

# ¿Es posible un abordaje más completo de la DM tipo 2?

## Más allá del control glucémico

Pedro Pablo Casado

Servicio de Medicina Interna  
Hospital Universitario La Princesa





CONGRESO NACIONAL  
DE MEDICINA GENERAL  
Y DE FAMILIA

San Sebastián 2017  
18-20 Mayo



**Ante un paciente con diabetes de reciente diagnóstico, sin síntomas cardinales y HbA1c de 9.1%, ¿qué tratamiento iniciaríais?:**



Ante un paciente con diabetes de reciente diagnóstico, sin síntomas cardinales y HbA1c de 9.1%, ¿qué tratamiento iniciaríais?:

?

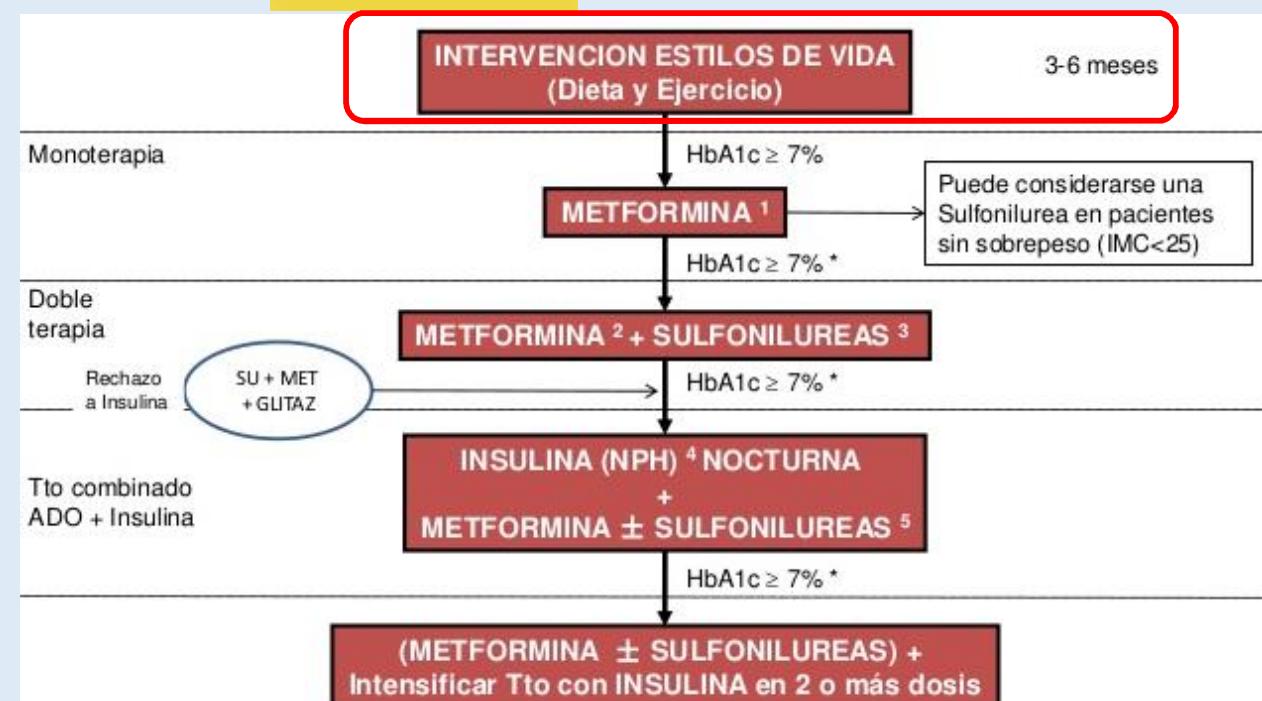
- ✓ Modificar los estilos de vida (MEV)
- ✓ MEV + Metformina
- ✓ MEV + Sulfonilurea
- ✓ MEV + 2 antidiabéticos
- ✓ MEV + 3 antidiabéticos
- ✓ Cerveza, hojas de menta, sangre de hipopótamo y sacrificios a los dioses



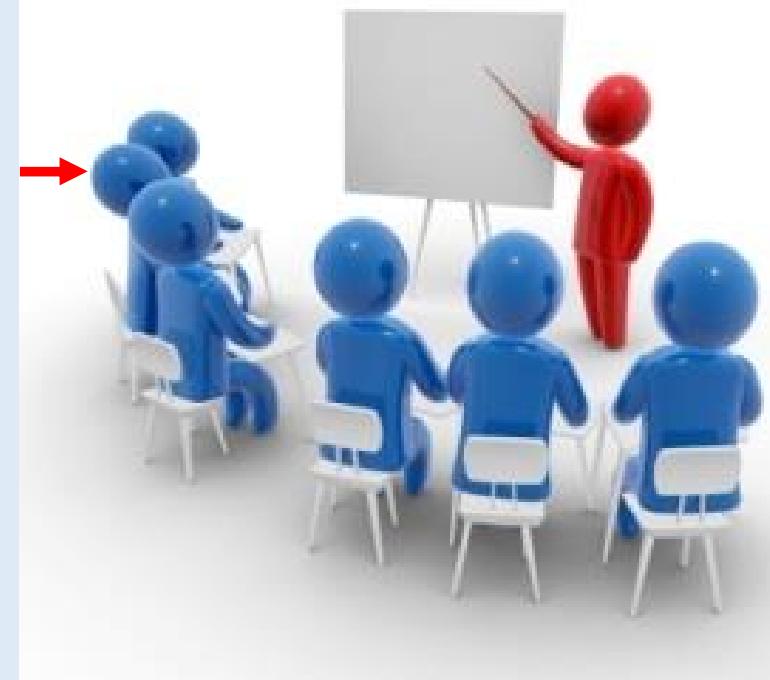
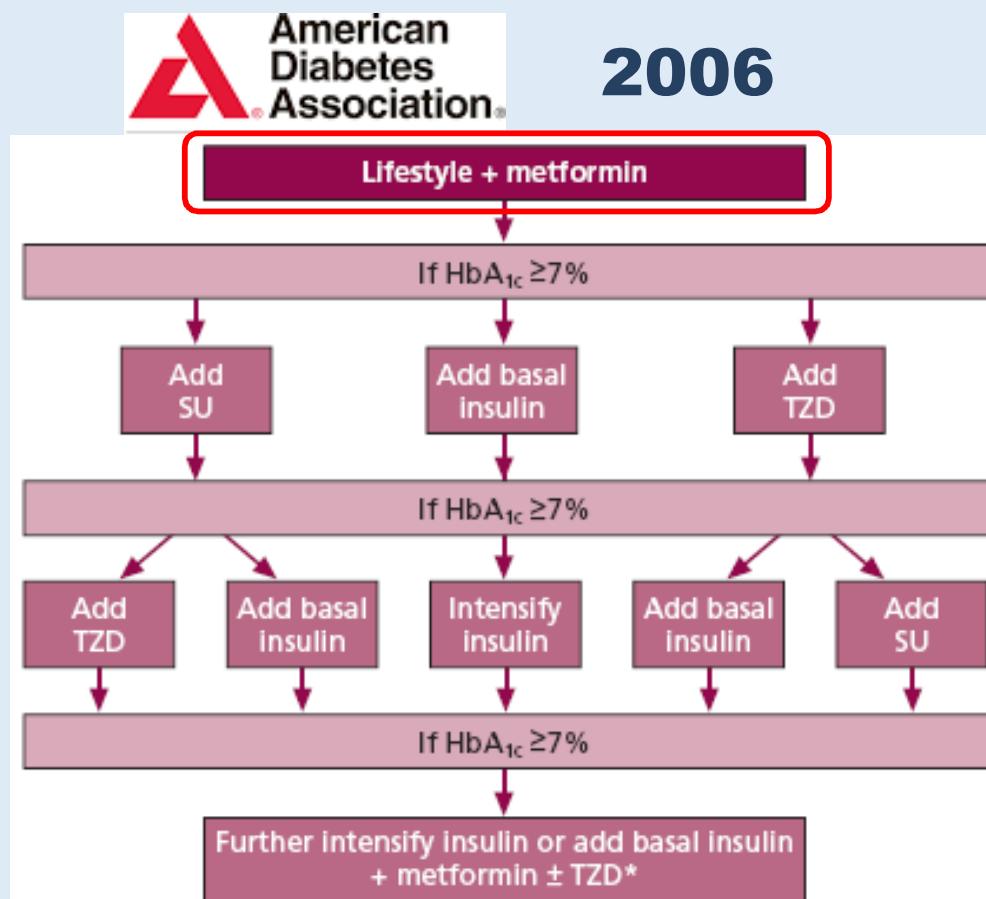
## Ante un paciente con diabetes de reciente diagnóstico, sin síntomas cardinales y HbA1c de 9.1%, ¿qué tratamiento iniciaríais?:



**2007**



## Ante un paciente con diabetes de reciente diagnóstico, sin síntomas cardinales y HbA1c de 9.1%, ¿qué tratamiento iniciaríais?:



## Ante un paciente con diabetes de reciente diagnóstico, sin síntomas cardinales y HbA1c de 9.1%, ¿qué tratamiento iniciaríais?:



National Institute for  
Health and Clinical Excellence

2007

HbA<sub>1c</sub> ≥6.5%\* after trial of  
lifestyle interventions

Metformin<sup>†</sup>

Consider sulfonylurea here if:

- not overweight (tailor the assessment of body-weight-associated risk according to ethnic group<sup>‡</sup>), or
- metformin is not tolerated or is contraindicated, or
- a rapid therapeutic response is required because of hyperglycaemic symptoms

HbA<sub>1c</sub> ≥6.5%\*

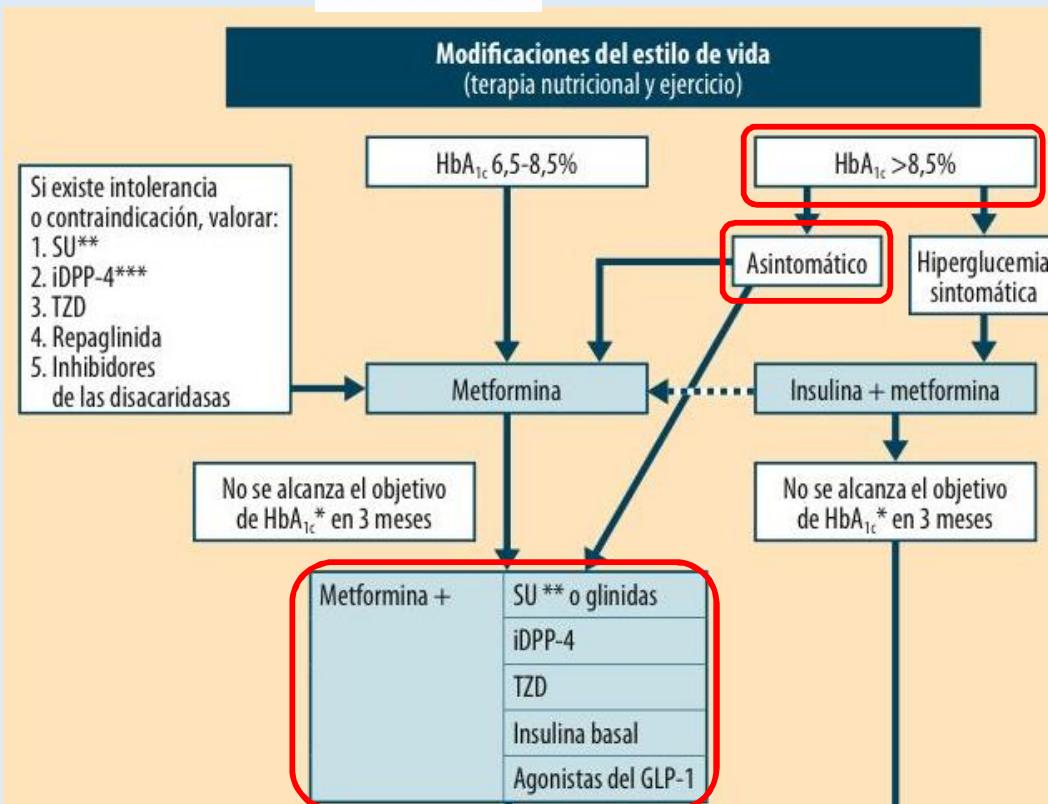
HbA<sub>1c</sub> <6.5%\*  
Monitor for  
deterioration



## Ante un paciente con diabetes de reciente diagnóstico, sin síntomas cardinales y HbA1c de 9.1%, ¿qué tratamiento iniciaríais?:



### 2010



# Ante un paciente con diabetes de reciente diagnóstico, sin síntomas cardinales y HbA1c de 9.1%, ¿qué tratamiento iniciaríais?:



Ante un paciente con diabetes de reciente diagnóstico, sin síntomas cardinales y HbA1c de 9.1%, ¿qué tratamiento iniciaríais?:

## Papiro de Ebers



1553 a.C





CONGRESO NACIONAL  
DE MEDICINA GENERAL  
Y DE FAMILIA

San Sebastián 2017  
18-20 Mayo



1553 a.C



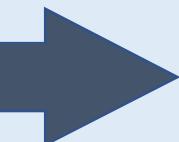
National Institute for  
Health and Clinical Excellence



2006 - 2007



2017





CONGRESO NACIONAL  
DE MEDICINA GENERAL  
Y DE FAMILIA

San Sebastián 2017  
18-20 Mayo



## ¿Control glucémico?





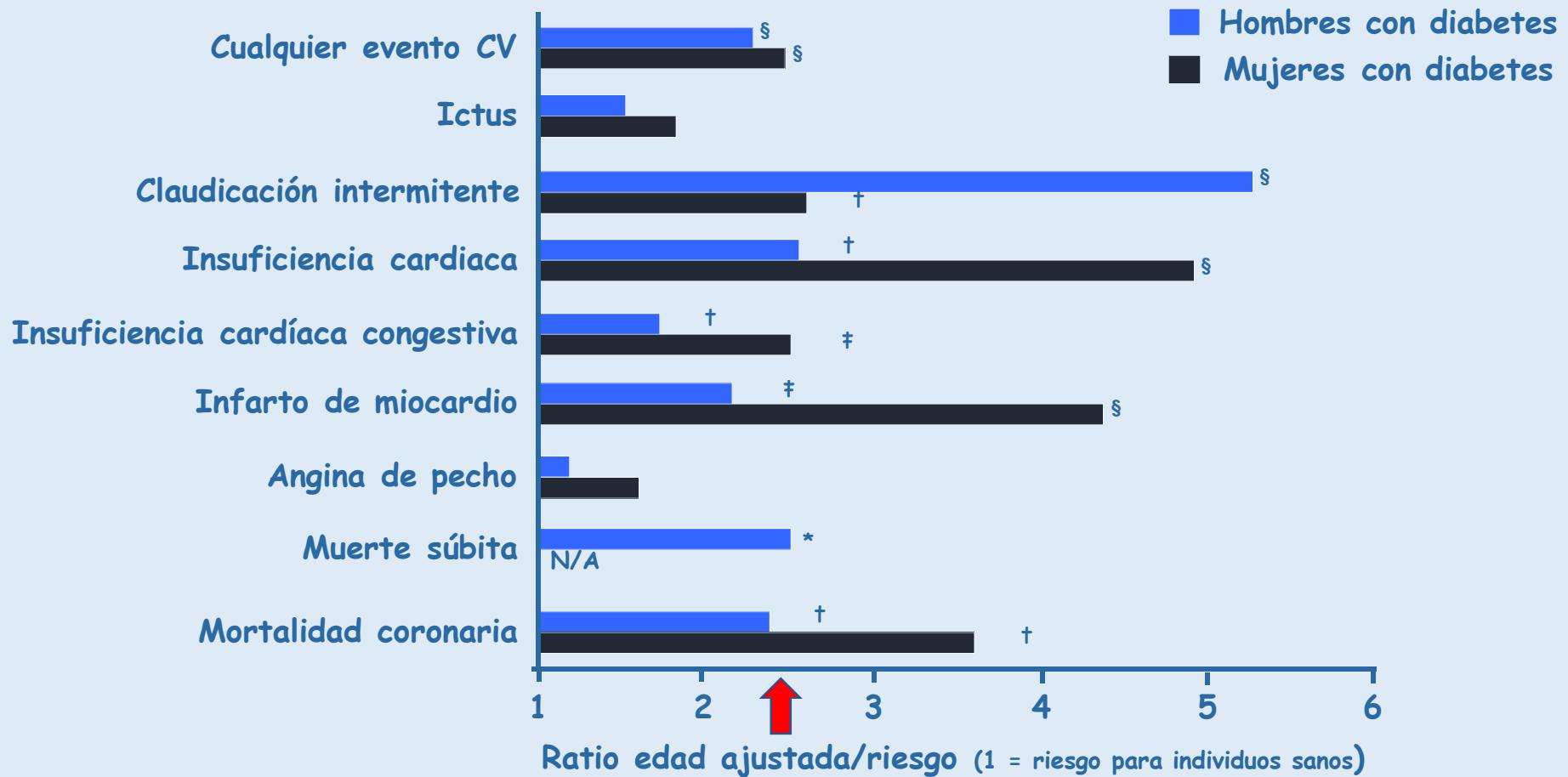
## Resultados de los estudios UKPDS,<sup>1,2</sup> ACCORD,<sup>3</sup> ADVANCE,<sup>4,5</sup> y VADT<sup>6,7\*</sup>

Estudio (HbA <sub>1c</sub> intensivo vs. convencional)	Complicaciones microvasculares	
	Corto plazo	Largo plazo
UKPDS 33 <sup>1,2</sup> (7,0% vs. 7,9%; T2D)	↓	↓
ACCORD <sup>3</sup> (6,4% vs. 7,5%; T2D)	↓	N/A
ADVANCE <sup>4,5</sup> (6,3% vs. 7,0%; T2D)	↓	↓
VADT <sup>6,7</sup> (6,9% vs. 8,4%; T2D)	↓	↓

\*Tan sólo el ensayo ACCORD no incluyó un seguimiento a largo plazo. N/A, no aplicable.

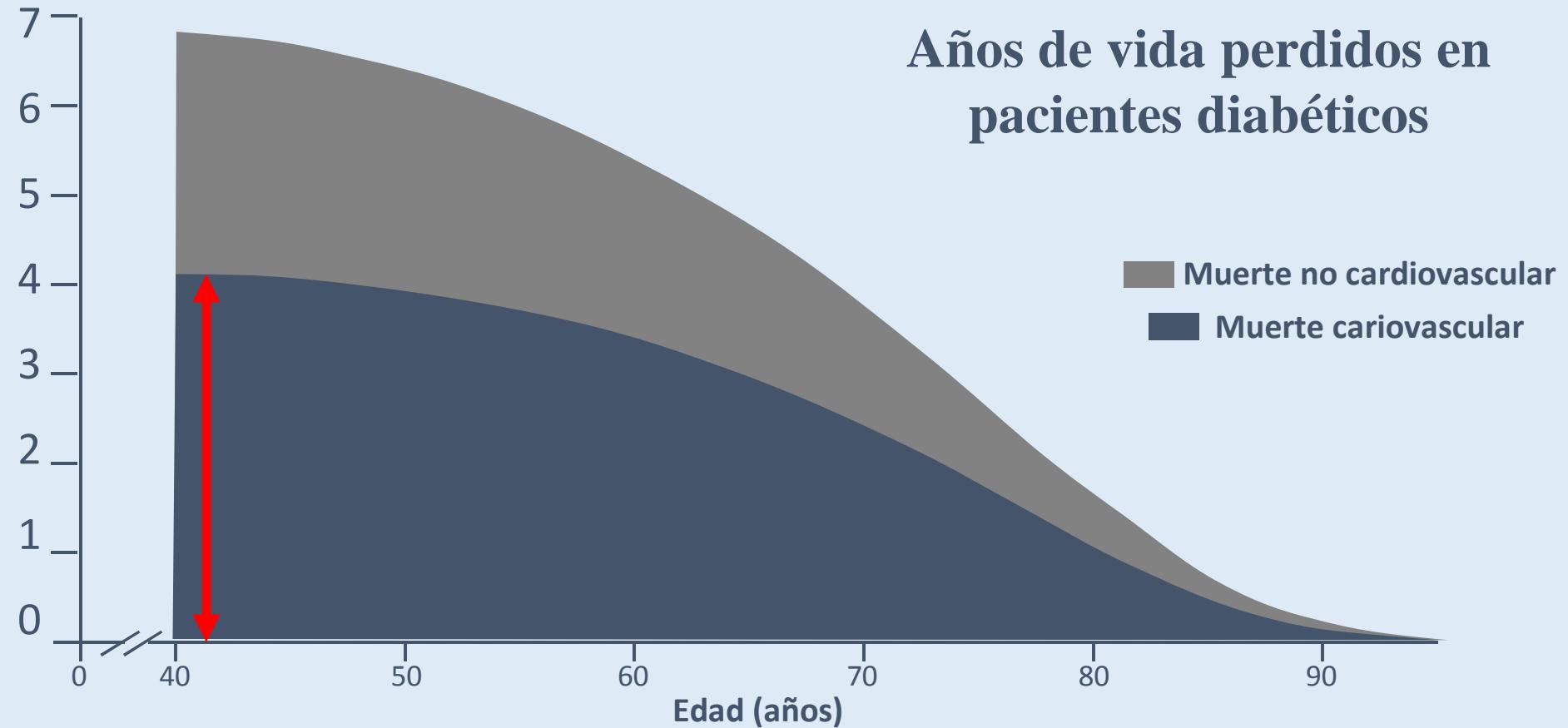
1. UKPDS. *Lancet* 1998;352:837. 53; 2. Holman RR, et al. *N Engl J Med* 2008;359:1565. 76; 3. Gerstein HC, et al. *N Engl J Med* 2008;358:2545. 59; 4. Patel A, et al. *N Engl J Med* 2008;358:2560. 72; 5. Zoungas S, et al. *N Engl J Med* 2014;371:1392. 406; 6. Duckworth W, et al. *N Engl J Med* 2009;360:129. 39; 7. Hayward RA, et al. *N Engl J Med* 2015;372:2197. 206.

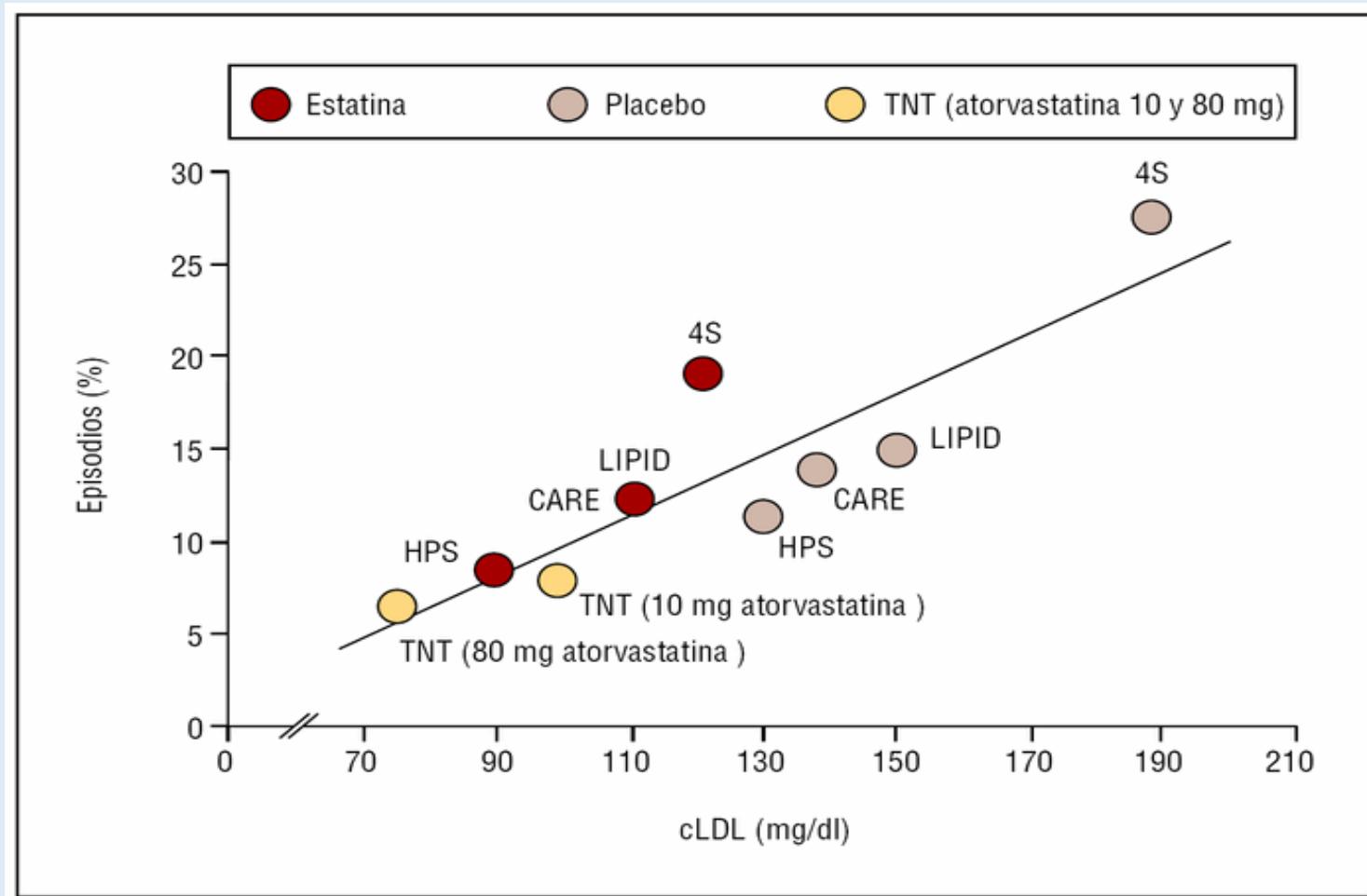
## RIESGO DE ENFERMEDAD CV EN DM-2



Adaptado de Kannel WB, et al. Am Heart J 1990; 120:672. 676.

## Años de vida perdidos en pacientes diabéticos





LaRosa JC, Grundy SM, Waters DD, Shear C, Barter P, Fruchart JC, et al. Treating to New Targets (TNT) Investigators. Intensive lipid lowering with atorvastatin in patients with stable coronary disease. *N Engl J Med.* 2005;352:1425-35.



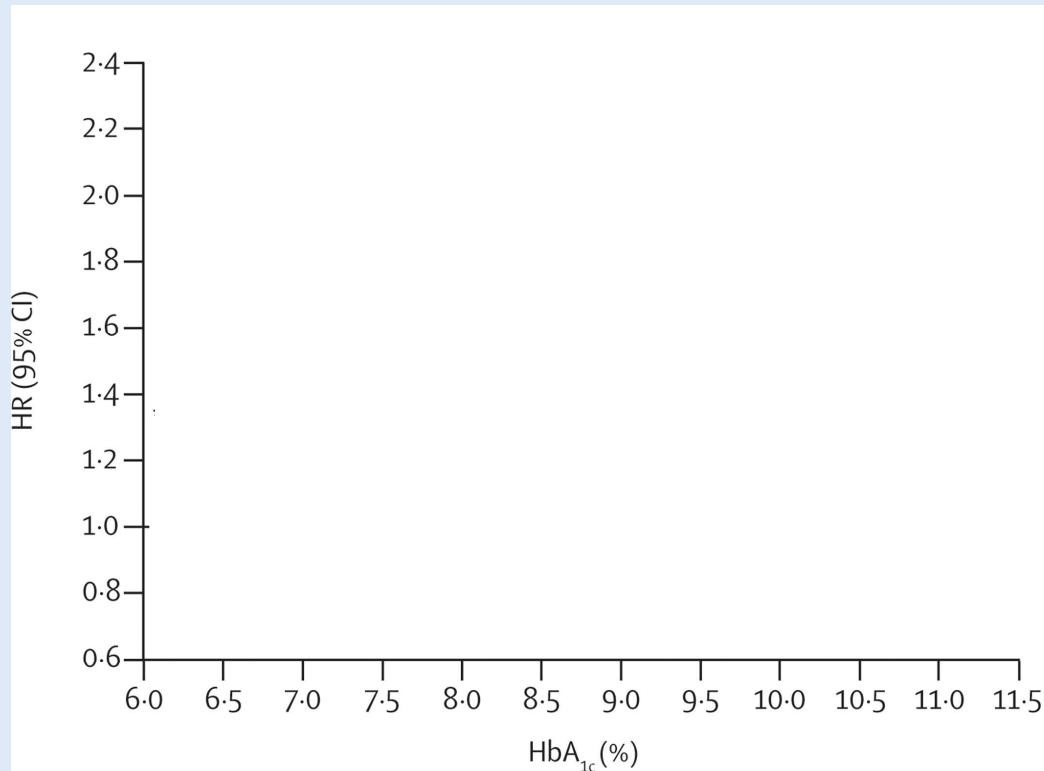
## Resultados de los estudios UKPDS,<sup>1,2</sup> ACCORD,<sup>3</sup> ADVANCE,<sup>4,5</sup> y VADT<sup>6,7\*</sup>

Estudio (HbA <sub>1c</sub> intensivo vs. convencional)	Complicaciones microvasculares	
	Corto plazo	Largo plazo
UKPDS 33 <sup>1,2</sup> (7,0% vs. 7,9%; T2D)	↓	↓
ACCORD <sup>3</sup> (6,4% vs. 7,5%; T2D)	↓	N/A
ADVANCE <sup>4,5</sup> (6,3% vs. 7,0%; T2D)	↓	↓
VADT <sup>6,7</sup> (6,9% vs. 8,4%; T2D)	↓	↓

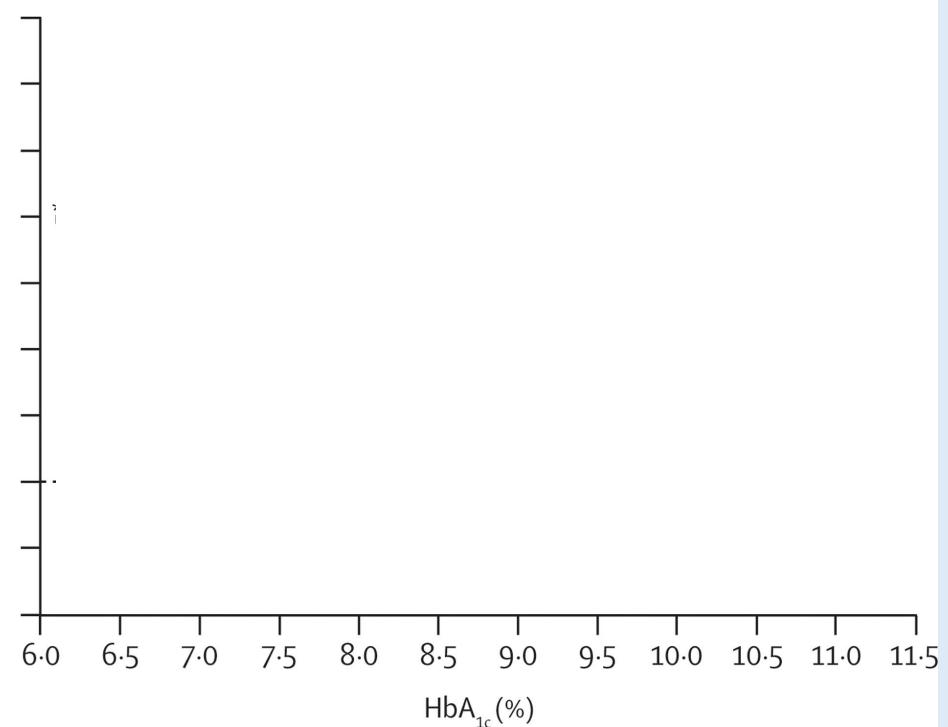
\*Tan sólo el ensayo ACCORD no incluyó un seguimiento a largo plazo. N/A, no aplicable.

1. UKPDS. *Lancet* 1998;352:837. 53; 2. Holman RR, et al. *N Engl J Med* 2008;359:1565. 76; 3. Gerstein HC, et al. *N Engl J Med* 2008;358:2545. 59; 4. Patel A, et al. *N Engl J Med* 2008;358:2560. 72; 5. Zoungas S, et al. *N Engl J Med* 2014;371:1392. 406; 6. Duckworth W, et al. *N Engl J Med* 2009;360:129. 39; 7. Hayward RA, et al. *N Engl J Med* 2015;372:2197. 206.

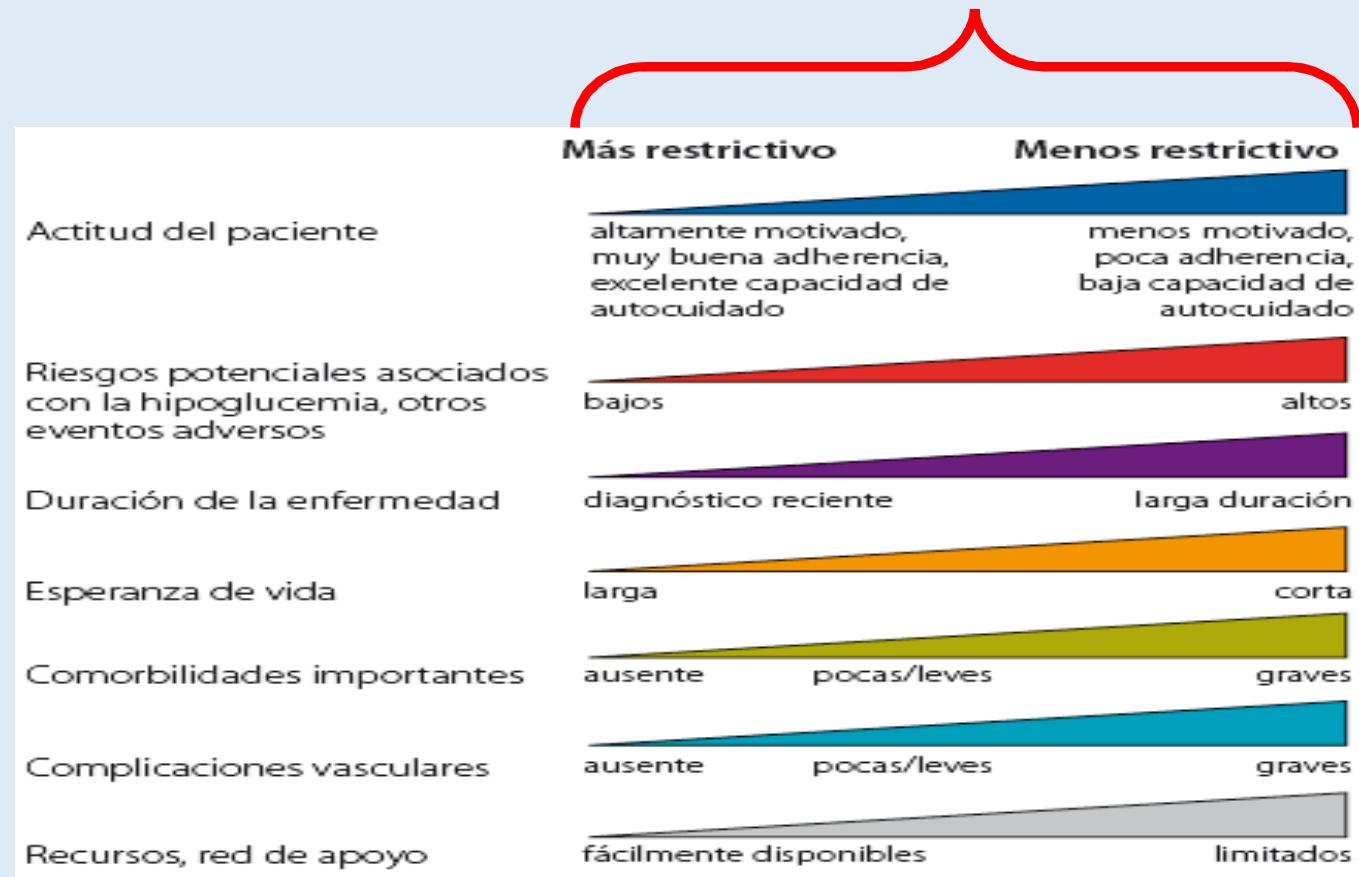
## ADO



## Insulina



Survival as a function of HbA<sub>1c</sub> in people with type 2 diabetes: a retrospective cohort study. Currie, Craig J et al. The Lancet , Volume 375 , Issue 9713 , 481 - 489



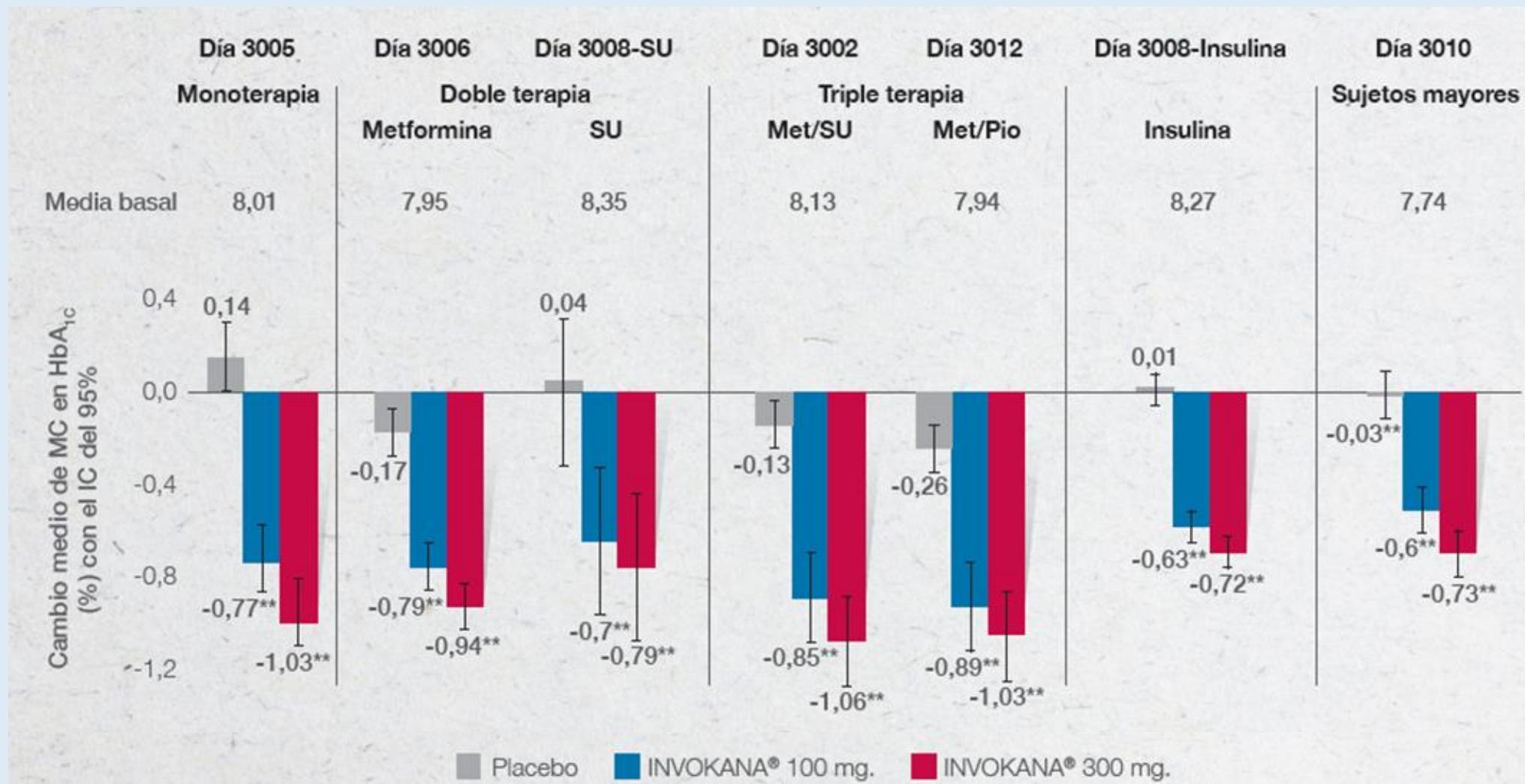


CONGRESO NACIONAL  
DE MEDICINA GENERAL  
Y DE FAMILIA

San Sebastián 2017  
18-20 Mayo



# ¿Qué más nos pueden ofrecer los inhibidores de los cotransportadores SGLT-2 para el manejo de nuestros pacientes diabéticos más allá del control glucémico?





CONGRESO NACIONAL  
DE MEDICINA GENERAL  
Y DE FAMILIA

San Sebastián 2017  
18-20 Mayo



## original article

*Diabetes, Obesity and Metabolism* 18: 783–794, 2016.

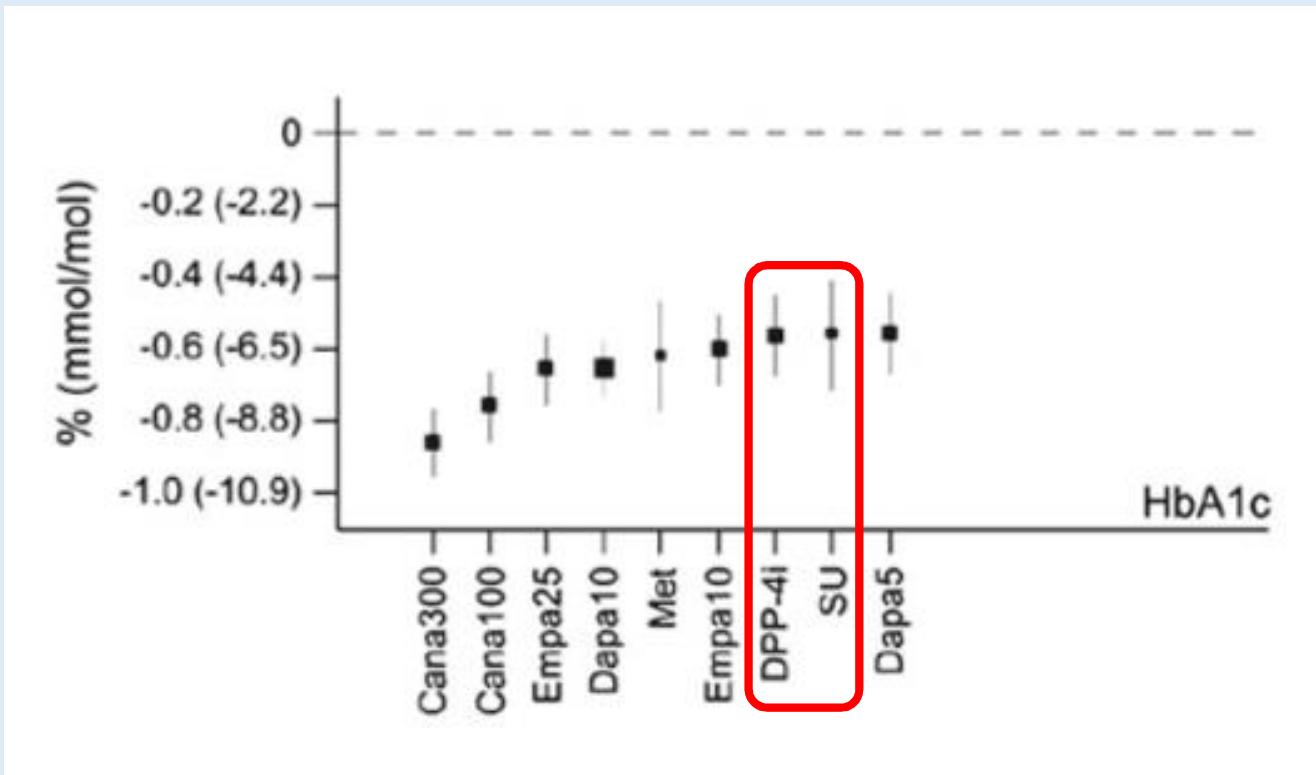
© 2016 John Wiley & Sons Ltd

# Efficacy and safety of sodium-glucose co-transporter-2 inhibitors in type 2 diabetes mellitus: systematic review and network meta-analysis

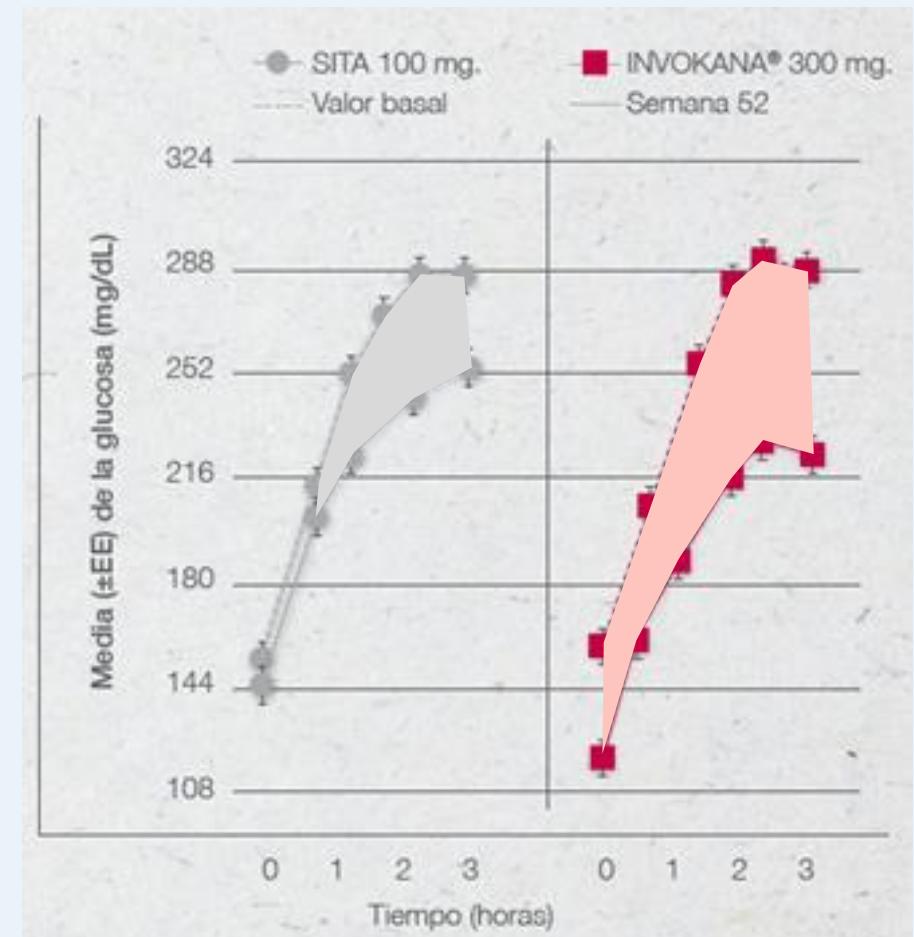
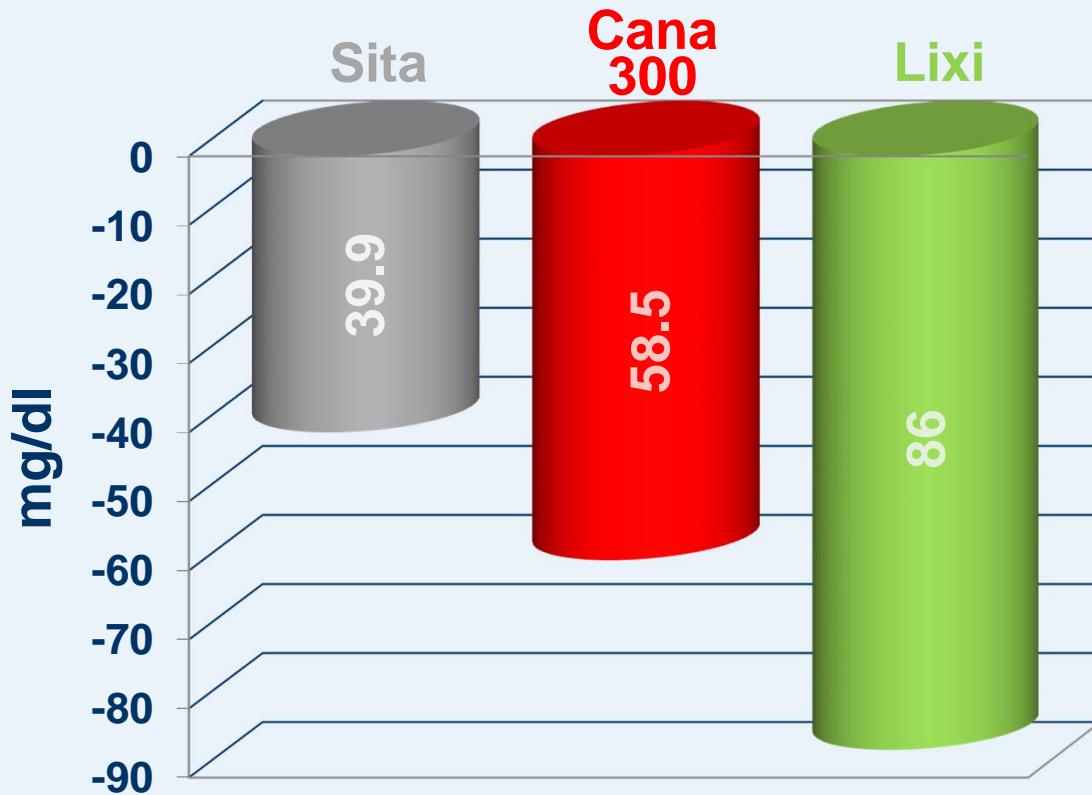
F. Zaccardi<sup>1,2</sup>, D. R. Webb<sup>1,2</sup>, Z. Z. Htike<sup>1,2</sup>, D. Youssef<sup>1,2</sup>, K. Khunti<sup>1,2</sup> & M. J. Davies<sup>1,2</sup>

<sup>1</sup> Diabetes Research Centre, University of Leicester, Leicester, UK

<sup>2</sup> Diabetes Research Center, Leicester Diabetes Centre, UHL NHS Trust, Leicester, UK



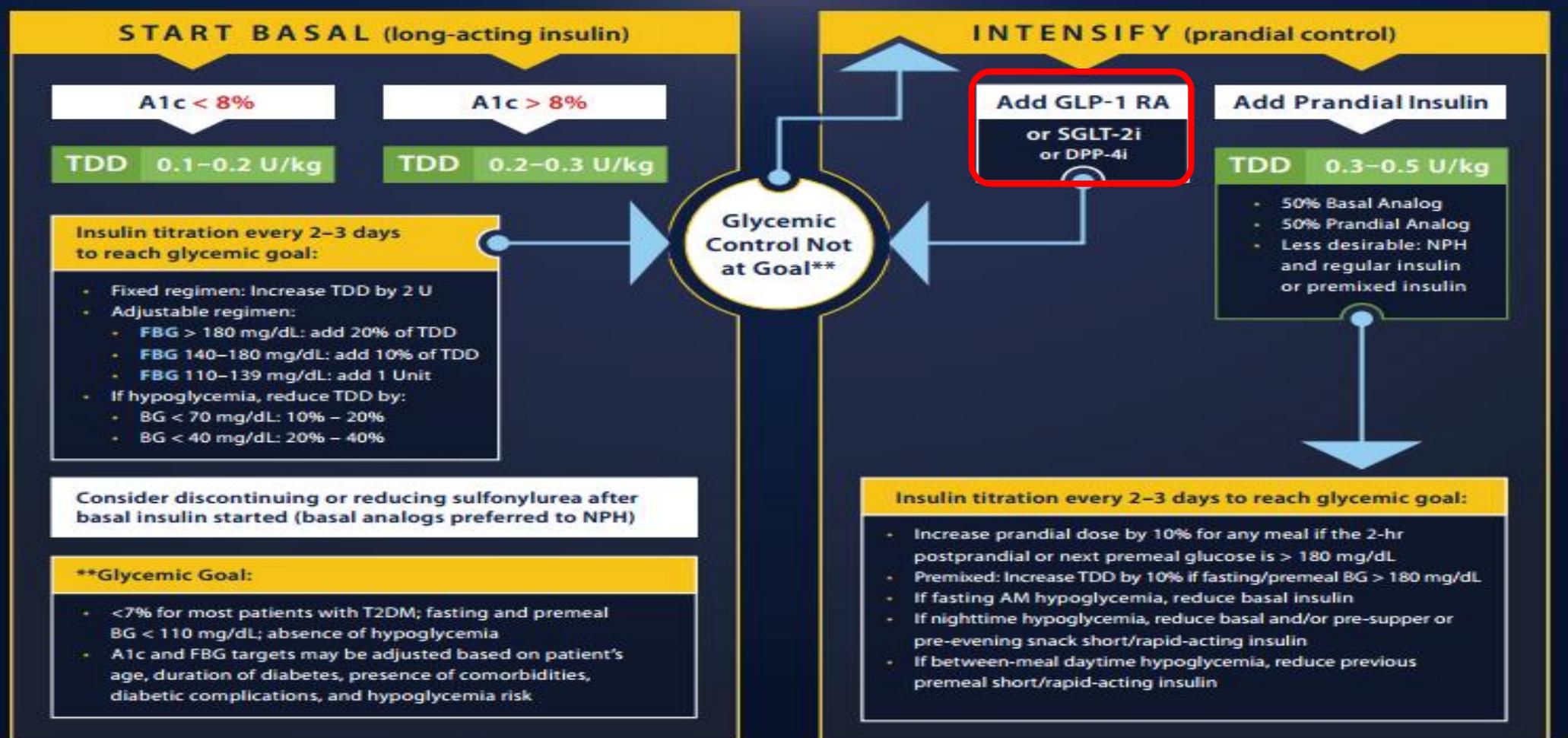
## Reducción de glucemia posprandial



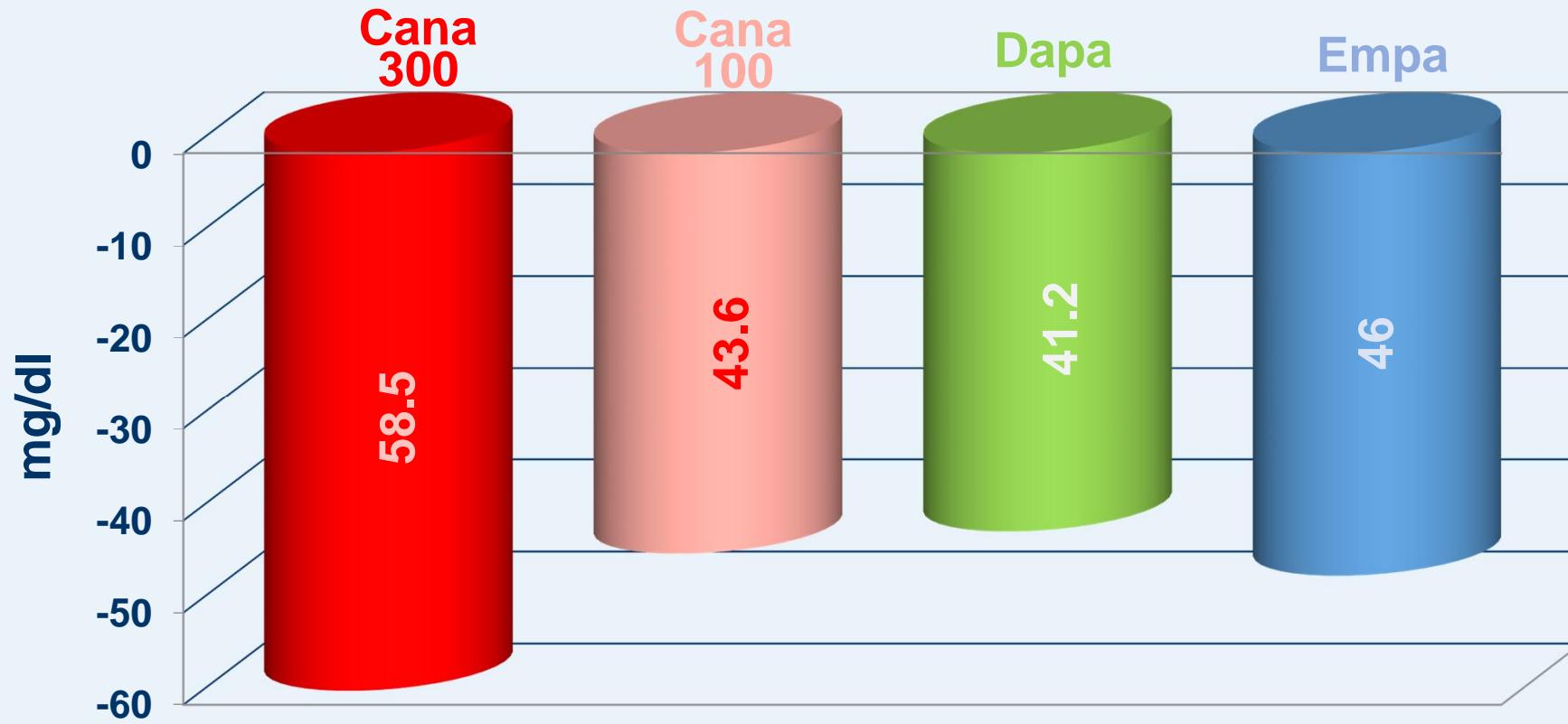
Schernthaner G et al. Canagliflozin compared with sitagliptin for patients with type 2 diabetes. Diabetes Care. 2013; 36(9):2508-15  
Raccah D. et al. Lixisenatide as add-on to oral anti-diabetic therapy. Diabetes/Metabolism Research and News 2014; 30:742-748



## ALGORITHM FOR ADDING/INTENSIFYING INSULIN



## Reducción de glucemia posprandial (glucosúricos)



Schernthaner G et al. Canagliflozin compared with sitagliptin for patients with type 2 diabetes. Diabetes Care. 2013; 36(9):2508-15  
Salsali A, et al. 71st ADA Scientific Sessions, San Diego, 24. 28 June [Poster 1104-P]. // Stenlöf K, et al. Efficacy and safety of canagliflozin monotherapy in subjects with type 2 diabetes mellitus. Diabetes, Obesity and Metabolism 15:372-382, 2013



CONGRESO NACIONAL  
DE MEDICINA GENERAL  
Y DE FAMILIA

San Sebastián 2017  
18-20 Mayo



## Efecto sobre el peso corporal

original article

*Diabetes, Obesity and Metabolism* 18: 783–794, 2016.

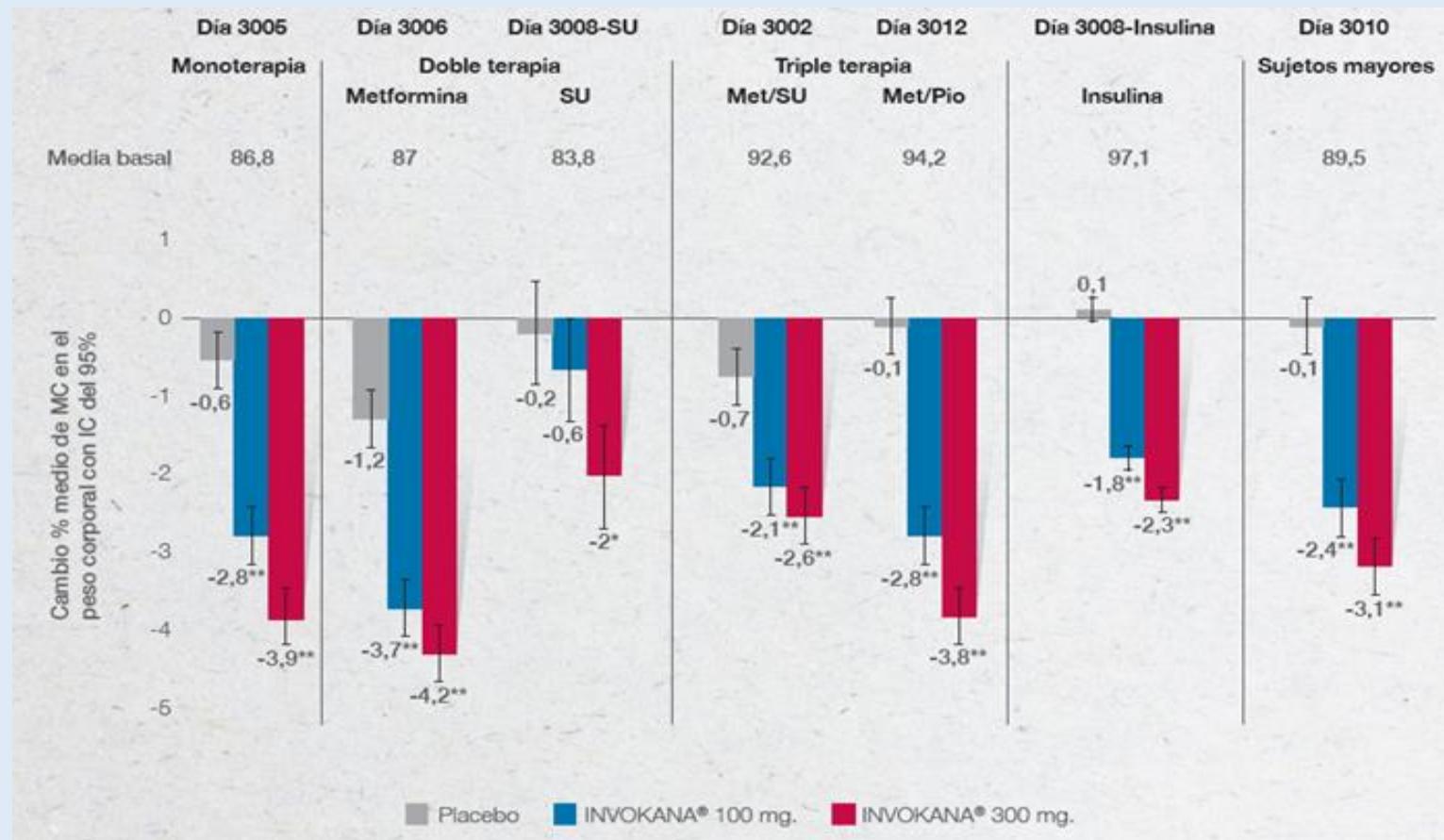
© 2016 John Wiley & Sons Ltd

# Efficacy and safety of sodium-glucose co-transporter-2 inhibitors in type 2 diabetes mellitus: systematic review and network meta-analysis

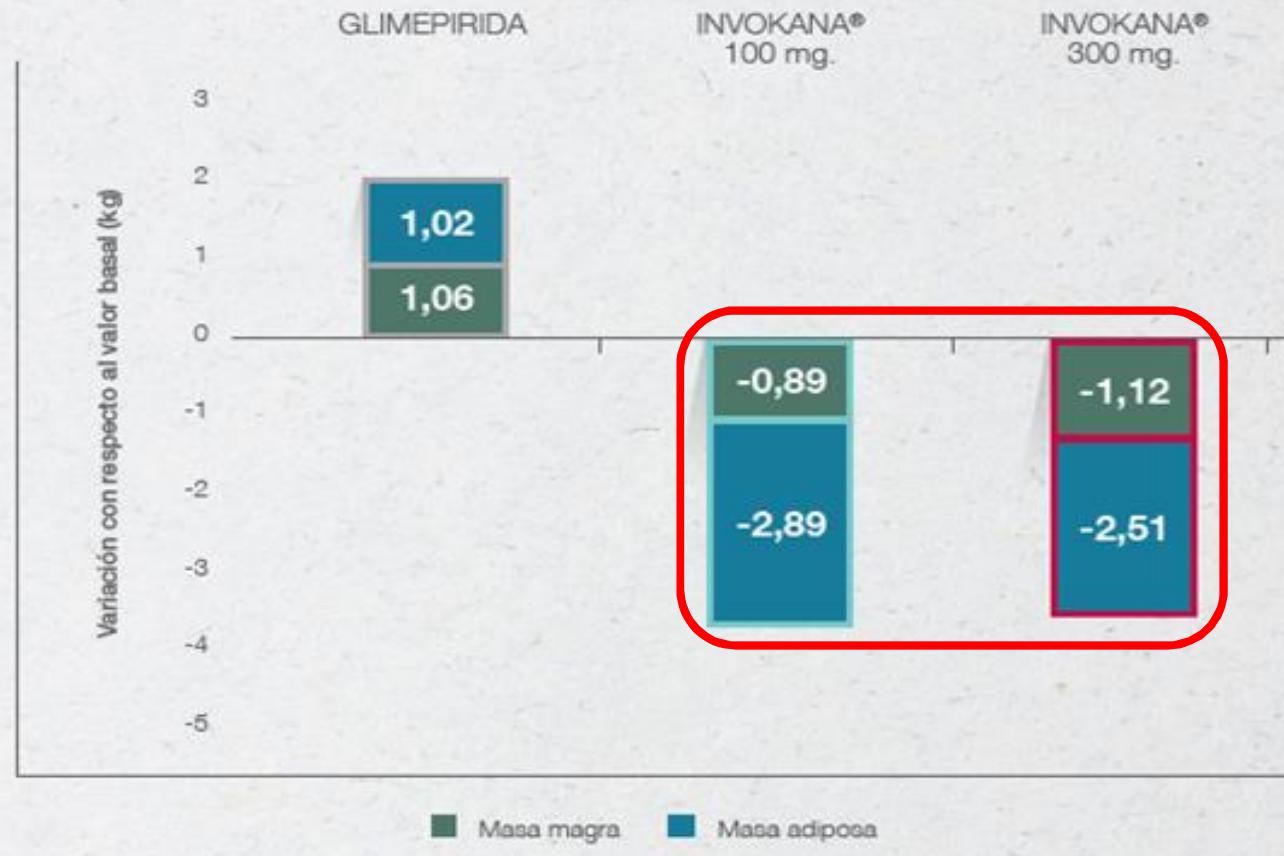
F. Zaccardi<sup>1,2</sup>, D. R. Webb<sup>1,2</sup>, Z. Z. Htike<sup>1,2</sup>, D. Youssef<sup>1,2</sup>, K. Khunti<sup>1,2</sup> & M. J. Davies<sup>1,2</sup>

<sup>1</sup> Diabetes Research Centre, University of Leicester, Leicester, UK

<sup>2</sup> Diabetes Research Center, Leicester Diabetes Centre, UHL NHS Trust, Leicester, UK



Efficacy and safety of sodium-glucose co-transporter-2 inhibitors in type 2 diabetes mellitus: systematic review and network meta-analysis. F. Zaccardi, DR. Webb et al. Diabetes, Obesity and Metabolism 2016. 18:783-794

COMPOSICIÓN CORPORAL EMPLEANDO EL ANÁLISIS DXA:  
CAMBIO MEDIO DESDE BASAL. A. DIA3009 (SEMANA 52)



CONGRESO NACIONAL  
DE MEDICINA GENERAL  
Y DE FAMILIA

San Sebastián 2017  
18-20 Mayo



Diabetes Ther (2017) 8:85–99  
DOI 10.1007/s13300-016-0217-4



CrossMark

ORIGINAL RESEARCH

## Liraglutide Versus SGLT-2 Inhibitors in People with Type 2 Diabetes: A Network Meta-Analysis

Maria Lorenzi · Uffe Jon Ploug · Jakob Langer · Rasmus Skovgaard ·  
Michael Zoratti · Jeroen Jansen

- Canagliflozina 300: - 2.27 Kg
- Canagliflozina 100: - 1.73 Kg
- Liraglutida 1.8 mg: - 1.59 Kg
- Liraglutida 1.2 mg: - 1.27 Kg



CrossMark

click for updates

Original Research

Safety and efficacy of canagliflozin in Japanese patients with type 2 diabetes mellitus: *post hoc* subgroup analyses according to body mass index in a 52-week open-label study

## Evalúa eficacia de canagliflozina según IMC

< 22 Kg/m<sup>2</sup>

22-25 Kg/m<sup>2</sup>

25-30 Kg/m<sup>2</sup>

> 30 Kg/m<sup>2</sup>

**Similares modificaciones de  
HbA1c y glucemia basal**



CONGRESO NACIONAL  
DE MEDICINA GENERAL  
Y DE FAMILIA

San Sebastián 2017  
18-20 Mayo



## Efecto sobre la Presión Arterial Sistólica

original article

*Diabetes, Obesity and Metabolism* 18: 783–794, 2016.

© 2016 John Wiley & Sons Ltd

# Efficacy and safety of sodium-glucose co-transporter-2 inhibitors in type 2 diabetes mellitus: systematic review and network meta-analysis

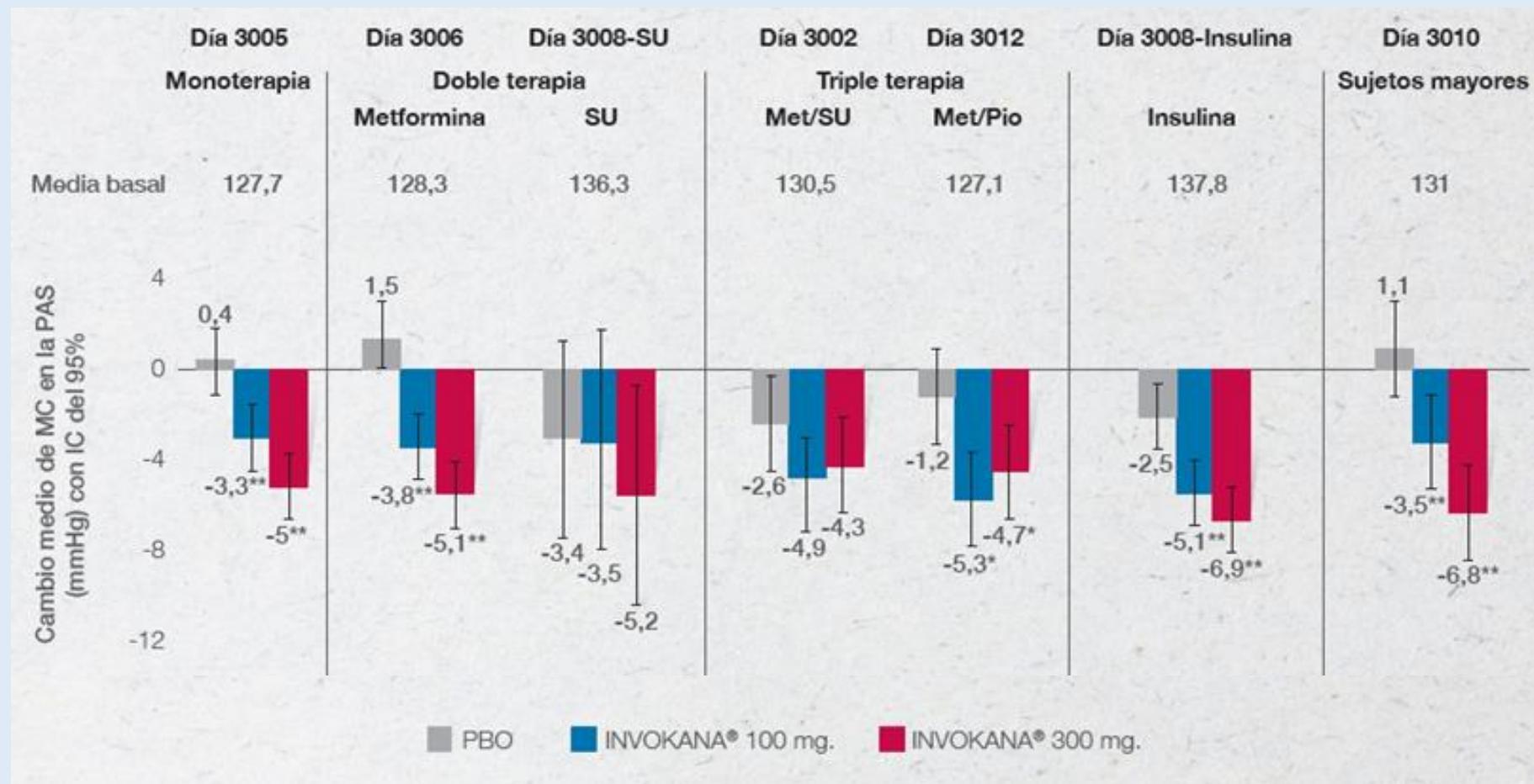
F. Zaccardi<sup>1,2</sup>, D. R. Webb<sup>1,2</sup>, Z. Z. Htike<sup>1,2</sup>, D. Youssef<sup>1,2</sup>, K. Khunti<sup>1,2</sup> & M. J. Davies<sup>1,2</sup>

<sup>1</sup> Diabetes Research Centre, University of Leicester, Leicester, UK

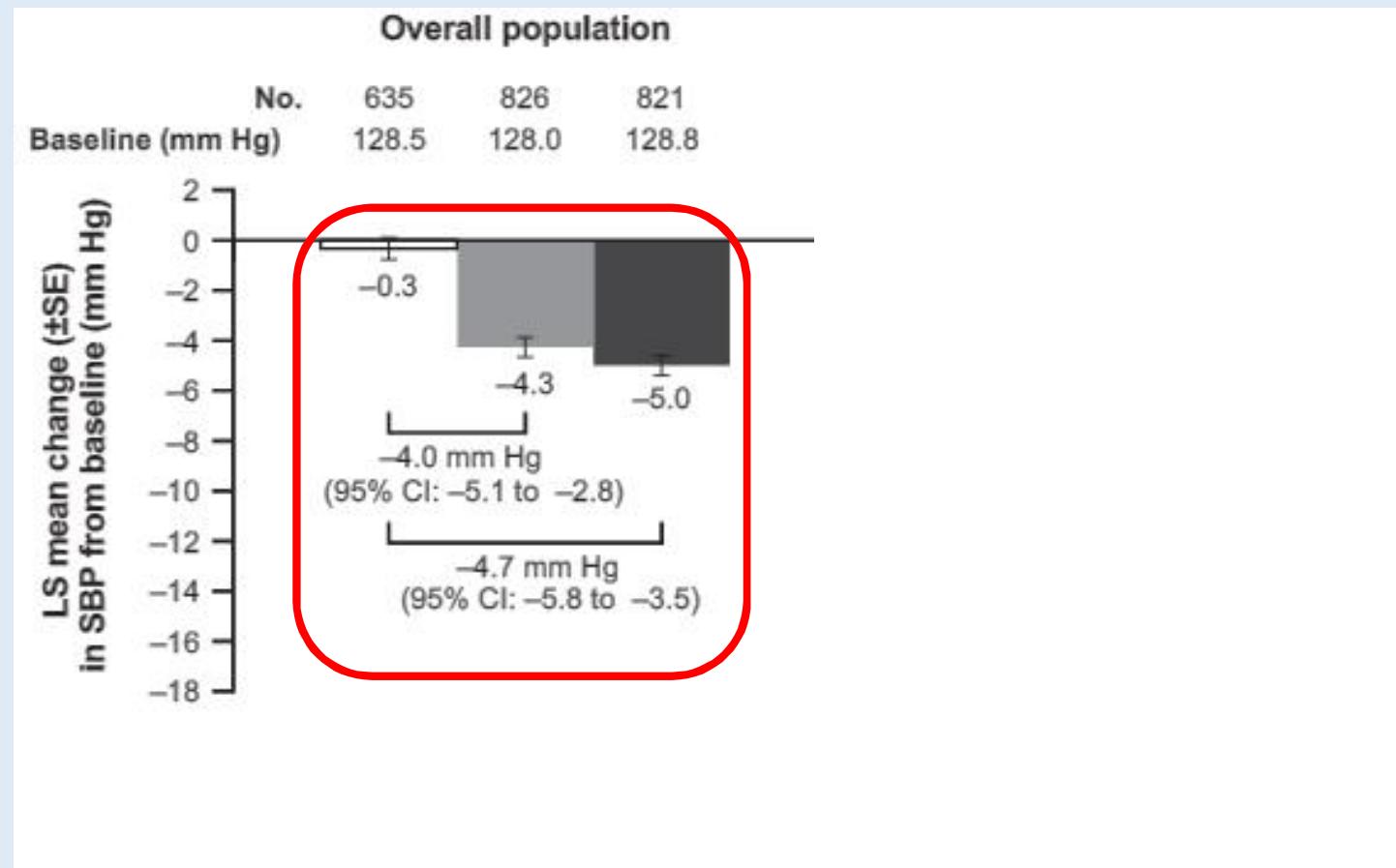
<sup>2</sup> Diabetes Research Center, Leicester Diabetes Centre, UHL NHS Trust, Leicester, UK

---

*Efficacy and safety of sodium-glucose co-transporter-2 inhibitors in type 2 diabetes mellitus: systematic review and network meta-analysis. F. Zaccardi, DR. Webb et al. Diabetes, Obesity and Metabolism 2016. 18:783-794*



Efficacy and safety of sodium-glucose co-transporter-2 inhibitors in type 2 diabetes mellitus: systematic review and network meta-analysis. F. Zaccardi, DR. Webb et al. Diabetes, Obesity and Metabolism 2016. 18:783-794



Weir MR, Januszewich A, et al. Effect of canagliflozin on blood pressure and adverse events related to osmotic diuresis and reduced intravascular volume in patients with type 2 diabetes mellitus. *J Clin Hypertens.* 2014 Dec; 16(12):875-82



CONGRESO NACIONAL  
DE MEDICINA GENERAL  
Y DE FAMILIA

San Sebastián 2017  
18-20 Mayo



## Efecto sobre el perfil lipídico

original article

*Diabetes, Obesity and Metabolism* 18: 783–794, 2016.

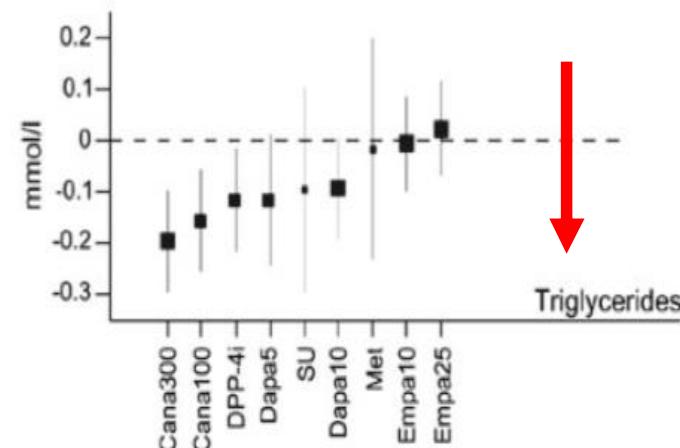
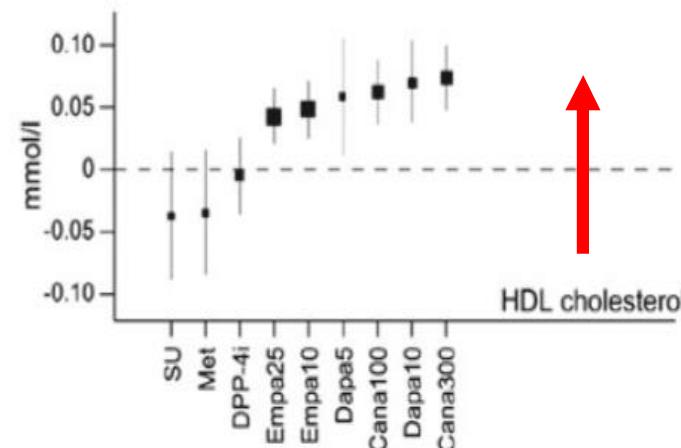
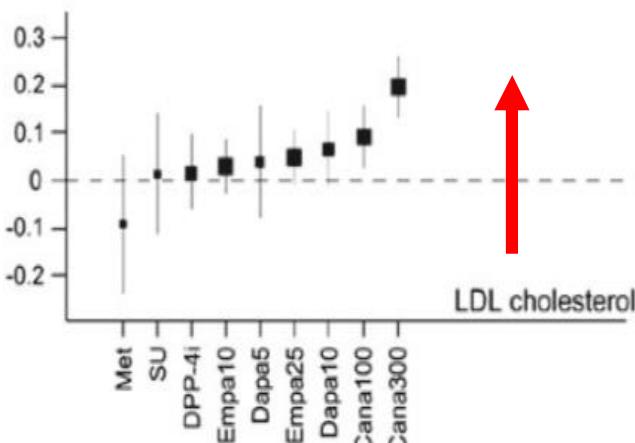
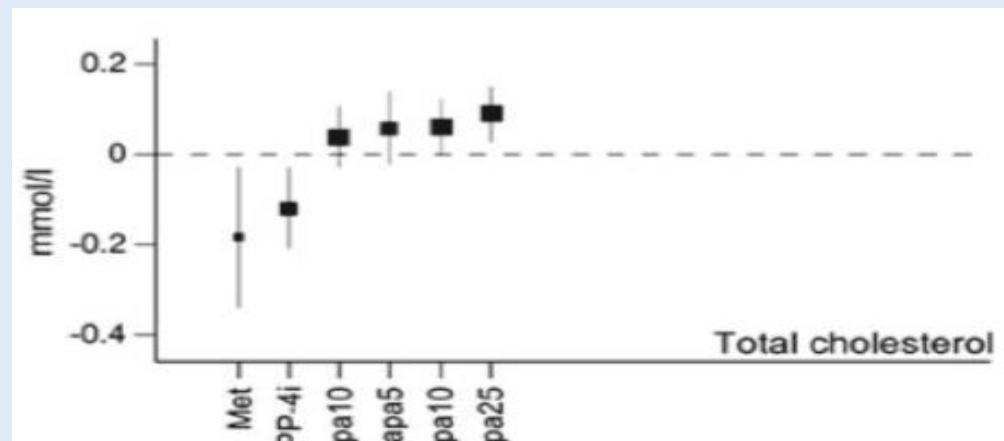
© 2016 John Wiley & Sons Ltd

# Efficacy and safety of sodium-glucose co-transporter-2 inhibitors in type 2 diabetes mellitus: systematic review and network meta-analysis

F. Zaccardi<sup>1,2</sup>, D. R. Webb<sup>1,2</sup>, Z. Z. Htike<sup>1,2</sup>, D. Youssef<sup>1,2</sup>, K. Khunti<sup>1,2</sup> & M. J. Davies<sup>1,2</sup>

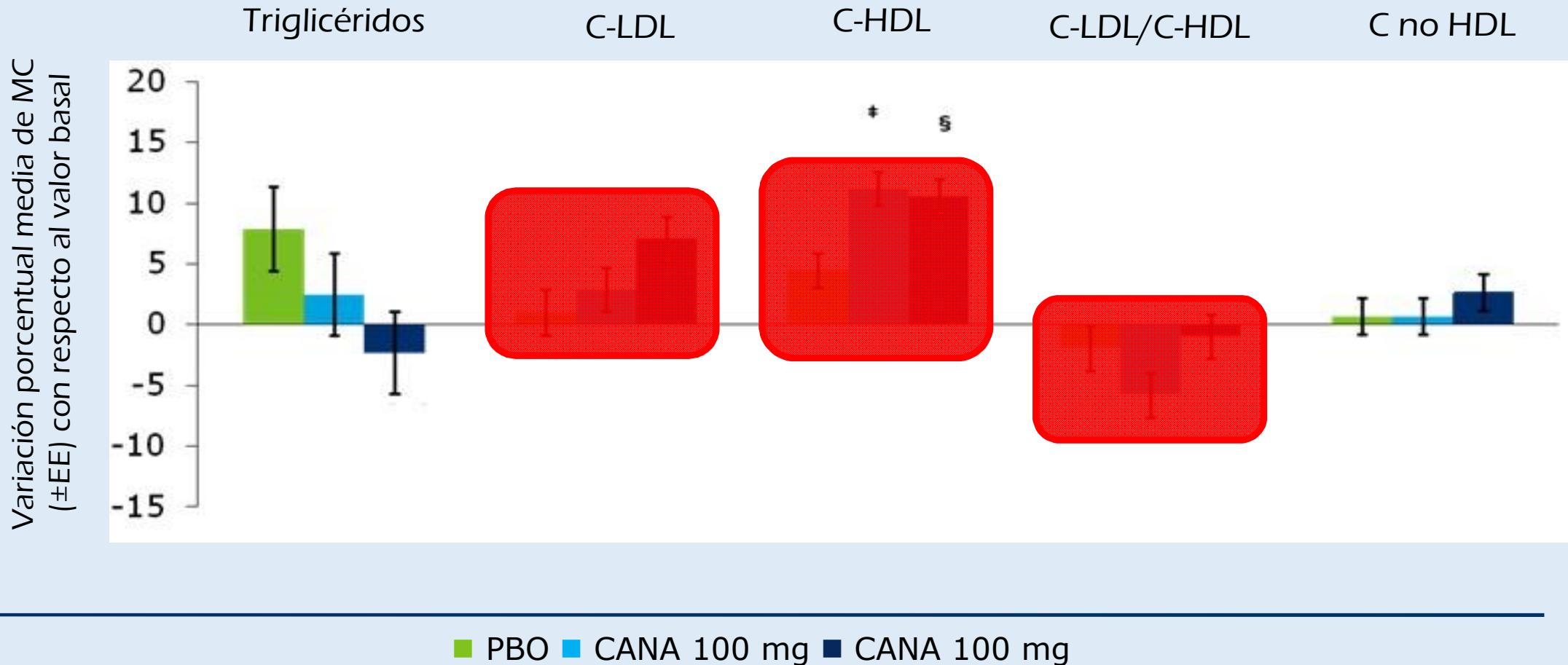
<sup>1</sup> Diabetes Research Centre, University of Leicester, Leicester, UK

<sup>2</sup> Diabetes Research Center, Leicester Diabetes Centre, UHL NHS Trust, Leicester, UK



Efficacy and safety of sodium-glucose co-transporter-2 inhibitors in type 2 diabetes mellitus: systematic review and network meta-analysis. F. Zaccardi, DR. Webb et al. Diabetes, Obesity and Metabolism 2016. 18:783-794

## Variación de los lípidos plasmáticos en ayunas en la semana 26 (LOCF)\*.





CONGRESO NACIONAL  
DE MEDICINA GENERAL  
Y DE FAMILIA

San Sebastián 2017  
18-20 Mayo



# ¿Efectos renales?



Skrtic M, Cherney D. Sodium-glucose cotransporter-2 inhibition and the potential for renal protection in diabetic nephropathy. [www.conephrolhypertens.com](http://www.conephrolhypertens.com) Volume 24, Number 1, January 2015



## Otros efectos extraglucémicos

- Reducción de la volemia (volumen plasmático)
- Aumento del hematocrito
- Disminución del ácido úrico
- ↑ Na<sup>+</sup> a nivel distal del túbulo (co-transportador Na-Glucosa)

Tto Farmacológico  
(ISGLT-2)

### Control glucémico:

- HbA1c
- Glucemia basal
- Glucemia posprandial

### Objetivos extraglucémicos:

- Peso
- Presión Arterial
- Perfil lipídico
- Efecto renal
- Otros

¿Prevención  
Macrovascular?





CONGRESO NACIONAL  
DE MEDICINA GENERAL  
Y DE FAMILIA

San Sebastián 2017  
18-20 Mayo



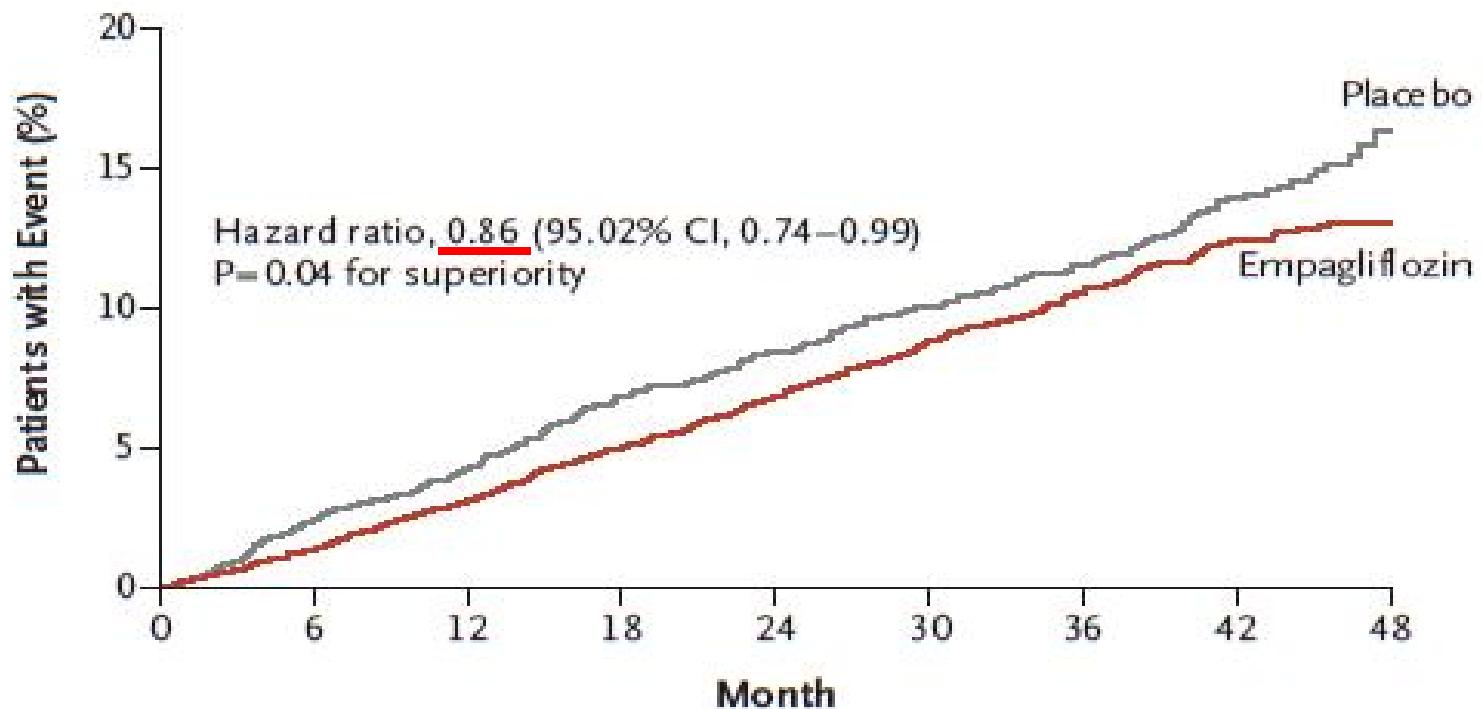
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

# Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes

Bernard Zinman, M.D., Christoph Wanner, M.D., John M. Lachin, Sc.D.,  
David Fitchett, M.D., Erich Bluhmki, Ph.D., Stefan Hantel, Ph.D.,  
Michaela Mattheus, Dipl. Biomath., Theresa Devins, Dr.P.H.,  
Odd Erik Johansen, M.D., Ph.D., Hans J. Woerle, M.D., Uli C. Broedl, M.D.,  
and Silvio E. Inzucchi, M.D., for the EMPA-REG OUTCOME Investigators

Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes. Bernard Zinman, M.D., Christoph Wanner, M.D., et al September 17, 2015 DOI: 10.1056/NEJMoa1504720

**A Primary Outcome****No. at Risk**

Empagliflozin	4687	4580	4455	4328	3851	2821	2359	1534	370
Placebo	2333	2256	2194	2112	1875	1380	1161	741	166



CONGRESO NACIONAL  
DE MEDICINA GENERAL  
Y DE FAMILIA

San Sebastián 2017  
18-20 Mayo



ACC.17

66<sup>th</sup> Annual Scientific Session & Expo

## LOWER RATES OF HOSPITALIZATION FOR HEART FAILURE AND ALL-CAUSE DEATH IN NEW USERS OF SGLT-2 INHIBITORS VERSUS OTHER GLUCOSE LOWERING DRUGS – REAL WORLD DATA FROM SIX COUNTRIES AND MORE THAN 300,000 PATIENTS: THE CVD-REAL STUDY

Mikhail Kosiborod, MD on behalf of the CVD-REAL Investigators and Study Team

WASHINGTON, DC  
**FRI • SAT • SUN**  
MARCH 17 – 19, 2017



## Data Sources: Health Records Across Six Countries



Truven MarketScan Claims & Encounters and linked Medicare



National full-population registries



National full-population registries



National full-population registries



Clinical Practice Research Datalink (CPRD) and  
The Health Improvement Network (THIN)



Diabetes Patienten Verlaufsdokumentation (DPV) initiative

HHF

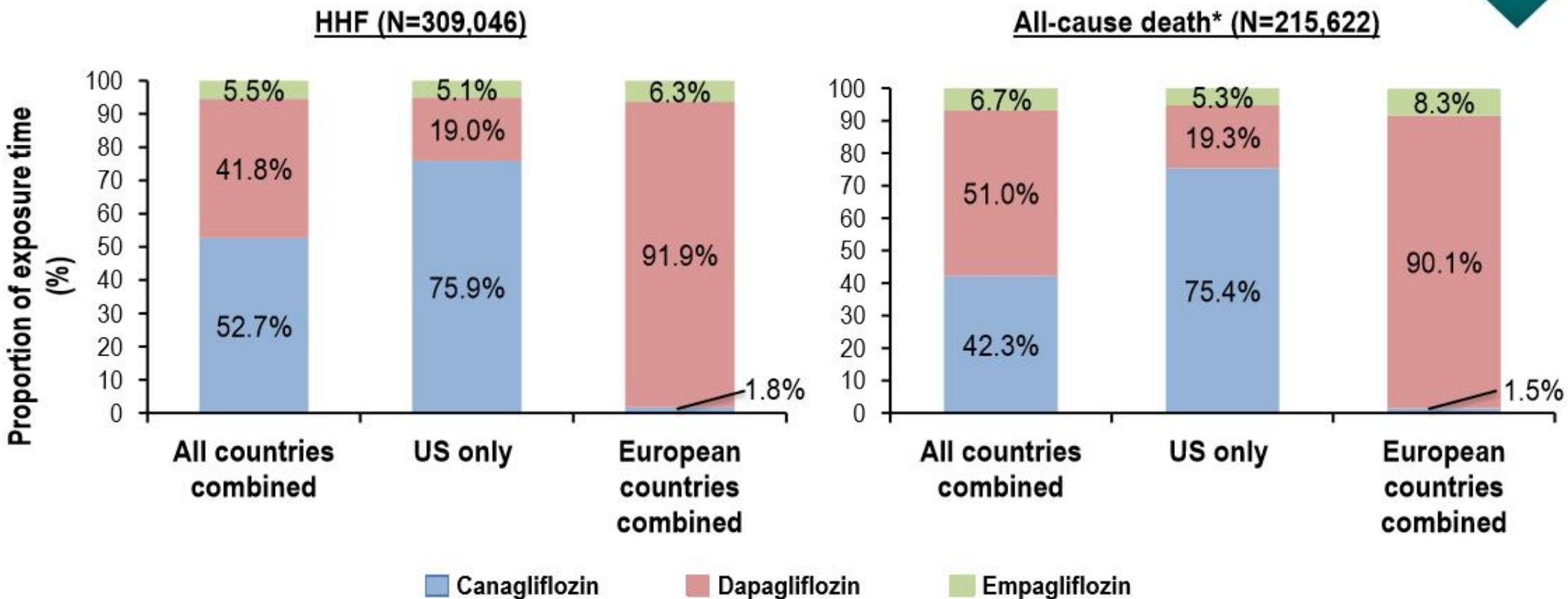
All-cause death  
and composite  
HHF/all-cause death



## Contribution of SGLT-2i compounds

**300.000****20% Prevención Secundaria**

ACC.17



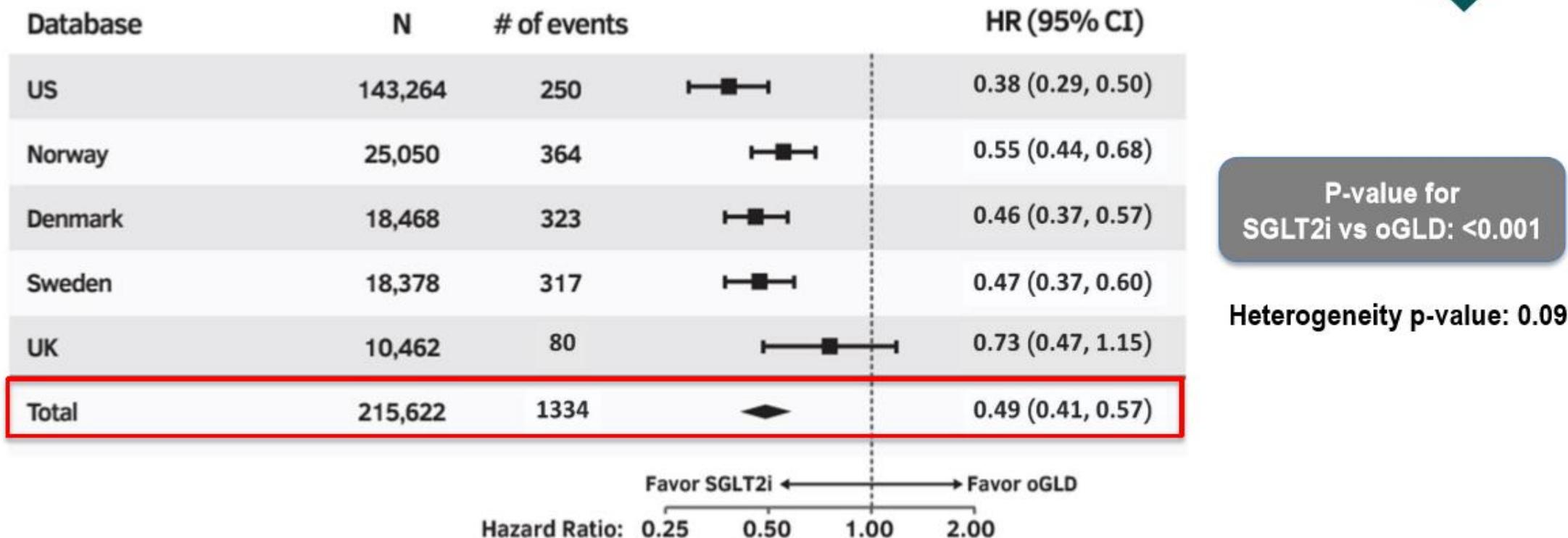


CVD REAL

# All-Cause Death



ACC.17

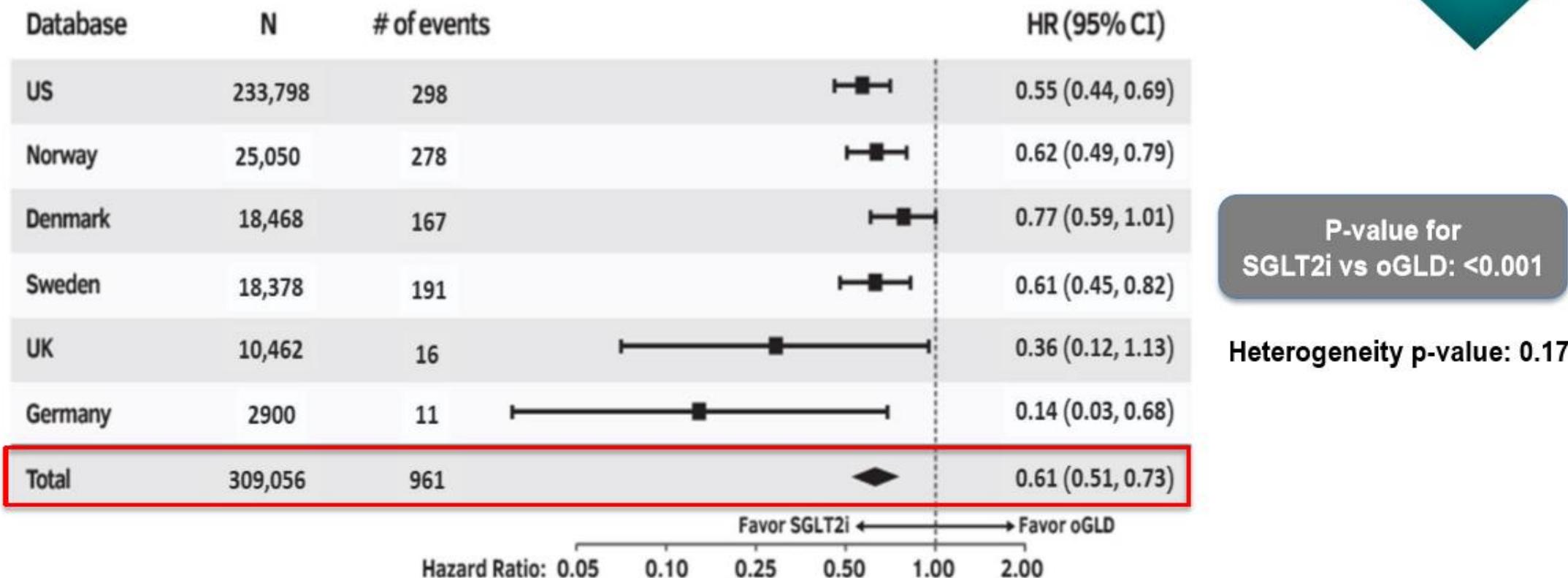




# HHF Primary Analysis



ACC.17





CONGRESO NACIONAL  
DE MEDICINA GENERAL  
Y DE FAMILIA

San Sebastián 2017  
18-20 Mayo



EXPERIENCE  
NEW HORIZONS  
IN DIABETES

SAN DIEGO, CA  
JUNE 9-13, 2017

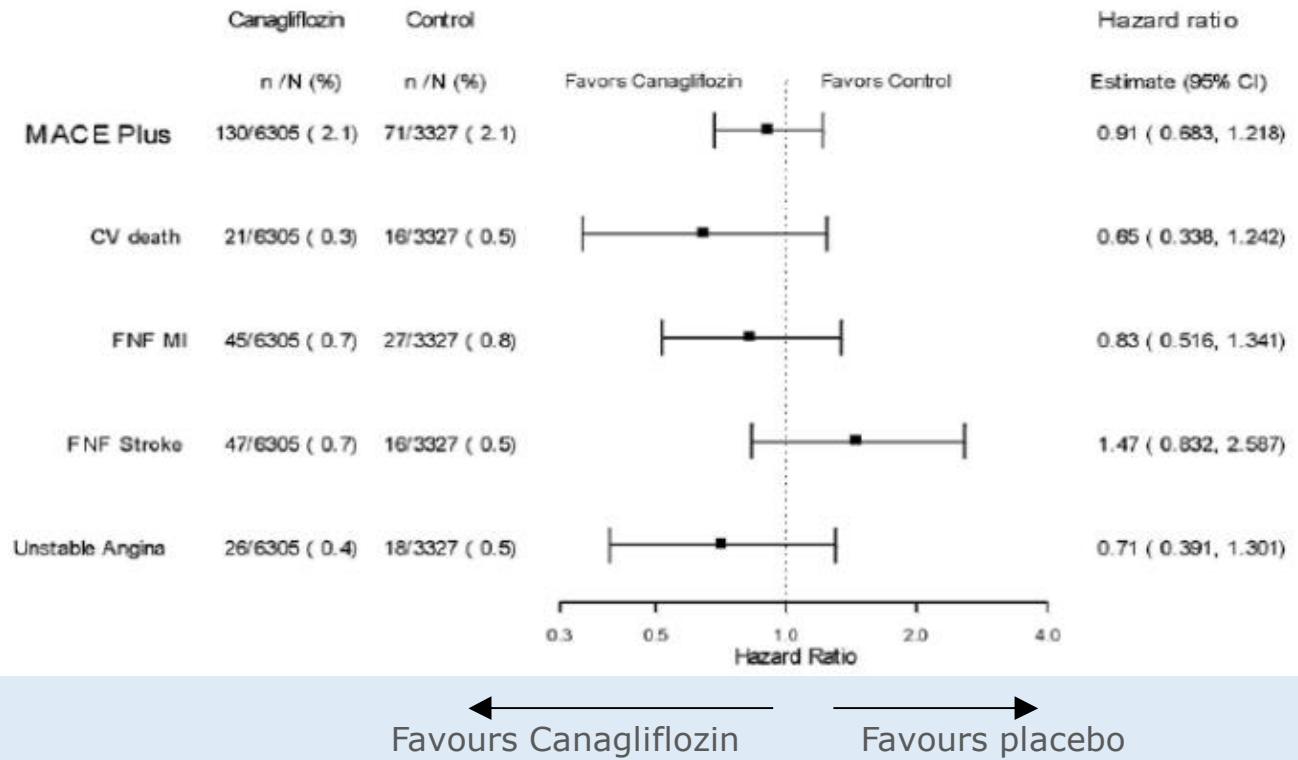
# CANVAS

## CANVAS-R

24:09:38:35

DAYS      HOURS      MINUTES      SECONDS

Figure 36: Forest Plot of Hazard Ratio for CV Components of the Primary Composite Endpoint (Phase 2/3 Studies)



**Add another agent best suited to the individual by prioritizing patient characteristics:**

PATIENT CHARACTERISTIC	CHOICE OF AGENT
<b>Priority:</b> Clinical cardiovascular disease	→ Antihyperglycemic agent with demonstrated CV outcome benefit (empagliflozin, liraglutide)
<ul style="list-style-type: none"><li>• Degree of hyperglycemia</li><li>• Risk of hypoglycemia</li><li>• Overweight or obesity</li><li>• Cardiovascular disease or multiple risk factors</li><li>• Comorbidities (renal, CHF, hepatic)</li><li>• Preferences &amp; access to treatment</li></ul>	<ul style="list-style-type: none"><li>• Consider relative A1C lowering</li><li>• Rare hypoglycemia</li><li>• Weight loss or weight neutral</li><li>• Effect on cardiovascular outcome</li><li>• See therapeutic considerations, consider eGFR</li><li>• See cost column; consider access</li></ul>



## GLYCEMIC CONTROL ALGORITHM



### LIFESTYLE THERAPY (Including Medically Assisted Weight Loss)

Entry A1C < 7.5%

Entry A1C ≥ 7.5%

Entry A1C > 9.0%

#### MONOTHERAPY\*

- ✓ Metformin
- ✓ GLP-1 RA
- ✓ SGLT-2i
- ✓ DPP-4i
- ⚠ TZD
- ✓ AGi
- ⚠ SU/GLN

If not at goal in 3 months  
proceed to Dual Therapy

#### DUAL THERAPY\*

- ✓ GLP-1 RA
- ✓ SGLT-2i
- ✓ DPP-4i
- ⚠ TZD
- ✓ Basal Insulin
- ✓ Colesevelam
- ✓ Bromocriptine QR
- ✓ AGi
- ⚠ SU/GLN

If not at goal  
in 3 months  
proceed to  
Triple Therapy

#### TRIPLE THERAPY\*

MET  
or other  
1st-line  
agent +  
2nd-line  
agent

- ✓ GLP-1 RA
- ✓ SGLT-2i
- ⚠ TZD
- ⚠ Basal insulin
- ✓ DPP-4i
- ✓ Colesevelam
- ✓ Bromocriptine QR
- ✓ AGi
- ⚠ SU/GLN

If not at goal in  
3 months proceed  
to or intensify  
insulin therapy

#### SYMPTOMS

NO YES

DUAL  
Therapy

INSULIN  
±  
Other  
Agents

TRIPLE  
Therapy

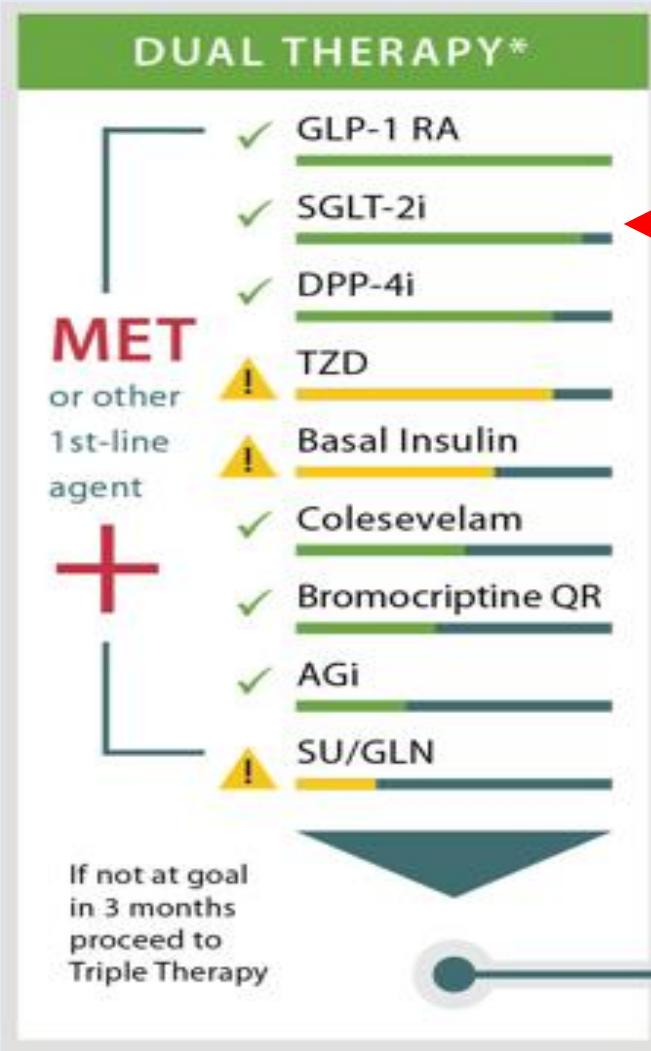
#### ADD OR INTENSIFY INSULIN

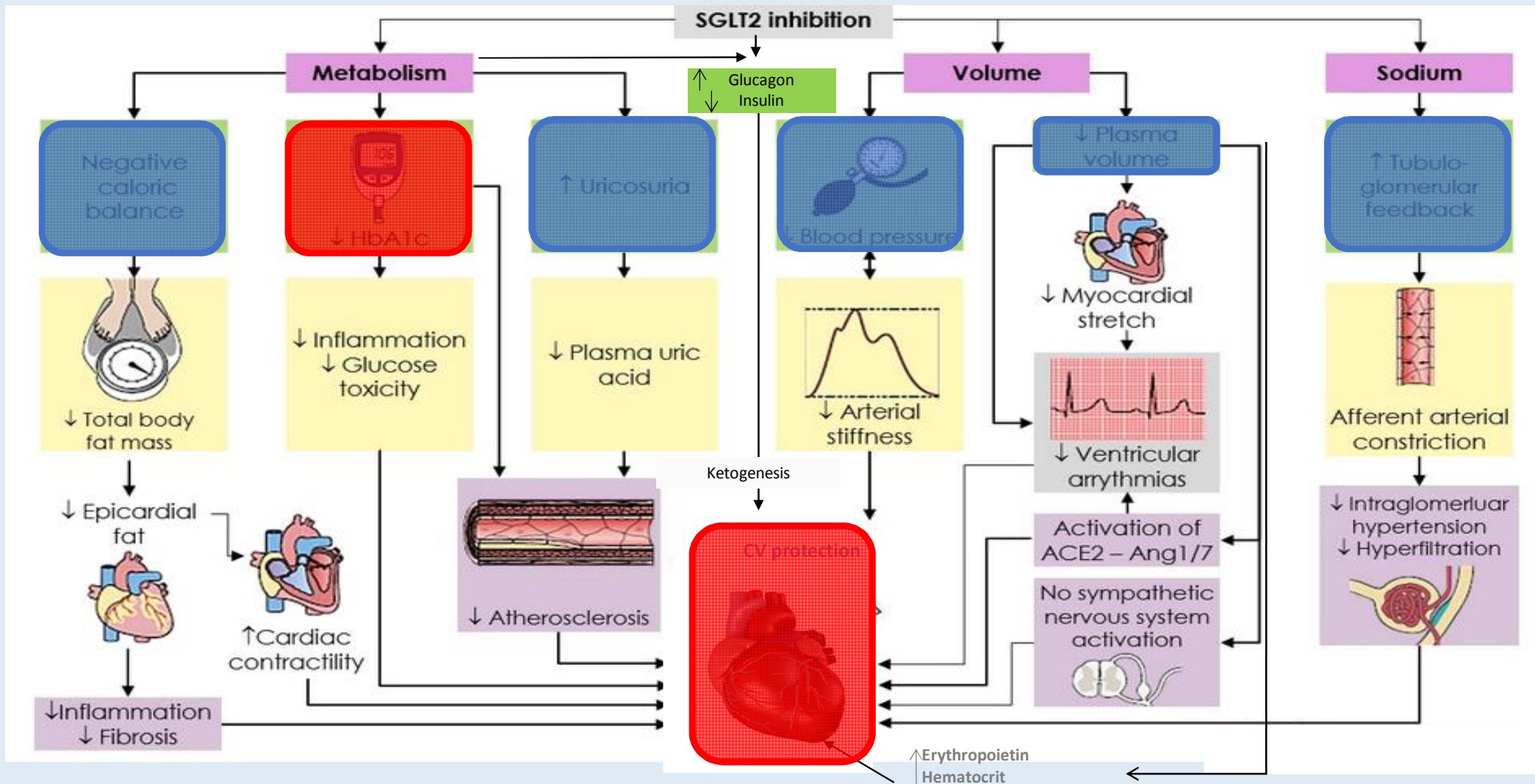
Refer to Insulin Algorithm

#### LEGEND

- ✓ Few adverse events and/or possible benefits
- ⚠ Use with caution

\* Order of medications represents a suggested hierarchy of usage;





Modificado de Heerspink HJ, et al. Circulation.2016 Sep 6;134(10):752-72

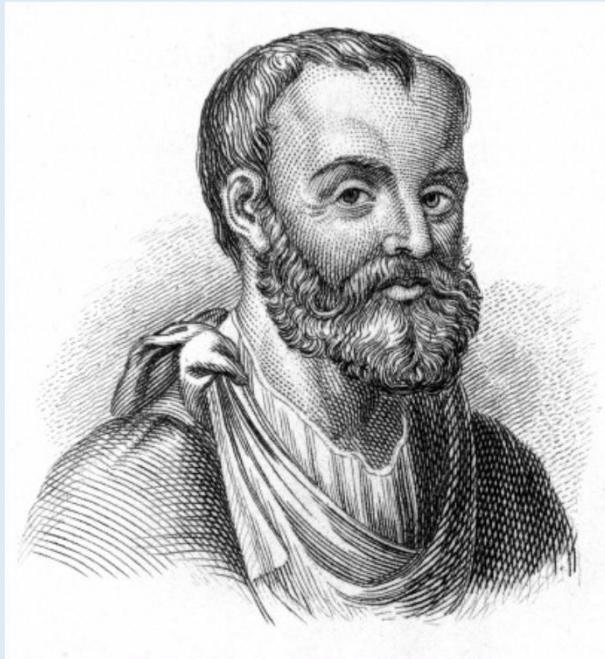


# CONCLUSIONES:

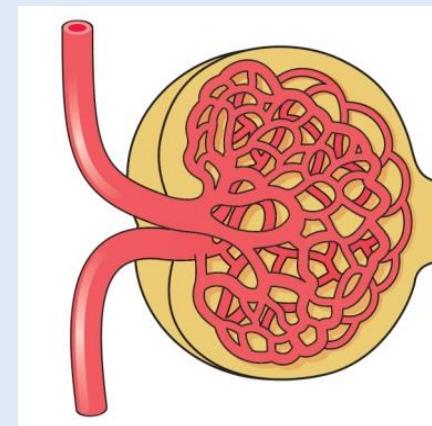
- Optimo control de parámetros glucémicos
- Efecto sobre multitud de parámetros extraglucémicos
- Parámetros subrogados → eventos macrovasculares
- Evidencia favorable previa
- Nueva evidencia favorable
- Futura evidencia

# Galenos

Pérgamo-Grecia 130-200 dC



Diabetes  
Enfermedad rara  
Sustrato renal  
Hidropesia en orina o diarrea en orina





CONGRESO NACIONAL  
DE MEDICINA GENERAL  
Y DE FAMILIA

San Sebastián 2017  
18-20 Mayo



*Gracias!!!*



CONGRESO NACIONAL  
DE MEDICINA GENERAL  
Y DE FAMILIA

San Sebastián 2017  
18-20 Mayo

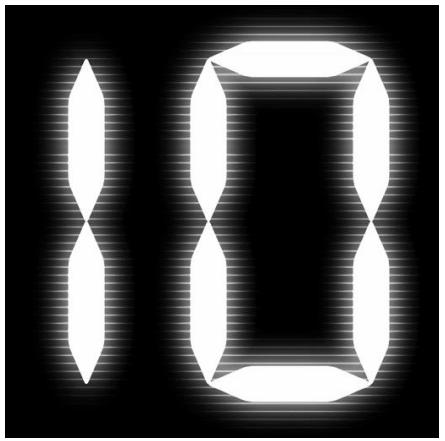




CONGRESO NACIONAL  
DE MEDICINA GENERAL  
Y DE FAMILIA

San Sebastián 2017  
18-20 Mayo

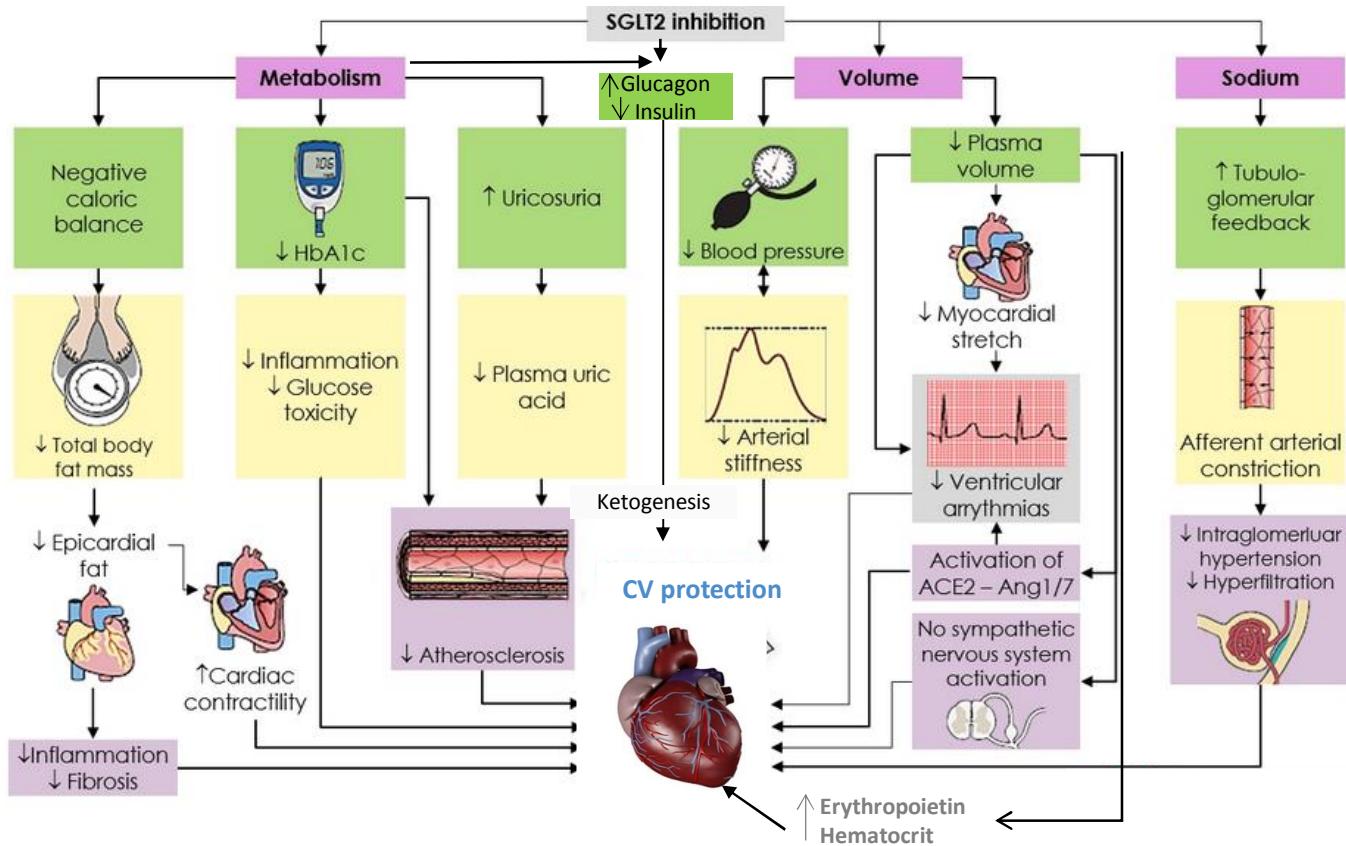




**02:09:38:35**

DAYS      HOURS      MINUTES      SECONDS

A digital timer or clock display. The main time value is shown as "02:09:38:35" in large, bold, white digits. Below this, there are four smaller labels: "DAYS", "HOURS", "MINUTES", and "SECONDS", each aligned with its respective colon separator. The entire display is contained within a dark rectangular box.



Modificado de Heerspink HJ, et al. Circulation.2016 Sep 6;134(10):752-72



## Liraglutide Versus SGLT-2 Inhibitors in People with Type 2 Diabetes: A Network Meta-Analysis

Maria Lorenzi · Uffe Jon Ploug · Jakob Langer · Rasmus Skovgaard ·  
Michael Zoratti · Jeroen Jansen

Placebo	1.27 (0.61, 1.90)	1.59 (0.96, 2.24)	1.73 (1.25, 2.20)	2.27 (1.79, 2.71)	2.05 (1.44, 2.66)	2.12 (1.39, 2.86)	1.70 (1.26, 2.13)	2.00 (1.56, 2.44)	-0.49 (-0.96, 0.01)
-1.27 (-1.90, -0.61)	<b>Liraglutide 1.2 mg</b>	0.32 (-0.23, 0.86)	0.46 (-0.27, 1.19)	<b>0.99 (0.31, 1.71)</b>	0.79 (-0.11, 1.66)	0.86 (-0.14, 1.82)	0.44 (-0.36, 1.23)	0.74 (-0.05, 1.53)	-1.75 (-2.39, -1.09)
-1.59 (-2.24, -0.96)	-0.32 (-0.86, 0.23)	<b>Liraglutide 1.8 mg</b>	0.15 (-0.59, 0.83)	0.68 (-0.03, 1.35)	0.47 (-0.44, 1.35)	0.54 (-0.46, 1.50)	0.12 (-0.68, 0.88)	0.42 (-0.38, 1.19)	-2.07 (-2.73, -1.43)
-1.73 (-2.20, -1.25)	-0.46 (-1.19, 0.27)	-0.15 (-0.83, 0.59)	<b>Canagliflozin 100 mg</b>	<b>0.53 (0.14, 0.94)</b>	0.32 (-0.43, 1.11)	0.38 (-0.47, 1.27)	-0.03 (-0.67, 0.62)	0.27 (-0.37, 0.93)	-2.22 (-2.67, -1.73)
-2.27 (-2.71, -1.79)	<b>-0.99 (-1.71, -0.31)</b>	-0.68 (-1.35, 0.03)	<b>-0.53 (-0.94, -0.14)</b>	<b>Canagliflozin 300 mg</b>	-0.20 (-0.98, 0.55)	-0.14 (-1.02, 0.73)	-0.56 (-1.20, 0.07)	-0.26 (-0.89, 0.38)	-2.74 (-3.16, -2.32)
-2.05 (-2.66, -1.44)	-0.79 (-1.66, 0.11)	-0.47 (-1.35, 0.44)	-0.32 (-1.11, 0.43)	0.20 (-0.55, 0.98)	<b>Dapagliflozin 10 mg</b>	0.06 (-0.66, 0.80)	-0.35 (-1.11, 0.41)	-0.05 (-0.81, 0.69)	-2.54 (-3.31, -1.75)
-2.12 (-2.86, -1.39)	-0.86 (-1.82, 0.14)	-0.54 (-1.50, 0.46)	-0.38 (-1.27, 0.47)	0.14 (-0.73, 1.02)	-0.06 (-0.80, 0.66)	<b>Dapagliflozin 5 mg</b>	-0.42 (-1.29, 0.44)	-0.12 (-0.98, 0.72)	-2.61 (-3.48, -1.71)
-1.70 (-2.13, -1.26)	-0.44 (-1.23, 0.36)	-0.12 (-0.88, 0.68)	0.03 (-0.62, 0.67)	0.56 (-0.07, 1.20)	0.35 (-0.41, 1.11)	0.42 (-0.44, 1.29)	<b>Empagliflozin 10 mg</b>	0.30 (-0.14, 0.75)	-2.19 (-2.83, -1.51)
-2.00 (-2.44, -1.56)	-0.74 (-1.53, 0.05)	-0.42 (-1.19, 0.38)	-0.27 (-0.93, 0.37)	0.26 (-0.38, 0.89)	0.05 (-0.69, 0.81)	0.12 (-0.72, 0.98)	-0.30 (-0.75, 0.14)	<b>Empagliflozin 25 mg</b>	-2.49 (-3.14, -1.81)
0.49 (-0.01, 0.96)	<b>1.75 (1.09, 2.39)</b>	<b>2.07 (1.43, 2.73)</b>	<b>2.22 (1.73, 2.67)</b>	<b>2.74 (2.32, 3.16)</b>	<b>2.54 (1.75, 3.31)</b>	<b>2.61 (1.71, 3.48)</b>	<b>2.19 (1.51, 2.83)</b>	<b>2.49 (1.81, 3.14)</b>	<b>Sitagliptin 100 mg</b>



**los inhibidores de los cotransportadores SGLT-2**