Mesa redonda

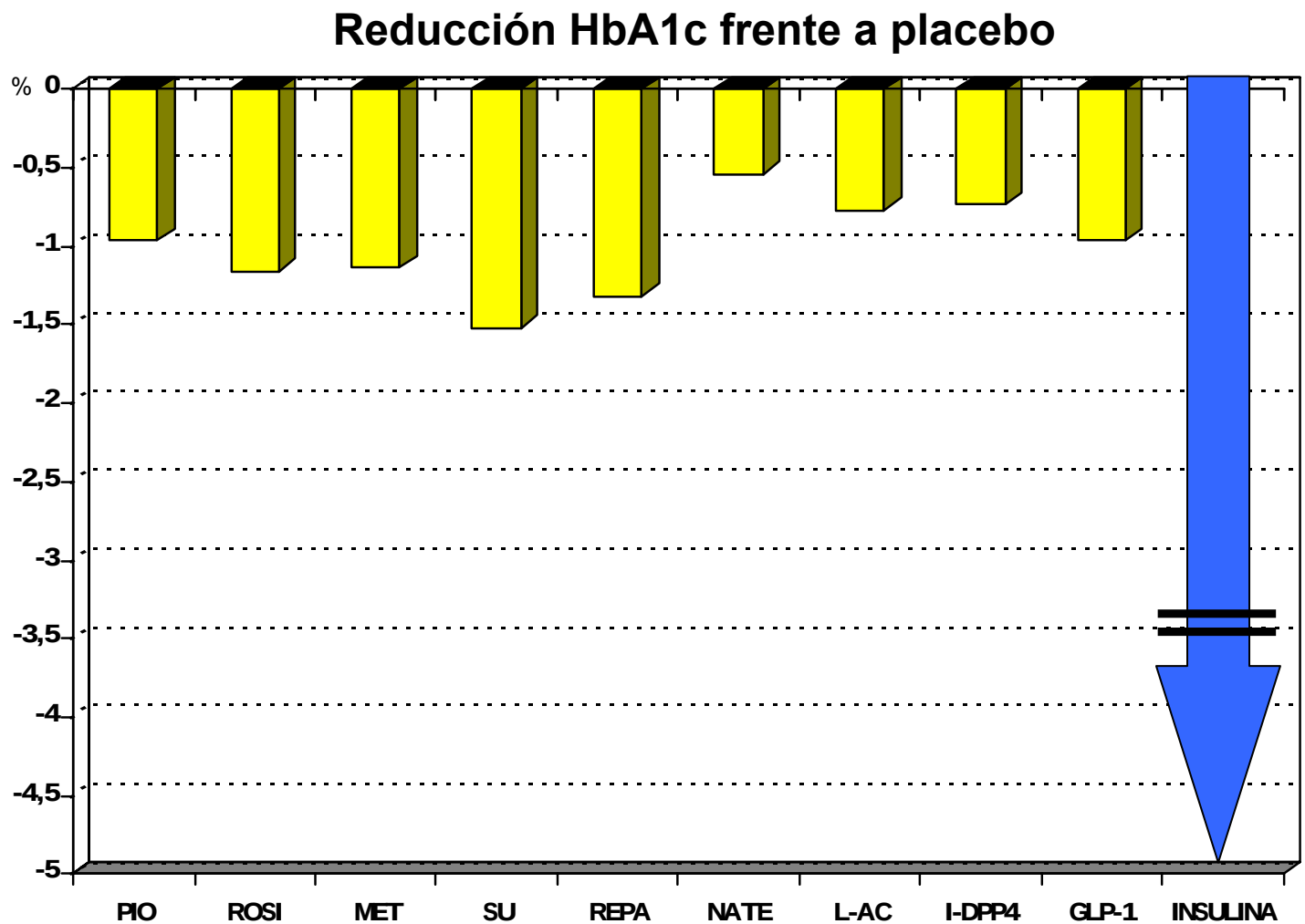
CONTROL DE LA GLUCEMIA EN PACIENTES CON DM TIPO 2: ¿QUÉ AÑADIMOS A LA METFORMINA?

INSULINIZACIÓN

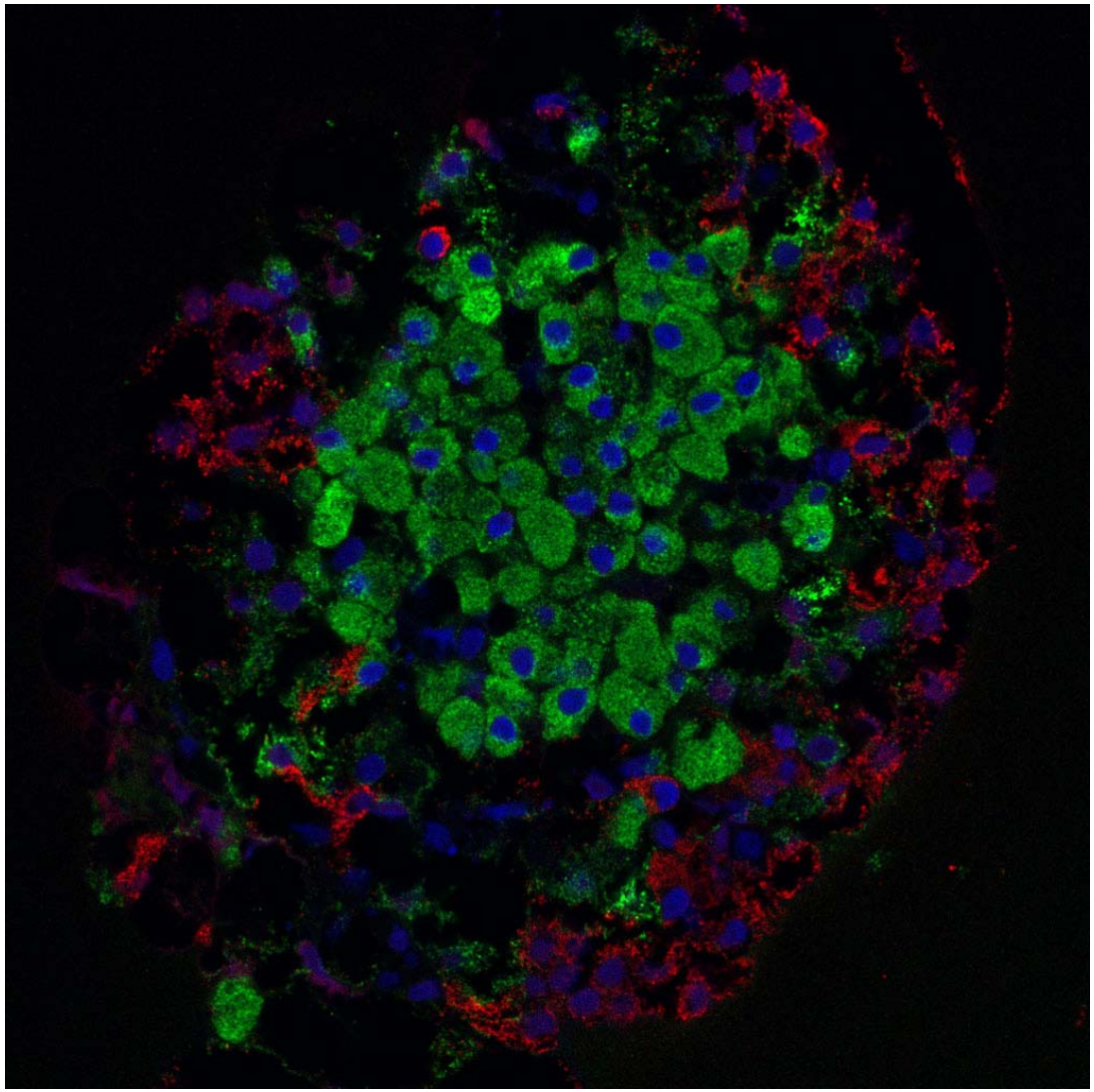
Ricardo Gómez Huelgas
Medicina Interna
Hospitla Carlos Haya - Málaga


INSUL
50 Units — 5 C.C.
10 Units per C
CONNAUGHT LABORA
UNIVERSITY OF TOR

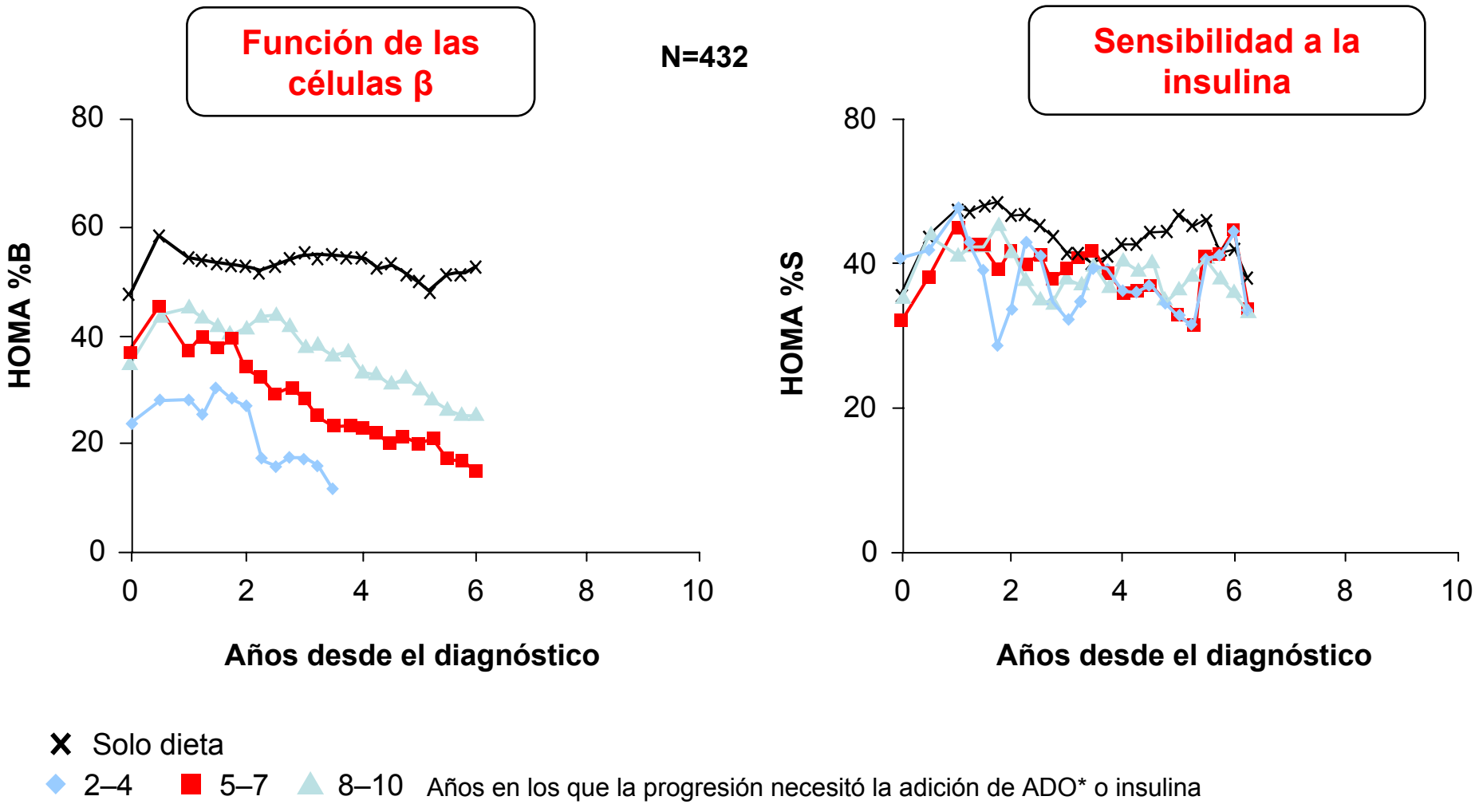
Eficacia hipoglucemiante de los fármacos antidiabéticos



Bolen S. Ann Intern Med 2007.
Amori RE. JAMA 2007.



Belfast Diet Study



HOMA=modelo de determinación de homeostasis; DMT2=diabetes mellitus tipo 2
*Tolbutamida, metformina
Adaptado de Levy J, et al. *Diabet Med*. 1998; 15: 290–296.

RESISTENCIA AL TRATAMIENTO CON INSULINA: otra forma de resistencia a la insulina en la DMT2

Epidemiology/Health Services/Psychosocial Research
ORIGINAL ARTICLE

Resistance to Insulin Therapy Among Patients and Providers

Results of the cross-national Diabetes Attitudes, Wishes, and Needs (DAWN) study

MARK PEYROT, PHD[1,2]
RICHARD R. RUBIN, PHD[2]
TORSTEN LAURITZEN, MD[3]
SOREN E. SKOVLUND, MSC[4]
FRANK J. SNOEK, PHD[5]
DAVID R. MATTHEWS, MD[6]
RÜDIGER LANDGRAF, MD[7]
LINE KLEINEBREIL[8]
ON BEHALF OF THE INTERNATIONAL DAWN ADVISORY PANEL*

OBJECTIVE — To examine the correlates of patient and provider attitudes toward insulin therapy.

RESEARCH DESIGN AND METHODS — Data are from surveys of patients with type 2 diabetes not taking insulin (*n* = 2,061) and diabetes care providers (nurses = 1,109; physicians = 2,681) in 13 countries in Asia, Australia, Europe, and North America. Multiple regression analysis is used to identify correlates of attitudes toward insulin therapy among patients, physicians, and nurses.

RESULTS — Patient and provider attitudes differ significantly across countries, controlling for individual characteristics. Patients rate the clinical efficacy of insulin as low and would blame themselves if they had to start insulin therapy. Self-blame is significantly lower among those who have better diet and exercise adherence and less diabetes-related distress. Patients who are not managing their diabetes well (poor perceived control, more complications, and diabetes-related distress) are significantly more likely to see insulin therapy as potentially beneficial. Most nurses and general practitioners (50–55%) delay insulin therapy until absolutely necessary, but specialists and opinion leaders are less likely to do so. Delay of insulin therapy is significantly less likely when physicians and nurses see their patients as more adherent to medication or appointment regimens, view insulin as more efficacious, and when they are less likely to delay oral diabetes medications.

CONCLUSIONS — Patient and provider resistance to insulin therapy is substantial, and for providers it is part of a larger pattern of reluctance to prescribe blood glucose–lowering medication. Interventions to facilitate timely initiation of insulin therapy will need to address factors associated with this resistance.

Diabetes Care 28:2673–2679, 2005

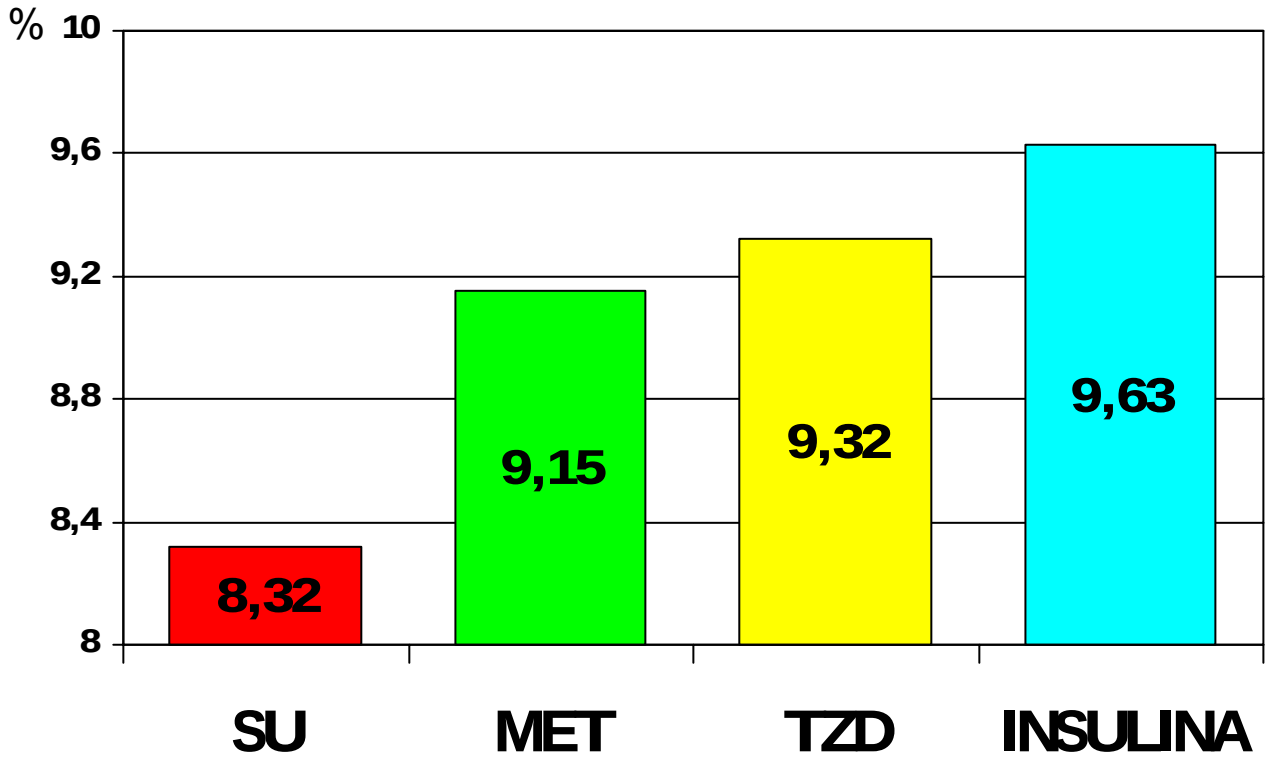
Type 2 diabetes is characterized by defects in both insulin secretion and insulin action. The defect in insulin secretion seems to be progressive; newly diagnosed patients in the U.K. Prospective Diabetes Study (1) had 50% of normal insulin secretion, and they had <25% of normal insulin secretion 6 years after diagnosis. As a consequence, good glycemic control in type 2 diabetes often requires insulin supplementation therapy (2). Unfortunately, many patients with type 2 diabetes who could benefit from insulin therapy do not receive it or do not receive it in a timely manner (3–6). Part of this gap appears to be attributable to resistance to taking insulin among patients and resistance to prescribing insulin among health care providers. This resistance is based on a variety of factors, primarily beliefs and perceptions regarding diabetes and its treatment, the nature and consequences of insulin therapy, and how

Am J Manag Care. 2007 November ; 13(11): 598–606.

Glycemic Response to Newly Initiated Diabetes Therapies

Andrew J. Karter, PhD, Howard H. Moffet, MPH, Jennifer Liu, MPH, Melissa M. Parker, MS, Ameena T. Ahmed, MD, Alan S. Go, MD, and Joe V. Selby, MD

HbA1c en el momento de la intensificación



Índice

- ¿Qué dicen las guías?
- Ventajas de la insulinización precoz
  - Reducir complicaciones micro-macrovasculares
  - Retrasar progresión de la diabetes
- Inconvenientes de la insulinización precoz
  - Hipoglucemias
  - Ganancia de peso
  - ¿Incremento del riesgo cardiovascular?
  - ¿Incremento del riesgo de cáncer?
  - Calidad de vida
- Conclusiones

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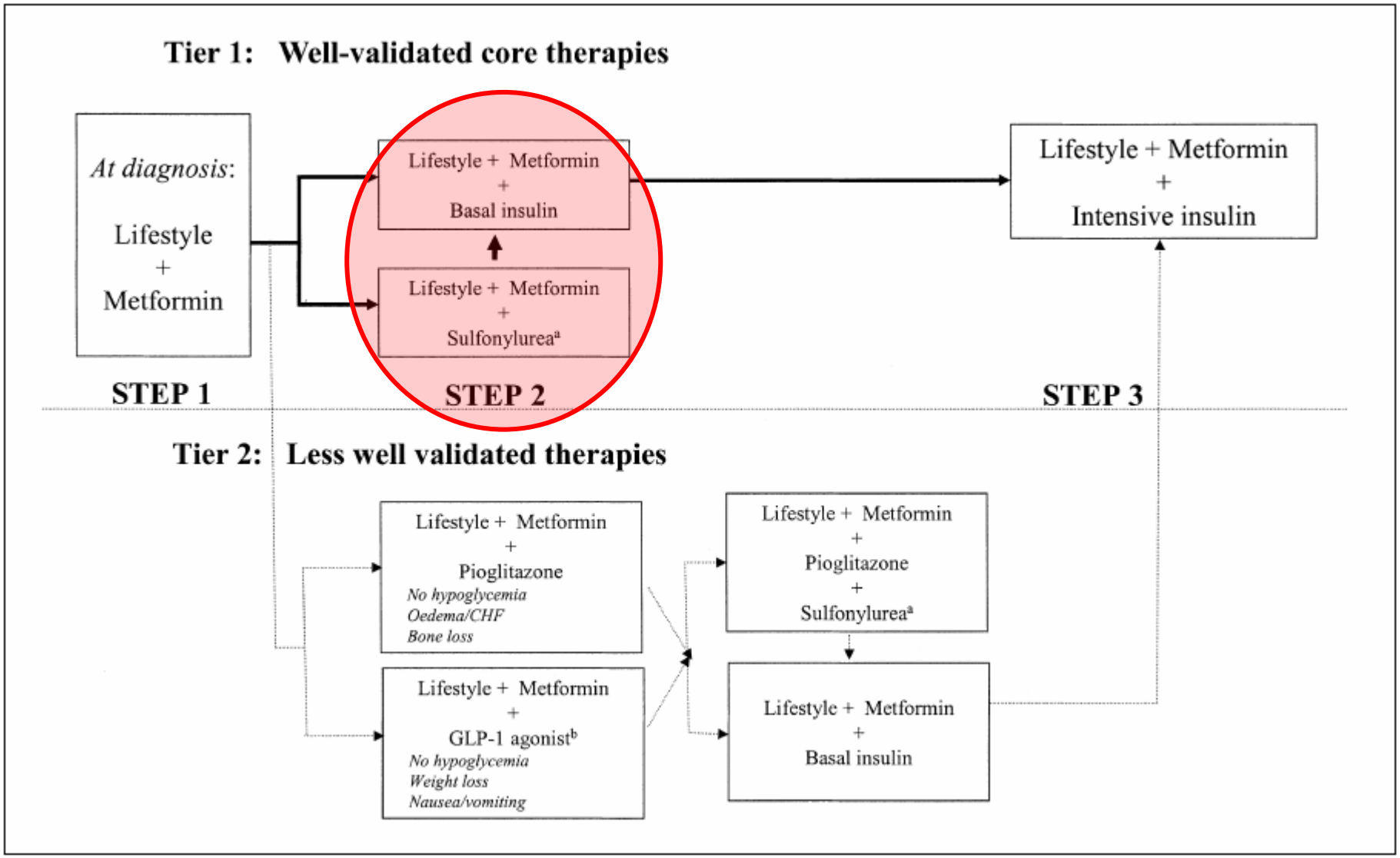
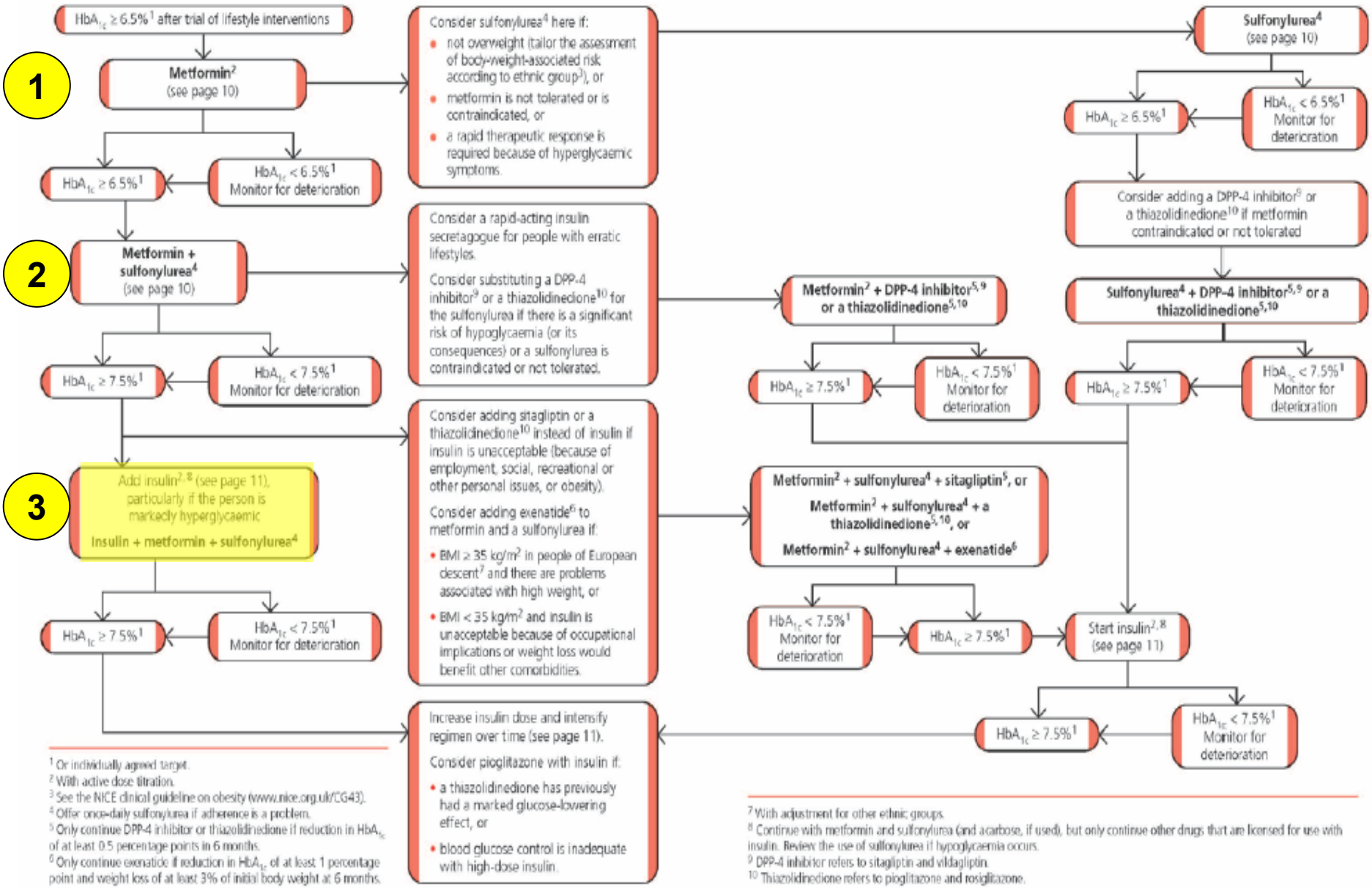
Algoritmo de tratamiento DMT2



A consensus statement of the American Diabetes Association and the European Association for the Study of Diabetes
Nathan DM et al. Diabetes Care 2009; 32:193–203.

1.2 Care pathway

Blood-glucose-lowering therapy



[1] Or individually agreed target.
[2] With active dose titration.
[3] See the NICE clinical guideline on obesity (www.nice.org.uk/CG43).
[4] Offer once-daily sulfonylurea if adherence is a problem.
[5] Only continue DPP-4 inhibitor or thiazolidinedione if reduction in HbA_{1c} of at least 0.5 percentage points in 6 months.
[6] Only continue exenatide if reduction in HbA_{1c} of at least 1 percentage point and weight loss of at least 3% of initial body weight at 6 months.
[7] With adjustment for other ethnic groups.
[8] Continue with metformin and sulfonylurea (and acarbose, if used), but only continue other drugs that are licensed for use with insulin. Review the use of sulfonylurea if hypoglycaemia occurs.
[9] DPP-4 inhibitor refers to sitagliptin and vildagliptin.
[10] Thiazolidinedione refers to pioglitazone and rosiglitazone.

ALGORITMO CANADIAN DIABETES ASSOCIATION 2008

ESTILOS de VIDA

Intervenciones sobre estilos de vida (dieta y actividad física)

HbA1c<9% → **Metformina**

HbA1c>9% → **Fármacos sin esperar efecto estilos de vida**
- **Metformina + otros F**
- **Insulina**

Hiperglucemia sintomática y descompensación metabólica → **Insulina ± Metformina**

Si no se alcanza objetivo → Añadir otro fármaco según ventajas e inconvenientes

Familia	HbA1c	Hipos	Ventajas	Inconvenientes
Glitazona	↓↓	Rara	Monoterapia persistente	Necesita 6-12 semanas para máx efecto Aumento de peso Edema, I.Cardiaca, fracturas en mujeres
Inhib Alfaglucos	↓	Rara	Control glucemia postprandial Peso neutral	Efectos gastrointestinal
Inhib DPP4	↓ o ↓↓	Rara	Control glucemia postprandial Peso neutral	Nuevo (seguridad desconocida)
Insulina	↓↓↓	Si	No tope de dosis Pautas flexibles	Ganancia peso
Meglitinida	↓ o ↓↓	Sí	Control glucemia postprandial	Requiere 2-3 dosis
Sulfonilurea	↓↓	Sí	Las nuevas menos hipoglucemias	Ganancia peso
Perdida peso	↓	No	Pérdida peso	Efectos gastrointest inal (Orlistat) Aumento frec cardiaca (sibutramina)

- Añadir otro F de diferente clase
- Añadir insulina basal bedtime a los FO
- Intensificar la dosis de insulina

AACE/ACE Diabetes Algorithm *For Glycemic Control*

A1C Goal ≤ 6.5%*

LIFESTYLE MODIFICATION

A1C 6.5 – 7.5%**

Monotherapy

MET	TZD [2]	DPP4 [1]	AGI [3]

2 - 3 Mos.***

Dual Therapy

MET	+	GLP-1 or DPP4 [1]
		TZD [2]
		Glinide or SU [5]
TZD	+	GLP-1 or DPP4 [1]
MET	+	Colesevelam
		AGI [3]

2 - 3 Mos.***

Triple Therapy

MET + GLP-1 or DPP4 [1]	+	TZD [2]
		Glinide or SU [4,7]

2 - 3 Mos.***

INSULIN ± Other Agent(s) [6]

A1C 7.6 – 9.0%

Dual Therapy [8]

MET	+	GLP-1 or DPP4 [1,10] or TZD [2]
		SU or Glinide [4,5]

2 - 3 Mos.***

Triple Therapy [9]

MET	+	GLP-1 or DPP4 [1]	+ TZD [2]
		GLP-1 or DPP4 [1]	+ SU [7]
		TZD [2]	

2 - 3 Mos.***

INSULIN ± Other Agent(s) [6]

A1C > 9.0%

Drug Name | *Under Treatment*

Symptoms | *No Symptoms*

INSULIN ± Other Agent(s) [6]

MET	+	GLP-1 or DPP4 [1]	± SU [7]
		TZD [2]	
		GLP-1 or DPP4 [1]	± TZD [2]

INSULIN ± Other Agent(s) [6]

AACE/ACE Algorithm for Glycemic Control Subcommittee

Cochairpersons:
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Harold Lebovitz, MD, FACE
Philip Levy, M.D., MACP
Rita S. Majercik, MD, FACP, FACE
Stanley S. Schwartz, MD, FACE

* If not appropriate for all patients

** For patients with diabetes and A1C <6.5%, pharmacologic Rx may be considered

*** If A1C goal not achieved safely

[1] DPP4 if ↑ PPG and ↑ FPG or GLP-1 if ↑↑ PPG

[2] TZD if metabolic syndrome and/or sonographic fatty liver disease (NAFLD)

[3] AGI if ↑ PPG

[4] Glinide if ↑↑ PPG or SU if ↑ FPG

[5] Low dose secretagogue recommended

[6] a) Discontinue insulin secretagogue with multidose insulin
b) Can use premix/nitrate with prandial insulin

[7] Decrease secretagogue by 50% when added to GLP-1 or DPP-4

[8] If A1C <8.5%, combination Rx with agents that cause hypoglycemia should be used with caution

[9] If A1C >8.5%, in patients on Dual Therapy, insulin should be considered

[10] GLP-1 not approved for initial combination Rx

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  - ¿Incremento del riesgo cardiovascular?
  - ¿Incremento del riesgo de cáncer?
  - Calidad de vida
- Conclusiones

Deng Xiaoping
(1904-1997)

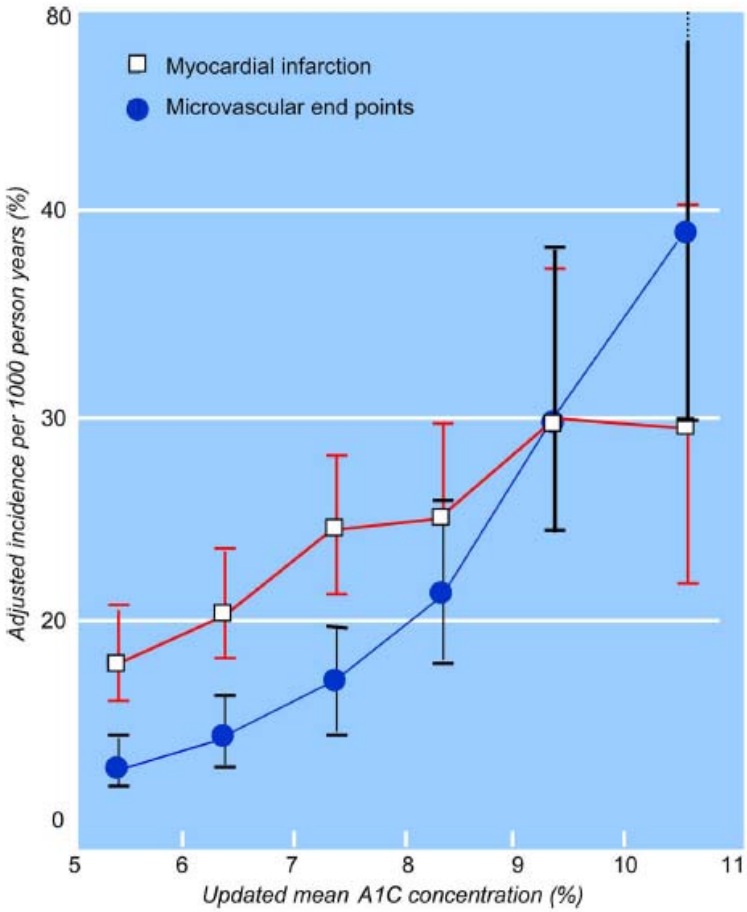
No importa que el gato sea blanco o negro mientras cace ratones.

BMJ

Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38

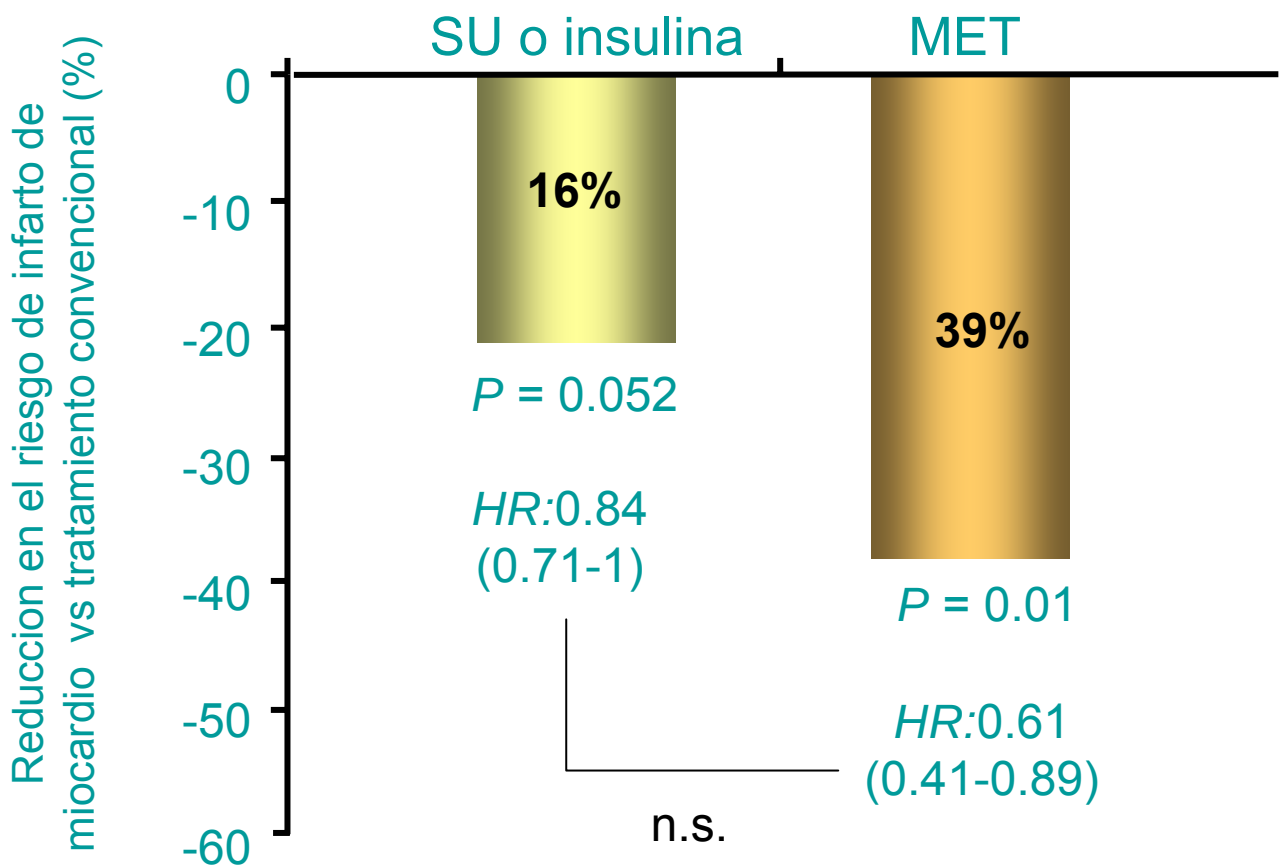
UK Prospective Diabetes Study Group

BMJ 1998;317:703-713



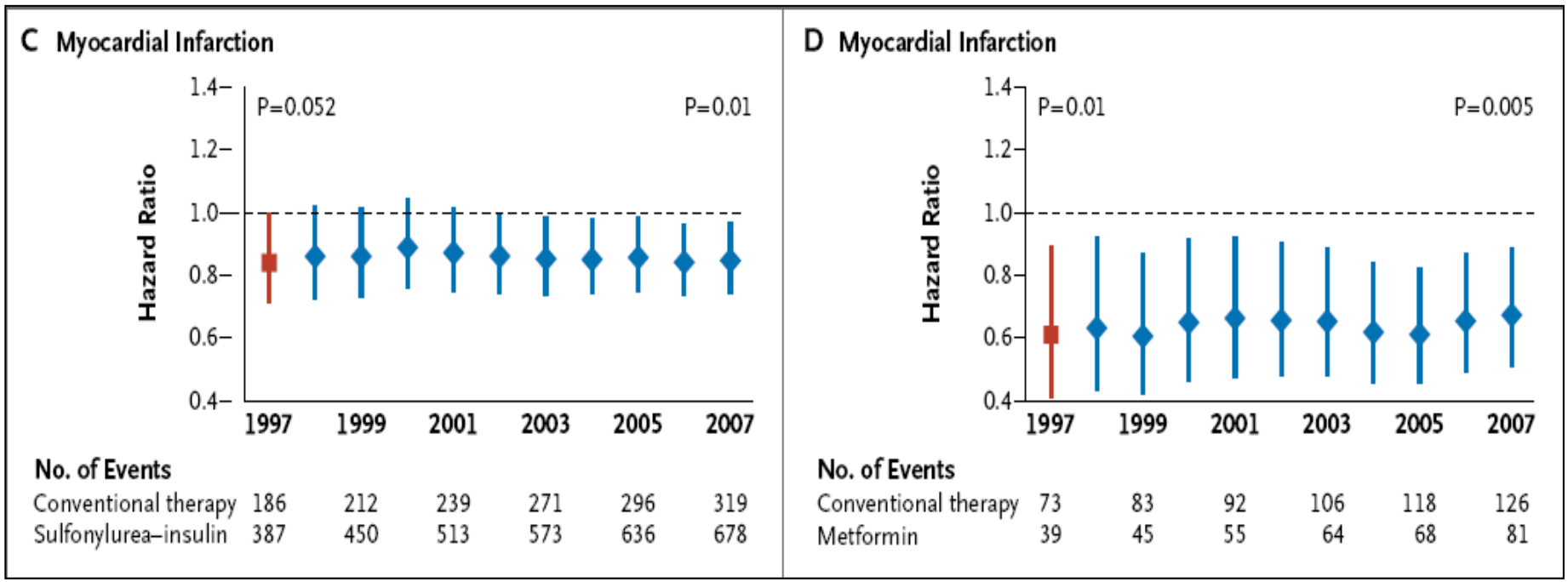
"no difference in the risk reduction of microvascular clinical end points was seen between insulin, sulfonylurea and meyformin; and thus, improved glycemic control, rather than any one therapy, is the principal factor"

UKPDS



UK Prospective Diabetes Study (UKPDS) Group. Lancet 1998; 352:854–865.

UKPDS: seguimiento a 10 años



Holman RR. NEJM 2008;359

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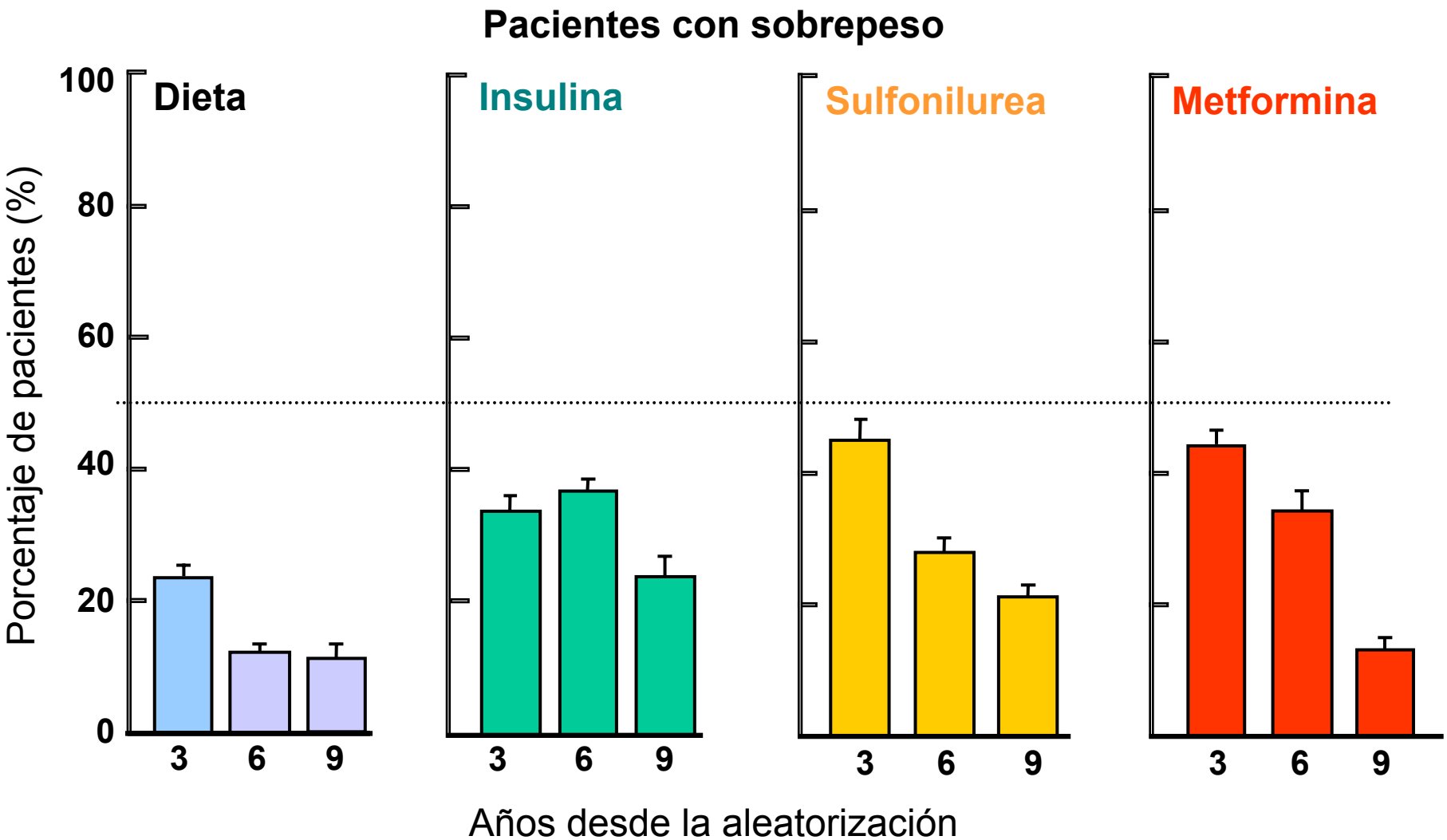
UKPDS: porcentaje de pacientes con HbA_{1c}<7,0% en monoterapia a los 3,6 y 9 años



Adaptado de Turner RC, *et al.* UKPDS 49. *JAMA* 1999; 281:2005–2012.

Ensayos clínicos con terapia antidiabética intensiva en diabetes tipo 2

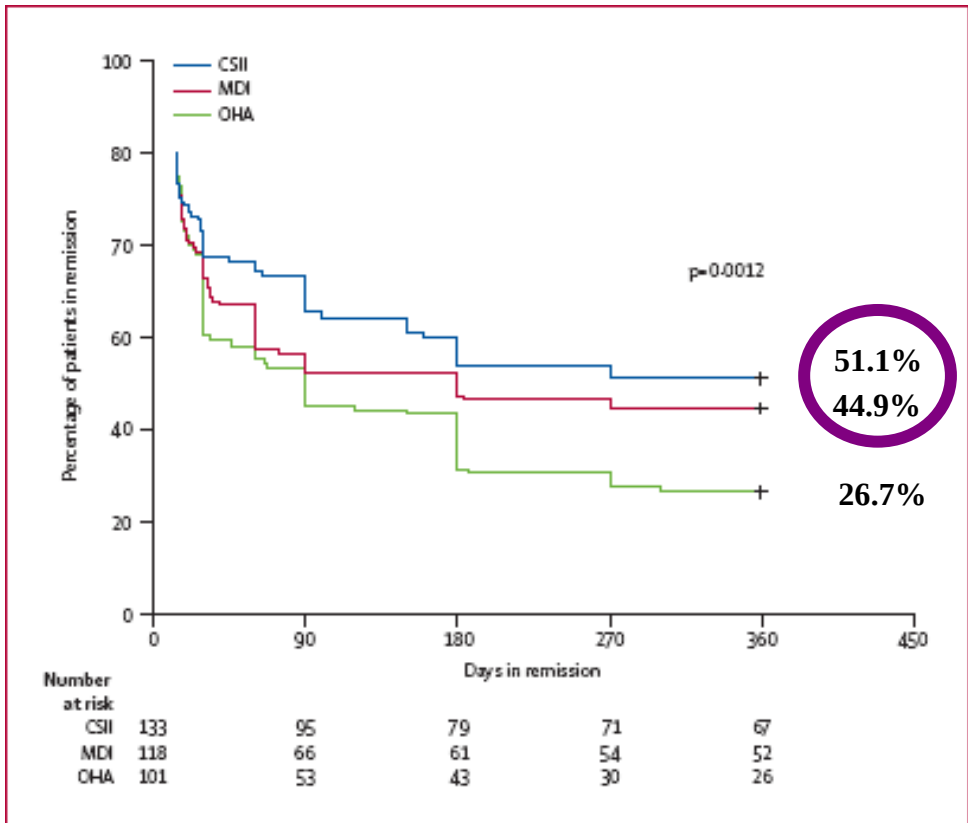
Study	N	Mean age (years)	Mean body-mass index (kg/m²)	Duration of type 2 diabetes	Baseline HbA_{1c} (%)	Type of therapy	Duration of therapy (days)	Patients who achieved euglycemia with therapy (%)	Patients with euglycemia at 6 months (%)	Patients with euglycemia at 1 year (%)
Li[6]	138	49	25	Newly diagnosed	10·1	CSII	14	91	67	47
Ilkova[7]	13	50	26·9	Newly diagnosed	11·0	CSII	14	92	69	N/A
Park[8]	91	54	NA	Mean 7·2 years	13·2	CSII	Mean 53·6 (SD 39)	34	~34	~34
Ryan[9]	16	52	30·8	Newly diagnosed	11·8	MDI	14–21	88	N/A	44
Weng[10]	382	51	25·0	Newly diagnosed	~9·7	CSII	14–35	97	N/A	51
Weng[10]	382	51	25·0	Newly diagnosed	~9·7	MDI	14–35	95	N/A	45
Weng[10]	382	51	25·0	Newly diagnosed	~9·7	OAD	14–35	84	N/A	27

NA=not available. CSII=continuous subcutaneous insulin infusion. MDI=multiple daily injections. OAD=oral antidiabetic agent.

Retnakaran R. Lancet 2008;371:1725-6.

Effect of intensive insulin therapy on β-cell function and glycaemic control in patients with newly diagnosed type 2 diabetes: a multicentre randomised parallel-group trial

Jianping Weng, Yanbing Li*, Wen Xu, Lixin Shi, Qiao Zhang, Dalong Zhu, Yun Hu, Zhiguang Zhou, Xiang Yan, Haoming Tian, Xingwu Ran, Zuojie Luo, Jing Xian, Li Yan, Fangping Li, Longyi Zeng, Yanming Chen, Liyong Yang, Sunjie Yan, Juan Liu, Ming Li, Zuzhi Fu, Hua Cheng*



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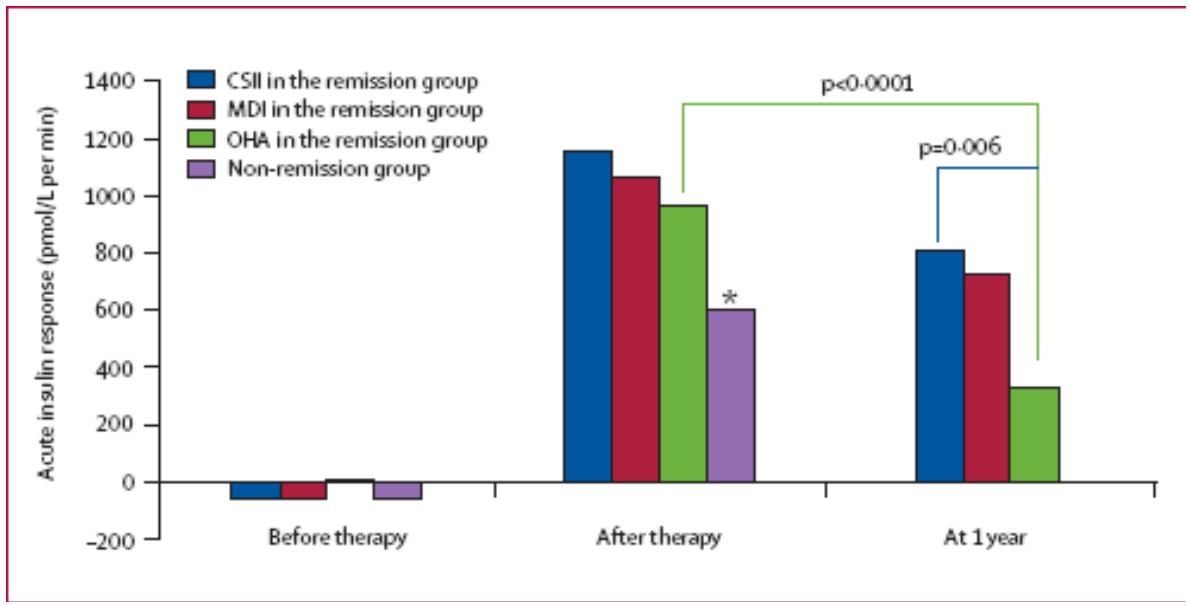


Early Insulin Treatment in Type 2 Diabetes

What are the pros?

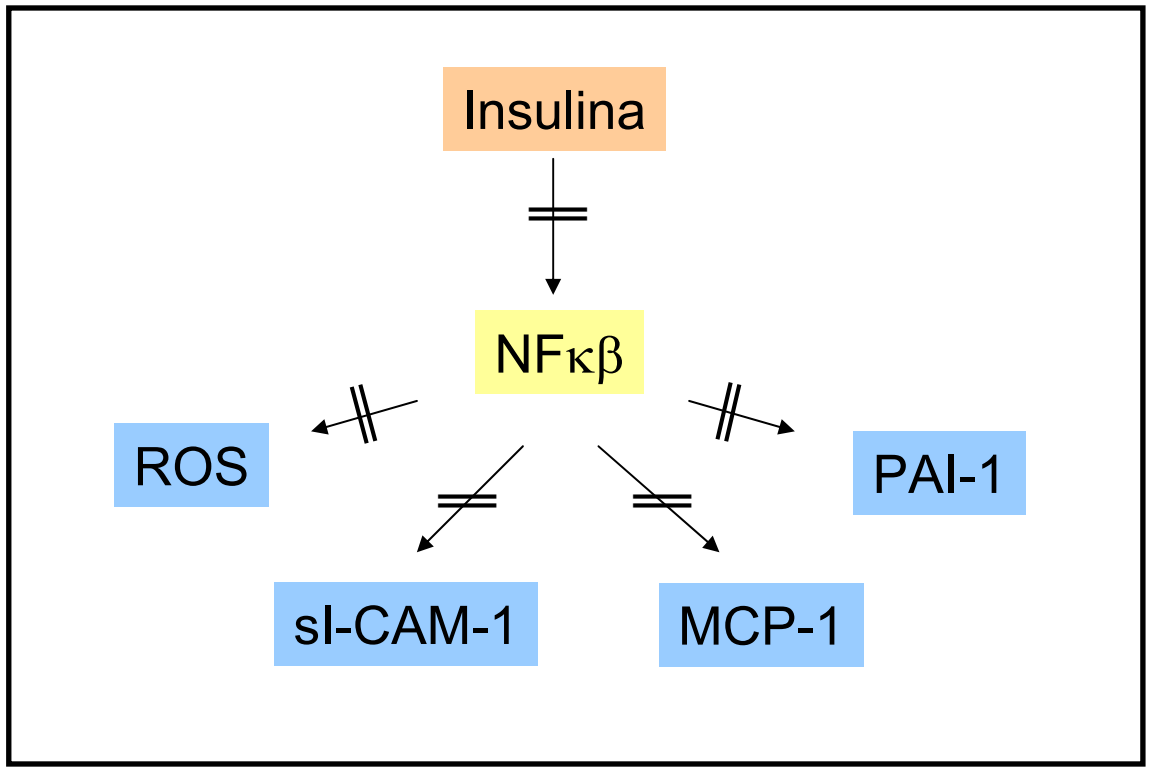
LUIGI F. MENEGHINI, MD, MBA

DIABETES CARE, VOLUME 32, SUPPLEMENT 2, NOVEMBER 2009

UNA ESTRATEGIA FISIOPATOLÓGICA

La insulinoterapia intensiva precoz en DMT2, con cobertura basal y prandial, puede preservar la función de la célula beta al revertir con rapidez la glucolipotoxicidad y el ambiente inflamatorio ocasionado por la hiperglucemia

Efectos antiinflamatorios de la insulina



Dandona P. J Clin Endocrinol Metab 2001;86:3257-65.
Dandona P. Curr Opin Clin Nutr Metab Care 2007;10:511-7

Early Insulin Treatment in Type 2 Diabetes

What are the pros?

LUIGI F. MENEGHINI, MD, MBA

DIABETES CARE, VOLUME 32, SUPPLEMENT 2, NOVEMBER 2009

- El tratamiento precoz, intensivo y transitorio en DMT2 de inicio proporciona
  - un rápido control metabólico
  - mínima ganancia de peso y bajo riesgo de hipoglucemia
  - restituye secreción fisiológica de insulina

- Continuar con terapias que mantengan euglucemia (metformina, TZD, incretinas)

- Reservar el tratamiento insulínico a largo plazo si claudica la función beta

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  - **Hipoglucemias**
  - Ganancia de peso
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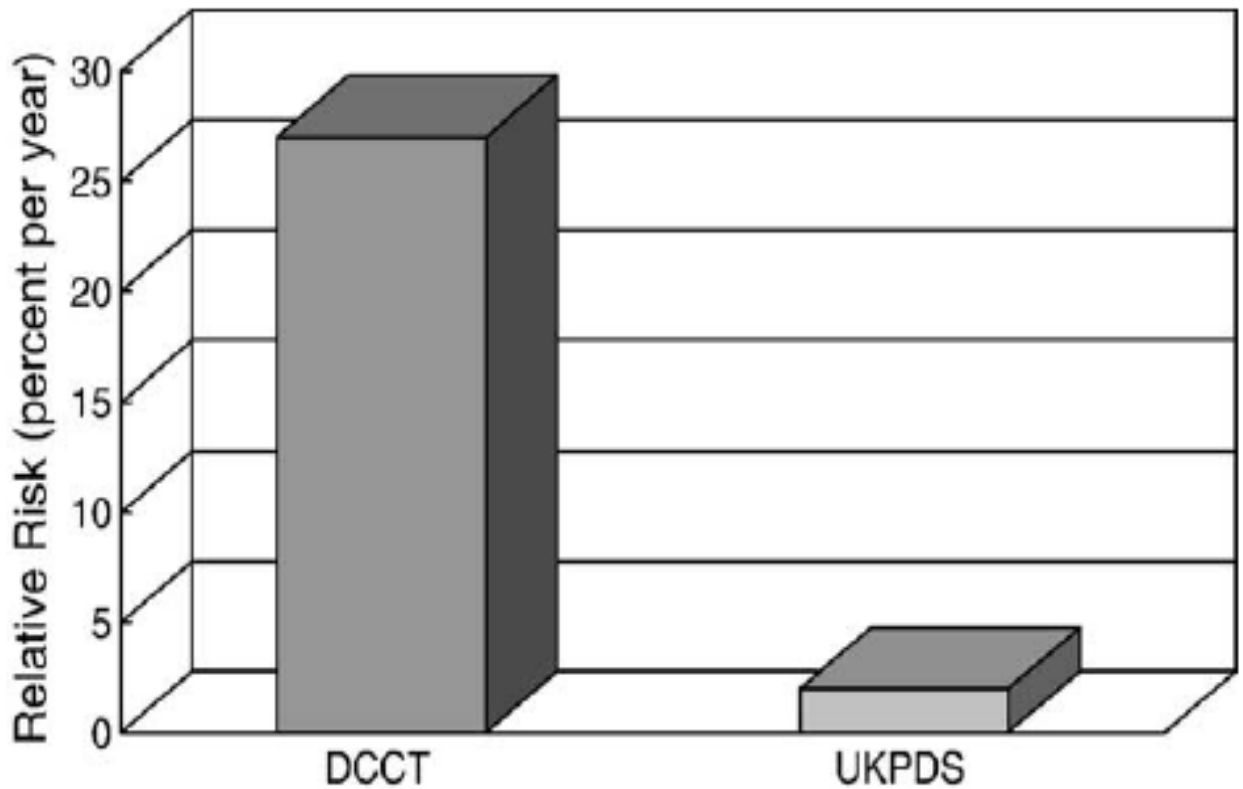
  - ¿Incremento del riesgo de cáncer?
  - Calidad de vida
- Conclusiones

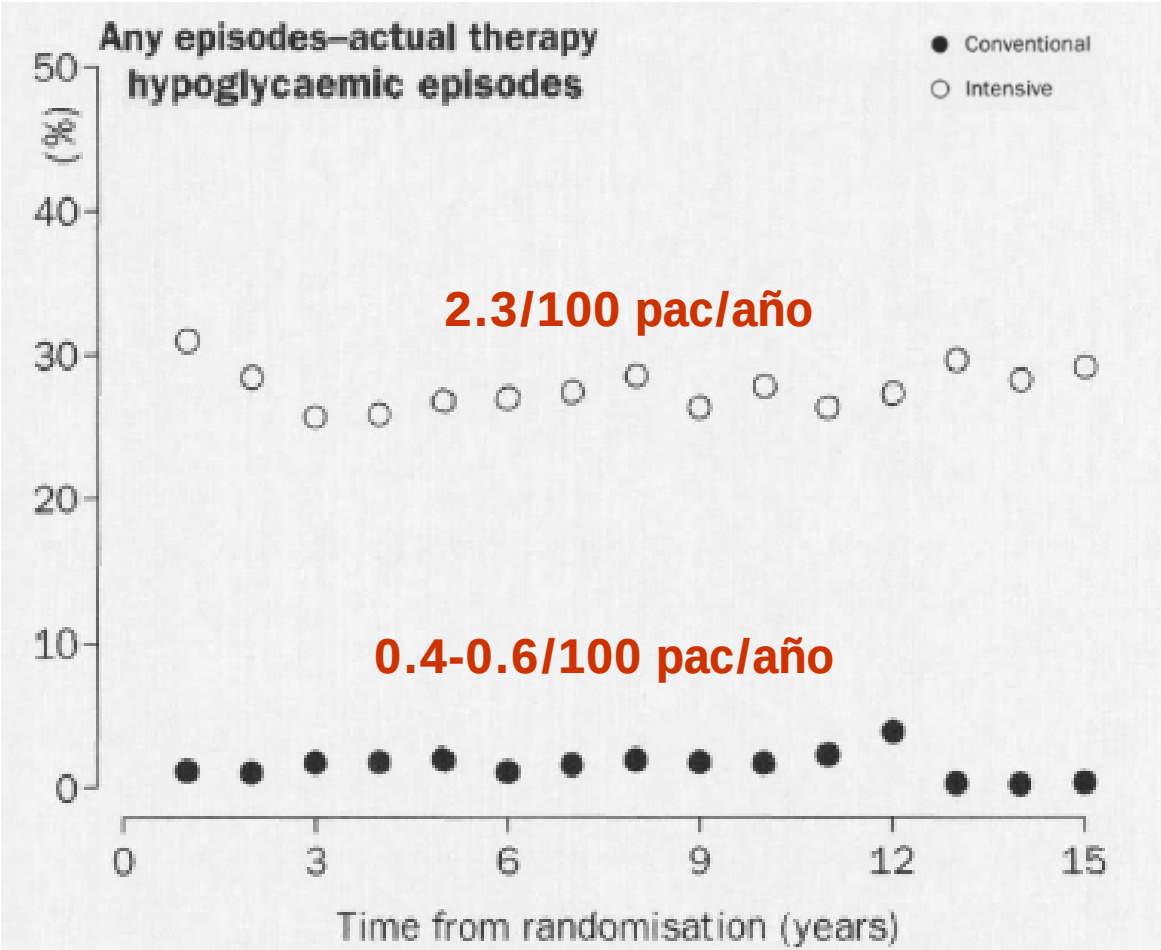
RIESGO RELATIVO DE HIPOGLUCEMIA GRAVE EN DIABETES TIPO 1 Y DIABETES TIPO 2



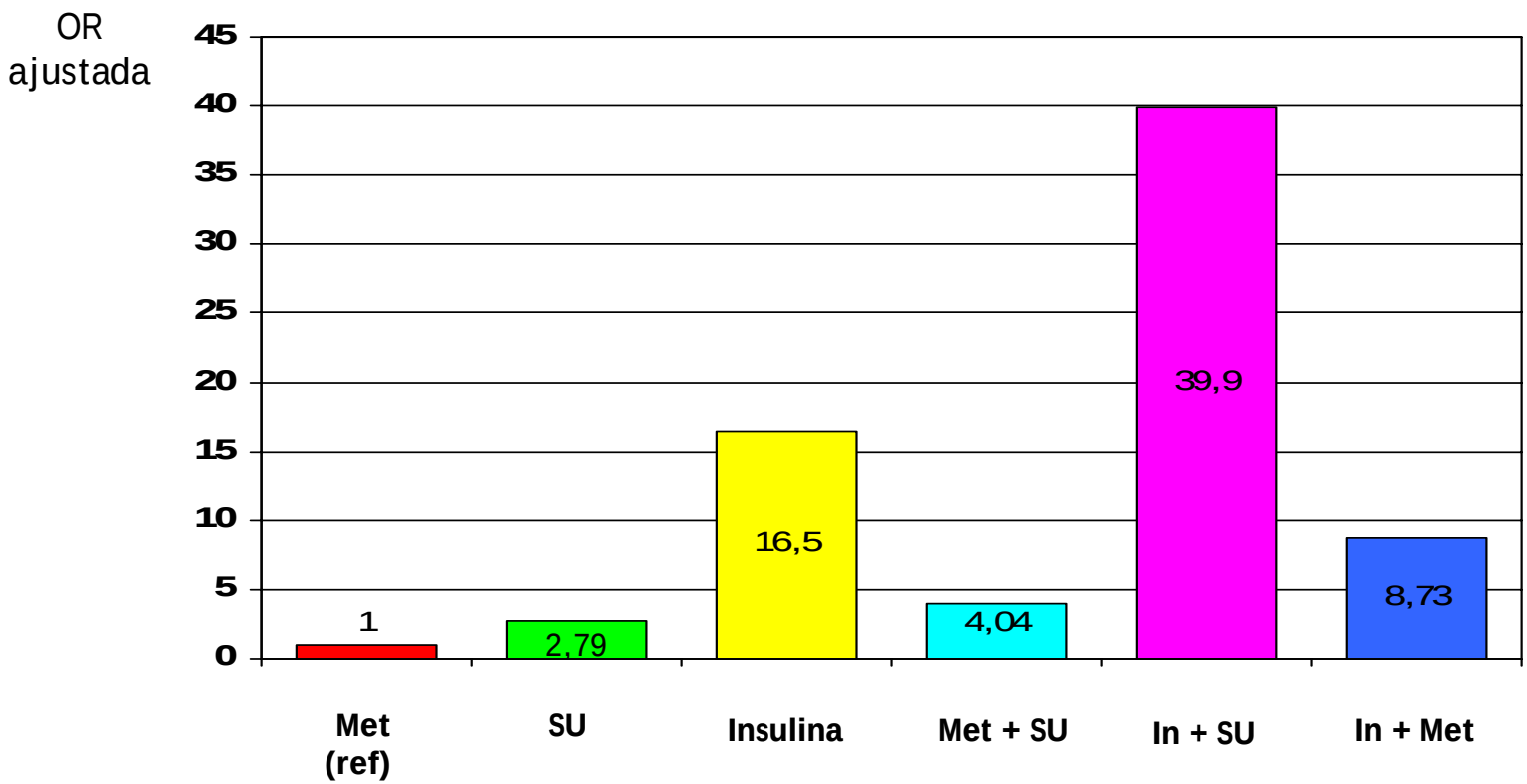
Del Prato S. Metab Clin Exp 2006;55 (suppl 1):S20-S27.

UKPDS 33

BMJ 1998; 352:837–53

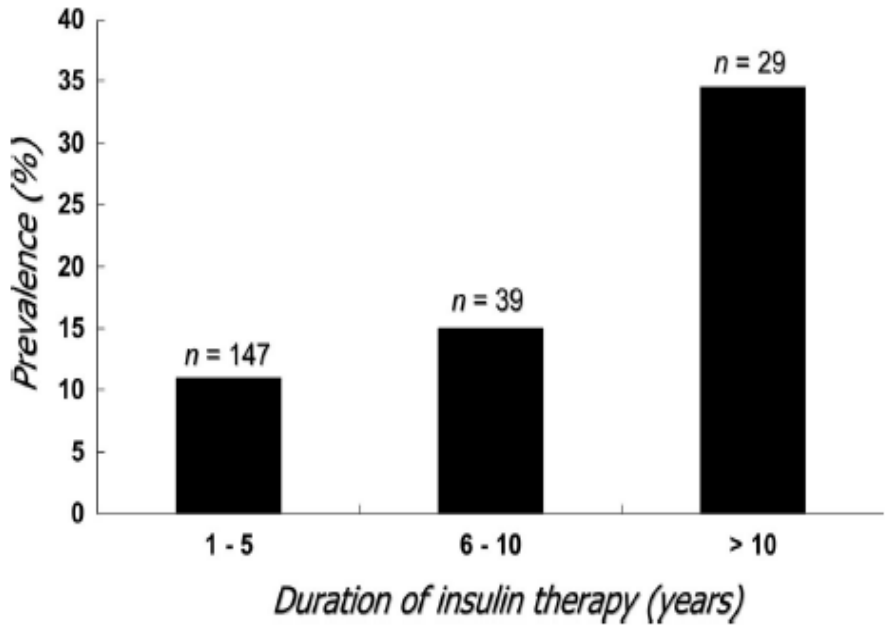


Riesgo de hipoglucemia grave en diabetes tipo 2



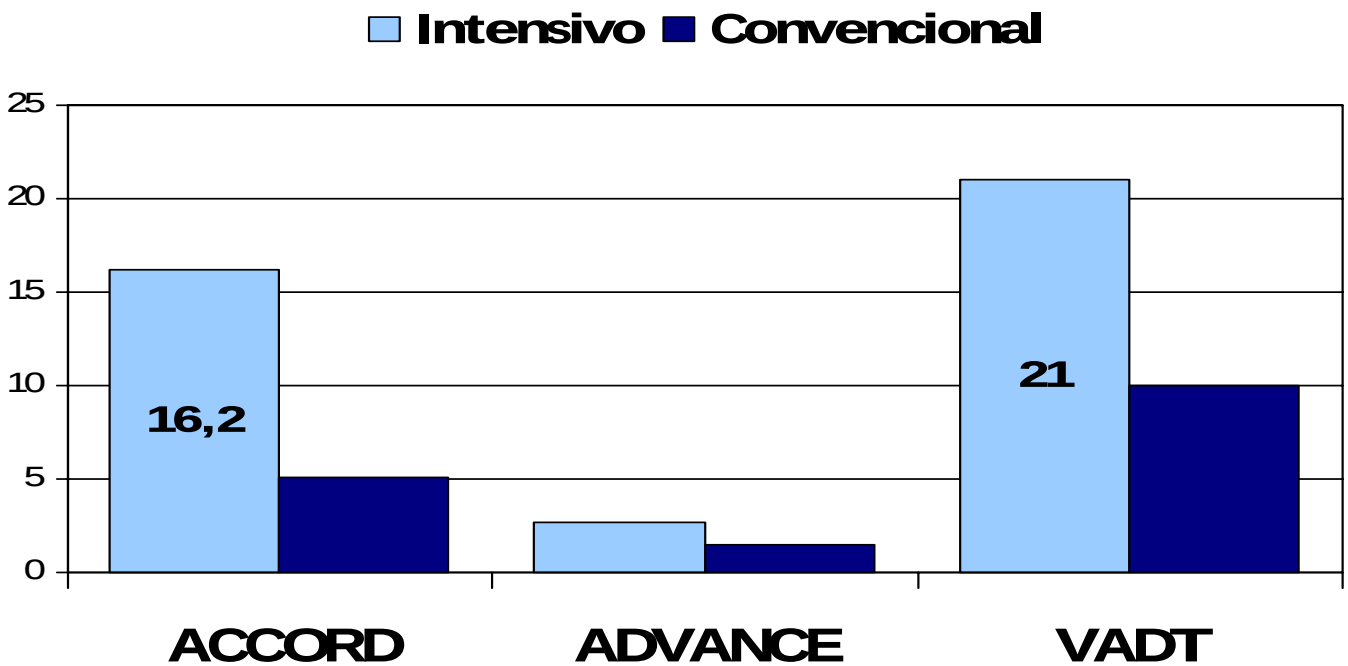
Bodner M. Diabetes Care 2008;31:2086-91.

Prevalencia de hipoglucemia grave en diabéticos tipo 2 tratados con insulina



Henderson JN. Diabet Med 2003;20:1016-21.

Tasa de hipoglucemias grave



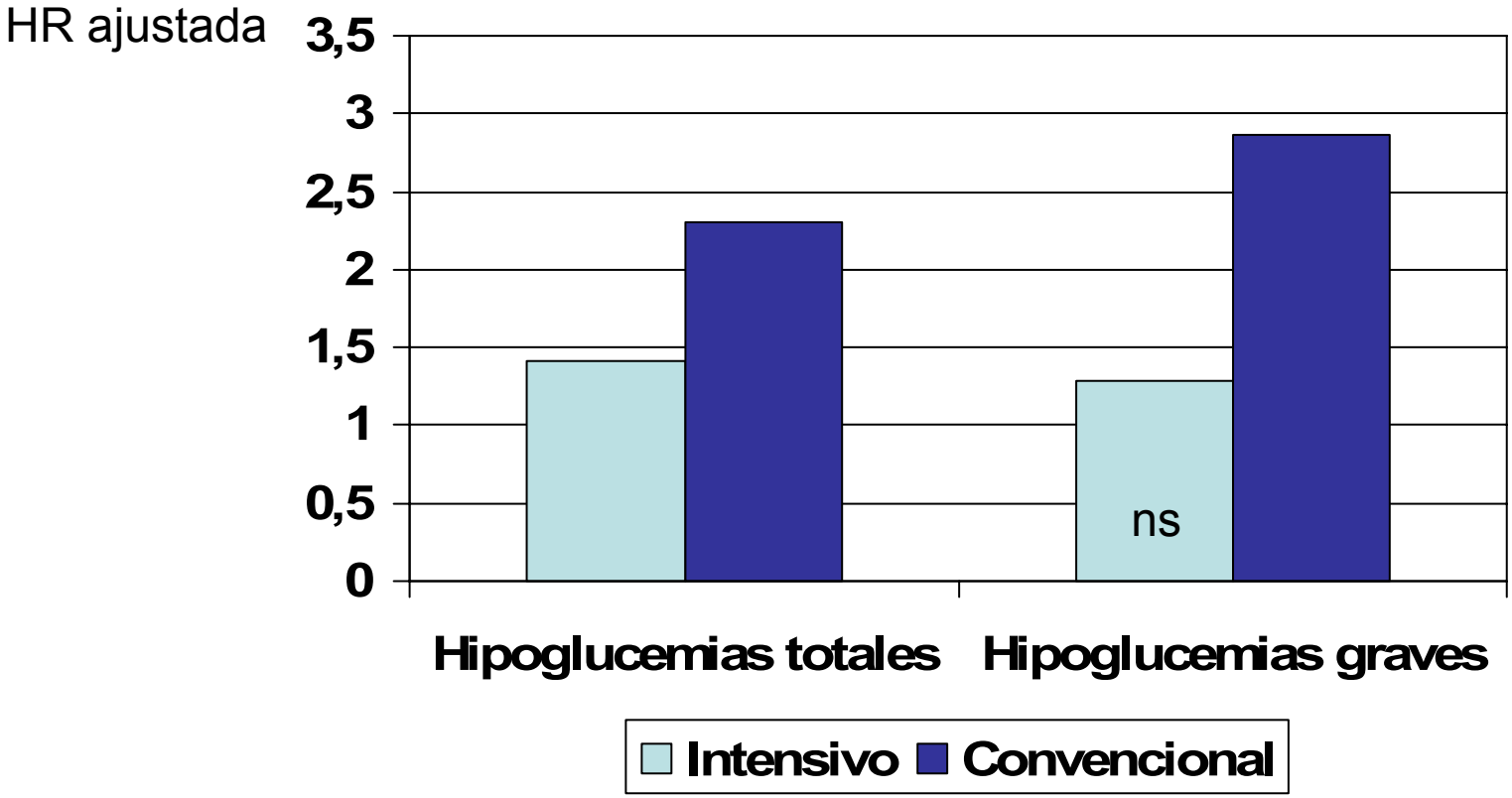
T. seguimiento	3,5 años	5 años	6 años

ADVANCE. N engl J Med 2008;358:2560-72.
ACCORD. N Engl J Med 2008;358:2545-59.
VADT. N Engl J Med 2008;360:

BMJ
BMJ 2009;339:b4909

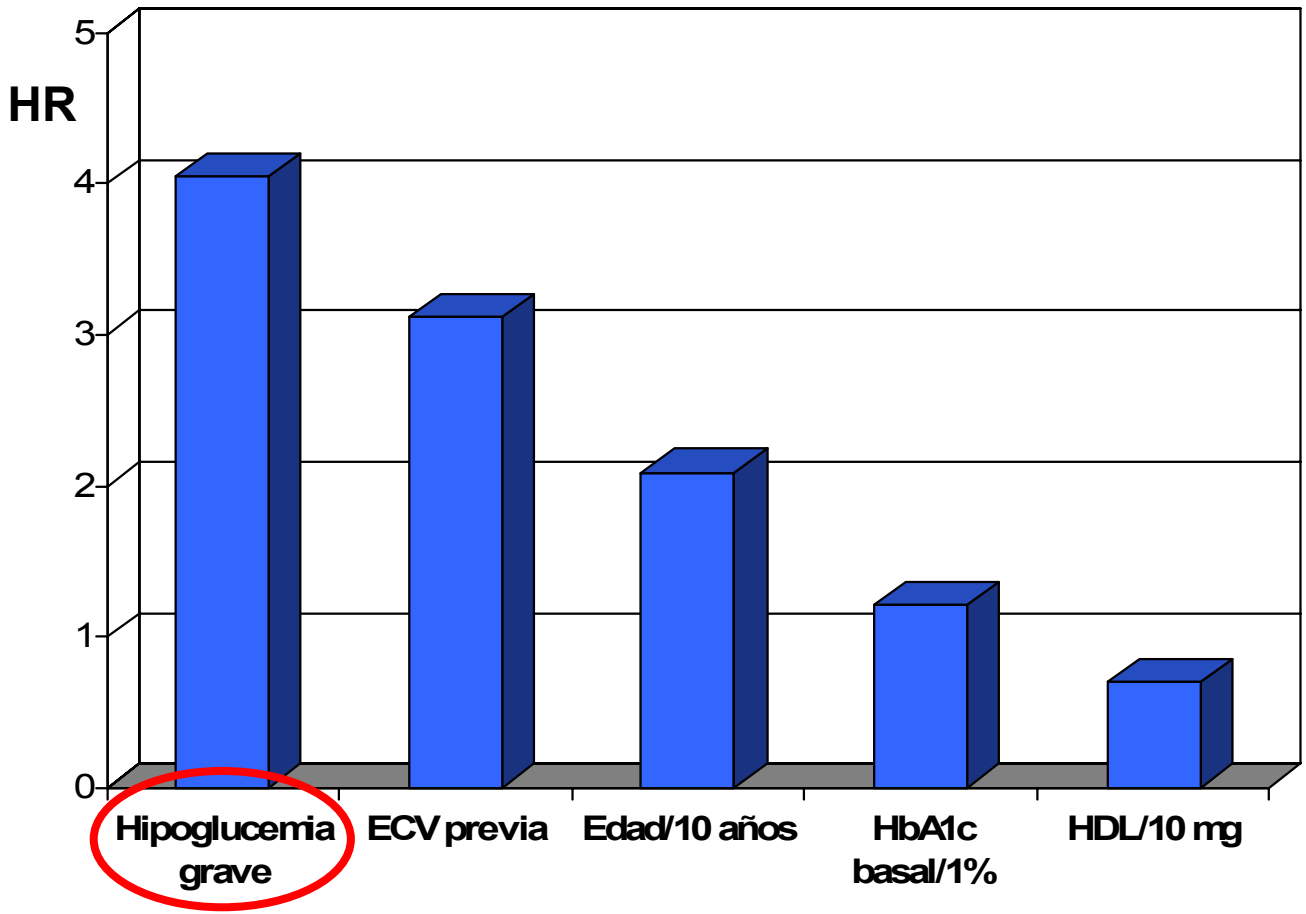
The association between symptomatic, severe hypoglycaemia and mortality in type 2 diabetes: retrospective epidemiological analysis of the ACCORD study

Riesgo de muerte en pacientes con hipoglucemia



VADT

PREDICTORES DE MUERTE CV



THE COCHRANE COLLABORATION®

Long-acting insulin analogues versus NPH insulin (human isophane insulin) for type 2 diabetes mellitus (Review)

Horvath K, Jeitler K, Berghold A, Ebrahim SH, Gratzer TW, Plank J, Kaiser T, Pieber TR, Siebenhofer A

Analysis 01.05. Comparison 01 Hypoglycaemia, Outcome 05 Nocturnal hypoglycaemia - Glargine vs. NPH

Review: Long-acting insulin analogues versus NPH insulin (human isophane insulin) for type 2 diabetes mellitus

Comparison: 01 Hypoglycaemia

Outcome: 05 Nocturnal hypoglycaemia - Glargine vs. NPH

Study	Glargine n/N	NPH n/N	Relative Risk (Random) 95% CI	Weight (%)	Relative Risk (Random) 95% CI
Eliaschewitz 2006	47/231	87/250		28.5	0.58 [0.43, 0.79]
Fritsche 2003	52/227	89/232		30.9	0.60 [0.45, 0.80]
Rosenstock 2001	81/259	104/259		40.6	0.78 [0.62, 0.98]
Total (95% CI)	717	741		100.0	0.66 [0.55, 0.80]

Total events: 180 (Glargine), 280 (NPH)

Test for heterogeneity chi-square=2.98 df=2 p=0.23 I^2 =32.8%

Test for overall effect z=4.20 p=0.00003

Analysis 01.06. Comparison 01 Hypoglycaemia, Outcome 06 Nocturnal hypoglycaemia - Detemir vs. NPH

Review: Long-acting insulin analogues versus NPH insulin (human isophane insulin) for type 2 diabetes mellitus

Comparison: 01 Hypoglycaemia

Outcome: 06 Nocturnal hypoglycaemia - Detemir vs. NPH

Study	Detemir n/N	NPH n/N	Relative Risk (Random) 95% CI	Weight (%)	Relative Risk (Random) 95% CI
Haak 2005	59/341	46/164		33.0	0.62 [0.44, 0.86]
Hermansen 2006	71/237	112/238		67.0	0.64 [0.50, 0.81]
Total (95% CI)	578	402		100.0	0.63 [0.52, 0.76]

Total events: 130 (Detemir), 158 (NPH)

Test for heterogeneity chi-square=0.02 df=1 p=0.88 I^2 =0.0%

Test for overall effect z=4.67 p<0.00001

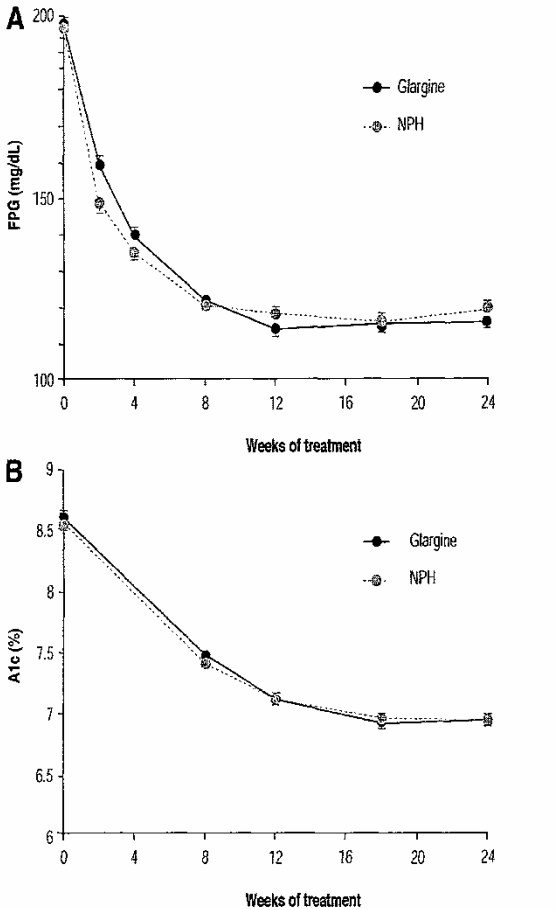
The Treat-to-Target Trial

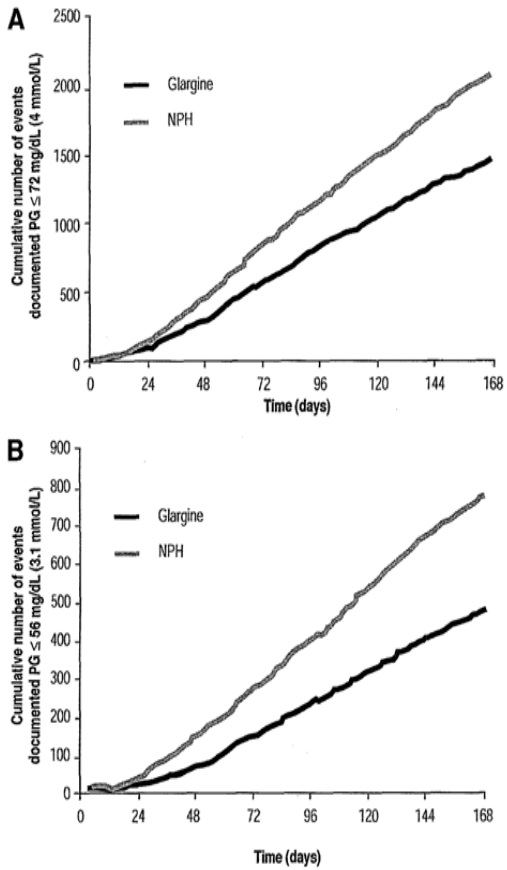
Randomized addition of glargine or human NPH insulin to oral therapy of type 2 diabetic patients

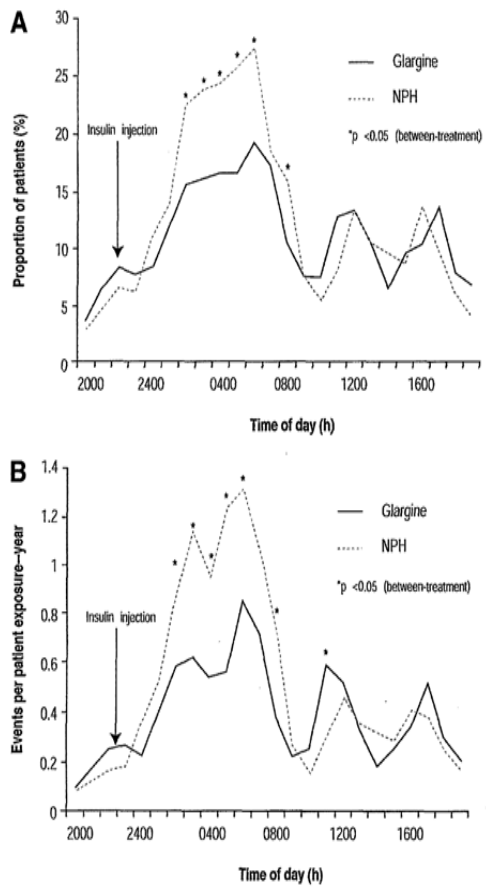
MATTHEW C. RIDDLE, MD[1]
JULIO ROSENSTOCK, MD[2]
JOHN GERICH, MD[3]

ON BEHALF OF THE INSULIN GLARGINE 4002 STUDY INVESTIGATORS*

Diabetes Care 26:3080–3086, 2003





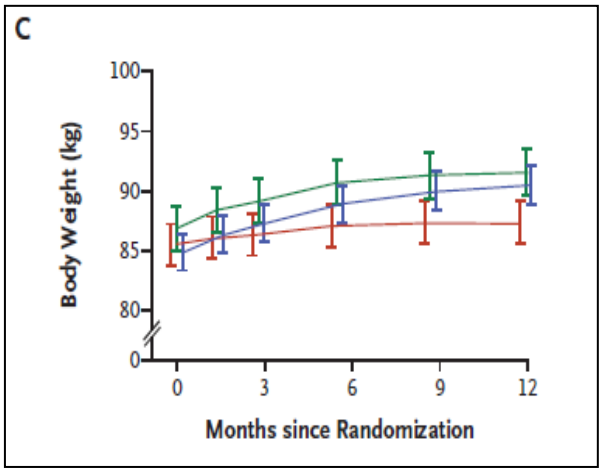


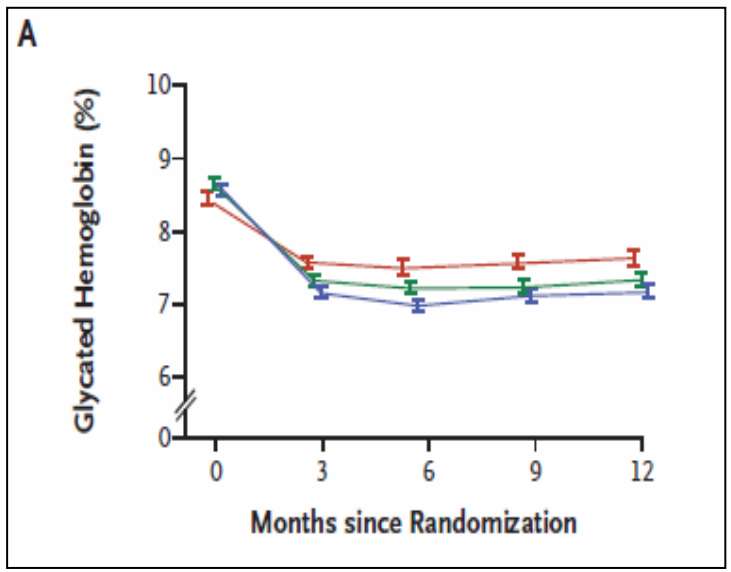
The NEW ENGLAND JOURNAL of MEDICINE

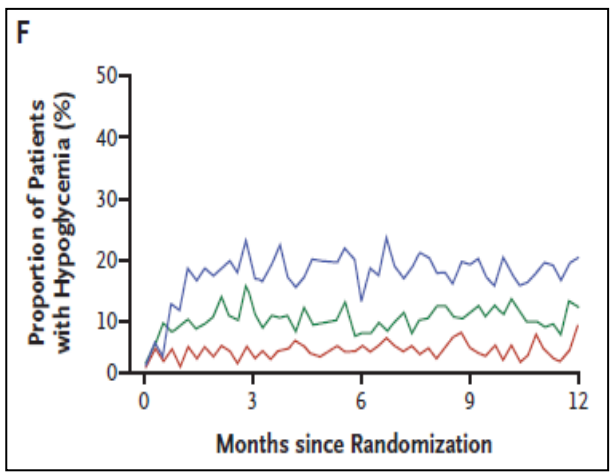
ORIGINAL ARTICLE

Addition of Biphasic, Prandial, or Basal Insulin to Oral Therapy in Type 2 Diabetes

Rury R. Holman, M.B., Ch.B., F.R.C.P., Kerensa I. Thorne, M.Sc., Andrew J. Farmer, D.M., F.R.C.G.P., Melanie J. Davies, M.D., F.R.C.P., Joanne F. Keenan, B.A., Sanjoy Paul, Ph.D., and Jonathan C. Levy, M.D., F.R.C.P., for the 4-T Study Group*







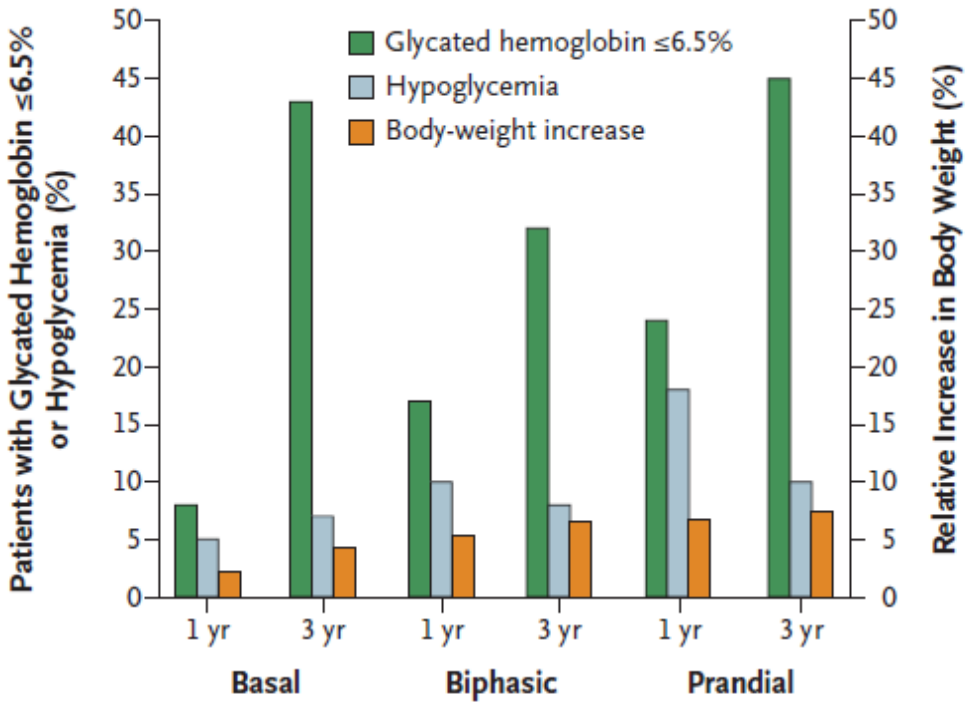
N Engl J Med 2007;357.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Three-Year Efficacy of Complex Insulin Regimens in Type 2 Diabetes

Rury R. Holman, M.B., Ch.B., F.R.C.P., Andrew J. Farmer, D.M., F.R.C.G.P., Melanie J. Davies, M.D., F.R.C.P., Jonathan C. Levy, M.D., F.R.C.P., Julie L. Darbyshire, M.A., M.Sc., Joanne F. Keenan, B.A., and Sanjoy K. Paul, Ph.D., for the 4-T Study Group*



	Basal		Biphasic		Prandial	
	1 yr	3 yr	1 yr	3 yr	1 yr	3 yr
Units insulin/kg body weight/day	0.49	1.03	0.53	0.78	0.61	0.94

Figure 1. Glycated Hemoglobin Level, Hypoglycemia, and Increase in Body Weight at 1 Year and 3 Years.

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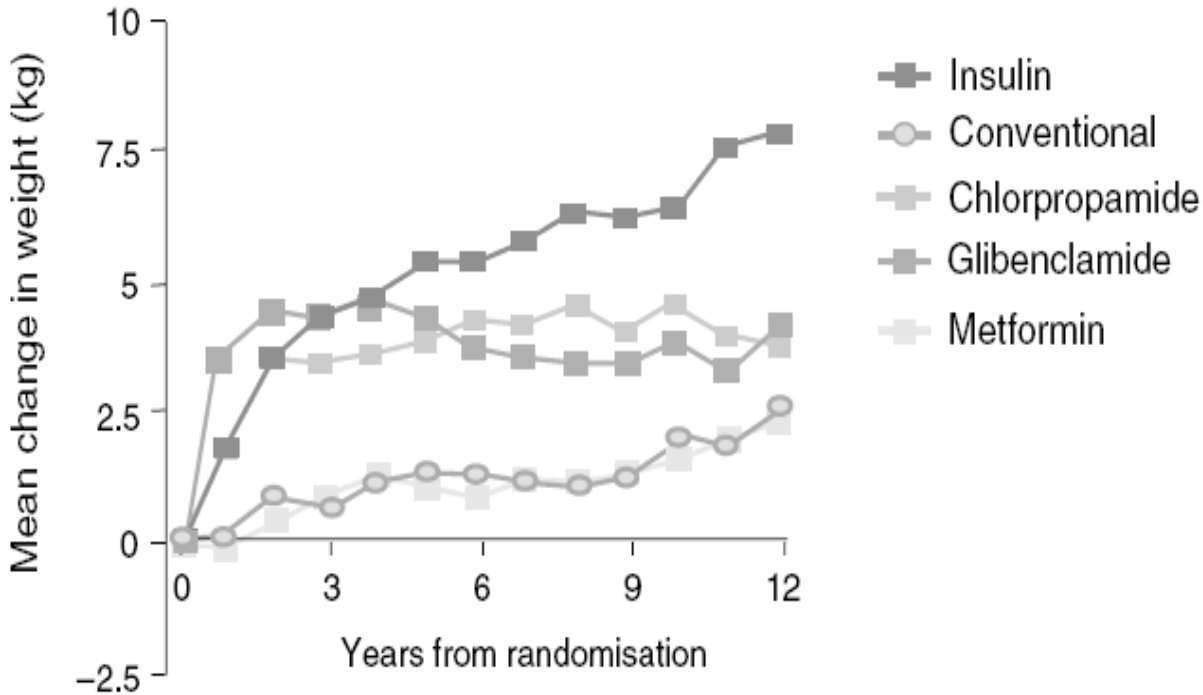
  - Hipoglucemias
  - **Ganancia de peso**
  - ¿Incremento del riesgo cardiovascular?
  - ¿Incremento del riesgo de cáncer?
  - Calidad de vida
- Conclusiones

Ganancia de peso y tratamiento antidiabético

UKPDS

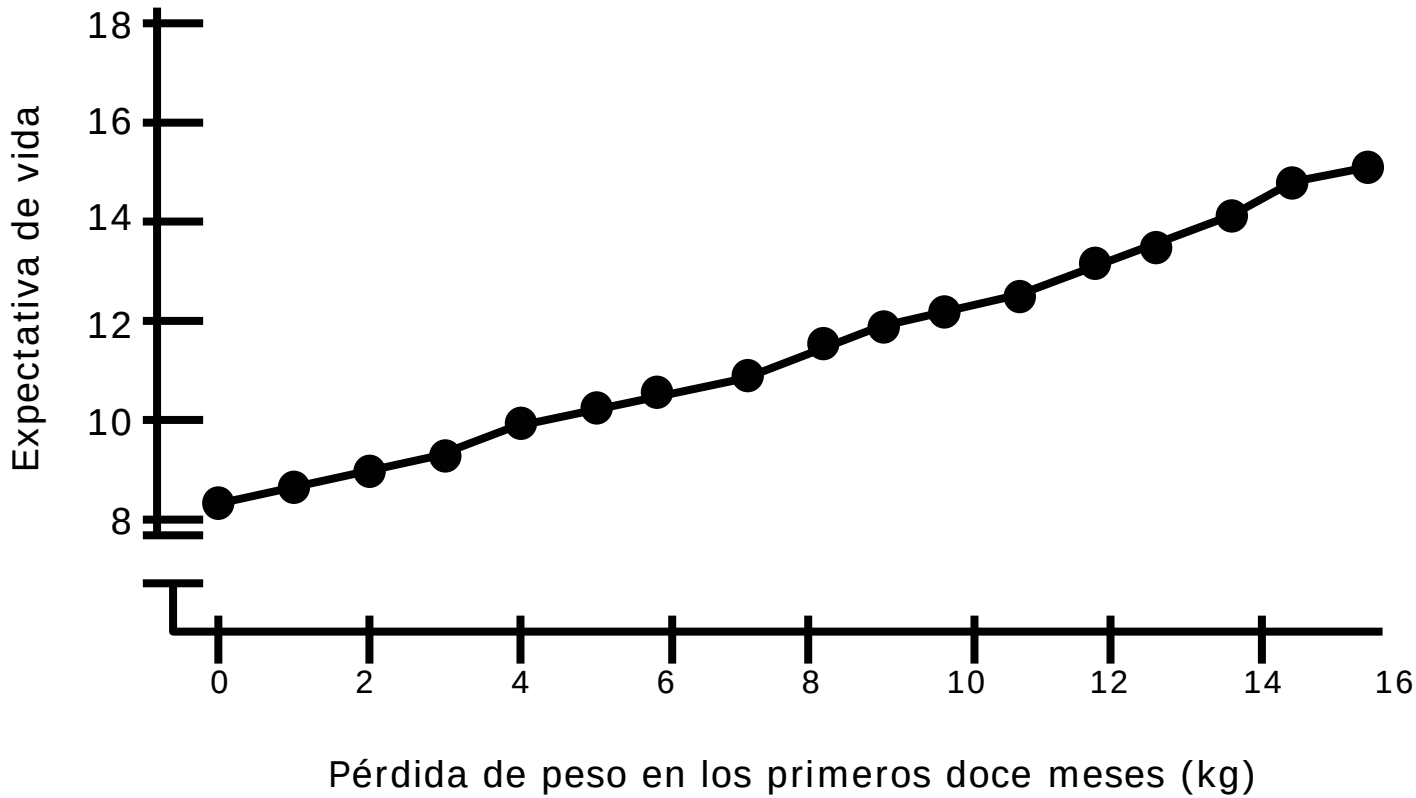


Lancet 1998;352:854-65.

Efectos adversos de la ganancia de peso

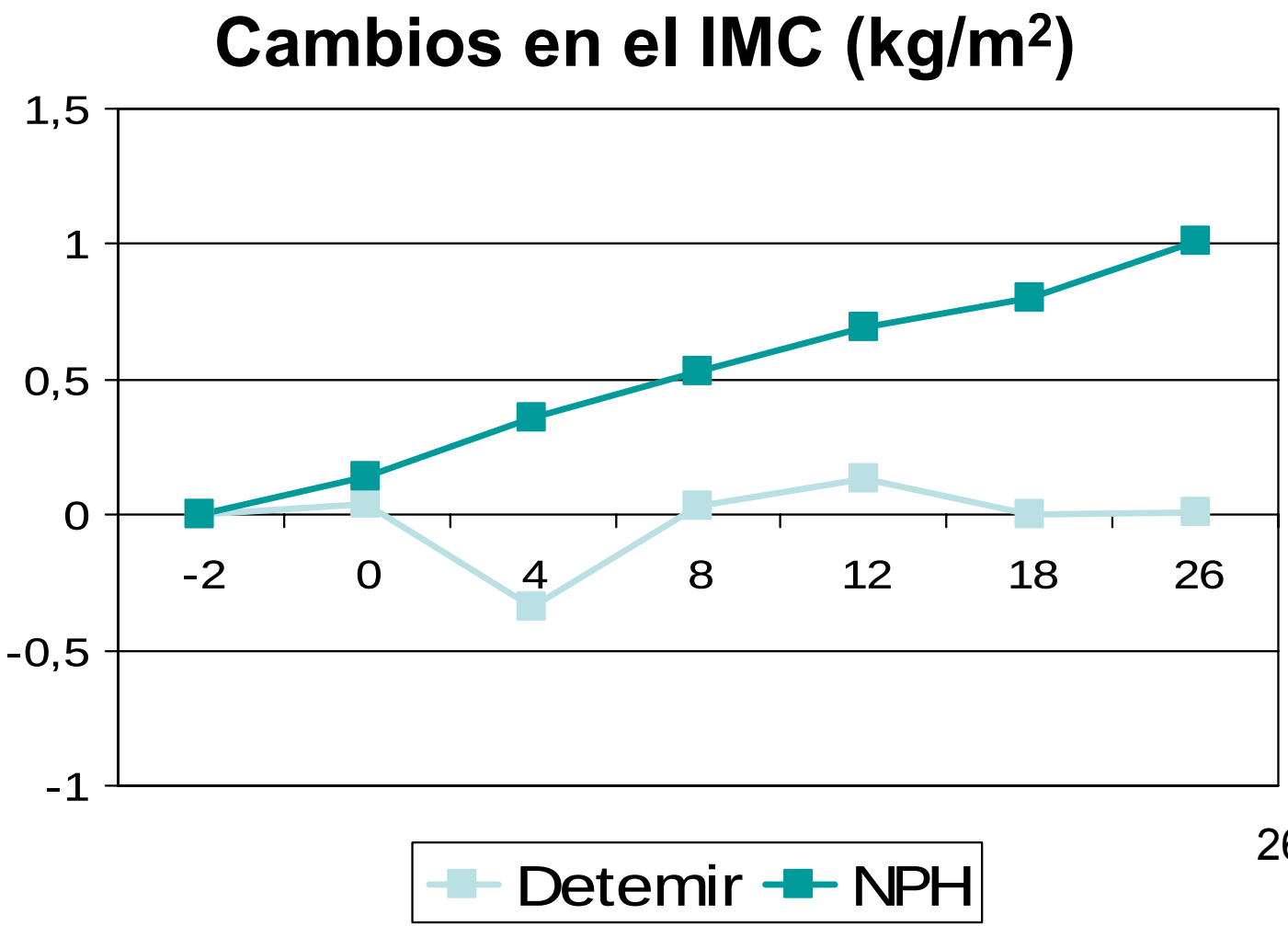
- riesgo vascular: dislipemia, HTA, control glucémico
- resistencia insulínica: ↑ dosis insulina
- deterioro células beta en DM tipo 2
- baja autoestima

La pérdida de peso aumenta la expectativa de vida en diabéticos tipo 2



Lean ME et al: Diab Med: 1990: 7: 228-233

Estudio PREDICTIVE



26 semanas

Índice

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  - Ganancia de peso
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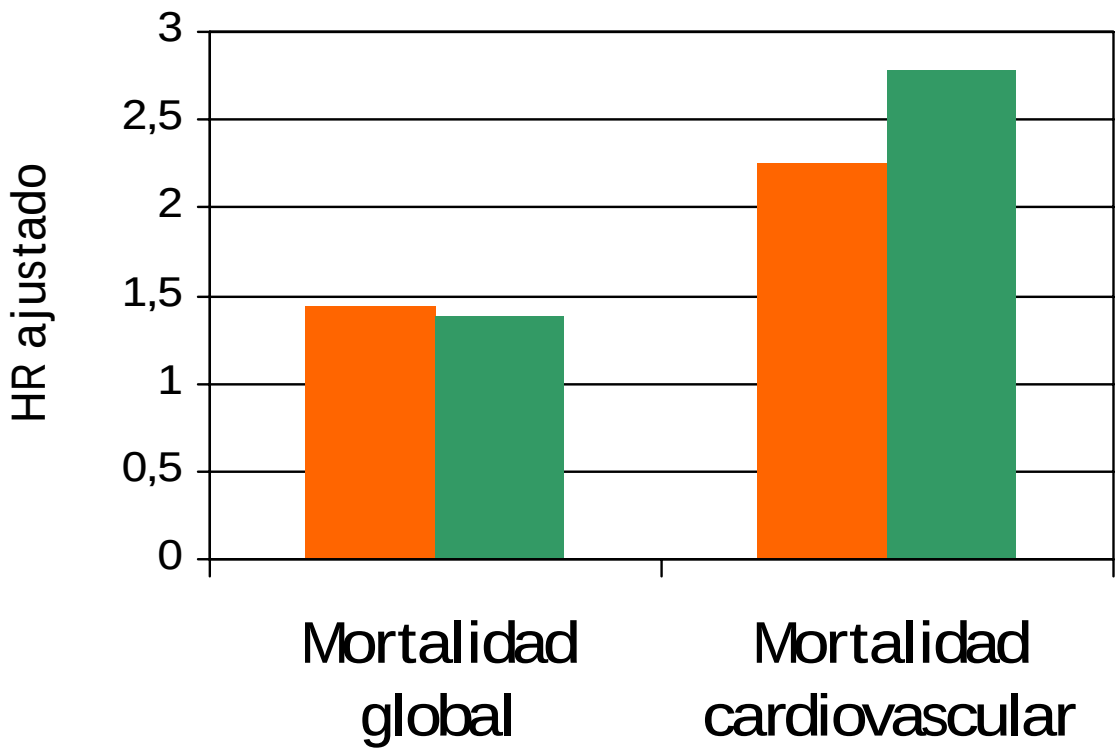
  - ¿Incremento del riesgo de cáncer?
  - Calidad de vida
- Conclusiones

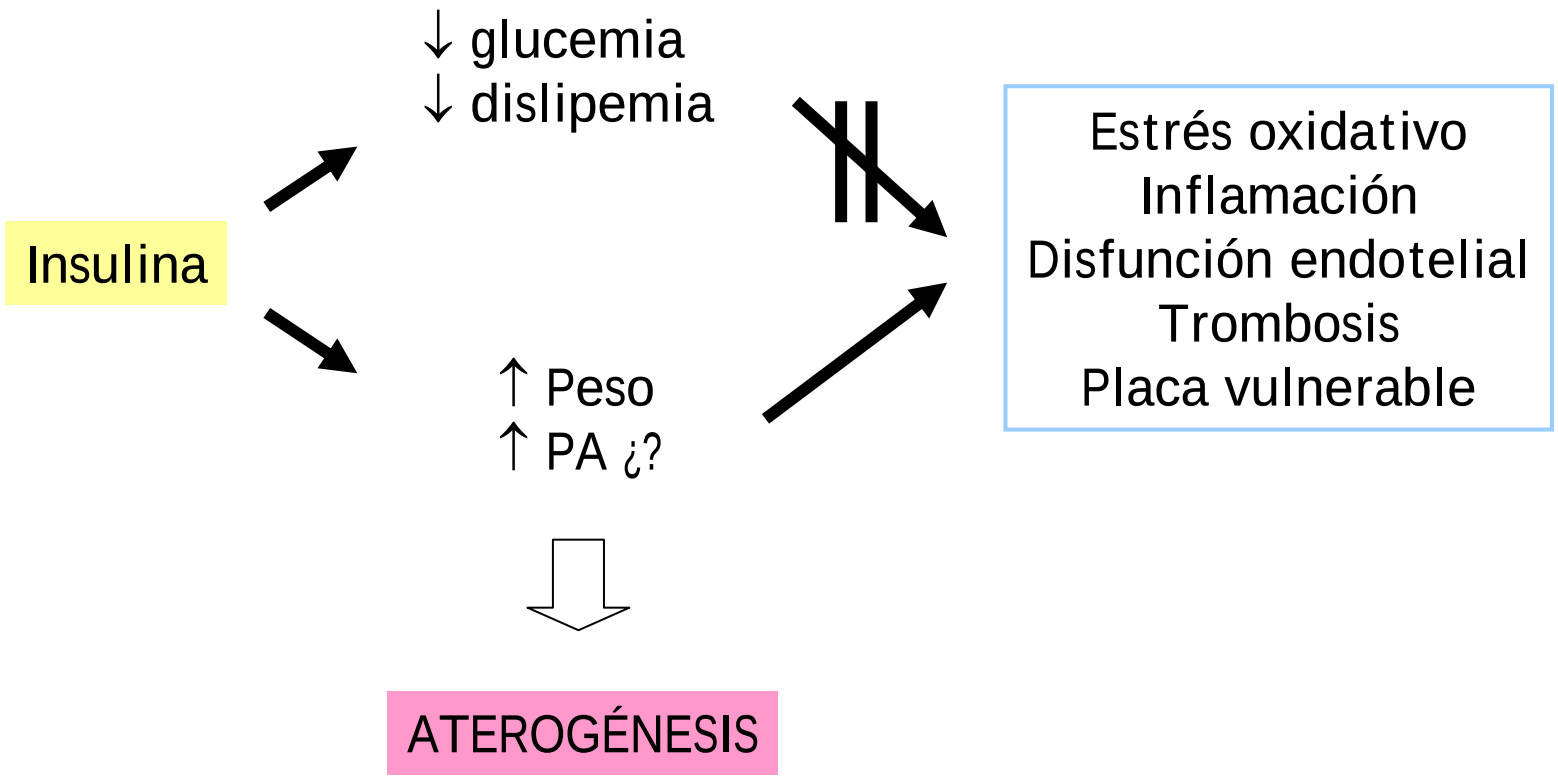
Estudio DECODE

Población no diabética con Síndrome Metabólico (OMS)



Hu G. Arch Intern Med 2004;164:1066-76

¿La insulina es aterogénica?



(Stern, 1999) (Bonadonna, 2004)

Rationale, design, and baseline characteristics for a large international trial of cardiovascular disease prevention in people with dysglycemia: The ORIGIN Trial (Outcome Reduction with an Initial Glargine Intervention)

The ORIGIN Trial Investigators *Hamilton, Ontario, Canada*

Aims Impaired fasting glucose (IFG), impaired glucose tolerance (IGT), and diabetes arise due to insufficient insulin secretion and are risk factors for cardiovascular (CV) events. Thus, targeting normal fasting glucose levels with insulin may reduce CV events. Previous studies suggest that ω-3 fatty acid supplements may reduce CV death; however, their effect in high-risk dysglycemic individuals is not known.

Methods People aged ≥50 years with evidence of CV disease and with IFG, IGT, newly detected or established diabetes (on 0 or 1 oral agent), and a local glycated hemoglobin <1.50% of the upper limit of normal for that assay were recruited and allocated to (*a*) either 1 daily injection of insulin glargine with the dose titrated to achieve a fasting plasma glucose ≤5.3 mmol/L (95 mg/dL), or standard glycemic care; and (*b*) either ω-3–acid ethyl esters 90 (1 g consisting of EPA 465 mg and DHA 375 mg) or identical placebo, according to a 2 × 2 factorial design. The 2 different primary outcomes for the insulin and ω-3 fatty acid arms are CV events and CV death, respectively.

Results A total of 12 612 (mean age 64, 35% women) people in 40 countries were randomized during a 2-year period ending December 2005. Eighty-two percent had established diabetes, 6% had new diabetes, and 12% had IGT or IFG; the mean fasting plasma glucose was 7.3 mmol/L (131 mg/dL).

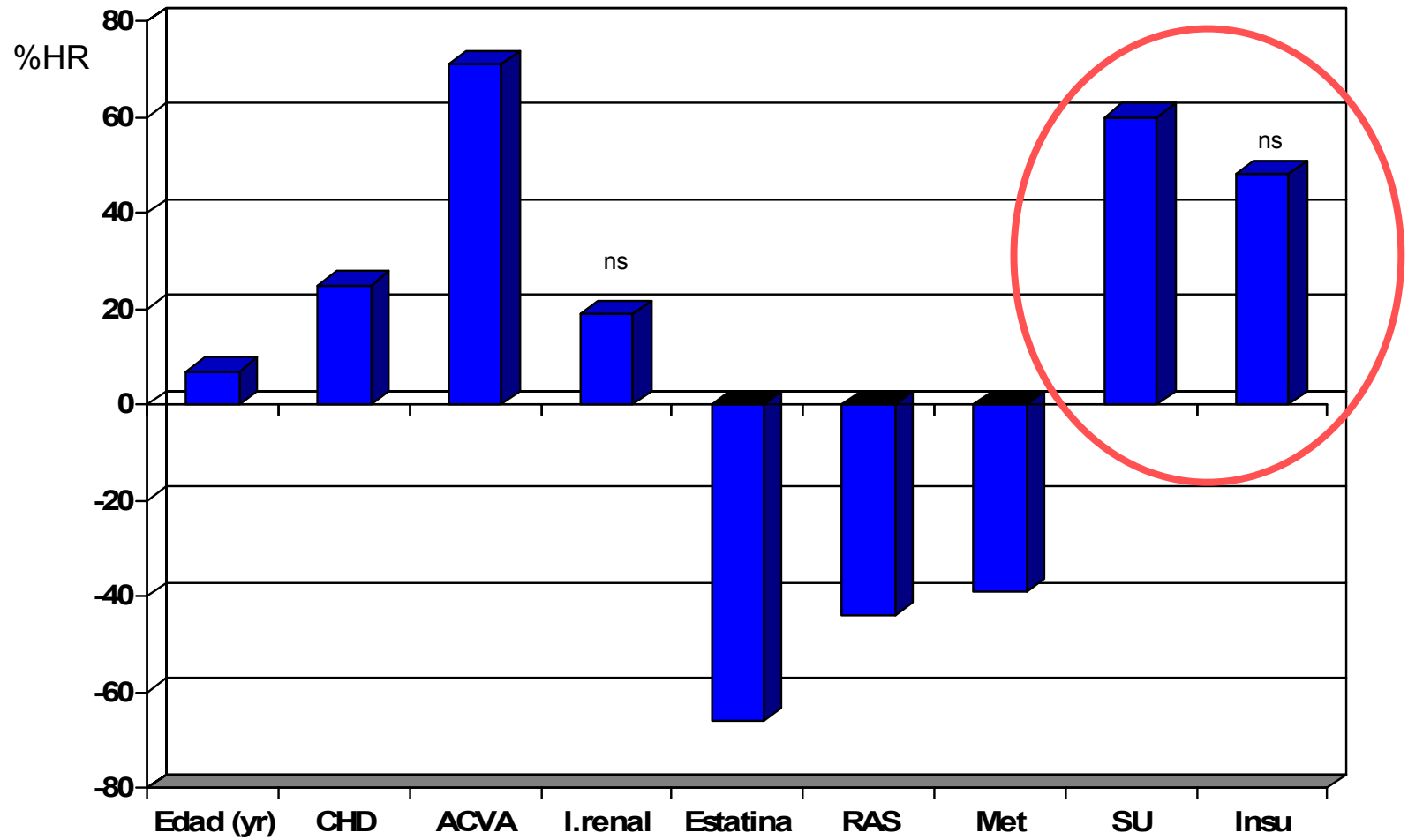
Conclusions The ORIGIN trial will determine whether or not either or both of these interventions can reduce CV events. (Am Heart J 2008;155:26-32.e6.)

Explaining the Decline in Early Mortality in Men and Women With Type 2 Diabetes

A population-based cohort study

JUDITH CHARLTON

Variables asociadas con mortalidad a los 2 años del diagnóstico de diabetes



Diabetes Care 31:1761–1766, 2008

European Heart Journal (2008) 29, 166–176
doi:10.1093/eurheartj/ehm518

The impact of glucose lowering treatment on long-term prognosis in patients with type 2 diabetes and myocardial infarction: a report from the DIGAMI 2 trial

Linda G. Mellbin[1]*, Klas Malmberg[1], Anna Norhammar[1], Hans Wedel[2], and Lars Rydén[1] for the DIGAMI 2 Investigators

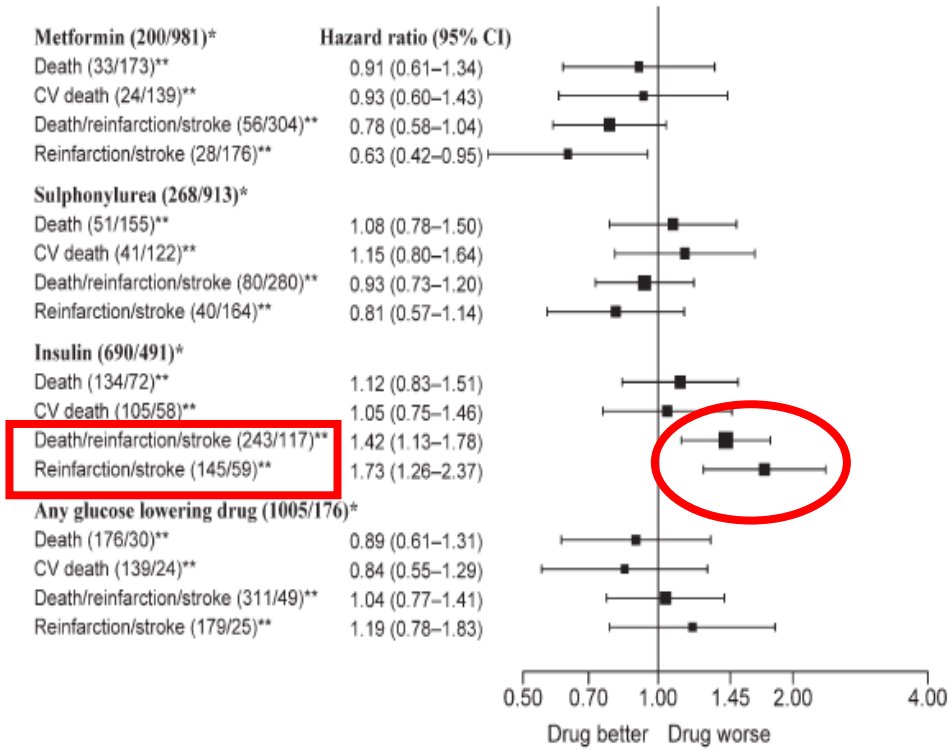
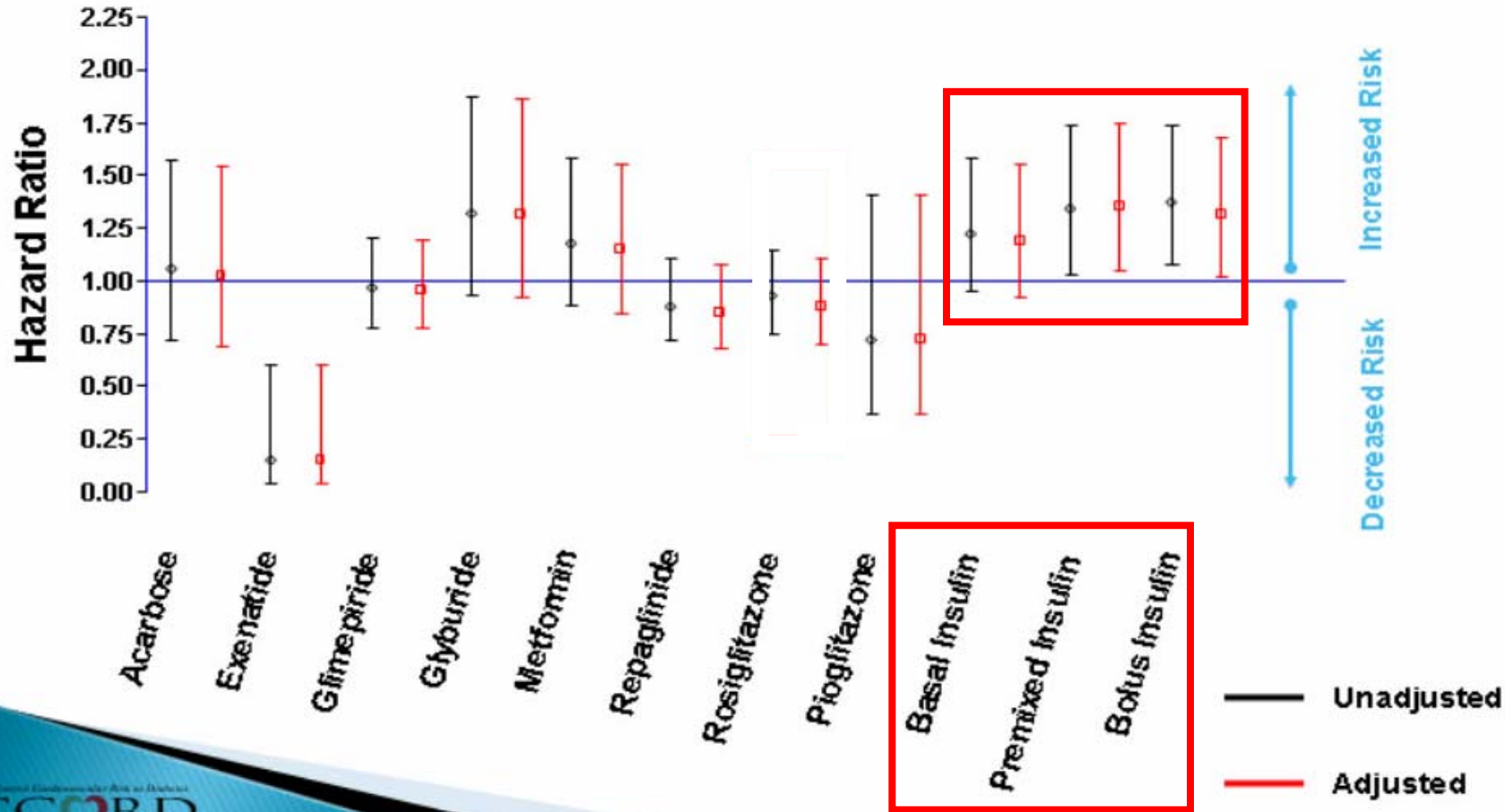


Figure 1 Effect of different updated glucose lowering treatments on mortality and morbidity. CV, cardiovascular

Conclusion Controlling for confounders including glycemic control, there was no significant difference in mortality between sulphonylureas, metformin, and insulin. In this *post hoc* analysis, the risk of non-fatal myocardial infarction and stroke increased significantly by insulin treatment while metformin was protective. It is emphasized that this observation is done in an epidemiological analysis and should encourage to further confirmation in randomized trials.

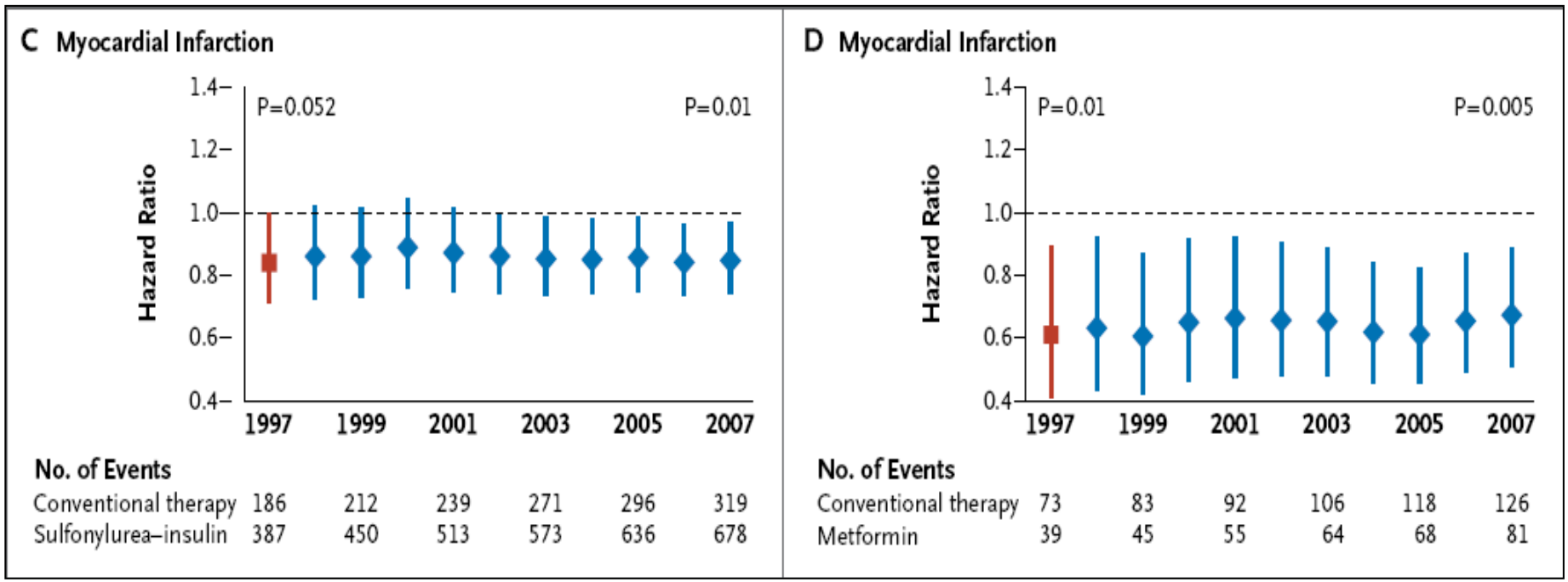
Mortality Hazard Ratios for Post-Randomization Prescription of Glycemia Medications After Also Adjusting for the Glycemia Intervention Effect



ACCORD

ADA 68th Scientific Sessions, June 6-10, San Francisco, 2008

UKPDS: seguimiento a 10 años



Holman RR. NEJM 2008;359

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  - Ganancia de peso
  - ¿Incremento del riesgo cardiovascular?
  - **¿Incremento del riesgo de cáncer?**
  - Calidad de vida
- Conclusiones

Risk of malignancies in patients with diabetes treated with human insulin or insulin analogues: a cohort study

Article
Use of insulin glargine and cancer incidence in Scotland: A study from the Scottish Diabetes Research Network Epidemiology Group

Insulin glargine use and short-term incidence of malignancies—a population-based follow-up study in Sweden

The influence of glucose-lowering therapies on cancer risk in type 2 diabetes

Diabetologia
DOI 10.1007/s00125-009-1440-6

ARTICLE

The influence of glucose-lowering therapies on cancer risk in type 2 diabetes

C. J. Currie · C. D. Poole · E. A. M. Gale

Received: 19 May 2009 / Accepted: 18 June 2009

Abstract

Aims/hypothesis The risk of developing a range of solid tumours is increased in type 2 diabetes, and may be influenced by glucose-lowering therapies. We examined the risk of development of solid tumours in relation to treatment with oral agents, human insulin and insulin analogues.

Methods This was a retrospective cohort study of people treated in UK general practices. Those included in the analysis developed diabetes >40 years of age, and started treatment with oral agents or insulin after 2000. A total of 62,809 patients were divided into four groups according to whether they received monotherapy with metformin or sulfonylurea, combined therapy (metformin plus sulfonylurea), or insulin. Insulin users were grouped according to treatment with insulin glargine, long-acting human insulin, biphasic analogue and human biphasic insulin. The outcome measures were progression to any solid tumour, or cancer of the breast, colon, pancreas or prostate. Confounding factors were accounted for using Cox proportional hazards models.

Results Metformin monotherapy carried the lowest risk of cancer. In comparison, the adjusted HR was 1.08 (95% CI 0.96–1.21) for metformin plus sulfonylurea, 1.36 (95% CI 1.19–1.54) for sulfonylurea monotherapy, and 1.42 (95% CI 1.27–1.60) for insulin-based regimens. Adding metformin to insulin reduced progression to cancer (HR 0.54, 95% CI 0.43–0.66). The risk for those on basal human insulin alone vs insulin glargine alone was 1.24 (95% CI 0.90–1.70). Compared with metformin, insulin therapy increased the risk of colorectal (HR 1.69, 95% CI 1.23–2.33) or pancreatic cancer (HR 4.63, 95% CI 2.64–8.10), but did not influence the risk of breast or prostate cancer. Sulfonylureas were associated with a similar pattern of risk as insulin.

Conclusions/interpretation Those on insulin or insulin secretagogues were more likely to develop solid cancers than those on metformin, and combination with metformin abolished most of this excess risk. Metformin use was associated with lower risk of cancer of the colon or pancreas, but did not affect the risk of breast or prostate cancer. Use of insulin analogues was not associated with increased cancer risk as compared with human insulin.

Keywords Cancer · Insulin · Insulin analogues · Metformin · Sulfonylureas · Survival · Type 2 diabetes

Abbreviations

LVD	Large vessel disease
OHA	Oral hypoglycaemic agent
THIN	The Health Information Network

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Bristol, UK

Introduction

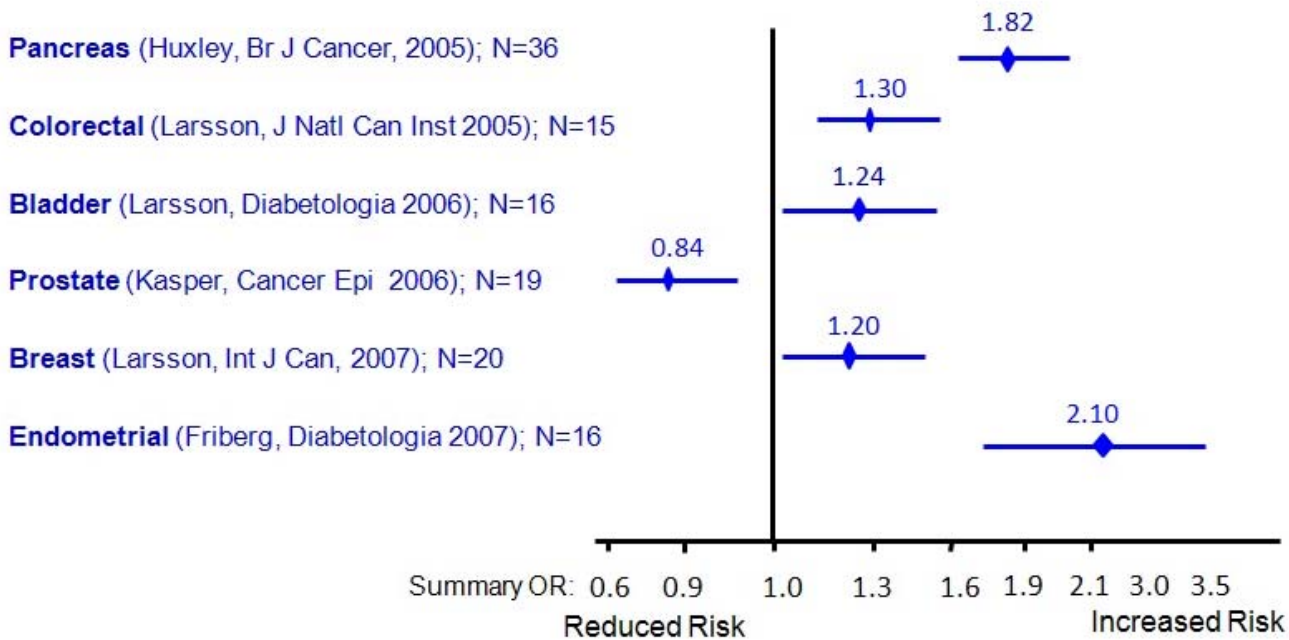
Type 2 diabetes is associated with an increased risk of mortality from a range of solid tumours, including cancers of the colon, breast and pancreas [1]. Similar associations

Diabetes y Cáncer

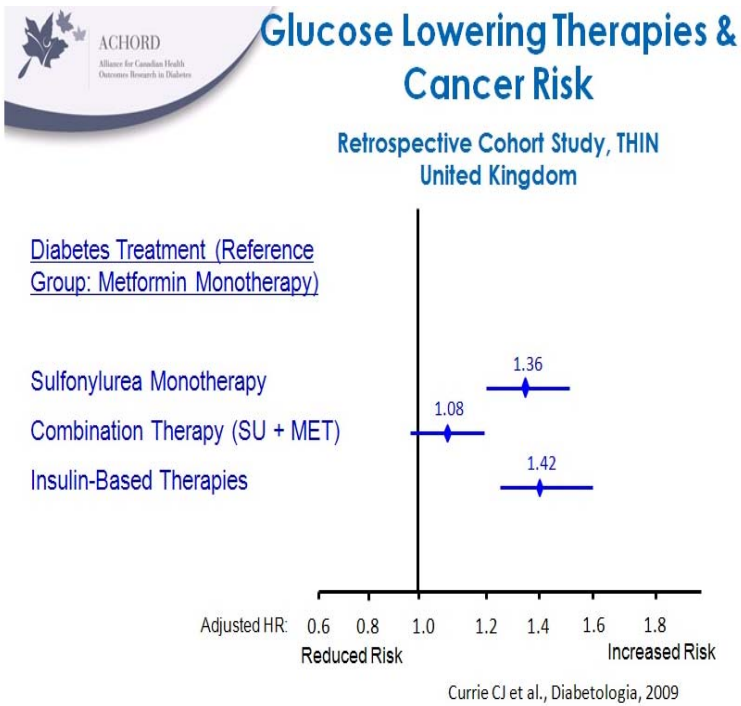
ACHORD
Alliance for Canadian Health Outcomes Research in Diabetes

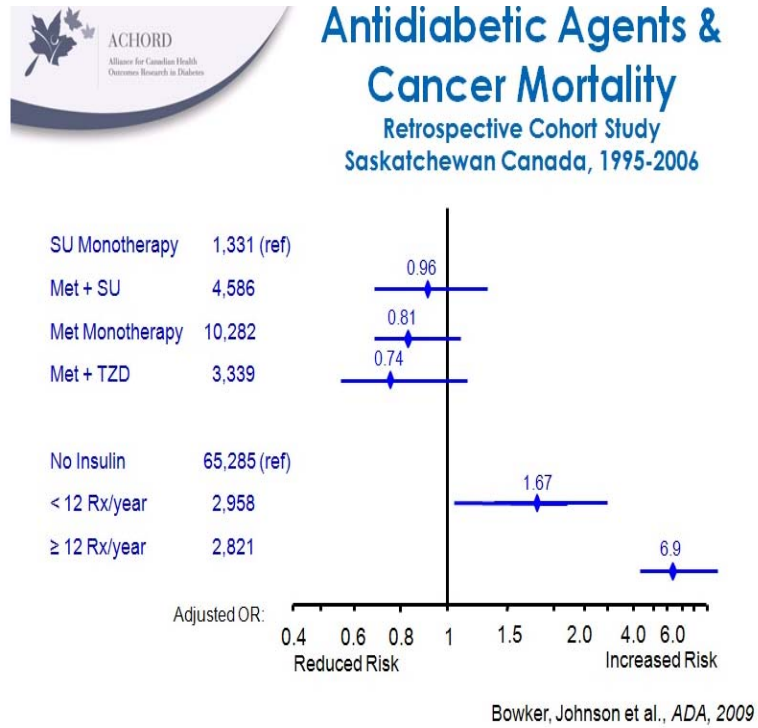
Diabetes & Cancer Risk

Meta-analyses, 2005-2007

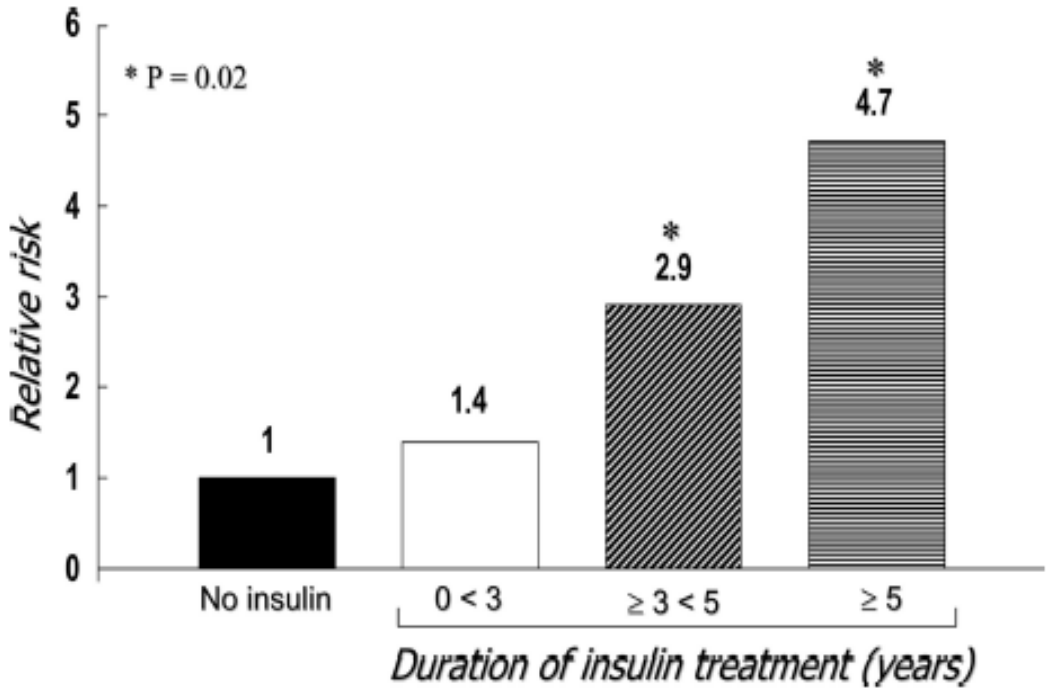


Hipoglucemiantes y Cáncer





Riesgo relativo de cáncer colorrectal en diabetes tipo 2 en relación con la duración del tratamiento con insulina



Yang YX. Gastroenterology 2004;127:1044-50.

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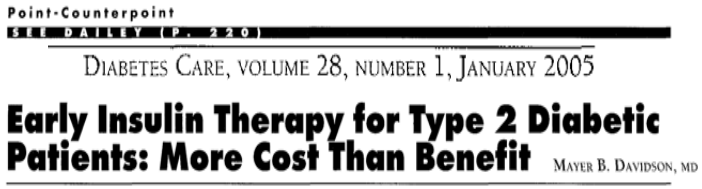

Costes sanitarios

- educación diabetológica
- revisiones frecuentes
- autocontrol

Impacto en calidad de vida:

- miedo a inyecciones
- necesidad de autocontroles
- modificación de hábitos (dieta, ejercicio, horarios)
- revisiones frecuentes
- estigma social

Diabetes Metab Res Rev. 2009 Sep;25 Suppl 1:S4-S10.

Insulin therapy and quality of life. A review.

Pouwer F, Hermanns N.

Conclusions.

Having multiple complications of diabetes is clearly associated with Decreased QoL. Results from large studies such as the Diabetes Control and Complications Trial (DCCT) and United Kingdom Prospective Diabetes Study (UKPDS) suggest that **intensive treatment itself does not impair QoL.** Recent findings further suggest that pump therapy, compared to multiple daily injections, has beneficial effects on QoL. The fact that multiple tools are used to assess QoL makes it **difficult to draw conclusions** regarding the effects of different types of insulin on QoL. More work on the standardization of the assessment of QoL in diabetes is urgently needed.

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CONCLUSIONES

1. No existe ninguna evidencia actual de que el uso precoz de insulina proporcione un beneficio añadido a largo plazo, más allá del control glucémico.

2. La insulina es un tratamiento insustituible en muchos pacientes para alcanzar los objetivos de control metabólico.

3. El uso de insulina se asocia a efectos adversos (hipoglucemia, ganancia de peso) (¿riesgo CV?, ¿cáncer?).

4. La insulina debe introducirse en su momento justo, tan pronto cuando no podamos conseguir el control glucémico con otros antidiabéticos.

5. Posible papel de la insulinización intensiva transitoria en diabetes tipo 2 de inicio, mal controlada

Muchas gracias por su atención