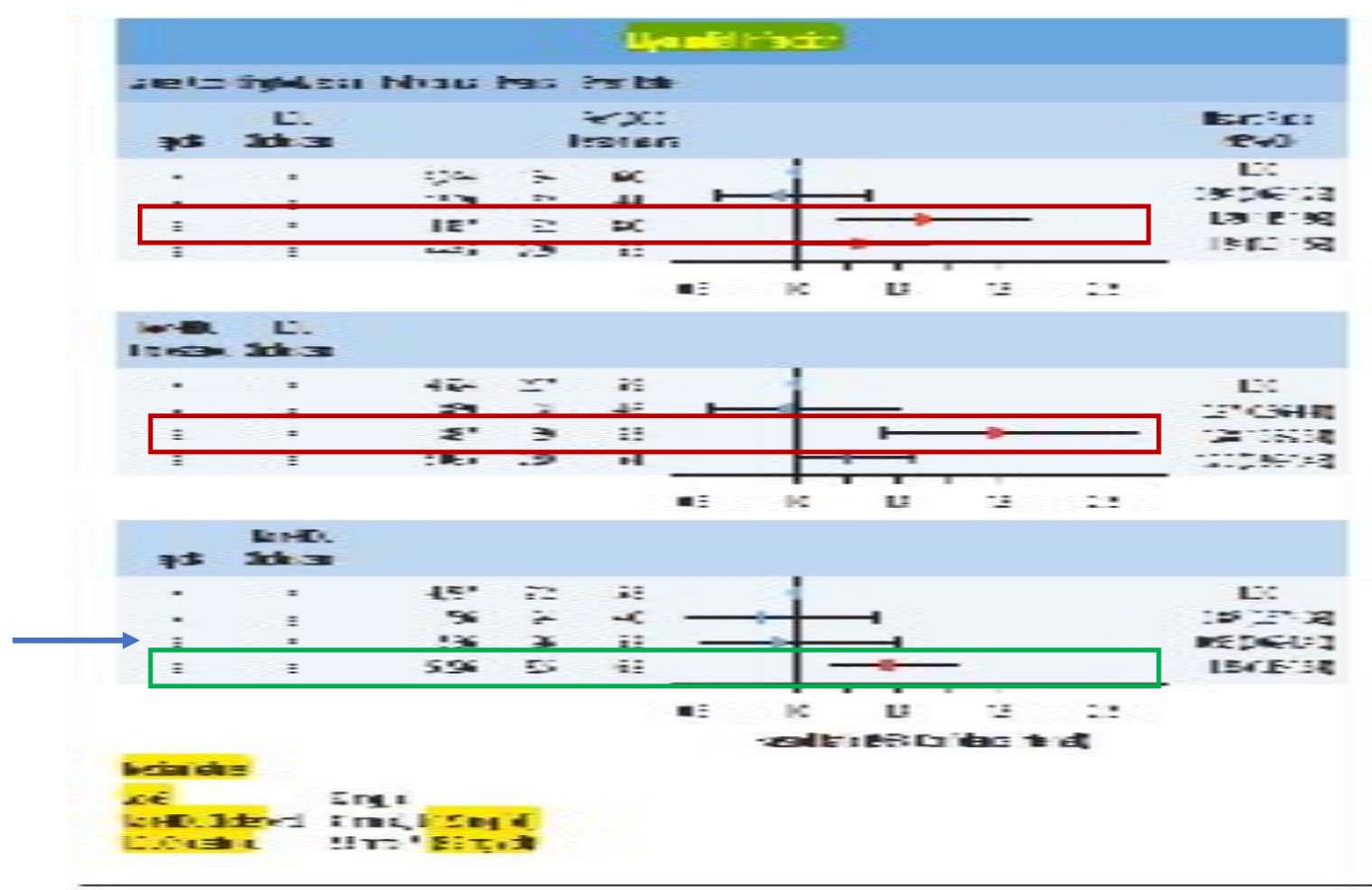
JACC VOL. 77, NO. 11, 2021

MARCH 23, 2021:1439-50





Apolipoprotein B and Non-HDL Cholesterol Better Reflect Residual Risk Than LDL Cholesterol in Statin-Treated Patients



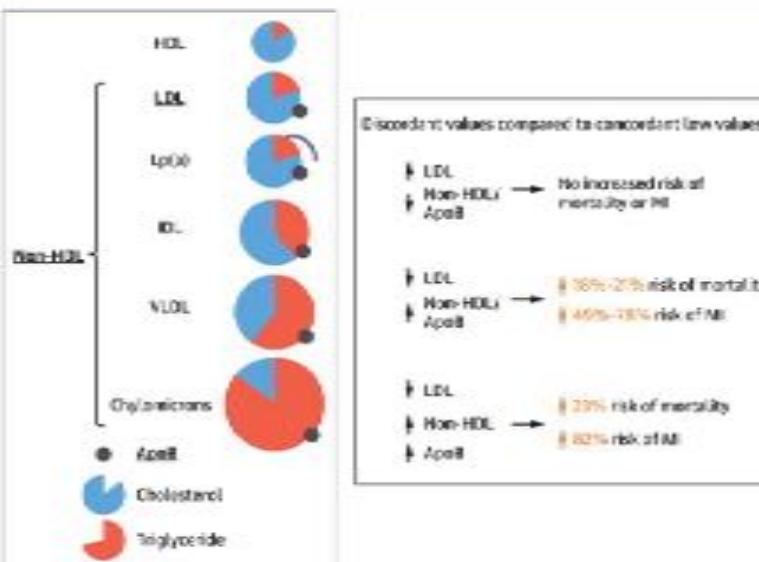
Residual risk is higher in patients with higher apoB and non-HDL cholesterol levels than in patients with higher LDL cholesterol levels. This suggests that apoB and non-HDL cholesterol better reflect residual risk than LDL cholesterol in statin-treated patients.





Apolipoprotein B and Non-HDL Cholesterol Better Reflect Residual Risk Than LDL Cholesterol in Statin-Treated Patients

CENTRAL ILLUSTRATION: Multivariable-Adjusted Risk of All-Cause Mortality and Myocardial Infarction in 13,015 Statin-Treated Patients From the Copenhagen General Population Study



Johannesen, C.D.L. et al. J Am Coll Cardiol. 2021;77(11):1439-50.

CONCLUSIONS In statin-treated patients, elevated apoB and non-HDL cholesterol, but not LDL cholesterol, are associated with residual risk of all-cause mortality and myocardial infarction. Discordance analysis demonstrates that apoB is a more accurate marker of all-cause mortality risk in statin-treated patients than LDL cholesterol or non-HDL cholesterol, and apoB in addition is a more accurate marker of risk of myocardial infarction than LDL cholesterol.

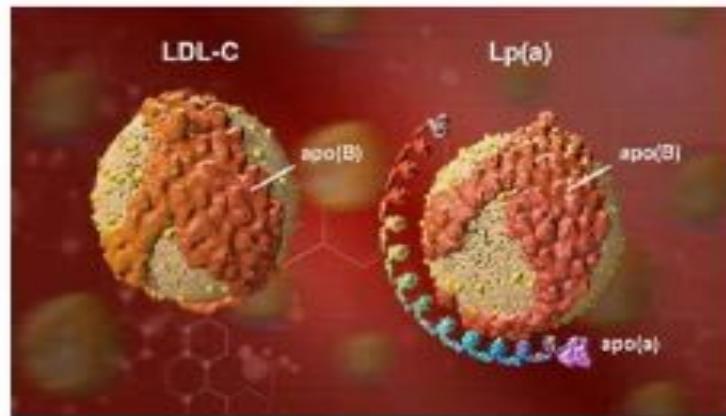
(J Am Coll Cardiol 2021;77:1439-50) © 2021 by the American College of Cardiology Foundation.



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Lipoproteína (a)



Lipoprotein(a) is comprised of an LDL-like particle with a second protein, called apolipoprotein(a), or apo(a), coiled around it.

Estándares SEA 2022 para el control global del riesgo cardiovascular

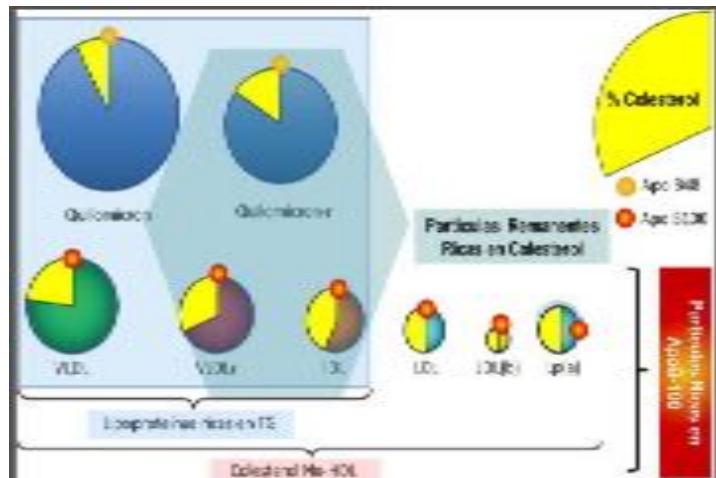


Tabla 4 Criterios diagnósticos

| Diagnóstico | Definición |
|--------------------------|---------------------------------|
| Hiperlipoproteinemia (a) | $Lp(a) \geq 50 \text{ mg/dL}$. |

Paciente de riesgo cardiovascular bajo-moderado

cLDL entre 115 y 190 mg/dL

Actividad física, abstinencia tabáquica y pérdida de peso si fuera necesaria. La prescripción de fármacos para disminuir el colesterol no está universalmente indicada y deberá considerarse de forma individualizada si un paciente presenta dos de los siguientes factores: edad (hombres > 45 años; mujeres > 50 años); IMC > 30 kg/m²; tabaquismo; HTA; antecedentes familiares de ECVA precoz; dislipemia aterogénica; SM; o $Lp(a) > 50 \text{ mg/dL}$.

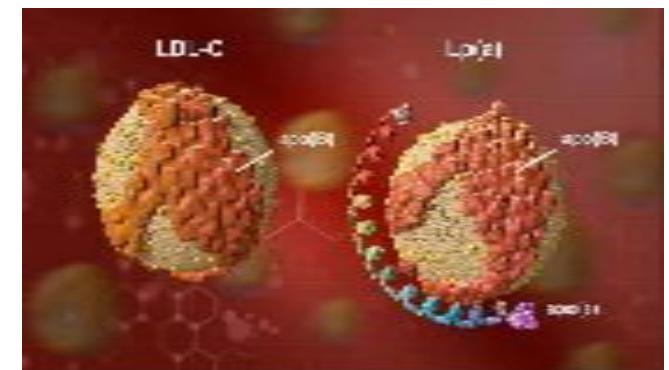
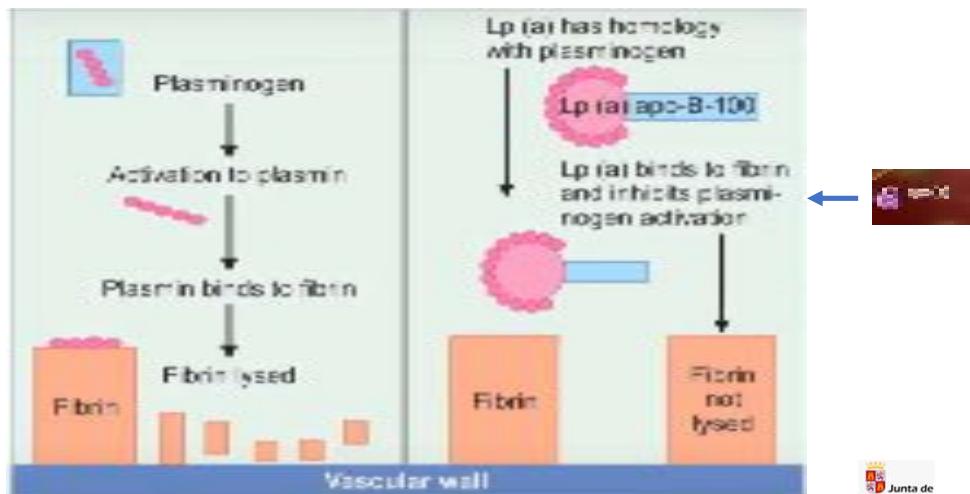
Si $Lp(a) > 50 \text{ mg/dL} \rightarrow$ "Considerar tratamiento"

por alto riesgo de evento isquémico (CI a los 30-40 años).

Lipoproteína (a)

Las elevaciones de Lp(a) se asocian a efectos proaterogénicos *de su fracción similar al LDL – apo(B)*.

- (1) Aterogénesis acelerada. presence of OxPL in Lp(a) particles.
- (2) Estado proinflamatorio.
- (3) Empeoramiento de la EA calcificada.
- (4) Estado protrombótico.



Lipoprotein(a) is composed of an LDL-like particle with a second protein, called apo lipoprotein(a), or apo(a), coiled around it.

Apo-A and Lp(a) are different

Apo-A constituent of HDL.

This "A" is written in capital letters.

It is anti-atherogenic.

Lp(a) constituent of LDL.

This "a" is written in small letters.

Highly atherogenic

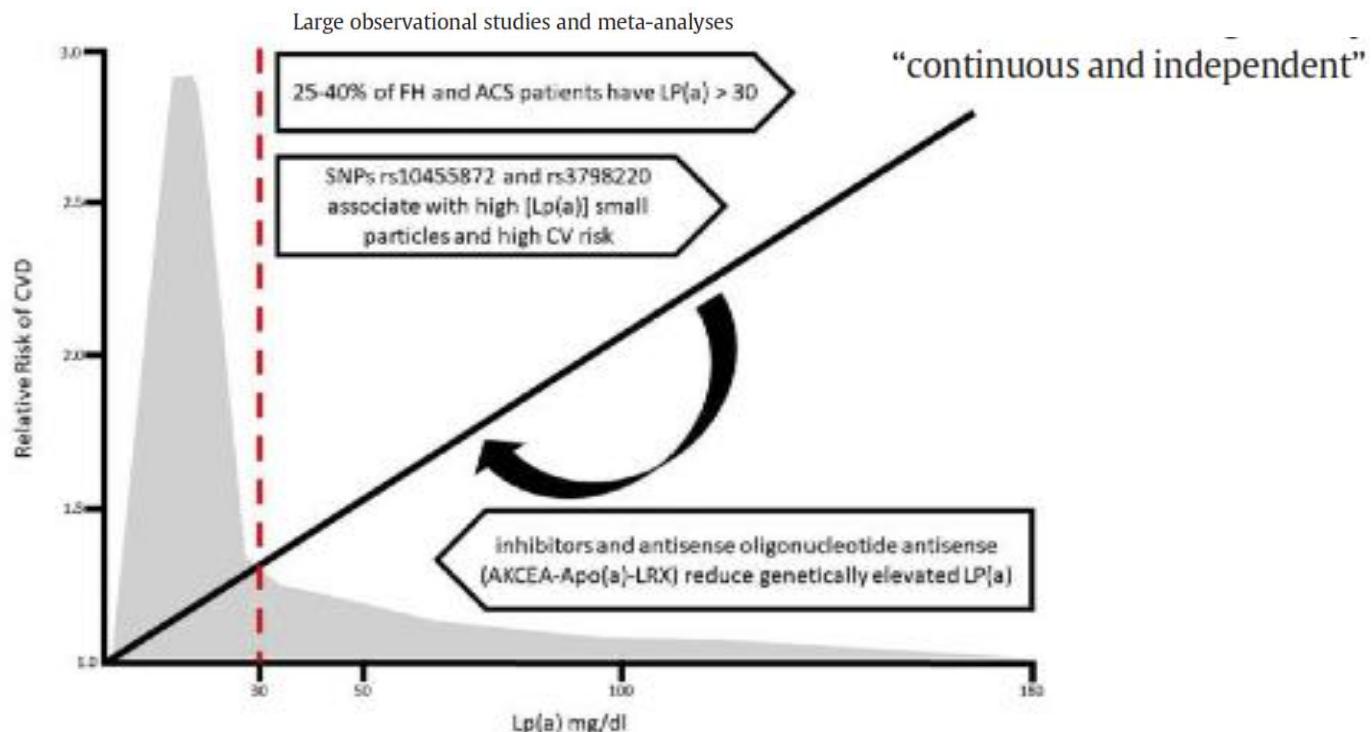


Fig. 1. The relationship between plasma concentrations of $Lp(a)$ and relative risk of CVD. Approximate values summarised from the studies cited in this paper. Text in arrows indicates factors for elevating $[Lp(a)]$ and promising therapeutic strategies to reduce $[Lp(a)]$. The grey shaded area shows the approximate distribution of $[Lp(a)]$ in the population. Abbreviations: ACS, acute coronary syndromes; CV, cardiovascular; FH, familial hypercholesterolaemia; $Lp(a)$, Lipoprotein(a); PCSK9 Proprotein convertase subtilisin/kexin type 9; SNP, single nucleotide polymorphism.

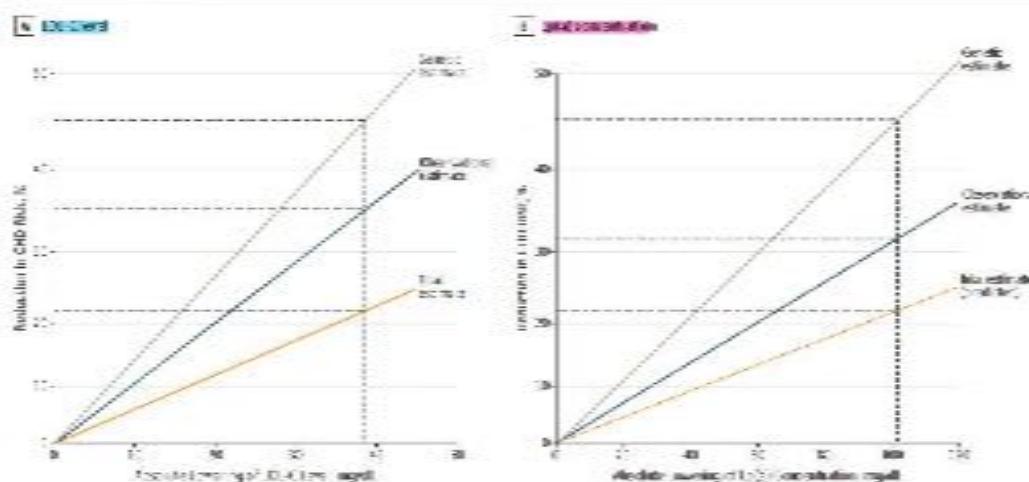
| | | | | |
|--|---|--------|---|--|
| O'Donghue MI, et al. 2019 ³ | Interventional: FOURIER -established ASCVD (statin, ezetimibe, evolocumab) | 25,096 | doubling of median baseline Lp (a) (37 mg/dL) | <ul style="list-style-type: none"> ● associated with increased risk independently of LDL-C level ● reduction of Lp(a) level on evolocumab therapy associated with decreased risk independently of LDL-C lowering |
| Bittner VA, et al. 2020 ⁴ | Interventional: ODYSSEY OUTCOMES - after ACS (statin, ezetimibe, alirocumab) | 18,924 | quartiles: <6.7 mg/dL, 6.7 to <21.2 mg/dL, 21.2 to <59.6 mg/dL, >59.6 mg/dL | <ul style="list-style-type: none"> ● higher baseline Lp(a) quartile associated with increased risk independently of LDL-C level ● reduction of Lp(a) levels on alirocumab therapy associated with decreased risk independently of LDL-C lowering |

Residual Lipid Risk

- CAD event risk reduction of 22%:
 - .. lowering LDL-C level by 38.7 mg/dL (approximately 1.0 mmol/L).
 - .. Lp(a) level would need to be lowered by 65.7 mg/dL.

Association of LPA Variants With Risk of Coronary Disease and the Implications for Lipoprotein(a)-Lowering Therapies A Mendelian Randomization Analysis

Figure 3. Estimates of Coronary Heart Disease (CHD) Risk Reduction With Lowering of Low-Density Lipoprotein Cholesterol (LDL-C) Level and Lipoprotein(a) (Lp(a)) Concentration



Genetic estimates of risk reduction from mendelian randomization known as the observational estimates from prospective cohort studies (blue line) and genetic estimates from genome-wide association studies (GWAS) (orange line) are shown. The vertical axis represents the reduction in CHD risk. The horizontal axis represents the reduction in LDL-C level and in Lp(a) concentration. The vertical dashed line at approximately 40 mg/dL on the x-axis corresponds to the horizontal dashed line at approximately 6% on the y-axis.

Abbreviations: CHD, coronary heart disease; LDL-C, low-density lipoprotein cholesterol; Lp(a), lipoprotein (a).

• linearly proportional

Table 2. Expected Clinical Benefit of Lowering Lp(a)

| Reduction in Lp(a) Concentration, mg/dL | Reduction in LDL-C Level for Equivalent CHD Risk Reduction, mg/dL (95% CI)* |
|---|---|
| 120 | 45.7 (34.1-65.4) |
| 100 | 38.1 (29.4-54.5) |
| 80 | 31.5 (22.7-43.1) |
| 50 | 13.0 (14.2-27.3) |
| 30 | 11.4 (8.5-16.4) |
| 20 | 7.6 (5.7-10.5) |
| 10 | 3.8 (2.8-5.5) |
| 5 | 1.9 (1.4-2.7) |

Abbreviations: CHD, coronary heart disease; LDL-C, low-density lipoprotein cholesterol; Lp(a), lipoprotein (a).

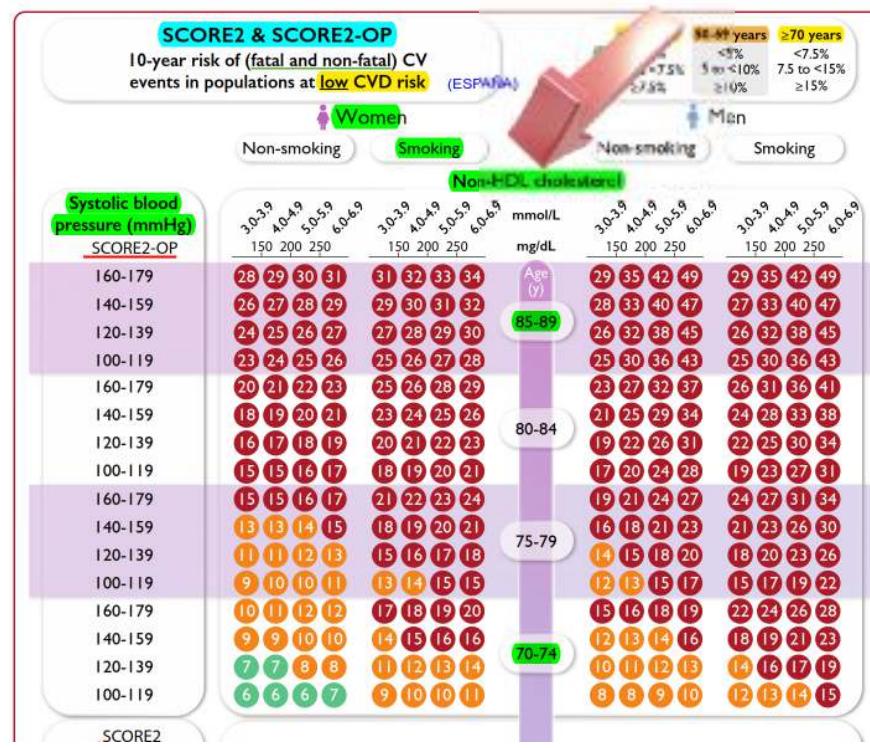
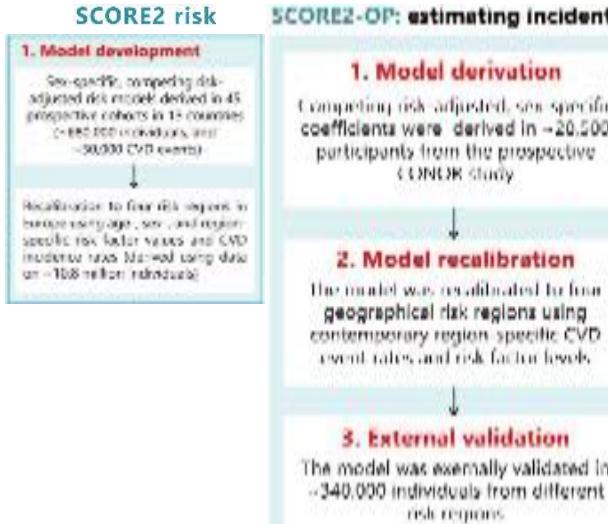




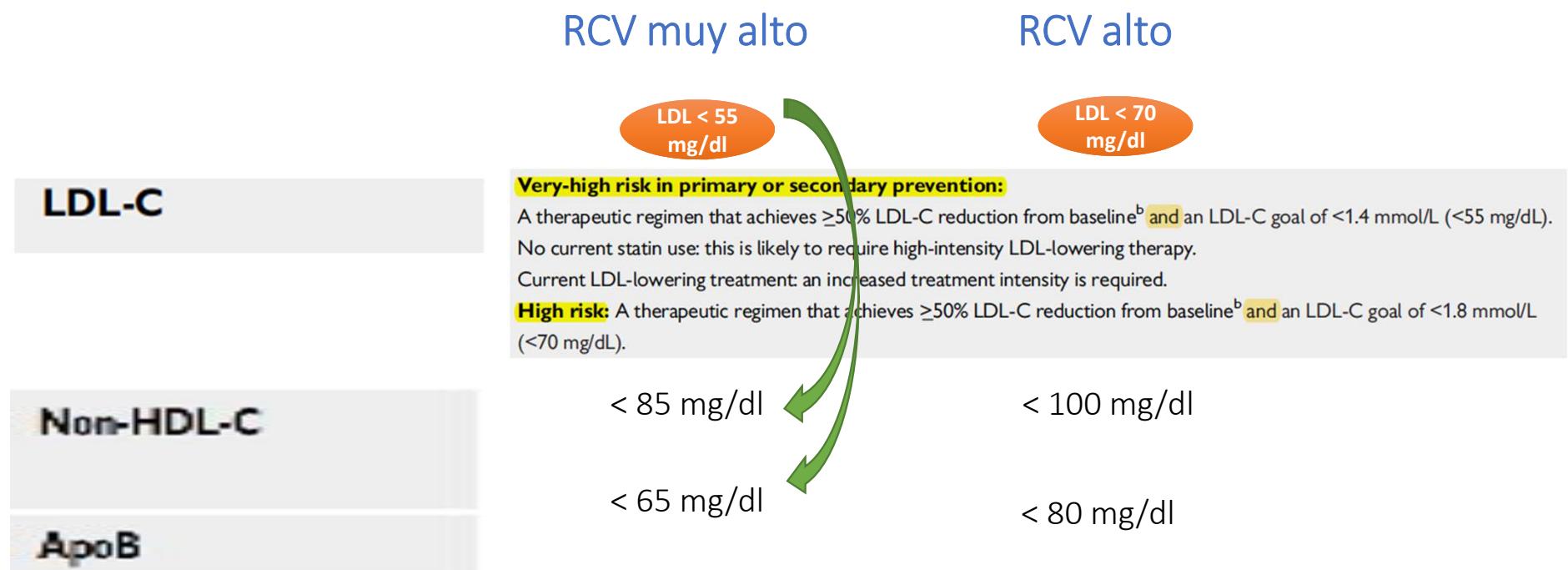
*Take
home message

Systematic Coronary Risk Estimation 2 and Systematic Coronary Risk Estimation 2-Older Persons – SCORE 2 / SCORE OP (≥ 70 años)

.. Risk charts for fatal and non-fatal (myocardial infarction, stroke) cardiovascular disease.



2021 ESC Guidelines on cardiovascular disease prevention in clinical practice



Triglycerides No goal, but <1.7 mmol/L (<150 mg/dL) indicates lower risk and higher levels indicate a need to look for other risk factors.



| Recommendations | Class | Level |
|--|-------|-------|
| For patients with ASCVD who experience a second vascular event within 2 years (not necessarily of the same type as the first event) while taking maximally tolerated statin therapy, an LDL-C goal of <1.0 mmol/L (<40 mg/dL) may be considered. | IIb | B |



Residual Lipid Risk

Objetivos tratamiento:

LDL-Col

Col NO-HDL

Apo B

Si Lp (a) > 50 mg/dl → “Considerar tratamiento”.

por alto riesgo de evento isquémico (CI a los 30-40 años).

Si Lp (a) > 50 mg/dl → Tratamiento ???

Objetivo primario o secundario ??? → Lp (a) < 50 mg/dL.