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Congreso de la Sociedad Andaluza
de Medicina Interna

13-15 de Mayo 2010
Hotel Meliá Sevilla



Dislipemia y Diabetes mellitus Tipo 2

Alfredo Michán Doña
Hospital SAS Jerez



Dislipemia y Diabetes mellitus tipo 2

- Potenciales conflictos de intereses.
 - En temas relacionados con la diabetes y/o dislipemia he actuado como consultor con MSD, Pfizer, participado en ensayos clínicos con MSD y Sanofi-Aventis y he impartido presentaciones financiadas por Almirall, Esteve, GSK, Lilly, MSD, Novartis, Novo Nordisk, Sanofi-Aventis, Servier,...



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**¿Qué es la diabetes
mellitus?**

Dislipemia diabética

Equivalente coronario

¿Qué hacer?

Y ahora,... ¿Qué?



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**¿Qué es la
diabetes
mellitus?**

¿Qué es la diabetes mellitus?



CRITERIOS DIAGNÓSTICOS ADA 2.010 DE LA DIABETES MELLITUS

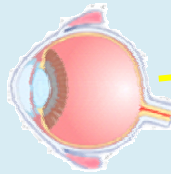
- **HbA1C \geq 6,5%:** El análisis deberá realizarse en un laboratorio utilizando un método certificado por el Programa nacional de estandarización de la glucohemoglobina (NGSP) de los Estados Unidos y estandarizado para el Estudio sobre el control de la diabetes y sus complicaciones (DCCT).
- **Glucemia en ayunas en plasma venoso >126 mg/dl (7,0 mmol/l):** el ayuno se define como la ausencia de ingesta calórica durante al menos 8 h.
- **Glucemia en plasma venoso a las 2 horas ≥ 200 mg/dl (11,1 mmol/l) durante la prueba de tolerancia oral a la glucosa (PTOG):** la prueba deberá realizarse tal y como lo describe la Organización Mundial de la Salud, es decir, con una carga de glucosa que contenga el equivalente a 75 g de glucosa anhidra disuelta en agua.
- **Paciente con síntomas clásicos de hiperglucemia o de crisis hiperglucémica:** glucemia al azar en plasma venoso ≥ 200 mg/dl (11,1 mmol/l).



La diabetes es una enfermedad caracterizada por la MICRO y la MACRO angiopatía

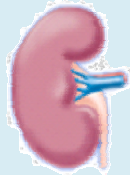
Retinopatía diabética

Principal causa de ceguera en adultos en edad laboral¹



Nefropatía diabética

Principal causa de insuficiencia renal terminal²



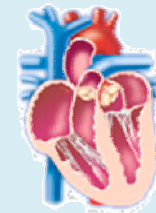
Ictus

Aumento de 2 a 4 veces en la mortalidad cardiovascular y los ictus^{3,4}



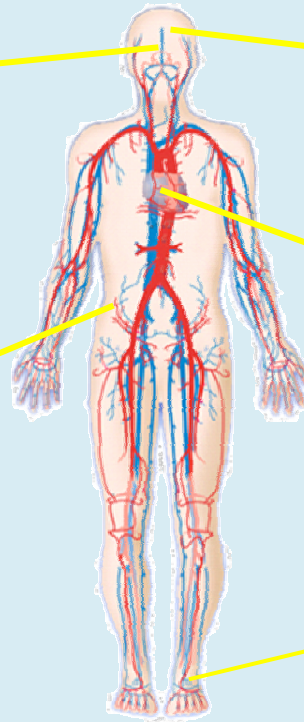
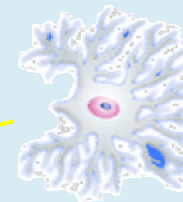
Enfermedad cardiovascular

8/10 pacientes diabéticos fallecen por eventos CV⁴



Neuropatía diabética

Principal causa de amputaciones no traumáticas de las extremidades inferiores⁵



¹Fong DS, et al. Diabetes Care 2003; 26(Suppl. 1):S99-S102. ²Molitch ME, et al. Diabetes Care 2003; 26(Suppl.1):S94-S98.

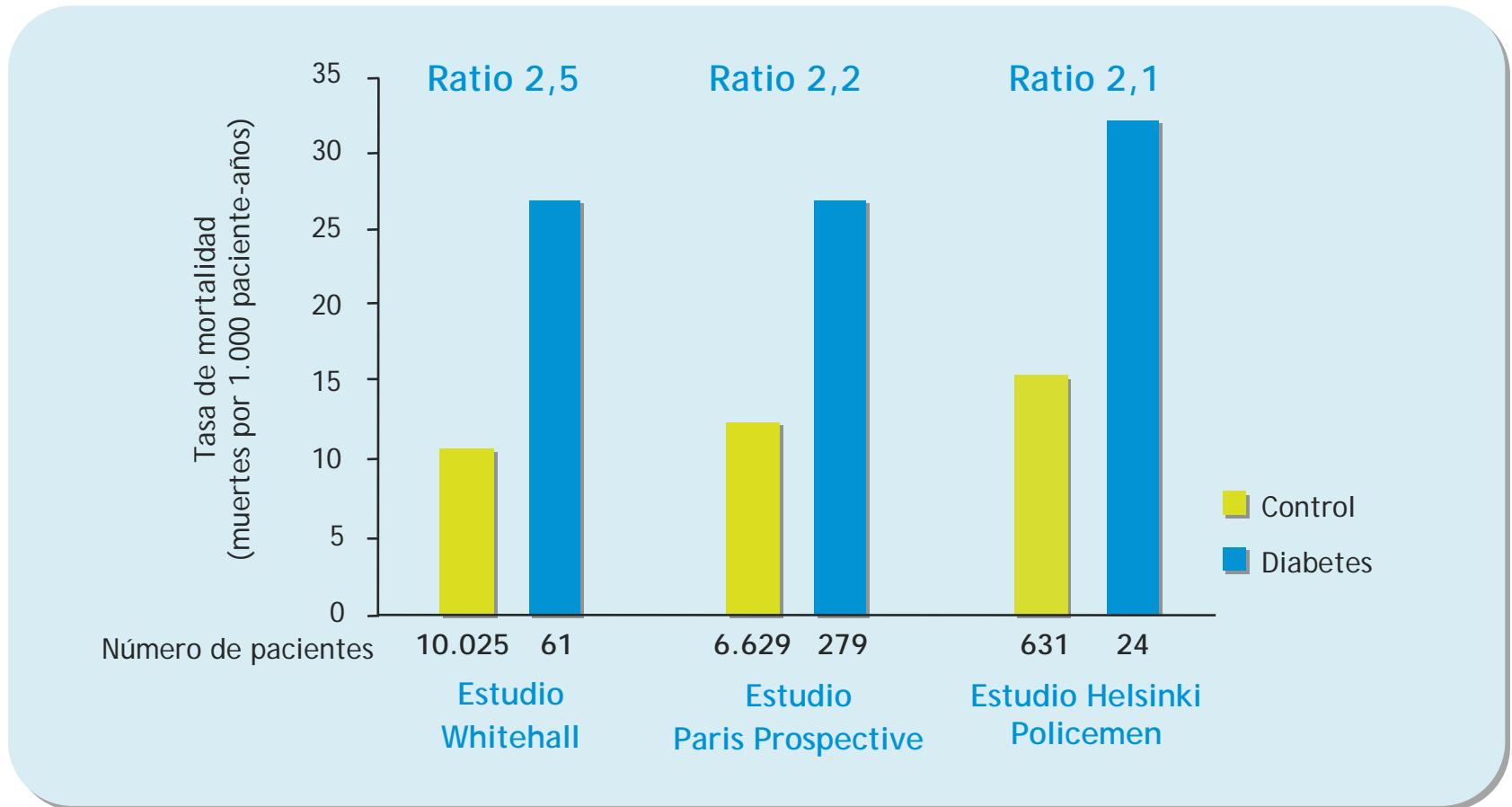
³Kannel WB, et al. Am Heart J 1990; 120:672-676. ⁴Gray RP & Yudkin JS. In Textbook of Diabetes 1997.

⁵Mayfield JA, et al. Diabetes Care 2003; 26(Suppl. 1):S78-S79.

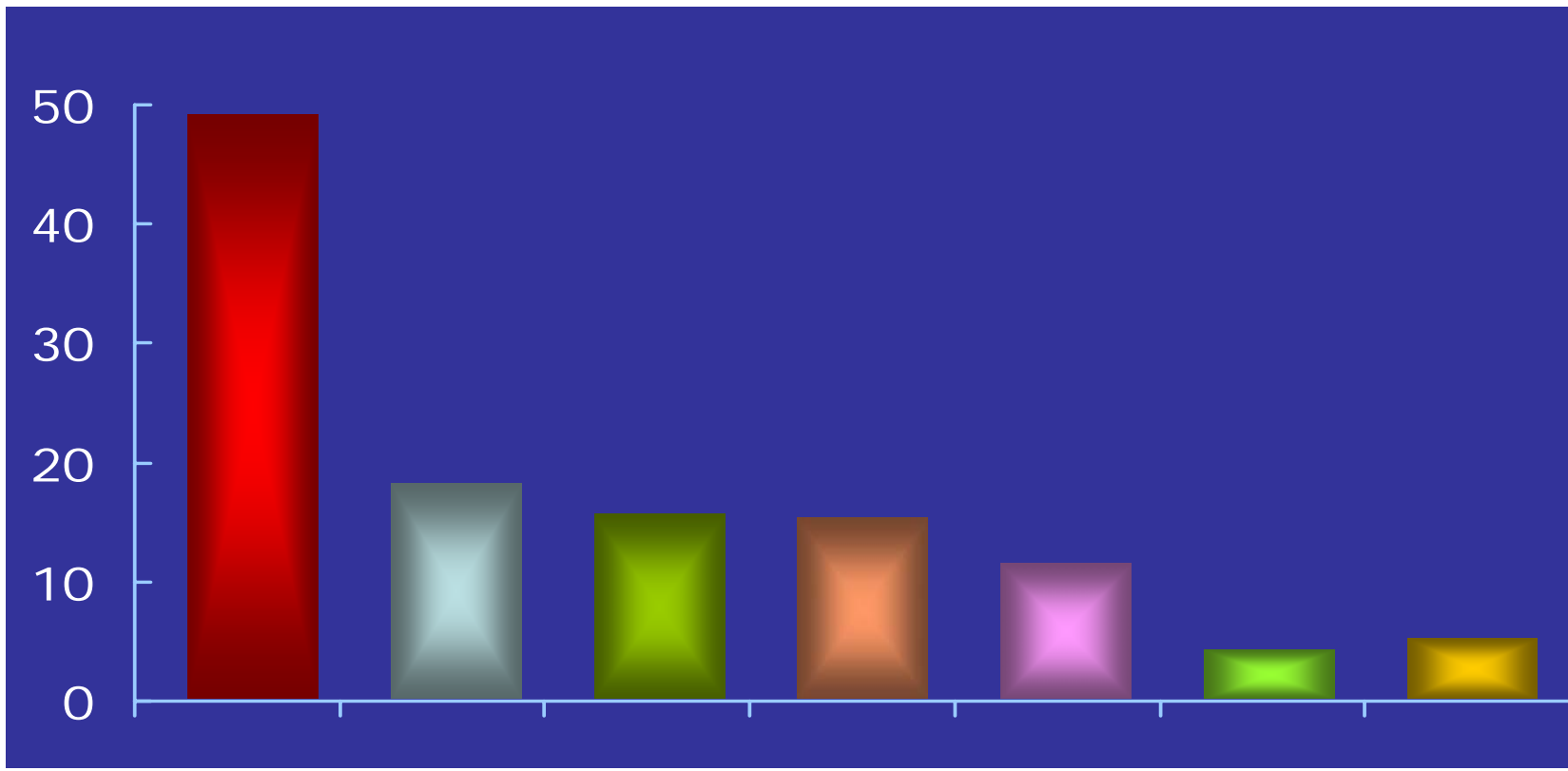
Blue Mountains Eye Study

- Población general de más de 49 años.
- Diabéticos: 199, con retinopatía 57: **28,6%**.
- Sin diabetes: 2.768, con retinopatía 268, **es decir un 9,7% de la población general tiene retinopatía y NO son diabéticos.**
- Criterios retinopatía:
 - Microhemorragias.
 - Hemorragias en llama.
 - Exudados duros.
 - Manchas de algodón.
 - Tratamiento previo con láser.

La tasa de mortalidad es doble en los pacientes con diabetes



Causas de muerte en la población diabética





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¿Qué es la diabetes
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Equivalente coronario

¿Qué hacer?

Y ahora,... ¿Qué?

Alteraciones lipoproteicas características en los pacientes con diabetes mellitus tipo 2



- **AUMENTADOS:**

- Triglicéridos.
- C-VLDL.
- C-no HDL.
- Apo B.
- LDL pequeñas y densas
- Lipemia postprandial.

- **DISMINUIDOS:**

- C-HDL.
- ApoA-1.

Alteraciones lipoproteicas características en los pacientes con diabetes mellitus tipo 2



- **La fisiopatología de estas alteraciones está íntimamente relacionada con un estado de insulinoresistencia.**
- **A diferencia de lo que ocurre en la diabetes mellitus tipo 1 , en la diabetes mellitus tipo 2 raramente se normalizan por completo con la optimización del control glicémico.**



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Factores de riesgo para el desarrollo de coronariopatía en la diabetes mellitus tipo 2: UKPDS 23.

Key messages

- Coronary artery disease is the major cause of mortality in patients with type 2 diabetes mellitus
- Patients without evidence of disease related to atheroma at diagnosis of type 2 diabetes mellitus had an increased standardised mortality ratio compared with the population of the United Kingdom
- 11% of patients in this study had a myocardial infarction or developed angina over a median of 8 years' follow up
- The potentially modifiable risk factors for coronary artery disease were increased concentrations of low density lipoprotein cholesterol, decreased concentrations of high density lipoprotein cholesterol, hypertension, hyperglycaemia, and smoking; these are also risk factors for coronary artery disease in the general population
- Evidence is needed on whether modifying these risk factors will reduce coronary artery disease in patients with type 2 diabetes mellitus

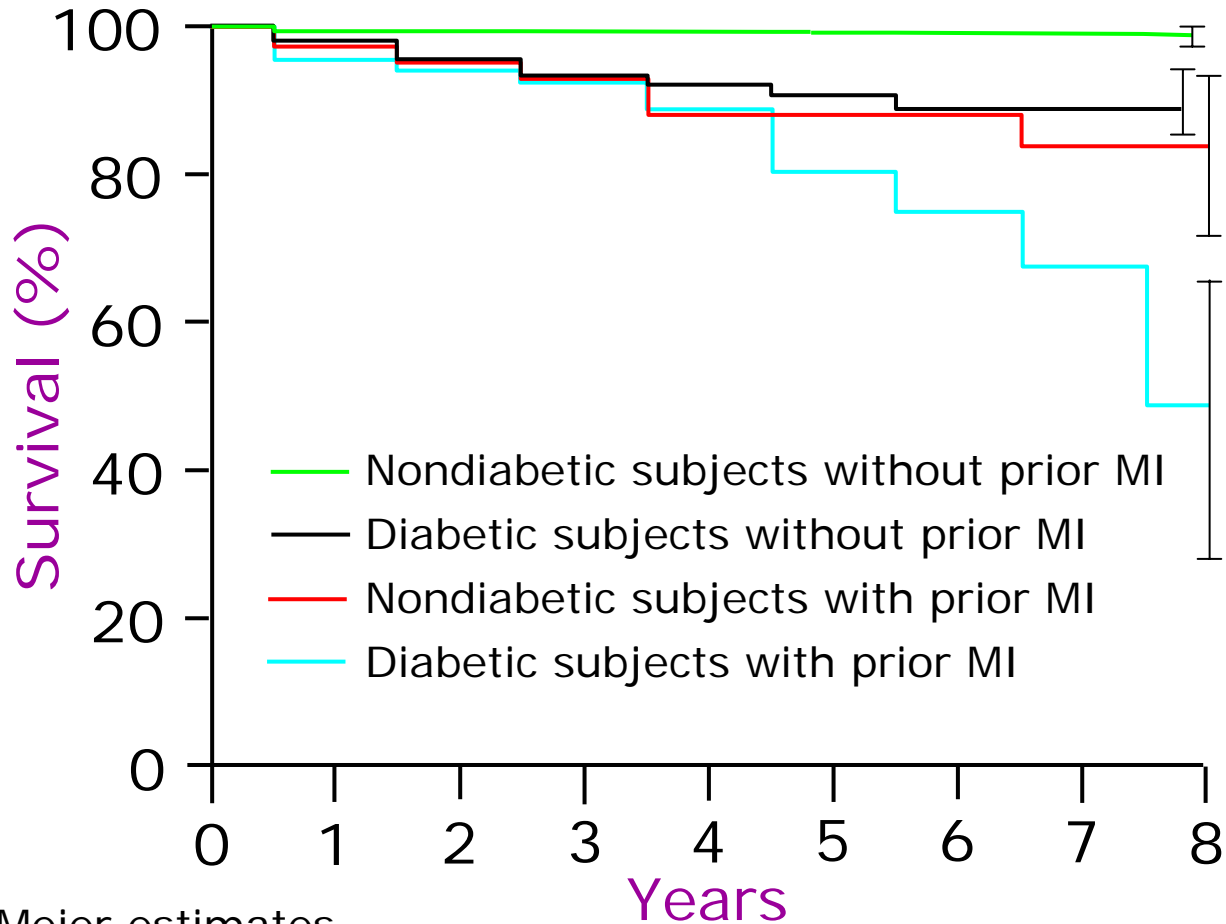
Riesgo de infarto mortal en DM2



- **METAANALISIS: 37 estudios de cohorte.**
- **Estudios publicados entre 1.996-2.005.**
- **n = 447.064 pacientes.**
- **Tasa de infarto mortal: No DM2 1,6/DM2 5,4.**
- **Mujeres/Hombres: 1,46.**



Probability of Death From CHD in Patients With NIDDM and in Nondiabetic Patients, With and Without Prior MI

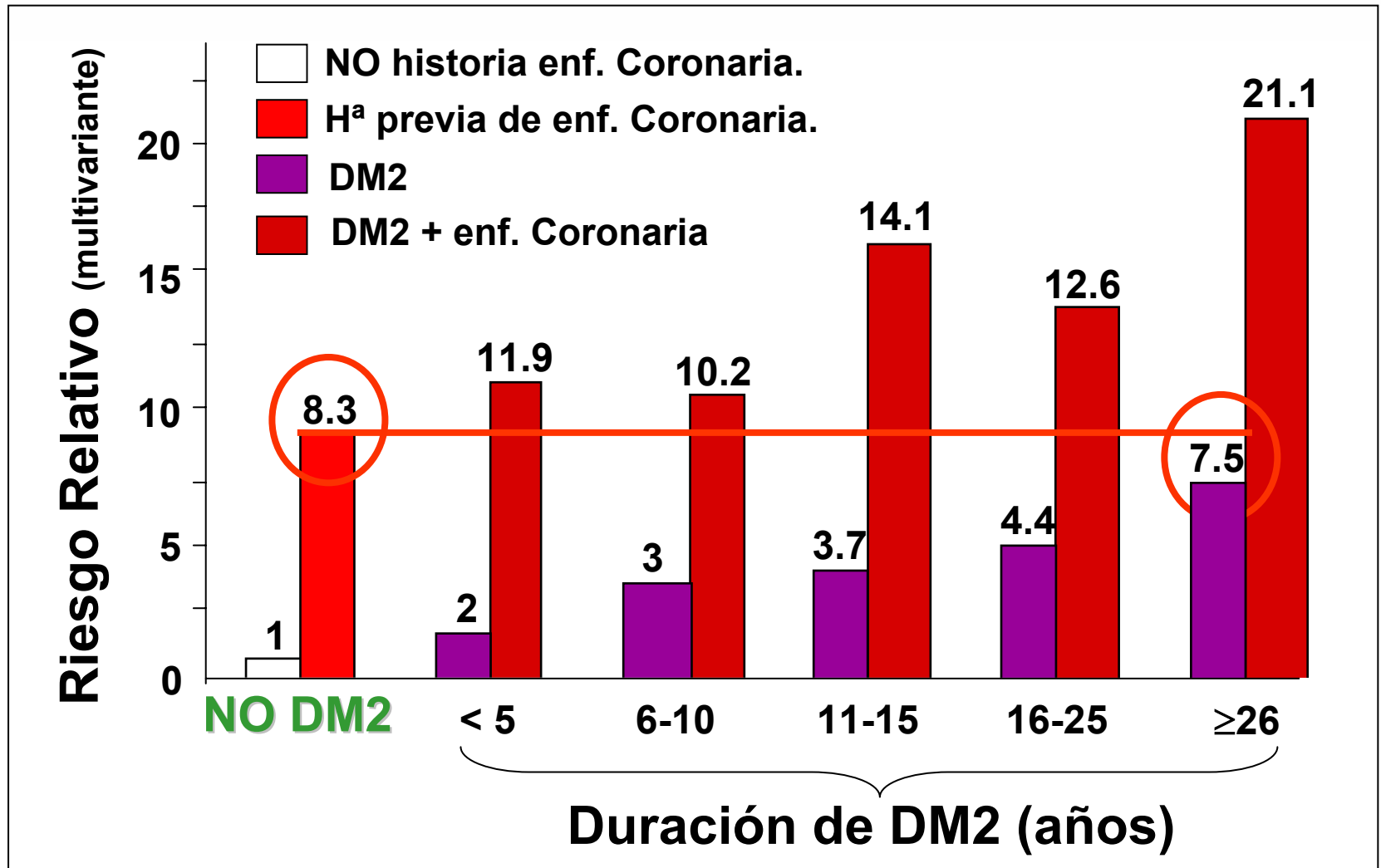


Kaplan-Meier estimates

Haffner SM et al. *N Engl J Med* 1998; 339:229–234.

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HPS: Muerte por enfermedad coronaria según duración DM2 (1.986-96, n= 51.316)



Adaptado de Cho E, et al. JACC 2.002;40:954-60.



La retinopatía predice la mortalidad coronaria

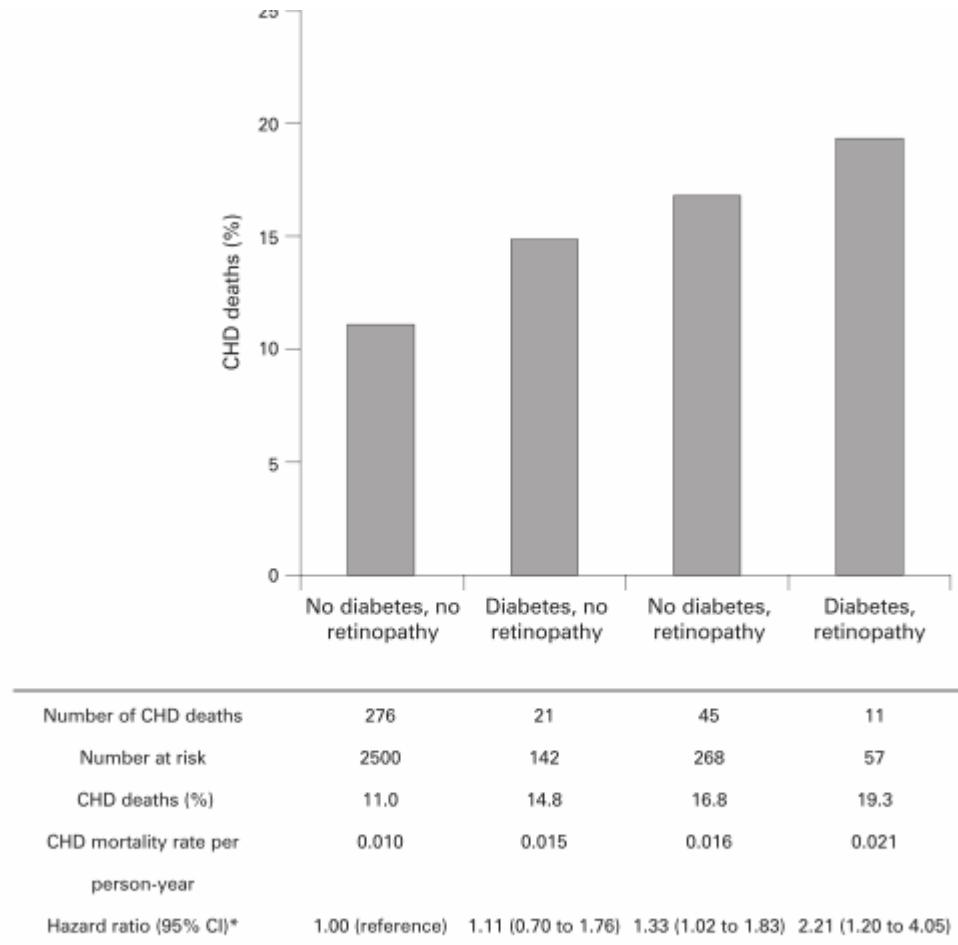


Figure 2 Coronary heart disease (CHD) deaths over 12 years, by diabetes and retinopathy. *Adjusted for age (continuously), gender, smoking (current, past and never), hypertension and diabetes.



- **Los pacientes diabéticos tipo 2 con síndrome metabólico presentan un riesgo vascular alto/muy alto.**



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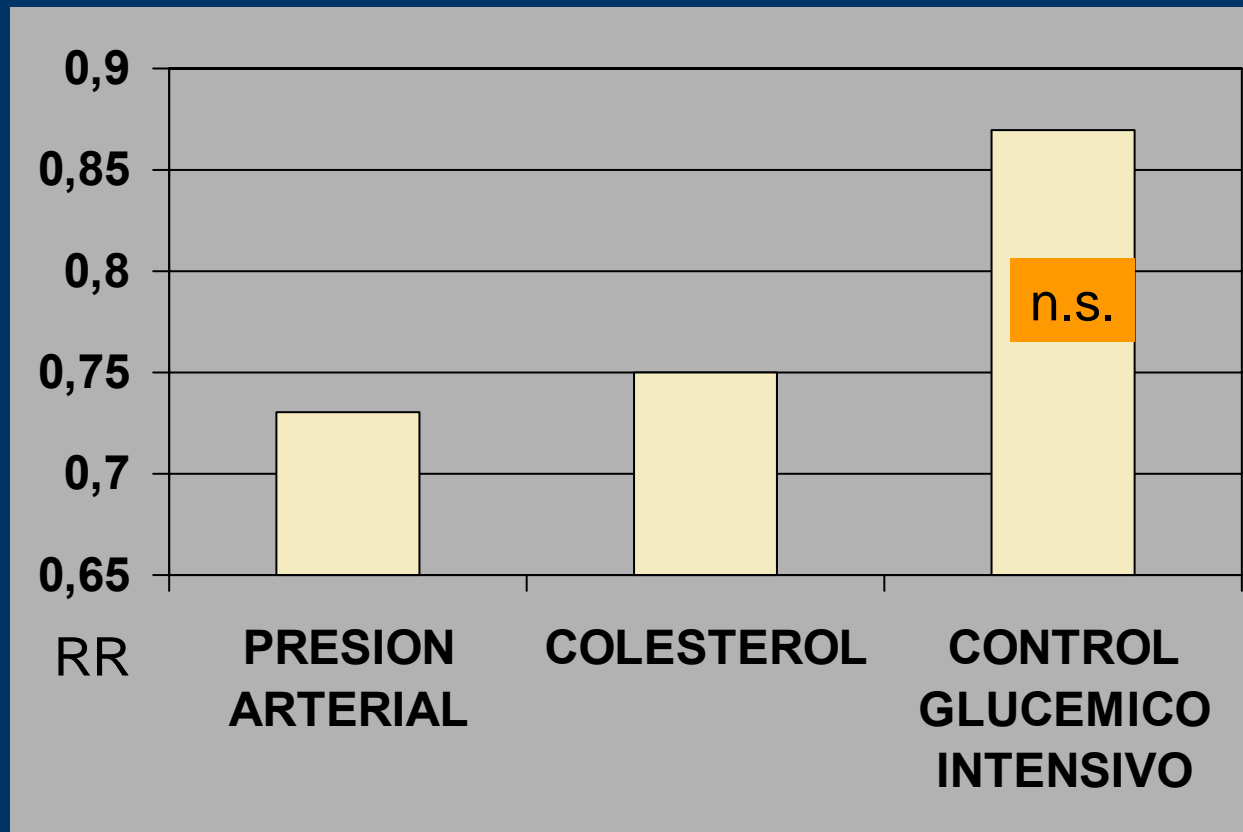
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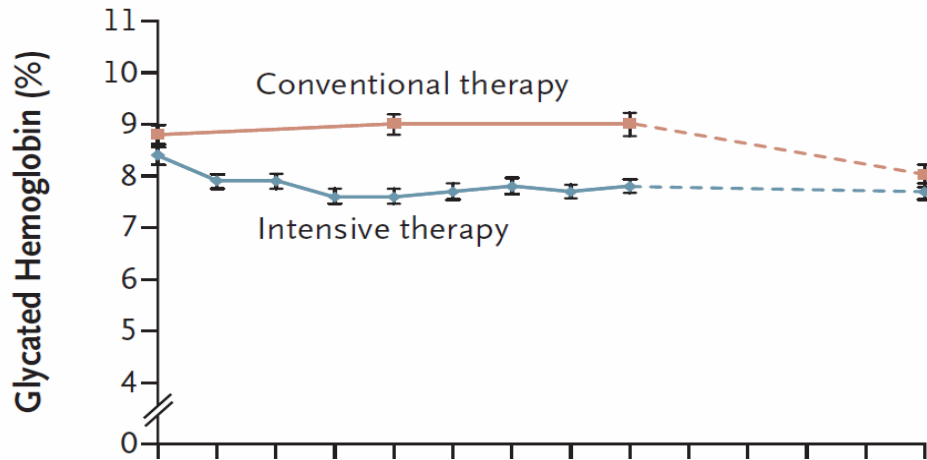
Metanálisis: Efecto de las intervenciones para prevenir eventos cardiovasculares en DM2



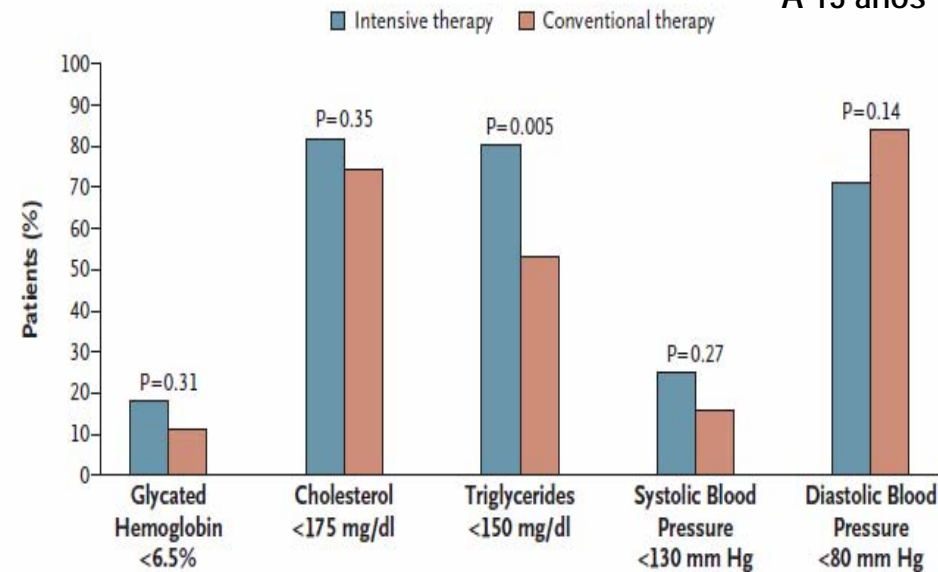
¿Cuál es la mejor estrategia para el tratamiento de la diabetes?



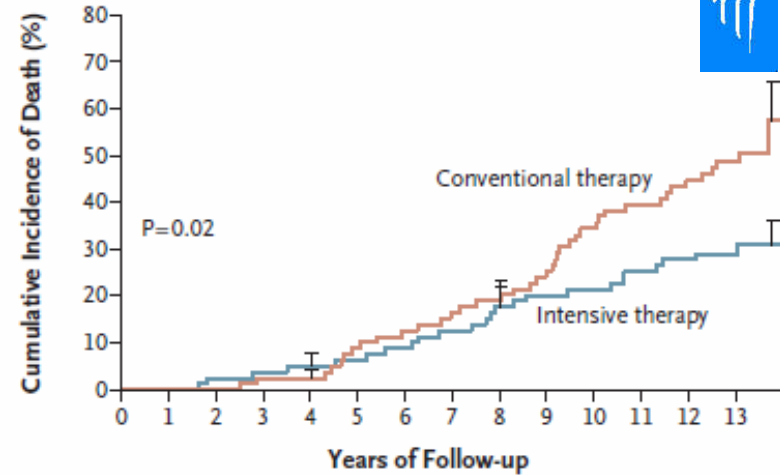
STENO 2 Gaede y cols, 2008,
Tratados 7,8 años, seguidos 5,5 años más



A 13 años



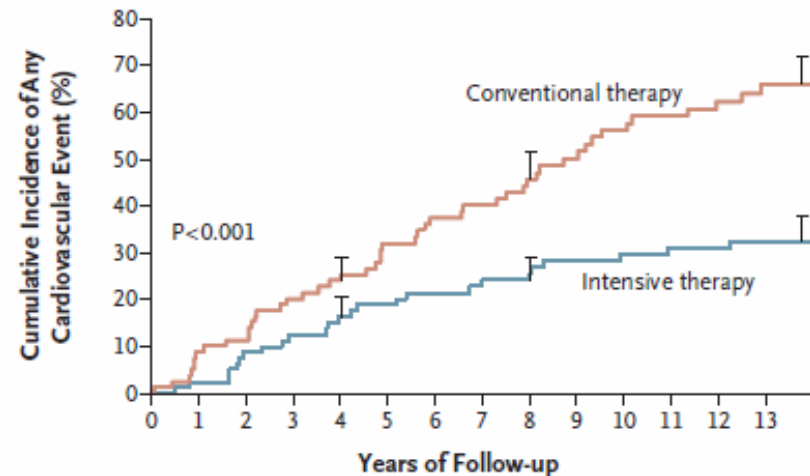
A



No. at Risk

Intensive therapy	80	78	75	72	65	62	57	39
Conventional therapy	80	80	77	69	63	51	43	30

B



No. at Risk

Intensive therapy	80	72	65	61	56	50	47	31
Conventional therapy	80	70	60	46	38	29	25	14

¿Qué condiciona este beneficio en el estudio STENO?



- **INFARTO AGUDO MIOCARDIO**

- HbA1c 13 %
- PAS 11%
- Tabaco 3%
- **Lípidos 73%**
 - HDL 25%
 - LDL 48%

- **ACCIDENTE CEREBRO-VASCULAR**

- HbA1c 3%
- PAS 25%
- Tabaco 8%
- **Lípidos 64%**
 - HDL 25%
 - LDL 39%



Factores de riesgo para el desarrollo de coronariopatía en la diabetes mellitus tipo 2: UKPDS 23.

Table 4 Stepwise selection of risk factors, adjusted for age and sex, in 2693 white patients with non-insulin dependent diabetes mellitus with dependent variable as time to first event. P values are significance of risk factor after accounting for all other risk factors in model

Position in model	Coronary artery disease (n=280)		Non-fatal or fatal myocardial infarction (n=192)		Fatal myocardial infarction (n=79)	
	Variable	P value	Variable	P value	Variable	P value
First	Low density lipoprotein cholesterol	<0.0001	Low density lipoprotein cholesterol	0.0022	Diastolic blood pressure	0.0012
Second	High density lipoprotein cholesterol	0.0001	Diastolic blood pressure	0.0074	Low density lipoprotein cholesterol	0.012
Third	Haemoglobin A _{1c}	0.0022	Smoking	0.025	Haemoglobin A _{1c}	0.024
Fourth	Systolic blood pressure	0.0065	High density lipoprotein cholesterol	0.026		
Fifth	Smoking	0.056	Haemoglobin A _{1c}	0.053		

Turner. BMJ 1.998; 316: 823-8.



Dr. de Cajón. Perogrullo Med J, 2.010.

“A la hora de establecer recomendaciones debe ofrecerse, en primer lugar, aquella que ha demostrado ser eficaz”.

METANALISIS “Cholesterol Treatment Trialists Collaboration” Eficacia terapia hipolipemiante con estatinas en DM2.



- 14 ensayos clínicos (4S, HPS, CARDS,...)
- n = 18.686 (DM1 1.466/DM2 17.220) VS 71.370 No DM.

– REDUCCIÓN DE MORBIMORTALIDAD

- **La terapia con estatinas debería considerarse en todos los pacientes diabéticos de alto riesgo vascular.**

CTT Collaborators. Lancet 2.008; 371: 117-25.



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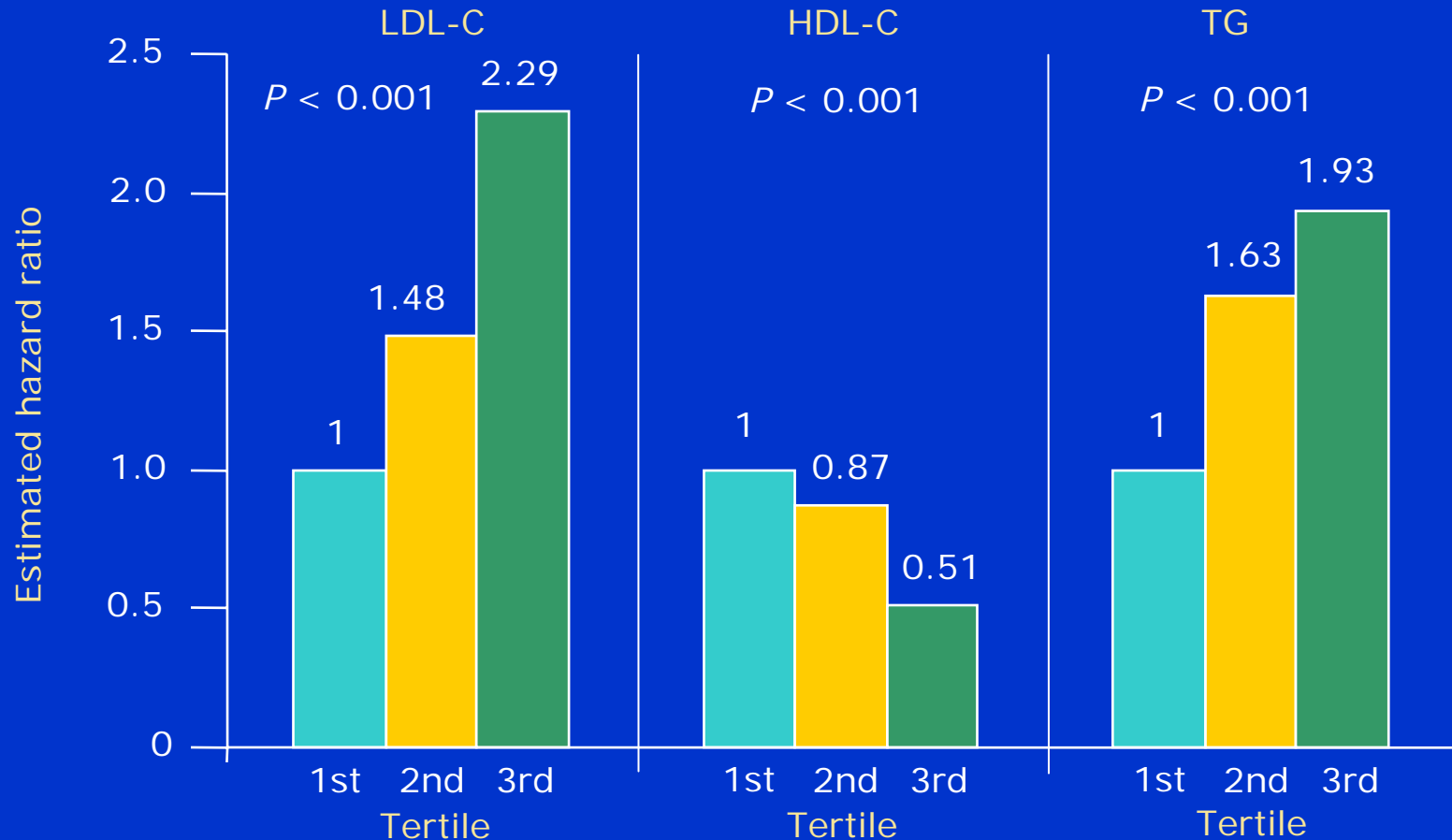
Equivalente coronario

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Potential Risk Factors for CHD in 2,693 White Patients With NIDDM

United Kingdom Prospective Diabetes Study

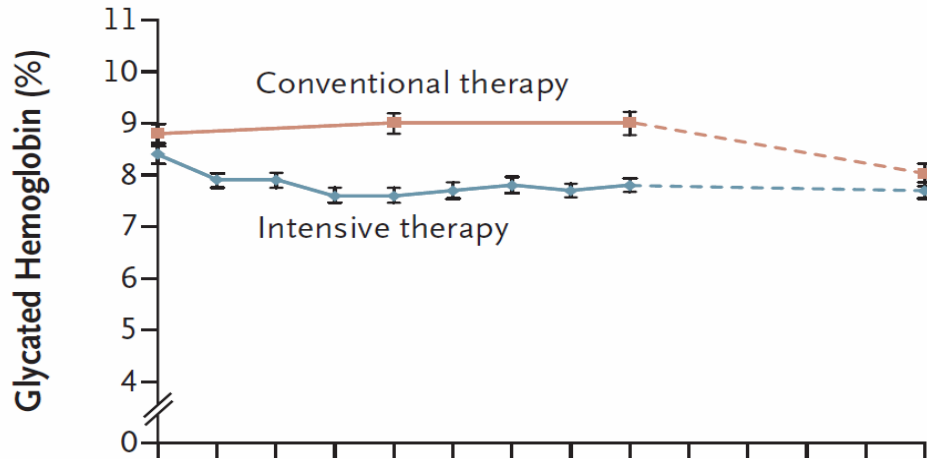


280 pts with CHD
Turner RC et al. *BMJ* 1998;316:823-828

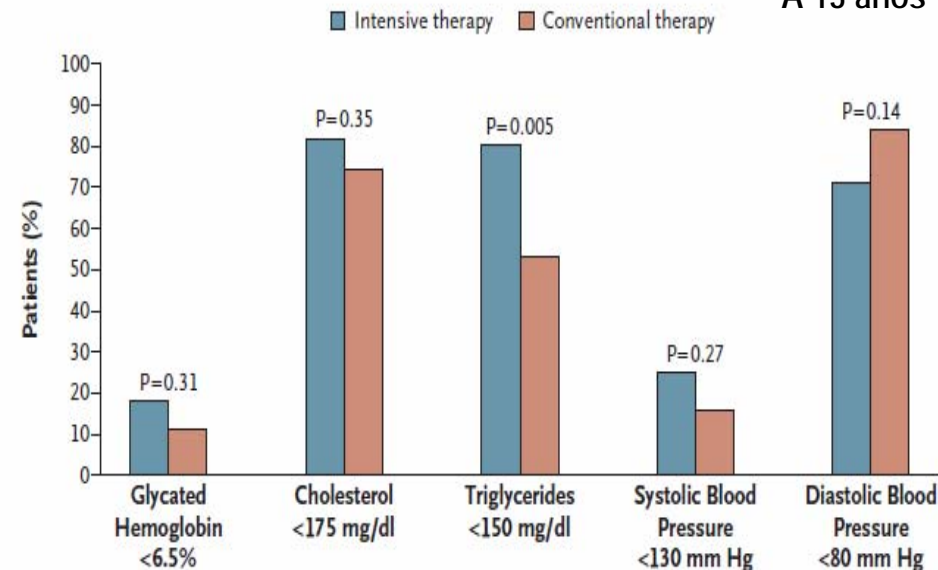
¿Cuál es la mejor estrategia para el tratamiento de la diabetes?



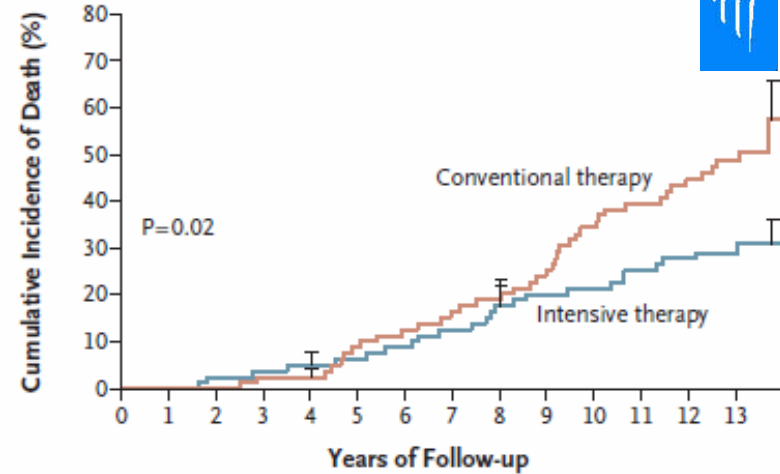
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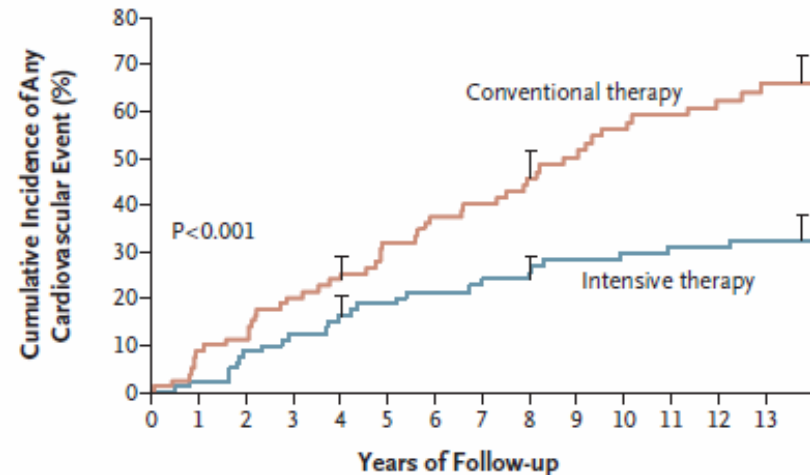
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ACCORD-Lípidos

NEJM -- Effects of Combination Lipid Therapy in Type 2 Diabetes Mellitus - Windows Internet Explorer

http://content.nejm.org/cgi/content/short/362/17/1563?query=TOC

NEJM -- Effects of Combination Lipid Therapy in ...

ORIGINAL ARTICLE

◀ Previous Volume 362:1563-1574 April 29, 2010 Number 17 Next ▶

Effects of Combination Lipid Therapy in Type 2 Diabetes Mellitus

The ACCORD Study Group

ABSTRACT

Background We investigated whether combination therapy with a statin plus a fibrate, as compared with statin monotherapy, would reduce the risk of cardiovascular disease in patients with type 2 diabetes mellitus who were at high risk for cardiovascular disease.

Methods We randomly assigned 5518 patients with type 2 diabetes who were being treated with open-label simvastatin to receive either masked fenofibrate or placebo. The primary outcome was the first occurrence of nonfatal myocardial infarction, nonfatal stroke, or death from cardiovascular causes. The mean follow-up was 4.7 years.

Results The annual rate of the primary outcome was 2.2% in the fenofibrate group and 2.4% in the placebo group (hazard ratio in the fenofibrate group, 0.92; 95% confidence interval [CI], 0.79 to 1.08; P=0.32). There were also no significant differences between the two study groups with respect to any secondary outcome. Annual rates of death were 1.5% in the fenofibrate group and 1.6% in the placebo group (hazard ratio, 0.91; 95% CI, 0.75 to 1.10; P=0.33). Prespecified subgroup analyses suggested heterogeneity in treatment effect according to sex, with a benefit for men and possible harm for women (P=0.01 for interaction), and a possible interaction according to lipid subgroup, with a possible benefit for patients with both a high baseline triglyceride level and a low baseline level of high-density lipoprotein cholesterol (P=0.057 for interaction).

Conclusions The combination of fenofibrate and simvastatin did not reduce the rate of fatal cardiovascular events, nonfatal myocardial infarction, or nonfatal stroke, as compared with simvastatin alone. These results do not support the routine use of combination therapy with fenofibrate and simvastatin to reduce cardiovascular risk in the majority of high-risk patients with type 2 diabetes. (ClinicalTrials.gov number, NCT00000620 [ClinicalTrials.gov].)

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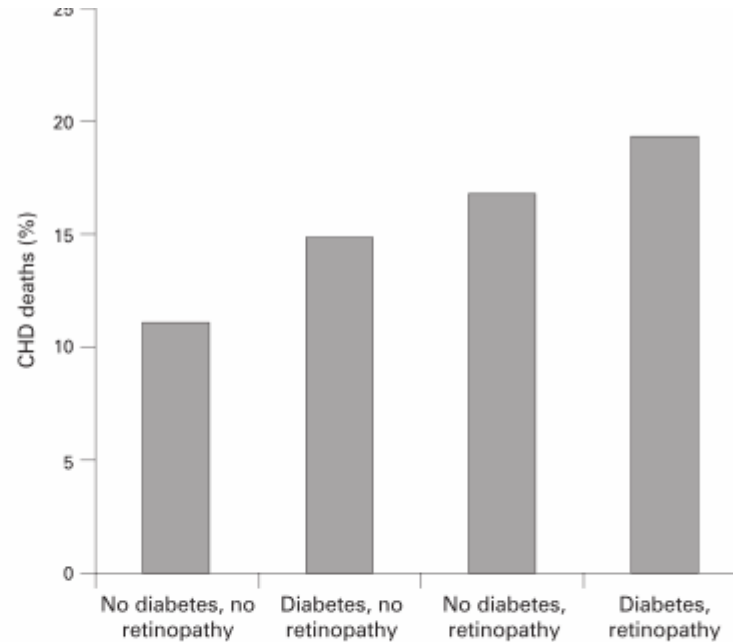
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La retinopatía predice la mortalidad coronaria

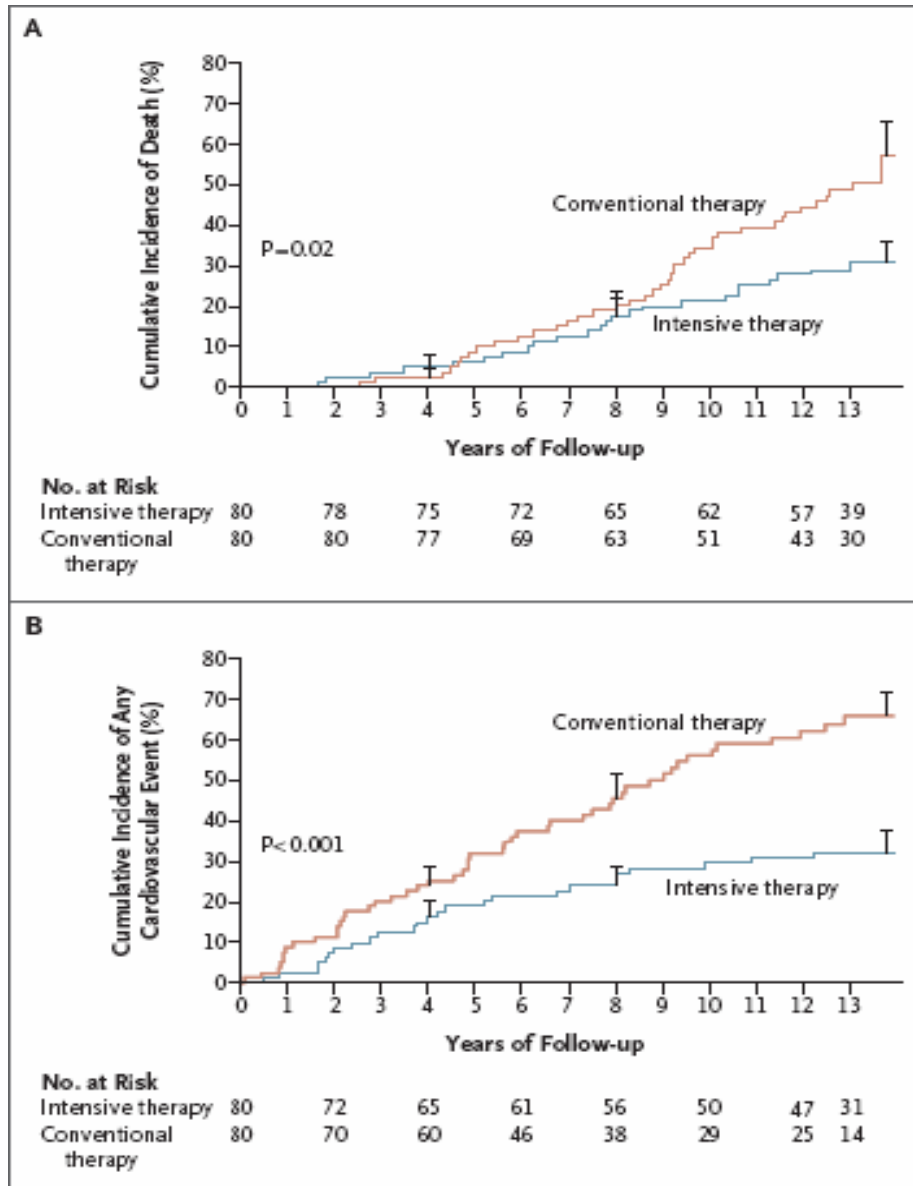


Number of CHD deaths	276	21	45	11
Number at risk	2500	142	268	57
CHD deaths (%)	11.0	14.8	16.8	19.3
CHD mortality rate per person-year	0.010	0.015	0.016	0.021
Hazard ratio (95% CI)*	1.00 (reference)	1.11 (0.70 to 1.76)	1.33 (1.02 to 1.83)	2.21 (1.20 to 4.05)

Figure 2 Coronary heart disease (CHD) deaths over 12 years, by diabetes and retinopathy. *Adjusted for age (continuously), gender, smoking (current, past and never), hypertension and diabetes.

Effect of a Multifactorial Intervention on Mortality in Type 2 Diabetes

Peter Gæde, M.D., D.M.Sc., Henrik Lund-Andersen, M.D., D.M.Sc., Hans-Henrik Parving, M.D., D.M.Sc., and Oluf Pedersen, M.D., D.M.Sc.



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[◀ Previous](#)

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