25 CONGRESO SEFAP • JEREZ
25-27 Mayo 2022

25 años SEFAP
De la calidad terapéutica a la calidad asistencial

Colesterol a debate: ¿Cuánto menos, mejor?

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SEFAP
SOCIEDAD ESPAÑOLA DE FARMACÉUTICOS DE ATENCIÓN PRIMARIA
Fundación Pro-Farmacéuticos de Atención Primaria de España

Efficacy and safety of more intensive lowering of LDL cholesterol: a meta-analysis of data from 170 000 participants in 26 randomised trials

*Cholesterol Treatment Trialists' (CTT) Collaboration**

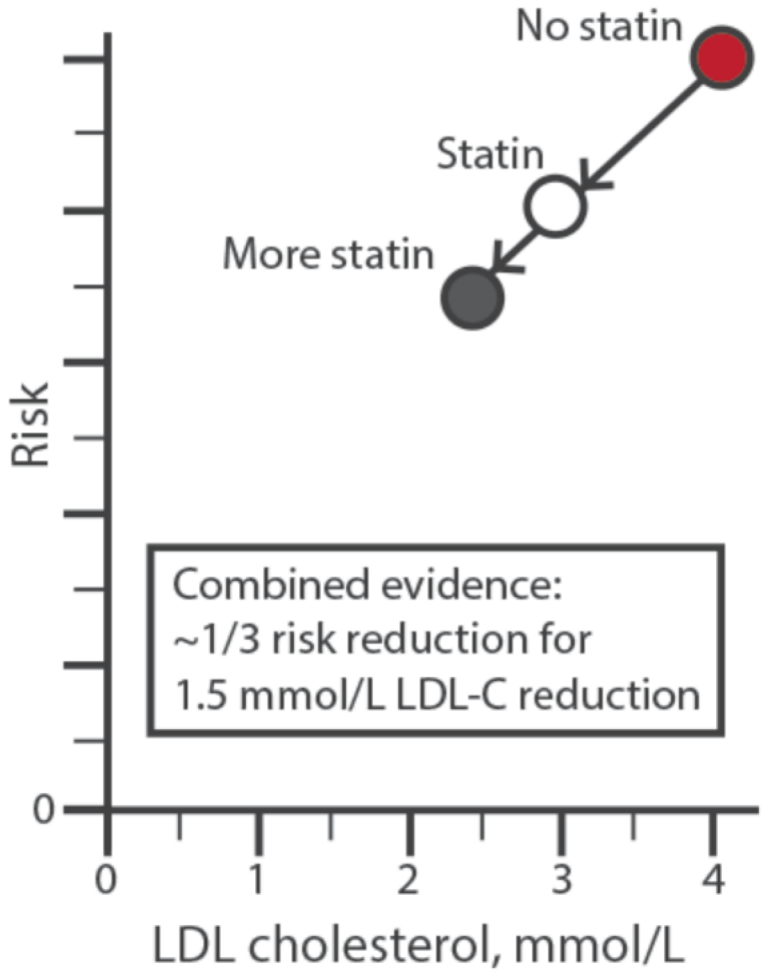
La reducción del cLDL mediante la terapia con estatinas reduce sustancialmente el riesgo de **eventos vasculares graves** (eventos coronarios graves, accidentes cerebrovasculares o la necesidad de revascularización coronaria) y la **mortalidad vascular** en aproximadamente una quinta parte por cada reducción de 1 mmol/L en el colesterol LDL logrado.

1 mmol/l ≈ 39 mg/dl

Reducciones adicionales en el cLDL con una terapia más intensiva con estatinas producen reducciones adicionales en la incidencia de eventos vasculares mayores

Fuente

Absolute effects on major vascular events of lowering LDL cholesterol with statin therapy



1,5 mmol/l ≈ 58 mg/dl

Fuente

ACC/AHA PREVENTION GUIDELINE

2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults

A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines

Fuente

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
VOL. 73, NO. 24, 2019

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CLINICAL PRACTICE GUIDELINE

2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol

A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines

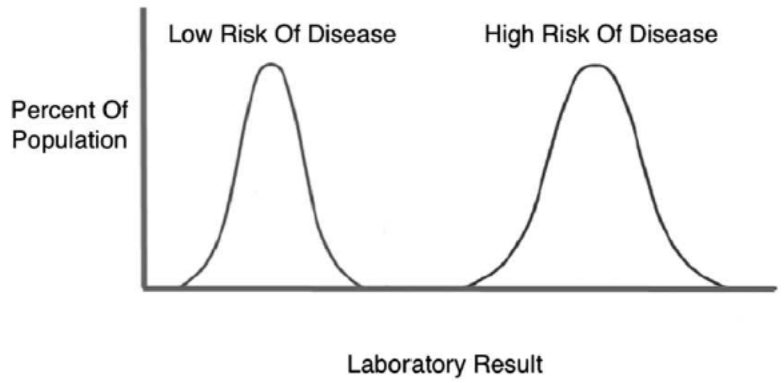
Fuente


ews Agency

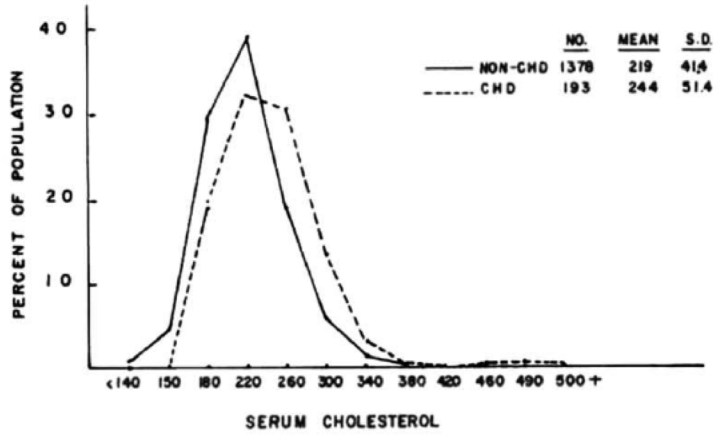
1.- Aproximadamente el 40% de las personas que sufren una enfermedad coronaria tienen un colesterol total <200 mg/dl

2.- Muchas personas con unos niveles elevados de colesterol jamás sufrirán un evento cardiovascular.

3.- Fármacos como el evacetrapib redujeron el cLDL (estudio ACCELERATE) en un 37% e incrementaron el cHDL en un 130% sin impacto en los eventos ni en la mortalidad.



Ideal Risk Factor



Framingham Heart Study

Fuente 1, 2

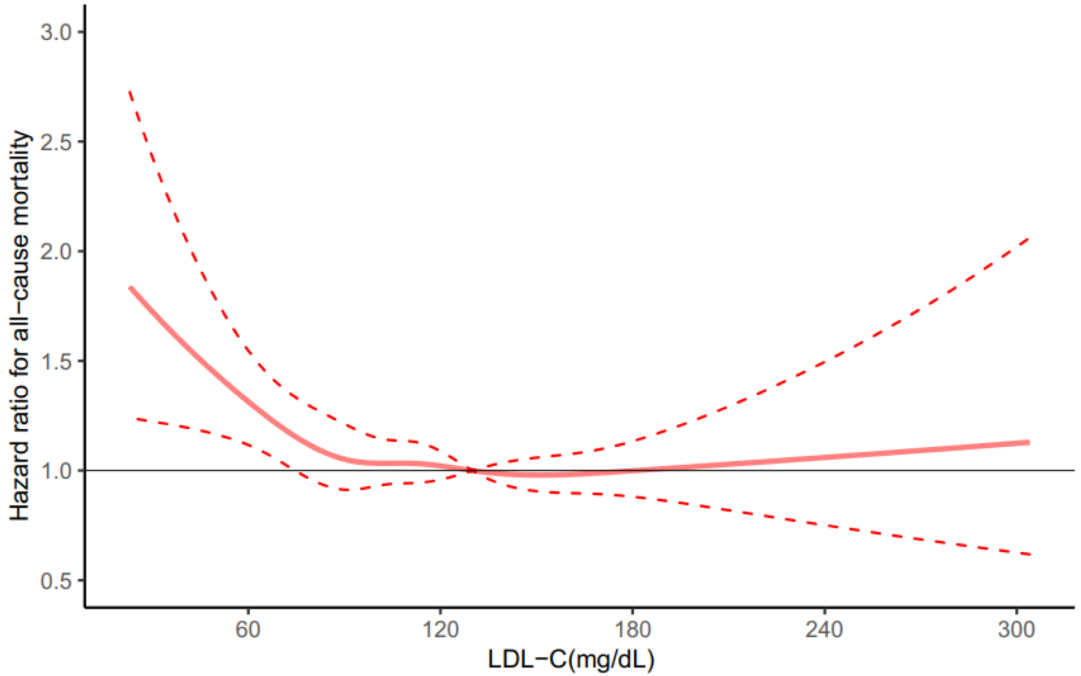
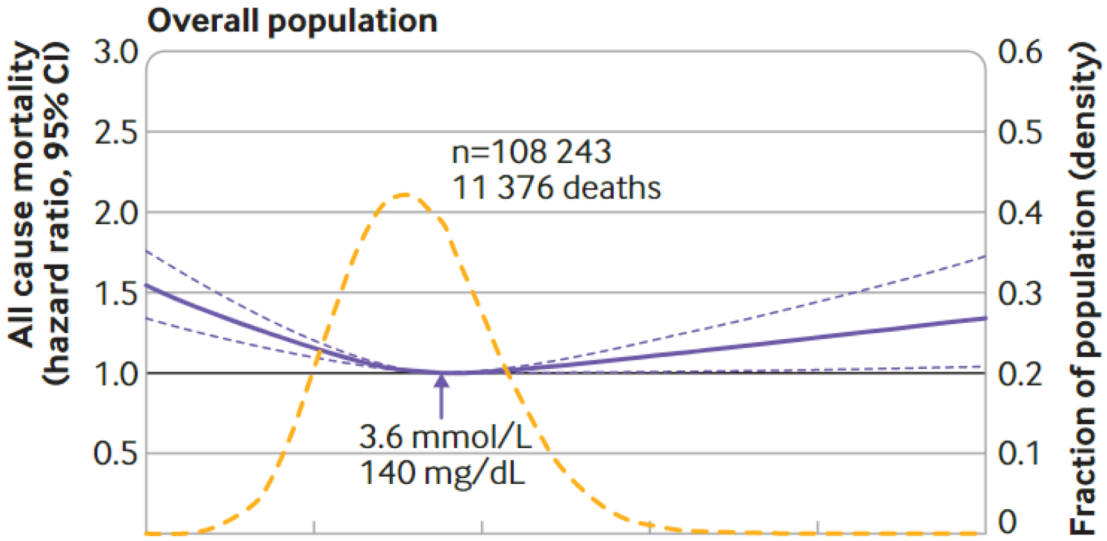


Figure 2. Spline plot of low-density lipoprotein cholesterol (LDL-C) level and all-cause mortality rate. The adjusted odd ratios and 95% confidence intervals (CIs) were calculated with logistic regression models after adjusting for age (continuous), sex, race, marital status, education level, smoking status, BMI (continuous), hypertension, diabetes, cardiovascular disease, cancer.



Fuente: 1, 2, 3, 4

EBM analysis: Primary care

Hit or miss: the new cholesterol targets

Robert DuBroff [1], Aseem Malhotra, [2] Michel de Lorgeril[3]

Table 1 Randomised controlled trials of cholesterol reduction in moderate-risk individuals (LDL-C reduction target ≥30%)

Study, year Quality score	Population size and characteristics	Intervention (drug class)	Study duration	LDL-C target met?	Mortality benefit? (NNT)	CVD benefit? (NNT)
WOSCOPS, 1995 A[36]	6595 men high cholesterol	Pravastatin 40 mg/day (statin)	4.9 years	No (LDL-C ↓26%)	No (RR 0.78; 95% CI 0.60 to 1.00)	Yes (RR 0.69; 95% CI 0.57 to 0.83) (45)
AFCAPS/TexCAPS, 1998 A[37]	6605 average cholesterol	Lovastatin 20–40 mg/day (statin)	5.2 years	No (LDL-C ↓26%)	No (OR 1.37; 95% CI 0.63 to 2.98)	Yes (RR 0.63; 95% CI 0.50 to 0.79) (71)
ALLHAT-LLT, 2002 B (open label)[38]	10 355 HBP	Pravastatin 40 mg/day (statin)	4.8 years	No (LDL-C ↓17%)	No (RR 0.99; 95% CI 0.89 to 1.11)	No (RR 0.91; 95% CI 0.79 to 1.04)
ASCOT-LLA, 2003 A[39]	10 305 HBP	Atorvastatin 10 mg/day (statin)	3.3 years	No (LDL-C ↓29%)	No (HR 0.87; 95% CI 0.71 to 1.06)	Yes (HR 0.64; 95% CI 0.50 to 0.83) (91)
PREVEND-IT, 2004 C (small population size)[40]	864 microalbuminuria	Pravastatin 40 mg/day (statin)	3.8 years	No (LDL-C ↓22%)	No (OR 1.50; 95% CI 0.42 to 5.35)	No (OR 0.85; 95% CI 0.44 to 1.61)
CARDS, 2004 A[41]	2838 T2DM	Atorvastatin 10 mg/day (statin)	3.9 years	Yes (LDL-C ↓31%)	No (HR 0.73; 95% CI 0.52 to 1.01)	Yes (RR 0.63; 95% CI 0.48 to 0.83) (31)
St Francis, 2005 A[42]	1005 CAC >80th percentile	Atorvastatin 20 mg/day (statin)	4.3 years	Yes (LDL-C ↓43%)	NR	No (OR 0.68; 95% CI 0.43 to 1.07)
4D, 2005 A[43]	1255 T2DM, haemodialysis	Atorvastatin 20 mg/day (statin)	4 years	Yes (LDL-C ↓42%)	No (RR 0.93; 95% CI 0.79 to 1.08)	No (RR 0.92; 95% CI 0.77 to 1.10)
ASPEN, 2006 A[44]	2410 T2DM	Atorvastatin 10 mg/day (statin)	4 years	No (LDL-C ↓29%)	No	No (HR 0.9; 95% CI 0.73 to 1.12)
MEGA, 2006 B (open label)[5]	7832 high cholesterol	Pravastatin 10–20 mg/day (statin)	5.3 years	No (LDL-C ↓15%)	No (HR 0.72; 95% CI 0.51 to 1.01)	Yes (HR 0.67; 95% CI 0.49 to 0.91) (125)
JUPITER, 2008 A[45]	17 800 LDL-C <130 mg/dL, hsCRP >2 mg/L	Rosuvastatin 20 mg/day (statin)	1.9 years	Yes (LDL-C ↓49%)	No (HR 0.81; 95% CI 0.63 to 1.04) (white subjects)	Yes (HR 0.55; 95% CI 0.43 to 0.69) (white subjects) (67)
AURORA, 2009 A[46]	2776 hemodialysis	Rosuvastatin 10 mg/day (statin)	3.8 years	Yes (LDL-C ↓43%)	No (HR 0.96; 95% CI 0.86 to 1.07)	No (HR 0.96; 95% CI 0.84 to 1.11)
ACAPS, 2010 C (small population size)[47]	919 early carotid atherosclerosis	Lovastatin 20–40 mg/day (statin)	3 years	No (LDL-C ↓28%)	Yes (OR 0.12; 95% CI 0.02 to 0.99) (9)	Yes (OR 0.35; 95% CI 0.12 to 0.98) (50)
SHARP, 2011 A[48]	9270 CKD	Simvastatin 20 mg + ezetimibe 10 mg/day (statin + CAI)	4.9 years	Yes (LDL-C ↓31%)	No (RR 1.01; 95% CI 0.75 to 1.35) CHD death	Yes (RR 0.83; 95% CI 0.74 to 0.94) (250)
HOPE-3, 2016 A[49]	12 705 HBP, intermediate risk	Rosuvastatin 10 mg/day (statin)	5.6 years	No (LDL-C ↓26%)	No (HR 0.93; 95% CI 0.80 to 1.08)	Yes (HR 0.76; 95% CI 0.64 to 0.91) (91)

CAC, coronary artery calcium score; CAI, cholesterol absorption inhibitor; CKD, chronic kidney disease; CVD, cardiovascular disease; HBP, high blood pressure; HR, hazard ratio; hsCRP, highly sensitive C reactive protein; LDL-C, low density lipoprotein cholesterol; NNT, number needed to treat (to prevent one death or cardiovascular event); NR, not reported; OR, odds ratio; PCSK9, proprotein convertase subtilisin/kexin type 9 inhibitor; RR, risk ratio; statin, HMG-CoA reductase inhibitor; T2DM, type 2 diabetes mellitus.

Fuente

Table 2 Randomised controlled trials of cholesterol reduction in high-risk individuals (LDL-C reduction target ≥50%)

Study, year Quality score	Population size and characteristics	Intervention (drug class)	Study duration	LDL-C target met?	Mortality benefit? (NNT)	CVD benefit? (NNT)
4 S, 1994 A[10]	4444 CHD	Simvastatin 20–40 mg/day (statin)	5.4 years	No (LDL-C ↓35%)	Yes (RR 0.70; 95% CI 0.58 to 0.85) (30)	Yes (RR 0.66; 95% CI 0.59 to 0.75) (15)
CARE, 1996 A[50]	4159 s/p MI	Pravastatin 40 mg/day (statin)	5 years	No (LDL-C ↓32%)	No	Yes (RR 0.76; 95% CI 0.64 to 0.91) (33)
LIPID, 1998 A[51]	9014 CHD	Pravastatin 40 mg/day (statin)	6.1 years	No (LDL-C ↓25%)	Yes (RR 0.78; 95% CI 0.69 to 0.87) (32)	Yes (RR 0.76; 95% CI 0.65 to 0.88) (34)
GISSI-P, 2000 C (study stopped and modified)[52]	4271 s/p MI	Pravastatin 20 mg/day (statin)	1.9 years	No (LDL-C ↓16%)	No (HR 0.84; 95% CI 0.61 to 1.14)	No (HR 0.90; 95% CI 0.71 to 1.15)
LIPS, 2002 A[53]	1677 s/p PCI	Fluvastatin 80 mg/day (statin)	3.9 years	No (LDL-C ↓27%)	No (RR 0.69; 95% CI 0.45 to 1.07)	Yes (RR 0.78; 95% CI 0.64 to 0.95) (19)
GREACE, 2002 B (open label)[54]	1600 CHD	Atorvastatin 10–80 mg/day (statin)	3 years	No (LDL-C ↓46%)	Yes (RR 0.57; 95% CI 0.39 to 0.78) (48)	Yes (RR 0.49; 95% CI 0.27 to 0.73) (26)
ALLIANCE, 2004 B (open label)[6]	2442 CHD	Atorvastatin 10–80 mg/day (statin)	4.3 years	No (LDL-C ↓11%)	No (HR 0.92; 95% CI 0.72 to 1.18)	Yes (HR 0.83; 95% CI 0.71 to 0.97) (29)
SPARCL, 2006 A[55]	4731 s/p TIA or CVA	Atorvastatin 80 mg/day (statin)	4.9 years	No (LDL-C ↓43%)	No (HR 1.03; 95% CI 0.84 to 1.25)	Yes (HR 0.80; 95% CI 0.69 to 0.92) (53)
CORONA, 2007 A[56]	5011 >60 years, ischaemic HF	Rosuvastatin 10 mg/day (statin)	2.7 years	No (LDL-C ↓45%)	No (HR 0.95; 95% CI 0.86 to 1.05)	No (HR 0.92; 95% CI 0.83 to 1.02)
SEAS, 2008 A[7]	1873 mild to moderate aortic stenosis	Simvastatin 40 mg + ezetimibe 10 mg/day (statin + CAI)	4.4 years	Yes (LDL-C ↓50%)	No (HR 1.04; 95% CI 0.79 to 1.36)	No (HR 0.96; 95% CI 0.83 to 1.12)
ENHANCE, 2008 C (small population size)[57]	720 FH on simvastatin 80 mg/day	Ezetimibe 10 mg/day (CAI)	2 years	No (LDL-C ↓17%)	No (OR 2.02; 95% CI 0.18 to 22.38)	No (OR 1.45; 95% CI 0.55 to 3.86)
ODYSSEY Long Term, 2015 A[58]	2341 high risk on statin	Alirocumab 150 mg/2 weeks (PCSK9)	1.5 years	Yes (LDL-C ↓62%)	NR	No (OR 0.91; 95% CI 0.61 to 1.35)
ODYSSEY COMBO I to 2015 C (small population size, short duration)[59]	316 high risk on statin	Alirocumab 75–150 mg/2 weeks (PCSK9)	1 year	No (LDL-C ↓46%)	NR	No (OR 1.03; 95% CI 0.25 to 4.22)
ODYSSEY FH1, 2015 C (small population size)[8]	486 FH	Alirocumab 75–150 mg/2 weeks (PCSK9)	1.5 years	Yes (LDL-C ↓58%)	No (OR 5.06; 95% CI 0.28 to 90.44)	No (OR 1.36; 95% CI 0.36 to 5.19)
ODYSSEY FH2, 2015 C (small population size)[8]	249 FH	Alirocumab 75–150 mg/2 weeks (PCSK9)	1.5 years	Yes (LDL-C ↓51%)	No deaths reported	No (OR 0.79; 95% CI 0.07 to 8.84)
IMPROVE-IT, 2015 A[27]	18 144 ACS on simvastatin 40 mg/day	Ezetimibe 10 mg/day (CAI)	6 years	No (LDL-C ↓24%)	No (HR 0.99; 95% CI 0.91 to 1.07)	Yes (HR 0.94; 95% CI 0.89 to 0.99) (56)
SPIRE 1&2, 2017 B (short study duration)[9]	27 438 high risk on statin	Bococizumab 150 mg/2 weeks (PCSK9)	1 year	Yes (LDL-C ↓64%)	No (HR 1.02; 95% CI 0.79 to 1.31)	No (HR 0.88; 95% CI 0.76 to 1.02)
HIJ-PROPER, 2017 B (open label)[60]	1734 ACS on pitavastatin	Ezetimibe 10 mg/day (CAI)	3.9 years	No (LDL-C ↓15%)	No (HR 0.70; 95% CI 0.47 to 1.04)	No (HR 0.89; 95% CI 0.76 to 1.04)
FOURIER, 2017 A[61]	27 564 ASCVD on statin	Evolocumab 140 mg/2 weeks or 420 mg/month	2.2 years	Yes (LDL-C ↓59%)	No (HR 1.04; 95% CI 0.91 to 1.19)	Yes (HR 0.85; 95% CI 0.79 to 0.92) (67)

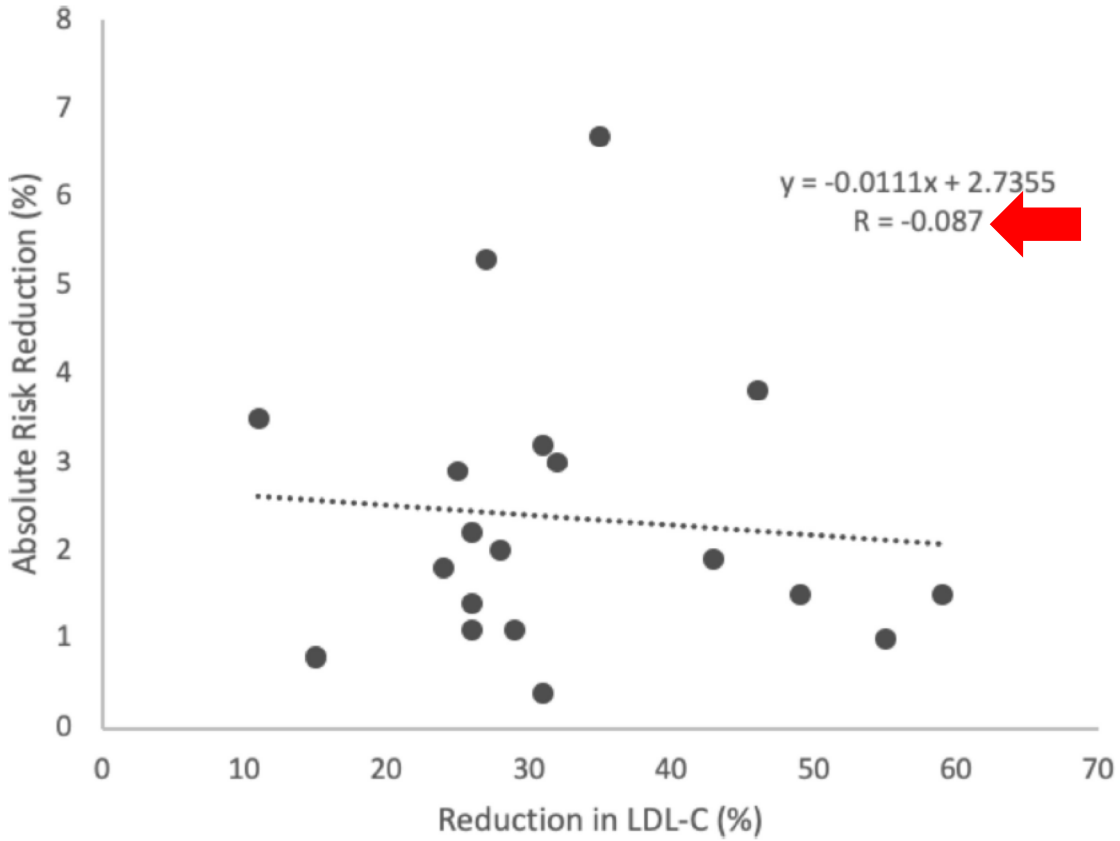


Figure 3 Relationship between the per cent reduction in low density lipoprotein cholesterol (LDL-C) and the absolute risk reduction in cardiovascular events (R, correlation coefficient).

Fuente

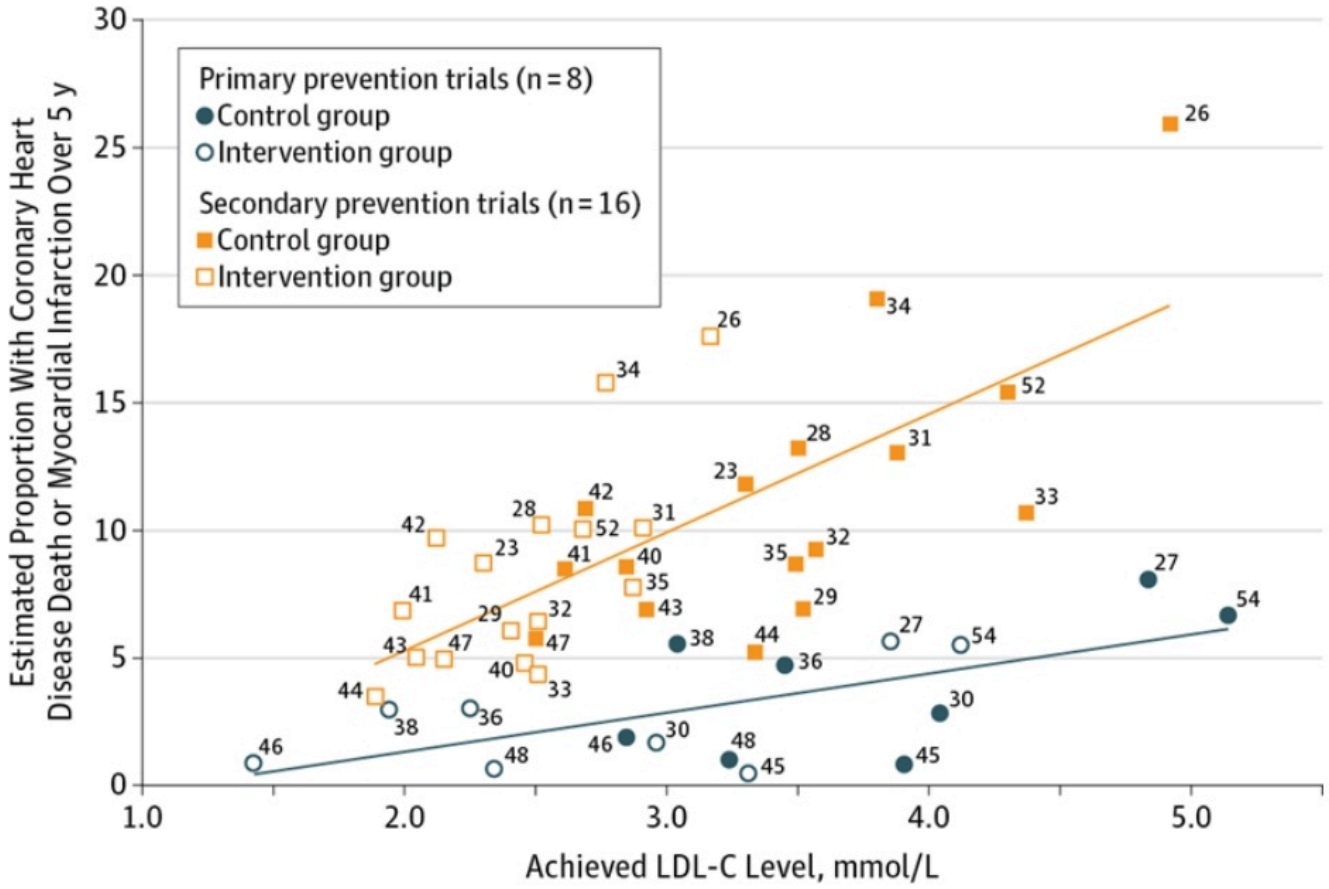
Original Investigation

September 27, 2016

Association Between Lowering LDL-C and Cardiovascular Risk Reduction Among Different Therapeutic Interventions

A Systematic Review and Meta-analysis

Michael G. Silverman, MD[1]; Brian



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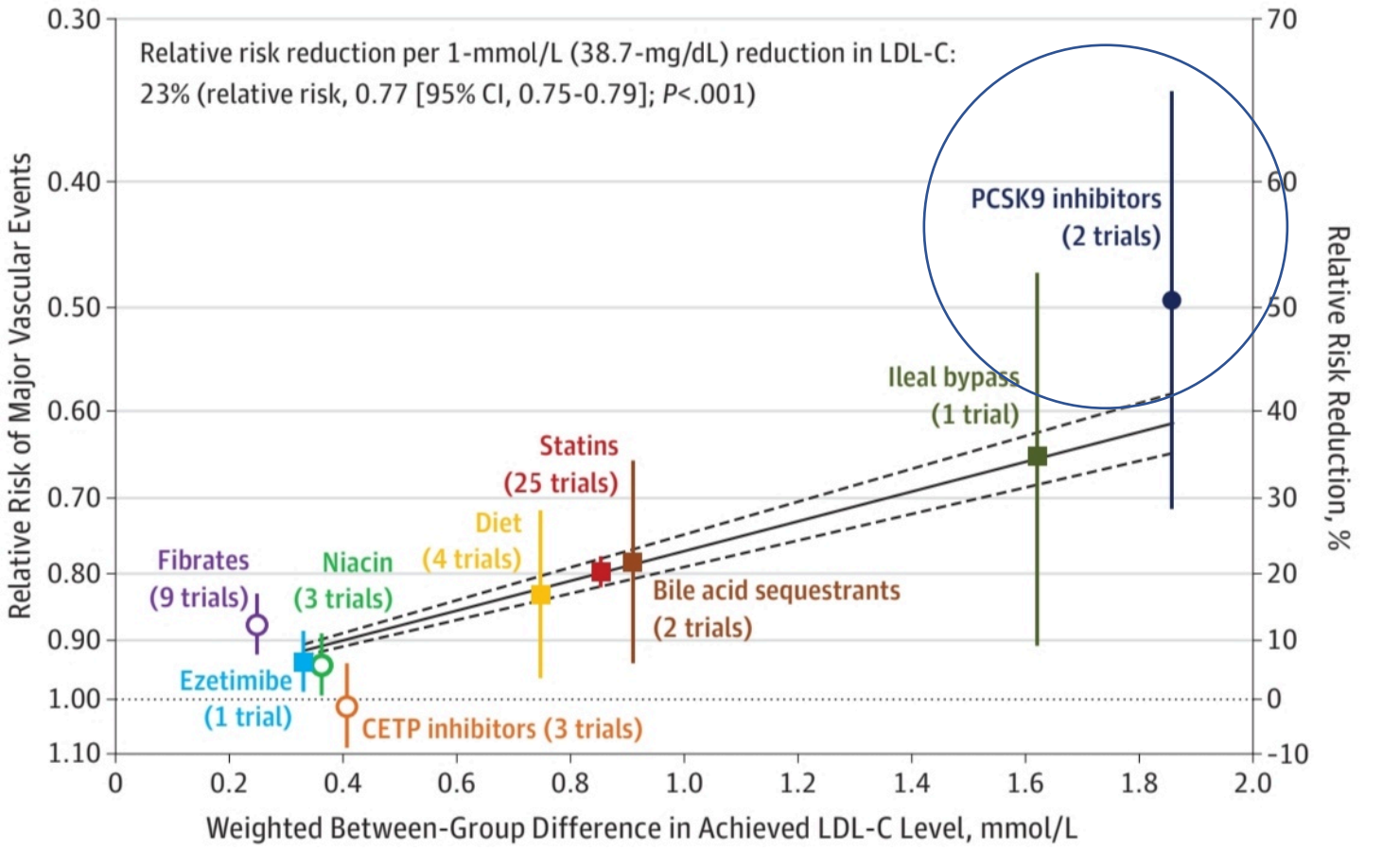
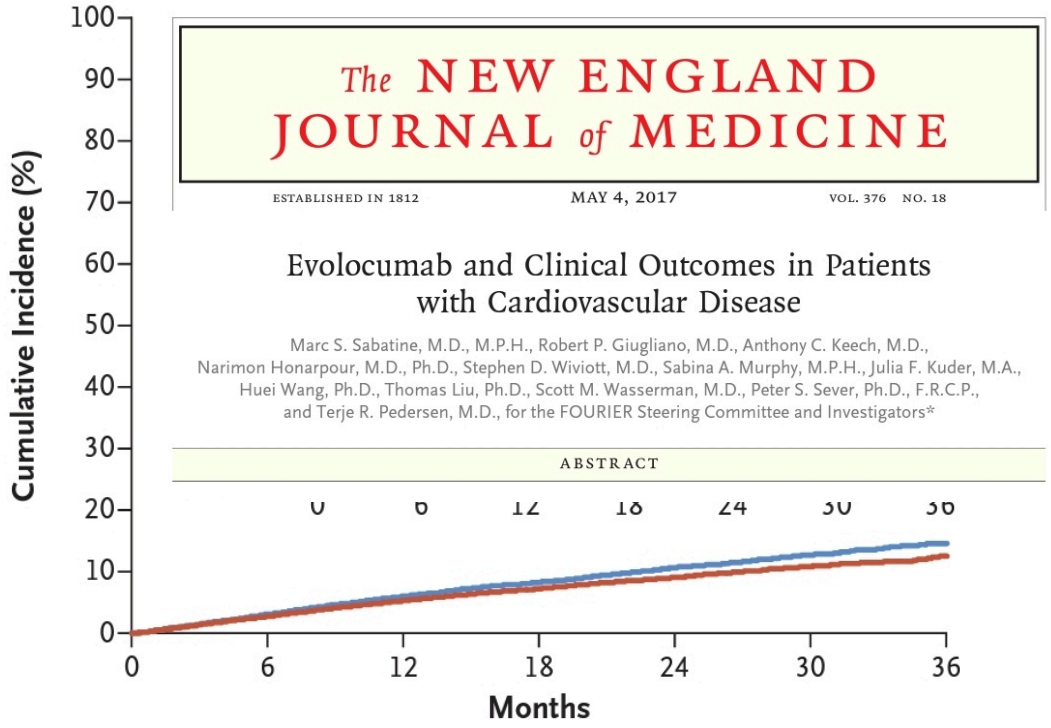


A Primary Efficacy End Point



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Evolocumab and Clinical Outcomes in Patients with Cardiovascular Disease

Marc S. Sabatine, M.D., M.P.H., Robert P. Giugliano, M.D., Anthony C. Keech, M.D., Narimon Honarpour, M.D., Ph.D., Stephen D. Wiviott, M.D., Sabina A. Murphy, M.P.H., Julia F. Kuder, M.A., Huei Wang, Ph.D., Thomas Liu, Ph.D., Scott M. Wasserman, M.D., Peter S. Sever, Ph.D., F.R.C.P., and Terje R. Pedersen, M.D., for the FOURIER Steering Committee and Investigators*

ABSTRACT

No. at Risk

Placebo	13,780	13,278	12,825	11,871	7610	3690	686
Evolocumab	13,784	13,351	12,939	12,070	7771	3746	689

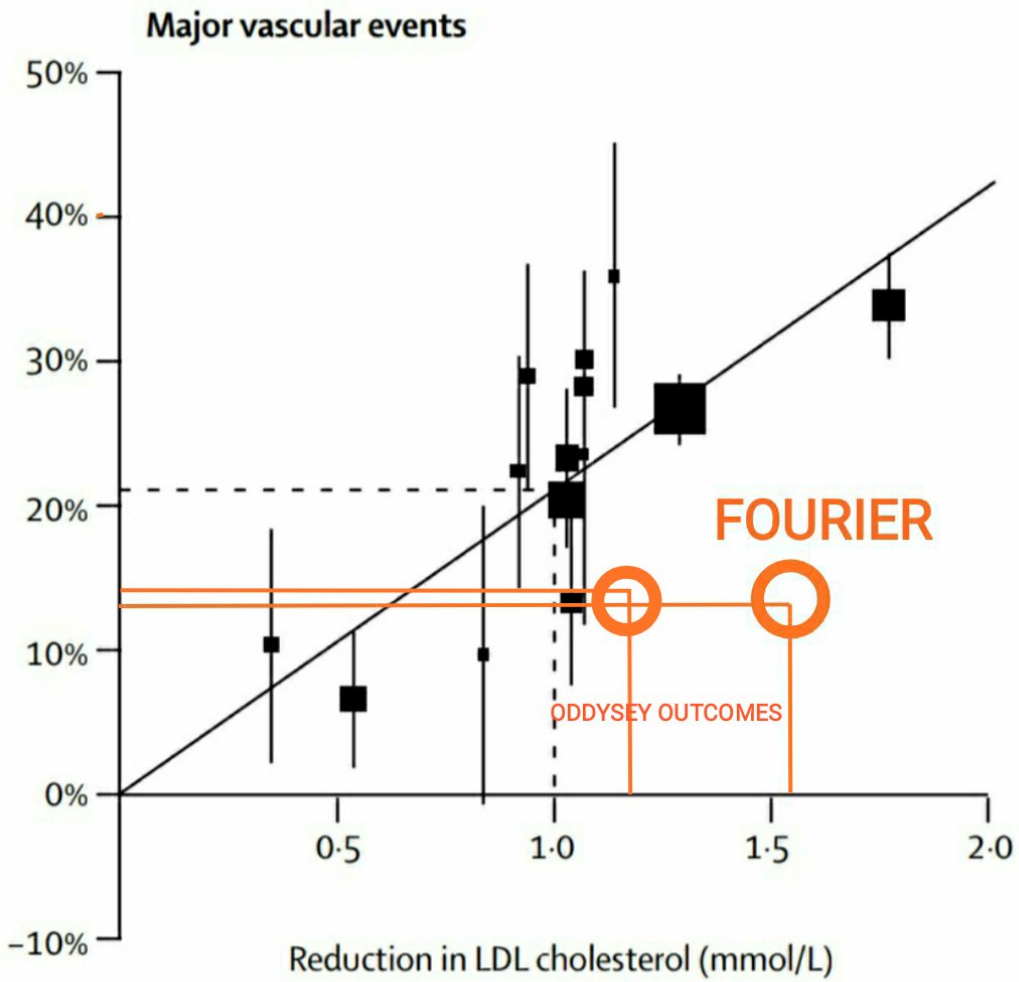


Tabla 10.1: Hoja de información al usuario (Fact Box)

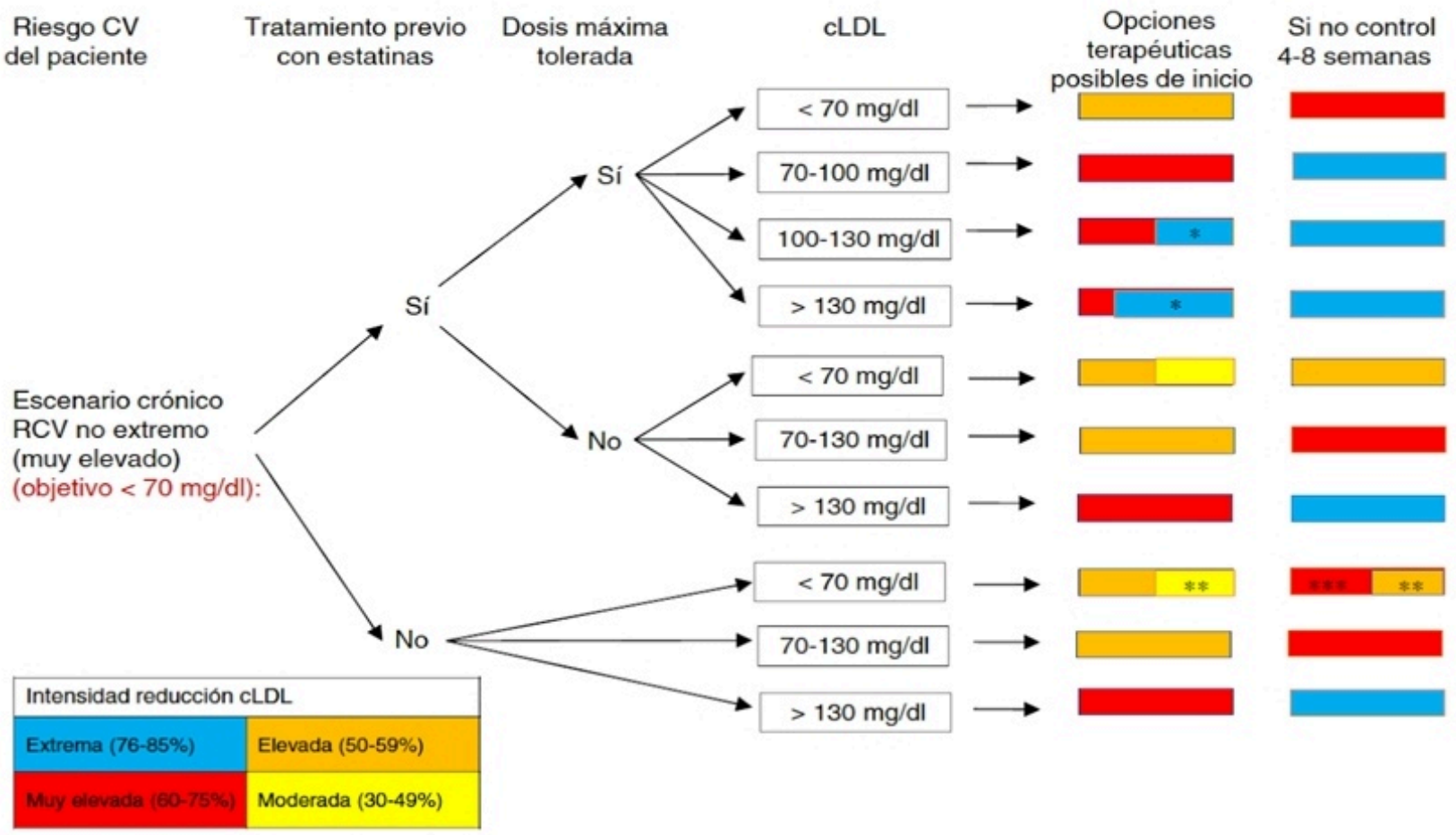
Estatinas frente a placebo en personas sin enfermedad cardiovascular (prevención primaria CV)

Número esperable de españoles de 60-65 años **que padecen un evento**, durante 3,5 años de tratamiento y seguimiento con estatina o con placebo, aplicando los resultados de la Revisión Sistemática GRADE(*) a los riesgos basales de España.

	De cada 1.000 personas tomando estatinas	De cada 1.000 personas tomando placebo	
Beneficios (personas que padecen un evento)			**NNT**
Mortalidad por cualquier causa	23	27	250
Mortalidad cardiovascular	5	6	1.000
Mortalidad por enfermedad coronaria	2	2	-
Infarto de miocardio	5	8	334
Accidente cerebrovascular	7	10	334
Daños añadidos (personas que padecen un evento)			**NNH**
Incidencia de Diabetes mellitus tipo 2	9	8	1.000
Mialgia	100	55	23

(*) Sánchez Robles GA, et al. Revisión GRADE de estatinas en población con ≥ 90% en prevención primaria cardiovascular. Sección 2: Variables de beneficio cardiovascular asociadas a estatinas. [Actualizado a 24-ene-2018.] Página web evalmed.es 22-feb-2018, Disponible en: http://evalmedicamento.weebly.com/evaluaciones/revision-grade-de-estatinas-en-prevencion-primaria-cardiovascular-seccion-1-diseno-material-y-metodos-actualizado-a-24-ene-2018-y-seccion-2-variables-de-beneficio-cardiovascular-asociadas-a-estatinasactualizado-a-24-ene-2018-oficina

¿Qué sentido tiene fijar objetivos de reducción de cLDL?



1.- Huir de la perspectiva ***colesterolocéntrica***: el cLDL es solo uno más de los factores de riesgo CV conocidos.

2.- Abordar DE VERDAD el riesgo cardiovascular de forma holística y multidisciplinar.

3.- La modificación de hábitos de vida, primero.

4.- Las estatinas, solo si el riesgo lo justifica. *Además de*; no *en vez de*.

5.- En ancianos >75 años sanos (prevención primaria) no hay evidencia sólida de la eficacia de las estatinas.

@quequesierra @rincondesisifo