Actualització teòrico-pràctica en dislipèmies mixtes

Auditori CAMFiC, 14 d'abril 2016

Aspectes terapèutics. Què diuen les guies?

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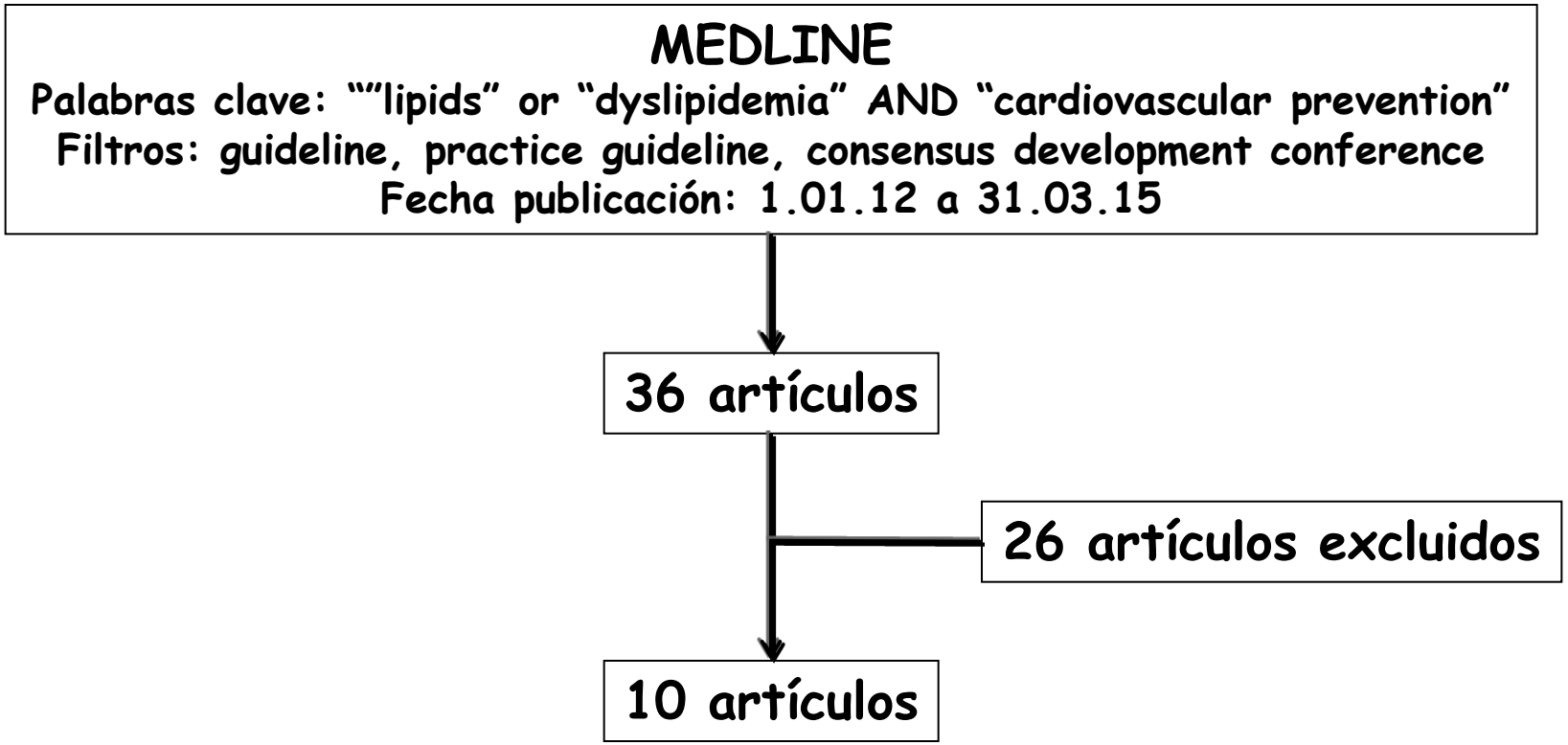
Dislipemia aterogénica en nuestro medio

- ✓ **Infradiagnosticada**
- ✓ **Infratratada**
- ✓ **Infracontrolada**

Dislipemia aterogénica en nuestro medio

- ✓ **Infradiagnosticada**
  - 27% de los pacientes con alto riesgo.
  - 34% de los pacientes con DM.
- ✓ **Infratratada**
  - < 2% de la población con dislipemia.
  - < 3% de la población con cardiopatía isquémica.
- ✓ **Infracontrolada**
  - 38% de los pacientes de alto riesgo (44% de los DM) tratados con estatinas tienen hiperTG.
  - 25% de los pacientes de alto riesgo (36% de los DM) tratados con estatinas tienen HDL bajo.

Guías clínicas – Sociedades científicas



Pedro-Botet J, et al. Clin Investig Arterioscl. 2016;28:65-70.

Listado de guías de práctica clínica seleccionadas

Guía	Año publicación
Comunidad Económica Europea	
• *Fifth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice*[10]	2012
• *European Society of Cardiology* (ESC) and *European Association for the Study of Diabetes* (EASD)[11]	2013
• *National Institute for Health and Care Excellence* (NICE) (UK)[15]	2014
América del Sur	
• *Sociedade Brasileira de Cardiologia*[13]	2013
Asia	
• *Japan Atherosclerosis Society* (JAS)[14]	2013
América del Norte	
• *Canadian Cardiovascular Society*[12]	2013
• *International Atherosclerosis Society* (IAS)[16]	2014
• *National Lipid Association* (NLA)[17]	2014
• *American College of Cardiology/American Heart Association* (ACC/AHA)[18]	2014
• *American Diabetes Association* (ADA)[19]	2015

Pedro-Botet J, et al. Clin Investig Arterioscl. 2016;28:65-70.

Analísis de las guías de práctica clínica

Parámetros evaluados:

1. Colesterol HDL
2. Triglicéridos
3. Dislipemia aterogénica
4. Colesterol no HDL
5. Apo B

De cada parámetro se valoraron los siguientes puntos:

a) Aparece en la guía?

b) Cuántas veces se cita?

c) Lo consideran un factor de riesgo?

d) Establecen algún objetivo terapéutico?

e) Proponen algún fármaco en concreto?

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart Association®

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

Neil J. Stone, Jennifer Robinson, Alice H. Lichtenstein, C. Noel Bairey Merz, Conrad B. Blum, Robert H. Eckel, Anne C. Goldberg, David Gordon, Daniel Levy, Donald M. Lloyd-Jones, Patrick McBride, J. Sanford Schwartz, Susan T. Shero, Sidney C. Smith, Jr, Karol Watson and Peter W.F. Wilson

Circulation. published online November 12, 2013;
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Print ISSN: 0009-7322. Online ISSN: 1524-4539

Nonstatin safety recommendations

Safety of Fibrates				
1. Gemfibrozil should not be initiated in patients on statin therapy because of an increased risk for muscle symptoms and rhabdomyolysis.	B (Moderate)	46	III: Harm	B
2. Fenofibrate may be considered concomitantly with a low- or moderate-intensity statin only if the benefits from ASCVD risk reduction or triglyceride lowering when triglycerides are ≥500 mg/dL are judged to outweigh the potential risk for adverse effects.	E (Expert)	—	IIb	C (14)
3. Renal status should be evaluated before fenofibrate initiation, within 3 months after initiation, and every 6 months thereafter. Assess renal safety with both a serum creatinine level and an eGFR based on creatinine.	B (Moderate)	66,67	I	B
• Fenofibrate should not be used if moderate or severe renal impairment, defined as eGFR <30 mL/min per 1.73 m^2, is present.			III: Harm	B
• If eGFR is between 30 and 59 mL/min per 1.73 m^2, the dose of fenofibrate should not exceed 54 mg/day.*				
• If, during follow-up, the eGFR decreases persistently to ≤30 mL/min per 1.73 m^2, fenofibrate should be discontinued.				

Future updates to the blood cholesterol guideline

- CQs for future guidelines could examine:
  1. the treatment of hypertriglyceridemia;
  2. the use of non–HDL-C in treatment decision making;
  3. whether on-treatment markers such as Apo B, Lp(a), or LDL particles are useful for guiding treatment decisions;
  4. the best approaches to using noninvasive imaging for refining risk estimates to guide treatment decisions;
  5. how lifetime ASCVD risk should be used to inform treatment decisions and the optimal age for initiating statin therapy to reduce lifetime risk of ASCVD;
  6. subgroups of individuals with heart failure or undergoing hemodialysis who might benefit from statin therapy;
  7. long-term effects of statin-associated new-onset diabetes and management;
  8. efficacy and safety of statins in patient groups excluded from RCTs to date (e.g., those who are HIV positive or have received a solid organ transplant); and
  9. role of pharmacogenetic testing.

Standards of Medical Care in Diabetes—2015: Summary of Revisions

Diabetes Care 2015;38(Suppl. 1):S4 | DOI: 10.2337/dc15-S003

8. Cardiovascular Disease and Risk Management

American Diabetes Association

Diabetes Care 2015;38(Suppl. 1):S49–S57 | DOI: 10.2337/dc15-S011

- Intensify lifestyle therapy and optimize glycemic control for patients with elevated triglyceride levels (≥150 mg/dL [1.7 mmol/L]) and/or low HDL cholesterol (<40 mg/dL [1.0 mmol/L] for men, <50 mg/dL [1.3 mmol/L] for women). **C** For patients with fasting triglyceride levels ≥500 mg/dL (5.7 mmol/L), evaluate for secondary causes and consider medical therapy to reduce risk of pancreatitis. **C**

- Combination therapy (statin/fibrate and statin/niacin) has not been shown to provide additional cardiovascular benefit above statin therapy alone and is not generally recommended. **A**

Journal of Clinical Lipidology (2014) 8, 473–488

Journal of Clinical Lipidology

Original Articles

National Lipid Association recommendations for patient-centered management of dyslipidemia: Part 1 – executive summary☆

Terry A. Jacobson, MD*, Matthew K. Ito, PharmD, Kevin C. Maki, PhD, Carl E. Orringer, MD, Harold E. Bays, MD, Peter H. Jones, MD, James M. McKenney, PharmD, Scott M. Grundy, MD, PhD, Edward A. Gill, MD, Robert A. Wild, MD, PhD, Don P. Wilson, MD, W. Virgil Brown, MD

Table 4 Criteria for clinical identification of the metabolic syndrome (any 3 or more of the listed components)[21]

Measure	Categorical cut points
1. Elevated waist circumference*	≥40 inches (≥102 cm) in men ≥35 inches (≥88 cm) in women
2. Elevated triglycerides (drug treatment with a triglyceride-lowering agent is an alternate indicator†)	≥150 mg/dL
3. Reduced HDL-C	<40 mg/dL in men <50 mg/dL in women
4. Elevated blood pressure (antihypertensive drug treatment in a patient with a history of hypertension is an alternate indicator)	Systolic ≥130 and/or diastolic ≥85 mm Hg
5. Elevated fasting glucose (drug treatment of elevated glucose is an alternate indicator‡)	≥100 mg/dL

National Lipid Association - 2014

Table 1 Classifications of cholesterol and triglyceride Levels in mg/dL

Non-HDL-C*	
<130	Desirable
130–159	Above desirable
160–189	Borderline high
190–219	High
≥220	Very high
LDL-C	
<100	Desirable
100–129	Above desirable
130–159	Borderline high
160–189	High
≥190	Very high
HDL-C	
<40 (men)	Low
<50 (women)	Low
Triglycerides	
<150	Normal
150–199	Borderline high
200–499	High
≥500	Very high†

HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; non-HDL-C, non–high-density lipoprotein cholesterol.

*Non-HDL-C = total cholesterol minus HDL-C.

†Severe hypertriglyceridemia is another term used for very high triglycerides in pharmaceutical product labeling.

Table 2 Treatment goals for non-HDL-C, LDL-C, and Apo B in mg/dL

	Treatment Goal		
Risk Category	Non-HDL-C	LDL-C	Apo B*
Low	<130	<100	<90
Moderate	<130	<100	<90
High	<130	<100	<90
Very High	<100	<70	<80

Apo, apolipoprotein; LDL-C, low-density lipoprotein cholesterol; non-HDL-C, non–high-density lipoprotein cholesterol.

*Apo B is a secondary, optional target of treatment.

Canadian Journal of Cardiology 29 (2013) 151–167

Society Guidelines

2012 Update of the Canadian Cardiovascular Society Guidelines for the Diagnosis and Treatment of Dyslipidemia for the Prevention of Cardiovascular Disease in the Adult

Todd J. Anderson, MD,[a] Jean Grégoire, MD,[b] Robert A. Hegele, MD,[c] Patrick Couture, MD, PhD,[d] G.B. John Mancini, MD,[e] Ruth McPherson, MD, PhD,[f] Gordon A. Francis, MD,[g] Paul Poirier, MD, PhD,[h] David C. Lau, MD, PhD,[a] Steven Grover, MD,[i] Jacques Genest, Jr, MD,[i] André C. Carpentier, MD,[j] Robert Dufour, MD,[k] Milan Gupta, MD,[l] Richard Ward, MD,[m] Lawrence A. Leiter, MD,[n] Eva Lonn, MD,[o] Dominic S. Ng, MD, PhD,[n] Glen J. Pearson, PharmD,[p] Gillian M. Yates, MN, NP,[q] James A. Stone, MD, PhD,[a] and Ehud Ur, MB[e]

[a] Libin Cardiovascular Institute of Alberta, University of Calgary, Calgary, Alberta, Canada; [b] Institut de Cardiologie de Montréal, Université de Montréal, Montréal, Québec, Canada; [c] Robarts Research Institute, London, Ontario, Canada; [d] Centre Hospitalier Universitaire de Québec, Québec City, Québec, Canada; [e] University of British Columbia, Vancouver, British Columbia, Canada; [f] University of Ottawa Heart Institute, Ottawa, Ontario, Canada; [g] St Paul's Hospital, University of British Columbia, Vancouver, British Columbia, Canada; [h] Institut Universitaire de cardiologie et de Pneumologie de Québec, Faculté de Pharmacie, Université Laval, Québec City, Québec, Canada; [i] McGill University Health Center, Montréal, Quebec, Canada; [j] Centre Hospitalier Universitaire de Sherbrooke, Sherbrooke, Québec, Canada; [k] Institut de Recherches Cliniques de Montréal, Montréal, Québec, Canada; [l] Department of Medicine, McMaster University, Hamilton, Ontario, Canada; [m] University of Calgary, Calgary, Alberta, Canada; [n] St Michael's Hospital, University of Toronto, Toronto, Ontario, Canada; [o] Population Health Research Institute, McMaster University, Hamilton, Ontario, Canada; [p] Mazankowski Alberta Heart Institute, University of Alberta, Edmonton, Alberta, Canada; [q] QE II Health Sciences Centre, Halifax, Nova Scotia, Canada

CANADÁ 2012

Objetivos terapéuticos

Risk level	Initiate therapy if	Primary target LDL C	Alternate target
High FRS ≥ 20%	Consider treatment in all (Strong, High)	≤ 2 mmol/L or ≥ 50% decrease in LDL-C (Strong, High)	➢ Apo B ≤ 0.8 g/L ➢ Non HDL-C ≤ 2.6 mmol/L (Strong, High)
Intermediate FRS 10%-19%	➢ LDL-C ≥ 3.5 mmol/L (Strong, Moderate) ➢ For LDL-C < 3.5 consider if: Apo B ≥ 1.2 g/L or Non-HDL-C ≥ 4.3 mmol/L (Strong, Moderate)	≤ 2 mmol/L or ≥ 50% decrease in LDL-C (Strong, Moderate)	➢ Apo B ≤ 0.8 mg/L ➢ Non HDL-C ≤ 2.6 mmol/L (Strong, Moderate)
Low FRS < 10%	➢ LDL-C ≥ 5.0 mmol/L ➢ Familial hypercholesterolemia (Strong, Moderate)	≥ 50% reduction in LDL-C (Strong, Moderate)	

- Colesterol no HDL es un mejor objetivo que apoB por la facilidad de su cálculo.
- En riesgo intermedio es donde se nombra a la DA.
- Tto no estatínico: subgrupo con HDL bajo y TG altos posible beneficio pero no concluyente.

Journal of Clinical Lipidology (2014) 8, 29–60

Journal of Clinical Lipidology

Original Articles

An International Atherosclerosis Society Position Paper: Global recommendations for the management of dyslipidemia—Full report

Expert Dyslipidemia Panel of the International Atherosclerosis Society*

Recommendations. When statin therapy fails to achieve an LDL-C goal of < 70 mg/dL (1.8 mmol/L) on maximal therapy, consideration should be given to use of either a bile acid resin or ezetimibe as an add-on drug to achieve this level. If non-HDL-C and triglycerides remain elevated when the LDL-C goal is achieved, consideration can be given to adding a fibrate, niacin, or high doses of n-3 fatty acids for triglyceride lowering. Any statin add-on therapy must be used with the recognition that risk-reduction efficacy has not been documented on combined-drug RCTs. Further, low doses of n-3 fatty acids seemingly do not reduce risk in routine secondary prevention.

www.cardiol.br

Arquivos Brasileiros de Cardiologia

www.arquivosonline.com.br

Sociedade Brasileira de Cardiologia • ISSN-0066-782X • Volume 101, Nº 4, Supl. 1, Outubro 2013

V Diretriz Brasileira De DisIipiDemias e preVenção Da aterosclerose

Autores da diretriz:

Xavier H. T., Izar M. C., Faria Neto J. R., Assad M. H., Rocha V. Z., Sposito A. C., Fonseca F. A., dos Santos J. E., Santos R. D., Bertolami M. C., Faludi A. A., Martinez T. L. R., Diament J., Guimarães A., Forti N. A., Moriguchi E., Chagas A. C. P., Coelho O. R., Ramires J. A. F.

BRASIL 2013

Tabela II. Valores referenciais do perfil lipídico para adultos maiores de 20 anos

Lípides	Valores (mg/dl)	Categoria
CT	< 200	Desejável
	200-239	Limítrofe
	≥ 240	Alto
LDL-C	< 100	Ótimo
	100-129	Desejável
	130-159	Limítrofe
	160-189	Alto
	≥ 190	Muito alto
HDL-C	> 60	Desejável
	< 40	Baixo
TG	<150	Desejável
	150-200	Limítrofe
	200-499	Alto
	≥ 500	Muito alto
Colesterol não-HDL	< 130	Ótimo
	130-159	Desejável
	160-189	Alto
	≥ 190	Muito alto

No DA
TG altos con HDL bajo cuando se refiere al estudio ACCORD
En este subgrupo posible beneficio de los fibratos pero pdte de + estudios)

Committee Report 1

Executive Summary of the Japan Atherosclerosis Society (JAS) Guidelines for the Diagnosis and Prevention of Atherosclerotic Cardiovascular Diseases in Japan −2012 Version

Tamio Teramoto, Jun Sasaki, Shun Ishibashi, Sadatoshi Birou, Hiroyuki Daida, Seitaro Dohi, Genshi Egusa, Takafumi Hiro, Kazuhiko Hirobe, Mami Iida, Shinji Kihara, Makoto Kinoshita, Chizuko Maruyama, Takao Ohta, Tomonori Okamura, Shizuya Yamashita, Masayuki Yokode and Koutaro Yokote

Committee for Epidemiology and Clinical Management of Atherosclerosis

Table 1. Dyslipidemia: Diagnostic Criteria for Screening (Fasting*)

Low-density lipoprotein cholesterol (LDL-C)	≥140 mg/dL	Hyper-LDL cholesterolemia
	120-139 mg/dL	Borderline hyper-LDL cholesterolemia**
High-density lipoprotein cholesterol (HDL-C)	<40 mg/dL	Hypo-HDL cholesterolemia
Triglycerides (TG)	≥150 mg/dL	Hypertriglyceridemia

• The LDL-C level is calculated using the Friedewald formula (TC − HDL-C − TG/5) (for TG < 400 mg/dL).
• If the TG level is ≥400 mg/dL or non-fasting blood is used, the non HDL-C (TC − HDL-C) level should be used with a cutoff value of LDL-C + 30 mg/dL.

*Fasting is defined as deprivation of food for at least 10 to 12 hours; however, the ingestion of noncaloric beverages, such as water and tea, is allowed.

**If a patient is found to have borderline hyper-LDL cholesterolemia during screening, he/she should be examined for any high-risk conditions and the need for treatment should be considered.

JAPÓN 2012

Table 2. Lipid Management Targets for Patients with Different Risk Levels

Therapeutic principle	Management category	Lipid management target (mg/dL)			
		LDL-C	HDL-C	TG	Non HDL-C
Primary prevention Drug therapy should be considered after lifestyle modification	Category I	<160	≥40	<150	<190
	Category II	<140			<170
	Category III	<120			<150
Secondary prevention Drug therapy should be considered, together with lifestyle modification	History of CAD	<100			<130

- For patients at low absolute risk, such as the young, the relative risk chart (Supplementary Table) should be used and changes in the absolute risk should be monitored carefully while encouraging the patient to modify their lifestyle.
- These values should be considered general, not mandatory, goals.
- A 20%-30% reduction in the level of LDL-C is considered to be a prime target for pharmacological intervention.
- The management target for the non HDL-C level is the secondary target to be used after a patient with hypertriglyceridemia has achieved the management target for the LDL-C level. The non HDL-C level should be used if blood is collected after meals or if the TG level is ≥400 mg/dL.
- For patients in any category, the management goals should generally be achieved via lifestyle modification.
- For patients in category I, drug therapy should be considered if the LDL-C level is ≥180 mg/dL.

No DA y solo una referencia a TG altos con HDL bajo en el apartado de tratamiento donde pautan fibratos o nicotínico.

European Heart Journal (2011) **32**, 1769–1818
doi:10.1093/eurheartj/ehr158

ESC/EAS GUIDELINES

ESC/EAS Guidelines for the management of dyslipidaemias

The Task Force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and the European Atherosclerosis Society (EAS)

Developed with the special contribution of: European Association for Cardiovascular Prevention & Rehabilitation†

European Heart Journal (2012) **33**, 1635–1701
doi:10.1093/eurheartj/ehs092

JOINT ESC GUIDELINES

European Guidelines on cardiovascular disease prevention in clinical practice (version 2012)

The Fifth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of nine societies and by invited experts)

5 JTF 2012

Parámetros lipídicos

	Estimación riesgo	Detección sistemática	Diana terapéutica
Colesterol total	SCORE	---	Si cLDL nd
Colesterol LDL	Principal	Principal	Principal
Colesterol no HDL	Alternativo	---	Secundario
Colesterol HDL	Indicado	---	No
Triglicéridos	Indicado	---	Casos
Apolipoproteína B	Alternativo	---	Secundario

5 JTF 2012

Objetivos terapéuticos

	Riesgo muy alto	Riesgo alto	Riesgo moderado
Colesterol LDL	< 70 mg/dl o ↓ ≥ 50%	< 100 mg/dl	< 115 mg/dl
Apo B	< 80 mg/dl	< 100 mg/dl	---
Colesterol no HDL	< 100 mg/dl	< 130 mg/dl	< 160 mg/dl
Triglicéridos	No objetivos concretos		
Colesterol HDL	No objetivos concretos		
Lipoproteína(a)	< 50 mg/dl	---	---

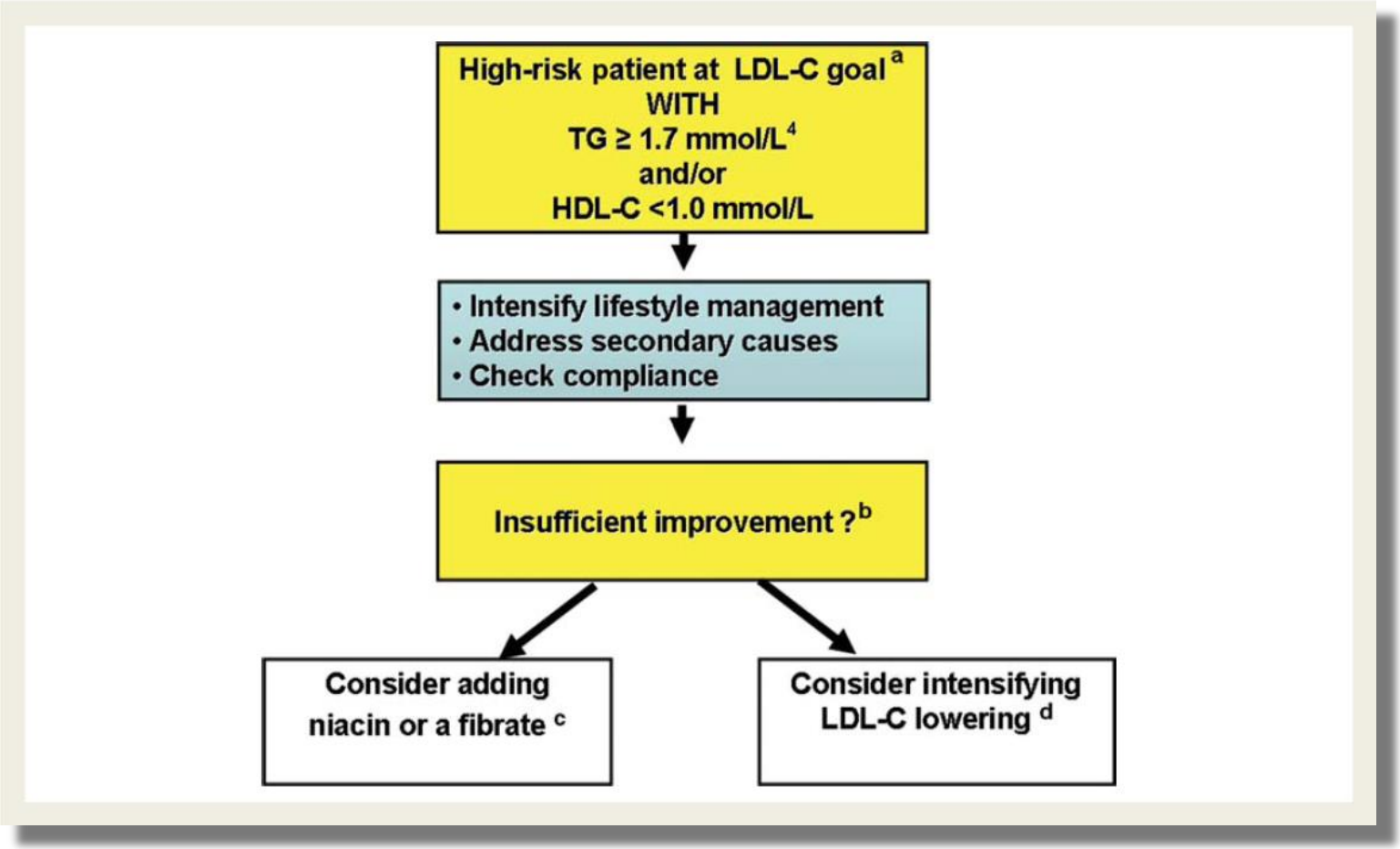
Recomendaciones para la determinación de lípidos como objetivo de tratamiento en la prevención CV

Recommendations	Class	Level
LDL-C is recommended as target for treatment.	I	A
TC should be considered as treatment target if other analyses are not available.	IIa	A
TG should be analysed during the treatment of dyslipidaemias with high TG levels.	IIa	B
Non-HDL-C should be considered as a secondary target in combined hyperlipidaemias, diabetes, the MetS or CKD.	IIa	B
Apo B should be considered as a secondary treatment target.	IIa	B
HDL-C is not		

Eur Heart J. 2011;32:1769-818.
Atherosclerosis. 2011;217:3-46.

European Heart Journal
doi:10.1093/eurheartj/ehr112

Triglyceride-rich lipoproteins and high-density lipoprotein cholesterol in patients at high risk of cardiovascular disease: evidence and guidance for management



Chapman J, et al. Eur Heart J. 2011;32:1345-61.

European Heart Journal (2013) 34, 3035–3087
doi:10.1093/eurheartj/eht108

ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD

Dyslipidaemia in diabetes			
Recommendations	**Class** [a]	**Level** [b]	**Ref.** [c]
Statin therapy is recommended in patients with T1DM and T2DM at very high-risk (i.e. if combined with documented CVD, severe CKD or with one or more CV risk factors and/or target organ damage) with an LDL-C target of <1.8 mmol/L (<70 mg/dL) or at least a ≥50% LDL-C reduction if this target goal cannot be reached.	I	A	227, 234, 238
Statin therapy is recommended in patients with T2DM at high risk (without any other CV risk factor and free of target organ damage) with an LDL-C target of <2.5 mmol/L (<100 mg/dL).	I	A	227, 234
Statins may be considered in T1DM patients at high risk for cardiovascular events irrespective of the basal LDL-C concentration.	IIb	C	-
It may be considered to have a secondary goal of non–HDL-C <2.6 mmol/L (<100 mg/dL) in patients with DM at very high risk and of <3.3 mmol/L (<130 mg/dL) in patients at high risk.	IIb	C	-
Intensification of statin therapy should be considered before the introduction of combination therapy with the addition of ezetimibe.	IIa	C	-
The use of drugs that increase HDL-C to prevent CVD in T2DM is not recommended.	III	A	251, 252, 256

6.4.4 Gaps in current knowledge

- The role of HDL particles in the regulation of insulin secretion in beta-cells needs further exploration.
- Efficiency and safety of drugs increasing or improving HDL-C particles is unclear.
- The relative contributions of HDL function and plasma HDL concentration in the pathogenesis of CVD should be clarified.

NICE National Institute for Health and Care Excellence

Offer atorvastatin 20 mg for the primary prevention of CVD to people who have a 10% or greater 10-year risk of developing CVD.

Offer atorvastatin 20 mg for the primary prevention of CVD to people with T2DM who have a 10% or greater 10-year risk of developing CVD.

Offer atorvastatin 20 mg for the primary or secondary prevention of CVD to people with CKD.

Estimate the level of risk using the QRISK2 assessment tool.

Start statin treatment in people with CVD with atorvastatin 80 mg. Use a lower dose of atorvastatin if any of the following apply:

- ✓ Potential drug interactions.
- ✓ High risk of adverse effects.
- ✓ Patient preference.

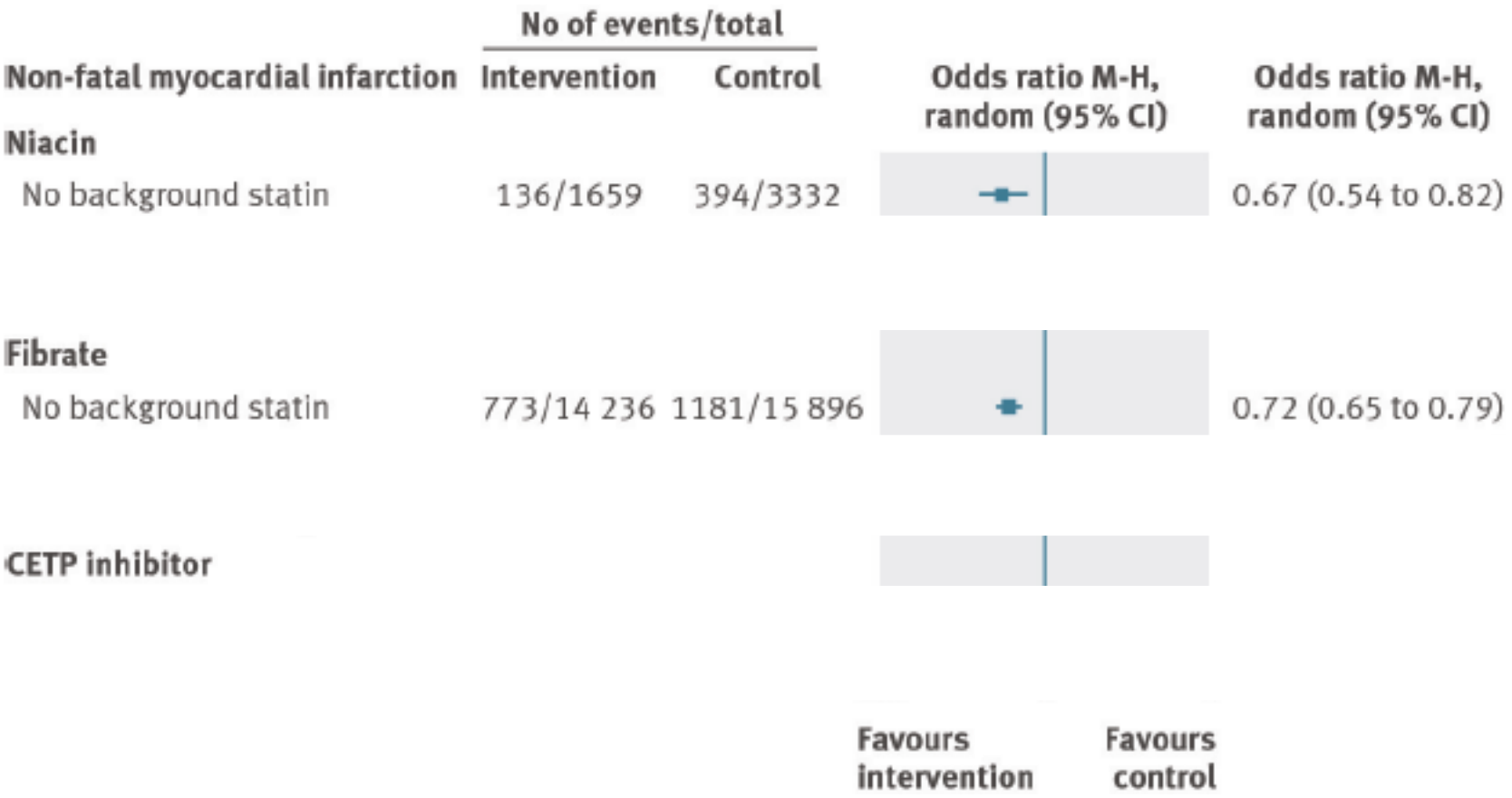
Aim for a greater than 40% reduction in non-HDL cholesterol.

Rabar S, et al. BMJ. 2014;349:g4356.

Conclusiones

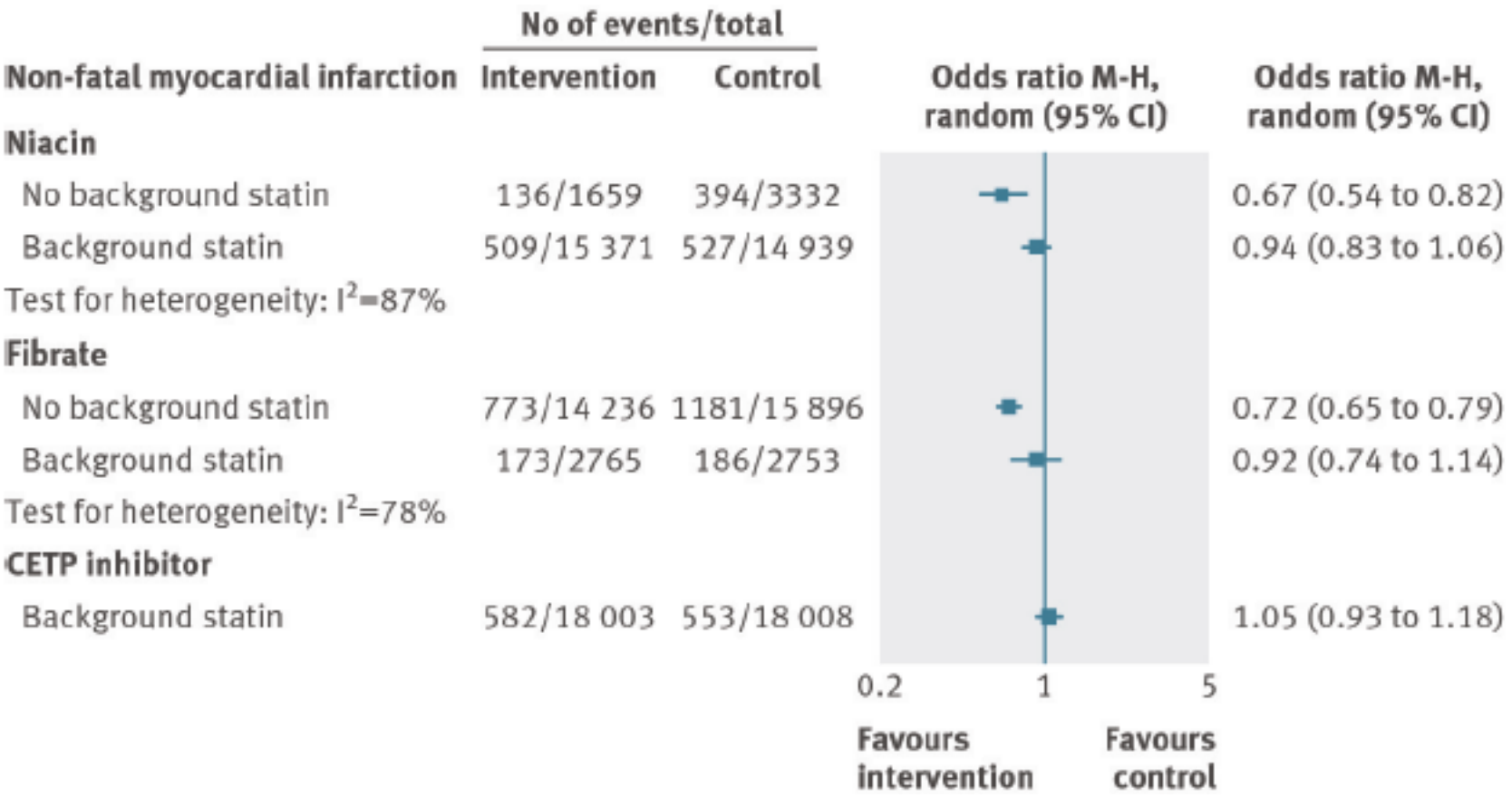
- Las guías americanas (excepto NLA) y NICE no consideran cHDL, ni TGs.
- NLA es pro-dislpemia aterogénica.
- Guía canadiense introduce colesterol no HDL y apoB como objetivo alternativo. Tratamiento no estatínico si cHDL bajo e hiperTG.
- IAS es pro colesterol no HDL
- Guía europea, Brasil y Japón: consideran cHDL y TGs, pero faltan evidencias.

Effect on cardiovascular risk of high density lipoprotein targeted drug treatments niacin, fibrates, and CETP inhibitors: meta-analysis of randomised controlled trials including 117,411 patients



Keene D, et al. BMJ. 2014;349:g4379.

Effect on cardiovascular risk of high density lipoprotein targeted drug treatments niacin, fibrates, and CETP inhibitors: meta-analysis of randomised controlled trials including 117,411 patients



Keene D, et al. BMJ. 2014;349:g4379.

Objetivos terapéuticos en triglicéridos y cHDL

	DM2	SM
OBJETIVO PRIMARIO		
cLDL		
• Obligado	<100	<100
• Opcional	<130 (1)	<130 (2)
Pacientes con CI		
• Obligado	<70	<70
• Opcional	<100 (1)	<100 (2)
OBJETIVOS SECUNDARIOS		
cHDL	>40 mg/dl(H) >50 mg/dl (M)	
C-no-HDL	Objetivo LDL + 30 mg/dl	
Triglicéridos	<150 mg/dl	

El riesgo de presentar un episodio CV: aumenta un 20% por cada incremento de TGs en 23 mg/dl, y disminuye un 40% por cada aumento de 7,5 mg/dl en cHDL.

(1) Sólo si DM sin SM, menos de 2 factores de riesgo, RCV < 20% a los 10 años.
(2) Sólo si RCV< 20% a los 10 años o desaparición del criterio diagnóstico de SM

Ascaso J, et al. Am J Cardiovasc Drugs. 2007;7:39-58.
Millán J, et al. Med Clin (Barc). 2007;128:786-94.

Contribución de los TGs y cHDL al RCV en pacientes de prevención secundaria con cLDL en objetivo

170 pacientes con ECV; 175 controles

High-Density Lipoprotein Quintile (mg/dl)	Triglyceride Quintile (mg/dl)				
	22–72	72–102	102–133	133–190	190–838
53–94	1.00	0.86	0.75	0.64	0.56
42–53	1.32	1.28	1.23	1.19	1.15
36–42	1.75	1.89	2.04	2.20	2.39
30–36	2.32	2.80	3.39	4.09	4.95
7–30	3.07	4.15	5.61	7.58	10.25

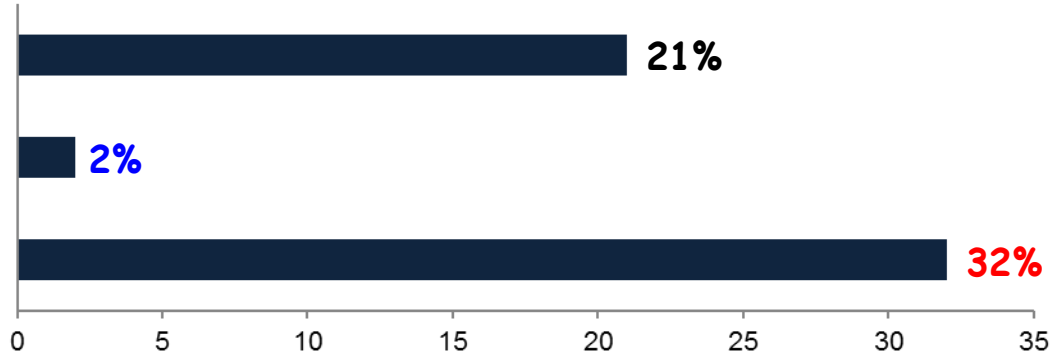
Carey VJ, et al. Am J Cardiol. 2010;106:757-63.

Alteraciones lipídicas y riesgo CV

C noHDL como objetivo terapéutico del riesgo CV

Incremento del riesgo CV en pacientes con cLDL controlado pero C no HDL fuera de objetivos terapéuticos

cLDL	C no HDL
≥ 2.6 mmol/L (≥ 100 mg/dL)	≥ 3.4 mmol/L (≥ 130 mg/dL)
≥ 2.6 mmol/L (≥ 100 mg/dL)	< 3.4 mmol/L (< 130 mg/dL)
< 2.6 mmol/L (< 100 mg/dL)	**≥ 3.4 mmol/L (≥ 130 mg/dL)**



Incremento del riesgo de ECV grave comparado con el nivel de referencia (cLDL <2,6 mmol/L [100 mg/dL] y C no HDL <3,4 mmol/L [130mg/dL])

Los pacientes que alcanzan el objetivo terapéutico en cLDL tienen un riesgo aumentado del 32% en episodios CVs si no alcanzan el objetivo en colesterol no HDL

Boekholdt SM, et al. JAMA. 2012;307:1302-9.

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A review of the evidence on reducing macrovascular risk in patients with atherogenic dyslipidaemia: A report from an expert consensus meeting on the role of fenofibrate–statin combination therapy

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Objetivo:

- Incrementar el conocimiento de la dislipemia aterogénica.
- Revisar la evidencia que apoya el tratamiento combinado fenofibrato-estatina para reducir el riesgo CV residual asociado a la dislipemia aterogénica.

Fenofibrato y reducción de episodios CVs

Optimización de los resultados en los pacientes con DM2

Estudio	Población de pacientes	Objetivos	
FIELD	• 9795 pacientes con DM2 • 22% de pacientes con ECV	**Todos los pacientes** Mediana TGs basales: 1,7 mmol/L **IM no mortal + muerte coronaria** **RRR 11% (p=0,16)**	**Pacientes con DA** NNT_5= 23 TGs ≥ 2,30 mmol/L y HDL < 1,30/1,29 mmol/L varón/mujer **Episodios CV totales (muerte CV, IM, ictus, revascularización)** **RRR 27% (p=0,005)**
ACCORD Lipid	• 5518 pacientes con DM2 • 37% de pacientes con ECV	**Todos los pacientes** Mediana TGs basales: 1,8 mmol/L **Muerte coronaria, IM no mortal + ictus no mortal** **RRR 8% (p=0,32)**	**Pacientes con DA** NNT_5= 20 TGs ≥ 2,3 mmol/L y cHDL ≤ 0,9 mmol/L **Muerte CV, IM no mortal IM + ictus no mortal** **RRR 31% (p=0,032)**

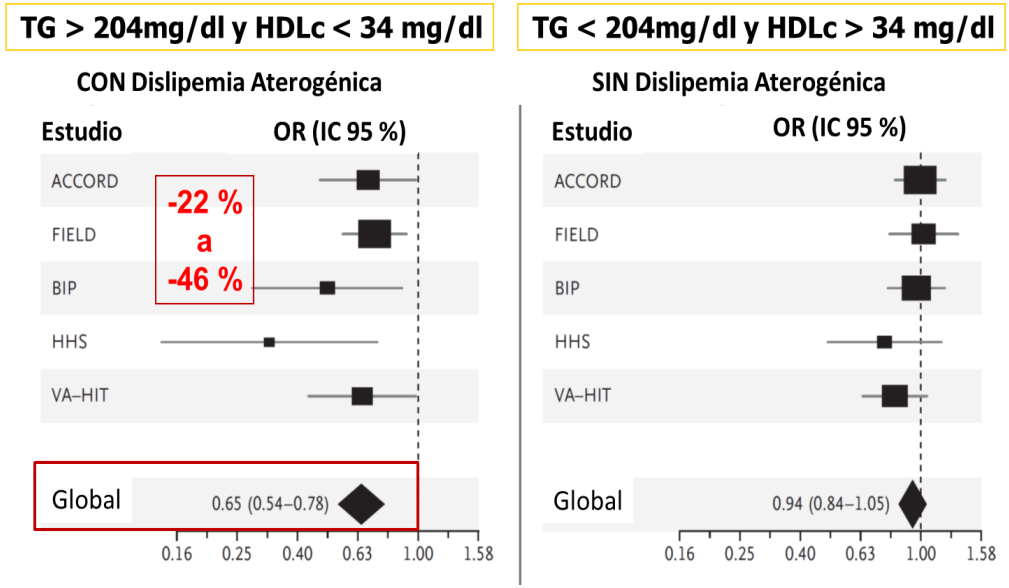
Fenofibrato reduce significativamente los episodios CVs en pacientes con DA

Keech A, et al. Lancet. 2005;366:1849-61.
Ginsberg HN, et al. N Engl J Med. 2010;362:1563-74.

Tratamiento combinado en paciente de alto RCV con dislipemia aterogénica

Impacto de los fibratos en los episodios CVs según el fenotipo lipídico

OR para episodios coronarios en pacientes con DA



En pacientes con DA el beneficio clínico de tratar con fibratos ha quedado demostrado en los estudios de intervención.

Sacks FM, et al. N Engl J Med. 2010; 363:692-4.

Dislipemia mixta

Principios de tratamiento farmacológico

- Los fibratos son eficaces
  - Perfil lipídico: cLDL, TG, cHDL
  - Efectos pleiotrópicos: inflamación, trombosis, antioxidante, estabilización endotelial

EFICACIA

- El fenofibrato sólo (FIELD) o en combinación con estatinas (ACCORD)
  - Reduce episodios coronarios (↓35%)
  - Es coste-efectiva (NNT: 20-25)

BENEFICIO CLÍNICO

- La combinación de estatina y fenofibrato
  - Es segura
  - Mejora el perfil lipídico global
  - Puede mejorar la adherencia (combinación fija)

SEGURIDAD