Perlas en el manejo de dislipidemias

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Conflictos de interés

- He recibido honorarios por conferencias, advisory board y/o investigación clínica de:
  - Astra Zeneca
  - Abbott Nutrición
  - Novartis Pharma Logistics Inc
  - Novartis Oncology
  - Novo Nordisk
  - Merck Sharp & Dohme
  - Roche
  - Glaxo SmithKline
  - Sanofi Aventis
  - Boehringer
  - Organon

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Objetivos

- Implicaciones y manejo de hipertrigliceridemia/dislipidemia mixta
- Guías 2013 manejo de dislipidemias (ATP IV)
- Cuánto tiempo se deben usar las estatinas?
- Cómo minimizar el riesgo de efectos adversos?
- Modificación de estilos de vida basado en la evidencia

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HIPERTRIGLICERIDEMIA/ DISLIPIDEMIA MIXTA

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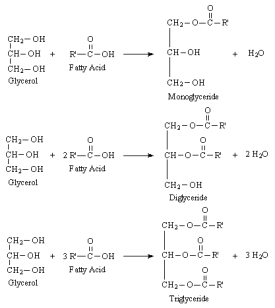
Ensamblaje en triglicéridos



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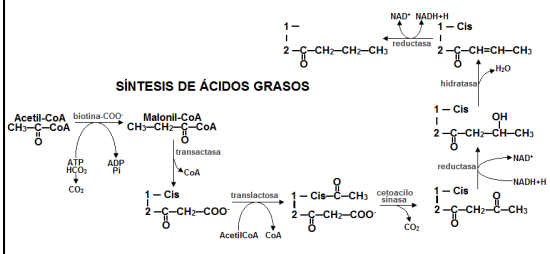

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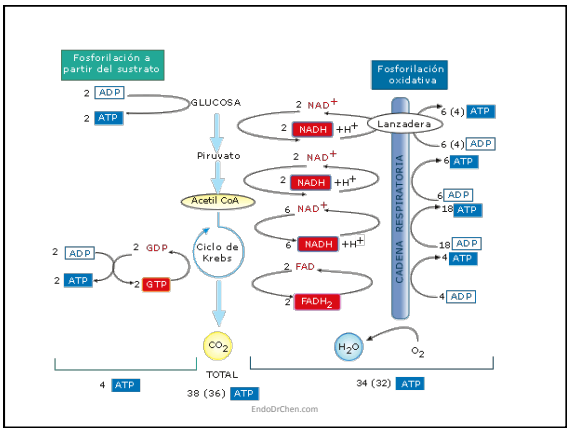

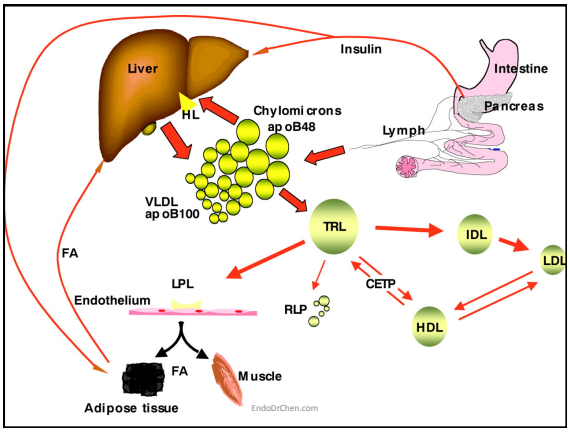

Triglicéridos y pancreatitis

- Hipertrigliceridemia (mayor a 1000 mg/dl) se ha observado entre 12 y 38% de pacientes con pancreatitis
- Pocos estudios controlados
- Al parecer niveles muy altos aumentan el RR 4.0
- Pancreatitis de otras causas pueden cursar con hipertrigliceridemia moderada

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Mecanismos

- Mediado por quilomicrones
- Alteración del flujo capilar que lleva a isquemia en lecho pancreático
- Liberación de lipasa aumenta ácidos grasos libres que son proinflamatorios

Gan SI. World J Gastroenterol. 2006;12(44):7197

Nueva clasificación

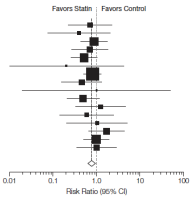
NCEP ATP III (3)			The Endocrine Society 2010[a]		
Normal	<150 mg/dl	<1.7 mmol/liter	Normal	<150 mg/dl	<1.7 mmol/liter
Borderline-high triglycerides	150–199 mg/dl	1.7–2.3 mmol/liter	Mild hypertriglyceridemia	150–199 mg/dl	1.7–2.3 mmol/liter
High triglycerides	200–499 mg/dl	2.3–5.6 mmol/liter	Moderate hypertriglyceridemia	200–999 mg/dl	2.3–11.2 mmol/liter
Very high triglycerides	≥500 mg/dl	≥5.6 mmol/liter	Severe hypertriglyceridemia	1000–1999 mg/dl	11.2–22.4 mmol/liter
			Very severe hypertriglyceridemia	≥2000 mg/dl	≥22.4 mmol/liter

Berglund L. J Clin Endocrinol Metab. 2012;97:2969

INTERVENCIÓN FARMACOLÓGICA

Estatinas

Source	Statin Cases	Statin Total	Control Cases	Control Total	Weight, %	Risk Ratio (95% CI)
Placebo- and standard care-controlled						
4S,[16] 1994	5	2223	7	2221	2.60	0.71 (0.23-2.25)
WOSCOPS,[17] 1995	2	3302	5	3293	1.28	0.40 (0.08-2.09)
CARE,[18] 1996	15	2081	17	2078	7.07	0.88 (0.44-1.77)
AFCAPS/TexCAPS,[19] 1998	7	3304	10	3301	3.67	0.70 (0.27-1.84)
LIPID,[20] 1998	12	4512	23	4502	7.02	0.52 (0.26-1.05)
GISSI Prevenzione,[21] 2000	0	2138	2	2133	0.37	0.20 (0.01-4.16)
HPS,[22] 2002	33	10269	41	10267	16.29	0.80 (0.51-1.27)
PROSPER,[23] 2002	5	2891	11	2913	3.07	0.46 (0.16-1.32)
GREACE,[24] 2002	0	800	0	800	0.22	1.00 (0.02-50.46)
ASCOT-LLA,[25] 2003	8	5168	16	5137	4.76	0.50 (0.21-1.16)
CARDS,[26] 2004	5	1428	4	1410	1.98	1.23 (0.33-4.61)
ASPEN,[27] 2006	3	1211	5	1199	1.67	0.59 (0.14-2.49)
MEGA,[28] 2006	3	3866	3	3966	1.34	1.03 (0.21-5.09)
CORONA,[29] 2007	12	2514	7	2497	3.94	1.70 (0.67-4.33)
JUPITER,[30] 2008	17	8901	17	8901	7.58	1.00 (0.51-1.96)
GISSI-HF,[31] 2008	7	2285	7	2289	3.12	1.00 (0.35-2.86)
Subtotal: $I^2 = 0.0\%$, $P = .87$					65.98	0.77 (0.62-0.97)



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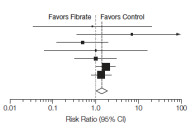
Preiss D. JAMA. 2012;308(8):804

Fibratos

Source	Fibrate Cases	Fibrate Total	Control Cases	Control Total	Weight, %	Risk Ratio (95% CI)
CORONARY Drug Project,[37] 1975	0	1103	1	2789	1.11	0.84 (0.03-20.71)
WHO-COOR[38] 1978	3	5331	0	5296	1.29	6.95 (0.35-134.66)
HHS,[40] 1987	3	2362	6	2347	5.89	0.50 (0.12-1.99)
VA-HIT,[41] 1999	1	1264	1	1267	1.47	1.00 (0.06-16.04)
BIP,[42] 2000	6	1548	6	1542	8.82	1.00 (0.32-3.10)
FIELD,[77] 2005	40	4895	23	4900	42.83	1.74 (1.04-2.91)
ACCORD Lipid,[43] 2010	31	2765	23	2753	38.59	1.34 (0.78-2.31)
Overall: $I^2 = 0.0\%$, $P = .61$					100.00	1.39 (1.00-1.95)



NNH 1 en 935

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Preiss D. JAMA. 2012;308(8):804

Fibratos y pancreatitis

- Clofibrato aumentaba el riesgo de colelitiasis
- Los fibratos nuevos tienen menor riesgo
- Aumentan la concentración de colesterol en la bilis
- No hay ensayos clínicos para triglicéridos mayores a 500 mg/dl

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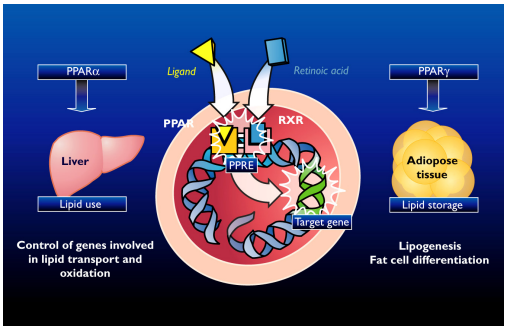
Preiss D. JAMA. 2012;308(8):804


PPARα
Ligand
Retinoic acid
PPARγ
PPAR
RXR
Liver
PPRE
Adiopose tissue
Lipid use
Target gene
Lipid storage
Control of genes involved in lipid transport and oxidation
Lipogenesis
Fat cell differentiation
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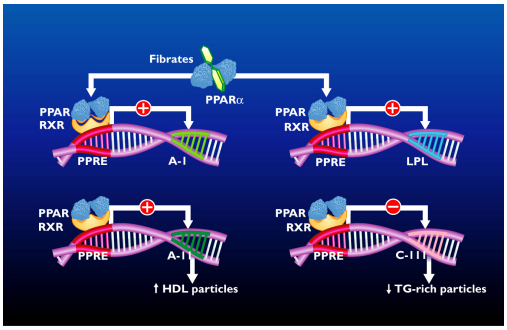
Fibrates
PPARα
PPAR
RXR
PPRE
A-I
LPL
A-II
C-III
↑ HDL particles
↓ TG-rich particles
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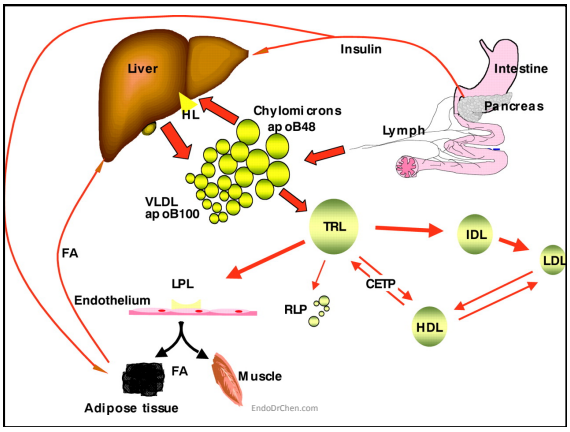
Liver
Insulin
Intestine
Pancreas
HL
Chylomicrons
apoB48
Lymph
VLDL
apoB100
TRL
IDL
LDL
FA
LPL
Endothelium
RLP
CETP
HDL
FA
Muscle
Adipose tissue
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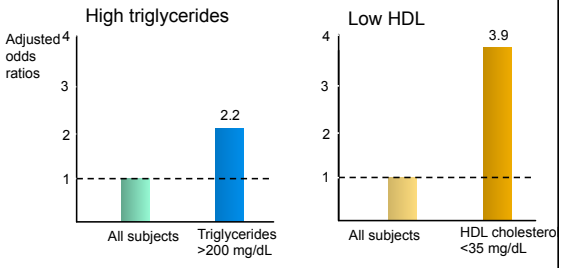
QUÉ HAY SOBRE EL IMPACTO CARDIOVASCULAR?

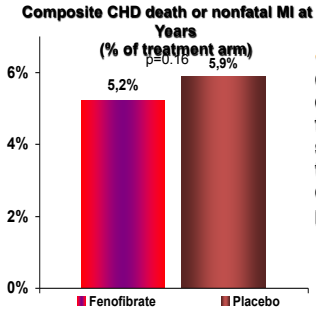
Triglycerides and HDL Cholesterol Predict CV Mortality in Type 2 Diabetes

313 Patients Followed for 7 Years



Laakso M et al. *Circulation*. 1993;88(part 1):1421-1430

FIELD: Primary Endpoint



- The primary composite endpoint of CHD death or non-fatal MI was not significantly lower in the fenofibrate group compared to the placebo group.

AHA 2005

Accord lipidos - resultados

Outcome	Fenofibrate (N=2765)		Placebo (N=2753)		Hazard Ratio (95% CI)	P Value
	no. of events	*rate/yr*	*no. of events*	*rate/yr*		
Primary outcome (major fatal or nonfatal cardiovascular event)	291	2.24	310	2.41	0.92 (0.79–1.08)	0.32*
Secondary outcomes						
Primary outcome plus revascularization or hospitalization for congestive heart failure	641	5.35	667	5.64	0.94 (0.85–1.05)	0.30
Major coronary disease event†	332	2.58	353	2.79	0.92 (0.79–1.07)	0.26
Nonfatal myocardial infarction	173	1.32	186	1.44	0.91 (0.74–1.12)	0.39
Stroke						
Any	51	0.38	48	0.36	1.05 (0.71–1.56)	0.80
Nonfatal	47	0.35	40	0.30	1.17 (0.76–1.78)	0.48
Death						
From any cause	203	1.47	221	1.61	0.91 (0.75–1.10)	0.33*
From cardiovascular cause	99	0.72	114	0.83	0.86 (0.66–1.12)	0.26
Fatal or nonfatal congestive heart failure	120	0.90	143	1.09	0.82 (0.65–1.05)	0.10

The Accord Study Group N Engl J Med. 2010

Y QUÉ TAL GEMFIBROZIL?

Helsinky Heart Study

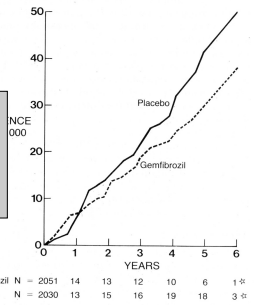
Perfil de lípidos de estos pacientes:

Colesterol total 269 →266

HDL 47 → 51

LDL 189 → 173

Triglicéridos 175 → 115



Heikki M. N Engl J Med. 1987;317:1237

VAHIT

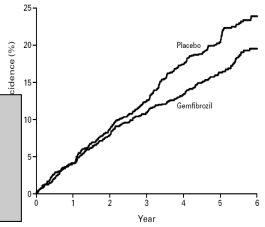
Perfil de lípidos de estos pacientes:

Colesterol total 177 →170

HDL 32 → 34

LDL 113 → 113

Triglicéridos 166 → 113



No. at Risk

Placebo	1267	1200	1118	1040	962	666	466
Gemfibrozil	1264	1201	1128	1067	1005	706	498

Figure 2. Kaplan–Meier Estimates of the Incidence of Death from Coronary Heart Disease and Nonfatal Myocardial Infarction in the Gemfibrozil and Placebo Groups.
The relative risk reduction was 22 percent (P=0.006), as derived from a Cox model.

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Bloomfield H. N Engl J Med. 1999;341:410

Gemfibrozil

- Mecanismo principal y que lo diferencia de los otros fibratos es la capacidad de aumentar HDL
- Es una alternativa válida para pacientes con HDL bajo y LDL normales

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HIPERTRIGLICERIDEMIA COMO MARCADOR DE RIESGO DE DM

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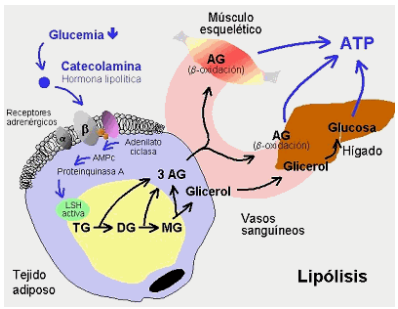

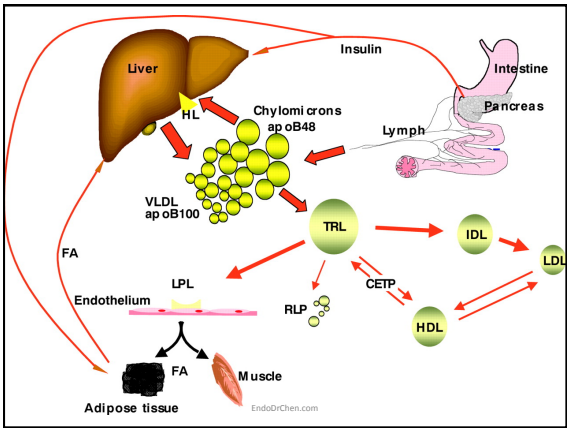

Variable	Hazard Ratio (95% CI)					P Value for Trend	P Value for Interaction
	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5		
Body-mass index†							
<25	1	1.48 (0.52–4.23)	1.64 (0.54–5.29)	1.71 (0.73–6.42)	1.73 (0.79–6.60)	<0.001	0.03
≥25	1	1.36 (0.86–2.15)	1.66 (1.02–2.68)	2.44 (1.43–4.16)	3.78 (1.95–7.35)	<0.001	
Triglyceride level							
<150 mg/dl	1	1.21 (0.63–2.29)	1.50 (0.76–2.97)	2.43 (1.14–5.23)	2.73 (1.28–6.67)	<0.001	0.87
≥150 mg/dl	1	1.41 (0.80–2.49)	1.90 (1.03–3.51)	2.37 (1.25–4.50)	3.24 (1.48–7.10)	<0.001	
Family history							
Negative	1	1.24 (0.66–2.35)	1.50 (0.78–2.87)	3.77 (1.62–8.77)	6.49 (2.25–18.86)	<0.001	0.37
Positive	1	1.96 (0.77–5.02)	2.51 (0.88–7.19)	2.57 (0.94–6.99)	4.58 (1.58–13.33)	<0.001	

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Tirosh A. N Engl J Med. 2005;353:1454

GUÍAS 2013 MANEJO DE DISLIPIDEMIAS AHA/ACC

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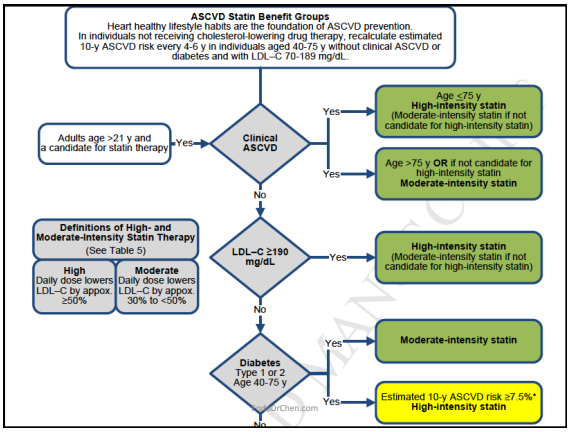

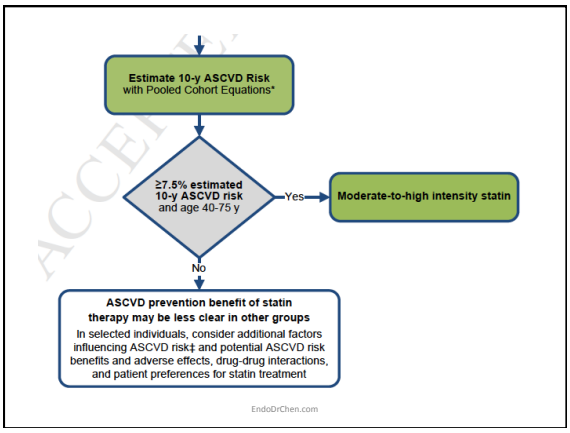

High-Intensity Statin Therapy	Moderate-Intensity Statin Therapy	Low-Intensity Statin Therapy
Daily dose lowers LDL–C on average, by approximately ≥50%	Daily dose lowers LDL–C on average, by approximately 30% to <50%	Daily dose lowers LDL–C on average, by <30%
Atorvastatin (40†)–80 mg **Rosuvastatin 20** *(40)* **mg**	**Atorvastatin 10** *(20)* **mg** **Rosuvastatin** *(5)* **10 mg** **Simvastatin 20–40 mg‡** **Pravastatin 40** *(80)* **mg** **Lovastatin 40 mg** *Fluvastatin XL 80 mg* **Fluvastatin 40 mg bid** *Pitavastatin 2–4 mg*	*Simvastatin 10 mg* **Pravastatin 10–20 mg** **Lovastatin 20 mg** *Fluvastatin 20–40 mg* *Pitavastatin 1 mg*

Highlights of 2013 Guidelines

- New **Pooled Cohort Equations** for atherosclerotic cardiovascular disease (ASCVD) risk assessment
  - Stroke now included in ASCVD risk assessment, in addition to myocardial infarction (MI)
  - Separate equations for nonwhite populations
- **Statin therapy** recommended in 4 groups:
  1. Adults with clinical ASCVD
  2. Adults with LDL-C ≥190 mg/dL
  3. Adults 40 to 75 years of age with diabetes
  4. Adults ≥7.5% estimated 10-year risk of ASCVD
- **No** LDL-C or non-HDL-C treatment targets

Primary Prevention: Central Role of Statin Therapy

- Statin therapy recommended for primary prevention of ASCVD
- Based on RCTs, statins reduce morbidity *and* mortality associated with ASCVD
- Cost-effective: many statins are now generic
- Lifestyle modification also critical to primary prevention efforts
  - DASH-like diet: high in fruits, vegetables, fish, and low in sweets, red meat, and sodium
  - Regular moderate to vigorous physical activity

Statin Therapy Recommended in Four Groups

1. Individuals with known ASCVD, without Class II-IV heart failure or receiving hemodialysis
2. Individuals with LDL-C ≥190 mg/dL
3. Individuals 40 to 75 years of age with diabetes and LDL-C 70-189 mg/dL
4. Individuals 40 to 75 years of age with estimated 10-year ASCVD risk ≥7.5% and LDL-C 70-189 mg/dL

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What about individuals of "intermediate risk" (<7.5% ASCVD risk)?

- Optional additional risk measurement tools to refine predicted risk
  - Family history of premature ASCVD?
  - High-sensitivity CRP
  - Coronary artery calcium
  - Ankle brachial Indices (ABI)

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ASCVD Risk Calculator

Search "ACC/AHA Prevention Guidelines risk calculator"

American Heart Association. | AMERICAN COLLEGE of CARDIOLOGY

2013 Prevention Guidelines Tools

CV RISK CALCULATOR

The American Heart Association and the American College of Cardiology are excited to provide a series of new cardiovascular prevention guidelines for the assessment of cardiovascular risk, lifestyle modifications that reduce risk, management of elevated blood cholesterol, and management of increased body weight in adults. To support the implementation of these guidelines, the new Pooled Cohort Equations CV Risk Calculator and additional Prevention Guideline Tools are available below. Others may be developed and available in the near future.

DOWNLOAD CV RISK CALCULATOR

This downloadable spreadsheet is a companion tool to the 2013 ACC/AHA Guideline on the Assessment of Cardiovascular Risk. The spreadsheet enables health care providers and patients to estimate 10-year and lifetime risks for atherosclerotic cardiovascular disease (ASCVD), defined as coronary death or nonfatal myocardial infarction, or fatal or nonfatal stroke, based on the Pooled Cohort Equations and the work of Lloyd-Jones, et al., respectively. The information required to estimate ASCVD risk includes age, sex, race, total cholesterol, HDL cholesterol, systolic blood pressure, blood pressure lowering medication use, diabetes status, and smoking status.

Estimates of 10-year risk for ASCVD are based on data from multiple community-based populations and are applicable to African-American and non-Hispanic white men and women 40 through 79 years of age. For other ethnic groups, we recommend use of the equations for non-Hispanic whites, though these estimates may underestimate the risk for persons from some race-ethnic groups, especially American Indians, some Asian Americans (e.g., of south Asian ancestry), and some Hispanics (e.g., Puerto Ricans), and may overestimate the risk for others, including some Asian Americans (e.g., of east Asian ancestry) and some Hispanics (e.g., Mexican Americans).

Estimates of lifetime risk for ASCVD are provided for adults 20 through 59 years of age and are shown as the lifetime risk for ASCVD for a 50-year old without ASCVD who has the risk factor values entered into the spreadsheet. The estimates of lifetime risk are most directly applicable to non-Hispanic whites. We recommend the use of these values for other race-ethnic groups, though as mentioned above, these estimates may represent under- and overestimates for persons of various ethnic groups. Because the primary use of these lifetime risk estimates is to facilitate the very important discussion regarding risk reduction through lifestyle change, the imprecision introduced is small enough to justify proceeding with lifestyle change counseling informed by these results.

Figure 1. Implementation of Risk Assessment Work Group Recommendations

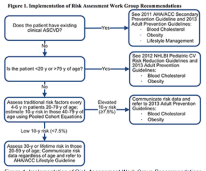

Figure 1. Implementation of Risk Assessment Work Group Recommendations

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Clinical Vignettes

ASCVD Risk Calculator

Pooled Cohort Equations

Risk Factor	Units	Value	Acceptable range of values	Optimal values
Sex	M or F		M or F	
Age	years		20-79	
Race	AA or WH		AA or WH	
Total Cholesterol	mg/dL		130-320	170
HDL-Cholesterol	mg/dL		20-100	50
Systolic Blood Pressure	mm Hg		90-200	110
Treatment for High Blood Pressure	Y or N		Y or N	N
Diabetes	Y or N		Y or N	N
Smoker	Y or N		Y or N	N

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ASCVD Risk Calculator

Pooled Cohort Equations

Risk Factor	Units	Value	Acceptable range of values	Optimal values
Sex	M or F	F	M or F	
Age	years	55	20-79	
Race	AA or WH	AA	AA or WH	
Total Cholesterol	mg/dL	210	130-320	170
HDL-Cholesterol	mg/dL	56	20-100	50
Systolic Blood Pressure	mm Hg	145	90-200	110
Treatment for High Blood Pressure	Y or N	Y	Y or N	N
Diabetes	Y or N	N	Y or N	N
Smoker	Y or N	N	Y or N	N

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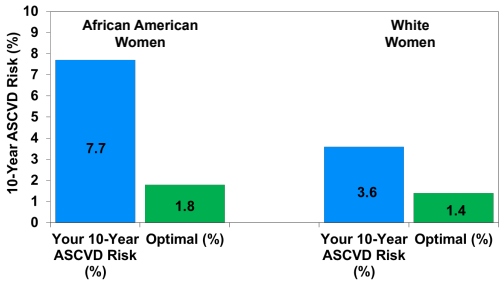
ASCVD Risk Calculator

55 yo AA and White Women



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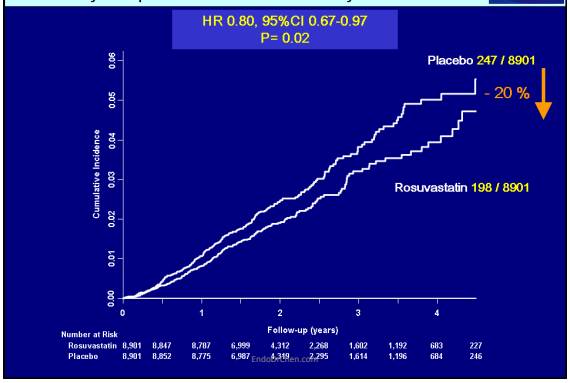
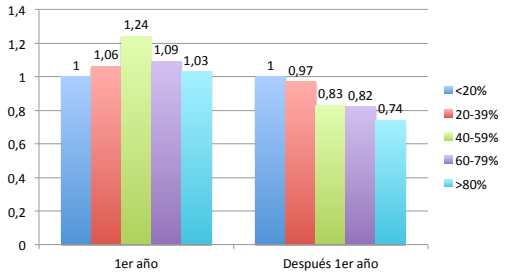
ES EL EFECTO HIPOLIPEMIANTE O ES LA ESTABILIZACIÓN DE LA PLACA?

JUPITER
Secondary Endpoint – All Cause Mortality



Adherencia a estatinas y eventos cardiovasculares



Perreault S. Am J Med. 2009;122:647-655

Reflexiones

- Podríamos usar esquemas alternativos de dosificación de estatinas?
- Indica esto que el efecto hipolipemiante es lo más importante o es más bien la parte estabilizadora de placa?

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CÓMO MINIMIZAR RIESGO DE EFECTOS ADVERSOS?

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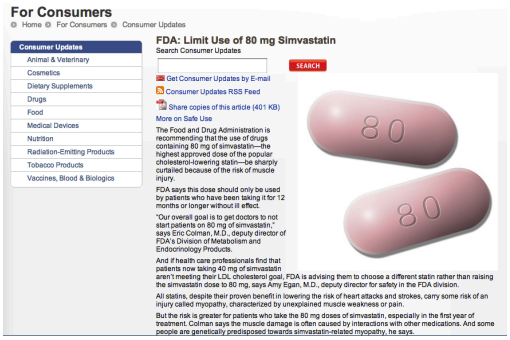

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FDA: Limit Use of 80 mg Simvastatin

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More on Safe Use

The Food and Drug Administration is recommending that the use of drugs containing 80 mg of simvastatin—the highest approved dose of the popular cholesterol-lowering statin—be sharply curtailed because of the risk of muscle injury.

FDA says this dose should only be used by patients who have been taking it for 12 months or longer without ill effect.

"Our overall goal is to get doctors to not start patients on 80 mg of simvastatin," says Eric Colman, M.D., deputy director of FDA's Division of Metabolism and Endocrinology Products.

And if health care professionals find that patients now taking 40 mg of simvastatin aren't meeting their LDL cholesterol goal, FDA is advising them to choose a different statin rather than raising the simvastatin dose to 80 mg, says Amy Egan, M.D., deputy director for safety in the FDA division.

All statins, despite their proven benefit in lowering the risk of heart attacks and strokes, carry some risk of an injury called myopathy, characterized by unexplained muscle weakness or pain.

But the risk is greater for patients who take the 80 mg doses of simvastatin, especially in the first year of treatment. Colman says the muscle damage is often caused by interactions with other medications. And some people are genetically predisposed towards simvastatin-related myopathy, he says.

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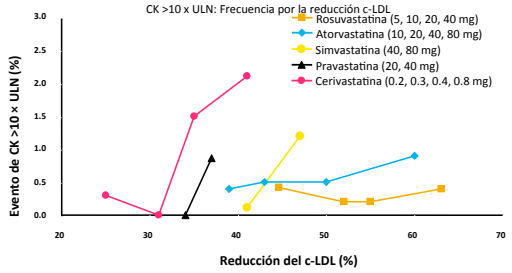
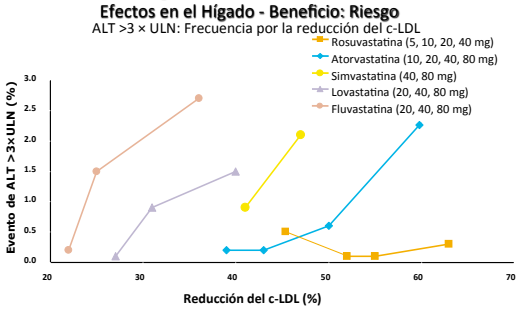
Seguridad de Rosuvastatina; Efectos en los Músculos - Beneficio: Riesgo



1.Brewer H *Am J Cardiol* 2003;92(Suppl):23K–29K
2.Davidson M *Exp Opin Drug Saf* 2004;3 (6):547-557

Seguridad de Rosuvastatina; Efectos en el Hígado - Beneficio: Riesgo



La elevación persistente es la elevación a >3 x ULN en 2 ocasiones sucesivas

1. Brewer H *Am J Cardiol* 2003;92(Suppl):23K–29K
2. Davidson M *Exp Opin Drug Saf* 2004;3 (6):547-557

Drugs

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Drug Safety and Availability

- Drug Alerts and Statements
- Importing Prescription Drugs
- Medication Guides
- Drug Safety Communications
- Drug Shortages
- Postmarket Drug Safety Information for Patients and Providers
- Information by Drug Class
- Medication Errors
- FDA Drug Safety Newsletter
- Drug Safety Podcasts
- Safe Use Initiative
- Drug Recalls
- Drug Integrity and Supply Chain Security

Resources for You

- FDA announces safety changes in labeling for some cholesterol-lowering drugs
- Infographic about Cholesterol and Statins (PDF - 2.5MB)

FDA Drug Safety Communication: Important safety label changes to cholesterol-lowering statin drugs

Safety Announcement
Additional Information for Patients
Additional Information for Healthcare Professionals
Data Summary
Lovastatin Dose Limitations
References

Facts about statins

- A class of prescription drugs used together with diet and exercise to reduce blood levels of low-density lipoprotein (LDL) cholesterol ("bad cholesterol")
- Marketed as single-ingredient products, including Lipitor (atorvastatin), Lescol (fluvastatin), Mevacor (lovastatin), Altoprev (lovastatin extended-release), Livalo (pitavastatin), Pravachol (pravastatin), Crestor (rosuvastatin), and Zocor (simvastatin)
- Also marketed as combination products, including Advicor (lovastatin/niacin extended-release), Simcor (simvastatin/niacin extended-release), and Vytorin (simvastatin/ezetimibe)

Safety Announcement

[2-28-2012] The U.S. Food and Drug Administration (FDA) has approved important safety label changes for the class of cholesterol-lowering drugs known as statins. These changes were made to provide the public with more information for the safe and effective use of statins and are based on FDA's comprehensive review of the statin class of drugs (see Data Summary below). The changes include the following:

Monitoring Liver Enzymes
Labels have been revised to remove the need for routine periodic monitoring of liver enzymes in patients taking statins. The labels now recommend that liver enzyme tests should be performed before starting statin therapy and as clinically indicated thereafter. FDA has concluded that serious liver injury with statins is rare and unpredictable in individual patients, and that routine periodic monitoring of liver enzymes does not appear to be effective in detecting or preventing serious liver injury.

Adverse Event Information
Information about the potential for generally non-serious and reversible cognitive side effects (memory loss, confusion, etc.) and reports of increased blood sugar and glycosylated hemoglobin (HbA1c) levels has been added to the statin labels. FDA continues to believe that the cardiovascular benefits of statins outweigh these small increased risks.

Drug Interactions
The lovastatin label has been extensively updated with new contraindications (situations when the drug should not be used) and dose limitations when it is taken with certain medicines that can

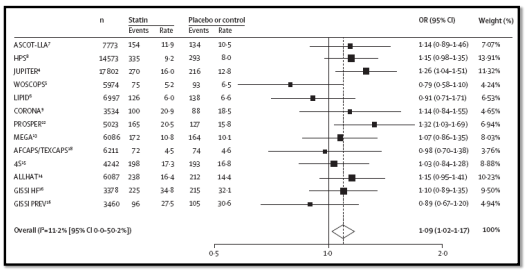
Infographic About Cholesterol and Statins

Deterioro cognitivo

- Demostrado en estudios observacionales, no en RCT
- 50% se produce en los primeros 2 meses de uso, 50% revierte al suspenderlo
- Datos preliminares parece que indicar que aquellos menos lipofílicos dan menos problemas (pravastatina y rosuvastatina)
- Una posible alternativa es pasar de estatina lipofílica a hidrofílicas

1. Rojas-Fernandez CH. Ann Pharmacother. 2012;46:549
2. Wagstaff LR. Pharmacotherapy. 2003;23:871.

Estatinas y riesgo de DM



Sattar N. Lancet. 2010;375:735

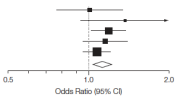
Estatinas y riesgo de DM

- NNH sería 1 en 255 por 4 años
- Durante estos 4 años si se tratan a 255 pacientes
  - Se reducen 5.4 eventos cardiovasculares
- El beneficio supera el riesgo!

Dosis de estatina

Incident Diabetes	Cases/Total, No. (%) Intensive Dose	Moderate Dose	OR (95% CI)
PROVE IT–TIMI 22,[18] 2004	101/1707 (5.9)	99/1688 (5.9)	1.01 (0.76-1.34)
A to Z,[17] 2004	65/1768 (3.7)	47/1736 (2.7)	1.37 (0.94-2.01)
TNT,[15] 2005	418/3798 (11.0)	358/3797 (9.4)	1.19 (1.02-1.38)
IDEAL,[16] 2005	240/3737 (6.4)	209/3724 (5.6)	1.15 (0.95-1.40)
SEARCH,[5] 2010	625/5398 (11.6)	587/5399 (10.9)	1.07 (0.95-1.21)
Pooled odds ratio	1449/16408 (8.8)	1300/16344 (8.0)	1.12 (1.04-1.22)

Heterogeneity: $I^2 = 0\%$; $P = .60$



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Preiss D. JAMA. 2011;305:2556

JUPITER

- Factores de riesgo:
  - Síndrome metabólico
  - IMC > 30 kg/m2
  - Alteración de glicemia en ayunas
  - Hba1c > 6%
- Uso de rosuvastatina
  - Aceleró el desarrollo de DM por 5.4 semanas

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Ridker P. Lancet. 2012;380:565

En pacientes que desarrollaron DM, el beneficio en reducción de eventos CV fue similar

134 casos de eventos CV o muerte prevenido por cada 54 casos nuevos de DM

	No major diabetes risk factors (n=6095)					One or more major diabetes risk factors (n=11508)				
	Rosuvastatin	Placebo	Δ	HR (95% CI)	p value	Rosuvastatin	Placebo	Δ	HR (95% CI)	p value
Primary endpoint	44 (0·69)	91 (1·45)	-47	0·48 (0·33-0·68)	0·0001	96 (0·80)	157 (1·31)	-61	0·61 (0·47-0·79)	0·0001
Primary endpoint, any death	118 (1·85)	174 (2·77)	-56	0·67 (0·53-0·85)	0·0007	175 (1·46)	262 (2·18)	-87	0·67 (0·55-0·81)	0·0001
Primary endpoint, VTE, any death	122 (1·92)	187 (2·99)	-65	0·64 (0·51-0·81)	0·0001	196 (1·64)	289 (2·41)	-93	0·68 (0·57-0·81)	0·0001
MI, stroke, any death	99 (1·55)	147 (2·33)	-48	0·67 (0·52-0·86)	0·002	139 (1·15)	202 (1·67)	-63	0·69 (0·56-0·86)	0·0006
Any death	89 (1·32)	113 (1·69)	-24	0·78 (0·59-1·03)	0·08	109 (0·85)	132 (1·02)	-23	0·83 (0·64-1·07)	0·15
Diabetes	12 (0·18)	12 (0·18)	0	0·99 (0·45-2·21)	0·99	258 (2·12)	204 (1·65)	54	1·28 (1·07-1·54)	0·01

Prevención de 86 casos de eventos CV o muerte con 0 casos nuevos de DM

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Ridker P. Lancet. 2012;380:565

Estatinas y lesiones osteomusculares

- RR 1.19 para todas las enfermedades musculoesqueléticas
- RR 1.13 para lesiones y enfermedades relacionadas
- RR 1.09 dolor musculoesquelético asociado a medicamentos

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Mansi I. JAMA Intern Med. Online June 3 2013

Diferencias farmacocinéticas

Caracterís-ticas	Atorvasta-tina	Lovastatina	Simvastatina	Pravastatina	Fluvastatina	Rosuvas-tatina
Biodisponi bilidad	12%	**<5%**	<5%	17%	24%	20%
Elimina-ción urinaria	**<2%**	10%	13%	20%	5%	10%
Elimina-ción Fecal	**98%**	83%	60%	70%	90%	90%
Unión a proteínas	>90%	>95%	95%	**50%**	98%	88%
Sustrato CYP	CYP3A4	CYP3A4	CYP3A4	**Sulfatación**	CYP2C9	CYP2C9
Lipofilici-dad	Lipofílico	Lipofílico	Lipofílico	**Hidrofílico**	**Hidrofílico**	**Hidrofílico**

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Riesgo de interacciones

- Inhibidores CYP3A4
  - Fluconazol, itraconazol, ketoconazol
  - Eritromicina, claritromicina
  - Omeprazole, lanzoprazole
  - Bloqueadores de canales de calcio
  - Fluoxetina, venlafaxina, paroxetina
  - Ciclosporina, tacrolimus
  - Jugo de toronja
- Inhibidores CYP2C9:
  - amiodarona

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MODIFICACIÓN DE ESTILOS DE VIDA BASADO EN EVIDENCIA

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Recomendaciones

- Las intervenciones que funcionan según las guías:
- Fibra
- Esteroles vegetales
- Grasas saturadas
- Reducir colesterol de la dieta

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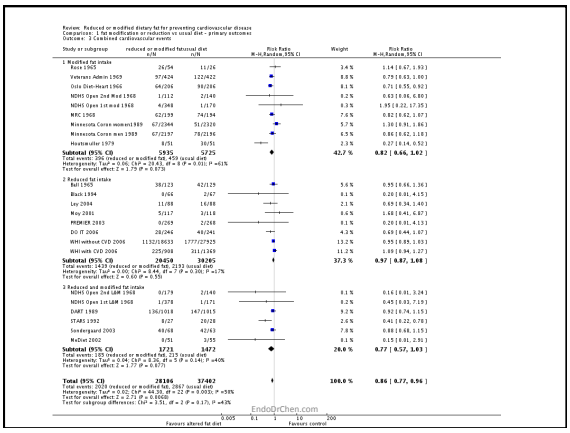
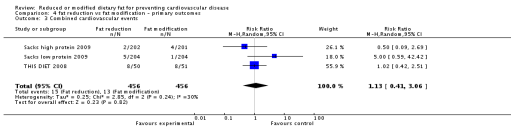


Eventos cardiovasculares



Hooper L Coch Dat Syst Rev. 2012;3:may 12

PREDIMED

- Hombres 55-80 años
- Mujeres 60-80 años
- DM ó 3 factores de riesgo:
  - Tabaquismo
  - HTA
  - LDL alto
  - HDL bajo
  - Sobrepeso u obesidad
  - Historia de enfermedad coronaria prematura

Estruch R. N Engl J Med. 2013.

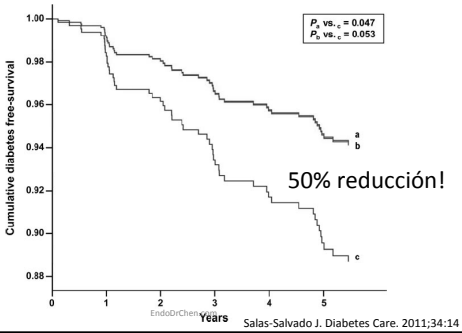
Mediterranean diet	
Recommended	
Olive oil*	≥4 tbsp/day
Tree nuts and peanuts†	≥3 servings/wk
Fresh fruits	≥3 servings/day
Vegetables	≥2 servings/day
Fish (especially fatty fish), seafood	≥3 servings/wk
Legumes	≥3 servings/wk
Sofrito‡	≥2 servings/wk
White meat	Instead of red meat
Wine with meals (optionally, only for habitual drinkers)	≥7 glasses/wk
Discouraged	
Soda drinks	<1 drink/day
Commercial bakery goods, sweets, and pastries§	<3 servings/wk
Spread fats	<1 serving/day
Red and processed meats	<1 serving/day

Estruch R. N Engl J Med. 2013.

Low-fat diet (control)	
Recommended	
Low-fat dairy products	≥3 servings/day
Bread, potatoes, pasta, rice	≥3 servings/day
Fresh fruits	≥3 servings/day
Vegetables	≥2 servings/wk
Lean fish and seafood	≥3 servings/wk
Discouraged	
Vegetable oils (including olive oil)	≤2 tbsp/day
Commercial bakery goods, sweets, and pastries§	≤1 serving/wk
Nuts and fried snacks	≤1 serving /wk
Red and processed fatty meats	≤1 serving/wk
Visible fat in meats and soups¶	Always remove
Fatty fish, seafood canned in oil	≤1 serving/wk
Spread fats	≤1 serving/wk
Sofrito‡	≤2 servings/wk

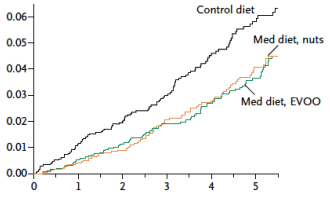
Estruch R. N Engl J Med. 2013.

Sobrevida libre de diabetes



Salas-Salvado J. Diabetes Care. 2011;34:14

Eventos cardiovasculares



Estruch R. N Engl J Med. 2013.

EL HACER EJERCICIO… SUSTITUYE HIPOLIPEMIANTE?

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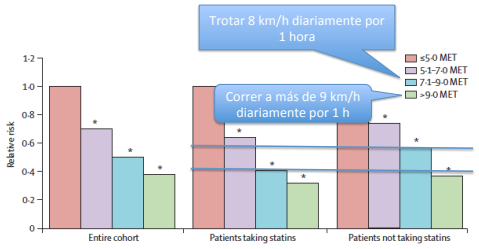
Interacción entre estatina y condición física



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Fokkinos PF. Lancet. 2012. Online nov 28.

Conclusiones

- Hipertrigliceridemia tiene implicación para pancreatitis y riesgo de DM, pero la intervención farmacológica no ha reducido riesgo de eventos CV
- Adherencia es fundamental para que haya beneficio a largo plazo
- Perfil de seguridad es diferente según cada estatina
- Modificación de estilos de vida y dieta mediterránea

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Número 147 www.ampmd.com Agosto 2013

ARTÍCULO DE REVISIÓN

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ABORDAJE PRÁCTICO DE DISLIPIDEMIA ASOCIADA CON RESISTENCIA A LA INSULINA

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