



## Cómo se entrelazan DM y enfermedad CV: terapias que disminuyen mortalidad

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## Conflictos de interés

- Conferencista: Astra Zeneca, Abbott Nutrición, Novartis, Novo Nordisk, Merck Sharp & Dohme, Roche, Glaxo SmithKline, Sanofi Aventis, Bayer, Pfizer
- Advisory Board: Novartis Oncology, Sanofi Aventis, Astra Zeneca, Novo Nordisk, Stendhal, Pfizer
- Investigación clínica: Astra Zeneca, Novartis Pharma Logistics Inc., Merck Sharp & Dohme, Glaxo SmithKline, Organon, Boehringer Ingelheim, Roche, Novo Nordisk

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## Agenda

- DM y enfermedad cardiovascular
- Medidas que reducen mortalidad CV en DM:
  - Estatinas
  - Antihipertensivos
  - Antiagregantes?
  - Antidiabéticos
- Abordaje práctico

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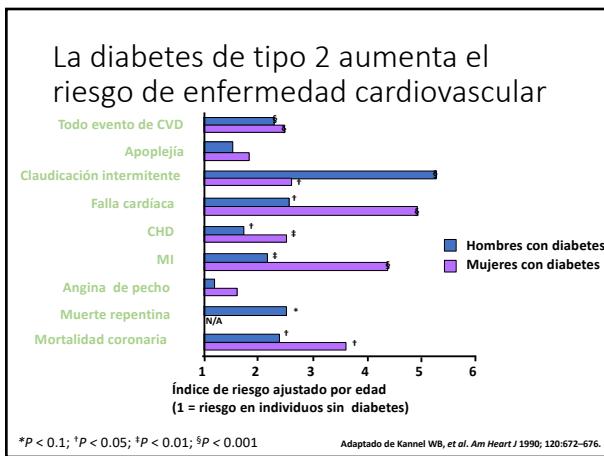
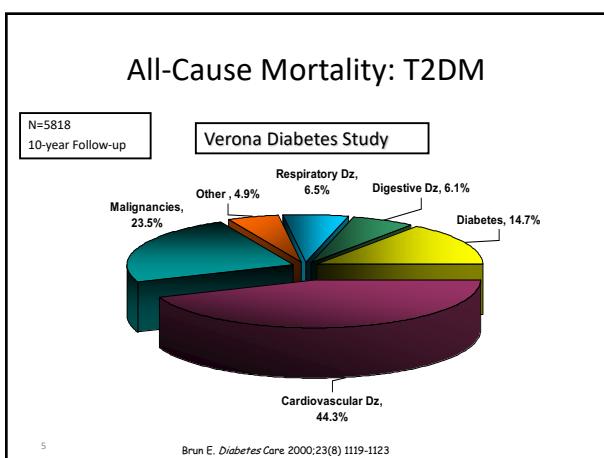


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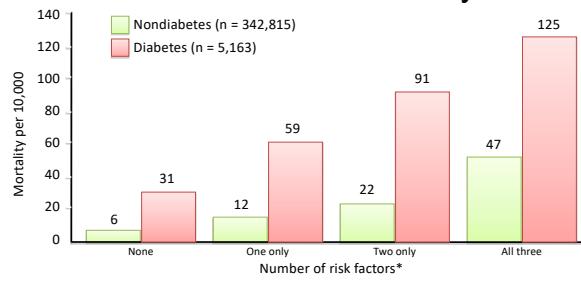


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## Relación DM y enfermedad cardiovascular



### MRFIT: Impact of Diabetes on Cardiovascular Mortality



\*Risk factors analyzed: smoking, hypercholesterolemia and hypertension.

Stamler J, et al. *Diabetes Care* 1993; 16(2):434-44

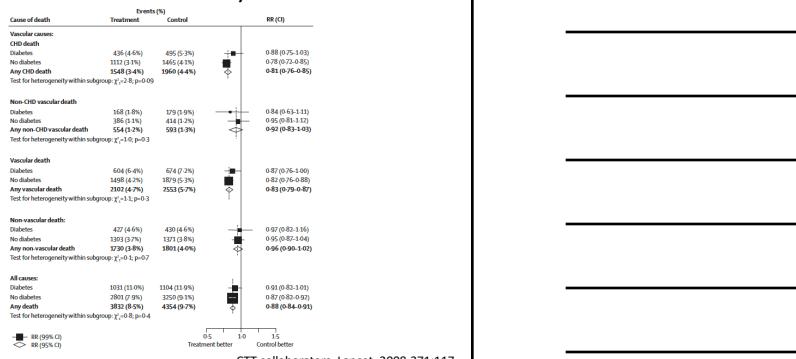
### Riesgo de DM post SCA

- 20% tiene DM usando criterios por CTG
- 16% tienen DM usando Hba1c

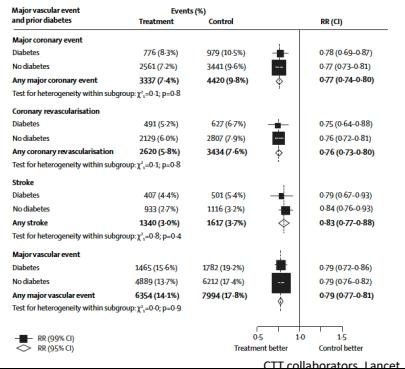
Karamat MA. BioMed Central. 2017

### Medidas extraglicémicas

## Metanálisis estatinas y mortalidad

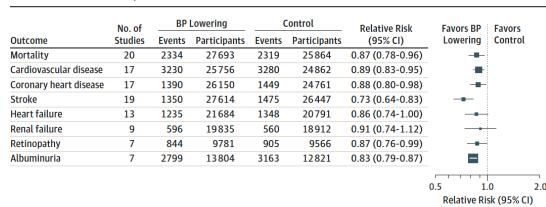


## Metanálisis estatinas en DM



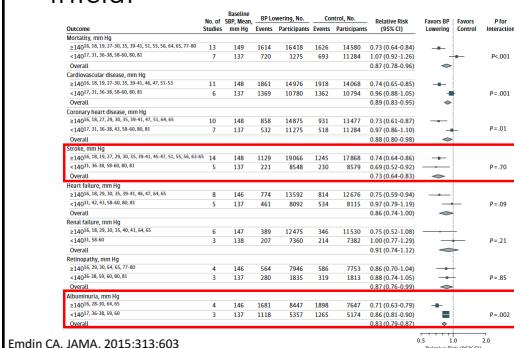
## Metanálisis: reducción de PA en DM

Figure 2. Standardized Associations Between 10-mm Hg Lower Systolic BP and All-Cause Mortality, Macrovascular Outcomes, and Microvascular Outcomes in Diabetic Patients



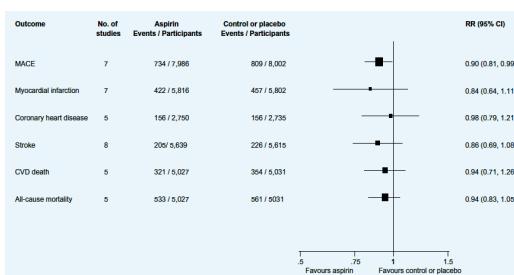
Emdin CA. JAMA. 2015;313:603

## Reducción de eventos según PA inicial



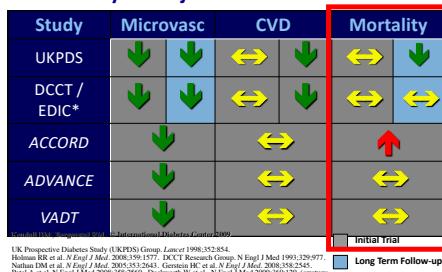
Emdin CA. JAMA. 2015;313:603

## Aspirina y mortalidad en prevención primaria en DM



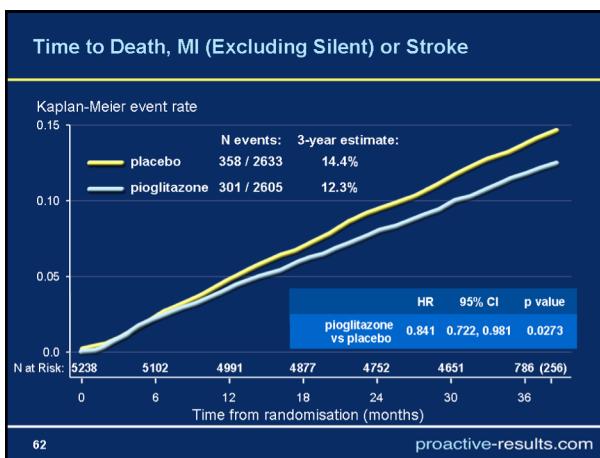
Kunutsor SK. Diab Med. 2017;34:316

## Impact of Intensive Therapy for Diabetes: Summary of Major Clinical Trials

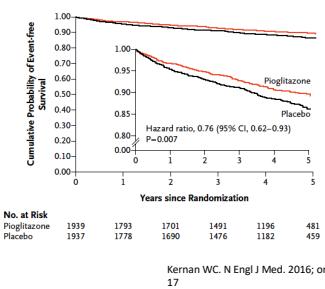


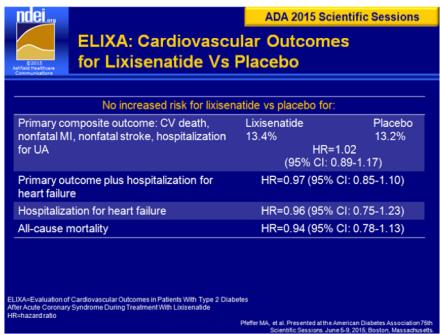
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## Antidiabéticos



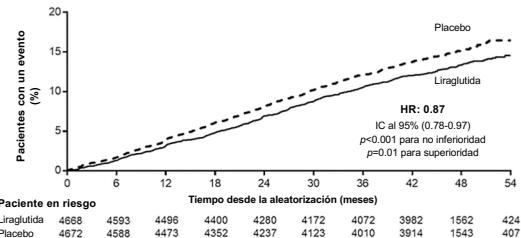
## IRIS: pioglitazona en ictus





## Desenlaces primarios

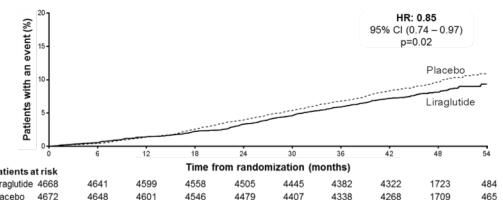
muerte por enfermedad CV, infarto de miocardio no fatal o accidente cerebrovascular no fatal



**LEADER**  
Liraglutide and empagliflozin in patients with type 2 diabetes mellitus: Evaluation of cardiovascular outcomes results

Marsi SP et al. N Engl J Med 2016;375:311-322

## All-cause death



The cumulative incidences were estimated with the use of the Kaplan-Meier method, and the hazard ratios with the use of the Cox proportional-hazard regression model. The hazard ratios are truncated at 54 months, because less than 10% of the patients had an observation time beyond 54 months. HR=hazard ratio.

Presented at the American Diabetes Association 76th Scientific Sessions, Session 3-CT-SY24, June 13-2016, New Orleans, LA, USA.

**LEADER**  
Liraglutide and empagliflozin in patients with type 2 diabetes mellitus: Evaluation of cardiovascular outcomes results

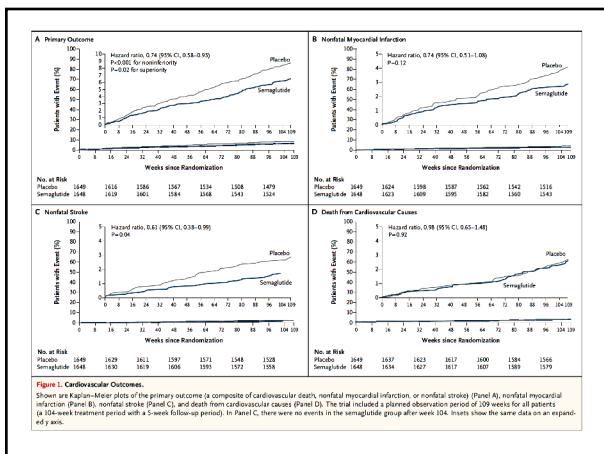
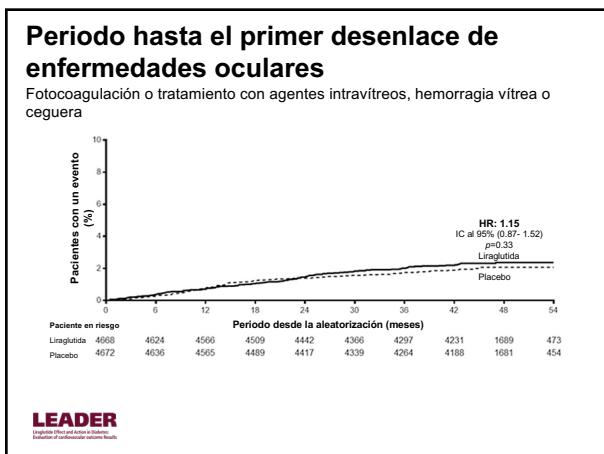
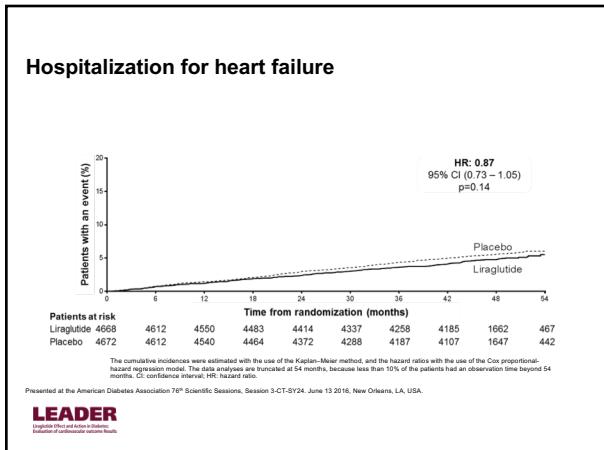
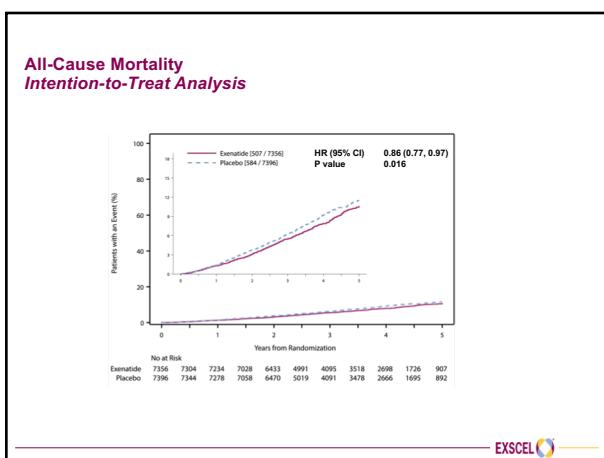
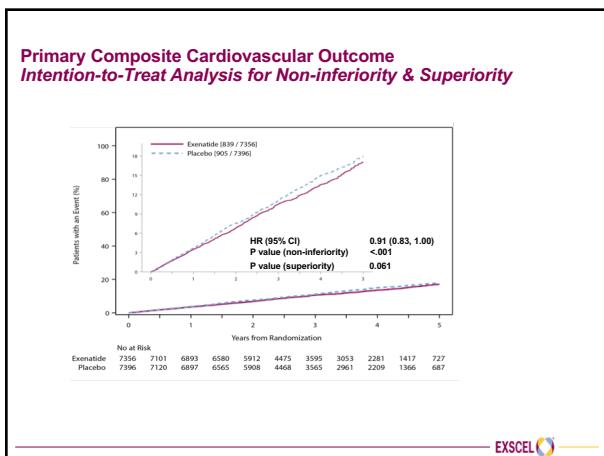
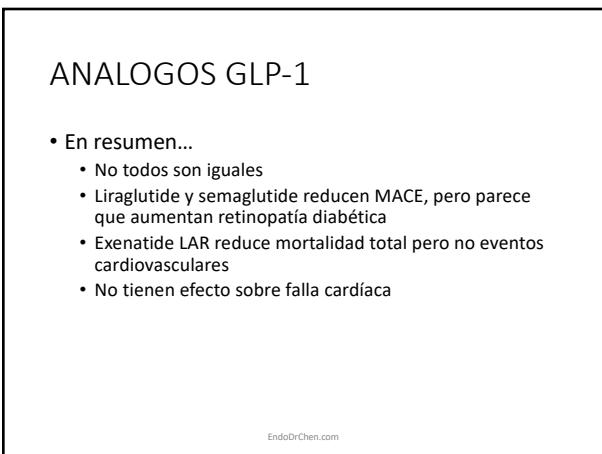
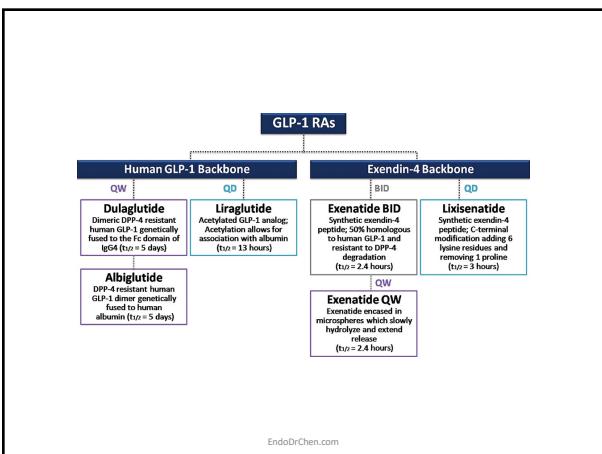
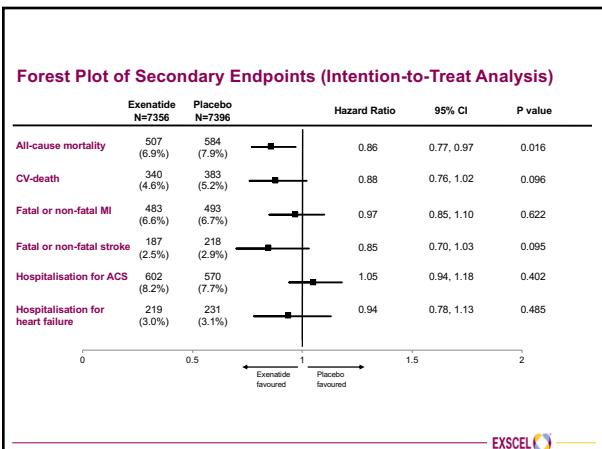
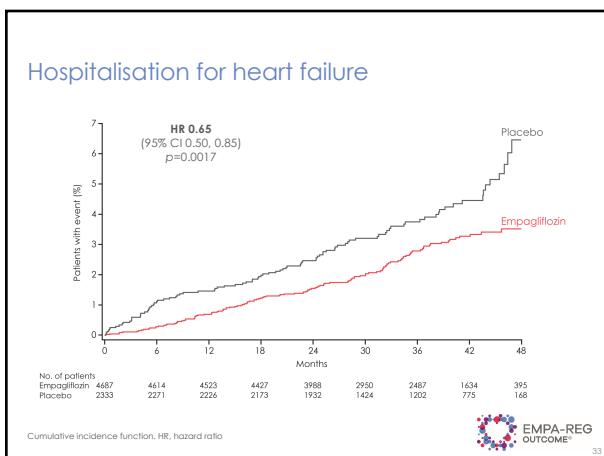
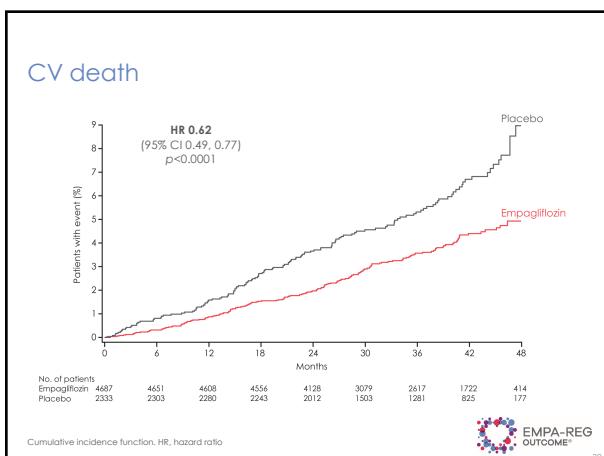
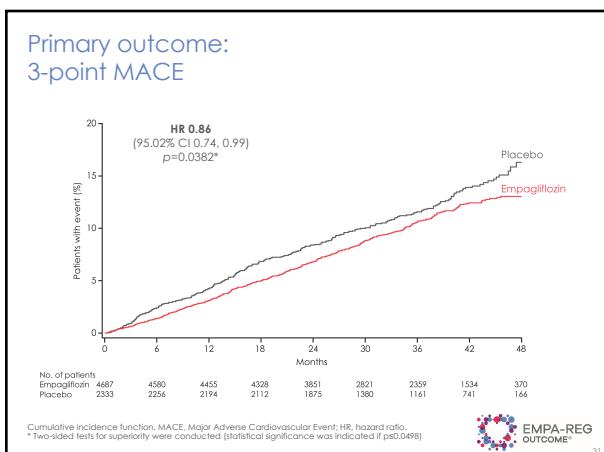


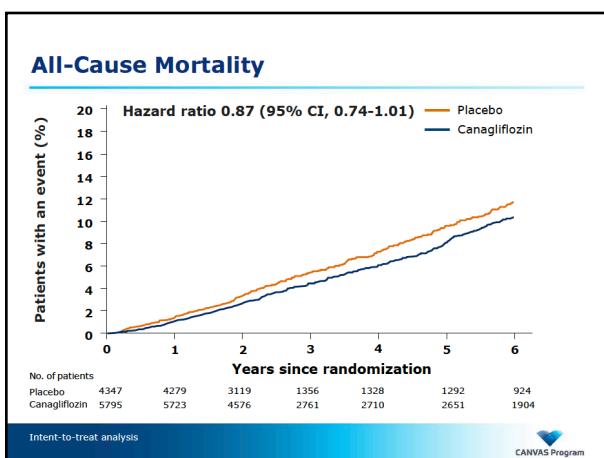
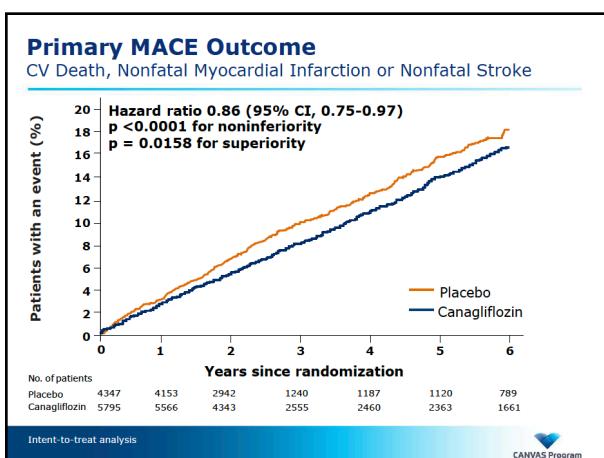
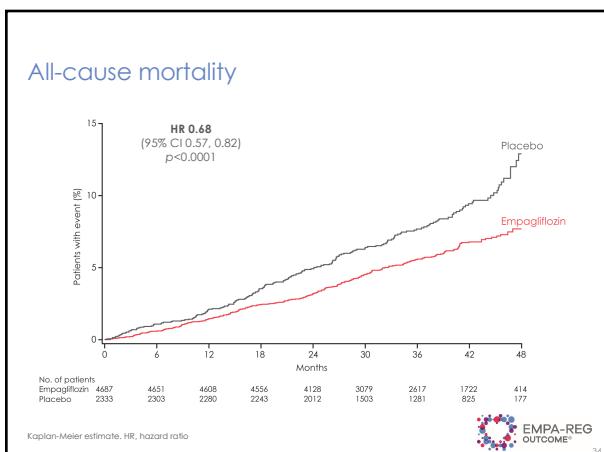
Table 2. Primary and Secondary Cardiovascular and Microvascular Outcomes.						
Outcome	Semaglutide [N=1648]		Placebo [N=1649]		Hazard Ratio (95% CI) <sup>a</sup>	P Value
	No. (%)	No./100 person-yr	No. (%)	No./100 person-yr		
Primary composite outcome <sup>b</sup>	108 (6.6)	3.24	146 (8.9)	4.44	0.74 (0.58–0.95)	<.0001 for noninferiority; 0.03 for superiority
Expanded composite outcome <sup>c</sup>	199 (12.1)	6.17	264 (16.0)	8.36	0.74 (0.62–0.89)	0.002
All-cause death, nonfatal myocardial infarction, or nonfatal stroke	122 (7.4)	3.66	158 (9.6)	4.81	0.77 (0.61–0.97)	0.03
Death						
From any cause	62 (3.8)	1.82	60 (3.6)	1.76	1.05 (0.74–1.50)	0.79
From cardiovascular cause	44 (2.7)	1.29	46 (2.8)	1.35	0.98 (0.65–1.48)	0.92
Nonfatal myocardial infarction	47 (2.9)	1.40	64 (3.9)	1.92	0.74 (0.51–1.08)	0.12
Nonfatal stroke	27 (1.6)	0.80	44 (2.7)	1.31	0.61 (0.38–0.99)	0.04
Hospitalization for unstable angina pectoris	22 (1.3)	0.65	27 (1.6)	0.80	0.82 (0.47–1.44)	0.49
Revascularization	83 (5.0)	2.50	126 (7.4)	3.85	0.65 (0.50–0.86)	0.003
Hospitalization for heart failure	59 (3.6)	1.76	54 (3.3)	1.61	1.11 (0.73–1.61)	0.57
Retinopathy complications <sup>d</sup>	59 (3.6)	1.49	29 (1.6)	0.86	1.78 (1.11–2.78)	0.03
New or worsening nephropathy <sup>e</sup>	62 (3.8)	1.84	100 (6.1)	3.06	0.64 (0.46–0.88)	0.005

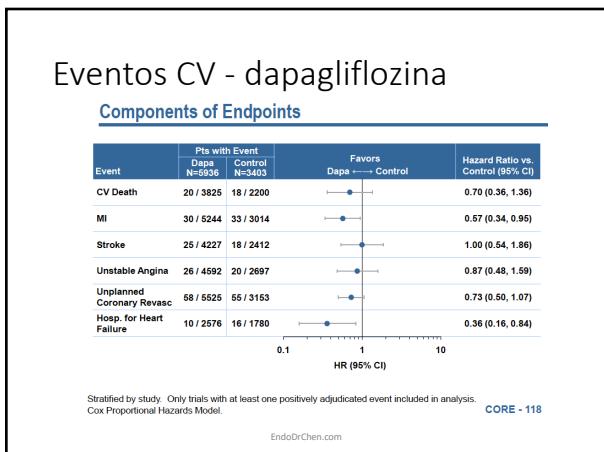
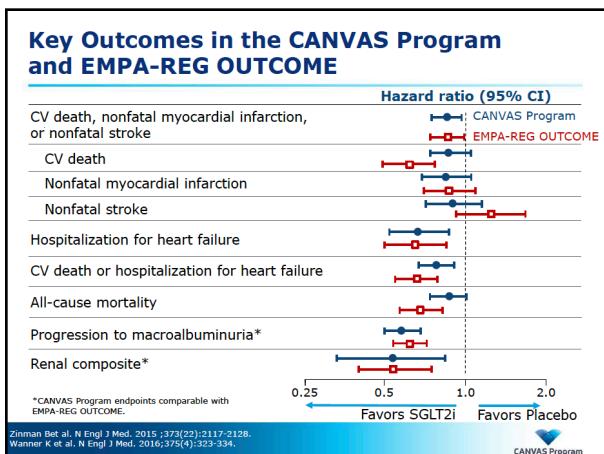
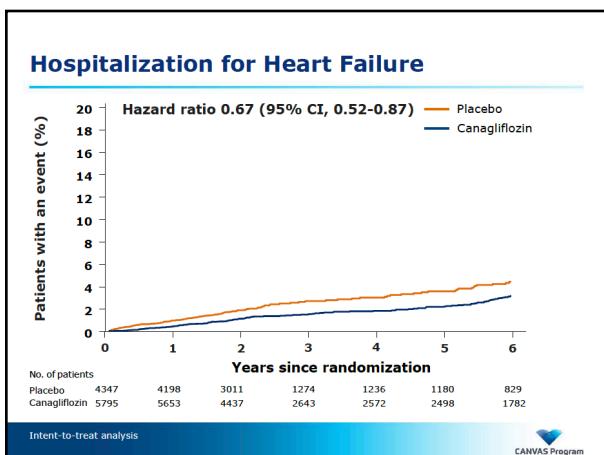
<sup>a</sup> Hazard ratios and P values were estimated with the use of a Cox proportional-hazards model with the study treatments as fixed factors and time as a continuous variable. Adjusting for age, sex, race, and baseline systolic blood pressure. <sup>b</sup> The primary composite outcome was the first occurrence of death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke. <sup>c</sup> Expanded composite outcome included death from cardiovascular causes, nonfatal myocardial infarction, nonfatal stroke, revascularization (coronary or peripheral), and hospitalization for unstable angina or heart failure. <sup>d</sup> Retinopathy complications include retinal hemorrhage, onset of diabetes-related blindness, and the need for treatment with an intravitreal injection. <sup>e</sup> New or worsening nephropathy includes persistent microalbuminuria, persistent doubling of the serum creatinine level and a creatinine clearance of less than 45 mL per minute per 1.73 m<sup>2</sup> of body-surface area (according to the Modification of Diet in Renal Disease criteria), or the need for continuous renal replacement therapy.

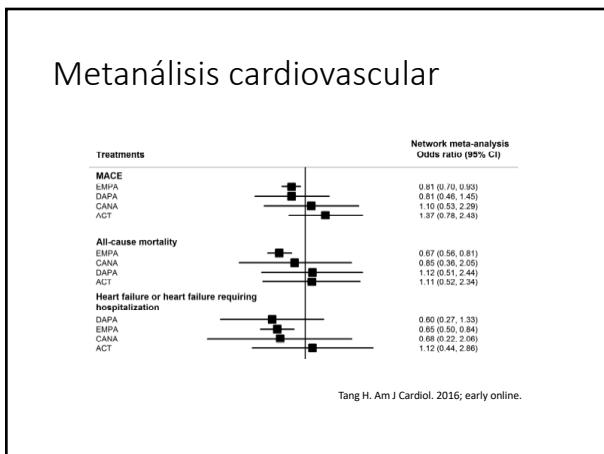
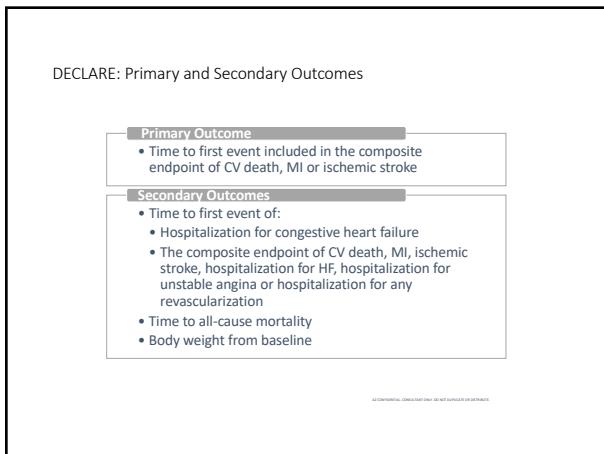
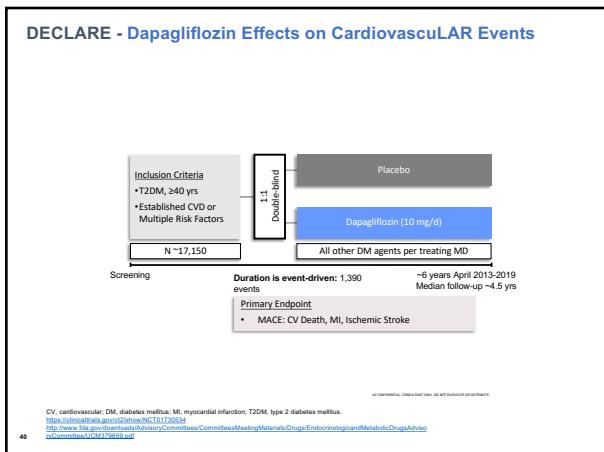




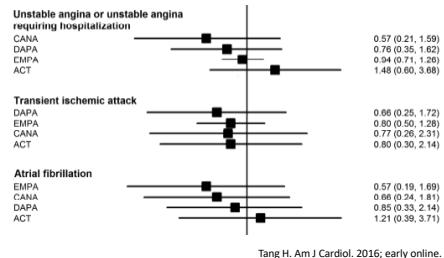






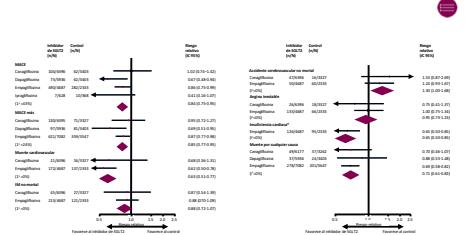


## Metanálisis cardiovascular



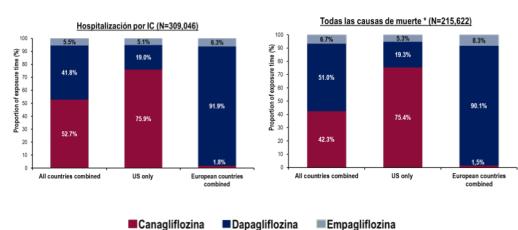
Tang H. Am J Cardiol. 2016; early online.

Los datos del metaanálisis sugieren una protección neta contra eventos cardiovasculares con inhibidores de SGLT-2

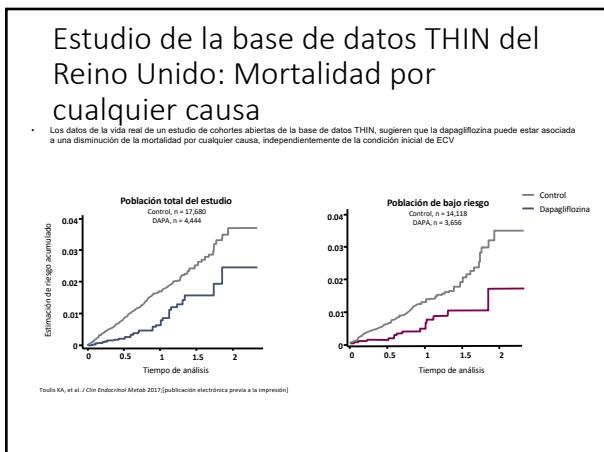
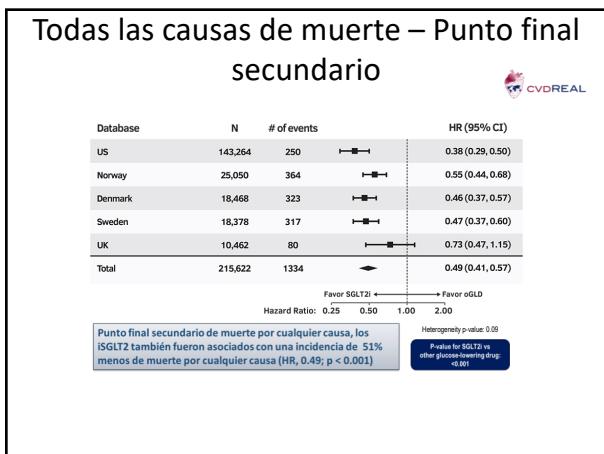
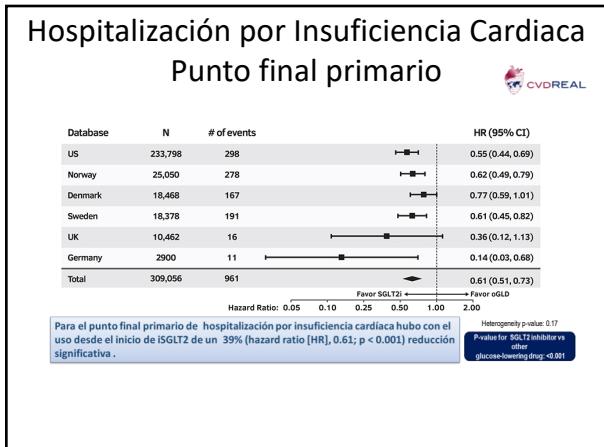


Wu JH, et al. Lancet Diabetes Endocrinol 2016;4:411-9

## Contribución de los iSGLT2

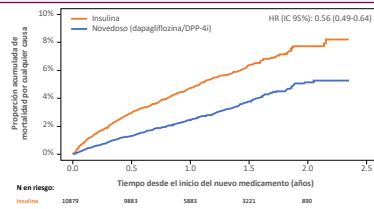


\*Data shown are for all-cause death; data for HFHF or all-cause death are similar



Registros nacionales suecos: Mortalidad por cualquier causa de los medicamentos hipoglucemiantes novedosos en comparación con insulina

Los medicamentos hipoglucemiantes novedosos se asociaron a un menor riesgo de mortalidad por cualquier causa en comparación con insulina

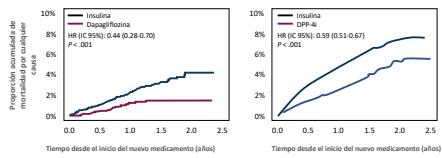


Hypertension et al. Diabetes Obes Metab 2017 [in press] © 2017 The Authors. Journal compilation © 2017 Diabetologia International Ltd. All rights reserved. DOI: 10.1111/diab.13742

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Registros nacionales suecos: Mortalidad por cualquier causa de dapagliflozina e inhibidores de DPP-4 en comparación con insulina

- Dapagliflozina se asoció con un 56% menos riesgo de mortalidad por cualquier causa en comparación con insulina
- Los inhibidores de DPP-4 se asociaron con un 41% menos riesgo de mortalidad por cualquier causa en comparación con insulina



Hypertension et al. Diabetes Obes Metab 2017 [in press] © 2017 The Authors. Journal compilation © 2017 Diabetologia International Ltd. All rights reserved. DOI: 10.1111/diab.13742

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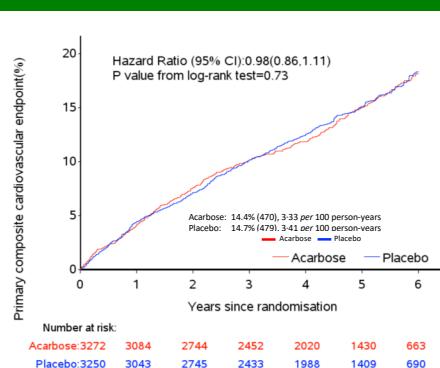
## Antidiabéticos con efecto neutro

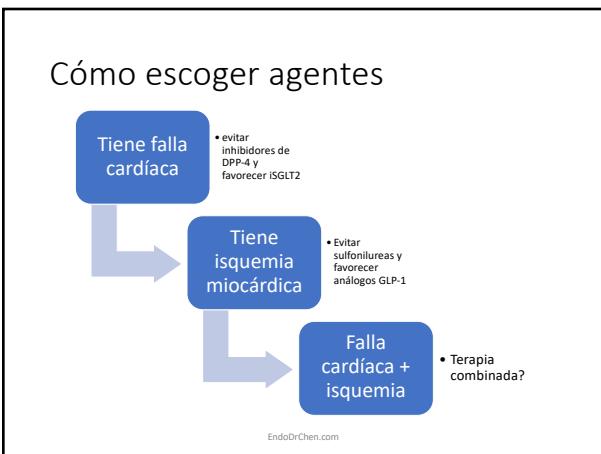
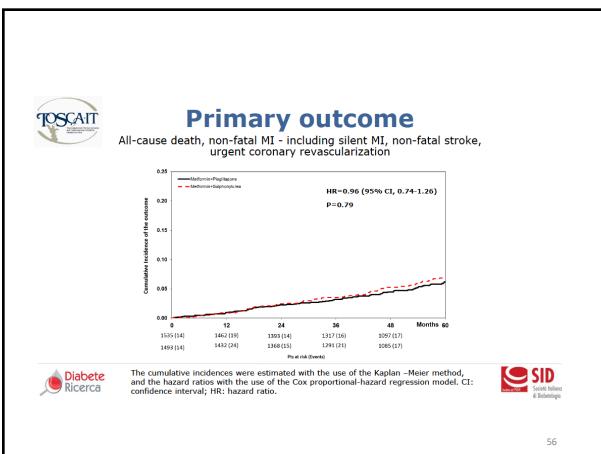
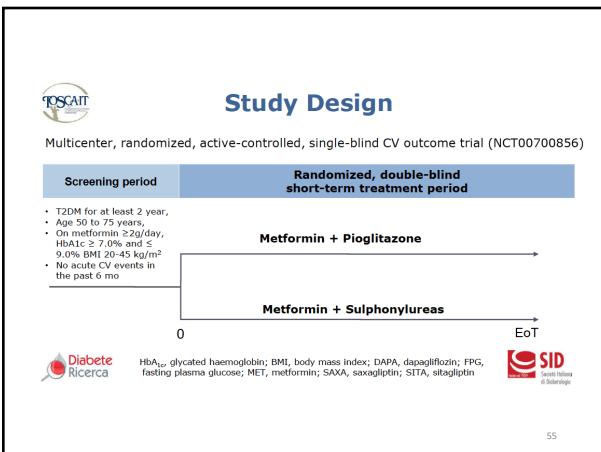
## Inhibidores de DPP4

- SAVOR, EXAMINE y TECOS todos han mostrado resultados neutros en MACE
- Saxagliptina y alogliptina con alertas por aumento de hospitalización por falla cardíaca
  - No claro el mecanismo
- Pendiente CAROLINA

## Insulinas

- ORIGIN y DEVOTE han mostrado que son neutros
- Efecto cardioprotector inicialmente mostrado en DIGAMI no se reprodujo en DIGAMI-2





## Combinación análogo GLP1 + iSGLT2

- DURATION8
  - Exenatide semanal: -1.54 kg
  - Dapagliflozina: -2.19 kg
  - Exenatide semanal + dapagliflozina: -3.41 kg
- Por qué efectos menores a los esperados?
- Papel de glucagon?
- No hay estudios con desenlaces CV con combinación

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## Conclusiones

- Hay una clara relación entre DM y enfermedad cardiovascular
  - Causa principal de muerte en DM
  - Pacientes con ECV tienen mayor riesgo de desarrollar DM
- Manejo de factores de riesgo como HTA y dislipidemia es crítico
- Los iSGLT-2 y algunos análogos GLP-1 han mostrado reducción de mortalidad cardiovascular

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## Preguntas...

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Puede descargar la presentación en:



[www.EndoDrChen.com](http://www.EndoDrChen.com)

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