Sulfonilureas

Dr. Pedro Conthe

Médico Clínico

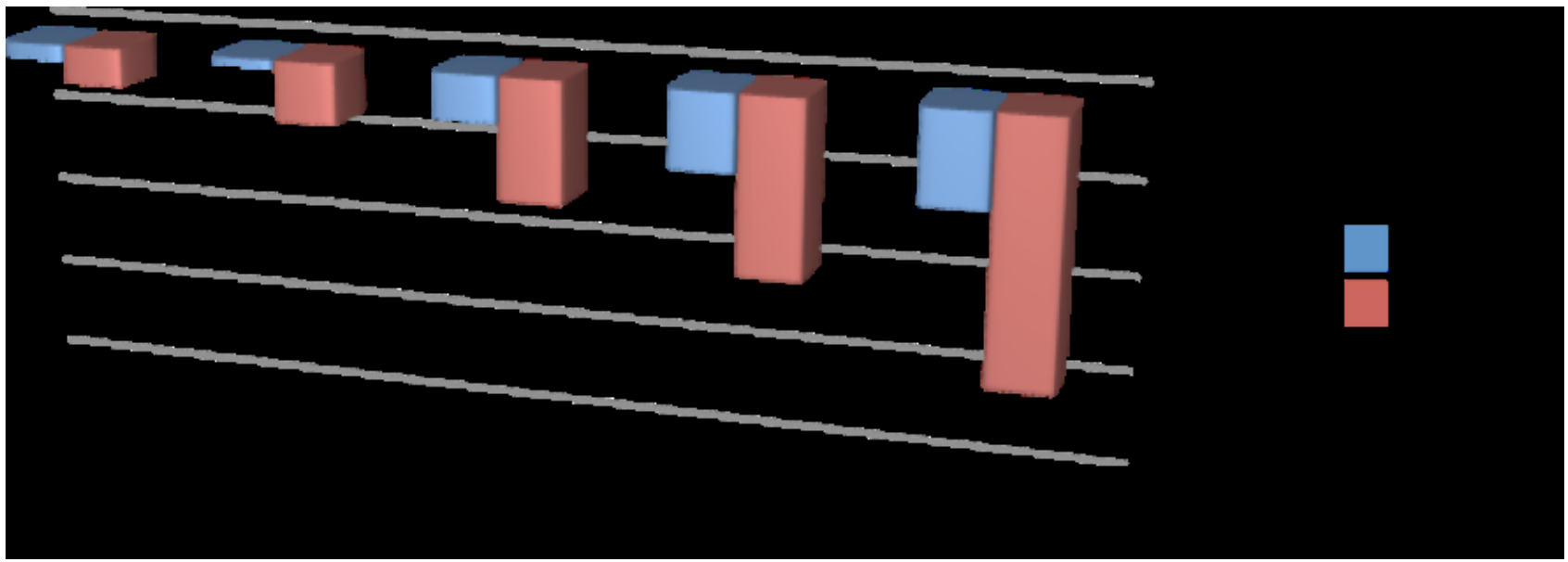
Real Madrid

"si tus dardos están bien afilados no tendrás que lanzar muchos"

A favor de SU

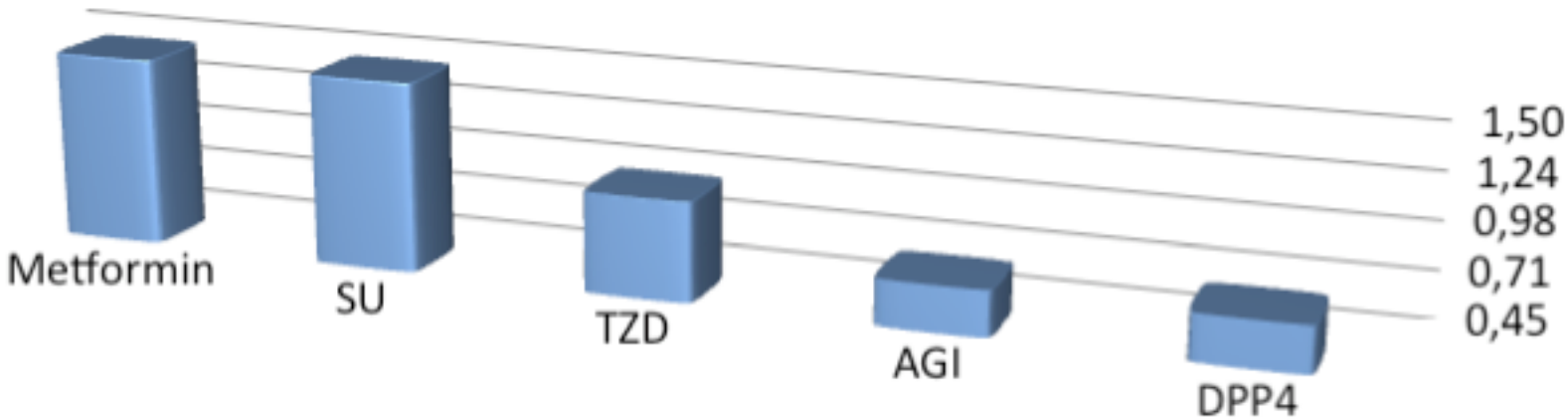
- Efectividad y uso en Control Glucémico
- Estudios largo plazo UKPDS, ADVANCE...
- Minimizar el peso y la hipoglucemia
- SU en las Guías, Recomendaciones

A1c:descenso según nivel de partida



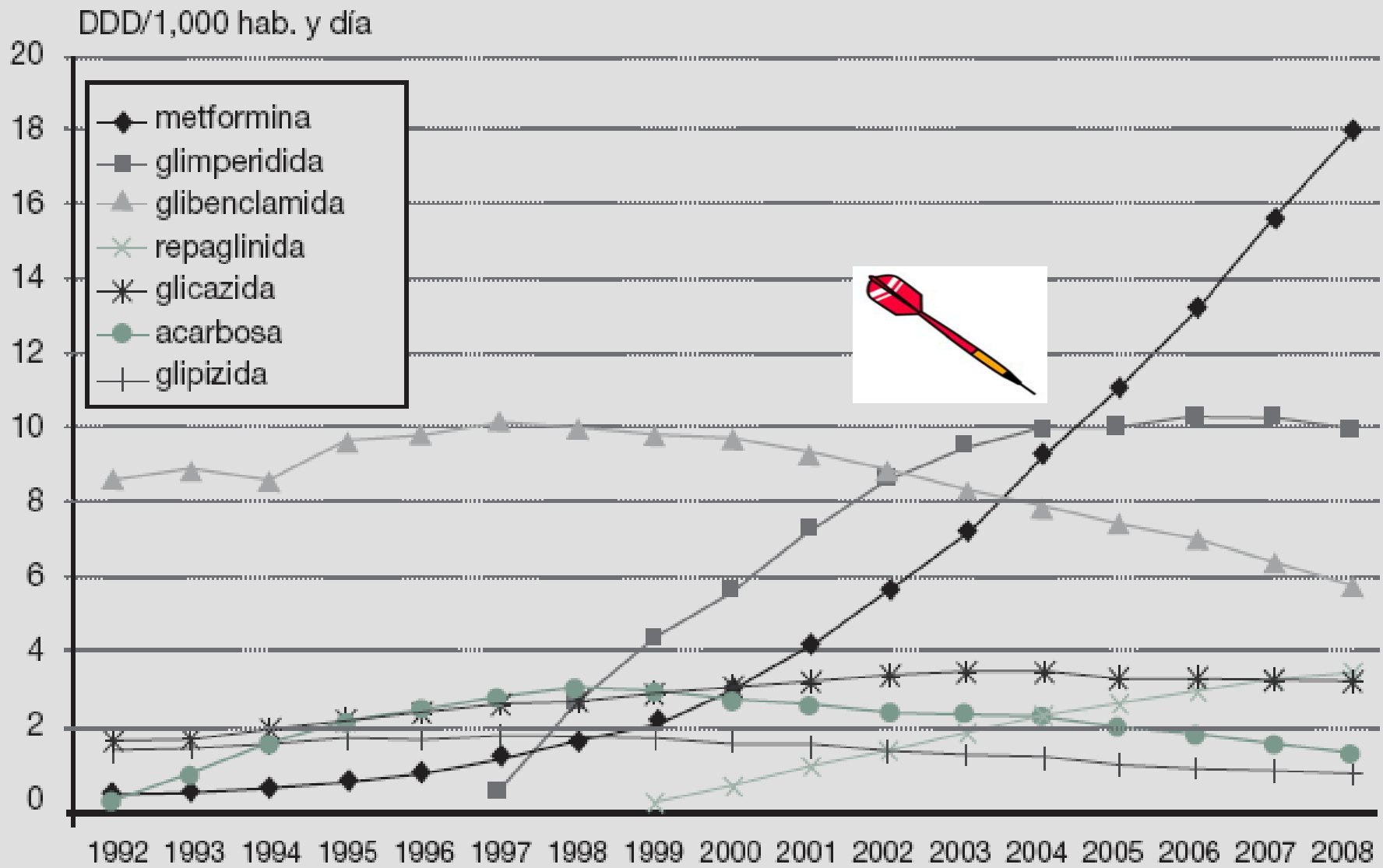
Bloomgarden et al, Diabetes Care 2006;29:2137

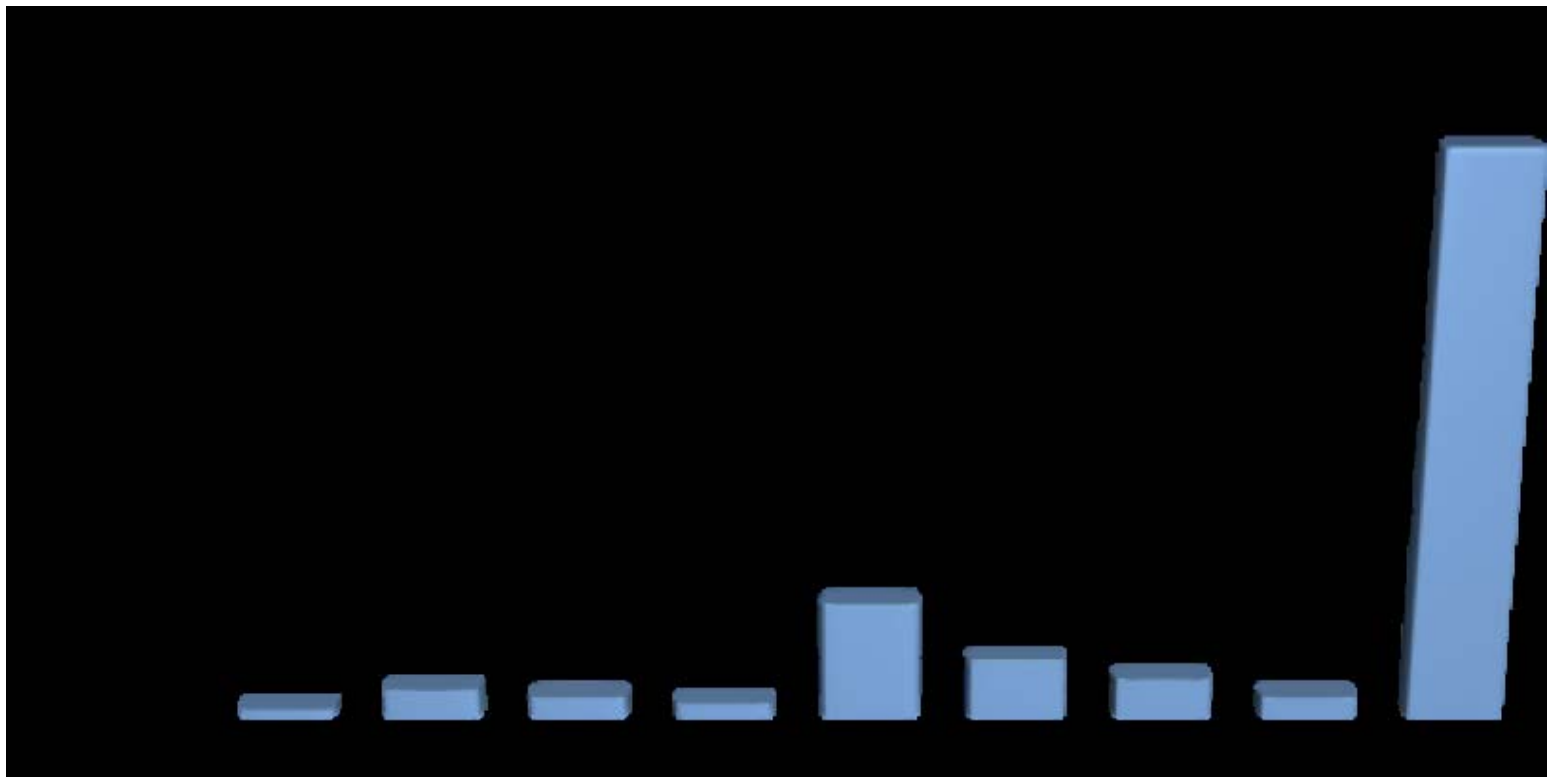
Descenso en A1c con distintos ADOs



Nathan et al. Diabetes Care 2008
(ADA/EASD guidelines)

Evolución de la utilización de algunos antidiabéticos orales en España (1992-2008)





Results

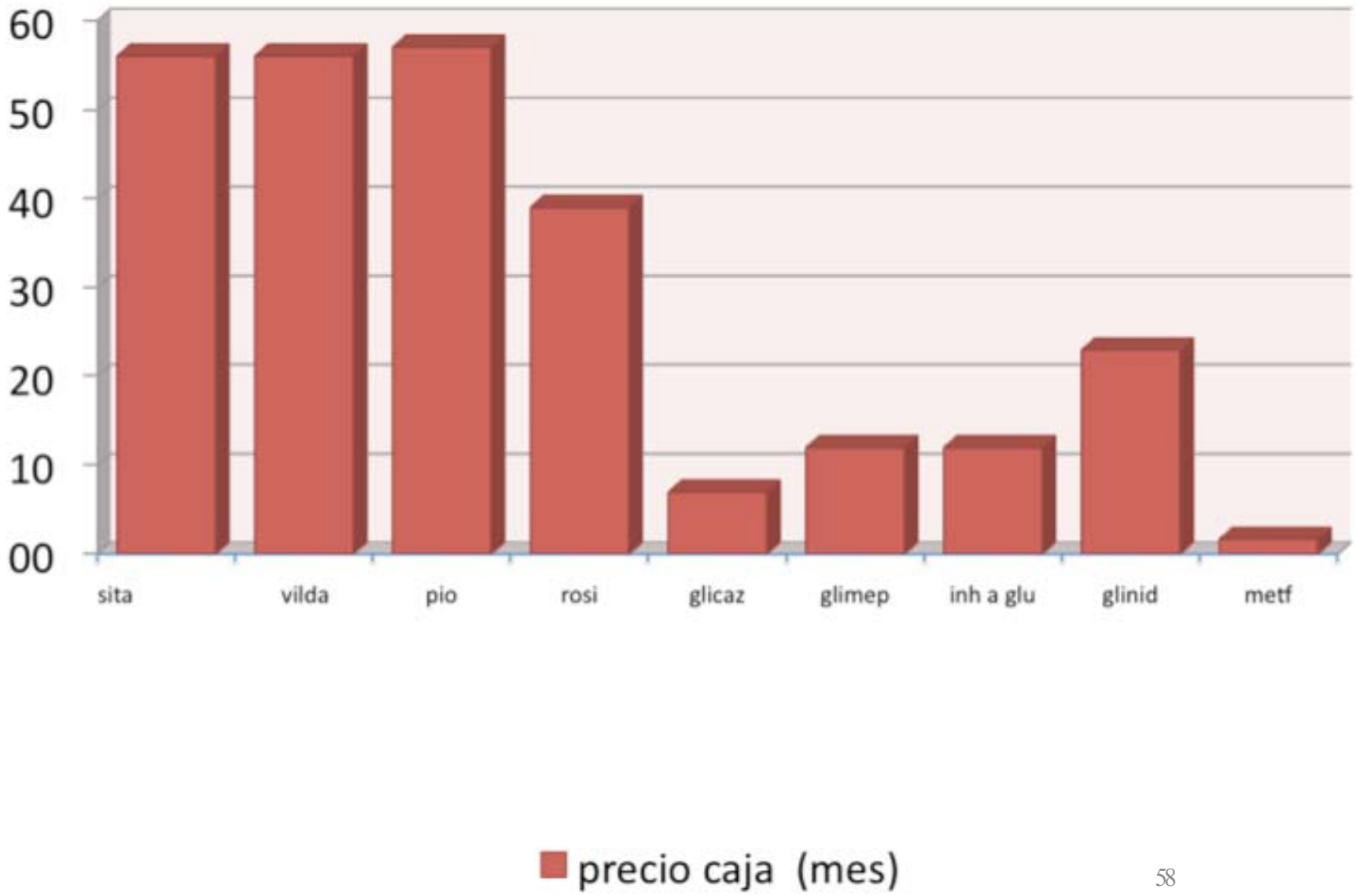
Treatment

At the end of the study

Combinations of ADO	Number of patients n= 1.202, n (%)
Metformina + SU	**530 (44,1)**
Metformina + Glitazonas	**191 (15,9)**
Metformina + Glinidas	**97 (8,1)**
Metformina + Insulina	**93 (7,7)**
Glitazonas + SU	**55 (4,6)**
Otros	**246 (19,6)**

(no datos de inhDPP4 inh 2008)

Diamond P Conthe, D Orozco et al. SEMI 2009


60
50
40
30
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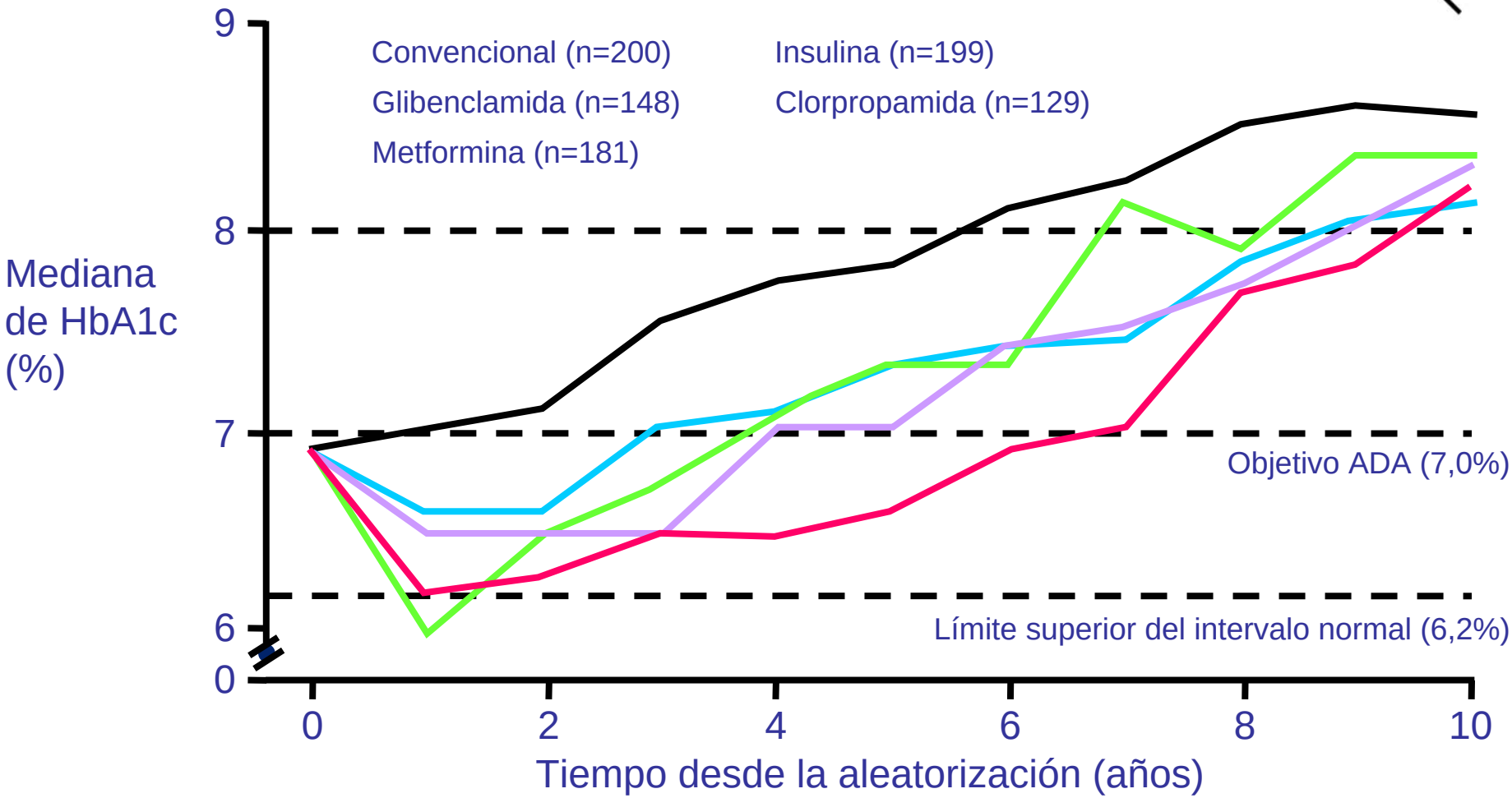
10
00
sita
vilda
pio
rosi
glicaz
glimep
inh a glu
glinid
metf
precio caja (mes)

UK Prospective Diabetes Study



UKPDS. Lancet 1998; 352: 854-865.

ORIGINAL ARTICLE

10-Year Follow-up of Intensive Glucose Control in Type 2 Diabetes

Rury R. Holman, F.R.C.P., Sanjoy K. Paul, Ph.D., M. Angelyn Bethel, M.D., David R. Matthews, F.R.C.P., and H. Andrew W. Neil, F.R.C.P.

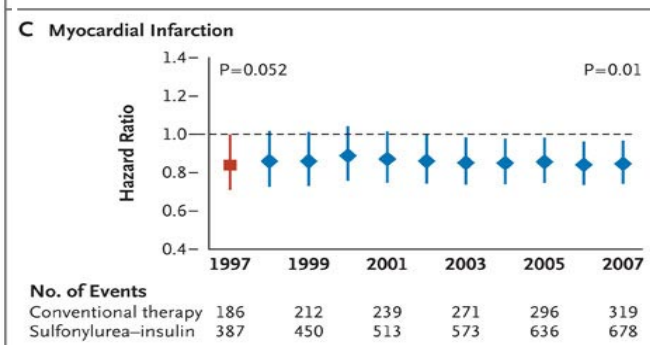
"Legacy effect"

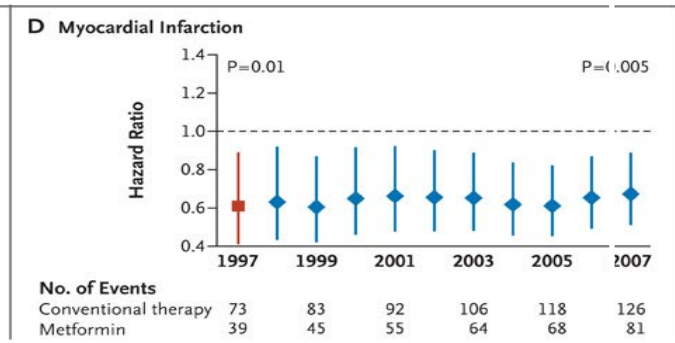
UKPDS Post-Trial

(10 años de seguimiento tras la finalización del Estudio)

Infarto de Miocardio

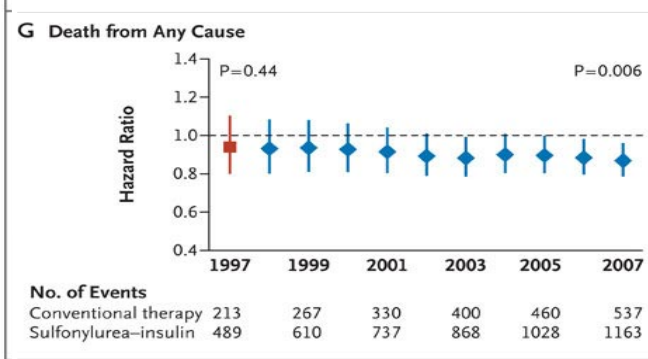
Sulfonilurea-Insulina | **Metformina**

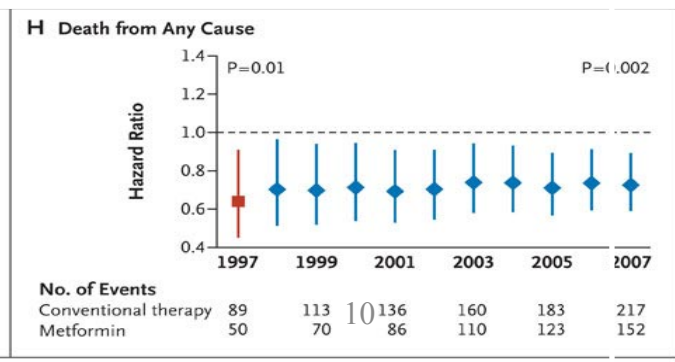




Mortalidad global

Sulfonilurea-Insulina | **Metformina**





Holman R et al.
N Engl J Med 2008;359:1577-1589

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JUNE 12, 2008 VOL. 358 NO. 24

Effects of Intensive Glucose Lowering in Type 2 Diabetes

The Action to Control Cardiovascular Risk in Diabetes Study Group*

ORIGINAL ARTICLE

Intensive Blood Glucose Control and Vascular Outcomes in Patients with Type 2 Diabetes

The ADVANCE Collaborative Group*

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Glucose Control and Vascular Complications in Veterans with Type 2 Diabetes

POSITION STATEMENT

Intensive Glycemic Control and the Prevention of Cardiovascular Events: Implications of the ACCORD, ADVANCE, and VA Diabetes Trials

A position statement of the American Diabetes Association and a scientific statement of the American College of Cardiology Foundation and the American Heart Association

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RICHARD BERGENSTAL, MD[2]
ROBERT O. BONOW, MD, MACC, FAHA[3]
JOHN BUSE, MD, PHD[4]
PRAKASH DEEDWANIA, MD, FACC, FAHA[5]
EDWIN A.M. GALE, MD[6]
BARBARA V. HOWARD, PHD[6,7]
M. SUE KIRKMAN, MD[8]
MIKHAIL KOSIBOROD, MD, FACC[9]
PETER REAVEN, MD[10]
ROBERT S. SHERWIN, MD[11]

Diabetes is defined by its association with hyperglycemia-specific microvascular complications; however, it also imparts a two- to fourfold risk of cardiovascular disease (CVD). Although microvascular complications can lead to significant morbidity and premature mortality, by far the greatest cause of death in people with diabetes is CVD.

Results from randomized controlled trials have demonstrated conclusively that the risk of microvascular complications can be reduced by intensive glycemic control in patients with type 1 (1,2) and type 2 diabetes (3–5). In the Diabetes Control and Complications Trial (DCCT), there was an ~60% reduction in development or progression of diabetic retinopathy, nephropathy, and neuropathy between the intensively treated group (goal A1C <6.05%, mean achieved A1C ~7%) and the standard group (A1C ~9%) over an average of 6.5 years. The relationship between glucose control (as reflected by the mean on-study A1C value) and risk of complications was log-linear and extended down to the normal A1C range (<6%) with no threshold noted.

In the UK Prospective Diabetes Study (UKPDS), participants newly diagnosed with type 2 diabetes were followed for 10 years, and intensive control (median A1C 7.0%) was found to reduce the overall microvascular complication rate by 25% compared with conventional treatment (median A1C 7.9%). Here, too, secondary analyses showed a continuous relationship between the risk of microvascular complications and glycemia extending into the normal range of A1C, with no glycemic threshold.

On the basis of these two large controlled trials, along with smaller studies and numerous epidemiologic reports, the consistent findings related to microvascular risk reduction with intensive glycemic control have led the American Diabetes Association (ADA) to recommend an A1C goal of <7% for most adults with diabetes (6), recognizing that more or less stringent goals may be appropriate for certain patients. Whereas many epidemiologic studies and meta-analyses (7,8) have clearly shown a direct relationship between A1C and CVD, the potential of intensive glycemic control to reduce CVD events has been less clearly defined. In the DCCT, there was a trend toward lower risk of CVD events with intensive control (risk reduction 41% [95% CI 10–68]), but the number of events was small. However, 9-year post-DCCT follow-up of the cohort has shown that participants previously randomized to the intensive arm had a 42% reduction ($P = 0.02$) in CVD outcomes and a 57% reduction ($P = 0.02$) in the risk of nonfatal myocardial infarction (MI), stroke, or CVD death compared with those previously in the standard arm (9).

The UKPDS of type 2 diabetes observed a 16% reduction in cardiovascular complications (combined fatal or nonfatal MI and sudden death) in the intensive glycemic control arm, although this difference was not statistically significant ($P = 0.052$), and there was no suggestion of benefit on other CVD outcomes such as stroke. However, in an epidemiologic analysis of the study cohort, a continuous association was observed such that for every percentage point of lower median on-study A1C (e.g., 8–7%) there was a statistically significant 18% reduction in CVD events, again with no glycemic threshold.

Because of ongoing uncertainty regarding whether intensive glycemic control can reduce the increased risk of CVD in people with type 2 diabetes, several large long-term trials were launched in the past decade to compare the effects of intensive versus standard glycemic con-

From the [1]University of Miami, Miami, Florida; the [2]International Diabetes Center at Park Nicollet, Minneapolis, Minnesota; the [3]Northwestern University Feinberg School of Medicine, Chicago, Illinois; the [4]University of North Carolina, Chapel Hill, North Carolina; the [5]VA Central California Healthcare System, University of California San Francisco, Fresno, California; the [6]University of Bristol, Bristol, U.K.; [7]MedStar Research Institute, Hyattsville, Maryland; the [8]American Diabetes Association, Alexandria, Virginia; the [9]Mid America Heart Institute of Saint Luke's Hospital and the University of Missouri-Kansas City, Kansas City, Missouri; the [10]Carl T. Hayden VA Medical Center, Phoenix, Arizona; and [11]Yale University School of Medicine, New Haven, Connecticut.

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DOI: 10.2337/dc08-9026

Effect of intensive control of glucose on cardiovascular outcomes and death in patients with diabetes mellitus: a meta-analysis of randomised controlled trials

Kausik K Ray, Sreenivasa Rao Kondapally Seshasai*, Shanelle Wijesuriya*, Rupa Sivakumaran*, Sarah Nethercott*, David Preiss, Sebhat Erqou, Naveed Sattar

	UKPDS-follow-up	Proactive	ADVANCE	VADT	ACCORD	Total
n	4620	5238	11140	1791	10251	33040
Years	10.1	2.9	5.0	5.6	3.5	4.95
Patient-years	46,237	15,059	55,700	10,030	35,879	162,905
Control	7·9%	7·6%	7·3%	8·4%	7·5%	7·5%
Intensve	7·0%	7·0%	6·5%	6·5%	6·4%	6·6%

Lancet 2009; 373: 1765–72

Effect of intensive control of glucose on cardiovascular outcomes and death in patients with diabetes mellitus: a meta-analysis of randomised controlled trials

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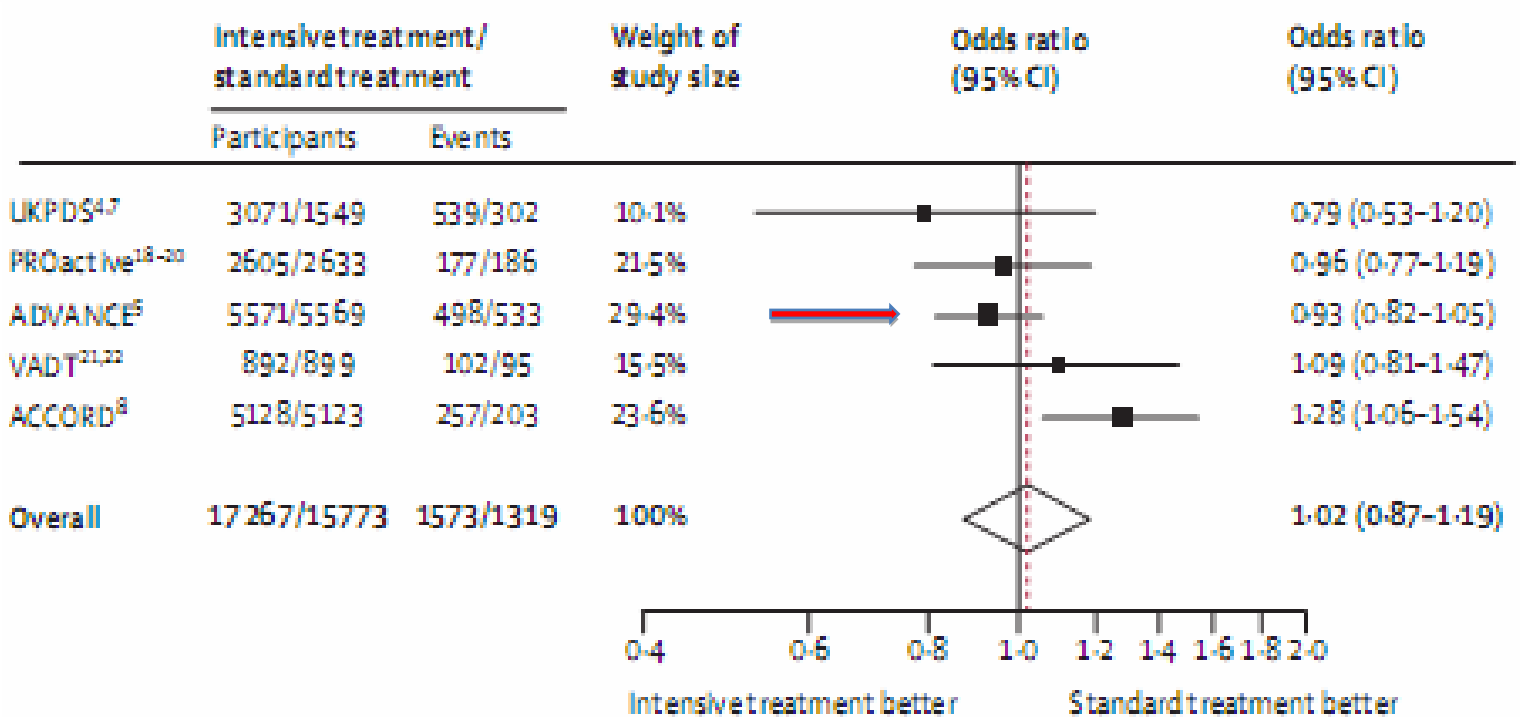
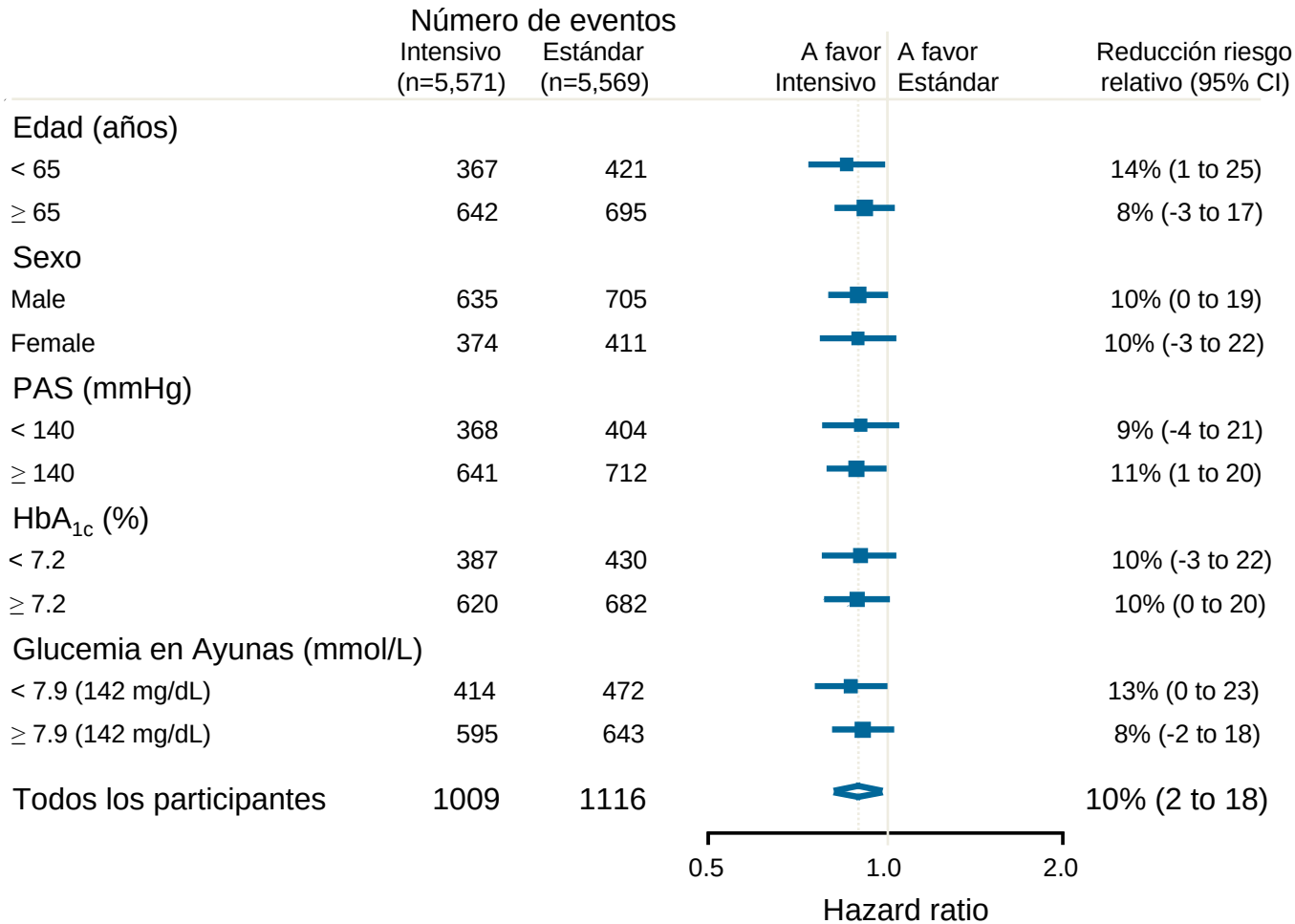


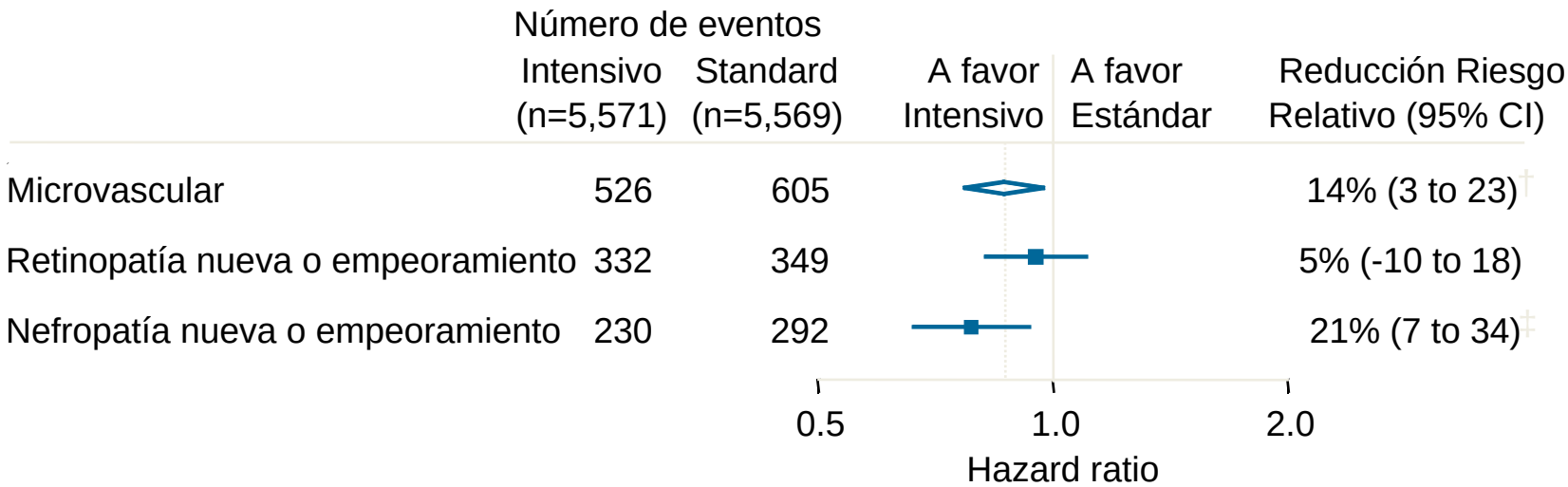
All-cause mortality

Lancet 2009; 373: 1765–72

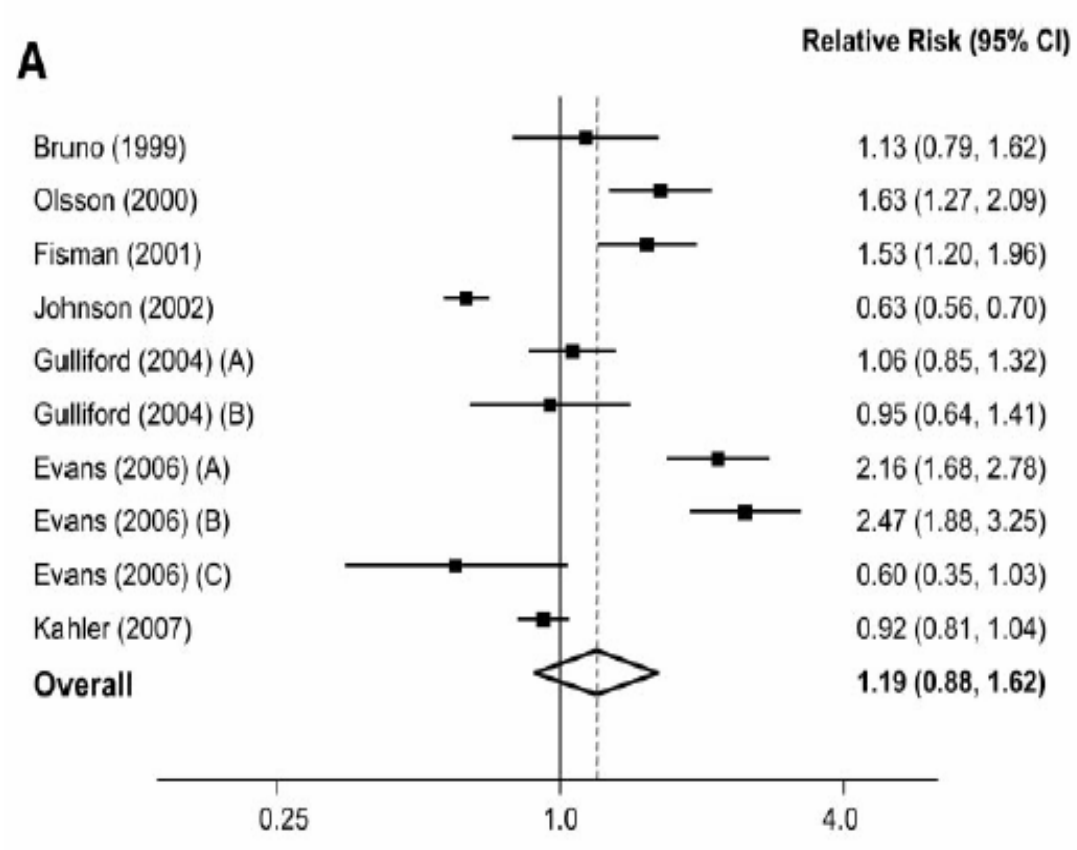
Efecto por edad, sexo, PAS y Control Glucémico: *Objetivo Primario Combinado*



Complicaciones Microvasculares



SULFONILUREAS +METFORMINA : mortalidad



Meta- analysis. Rao et al. Diabetes Care 31:1672–1678, 2008

Effect of Second-Generation Sulfonylureas on Survival in Patien With Diabetes Mellitus After Myocardial Infarction

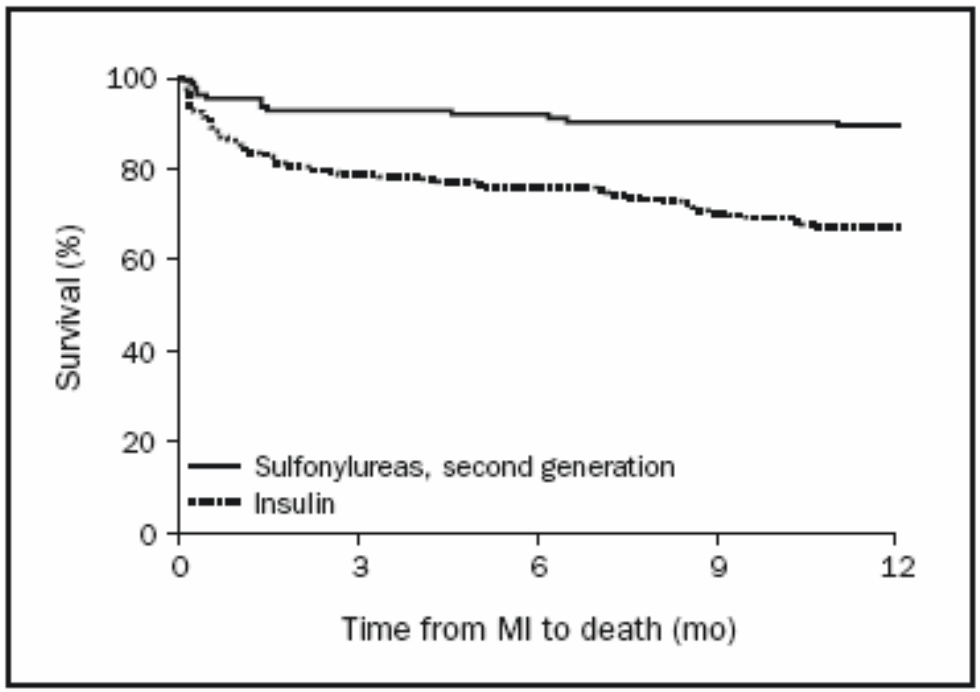
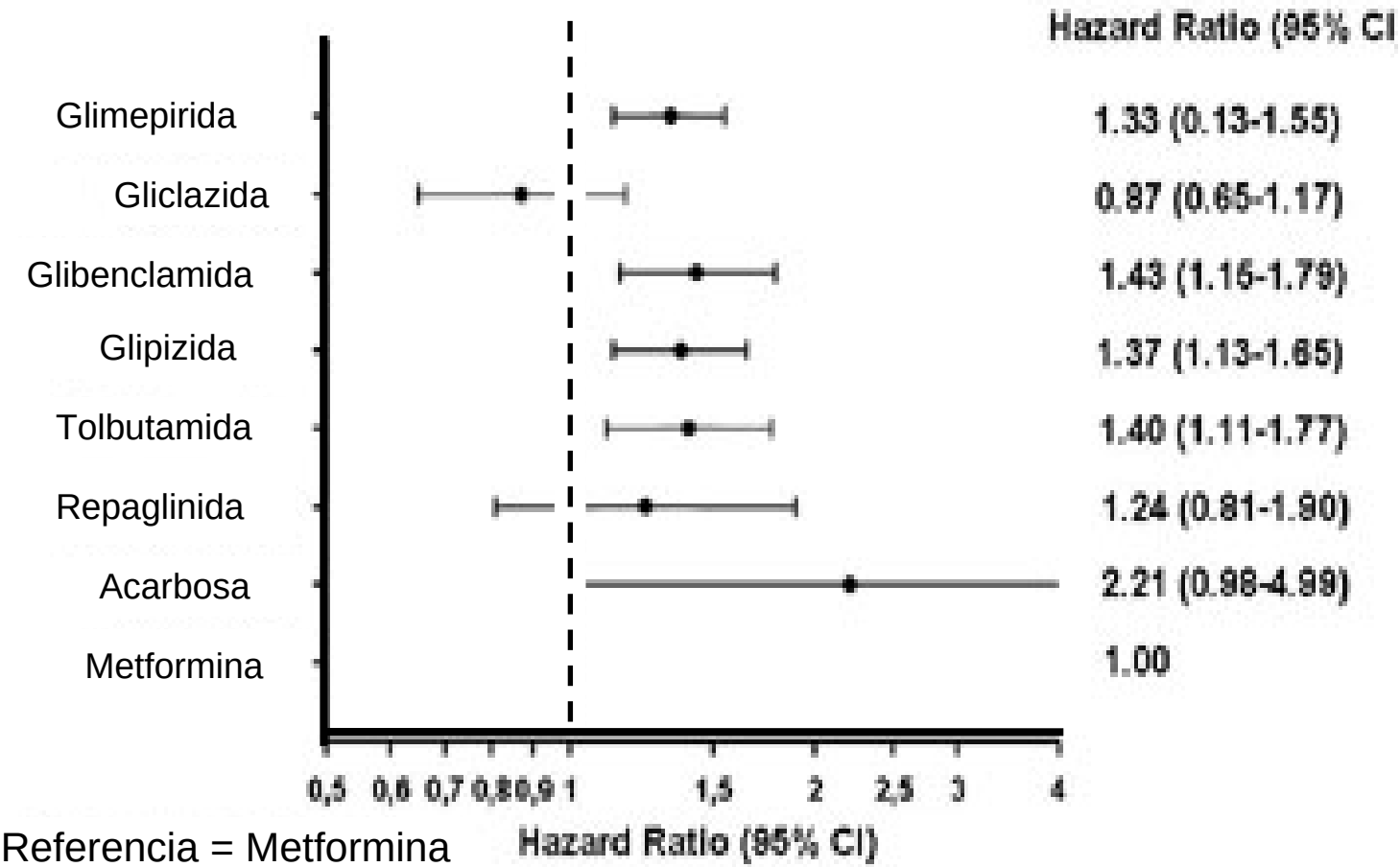


FIGURE 2. Survival after myocardial infarction (MI) for diabetic patients treated with second-generation sulfonylureas and those treated with insulin.

Arruda-Olson et al. Mayo Clin Proc. 2009;84(1):28-33

Riesgo de Muerte en relación con utilización de Antidiabéticos orales (Pacientes con DM e IAM previo)

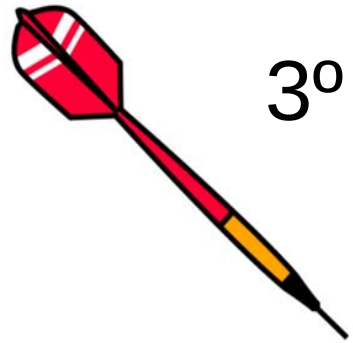
Mortalidad Global



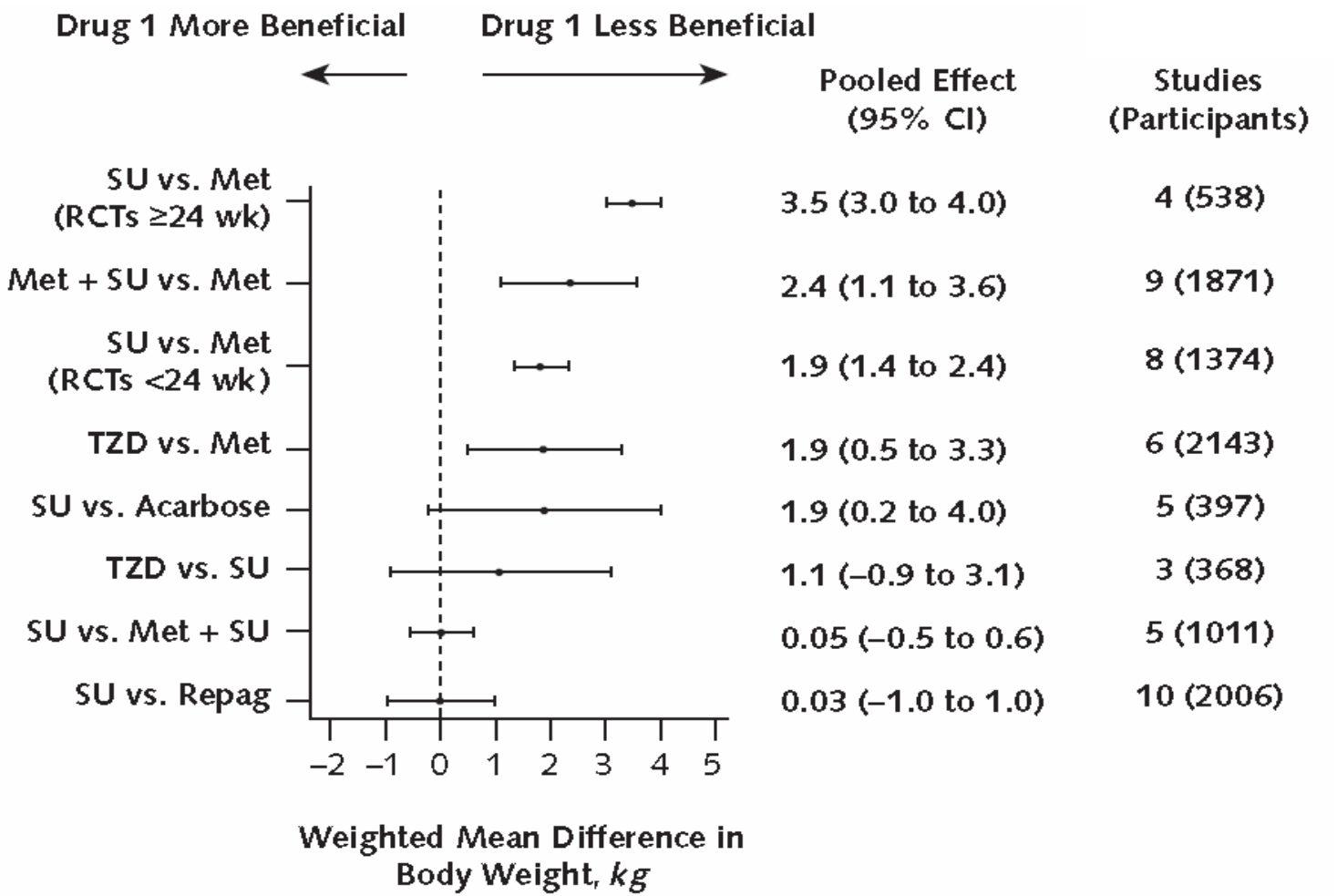
Referencia = Metformina

Schramml et al Steno Diabetes Center Eur Heart J. 2009:30, 304

El tema del peso…

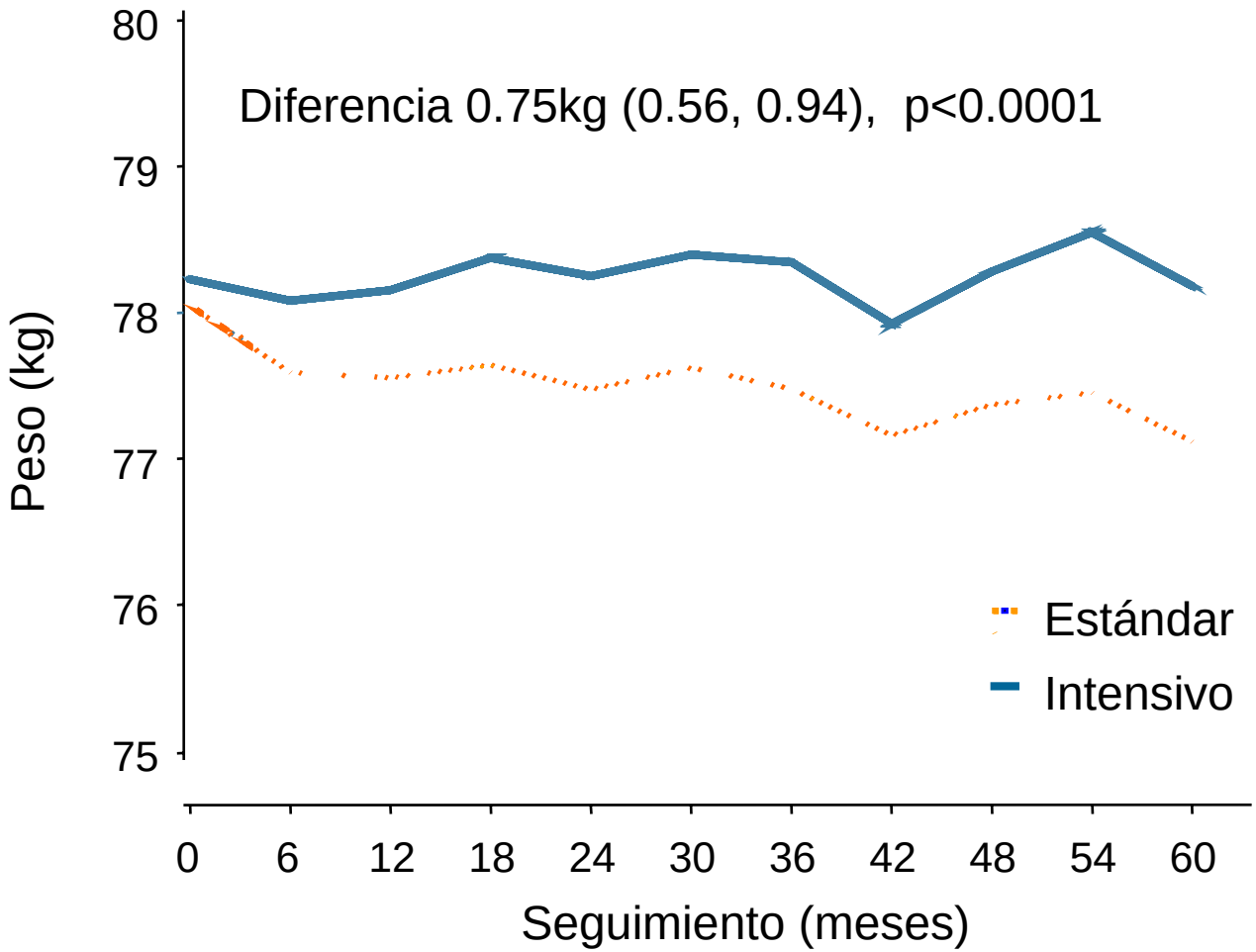


3º



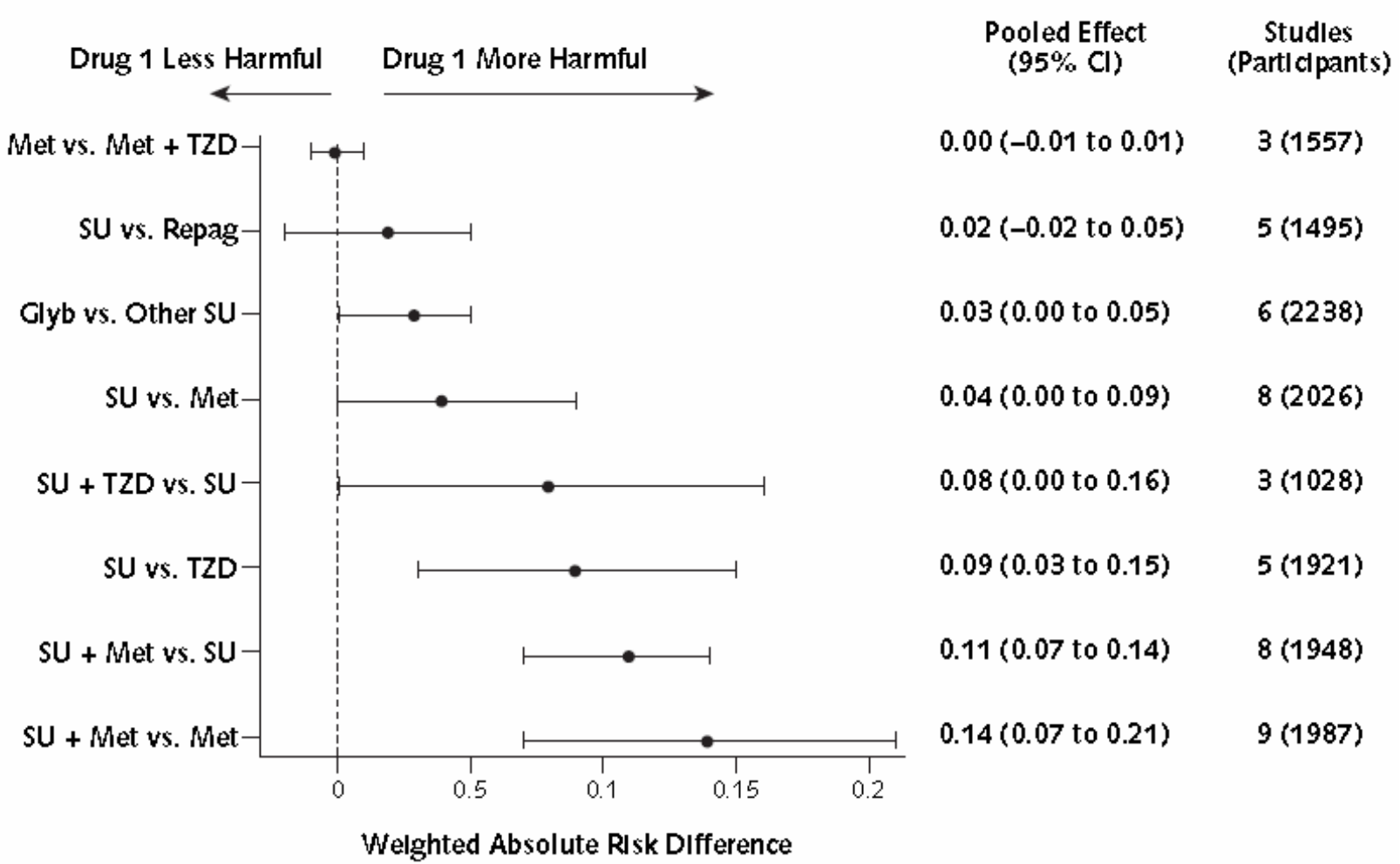
Bolen S, et al. Ann Intern Med. 2007;147

Diferencia en el Peso Corporal



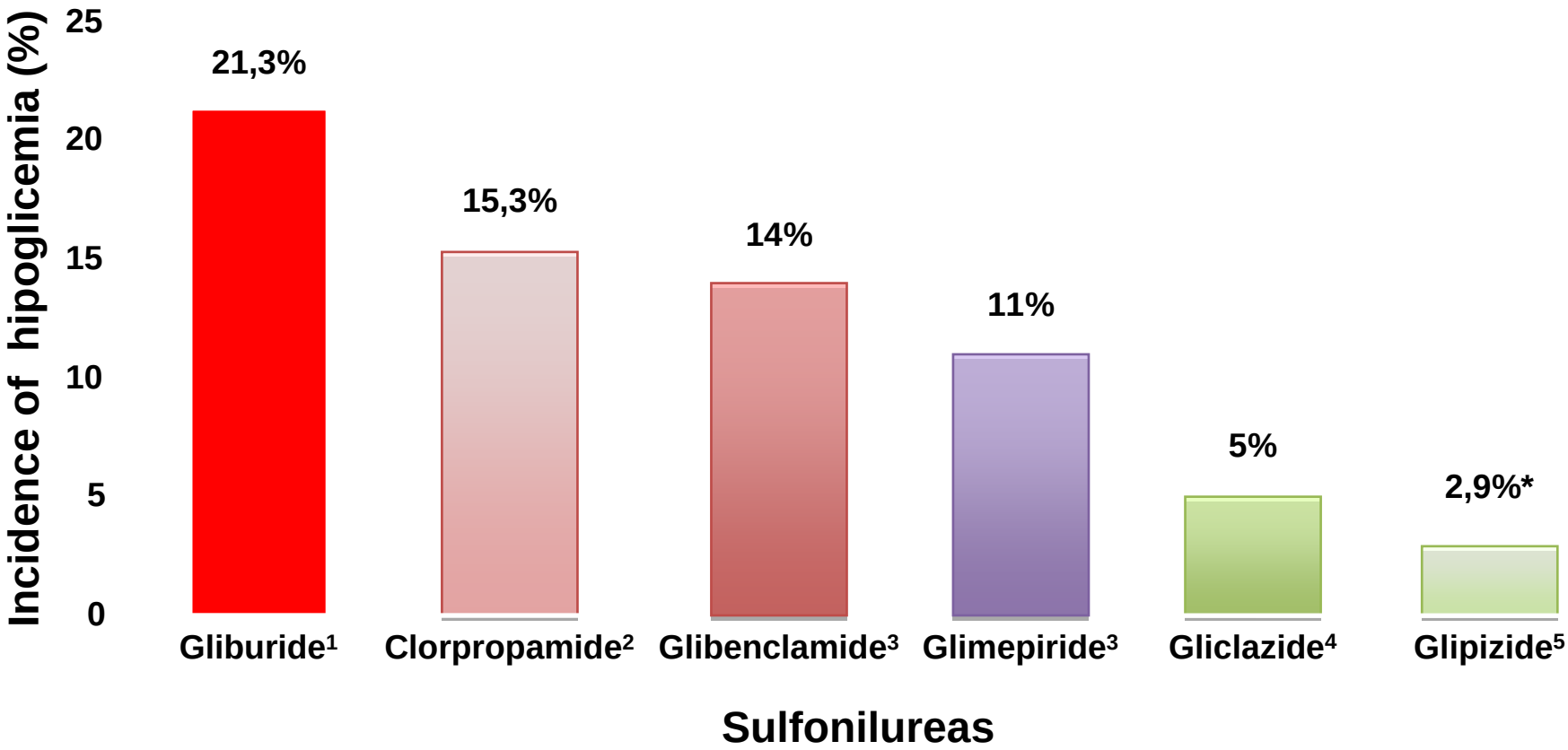
El tema de la hipoglucemia…

3º



Bolen S, et al. Ann Intern Med. 2007;147(6):386-399.

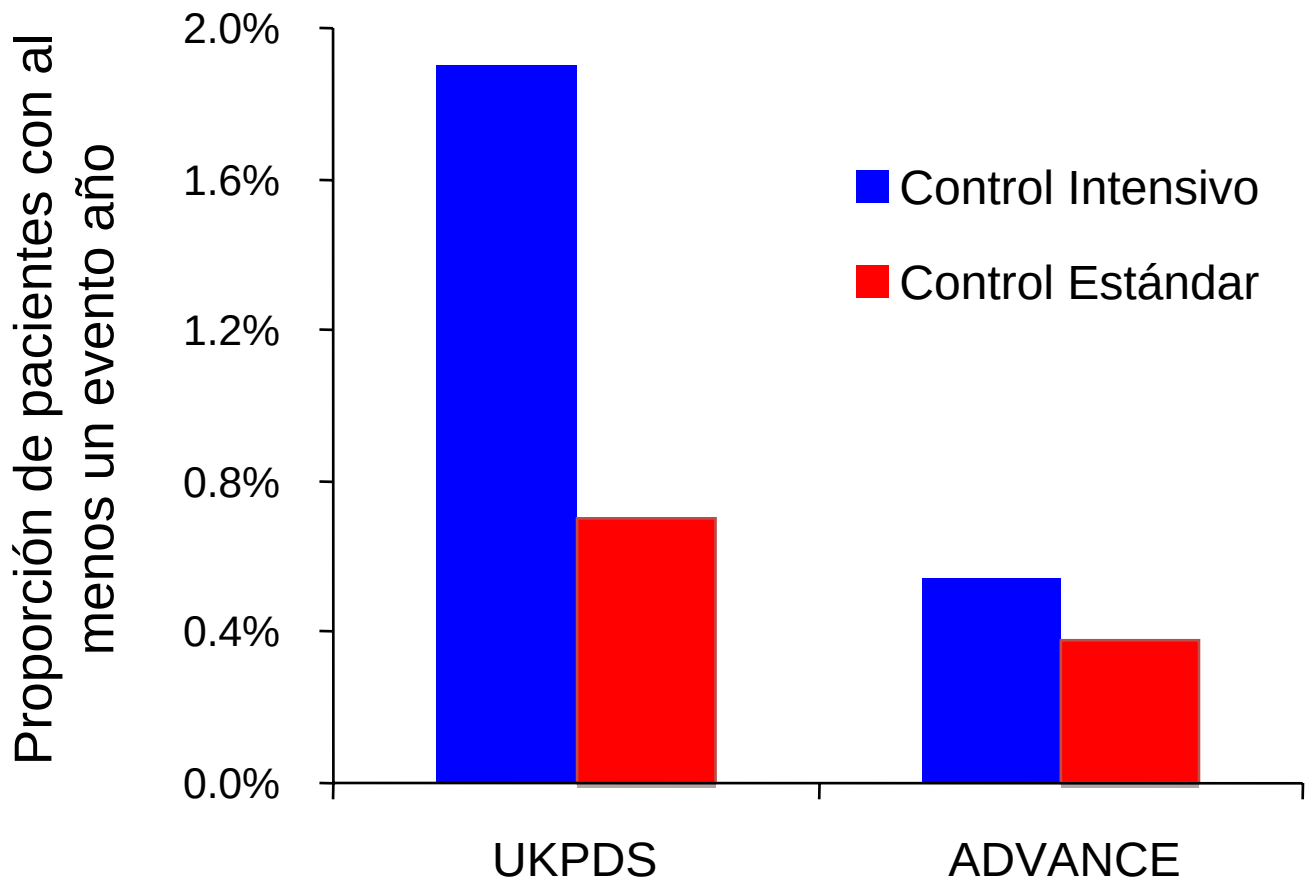
Hipoglucemia y Sulfonilureas



- *Glu $\leq$ 50 mg/dL (2,75 mmol/L)

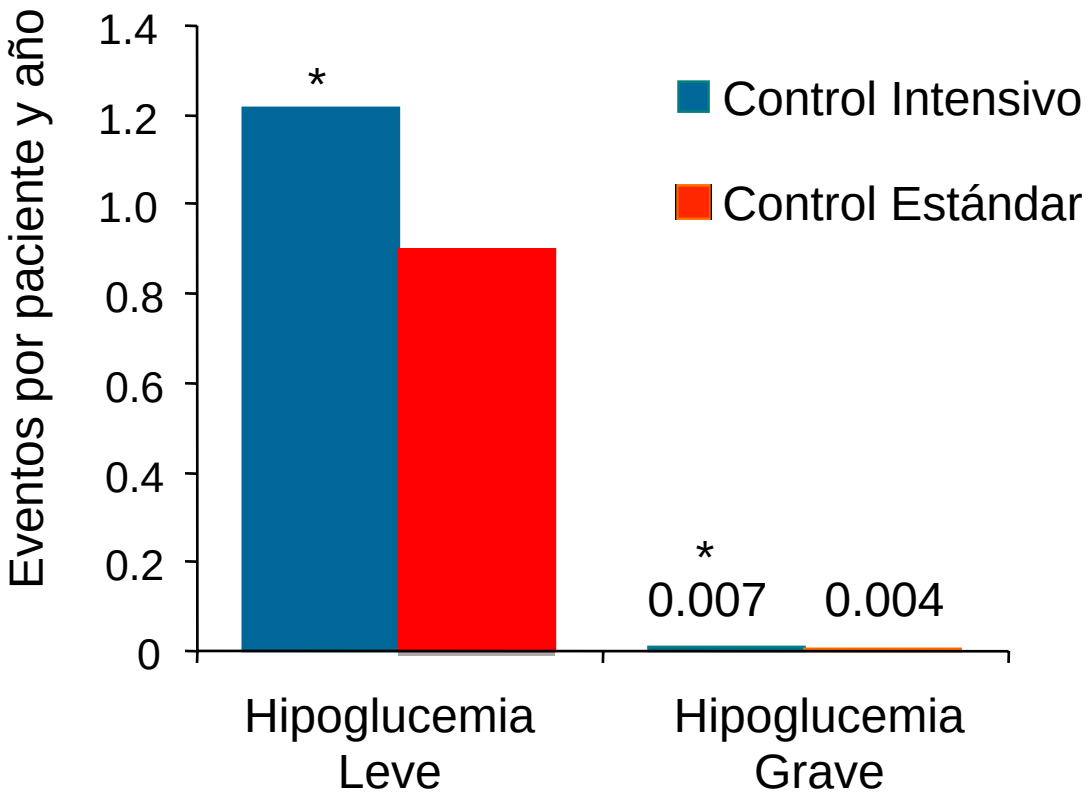
•1. Glucovance [prospect]. Princeton, NJ: Bristol-Myers Squibb Company; 2004. 2. UKPDS Group. *Lancet* 1998; 352: 837–853. 3. Draeger KE, et al. *Horm Metab Res*. 1996; 28: 419–425. 4. McGavin JK, et al. *Drugs* 2002; 62; 1357–1364. 5. Metaglip [prospect]. Princeton, NJ: Bristol-Myers Squibb Company; 2002

Tasas de Hipoglucemia Grave



Tasa de Hipoglucemia

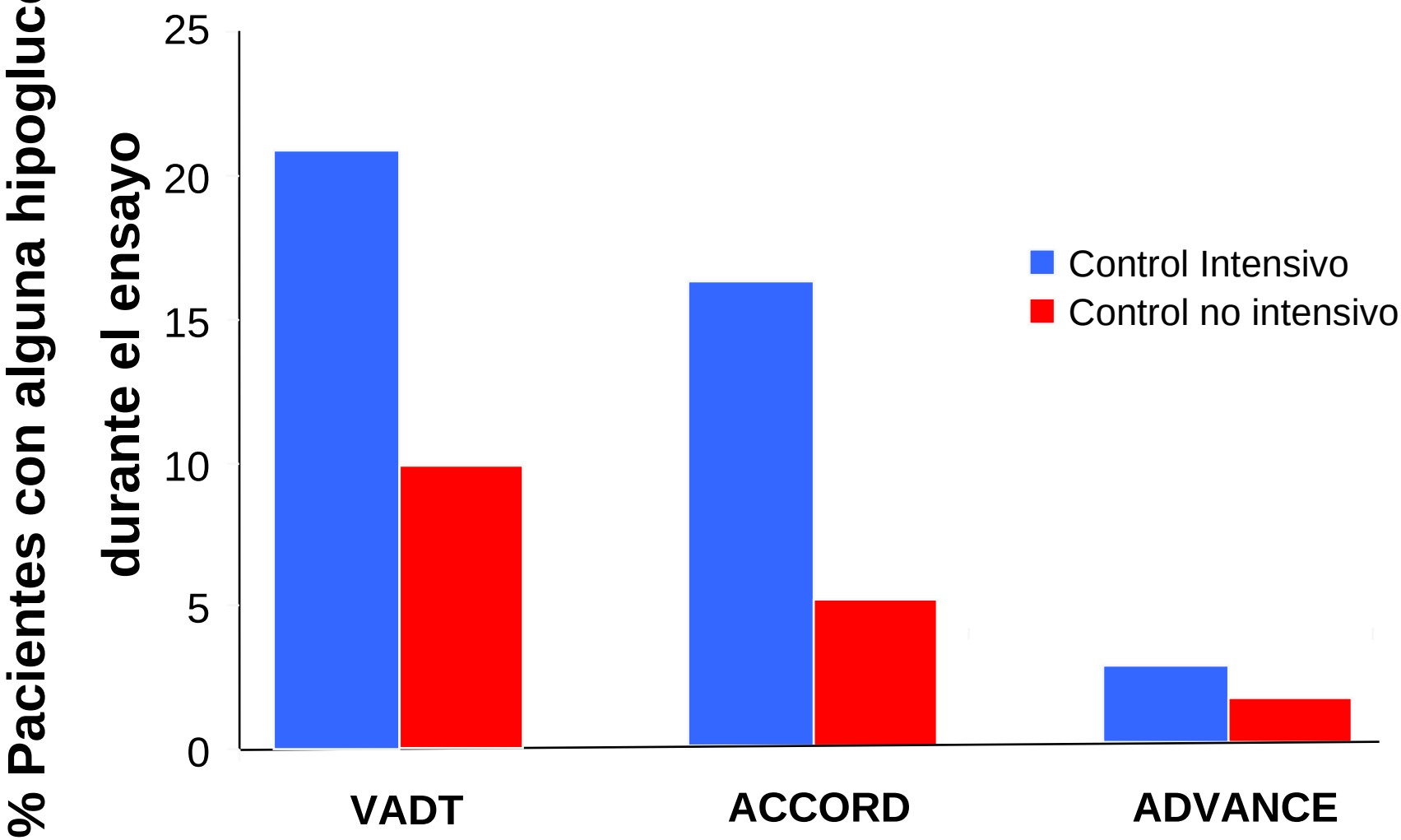
Leve y Grave



*p<0.001

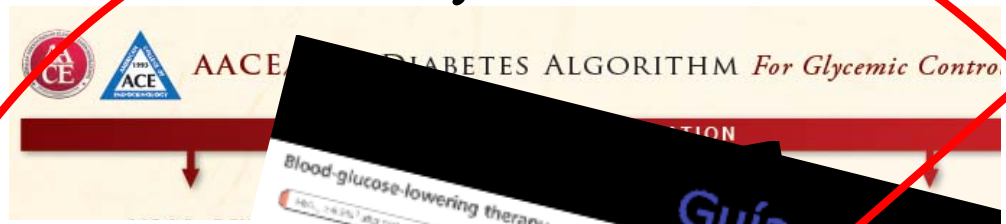
ADVANCE

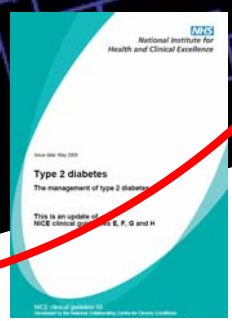
Hipoglicemia severa en los ensayos recientes de tratamiento intensivo en diabetes tipo 2



Consensos y Guías Clínicas

4º

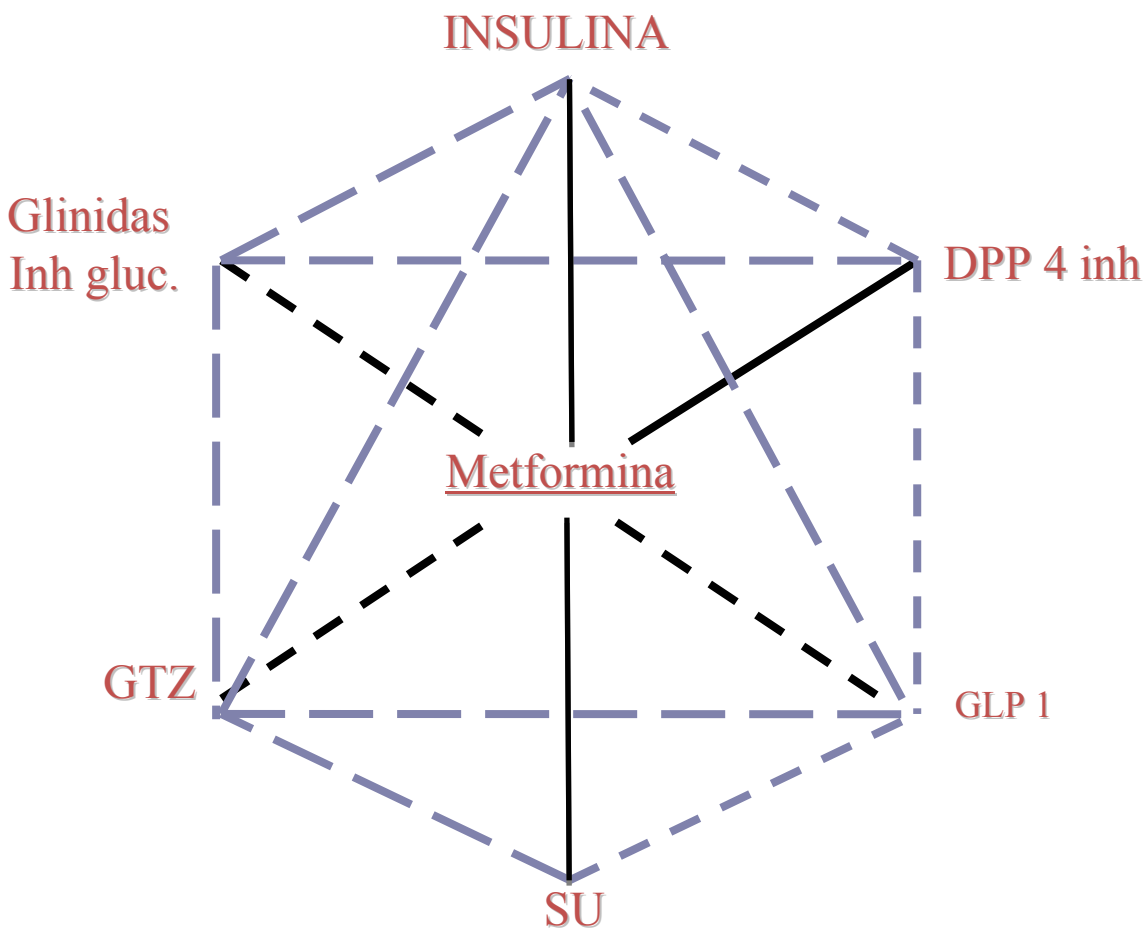




El objetivo A1c <7 % corresponde a un intervalo de normalidad del 4-6 %. Para otros valores de normalidad el objetivo debe calcularse (media + 4DE).
Se debe individualizar según las características del paciente.

"mi guía"

Tratamiento combinado en la Diabetes Mellitus tipo 2



1º Metformina de inicio

2º INDIVIDUALIZAR combinación según perfil

3º Intensificar (3-6 meses) hasta objetivos (A1c 6,5% - 7,5 %)

J L PALMA
glitazonas

JG CEREZO
GLP$_1$

R G HUELGAS
insulina

J.G.ALEGRIA
Inh-DPP$_4$

P CONTHE
su

1ª pregunta

¿Qué sulfonilureas no utilizaría por elevadas tasas de hipoglucemias severas?

- Glibenclamida
- Glimepirida
- Glicazida
- Glipizida
- Glipentida

1ª pregunta

¿Qué sulfonilureas no utilizaría por elevadas tasas de hipoglucemias severas?

- Glibenclamida
- Glimepirida
- Glicazida
- Glipizida
- Glipentida

2ª pregunta

¿Qué tienen en común las recomendaciones terapeúticas vigentes en control glucémico de DM tipo 2?

- Utilizar sulfonilureas de inicio y en combinación
- Empezar con 2 fármacos hipoglucemiantes
- La Insulina debe relegarse para casos avanzados
- Con dieta y ejercicio se pueden controlar muchos pacientes
- De inicio metformina al diagnóstico e individualizar

2ª pregunta

¿Qué tienen en común las recomendaciones terapeúticas vigentes en control glucémico de DM tipo 2?

- Utilizar sulfonilureas de inicio y en combinación
- Empezar con 2 fármacos hipoglucemiantes
- La Insulina debe relegarse para casos avanzados
- Con dieta y ejercicio se pueden controlar muchos pacientes
- De inicio metformina al diagnóstico e individualizar

- pregunta

  ¿En qué programa se ha basado esta charla?