Nous antidiabètics orals. A qui? Quan? Com?

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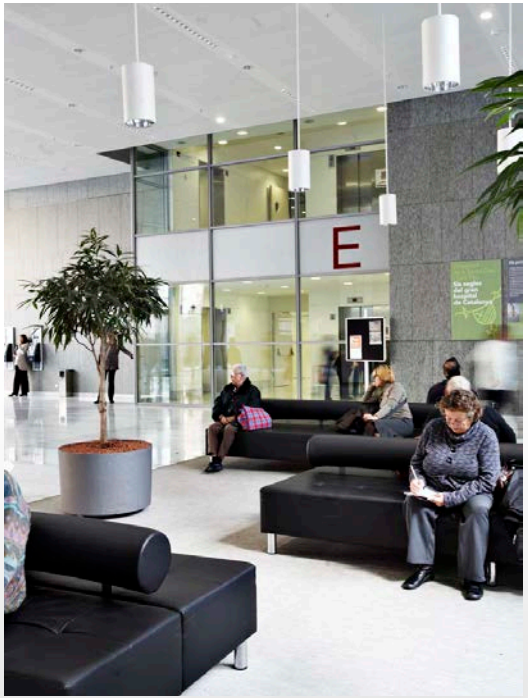
1. DM2 i Cardiologia…
2. Tractament de la DM2 i pronòstic CV
3. Noves guies
4. Conclusions



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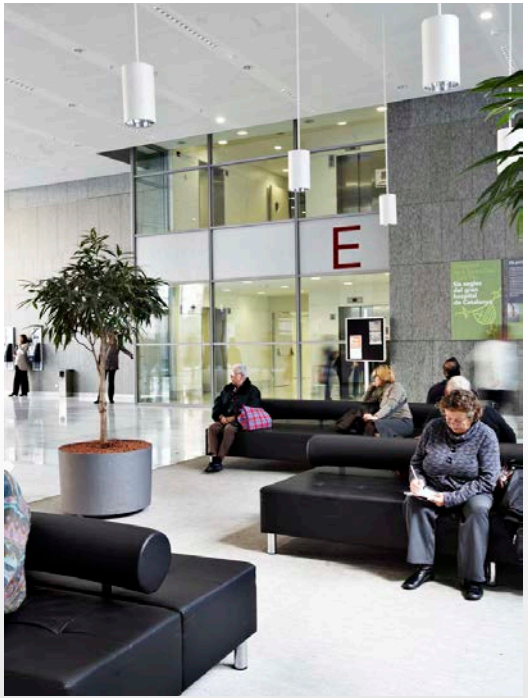
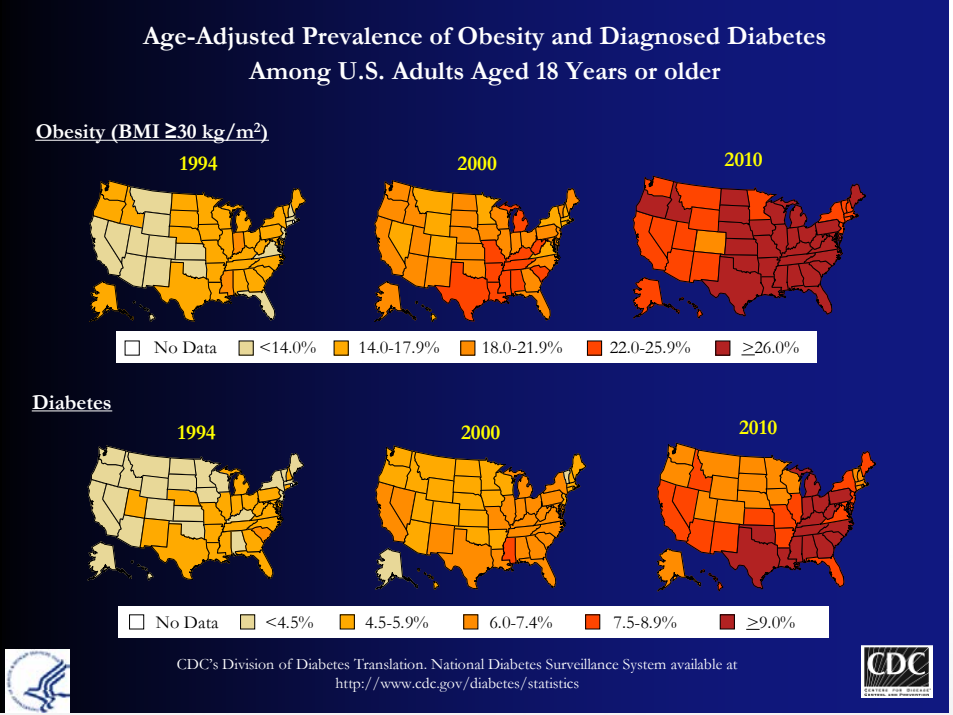
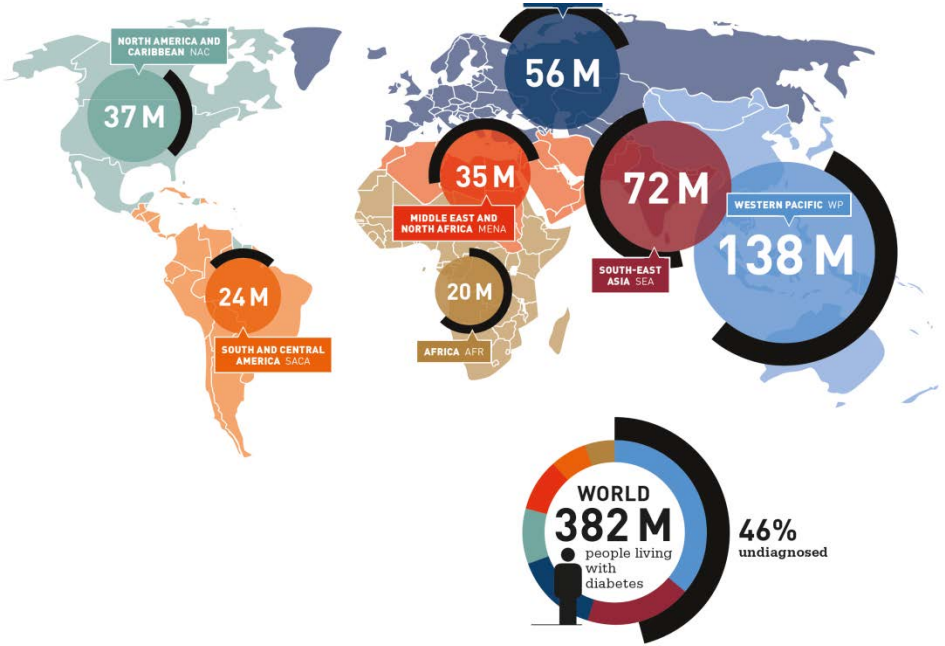
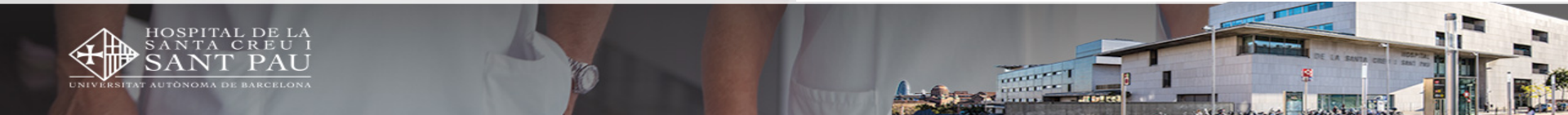




Prevalència actual de DM al món



Cardiopatia isquèmica i d'altres cardiopaties causen més del 50% de la mortalitat dels pacients diabètics



Control d'HbA1c I malaltia cardiovascular

Per què els cardiòlegs han "negligit" el maneig de la diabetes tot I que els pacients DM2 són aproximadament 1/3 dels nostres pacients?

- Nivells perfectes d'HbA1c no impedeixen complicacions cardíaques
- Hi ha moltes famílies terapèutiques
- STENO: tractament holístic té molt més impacte pronòstic que només el clàssic tractament antihiperglucemiant
- No impacte sobre la mortalitat CV
- Qüestions de seguretat: hipoglicèmia, FDA...

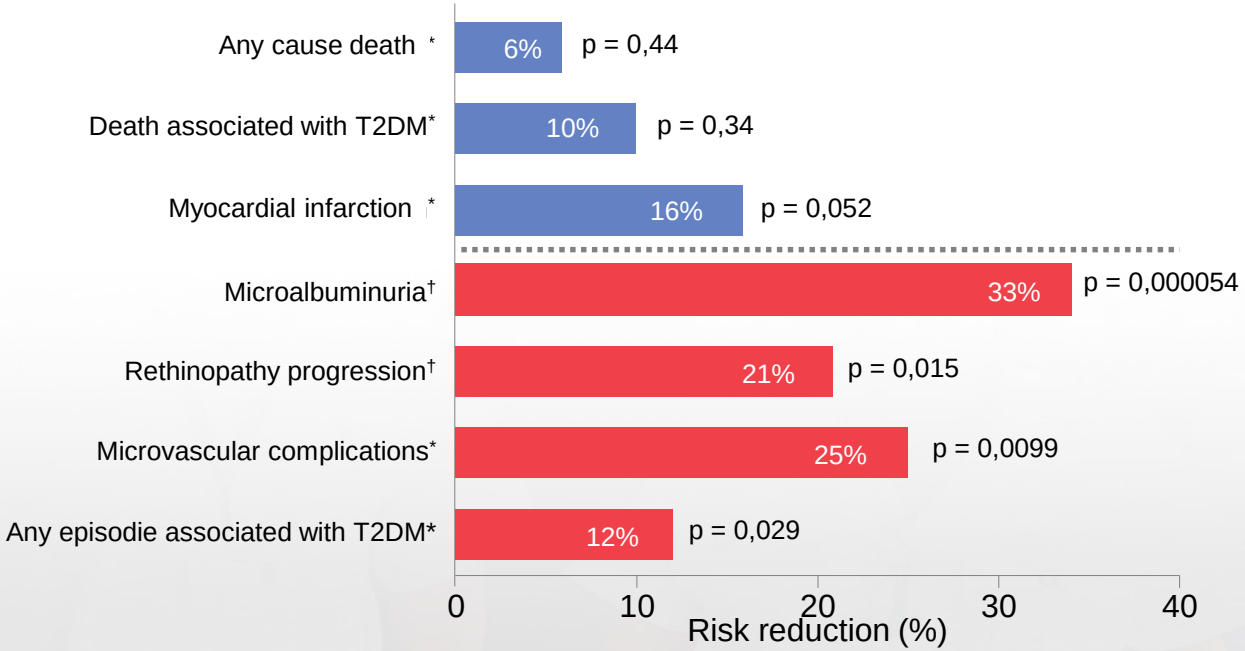
Tractament hipoglucemiant intensiu ha comfirmat benefici pronòstic microvascular però no macrovascular

Study[1]	Year of enrolment	Baseline HbA_{1c} Control vs intensive	Mean duration of diabetes at baseline (years)	Microvascular	CVD	Mortality
UKPDS	1977	9% → 7.9% vs 7%	Newly diagnosed	↓	↔	↔
ACCORD[1–3]	1999	8.3% → 7.5% vs 6.4%	10.0	↓*	↔	↑
ADVANCE	2001	7.5% → 7.3% vs 6.5%	8.0	↓	↔	↔
VADT	2000	9.4% → 8.4% vs 6.9%	11.5	↓	↔	↔

*No change in primary microvascular composite but significant decreases in micro/macroalbuminuria[2,3]
†No change in major clinical microvascular events but significant reduction in ESRD (p=0.007)[5]

1. Table adapted from Bergenstal *et al. Am J Med* 2010;123:374.e9; 2. Genuth *et al. Clin Endocrinol Metab* 2012;97:41;
3. Ismail-Beigi *et al. Lancet* 2010;376:419; 4. Hayward *et al. N Engl J Med* 2015;372:2197; 5. Zoungas *et al. N Engl J Med* 2014;371:1392

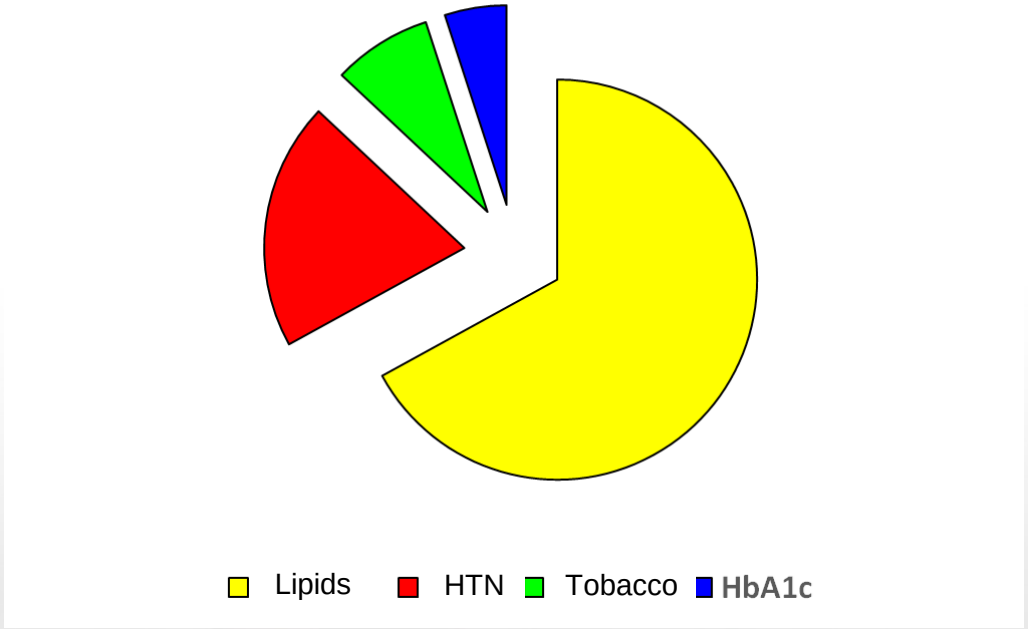
UKPDS: Intensive glycaemic control reduced microvascular episodes but not macrovascular episodes



Median FU: 10 years; † assessed as suboridanated endpoint.

UKPDS 33. Lancet 1998;352:837–53

Prevenció CV a DM2: estrategia multifactorial



Gaede P et al. NEJM 2008;358:580-591

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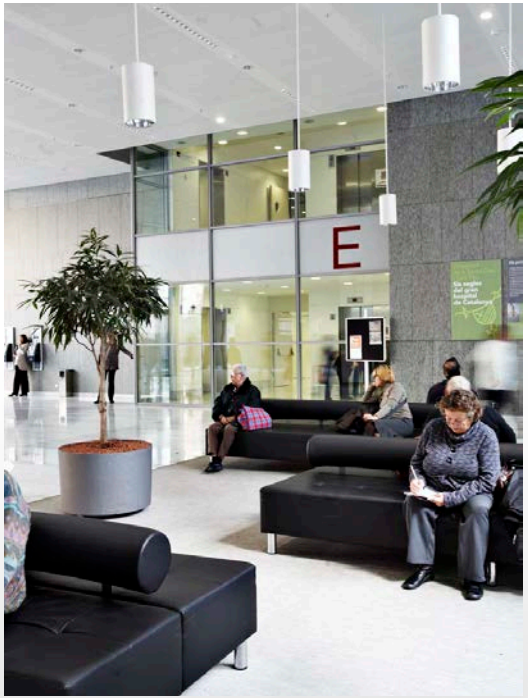
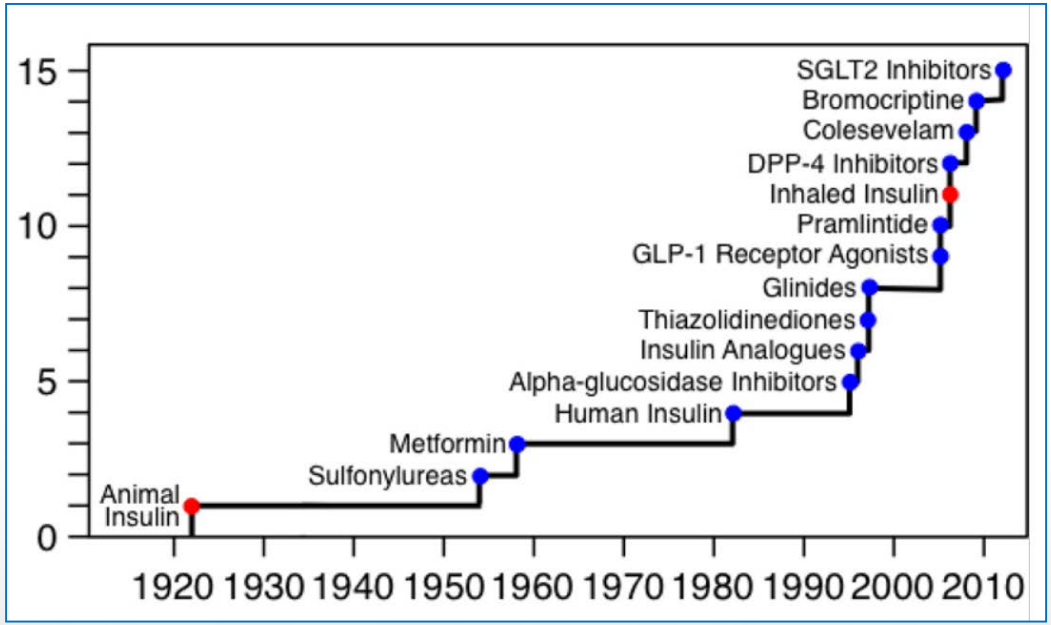


Wide range of hypoglycemiant drugs



Kahn SE. *et al*. Lancet 2014;383:1068-83

The New York Times

F.D.A. to Restrict Avandia, Citing Heart Risk

By GARDINER HARRIS SEPT. 23, 2010

A bottle of the controversial diabetes drug Avandia. Joe Raedle/Getty Images

WASHINGTON — In a highly unusual coordinated announcement, drug regulators in Europe and the United States said Thursday that Avandia, the controversial diabetes medicine, would no longer be widely available.

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

European Medicines Agency - Science, medicines, health

European Medicines Agency recommends suspension of Avandia, Avandamet and Avaglim

23/09/2010

European Medicines Agency recommends suspension of Avandia, Avandamet and Avaglim

Anti-diabetes medication to be taken off the market

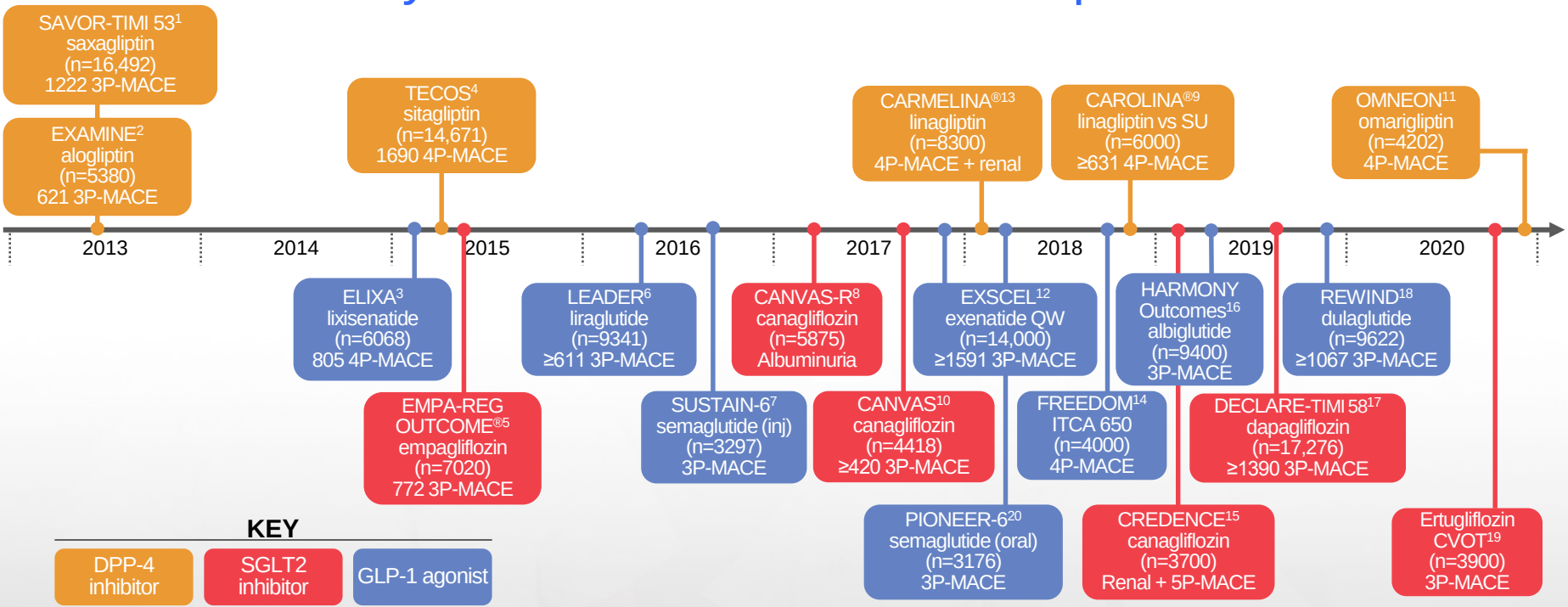
The European Medicines Agency today recommended the suspension of the marketing authorisations for the rosiglitazone-containing anti-diabetes medicines Avandia, Avandamet and Avaglim. These medicines will stop being available in Europe within the next few months.

Patients who are currently taking these medicines should make an appointment with their doctor to discuss suitable alternative treatments. Patients are advised not to stop their treatment without speaking to their doctor.

Doctors should stop prescribing rosiglitazone-containing medicines. Patients taking rosiglitazone-containing medicines should be reviewed in a timely manner to amend their treatment.

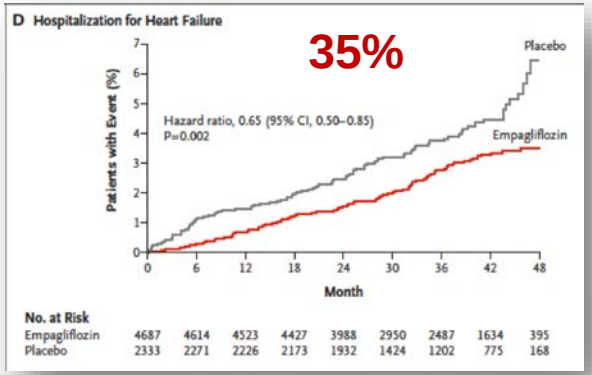
The current review of rosiglitazone by the Agency's Committee for Medicinal Products for Human Use (CHMP) was initiated on 9 July 2010 following the availability of new studies questioning the cardiovascular safety of the medicine.

CV safety studies with the new therapeutic families



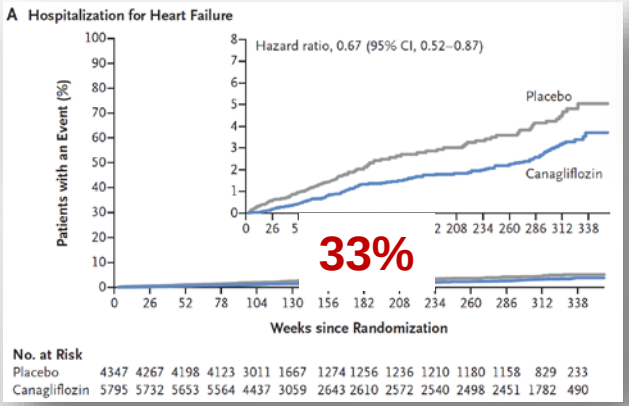
Adapted from Johansen OE. *World J Diabetes* 2015;6:1092

EMPA-REG OUTCOME®



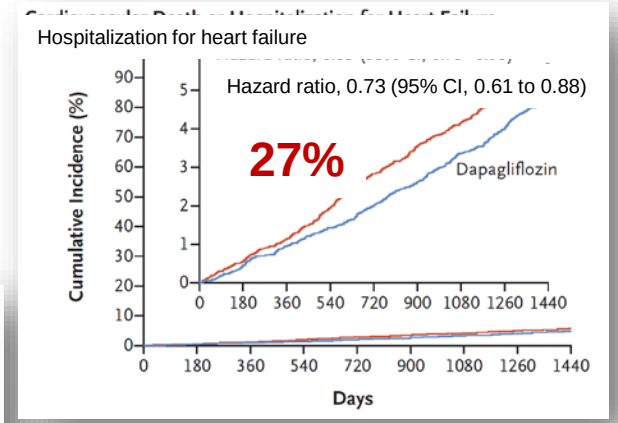
N Engl J Med 2015; 373:2117-2128

CANVAS Program



N Engl J Med 2017; 377:644-657

DECLARE TIMI-58



NEJM.org. DOI: 10.1056/NEJMoa1812389

HOSPITAL DE LA SANTA CREU I SANT PAU
UNIVERSITAT AUTÒNOMA DE BARCELONA

ar-GLP1: “glutides”

LEADER®
Liraglutide Effect and Action in Diabetes: Evaluation of cardiovascular outcome Results

13% MACE
3 años

N Engl J Med 2016;375: 1834-44.

SUSTAIN
SEMAGLUTIDE UNABATED SUSTAINABILITY IN TREATMENT OF TYPE 2 DIABETES

26% MACE
2 años

N Engl J Med 2016; 375:311-322

Harmony Outcomes

22% MACE
1,8 años

Lancet. 2018 Oct 1.
pii: S0140-6736(18)32261-X.

REWIND

22% MACE
5,4 años

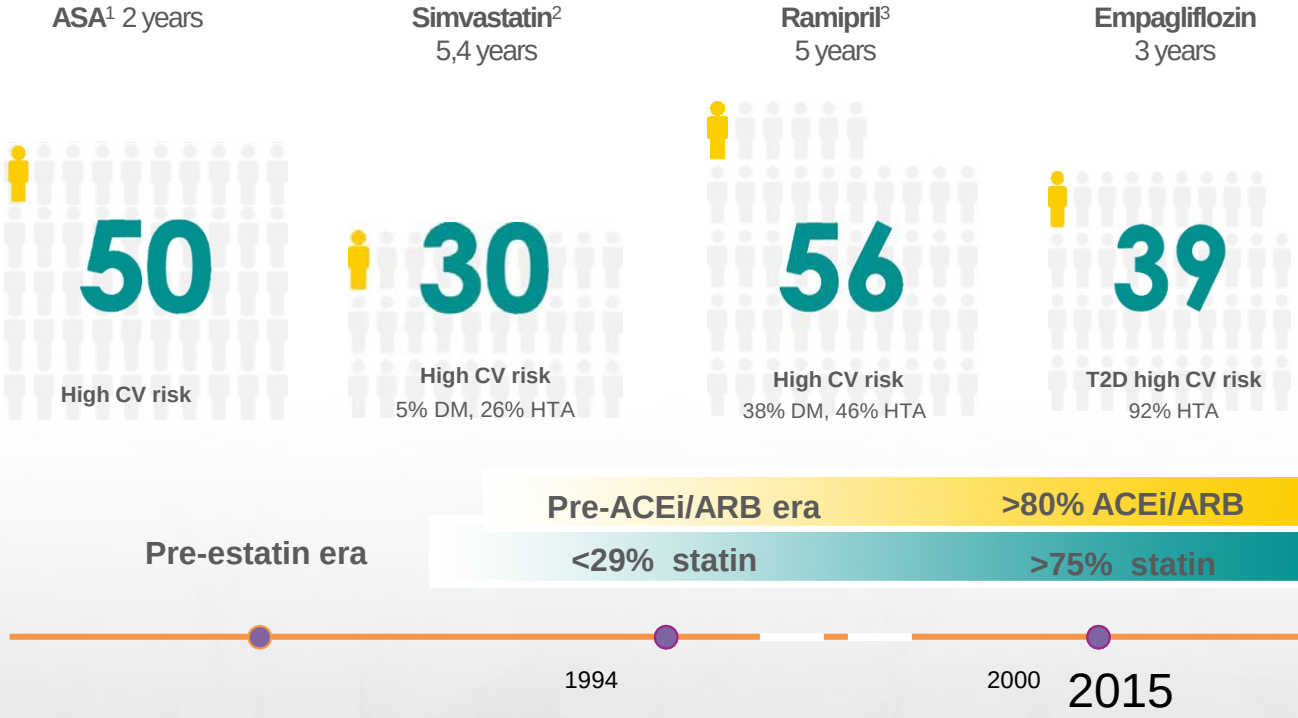
Lancet 2019 ;394:121130.

PIONEER 6

51%
mort CV
49%
mort T
1,5 años

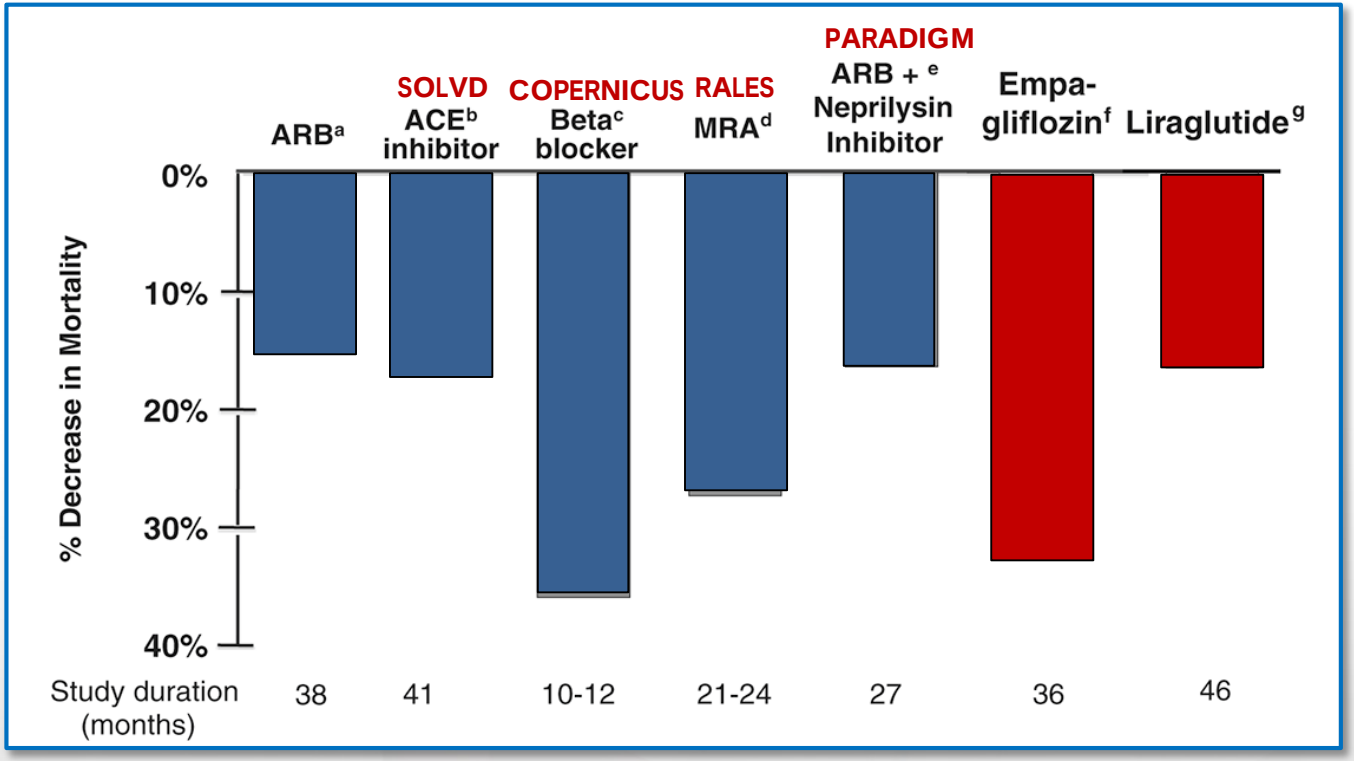
N Engl J Med;
doi:10.1056/NEJMoa1901118.

NNT to prevent one death in clinical trials in high CV risk patients



1. Newman, DH. Aspirin to Prevent Cardiovascular Disease in Patients with Known Heart Disease or Strokes. Availabe at: http://www.thennt.com/nnt/aspirin-for-cardiovascular-prevention-after-prior-heart-attack-or-stroke 2. 4S Investigators. Lancet 1994; 344: 1383-89. 3. Yusuf S, Sleight P, Pogue J, et al. N Engl J Med 2000; 342:145-53. 4. Zinman B, et al. N Engl J Med. 2015; 373(22):2117-28.

Any cause mortality in different clinical trials



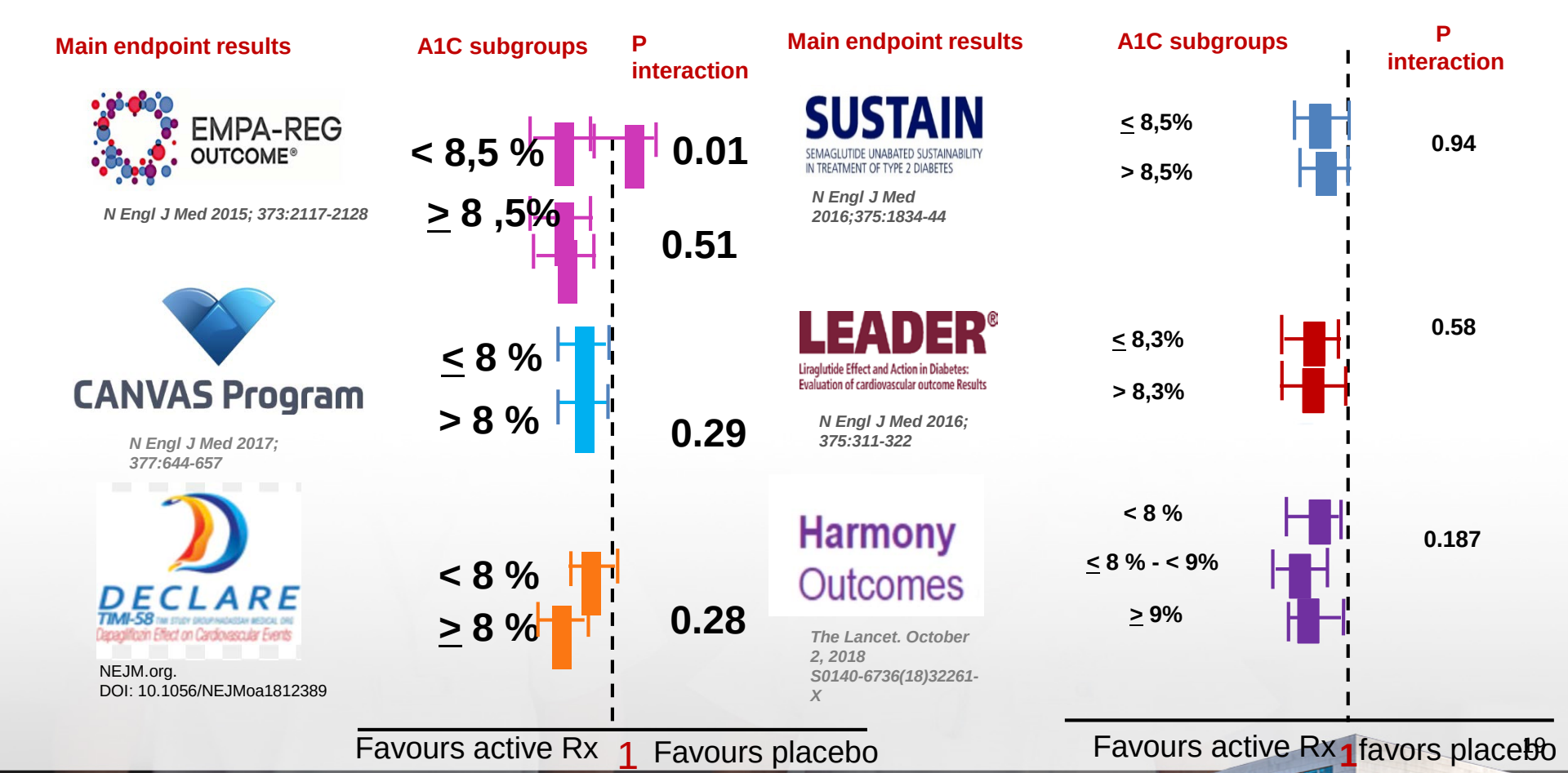
Fitchett DH et al EurJ Heart Failure 2016

Change of paradigm in T2D
(a new era)

1

Benefit

Regardless A1C


Main endpoint results
A1C subgroups
P interaction
EMPA-REG OUTCOME®
N Engl J Med 2015; 373:2117-2128
< 8,5 %
≥ 8 ,5%
0.01
0.51
CANVAS Program
N Engl J Med 2017; 377:644-657
≤ 8 %
> 8 %
0.29
DECLARE TIMI-58
Dapagliflozin Effect on Cardiovascular Events
NEJM.org.
DOI: 10.1056/NEJMoa1812389
< 8 %
≥ 8 %
0.28
Favours active Rx
1
Favours placebo
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SUSTAIN
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N Engl J Med 2016;375:1834-44
≤ 8,5%
> 8,5%
0.94
LEADER®
Liraglutide Effect and Action in Diabetes: Evaluation of cardiovascular outcome Results
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≤ 8,3%
> 8,3%
0.58
Harmony Outcomes
The Lancet. October 2, 2018
S0140-6736(18)32261-X
< 8 %
≤ 8 % - < 9%
≥ 9%
0.187
Favours active Rx
1
favors placebo
10

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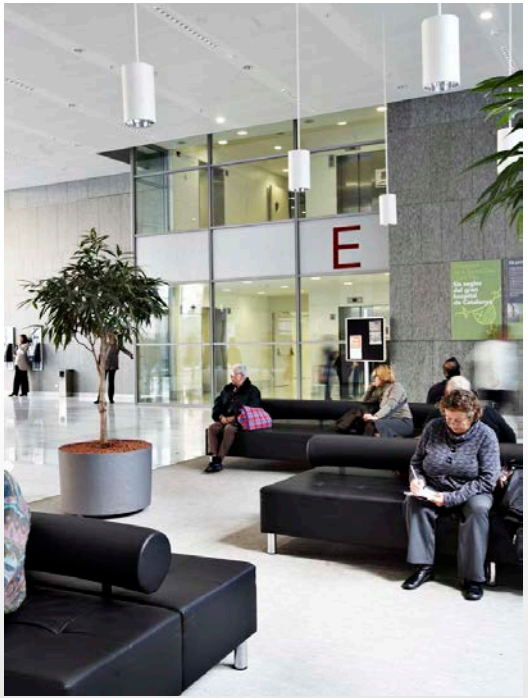


T2D treatment and CV outcomes

Table 7 Cardiovascular risk categories in patients with diabetes[a]

Very high risk	Patients with DM **and** established CVD **or** other target organ damage[b] **or** three or more major risk factors[c] **or** early onset T1DM of long duration (>20 years)
High risk	Patients with DM duration ≥10 years without target organ damage plus any other additional risk factor
Moderate risk	Young patients (T1DM aged <35 years or T2DM aged <50 years) with DM duration <10 years, without other risk factors

CV = cardiovascular; CVD = cardiovascular disease; DM = diabetes mellitus; T1DM = type 1 diabetes mellitus; T2DM = type 2 diabetes mellitus.

[a]Modified from the 2016 European Guidelines on cardiovascular disease prevention in clinical practice.[27]

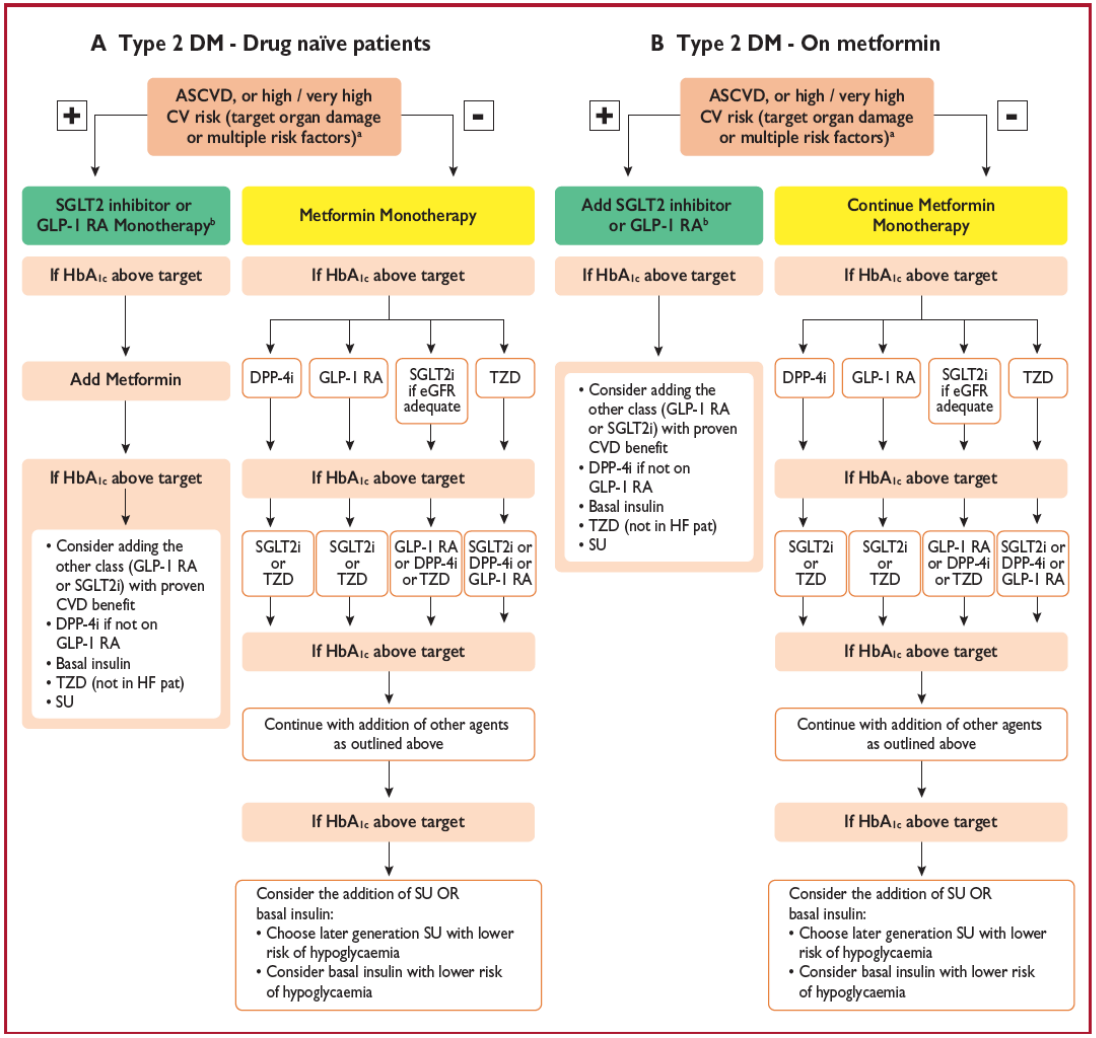
[b]Proteinuria, renal impairment defined as eGFR ≥30 mL/min/1.73 m^2, left ventricular hypertrophy, or retinopathy.

[c]Age, hypertension, dyslipidemia, smoking, obesity.

Eur Heart J 2019;00,169
doi:10.1093/eurheartj/ehz486

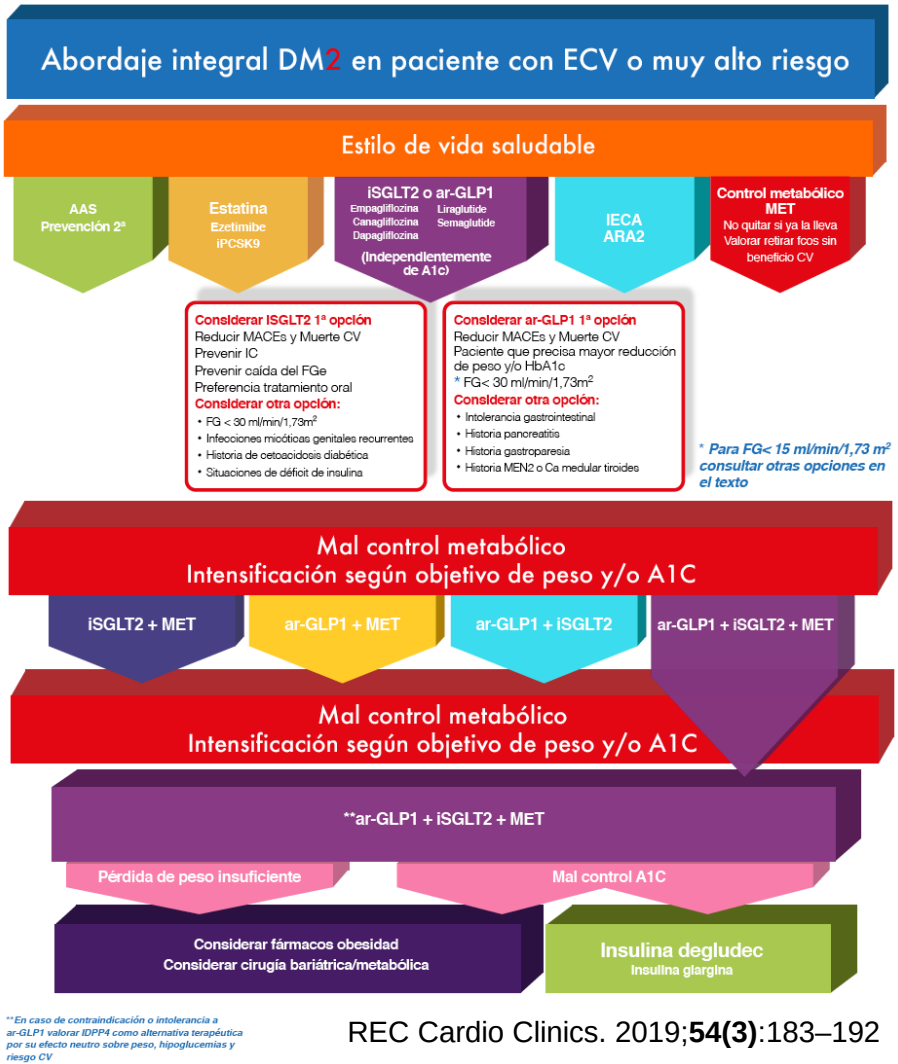
ESC Guidelines

ESC Guidelines



Eur Heart J 2019;00,169
doi:10.1093/eurheartj/ehz486

SEC algorithm



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REC Cardio Clinics. 2019;**54(3)**:183–192

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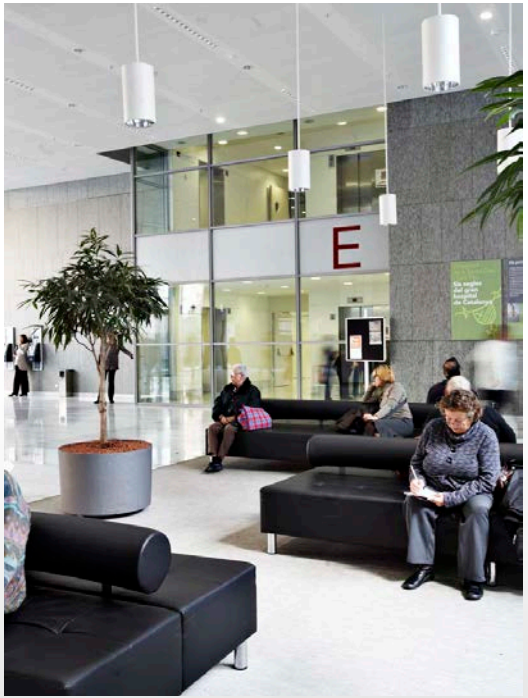

Conclusions

- No tenim excusa per no tractar el pronòstic CV de la DM2
- Estratificació per risc (més que P1 i P2): implicacions en objectius terapèutics
- Nou algoritme de tractament: metformina no té perquè ser el primer pas…


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