

VII



Reunión de Riesgo Vascular

Palacio de Congresos. Valencia
5 y 6 de Mayo 2011



**¿Qué ha habido
de NUEVO
en diabetes mellitus
en 2010?**

Ricardo Gómez Huelgas
Medicina Interna
Hospital Carlos Haya. Málaga.

No voy a hablar de...

- UKPDS
- STENO-2
- Efecto incretina
- Efecto memoria

Sólo incluir...

- Estudios de 2010-2011

GUIÓN

- Epidemiología
- Prevención
- Manejo de los factores de riesgo en la DMT2
- Hipoglucemia
- HbA1c y diagnóstico de DMT2
- Conclusiones

GUIÓN

- Epidemiología
- Prevención
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- Conclusiones

Estudio di@bet.es

Datos globales de prevalencia en población >18 años

	%	Nº total
Diabetes conocida	8.1	3.111.641
Diabetes no conocida	3.9	1.514.916
Diabetes total	12	4.626.557
Tolerancia anormal a la glucosa	7.9	3.028.706
Glucemia basal alterada	3.6	1.398.183
Obesidad	28.2	10.863.431
Síndrome metabólico	20.8	8.022.026
Sedentarismo	50.3	19.400.237
Tabaquismo	27.8	10.724.239

GUIÓN

- Epidemiología
- **Prevención**
- Manejo de los factores de riesgo en la DMT2
- Hipoglucemia
- HbA1c y diagnóstico de DMT2
- Conclusiones



Reduction in the Incidence of Type 2 Diabetes With the Mediterranean Diet

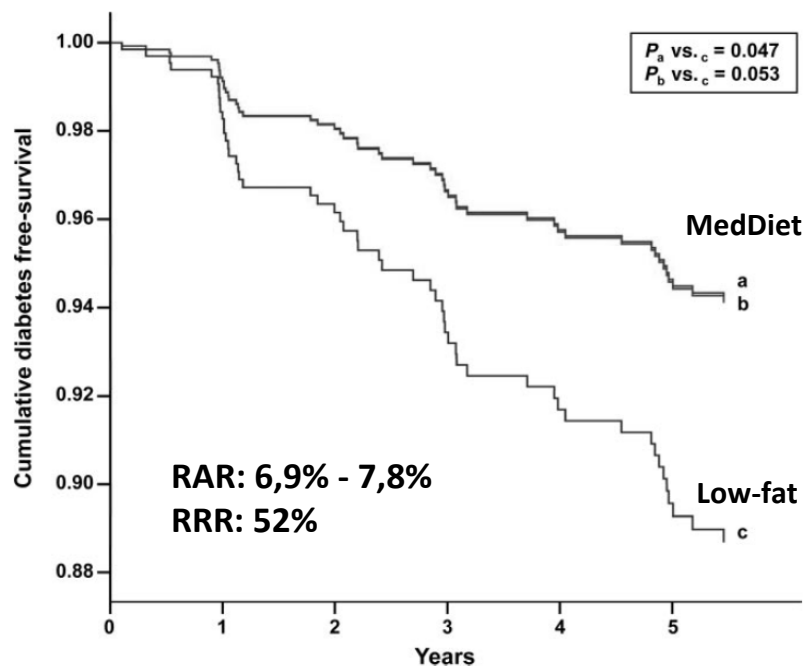
Results of the PREDIMED-Reus nutrition intervention randomized trial



JORDI SALAS-SALVADÓ, MD, PHD^{1,2}
MONICA BULLÓ, BSC, PHD^{1,2}
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MIGUEL ÁNGEL MARTÍNEZ-GONZÁLEZ, MD,
PHD^{2,3}
NÚRIA IBARROLA-JURADO, RD^{1,2}
JOSEP BASORA, MD^{1,2,4}
RAMON ESTRUCH, MD, PHD^{2,5}

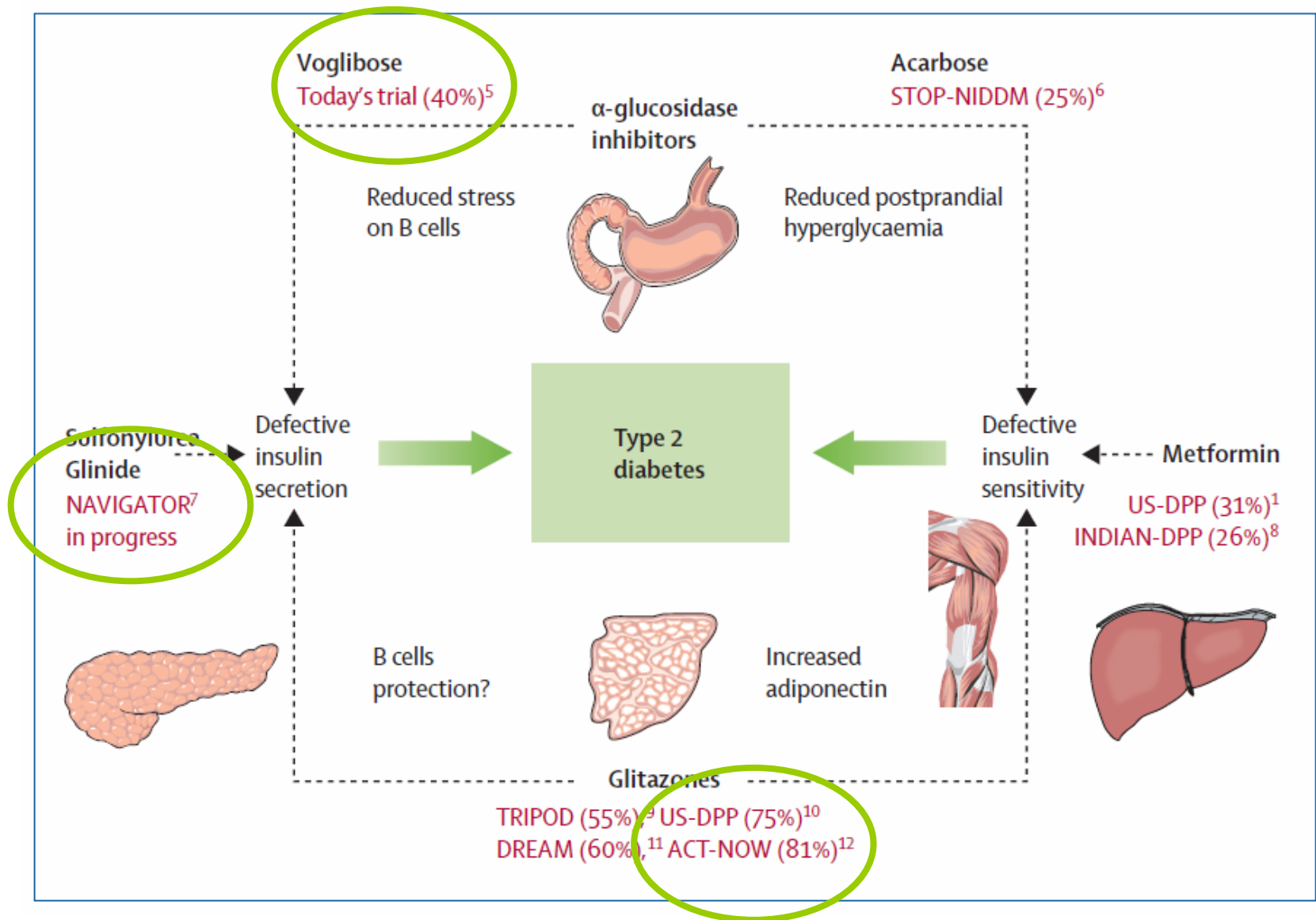
MARIA ISABEL COVAS, DPHARM, PHD^{2,6}
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FERNANDO AROS, MD, PHD^{2,8}
VALENTINA RUIZ-GUTIERREZ, DPHARM, PHD⁹
EMILIO ROS, MD, PHD^{2,10}
FOR THE PREDIMED STUDY
INVESTIGATORS

Diabetes Care 34:14–19, 2011



- La dieta mediterránea sin restricción calórica previene la diabetes en sujetos de alto riesgo vascular.
- La reducción del riesgo de diabetes ocurrió sin cambios en el peso corporal ni en la actividad física.

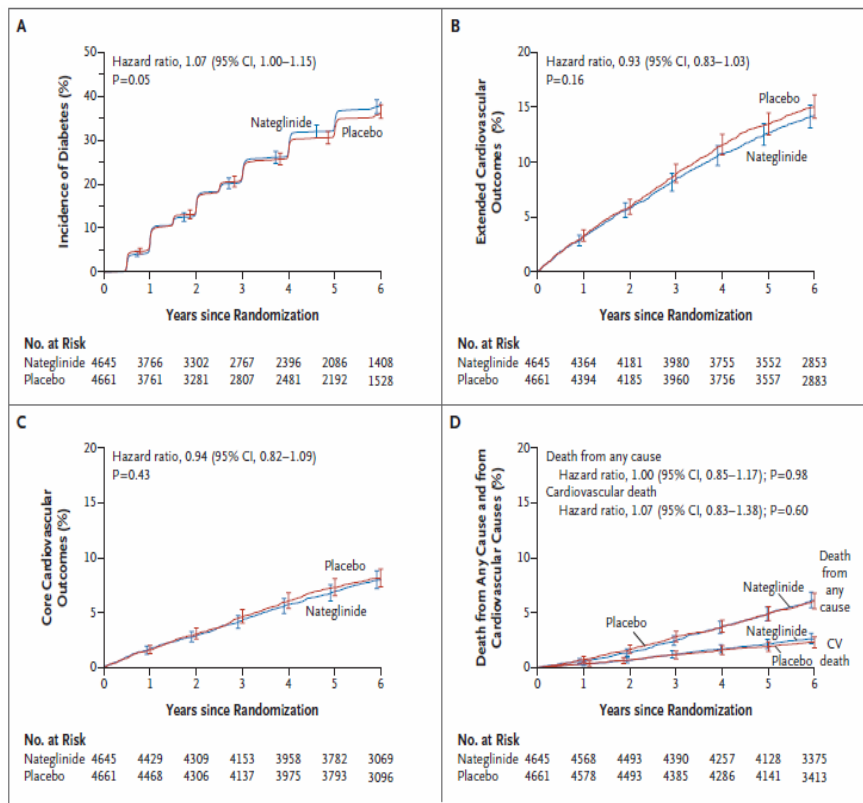
PREVENCIÓN FARMACOLÓGICA DE LA DIABETES TIPO 2



ORIGINAL ARTICLE

Effect of Nateglinide on the Incidence of Diabetes and Cardiovascular Events

The NAVIGATOR Study Group*



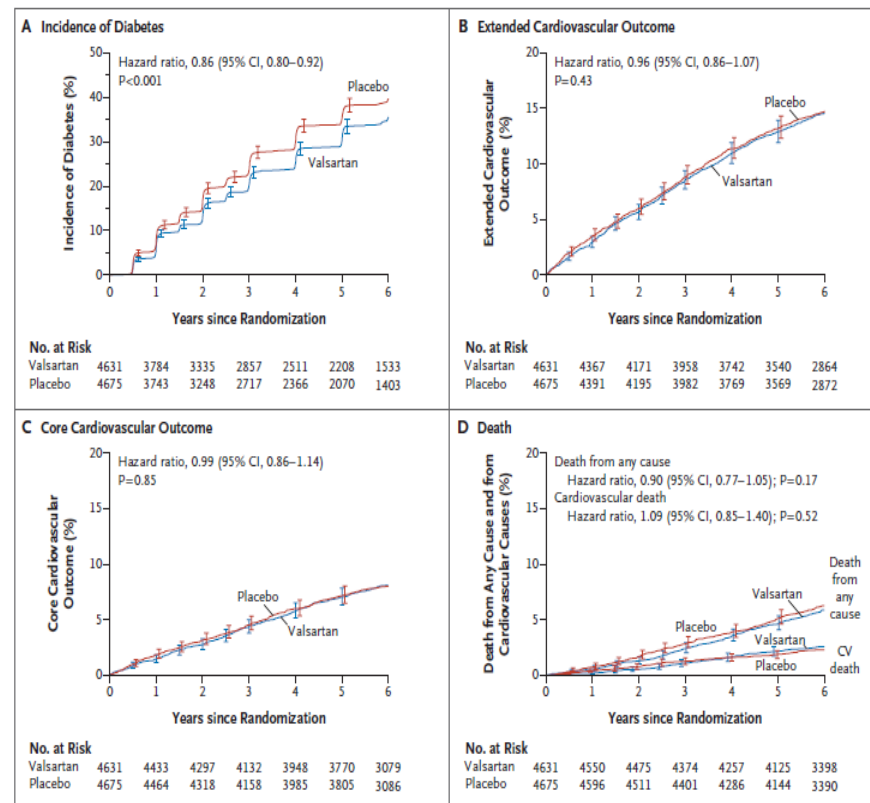
NATEGLINIDA n.s.
↑ hipoglucemias

n: 9306
ITG + ECV o FRCV
t: 5 años

ORIGINAL ARTICLE

Effect of Valsartan on the Incidence of Diabetes and Cardiovascular Events

The NAVIGATOR Study Group*



VALSARTAN: -14% DM
n.s. ECV



Pioglitazone for Diabetes Prevention in Impaired Glucose Tolerance

Ralph A. DeFronzo, M.D., Devjit Tripathy, M.D., Ph.D., Dawn C. Schwenke, Ph.D., MaryAnn Banerji, M.D., George A. Bray, M.D., Thomas A. Buchanan, M.D., Stephen C. Clement, M.D., Robert R. Henry, M.D., Howard N. Hodis, M.D., Abbas E. Kitabchi, M.D., Ph.D., Wendy J. Mack, Ph.D., Sunder Mudaliar, M.D., Robert E. Ratner, M.D., Ken Williams, M.Sc., Frankie B. Stentz, Ph.D., Nicolas Musi, M.D., and Peter D. Reaven, M.D., for the ACT NOW Study

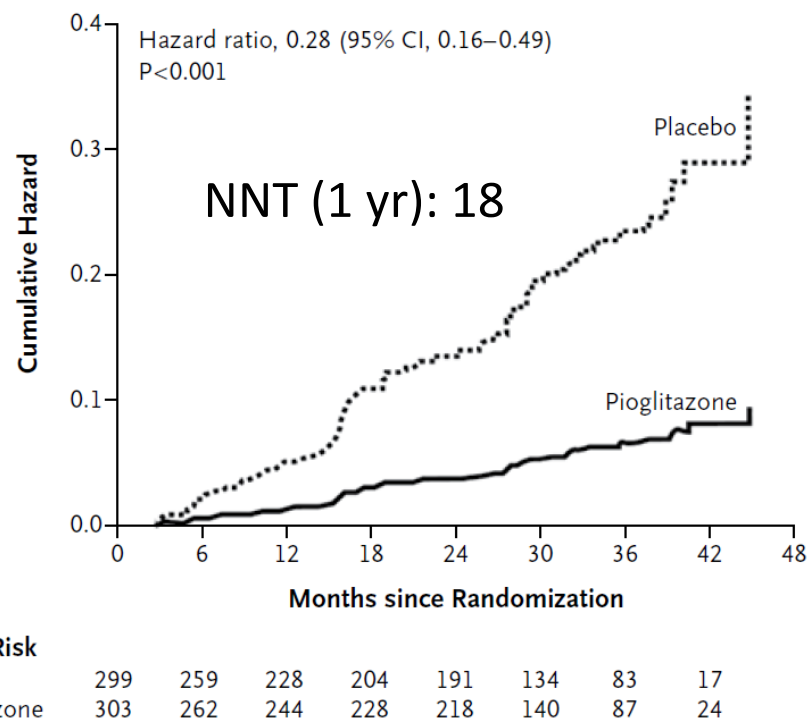


Figure 2. Kaplan–Meier Plot of Hazard Ratios for Time to Development of Diabetes.

Low-dose combination therapy with rosiglitazone and metformin to prevent type 2 diabetes mellitus (CANOE trial): a double-blind randomised controlled study

Bernard Zinman, Stewart B Harris, Jan Neuman, Hertz C Gerstein, Ravi R Retnakaran, Janet Raboud, Ying Qi, Anthony J G Hanley

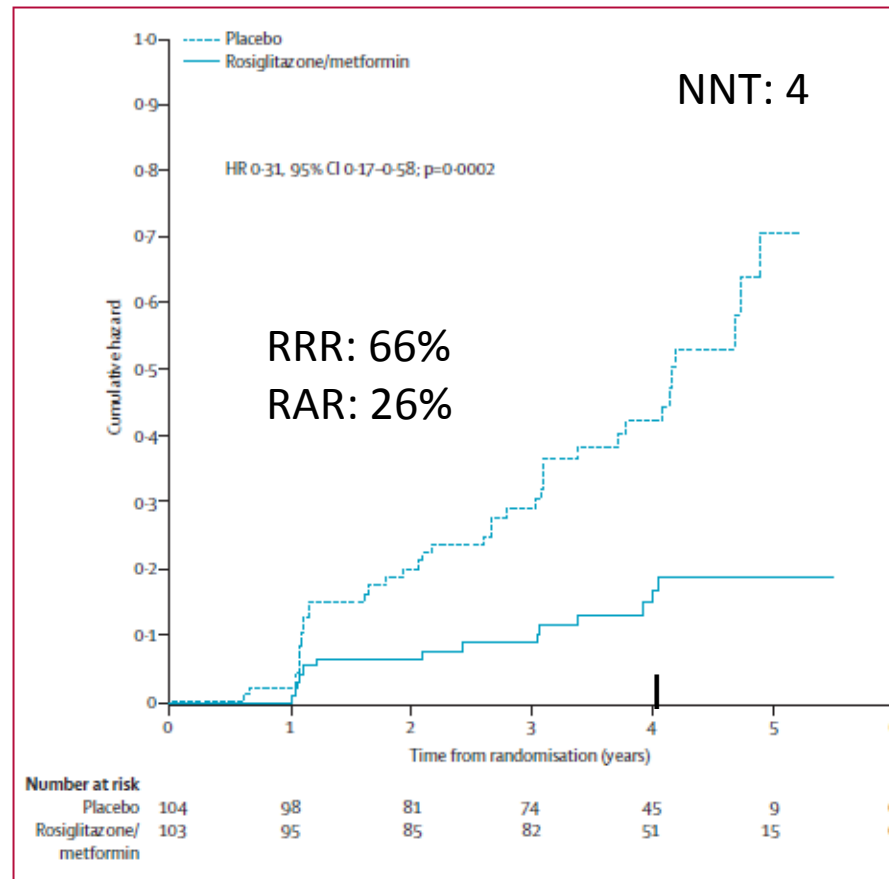


Figure 2: Time to occurrence of the development of diabetes
HR=hazard ratio.

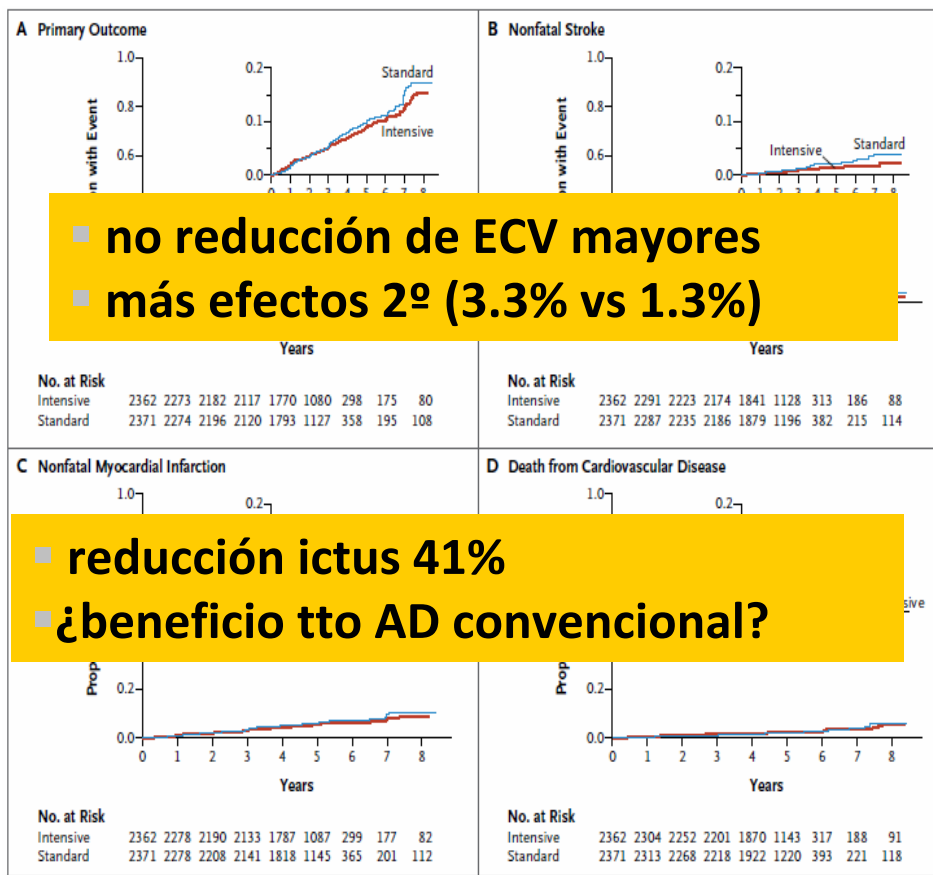
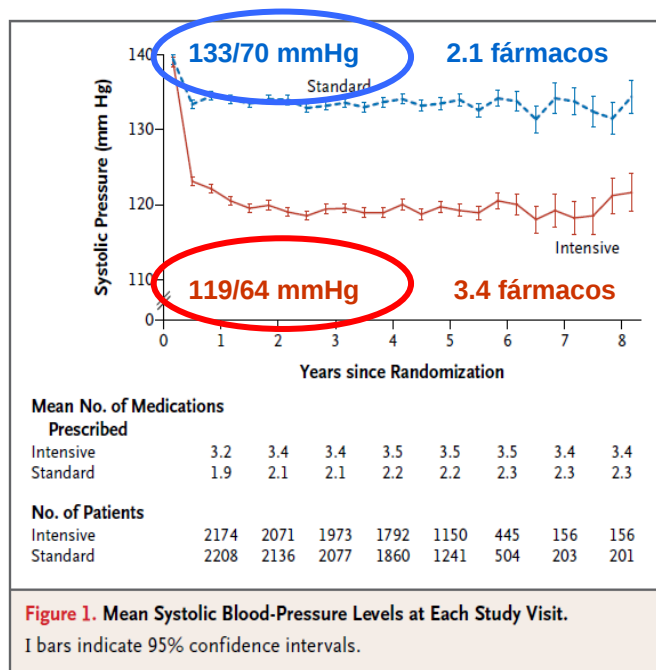
GUIÓN

- Epidemiología
- Prevención
- Manejo de los factores de riesgo en la DMT2
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- Conclusiones

ORIGINAL ARTICLE

Effects of Intensive Blood-Pressure Control in Type 2 Diabetes Mellitus

The ACCORD Study Group*



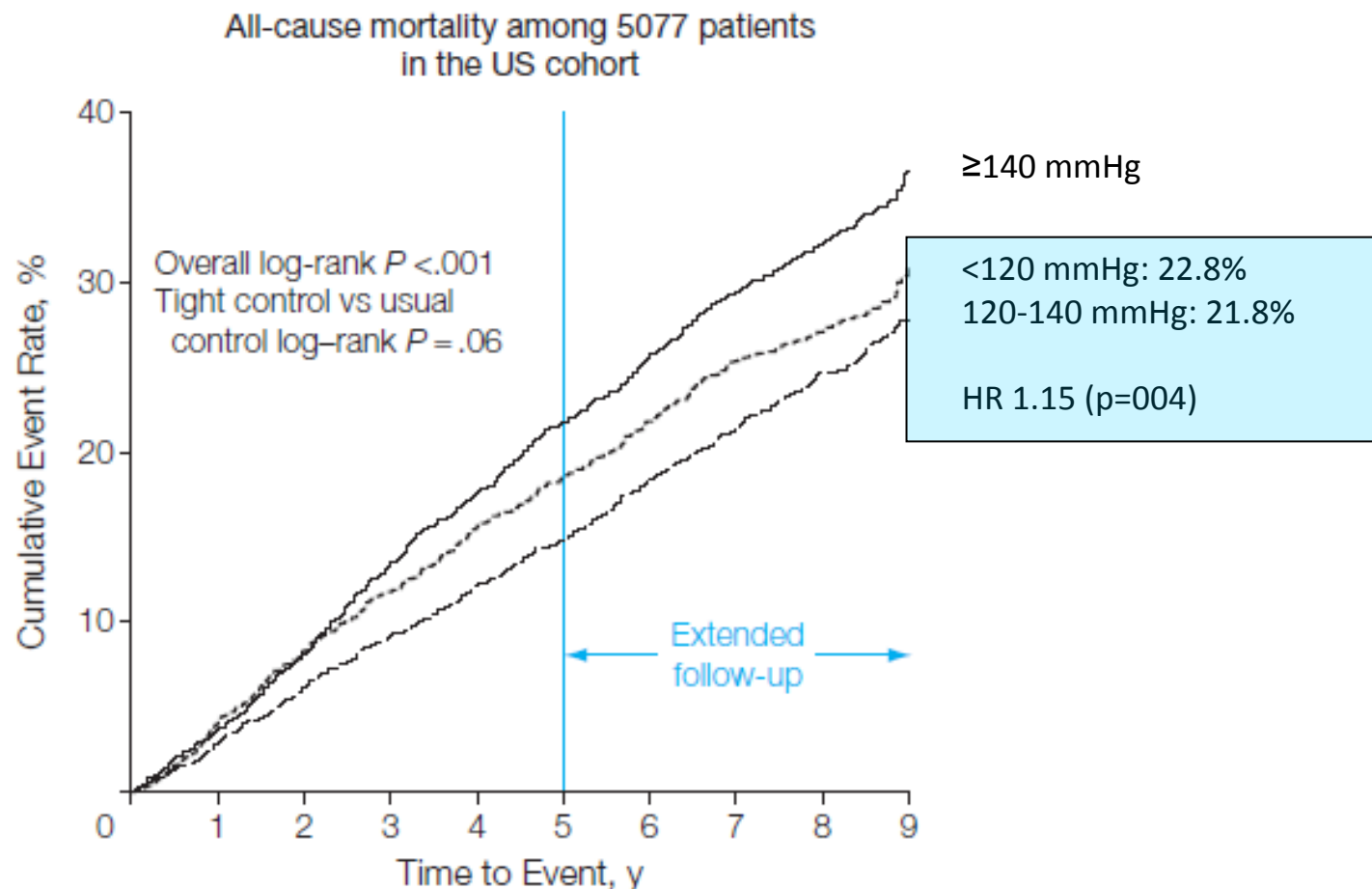
ACCORD-BP

¿PAS <120 vs <140?

Tight Blood Pressure Control and Cardiovascular Outcomes Among Hypertensive Patients With Diabetes and Coronary Artery Disease

Rhonda M. Cooper-DeHoff; Yan Gong; Eileen M. Handberg; et al.

INVEST



Blood Pressure and Cardiovascular Disease Risk in the Veterans Affairs Diabetes Trial

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FOR THE VADT STUDY GROUP

Diabetes Care 34:34–38, 2011

Table 2—HRs for separated SBP and DBP categories relative to each reference category at baseline and On-Study

	Baseline			On-Study		
	HR	95% CI	P	HR	95% CI	P
DBP (mmHg)						
70–79	Reference			Reference		
<70	1.482	1.179–1.862	<0.001	1.491	1.206–1.844	<0.001
≥80	1.030	0.825–1.287	0.79	1.049	0.814–1.351	0.71
SBP (mmHg)						
105–129	Reference			Reference		
<105	0.974	0.591–1.603	0.92	1.364	0.977–1.904	0.07
130–139	1.004	0.786–1.283	0.97	0.938	0.733–1.201	0.61
≥140	1.508	1.203–1.890	<0.001	1.469	1.157–1.867	0.002

Table 3—HRs for combined SBP and DBP categories relative to a reference category at baseline and On-Study

BP (mmHg)	Baseline			On-Study		
	HR	95% CI	P	HR	95% CI	P
105–129/70–79	Reference			Reference		
<105/<70	1.609	0.930–2.787	0.09	2.103	1.437–3.079	<0.001
105–129/<70	1.370	1.019–1.843	0.04	1.472	1.121–1.934	0.006
130–139/<70	1.682	1.061–2.667	0.03	1.379	0.908–2.096	0.13
≥140/<70	1.785	1.060–3.004	0.03	2.042	1.276–3.269	0.003
<105/70–79	0.441	0.109–1.790	0.25	0.633	0.156–2.574	0.52
130–139/70–79	0.871	0.592–1.281	0.48	0.942	0.632–1.404	0.77
≥140/70–79	1.495	1.033–2.164	0.03	1.486	1.005–2.198	0.05
<105/≥80*				3.273	0.455–23.55	0.24
105–129/≥80	0.939	0.634–1.393	0.76	1.011	0.655–1.562	0.96
130–139/≥80	0.982	0.675–1.432	0.93	0.957	0.611–1.487	0.85
≥140/≥80	1.499	1.130–1.990	0.005	1.536	1.104–2.137	0.01

*Insufficient number in this BP category at baseline for analysis.

CONCLUSIONS — Increased risk of CVD events with SBP ≥140 mmHg emphasizes the urgency for treatment of systolic hypertension. Increased risk with DBP <70 mmHg, even when combined with SBP in guideline-recommended target ranges, supports a new finding in patients with type 2 diabetes. The results emphasize that DBP <70 mmHg in these patients was associated with elevated CVD risk and may best be avoided.

ACCORD – LIPIDS

¿estatina o estatina + fibrato?

The NEW ENGLAND JOURNAL of MEDICINE

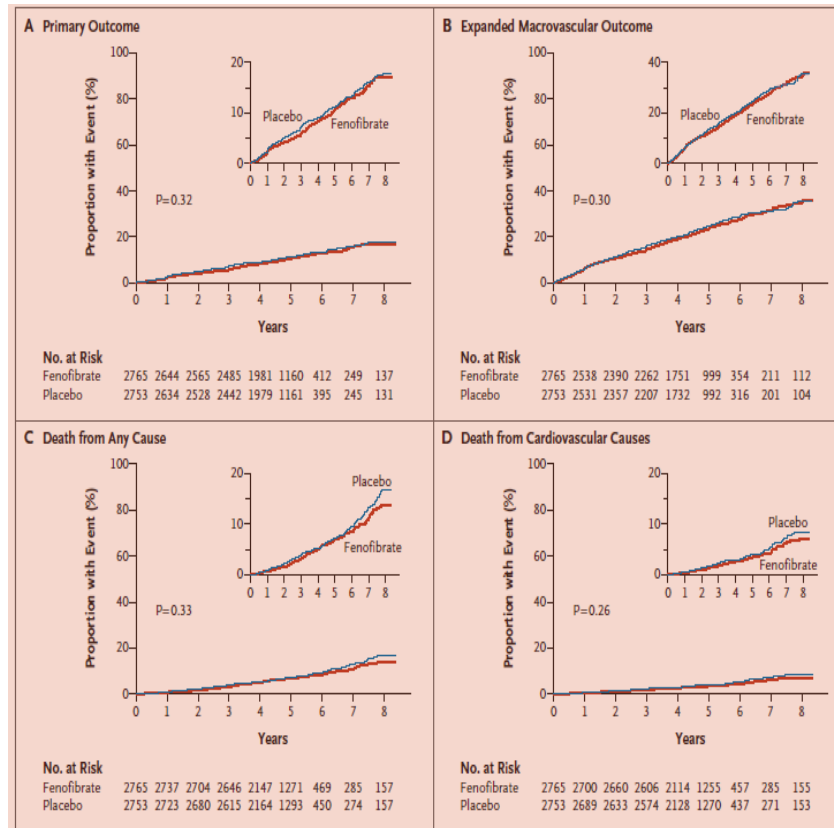
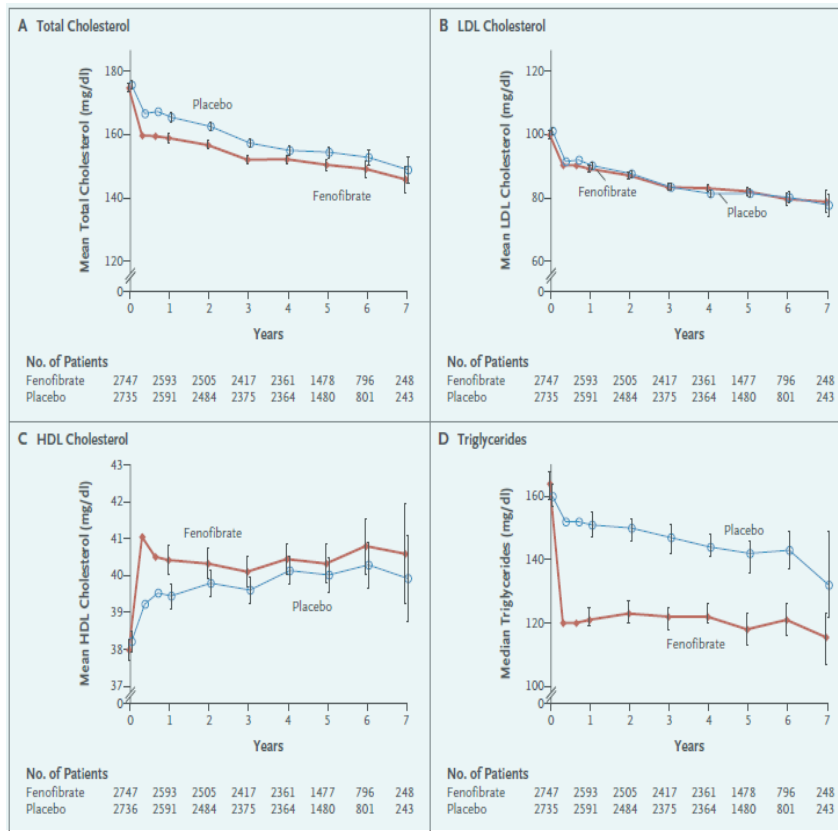
ORIGINAL ARTICLE

NEJM



Effects of Combination Lipid Therapy in Type 2 Diabetes Mellitus

The ACCORD Study Group*

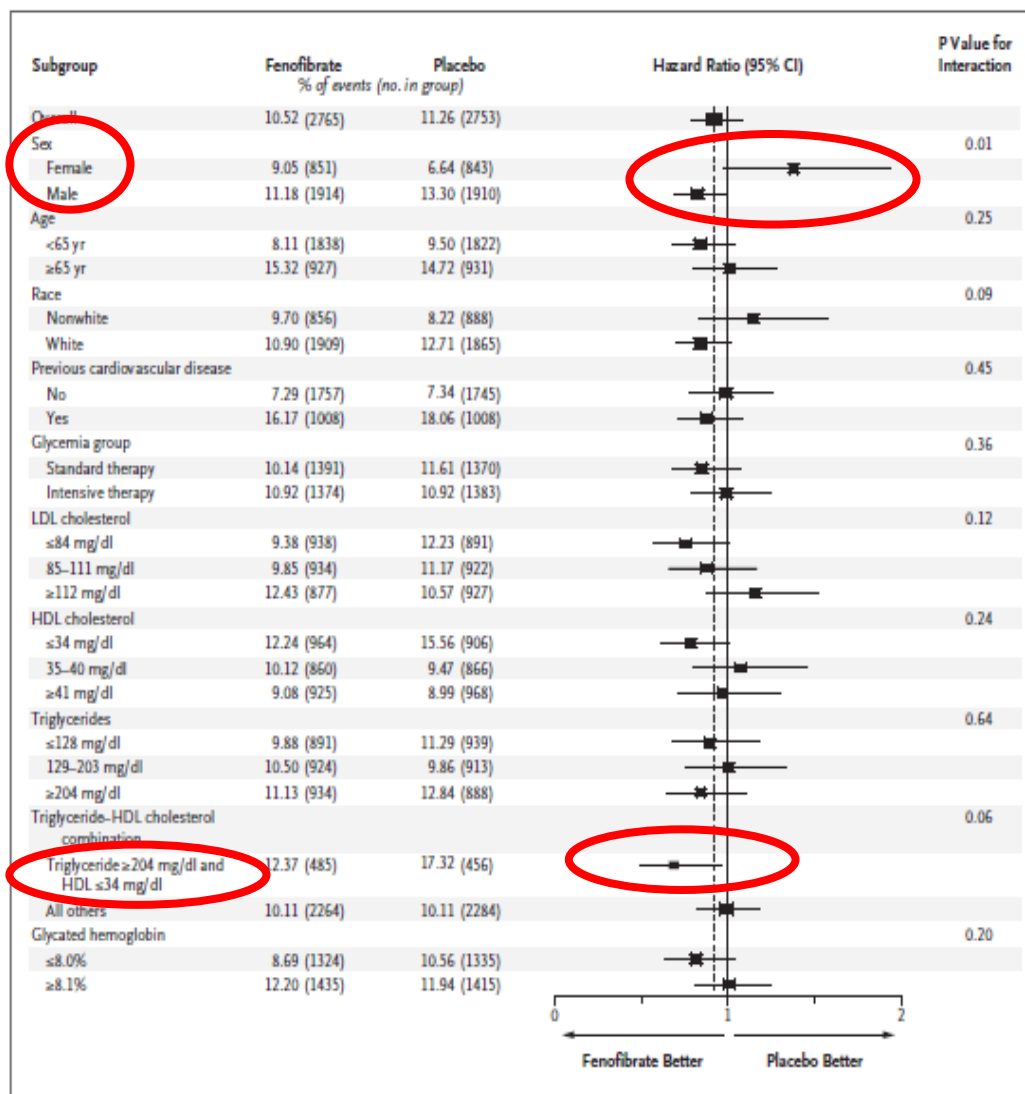




ORIGINAL ARTICLE

Effects of Combination Lipid Therapy in Type 2 Diabetes Mellitus

The ACCORD Study Group*





ORIGINAL ARTICLE



Effects of Medical Therapies on Retinopathy Progression in Type 2 Diabetes

The ACCORD Study Group and ACCORD Eye Study Group*

Table 2. Effects of Intensive Glycemic Control, Fenofibrate, and Intensive Blood-Pressure Control on Progression of Diabetic Retinopathy and Moderate Vision Loss.*

Treatment	Progression of Diabetic Retinopathy <i>no./total no. (%)</i>	Adjusted Odds Ratio (95% CI)	P Value	Moderate Vision Loss <i>no./total no. (%)</i>	Adjusted Hazard Ratio (95% CI)	P Value
Glycemia therapy		0.67 (0.51–0.87)	0.003		0.95 (0.80–1.13)	0.56
Intensive	104/1429 (7.3)			266/1629 (16.3)		
Standard	149/1427 (10.4)			273/1634 (16.7)		
Dyslipidemia therapy†		0.60 (0.42–0.87)	0.006		1.04 (0.83–1.32)	0.73
With fenofibrate	52/806 (6.5)			145/908 (16.0)		
With placebo	80/787 (10.2)			136/893 (15.2)		
Antihypertensive therapy		1.23 (0.84–1.79)	0.29		1.27 (0.99–1.62)	0.06
Intensive	67/647 (10.4)			145/749 (19.4)		
Standard	54/616 (8.8)			113/713 (15.8)		

* Moderate vision loss was defined as loss of visual acuity by three or more lines in either eye.

† Dyslipidemia therapy consisted of simvastatin plus either fenofibrate or placebo.

CONCLUSIONS

Intensive glycemic control and intensive combination treatment of dyslipidemia, but not intensive blood-pressure control, reduced the rate of progression of diabetic retinopathy.

Long-term Effects of a Lifestyle Intervention on Weight and Cardiovascular Risk Factors in Individuals With Type 2 Diabetes Mellitus

Four-Year Results of the Look AHEAD Trial

Arch Intern Med. 2010;170(17):1566-1575

The Look AHEAD Research Group

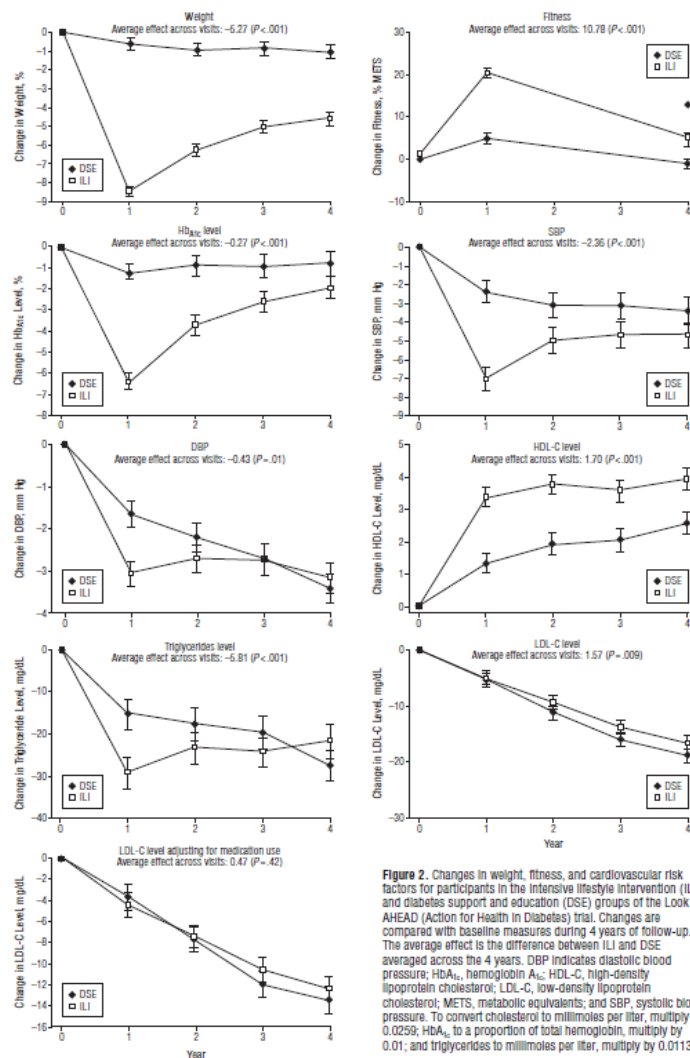


Figure 2. Changes in weight, fitness, and cardiovascular risk factors for participants in the intensive lifestyle intervention (ILI) and diabetes support and education (DSE) groups of the Look AHEAD (Action for Health in Diabetes) trial. Changes are compared with baseline measures during 4 years of follow-up. The average effect is the difference between ILI and DSE averaged across the 4 years. DBP indicates diastolic blood pressure; HbA_{1c}, hemoglobin A_{1c}; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; METS, metabolic equivalents; and SBP, systolic blood pressure. To convert cholesterol to millimoles per liter, multiply by 0.0259; HbA_{1c} to a proportion of total hemoglobin, multiply by 0.01; and triglycerides to millimoles per liter, multiply by 0.0113.

La MEV intensiva en DMT2 produce beneficios a largo plazo (4 años):

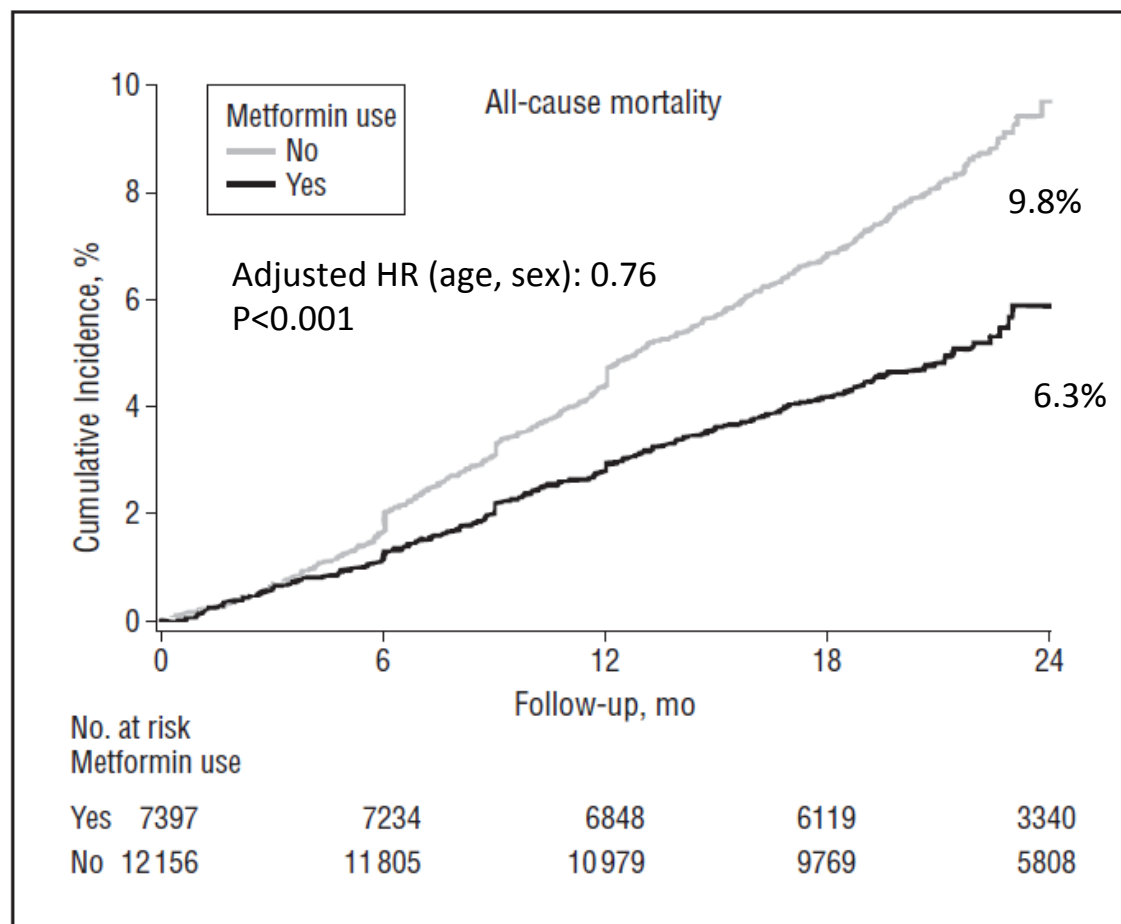
- pérdida de peso
- mejora capacidad física
- mejora control glucémico
- reduce PAS y PAD
- mejora perfil lipídico

Metformin Use and Mortality Among Patients With Diabetes and Atherothrombosis

Ronan Roussel, MD, PhD; Florence Travert, MD, PhD; Blandine Pasquet, MSc; Peter W. F. Wilson, MD; Sidney C. Smith Jr, MD; Shinya Goto, MD, PhD; Philippe Ravaut, MD, PhD; Michel Marre, MD, PhD; Avi Porath, MD, MPH; Deepak L. Bhatt, MD, MPH; P. Gabriel Steg, MD; for the Reduction of Atherothrombosis for Continued Health (REACH) Registry Investigators

Arch Intern Med. 2010;170(21):1892-1899

REACH

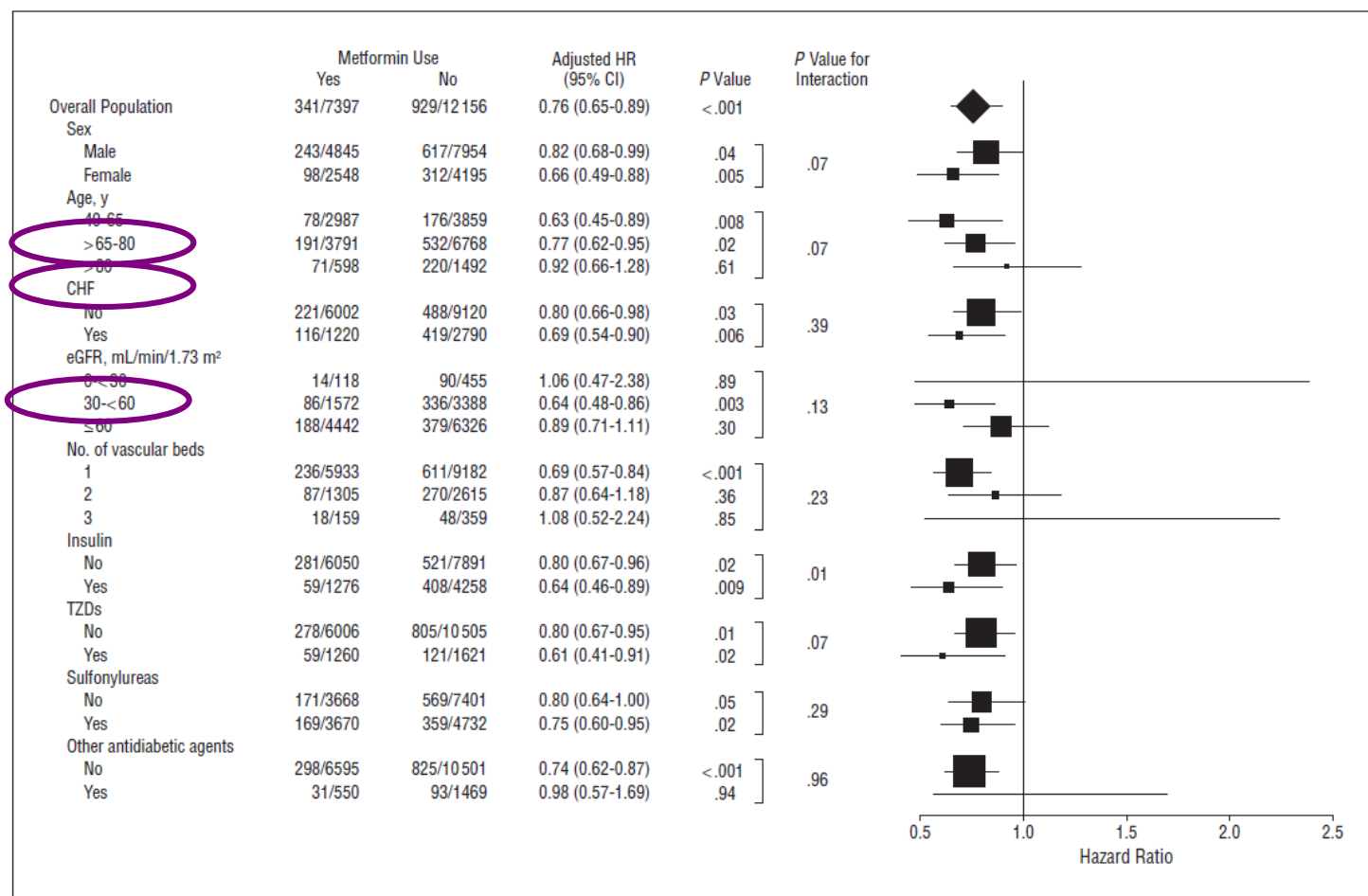


Metformin Use and Mortality Among Patients With Diabetes and Atherothrombosis

Ronan Roussel, MD, PhD; Florence Travert, MD, PhD; Blandine Pasquet, MSc; Peter W. F. Wilson, MD; Sidney C. Smith Jr, MD; Shinya Goto, MD, PhD; Philippe Ravaut, MD, PhD; Michel Marre, MD, PhD; Avi Porath, MD, MPH; Deepak L. Bhatt, MD, MPH; P. Gabriel Steg, MD; for the Reduction of Atherothrombosis for Continued Health (REACH) Registry Investigators

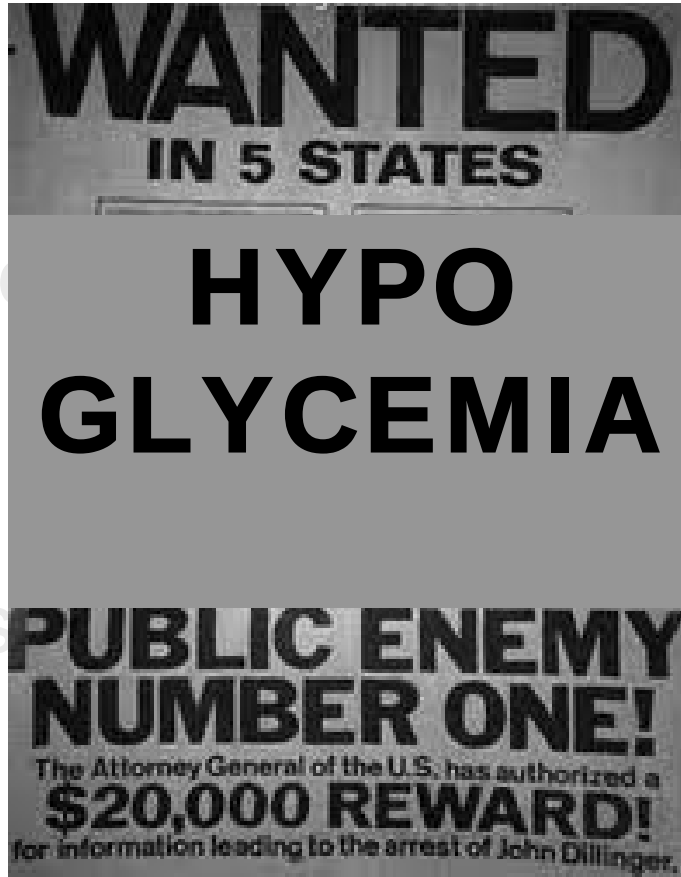
Arch Intern Med. 2010;170(21):1892-1899

REACH



GUIÓN

- Epidemiología
- Prevención
- Manejo de los factores de riesgo en la DMT2
- Hipoglucemia
- HbA1c y diagnóstico
- Conclusiones





ACCORD

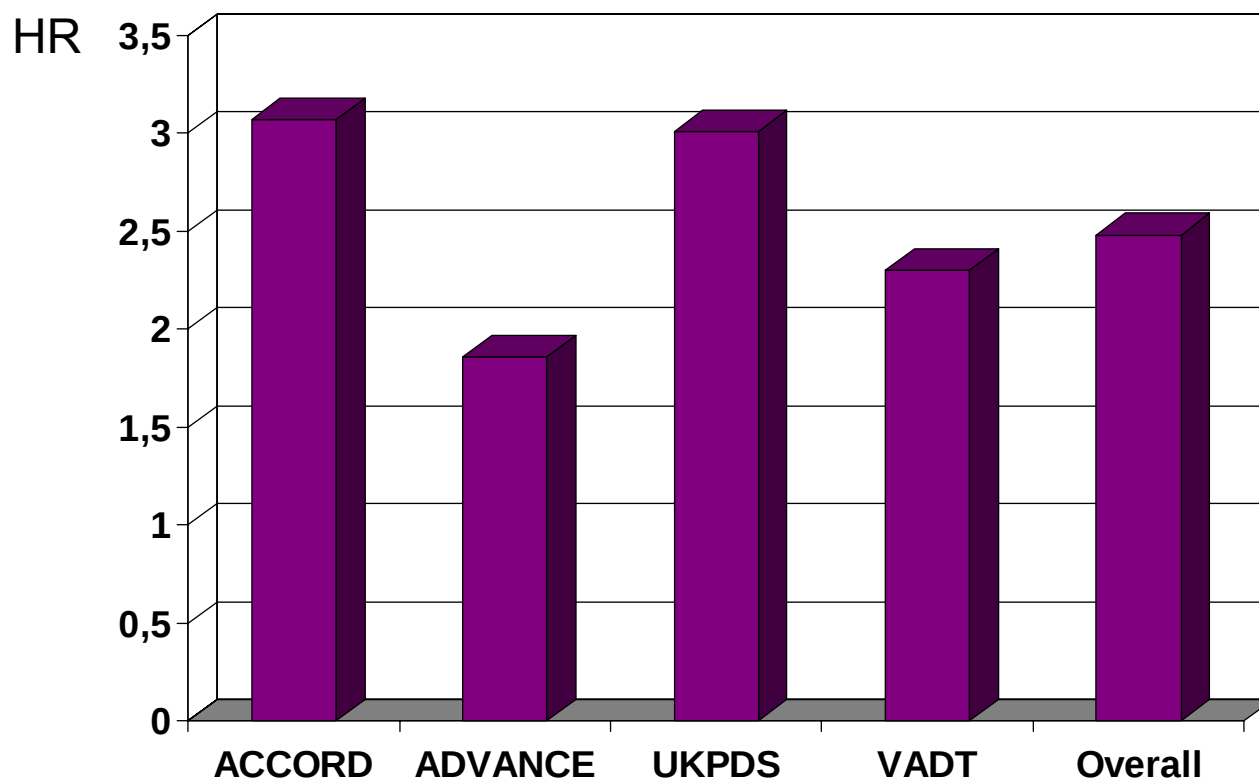
Causas de muerte

Cause of death	Intensive-treatment group	Standard-treatment group
Unexpected/presumed CVD	86	67
Myocardial infarction	19	13
Congestive heart failure	23	16
Cardiovascular procedure	10	3
Arrhythmia	4	10
Noncardiovascular procedure	1	3
Stroke	9	11
Other CVD	8	10
Cancer	65	63
Non-cancer/CVD	50	35
Indeterminate	7	11
Total	282	242

Intensive glucose control and macrovascular outcomes in type 2 diabetes

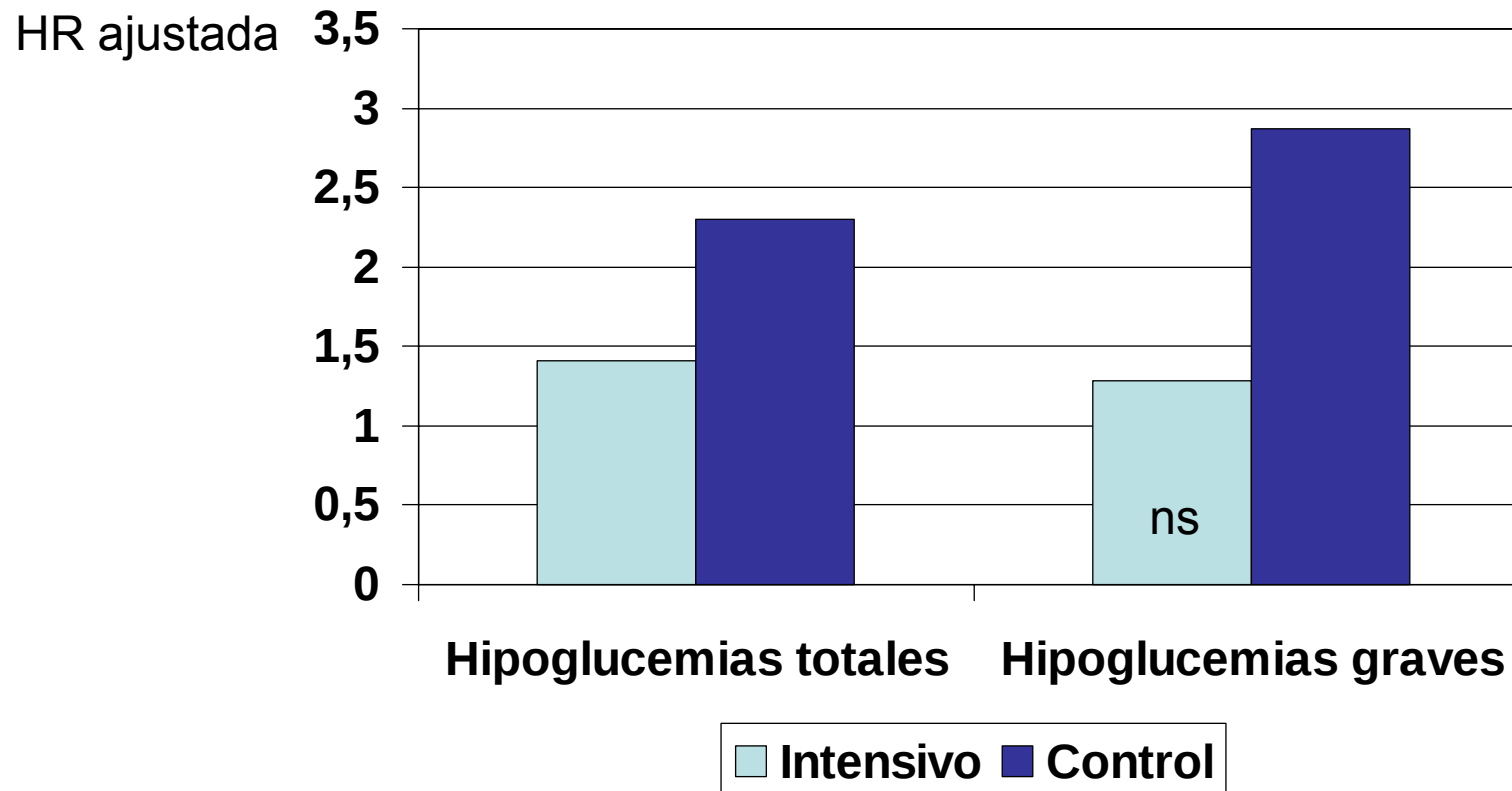
F. M. Turnbull · C. Abaira · R. J. Anderson · R. P. Byington · J. P. Chalmers ·
W. C. Duckworth · G. W. Evans · H. C. Gerstein · R. R. Holman · T. E. Moritz ·
B. C. Neal · T. Ninomiya · A. A. Patel · S. K. Paul · F. Travert · M. Woodward

Riesgo de hipoglucemia grave asociado al control glucémico intensivo



The association between symptomatic, severe hypoglycaemia and mortality in type 2 diabetes: retrospective epidemiological analysis of the ACCORD study

Riesgo de muerte en pacientes con hipoglucemia



ORIGINAL ARTICLE

Severe Hypoglycemia and Risks of Vascular Events and Death

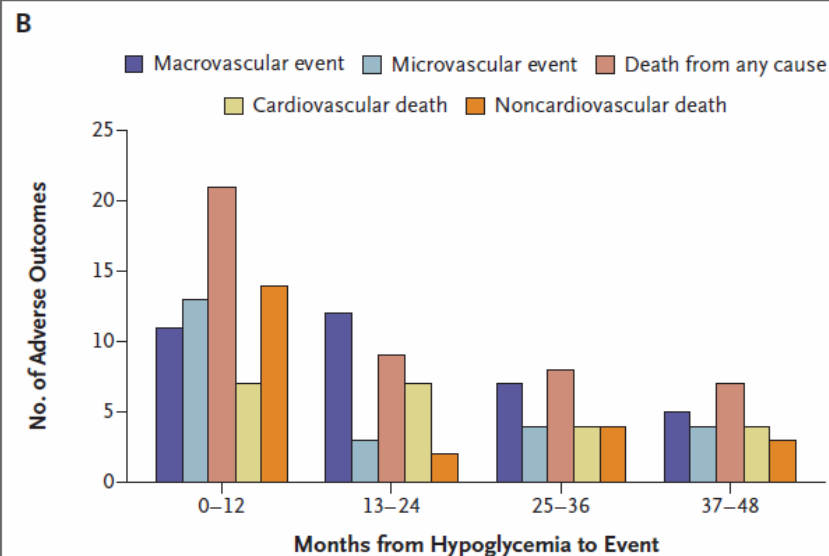
Sophia Zoungas **N Engl J Med** 2010;363:1410-8.

No se demuestra:

- relación dosis – efecto
- relación temporal

Table 2. Unadjusted, Annualized Mortality Rates and Hazard Ratios According to Treatment Group and Status with Respect to Severe Hypoglycemia.

Severe Hypoglycemia	Deaths (N = 1031)		Unadjusted Hazard Ratio (95% CI)
	Intensive Glucose Control	Standard Glucose Control	
	no. of deaths/no. of person-yr (% per yr)		
No episodes	472/26,034 (1.8)	514/26,392 (1.9)	0.93 (0.82–1.06)
One or more episodes	26/718 (3.6)	19/369 (5.1)	0.67 (0.37–1.21)



Effect of Intensive Compared With Standard Glycemia Treatment Strategies on Mortality by Baseline Subgroup Characteristics

The Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial

JORGE CALLES-ESCAÑÓN, MD¹

Diabetes Care 33:721–727, 2010

- No se objetivó un incremento de mortalidad con tratamiento intensivo por EDAD, DURACIÓN DE DIABETES, ANTECEDENTES DE ECV

- Factores asociados con mayor mortalidad con terapia intensiva:
 - **NEUROPATÍA** (Michigan) HR 1.95 (1.41–2.69)
 - HbA1c $\geq 8.5\%$ HR 1.64 (1.22–2.22)
 - Consumo de AAS HR 1.45 (1.13–1.85)

Efecto de la neuropatía autonómica cardíaca en la mortalidad

ACCORD

Table 2—HR (95% CI) for all-cause and CVD mortality in participants with CAN compared with participants without CAN

Measure	All-cause mortality*		CVD mortality*	
	HR (95% CI): CAN+/CAN−	P	HR (95% CI): CAN+/CAN−	P
CAN1	1.55 (1.09–2.21)	0.016	1.94 (1.20–3.12)	0.007
CAN2	2.14 (1.37–3.37)	0.0009	2.62 (1.40–4.91)	0.003
CAN3	2.07 (1.14–3.76)	0.02	2.95 (1.33–6.53)	0.008

*Adjusted for treatment allocation, CVD history, and other prespecified covariates including baseline age, sex, ethnicity, diabetes duration, A1C, BMI, SBP and DBP, LDL cholesterol, triglycerides, microalbumin-to-creatinine ratio, and use of TZDs, insulin, β -blockers, ACE inhibitors/angiotensin-receptor blockers, statins, alcohol, and cigarettes.

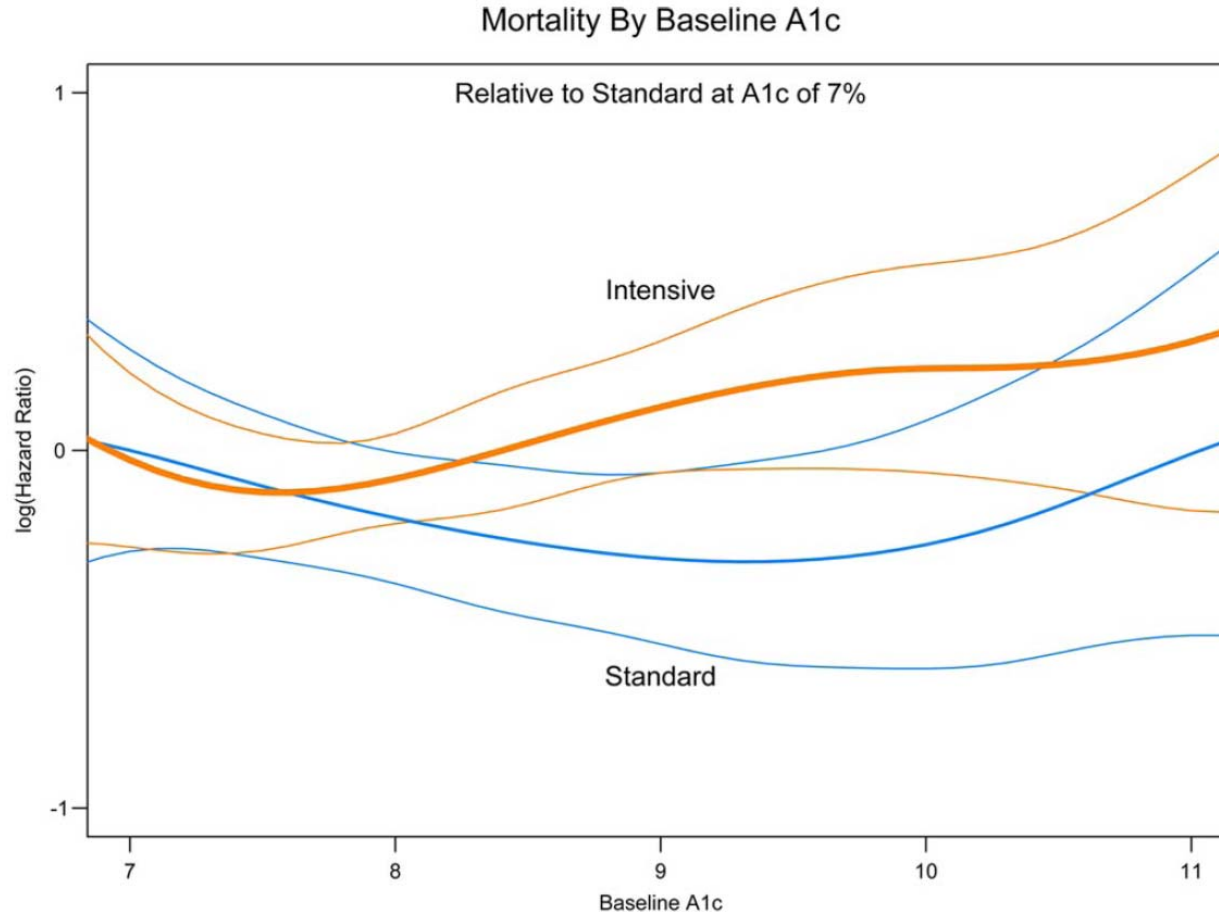
Insuficiencia Autonómica Asociada a Hipoglucemia (HAAF)

Factores de riesgo

- **Deficiencia absoluta de insulina/glucagón**
- **Historia de hipoglucemia grave y/o asintomática.**
- **Tratamiento intensivo en pacientes con glucemia media elevada.**

ACCORD

Análisis de mortalidad por subgrupos



GUIÓN

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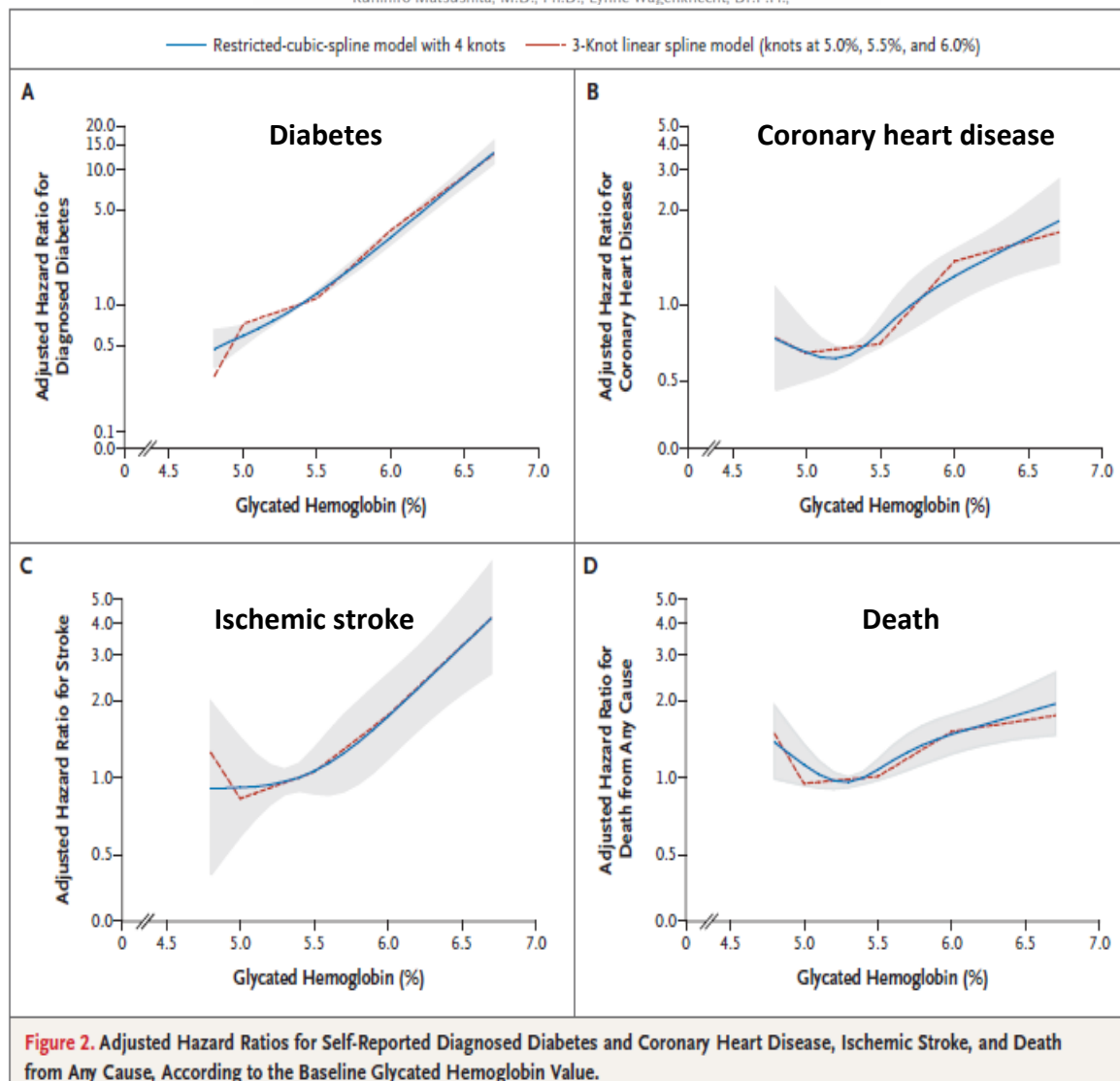
Is haemoglobin A1c a step forward for diagnosing diabetes?

	Glucosa	HbA1c
Ventajas	• Método diagnóstico tradicional • Medición directa de la molécula • No influencia de factores no glucémicos • Poca variación entre laboratorios • Facilidad • Disponibilidad • Barato	• Marcador de control glucémico • No requiere ayuno • Mayor estabilidad preanalítica • Carga glucémica • Menor variabilidad individual • No modificación por factores agudos (ejercicio, estrés) • Mejor predictor de complicaciones diabéticas • Mejor predictor de riesgo CV
Inconvenientes	• Requiere ayuno ≥ 8 horas • Poca estabilidad preanalítica • Medida puntual • Mayor variabilidad individual • Se altera por ejercicio, estrés • Diferencias según muestra: plasma (recomendada) / sangre completa / capilar / venosa / arterial • Puede requerir TTGO • TTGO: costes, molestias, limitaciones (cirugía gástrica)	• Marcador subrogado • Variación por edad y raza • No aplicable en embarazo, anemia, hemoglobinopatías, insuficiencia renal • Mayor variabilidad entre laboratorios • Accesibilidad • Costes



Glycated Hemoglobin, Diabetes, and Cardiovascular Risk in Nondiabetic Adults

Elizabeth Selvin, Ph.D., M.P.H., Michael W. Steffes, M.D., Ph.D., Hong Zhu, B.S.,
Kunihiro Matsushita, M.D., Ph.D., Lynne Wagenknecht, Dr.P.H.,

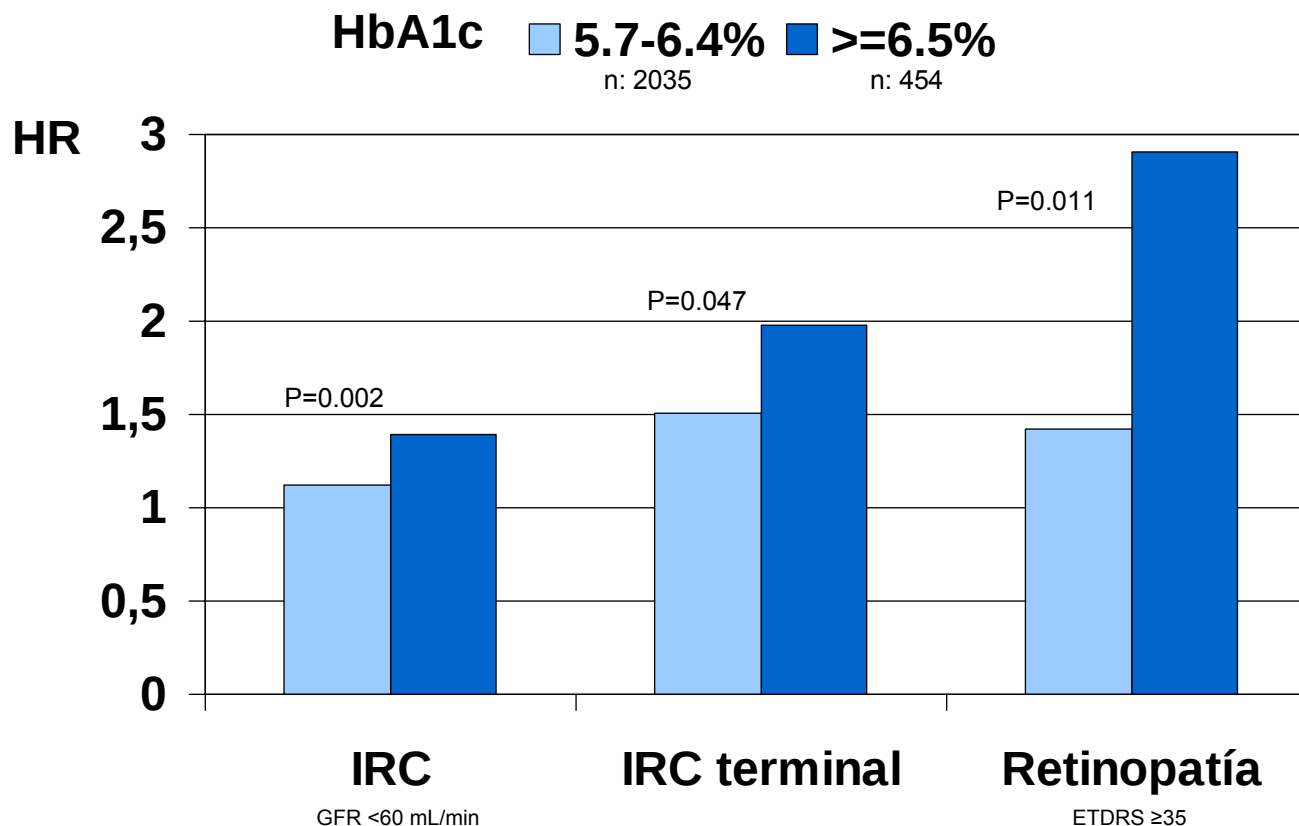


Glycated Hemoglobin and the Risk of Kidney Disease and Retinopathy in Adults With and Without Diabetes

Elizabeth Selvin,^{1,2} Yang Ning,³ Michael W. Steffes,⁴ Lori D. Bash,⁵ Ronald Klein,⁶ Tien Y. Wong,^{7,8} Brad C. Astor,^{1,2} A. Richey Sharrett,¹ Frederick L. Brancati,^{1,2} and Josef Coresh^{1,2,4}

Diabetes 60:298–305, 2011

Pronóstico microvascular en población no diabética (ARIC)



n: 11357
t: 14 años
773 DM autorreportada o tto AD

Prevalence of Diabetes and High Risk for Diabetes Using A1C Criteria in the U.S. Population in 1988-2006

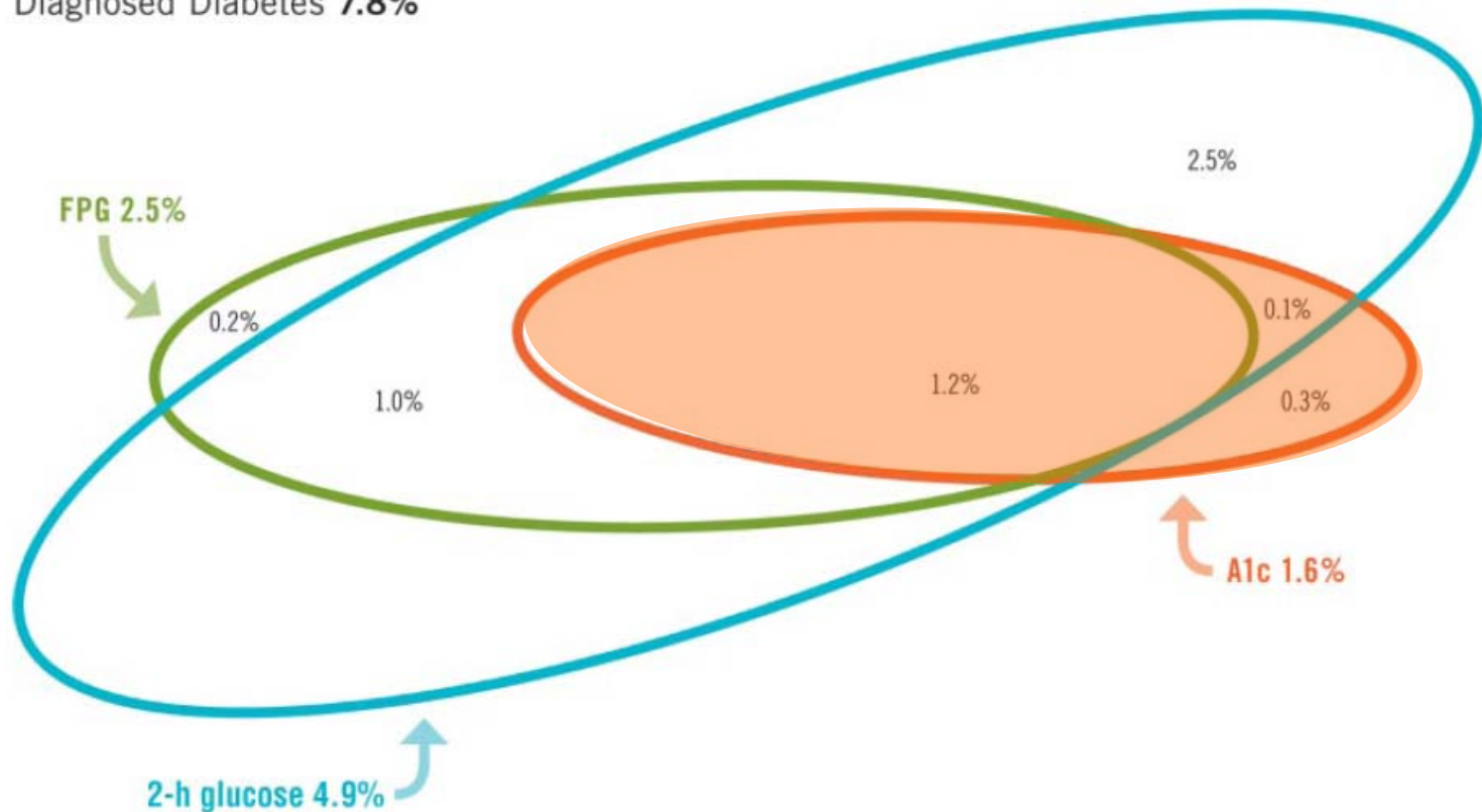
CATHERINE C. COWIE, PHD¹
KEITH F. RUST, PHD²
DANITA D. BYRD-HOLT, BBA³
EDWARD W. GREGG, PHD¹

EARL S. FORD, MD²
LINDA S. GEISS, MS⁴
KATHLEEN E. BAINBRIDGE, PHD³
JUDITH E. FRADKIN, MD¹

Diabetes Care 33:562-568, 2010

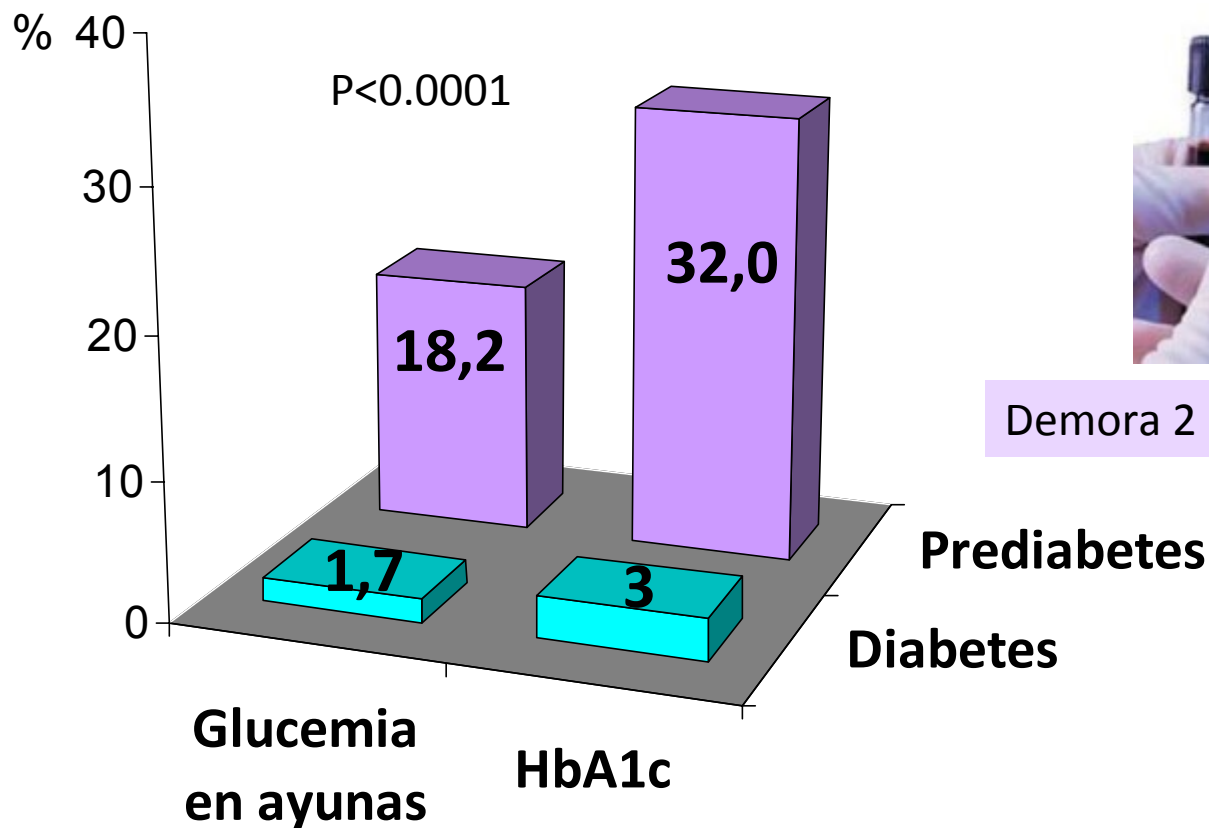
No Diabetes **86.9%**

Diagnosed Diabetes **7.8%**



CONCLUSIONS — “Using A1C criteria, prevalences of undiagnosed diabetes and high risk of diabetes were one-third that and one-tenth that, respectively, using glucose criteria.”

Prevalencia de disglucemia en población adulta no diabética de Málaga



Demora 2 h = ↓ 12 mg/dL

GUIÓN

- Epidemiología
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- Manejo de los factores de riesgo en la DMT2
- Hipoglucemia
- HbA1c y diagnóstico de DMT2
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CONCLUSIONES -1

- **Prevalencia** de DM en España: 12%
- **Prevención:**
 - Beneficio de dieta mediterránea
 - Metformina (+ glitazona) en prediabéticos de alto riesgo
- **Manejo de los factores de riesgo en la DMT2**
 - Objetivo general TA <130/80 mmHg
 - Evitar PAS <120 mmHg y PAD <70 mmHg en diabéticos de alto riesgo
 - Potenciales beneficios de terapia hipolipemiente combinada:
 - dislipemia aterogénica (varones)
 - prevención de retinopatía

CONCLUSIONES -2

■ **Hipoglucemia**

- Marcador de mortalidad y ECV, con independencia del tratamiento empleado
- Factores de riesgo de hipoglucemia:
 - tratamiento intensivo
 - ancianos
 - mal control metabólico
 - Insuficiencia autonómica asociada a hipoglucemia
- Evitar terapia hipoglucemiante intensiva en pacientes con neuropatía (cardiaca)

■ **HbA1c y diagnóstico de DMT2**

- Mejor instrumento diagnóstico en la práctica clínica real
- Marcador pronóstico micro-macrovascular y de mortalidad

MENSAJE FINAL

- 1. INDIVIDUALIZAR OBJETIVOS glucémicos, tensionales y lipídicos**
- 2. EVITAR HIPOGLUCEMIAS**
- 3. UTILIDAD de la HbA1c como marcador de riesgo cardiometabólico**

VII



Reunión de Riesgo Vascular

Palacio de Congresos. Valencia
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MUCHAS GRACIAS

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