XXXII Congreso Nacional de la SEMI

XIV Congreso de la Sociedad Canaria de Medicina Interna

26-28 Octubre 2011

LAS SULFONILUREAS A DEBATE

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redGDPS
Red de Grupos de Estudio de la Diabetes
EN ATENCIÓN PRIMARIA DE LA SALUD

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A FAVOR DE LAS SULFONILUREAS

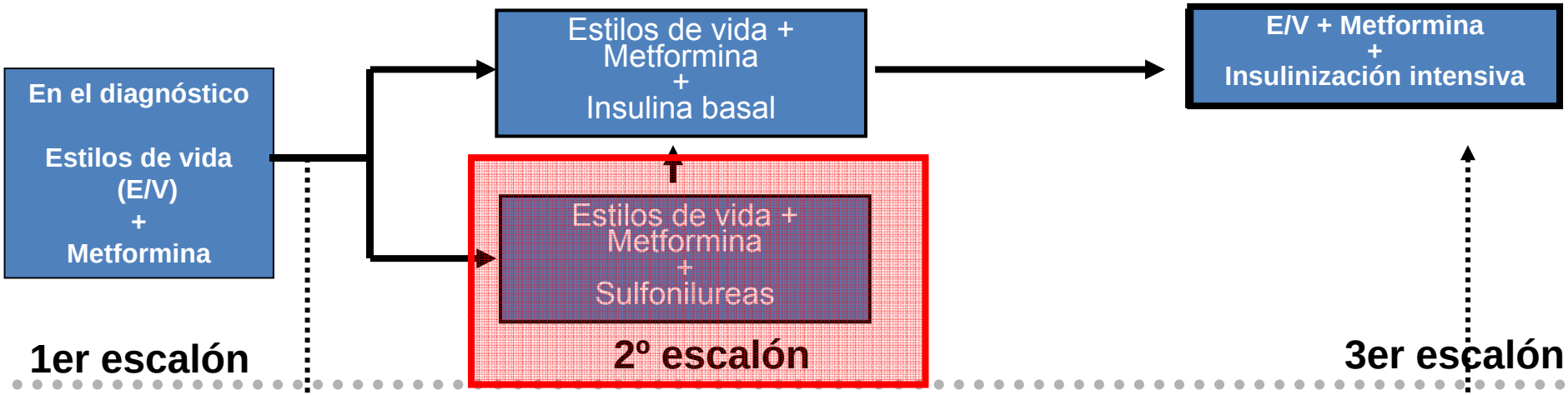
- Posición de las SU en las Guías de Tratamiento
- Ventajas de las SU
- Problemas atribuidos a las SU
- Conclusiones

Algoritmo de tratamiento DM2 ADA/EASD 2008

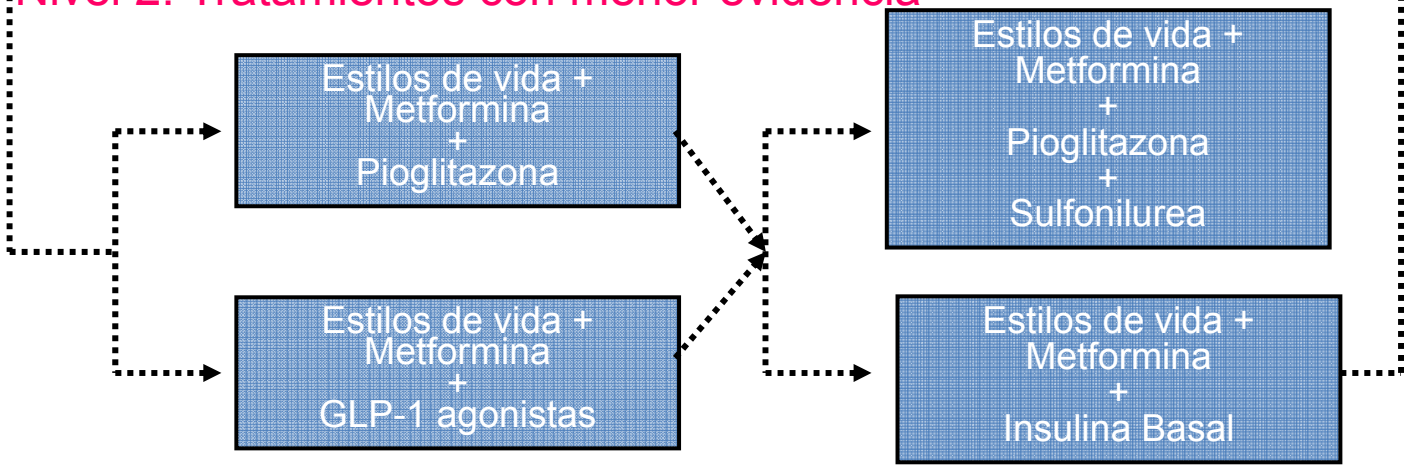
Medical Management of Hyperglycemia in Type 2 Diabetes: A Consensus Algorithm for the Initiation and Adjustment of Therapy

A consensus statement of the American Diabetes Association and the European Association for the Study of Diabetes

Nivel 1: Tratamientos básicos con buena evidencia

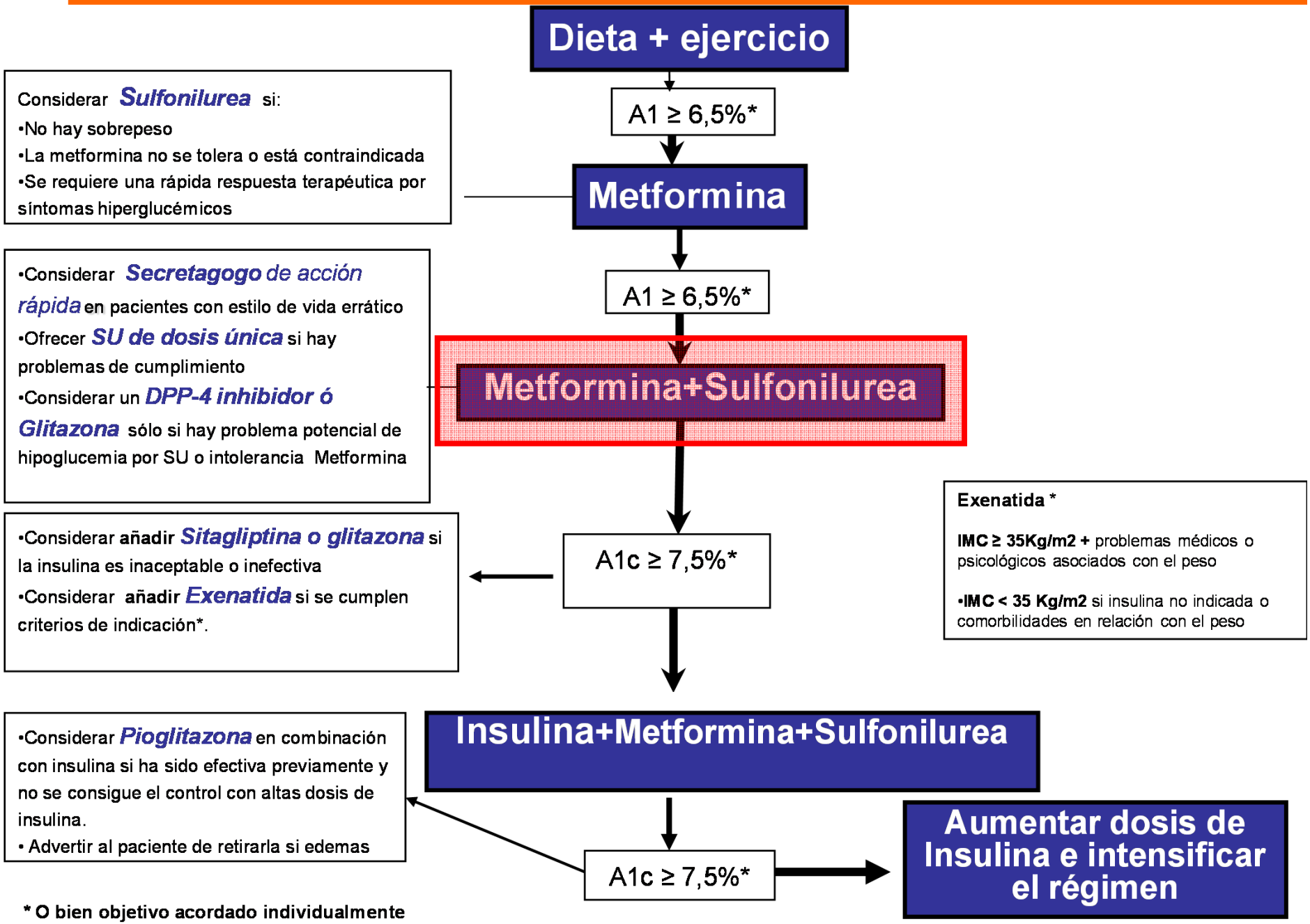


Nivel 2: Tratamientos con menor evidencia



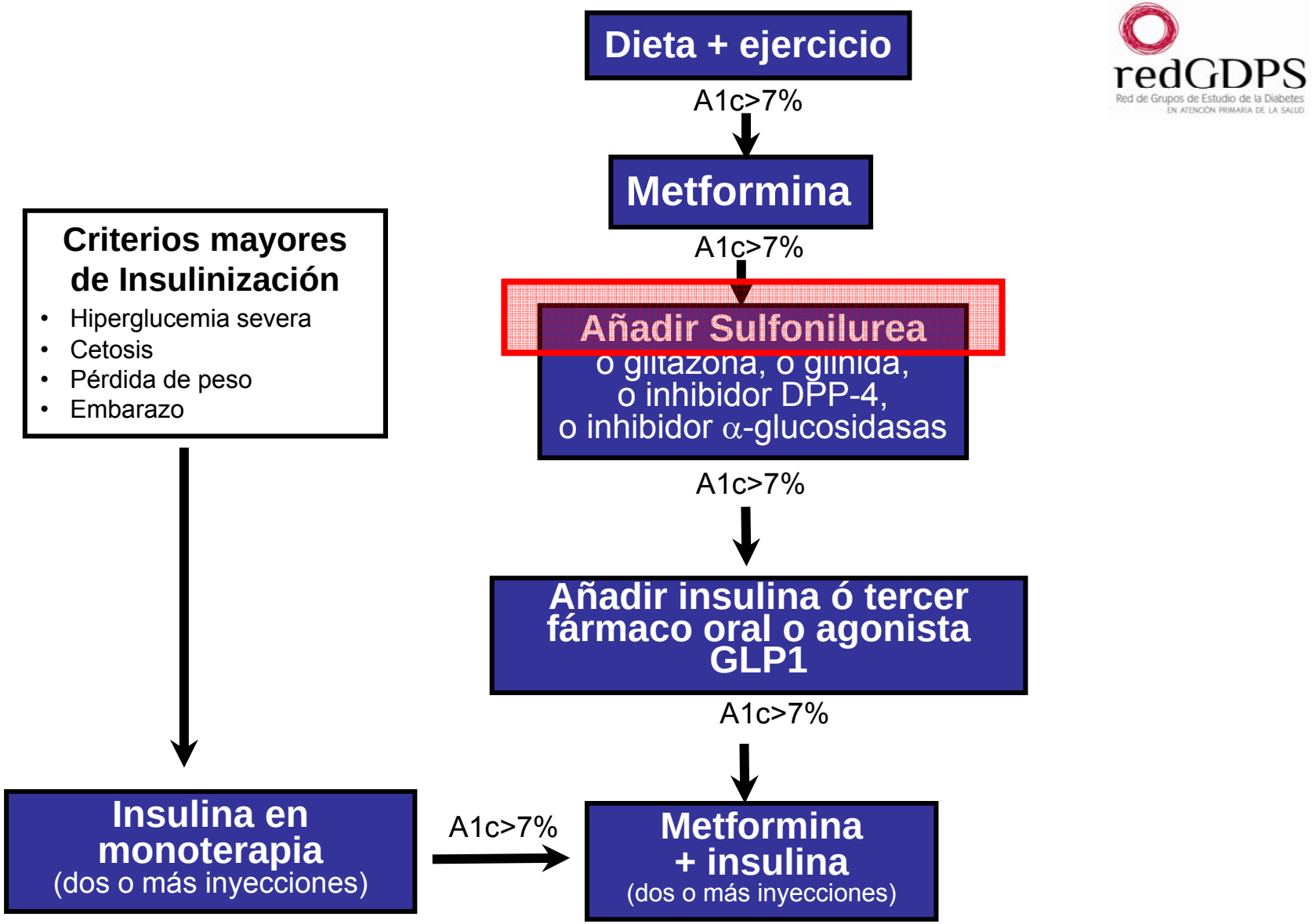
Nathan D. Diabetes Care 2008;31:1–11.

Algoritmo de tratamiento de la DM2 - NICE 2009



*** O bien objetivo acordado individualmente**

Algoritmo de tratamiento de la DM2. GEDAPS 2009



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

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

*2 - 3 Mos.****

Triple Therapy

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

*2 - 3 Mos.****

Triple Therapy [9]

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

*2 - 3 Mos.****

INSULIN ± Other Agent(s) [6]

A1C > 9.0%

Drug Naive | *Under Treatment*

Symptoms | *No Symptoms*

INSULIN ± Other Agent(s) [6]

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

INSULIN ± Other Agent(s) [6]

AACE/ACE Algorithm for Glycemic Control Subcommittee

Co chairpersons:
Helena W. Rodbard, MD, FACP, MACE
Paul S. Jellinger, MD, MACE

Zachary T. Bloomgarden, MD, FACE
Jaime A. Davidson, MD, FACP, MACE
Daniel Einhorn, MD, FACP, FACE
Alan J. Garber, MD, PhD, FACE
James R. Gavin III, MD, PhD
George Grunberger, MD, FACP, FACE
Yehuda Handelsman, MD, FACP, FACE
Edward S. Horton, MD, FACE
Harold Lebovitz, MD, FACE
Philip Levy, MD, MACE
Etie S. Moghissi, MD, FACP, FACE
Stanley S. Schwartz, MD, FACE

* May not be 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 nonalcoholic 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 pramlintide with prandial insulin

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

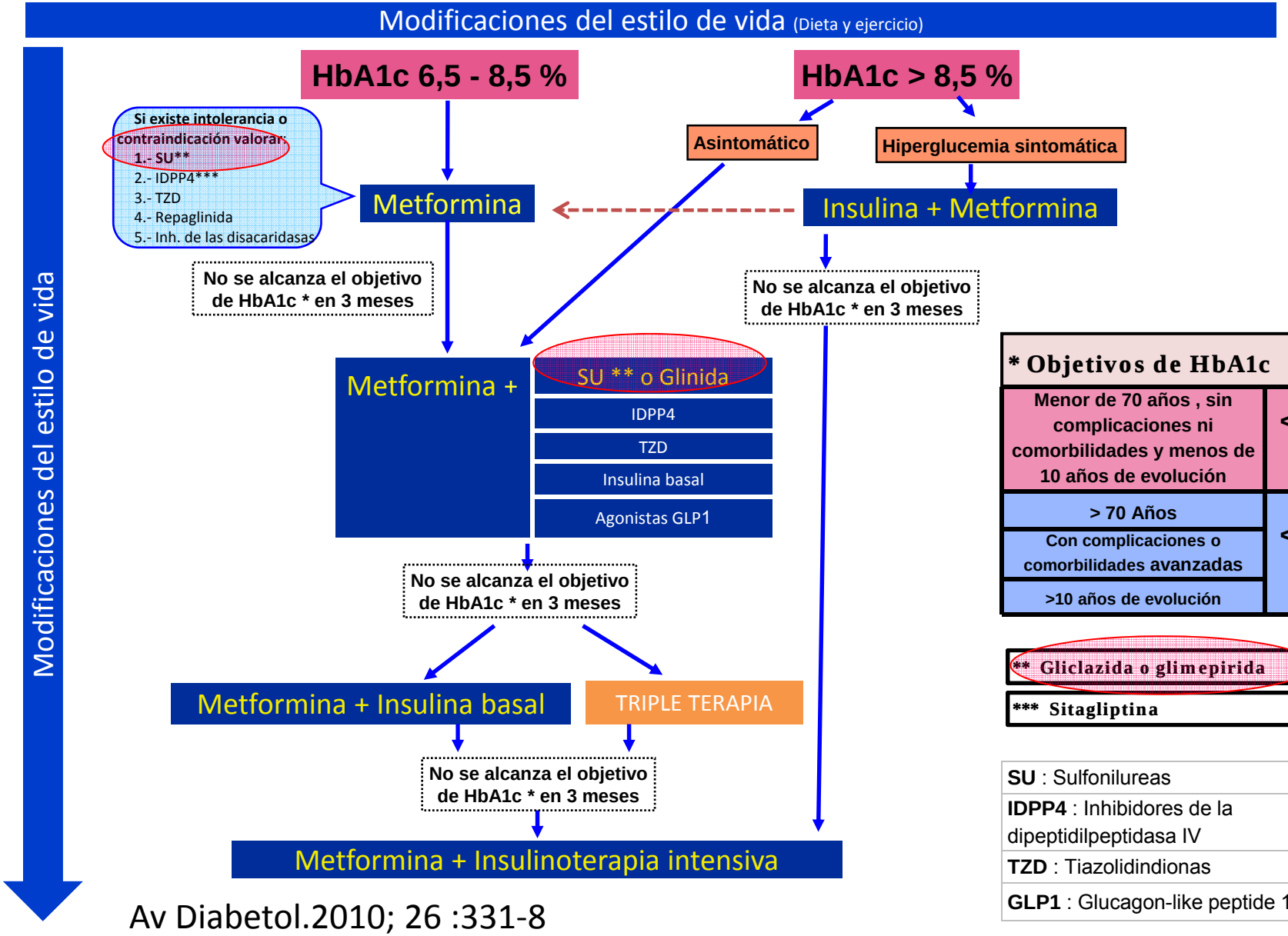
8 If A1C < 8.5%, combination Rx with agents that cause hypoglycemia should be used with caution

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

10 GLP-1 not approved for initial combination Rx

Available at www.aace.com/pub

Tratamiento de la hiperglucemia en la diabetes tipo 2. Algoritmo de la Sociedad Española de Diabetes



* Objetivos de HbA1c	
Menor de 70 años , sin complicaciones ni comorbilidades y menos de 10 años de evolución	<6,5 %
> 70 Años Con complicaciones o comorbilidades avanzadas >10 años de evolución	<7,5 %

** Gliclazida o glimepirida

*** Sitagliptina

SU : Sulfonilureas
IDPP4 : Inhibidores de la dipeptidilpeptidasa IV
TZD : Tiazolidindionas
GLP1 : Glucagon-like peptide 1

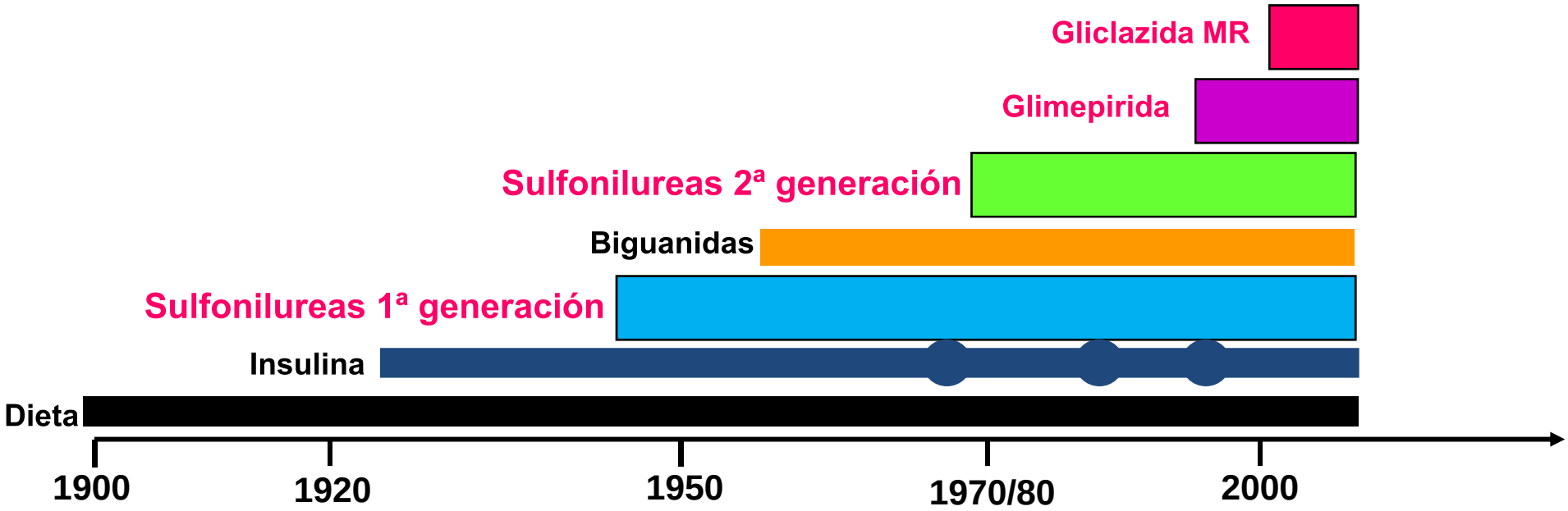
Av Diabetol.2010; 26 :331-8

VENTAJAS DE LAS SULFONILUREAS

Beneficios clínicos

- **Experiencia de uso**
- **Eficacia** descenso HbA1c
- **Rapidez** descenso glucemia
- Reducción de **objetivos finales**
- **“Memoria metabólica”**
- Reducción de complicaciones **microvasculares**
- **Coste**

EXPERIENCIA USO



EFICACIA comparativa de los antidiabeticos orales sobre la HbA1c

REVIEW | Annals of Internal Medicine

Systematic Review: Comparative Effectiveness and Safety of Oral Medications for Type 2 Diabetes Mellitus

Shari Bolen, MD, MPH; Leonard Feldman, MD; Jason Vassy, MD, MPH; Lisa Wilson, BS, ScM; Hsin-Chieh Yeh, PhD; Spyridon Marinopoulos, MD, MBA; Crystal Wiley, MD, MPH; Elizabeth Selvin, PhD; Renee Wilson, MS; Eric B. Bass, MD, MPH; and Frederick L. Brancati, MD, MHS

		estudios	Δ HbA1c*	IC 95%
Metformina	vs control	15	-1,14	-1,40 a -0,87
Sulfonilureas	vs control	11	-1,52	-1,75 a -1,28
Pioglitazona	vs control	9	-0,97	-1,18 a -0,75
Rosiglitazona	vs control	8	-1,16	-0,39 a -0,92
Repaglinida	vs control	4	-1,32	-1,90 a -0,80
Nateglinida	vs control	4	-0,54	-0,80 a -0,27
Acarbosa	vs control	28	-0,77	-0,90 a -0,64

* Diferencias medias ajustadas

Bolen S et al. Ann Int Med 2007; 147:386-99

Beneficios del tratamiento de la DM2

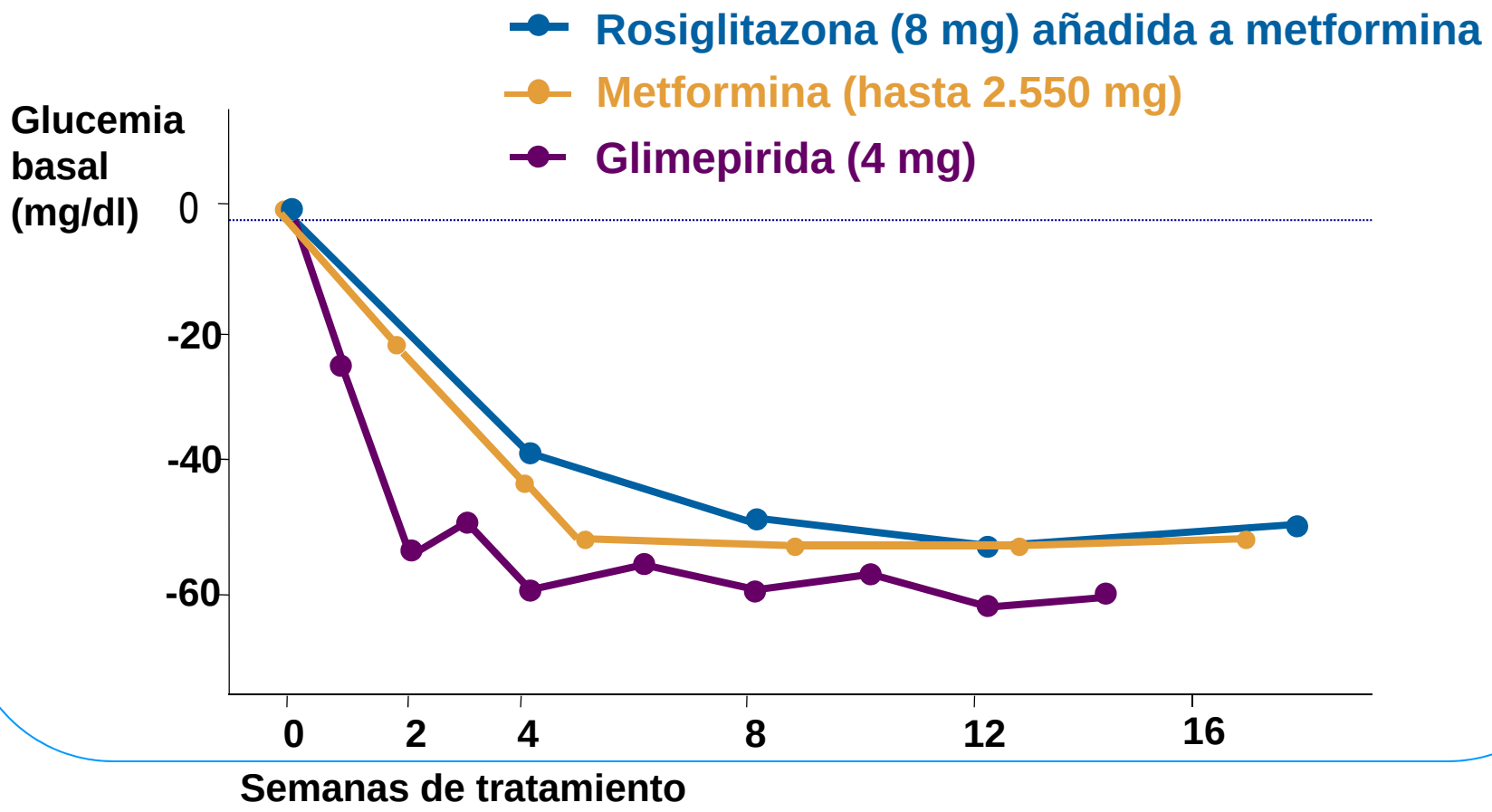
UKPDS 35: Estudio Observacional Prospectivo

Reducción del riesgo por 1 punto de descenso de la HbA1c

Cualquier indicador final	21 %
Complicaciones Microvasculares	37 %
Muerte relacionada con la DM	21 %
Infarto Agudo de Miocardio	14 %
Accidente Vascular Cerebral	12 %
Insuficiencia cardiaca	16 %

UKPDS 35. BMJ 2000; 321:405-412.

RAPIDEZ: **Tiempo de acción de los ADOS**



DeFronzo RA et al. ***N Engl J Med. 1995;333:541-549****; Fonseca V et al.* ***JAMA 2000;283:1695-1702****; Goldberg RB et al.* ***Diabetes Care. 1996;19:849-856***

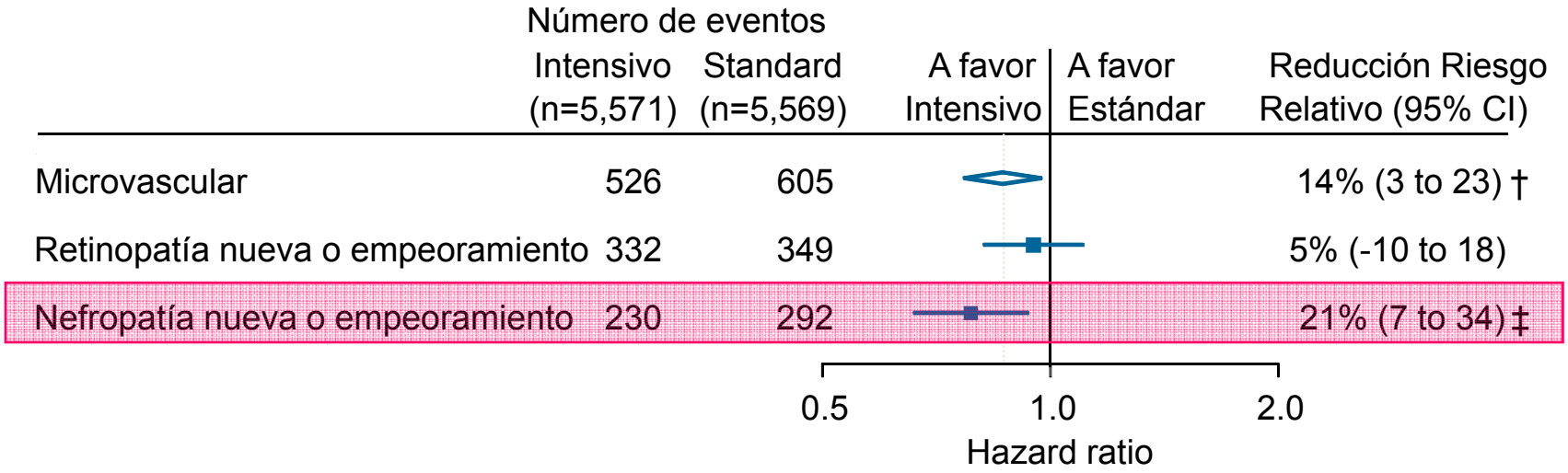
Persistencia del beneficio del control glucémico ("memoria metabólica")

	UKPDS (1998)	UKPDS(2008)
Eventos relacionados	0,88 (0,79-0,99)	0,91 (0,83-0,99)
Mortalidad diabetes	0,90 (0,73- 1,11)	0,83 (0,73- 0,96)
Mortalidad total	0,94 (0,8 – 1,1)	0,87 (0,79 - 0,96)
IAM	0,84 (0,71-1)	0,85 (0,74 – 0,97)
ACVA	1,11 (0,81-1,51)	0,91 (0,75 – 1,13)
Vasculop. periférica	0,65 (0,36-1,18)	0,82 (0,56 -1,19)
Microangiopatía	0,75 (0,6-0,93)	0,76 (0,64 – 0,89)

UKPDS (2008). N Engl J Med. 2008;359:1577

Beneficio microangiopatía DM2

Nefropatía : HR 0.79 (0.66-0.93)



†P=0.01

‡P=0.006

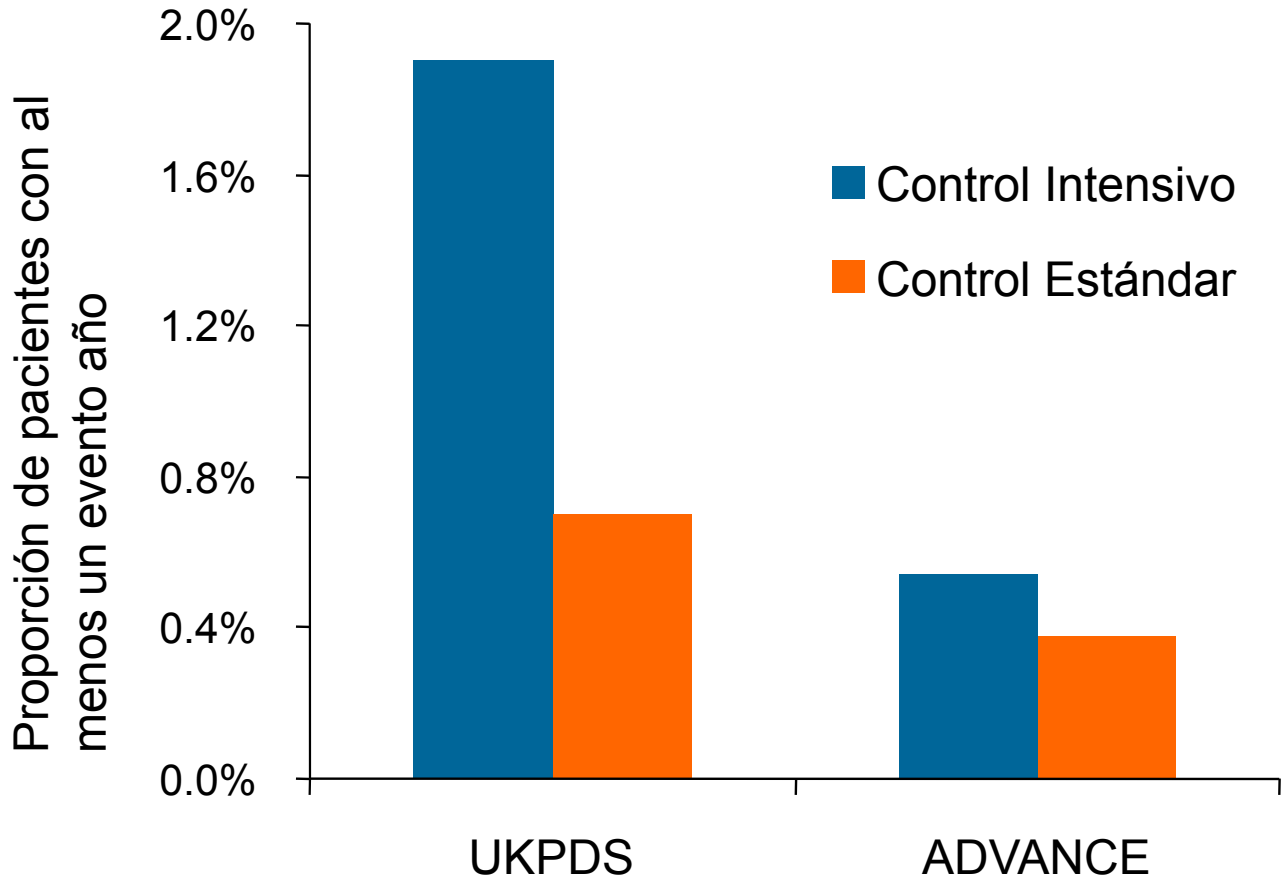
New Eng J Med 2008:358:2560

PROBLEMAS ATRIBUIDOS A LAS SULFONILUREAS ¿MITOS O REALIDAD?

- **Hipoglucemia**
- **Ganancia de peso**
- **Efectos adversos cardiovasculares**
- **Pérdida de eficacia (“agotamiento” de la célula beta)**

HIPOGLUCEMIAS

Comparativa Tasas de Hipoglucemia Grave



N Engl J Med 2008;358:2560-72

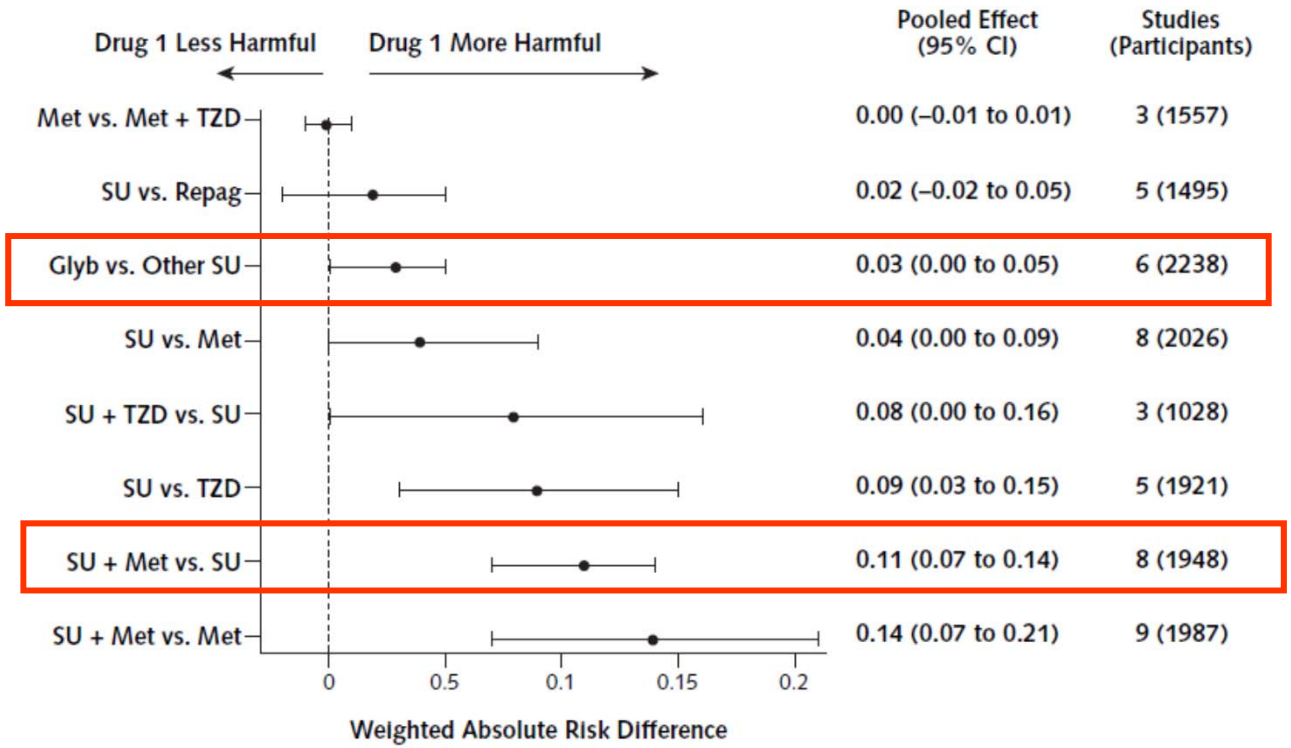
HIPOGLUCEMIAS

REVIEW | Annals of Internal Medicine

Systematic Review: Comparative Effectiveness and Safety of Oral Medications for Type 2 Diabetes Mellitus

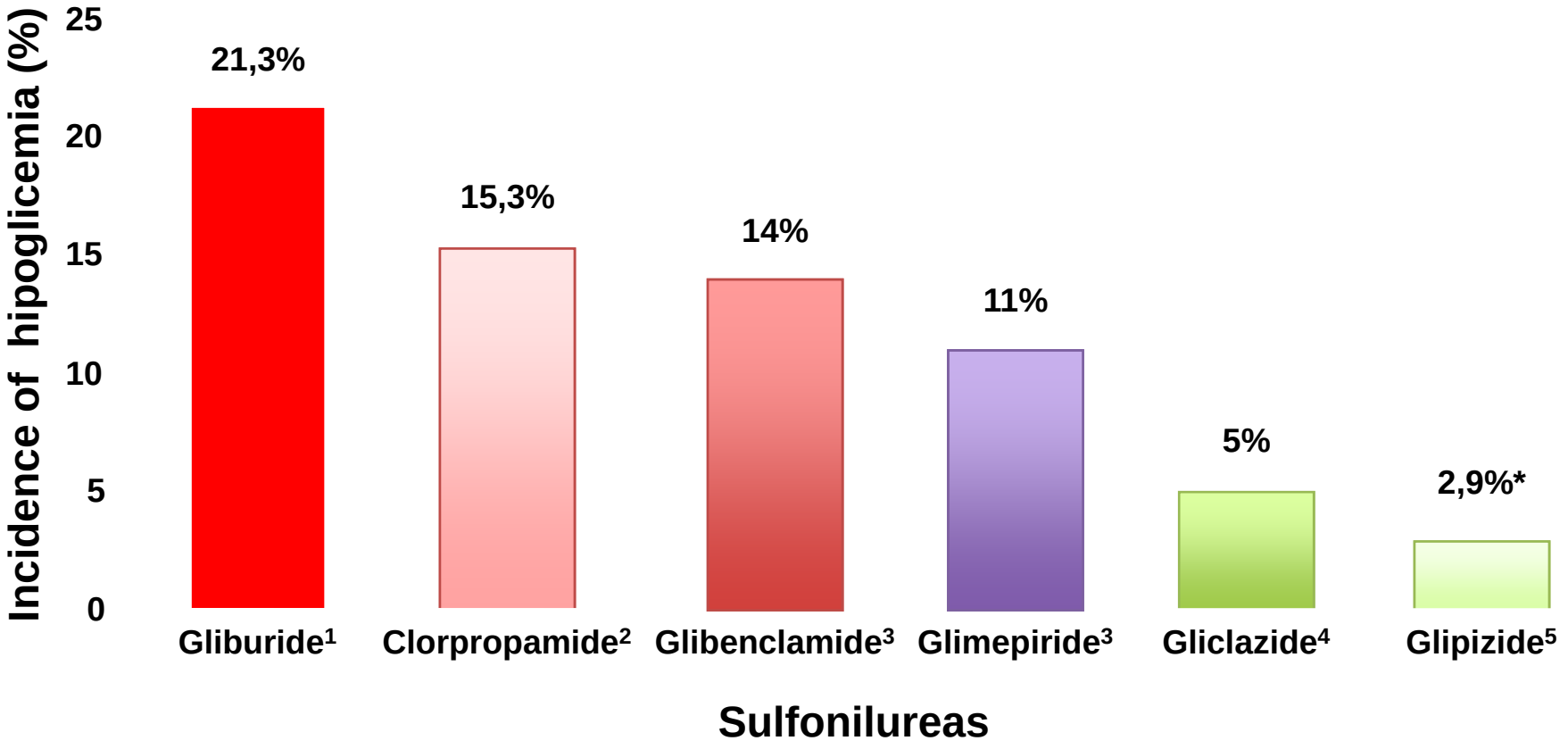
Shari Bolen, MD, MPH; Leonard Feldman, MD; Jason Vassy, MD, MPH; Lisa Wilson, BS, ScM; Hsin-Chieh Yeh, PhD; Spyridon Marinopoulos, MD, MBA; Crystal Wiley, MD, MPH; Elizabeth Selvin, PhD; Renee Wilson, MS; Eric B. Bass, MD, MPH; and Frederick L. Brancati, MD, MHS

Figure 3. Pooled hypoglycemia results for randomized trials, by drug comparison.



Ann Intern Med. 2007;147:386-399

Hipoglucemia y Sulfonilureas



- *Glu δ 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

HIPOGLUCEMIAS

ORIGINAL ARTICLE

Severe Hypoglycemia and Risks of Vascular Events and Death

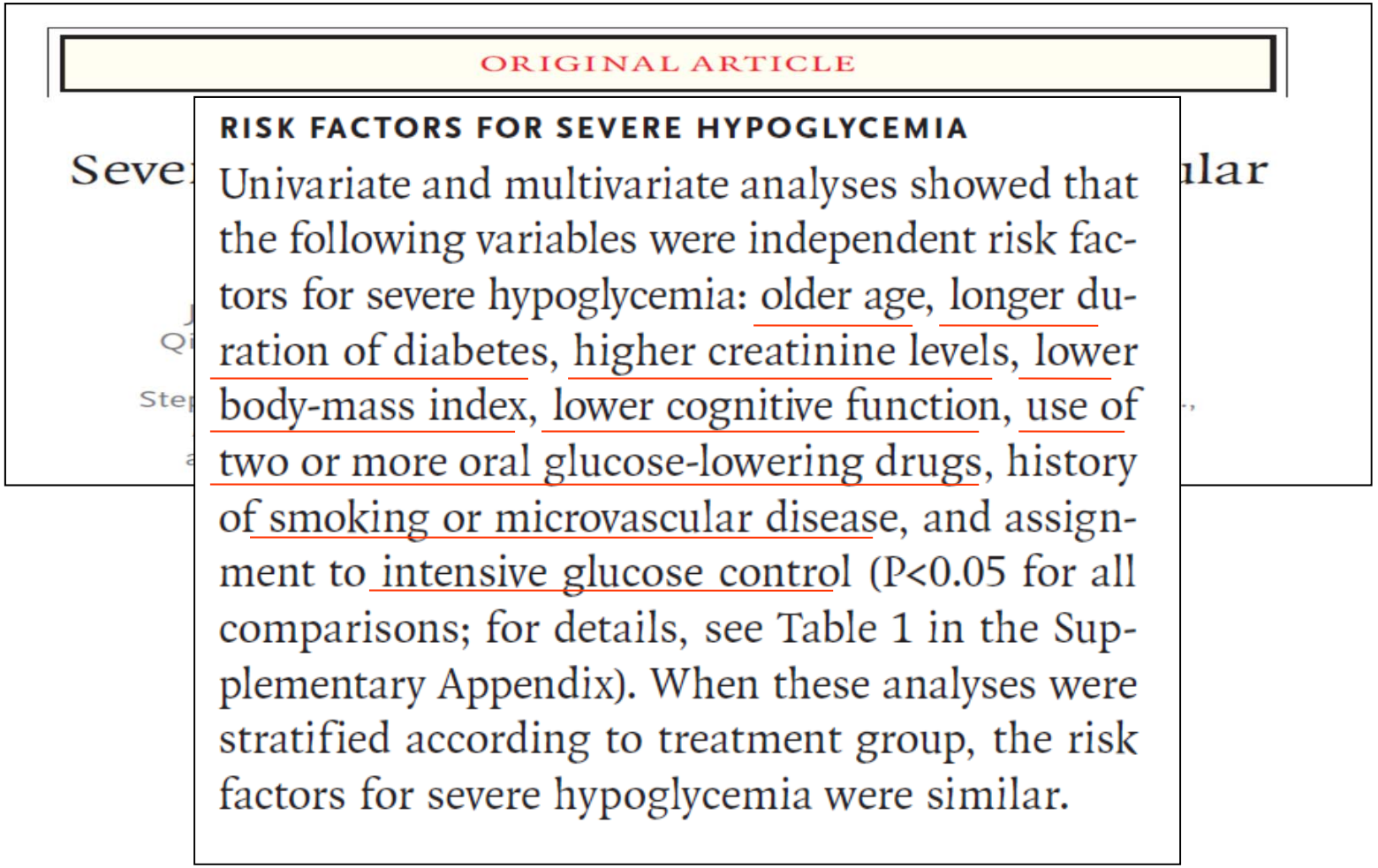
Sophia Zoungas, M.D., Ph.D., Anushka Patel, M.D., Ph.D., John Chalmers, M.D., Ph.D., Bastiaan E. de Galan, M.D., Ph.D., Qiang Li, M.Biostat., Laurent Billot, M.Sc., Mark Woodward, Ph.D., Toshiharu Ninomiya, M.D., Ph.D., Bruce Neal, M.D., Ph.D., Stephen MacMahon, D.Sc., Ph.D., Diederick E. Grobbee, M.D., Ph.D., Andre Pascal Kengne, M.D., Ph.D., Michel Marre, M.D., Ph.D., and Simon Heller, M.D., for the ADVANCE Collaborative Group

CONCLUSIONS

Severe hypoglycemia was strongly associated with increased risks of a range of adverse clinical outcomes. It is possible that severe hypoglycemia contributes to adverse outcomes, but these analyses indicate that hypoglycemia is just as likely to be a marker of vulnerability to such events. (Funded by Servier and the National Health and Medical Research Council of Australia; ClinicalTrials.gov number, NCT00145925.)

N Engl J Med 2010;363:1410-8

HIPOGLUCEMIAS



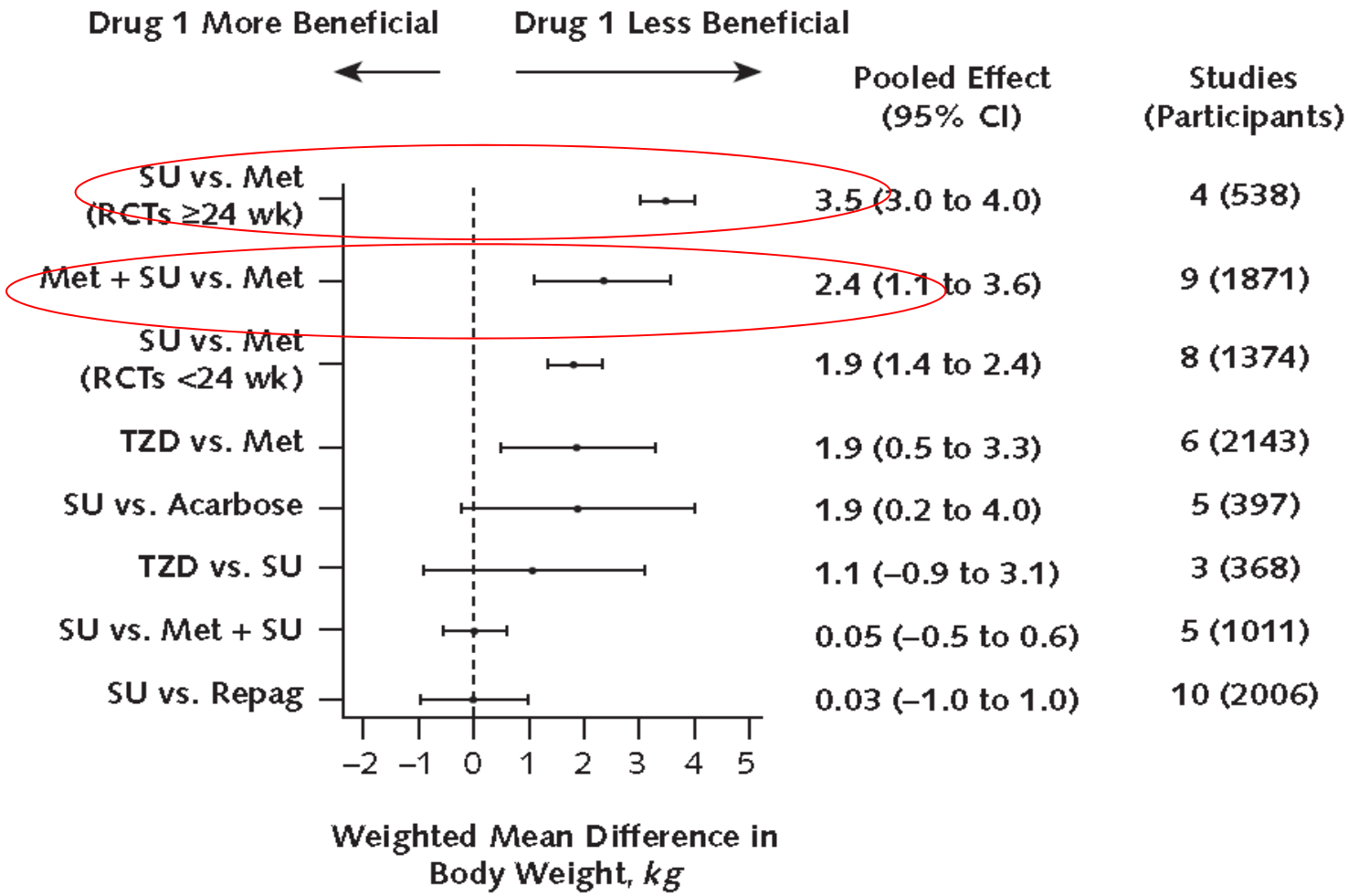
ORIGINAL ARTICLE

RISK FACTORS FOR SEVERE HYPOGLYCEMIA

Univariate and multivariate analyses showed that the following variables were independent risk factors for severe hypoglycemia: older age, longer duration of diabetes, higher creatinine levels, lower body-mass index, lower cognitive function, use of two or more oral glucose-lowering drugs, history of smoking or microvascular disease, and assignment to intensive glucose control ($P<0.05$ for all comparisons; for details, see Table 1 in the Supplementary Appendix). When these analyses were stratified according to treatment group, the risk factors for severe hypoglycemia were similar.

N Engl J Med 2010;363:1410-8

Peso



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

JAMA®

Online article and related content current as of April 14, 2010.

Effect of Noninsulin Antidiabetic Drugs Added to Metformin Therapy on Glycemic Control, Weight Gain, and Hypoglycemia in Type 2 Diabetes

Olivia J. Phung; Jennifer M. Scholle; Mehak Talwar; et al.

JAMA. 2010;303(14):1410-1418 (doi:10.1001/jama.2010.405)

http://jama.ama-assn.org/cgi/content/full/303/14/1410

	HbA_{1c} (% cambio) (95% IC)	Hipoglucemia (RR) (95% IC)	Peso (kg) (95% IC)	Otros efectos adversos
Inhibidores α-glucosidasas	-0,64 0,26/1,03	0,42 0,01-9	-1,8 -3,79/0,21	Flatulencia meteorismo
Sulfonilureas	-0,79 0,62/0,79	4,57 2,11-11,45	+2,06 1,15/2,96	
Glinidas	-0,65 0,36/0,97	7,5 2,12-41,52	+1,77 0,46/3,28	
Glitazonas	-0,85 0,66/1,08	0,56 0,19/1,69	+2,08 0,98/3,18	Edemas, anemia Insuficiencia cardíaca Fracturas en mujeres
Inhibidores DPP-4	-0,78 0,64/0,93	0,63 0,26/1,71	-0,14 -0,94/0,63	I. Respiratoria, ITU
Análogos GLP1	-0,97 0,78/1,19	0,89 0,22/3,96	-1,74 -3,11/-0,48	Vómitos

JAMA. 2010; 303(14): 1410-1418.

EFECTOS ADVERSOS CARDIOVASCULARES

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

In ADOPT (A Diabetes Outcome Progression Trial) (28), the incidence of cardiovascular events was lower with glyburide than with rosiglitazone or metformin (1.8%, 3.4%, and 3.2%, respectively; $P < 0.05$). This effect was mainly driven by fewer congestive heart failure events and a lower rate of nonfatal myocardial infarction events in the glyburide group. Loss to follow-up was high (40%) and was disproportionate among the groups and therefore may account for some differences among groups.

N Engl J Med 2006;355:2427-43

EFECTOS ADVERSOS CARDIOVASCULARES

REVIEW ARTICLE

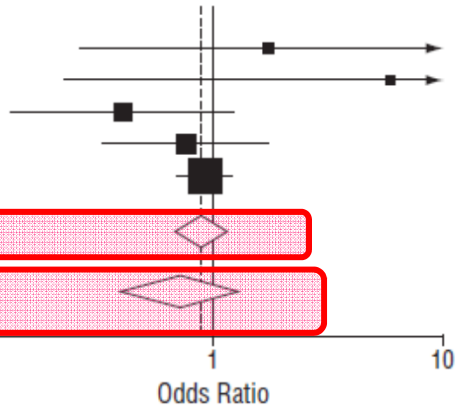
Cardiovascular Outcomes in Trials of Oral Diabetes Medications

A Systematic Review

Elizabeth Selvin, PhD, MPH; Shari Bolen, MD, MPH; Hsin-Chieh Yeh, PhD; Crystal Wiley, MD, MPH;

B

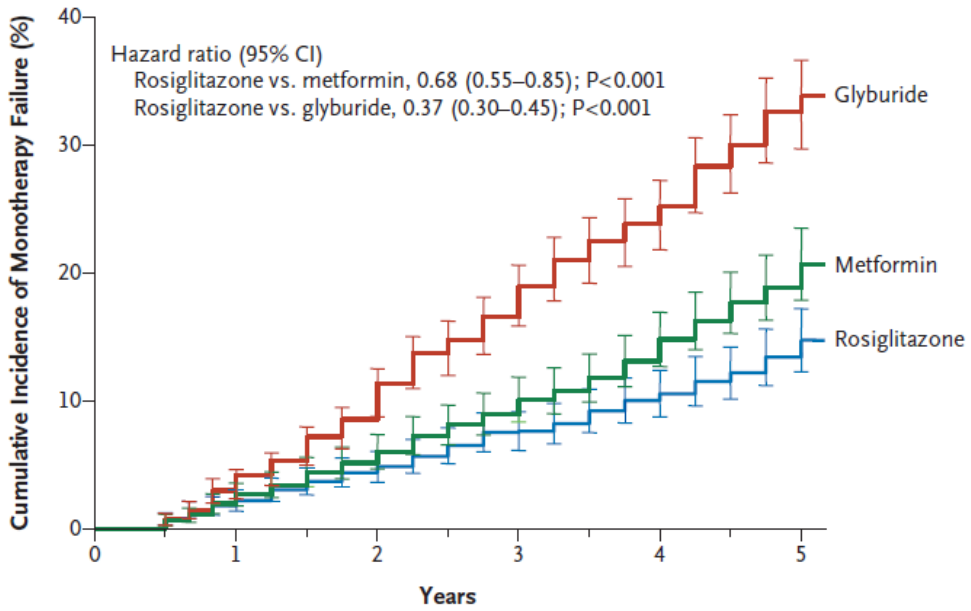
Source	OR (95% CI)	Weight, %
Hermann et al,[41] 1994	1.74 (0.27-11.11)	1.07
Lawrence et al,[44] 2005	5.93 (0.23-151.78)	0.20
Marbury et al,[45] 1999	0.41 (0.14-1.21)	7.72
St John Sutton et al,[53] 2002	0.76 (0.34-1.70)	8.52
UKPDS Group,[1] 1998 (UKPDS 33)	0.92 (0.72-1.18)	82.48
Overall pooled OR	0.89 (0.71-1.11)	100.00
Pooled OR, excluding UKPDS 33	0.72 (0.41-1.28)	



Arch Intern Med. 2008;168(19):2070-2080

AGOTAMIENTO DE CÉLULA BETA

The NEW ENGLAND JOURNAL of MEDICINE

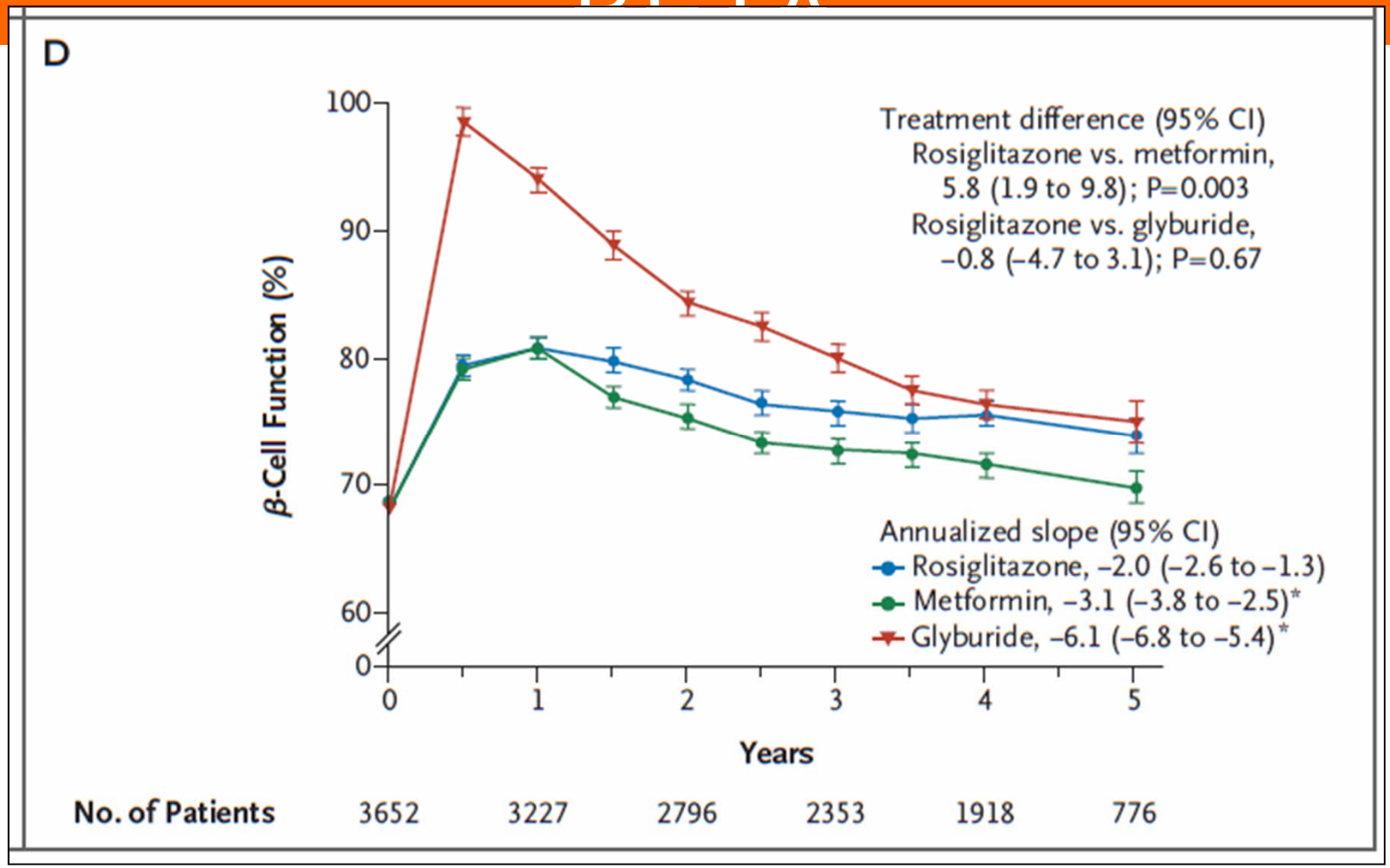


No. at Risk						
Rosiglitazone	1393	1207	1078	957	844	324
Metformin	1397	1205	1076	950	818	311
Glyburide	1337	1114	958	781	617	218

Figure 2. Kaplan–Meier Estimates of the Cumulative Incidence of Monotherapy Failure at 5 Years.

N Engl J Med 2006;355:2427-43

AGOTAMIENTO DE CÉLULA BETA



CONCLUSIONES

- **Las SU han demostrado beneficios en reducción de complicaciones microvasculares y macrovasculares**

- **La mayor contraindicación de las SU es la falta de indicación. Debemos individualizar los objetivos de tratamiento en cada paciente antes de indicar un fármaco hipoglucemiante.**

- **Las hipoglucemias pueden reducirse con educación adecuada, eligiendo las SU de vida media más corta y evitándolas en los pacientes de mayor riesgo para padecerlas**

- **Las SU son actualmente los antidiabéticos orales con mayor experiencia de uso y con un perfil de seguridad adecuado en relación a sus beneficios y coste.**

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26-28 Octubre 2011

world diabetes day

14 November

Muchas Gracias

Costa Meloneras

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