OTTIMIZZAZIONE TERAPEUTICA DELLE PERSONE CHE VIVONO CON HIV: TERAPIE DUPLICE, TRIPLICE E NUOVE OPZIONI PER HTE

Milano, 16 Maggio 2025
Centro Congressi StarHotels Ritz

Prevenzione cardiovascolare nelle PWH: il punto di vista del cardiologo

Aldo P Maggioni
Centro Studi ANMCO-Heart Care Foundation
Firenze

DISCLOSURES

Nessun conflitto di interesse per questa presentazione

Outside the present work:

Director of the **ANMCO Research Center** that receives **public grants** of research from Oxford University, NIH, Canadian Government, PHRI, SID and **private grants** of research from Bayer, Sanofi-Aventis, Amgen, AstraZeneca, Menarini, Boehringer Ingelheim, DalCor.

Member of Trial Committees (SC, EC, CEC, DSMB) sponsored by Novartis, AstraZeneca, Bayer, Sanofi.

Le aree cardiometaboliche da considerare le principali novità

- Ipercolesterolemia
- Diabete mellito
- Obesità
- Malattia renale cronica

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I fenotipi di pazienti da considerare a maggior rischio e i loro target di LDL-C

Fenotipo	Target
• Ipercolesterolemia familiare omozigote o eterozigote	<55mg/dL
• Paziente con un precedente aterotrombotico (coronarico, cerebrale, periferico)	<55mg/dL <40 mg/dL se episodi ripetuti
• Paziente con diabete mellito	<70mg/dL <55 mg/dL se con altri FRC
• Paziente con insufficienza renale cronico	<70mg/dL <55 mg/dL se con altri FRC

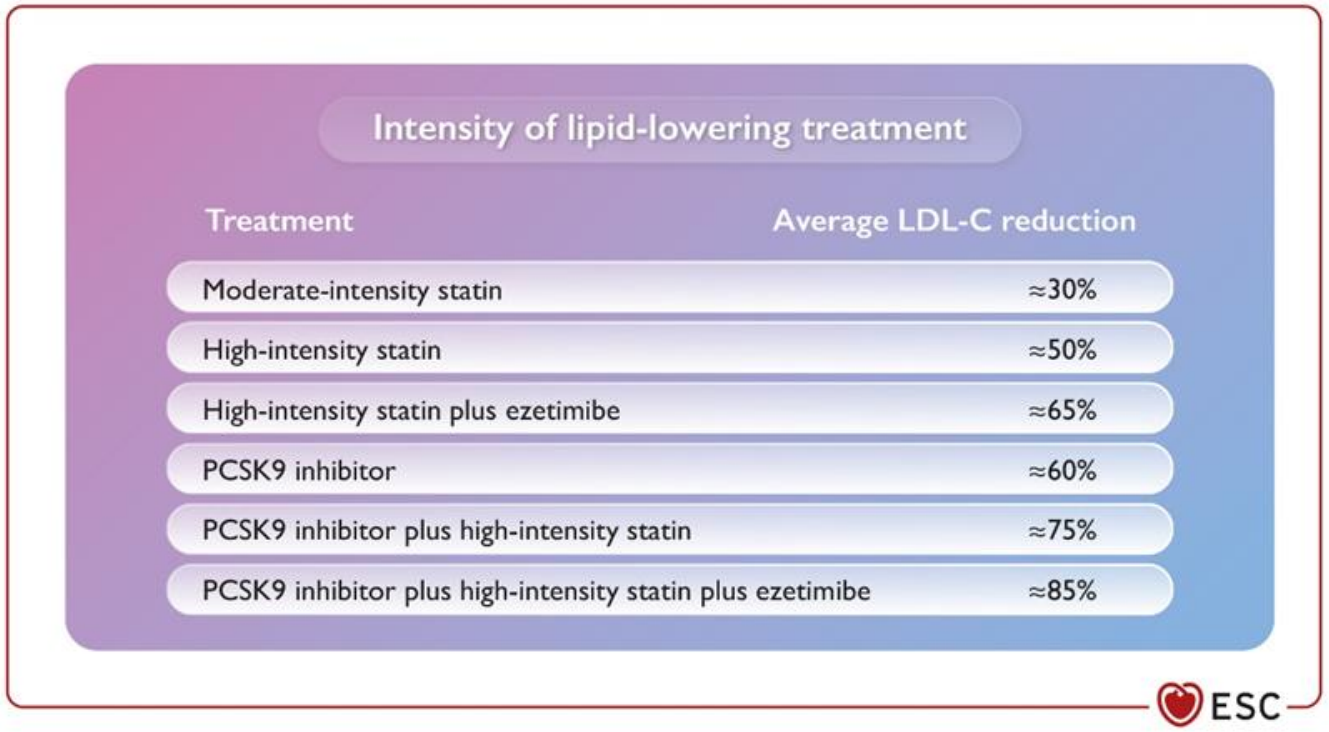
Aggiungiamo ?

- **Paziente che vive con HIV** — **<70mg/dL
<55 mg/dL se con altri FRC**

Colesterolo LDL

Sono raggiungibili questi target?
Come?

Le strategie di prevenzione dirette al controllo della colesterolemia LDL



Expected low-density lipoprotein cholesterol reductions for combination therapies

Le (relative) novità:

- **Acido bempedoico (-20%)**
- **Inclisiran (-45/-50%)**

52.2% In-patients

47.8% Out-patients

189 Cardiology Units

Sept 2023 - Feb 2024

4790 pts with prior atherothrombotic event

- CAD (98%)
- CVD (6.1%)
- PAD (6.9%)

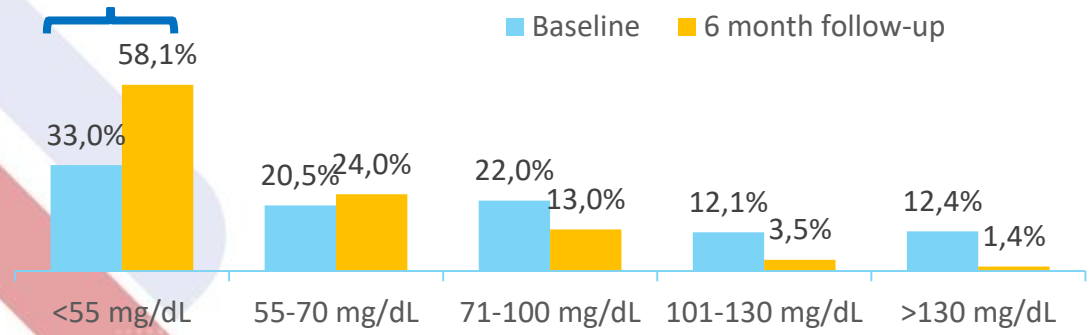
Primary endpoint (6 Months)

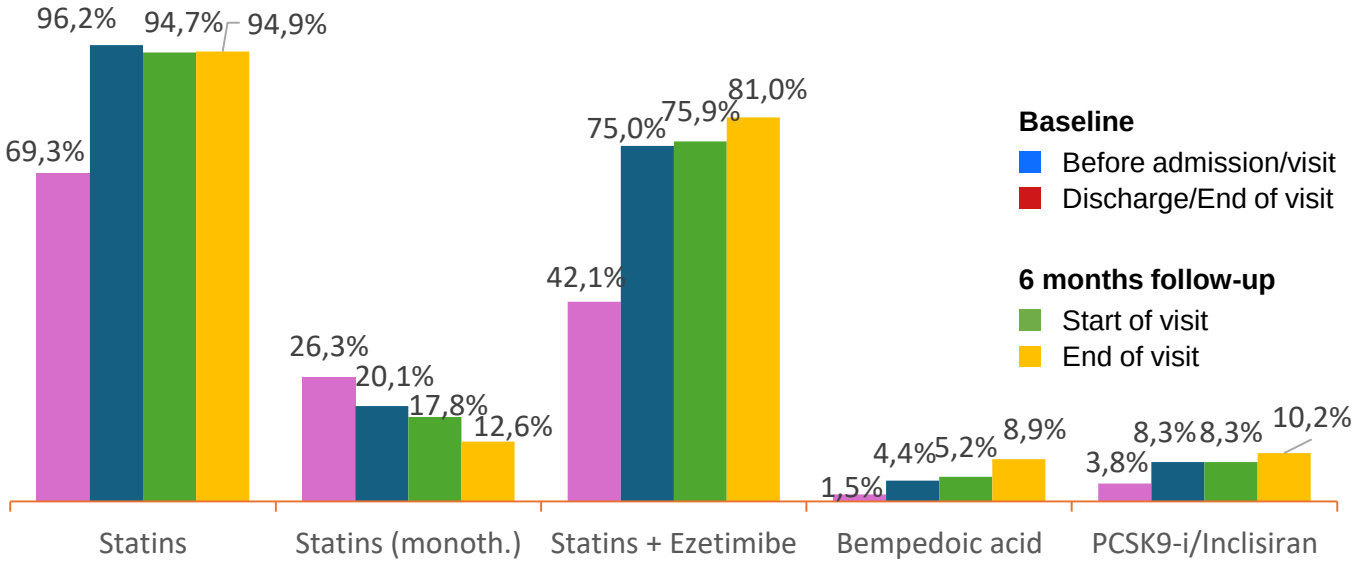
% patients achieving LDL-c <55 mg/dL

Lipid Lowering Drugs (n. 4334)

LDL Cholesterol (n. 4334 pts)

+76.1% relative
+25.1% absolute





BRING·UP PREVENZIONE

52.2% In-patients

47.8% Out-patients

189 Cardiol

CAD (98%)

CVD (6.1%)

PAD (6.9%)

Primary endpoint (6 Months)

% patients achieving LDL-c <55 mg/dL

La ricetta:

Formazione

Partecipazione

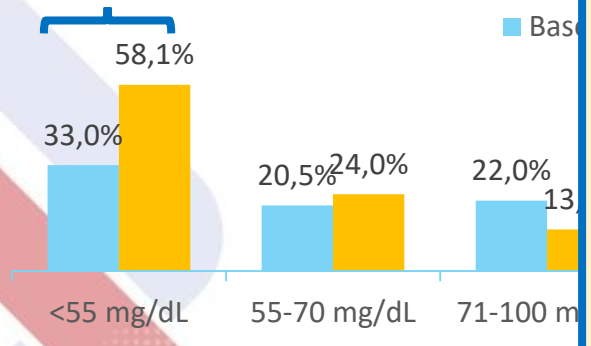
Raccolta dati guidata

Discussione dei risultati

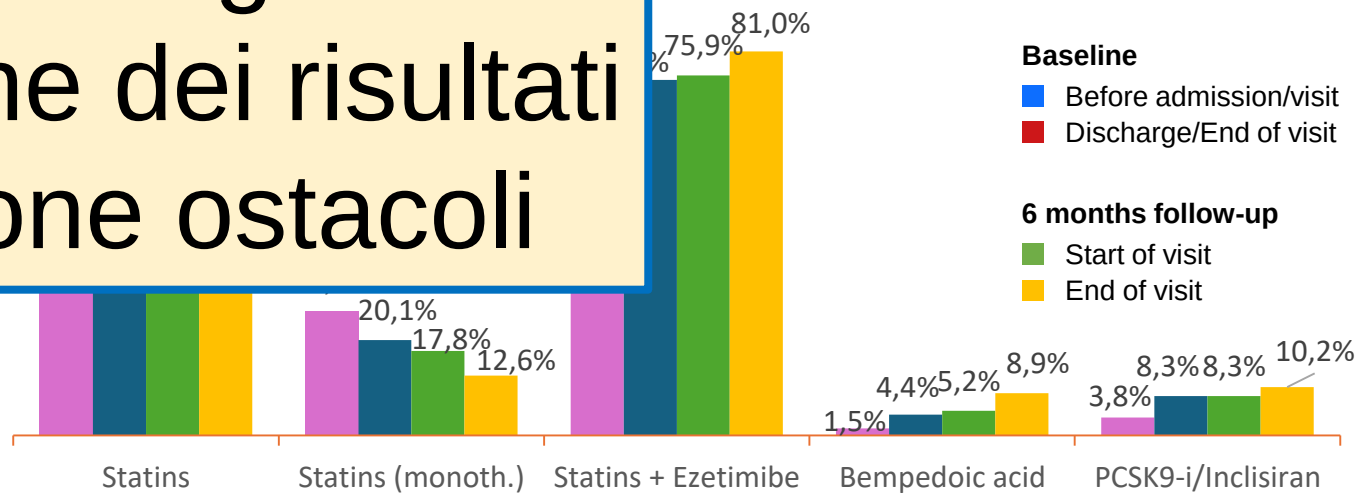
Valutazione ostacoli

s (n. 4334)

+76.1% relative
+25.1% absolute



LDL Cholesterol (n. 4334 pts)



Le aree cardiometaboliche da considerare le principali novità

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ESC
European Society of Cardiology

European Heart Journal (2023) **44**, 4043–4140
https://doi.org/10.1093/eurheartj/ehad192

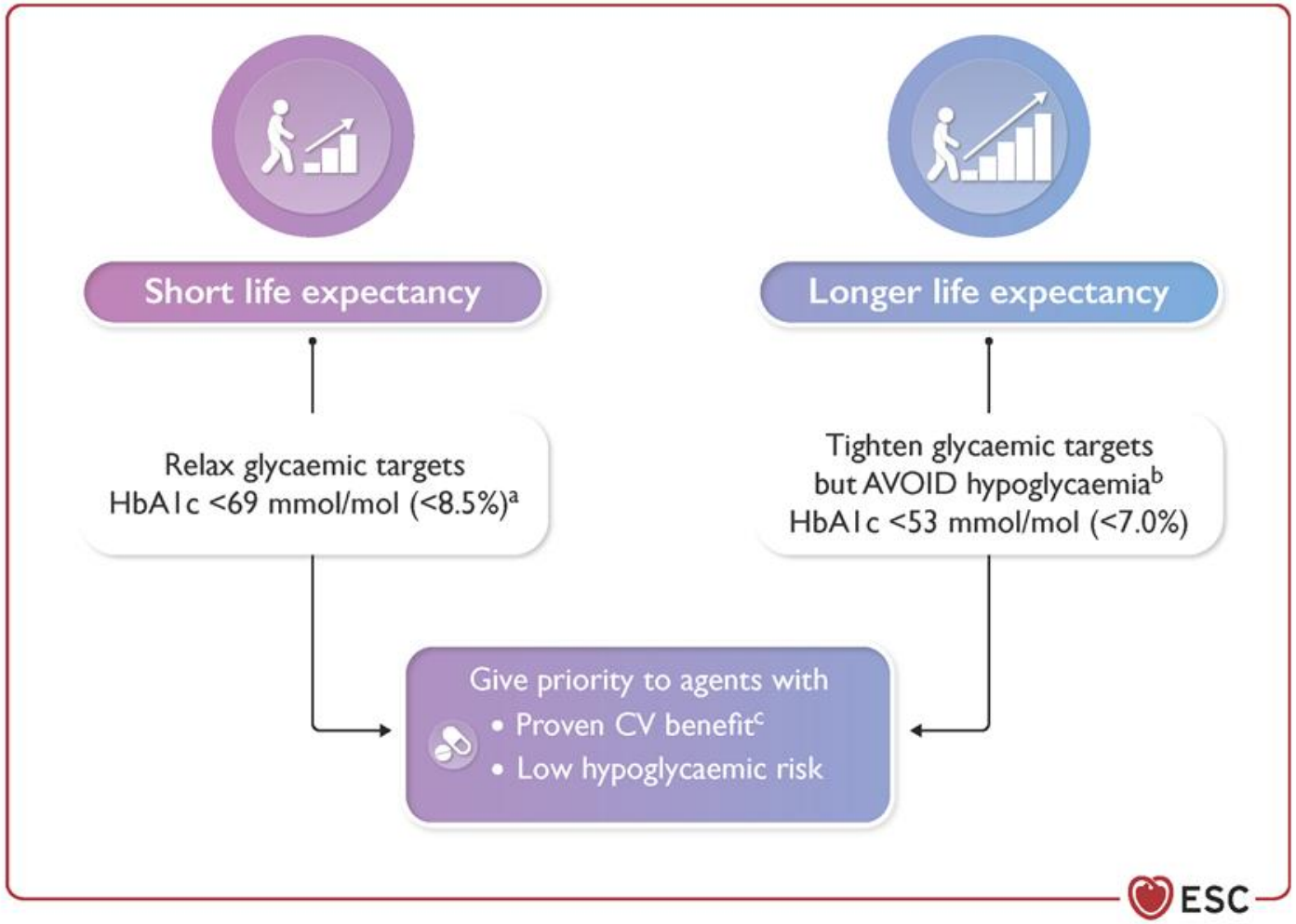
ESC GUIDELINES

2023 ESC Guidelines for the management of cardiovascular disease in patients with diabetes

Developed by the task force on the management of cardiovascular disease in patients with diabetes of the European Society of Cardiology (ESC)

Figure 4

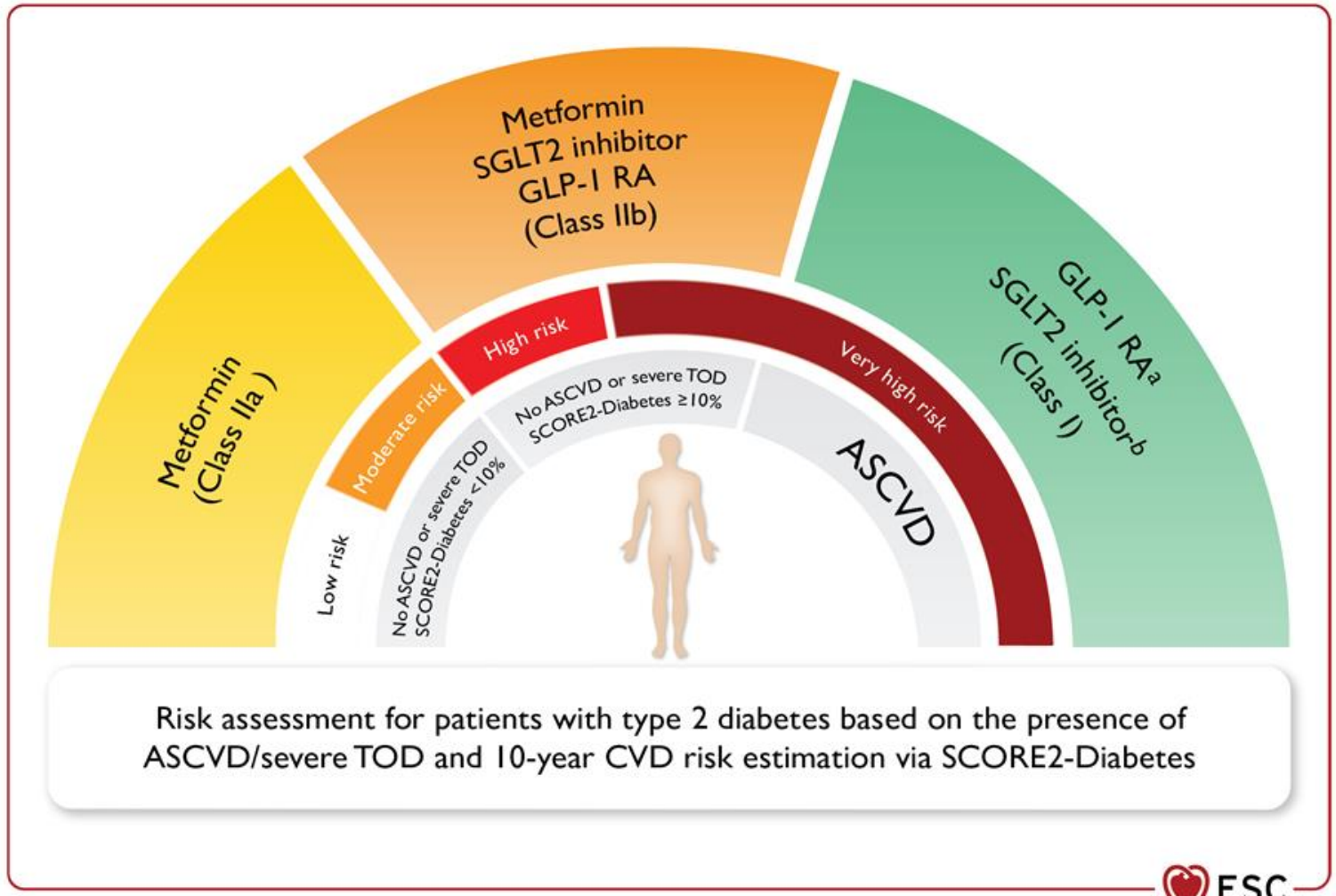
Simple guide to glycaemic targets in patients with type 2 diabetes and cardiovascular disease



2023 ESC Guidelines for the management of cardiovascular disease in patients with diabetes
(European Heart Journal; 2023 – doi:10.1093/eurheartj/ehad192)

Figure 7

Glucose-lowering treatment for patients with type 2 diabetes to reduce cardiovascular risk based on the presence of ASCVD/severe target-organ damage and 10-year cardiovascular disease risk estimation via SCORE2-Diabetes

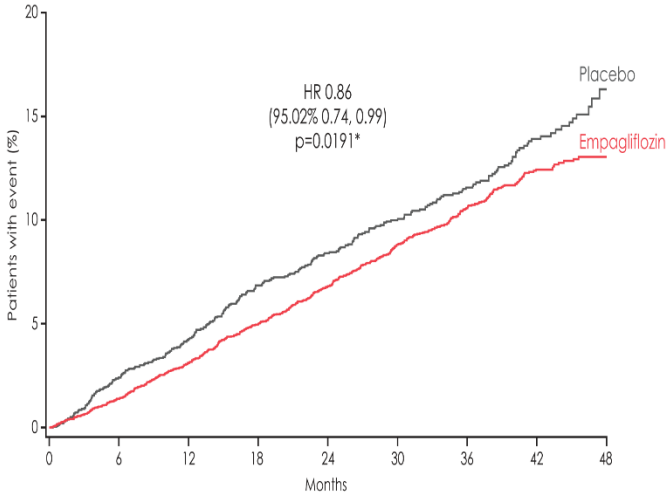


2023 ESC Guidelines for the management of cardiovascular disease in patients with diabetes
(European Heart Journal; 2023 – doi:10.1093/eurheartj/ehad192)

SGLT-2 inhibitors

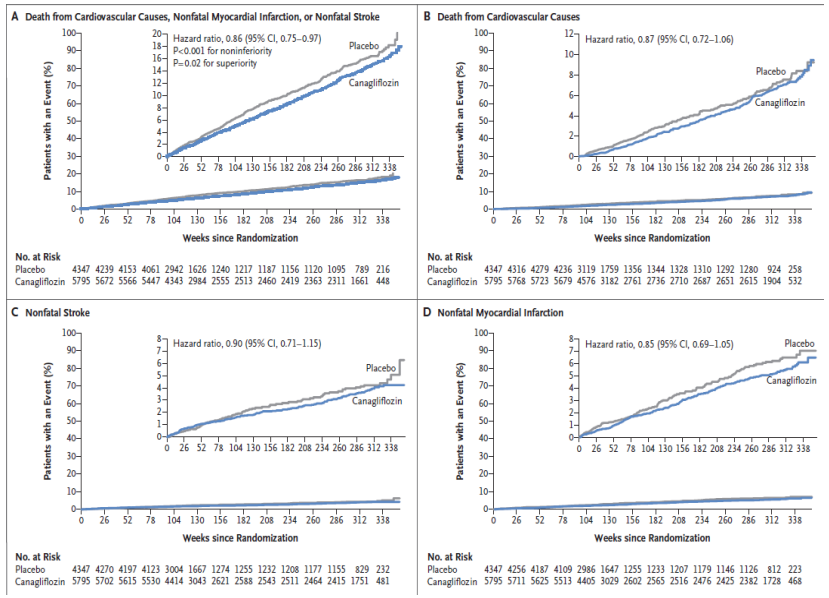
EMPA-REG Outcome

HR 0.86
(95.02% CI 0.74, 0.99)
p=0.0382*



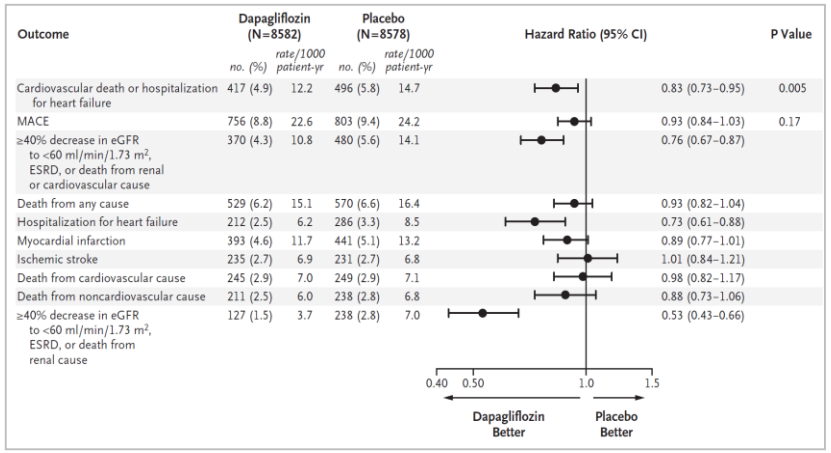
Zinman B et al. N Engl J Med 2015;373:2117-28.

CANVAS Trial



N Engl J Med 2017;377:644-57

DECLARE Trial



N Engl J Med 2019;380:347-357. Epub 2018 Nov 10.

In pazienti diabetici ad alto rischio CV (prevenzione secondaria e primaria ad alto rischio), l'utilizzo di SGLT2-I ha ridotto significativamente il rischio di:
- morte CV, infarto e stroke non fatali,
- ospedalizzazioni per scompenso cardiaco
con un profilo di sicurezza/ tollerabilità accettabili

GLP-1 Receptor Agonists for the Reduction of Atherosclerotic Cardiovascular Risk in Patients With Type 2 Diabetes

Nikolaus Marx, MD; Mansoor Husain, MD; Michael Lehrke, MD; Subodh Verma, MD, PhD; Naveed Sattar, FMedSci, PhD

GLP1 RA

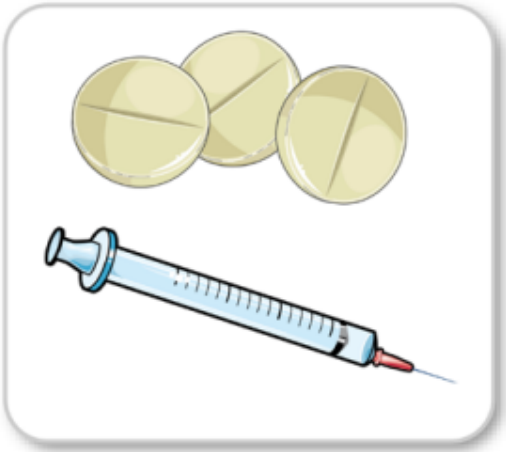
	ELIXA (n=6068)	LEADER (n=9340)	SUSTAIN 6 (n=3297)	EXSCEL (n=14752)	HARMONY OUTCOMES (n=9463)	REWIND (n=9903)	PIONEER-6 (n=3183)	AMPLITUDE-O (n=4076)
Drug	Lixisenatide	Liraglutide	Semaglutide	Exenatide	Albiglutide	Dulaglutide	Semaglutide	Efpeglenatide

GLP-1 receptor agonists

Effects on CV outcomes

(HR; 95%CI)

- MACE 0.86 (0.80 to 0.93)
- MI 0.90 (0.83 to 0.98)
- Stroke 0.83 (0.76 to 0.92)
- CV death 0.87 (0.80 to 0.94)



Effects on risk factors

glucose | weight | blood pressure

HbA1 ~ 1.5 % | ~ 4% | ~ 3 mmHg

Side effects

- GI side effect
- Local reaction at injection side
- Use with caution in patients with history of pancreatitis

Patient profile

- ASCVD
- Overweight / obese
- High risk of stroke

Treatments aspects

- Start with low dose
- Increase dose slowly
- Use ≤ 32 gauge needle
- Adjust insulin / SU dose
- Recommend small meals

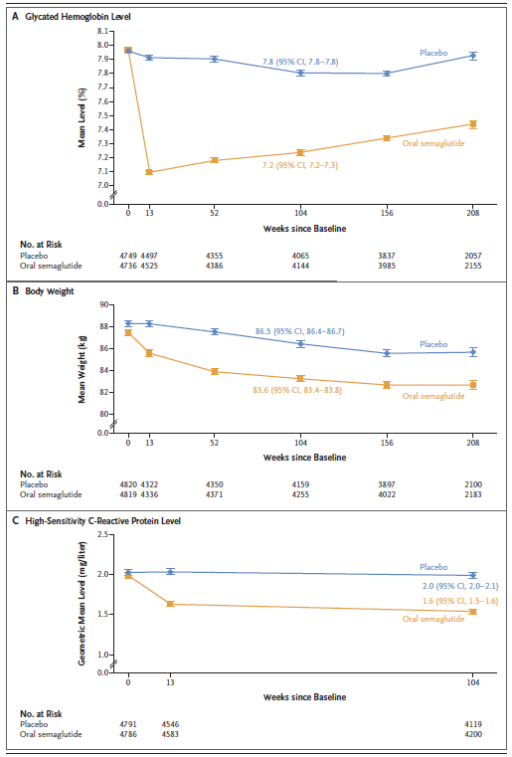
Circulation. 2022;146:1882–1894.

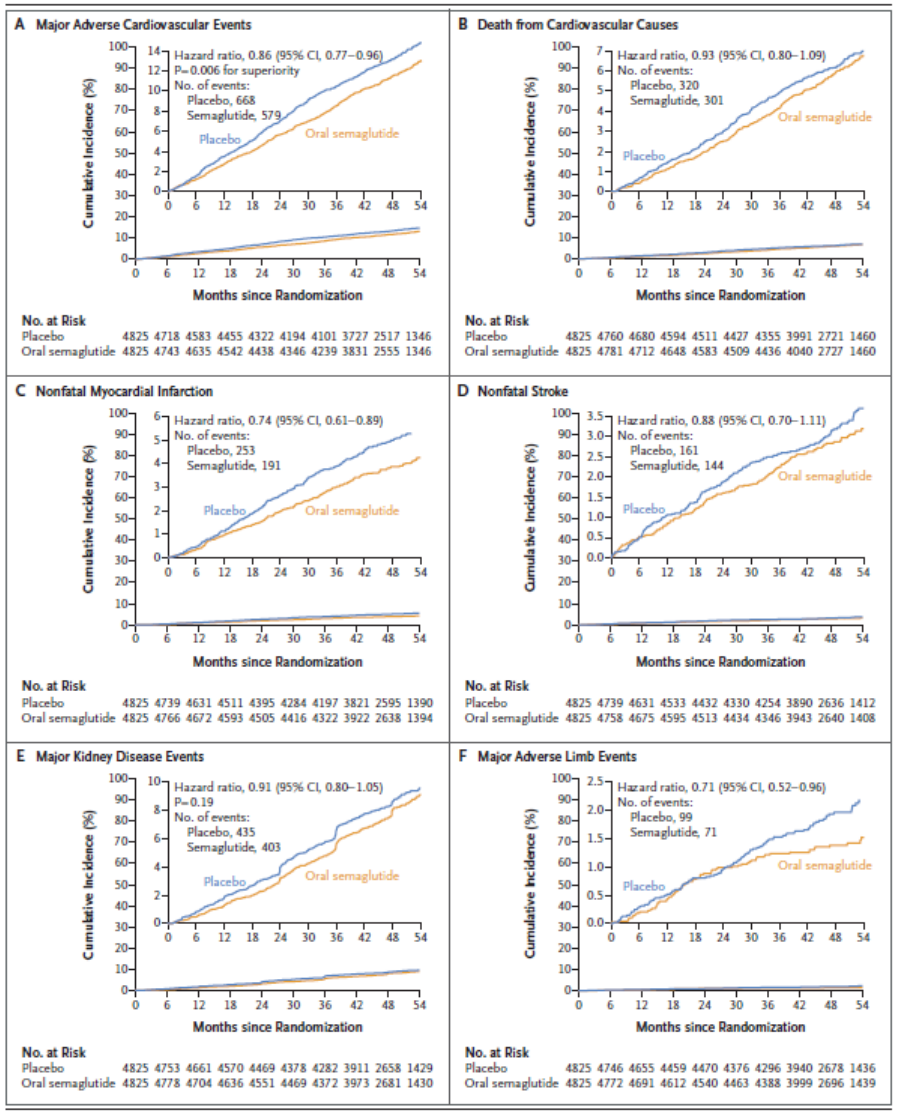
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Oral Semaglutide and Cardiovascular Outcomes in High-Risk Type 2 Diabetes

D.K. McGuire,[1,2] N. Marx,[3] S.L. Mulvagh,[4] J.E. Deanfield,[5] S.E. Inzucchi,[6] R. Pop-Busui,[7] J.F.E. Mann,[8,9] S.S. Emerson,[10] N.R. Poulter,[11] M.D.M. Engelmann,[12] M.S. Ripa,[12] G.K. Hovingh,[12] K. Brown-Frandsen,[12] S.C. Bain,[13] M.A. Cavender,[14] M. Gislum,[12] J.-P. David,[12] and J.B. Buse,[14] for the SOUL Study Group*





9650 patients

- T2DM with a HbA1c 6.5 to 10.0%
- known atherosclerotic cardiovascular disease
- chronic kidney disease
- or both

Oral semaglutide max dose 14mg vs **placebo**

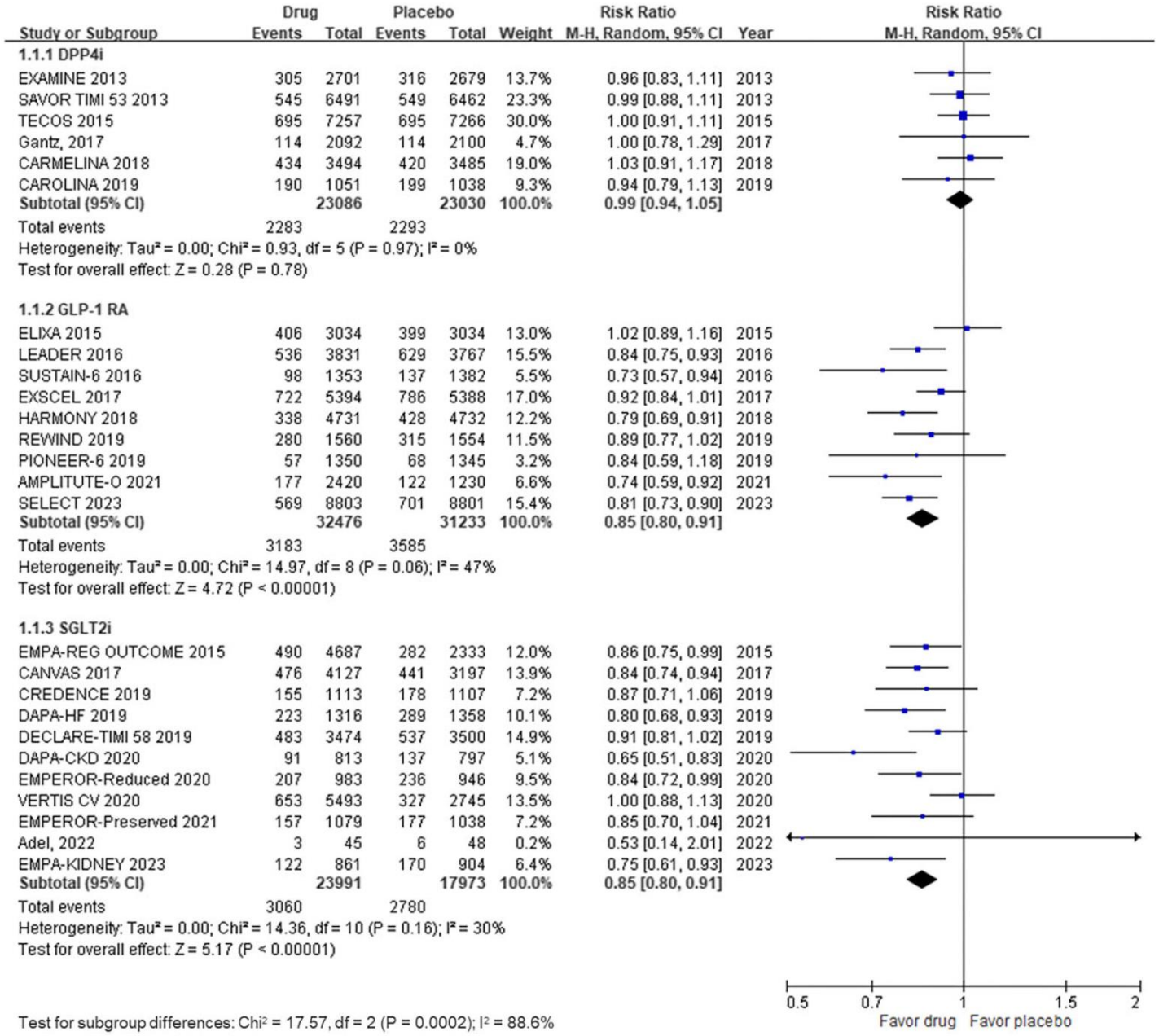
The incidence of adverse events that led to discontinuation of oral semaglutide or placebo was higher among participants receiving oral semaglutide, a difference that was largely due to gastrointestinal symptoms.

In this randomized, placebo-controlled trial involving persons with type 2 diabetes and atherosclerotic cardiovascular disease, chronic kidney disease, or both, daily oral semaglutide was superior to placebo in reducing the risk of major adverse cardiovascular events.

ESC European Society of Cardiology
European Heart Journal - Cardiovascular Pharmacotherapy (2025) **11**, 174–189
https://doi.org/10.1093/ehjcvp/pvae093
ORIGINAL ARTICLE
Heart failure/cardiomyopathy

Comparative cardiovascular effectiveness of glucagon-like peptide-1 receptor agonists and sodium–glucose cotransporter-2 inhibitors in atherosclerotic cardiovascular disease phenotypes: a systematic review and meta-analysis

Yu-Min Lin[1], Jheng-Yan Wu[2,3], Mei-Chuan Lee[4], Chen-Lun Su[5], Han Siong Toh[6,7], Wei-Ting Chang[8], Sih-Yao Chen[9], Fang-Hsiu Kuo[9], Hsin-Ju Tang[10], and Chia-Te Liao[8,*]



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World Health Organization

Obesity and overweight

Overview

1 March 2

Overweight is a condition of excessive fat deposits.

Obesity is a chronic complex disease defined by excessive fat deposits that can impair health. Obesity can lead to increased risk of type 2 diabetes and heart disease, it can affect bone health and reproduction, it increases the risk of certain cancers. Obesity influences the quality of living, such as sleeping or moving.

Key fa

- In 202
- World obesit
- In 202 millior
- In 2022, 43% of adults aged 18 years and over were overweight and 16% were living with obesity.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Semaglutide and Cardiovascular Outcomes in Obesity without Diabetes

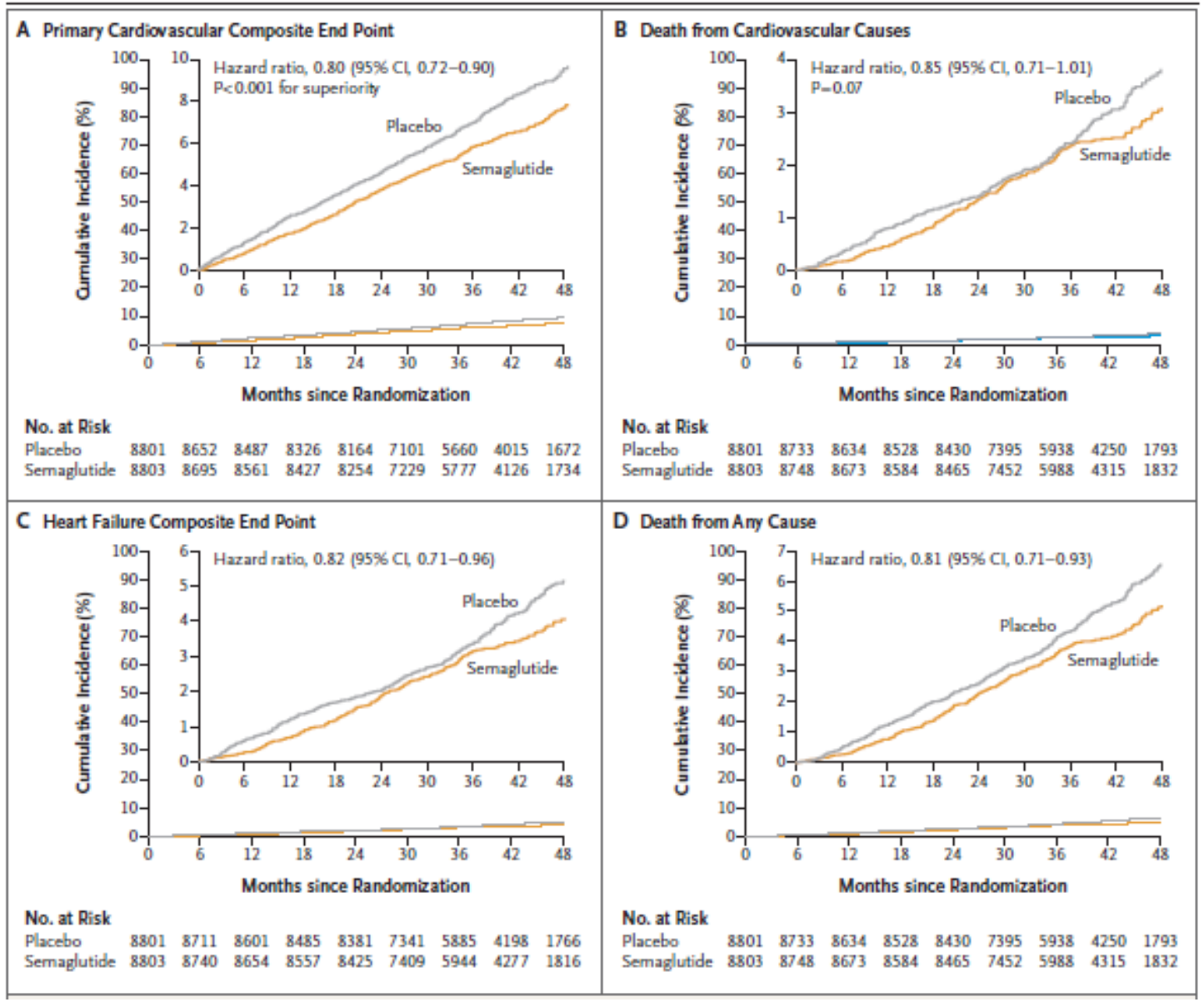
A. Michael Lincoff, M.D., Kirstine Brown-Frandsen, M.D., Helen M. Colhoun, M.D., John Deanfield, M.D., Scott S. Emerson, M.D., Ph.D., Sille Esbjerg, M.Sc., Søren Hardt-Lindberg, M.D., Ph.D., G. Kees Hovingh, M.D., Ph.D., Steven E. Kahn, M.B., Ch.B., Robert F. Kushner, M.D., Ildiko Lingvay, M.D., M.P.H., Tugce K. Oral, M.D., Marie M. Michelsen, M.D., Ph.D., Jorge Plutzky, M.D., Christoffer W. Tornøe, Ph.D., and Donna H. Ryan, M.D., for the SELECT Trial Investigators*

17604 patients

- ≥45 years
- Preexisting CV disease
- BMI > 27
- No history of diabetes

Primary end point:
A composite of death from CV causes, nonfatal myocardial infarction, or nonfatal stroke.

Once-weekly **sc semaglutide** 2.4 mg or placebo.
Mean **follow-up** of 39.8 months.



N Engl J Med 2023;389:2221-2232.

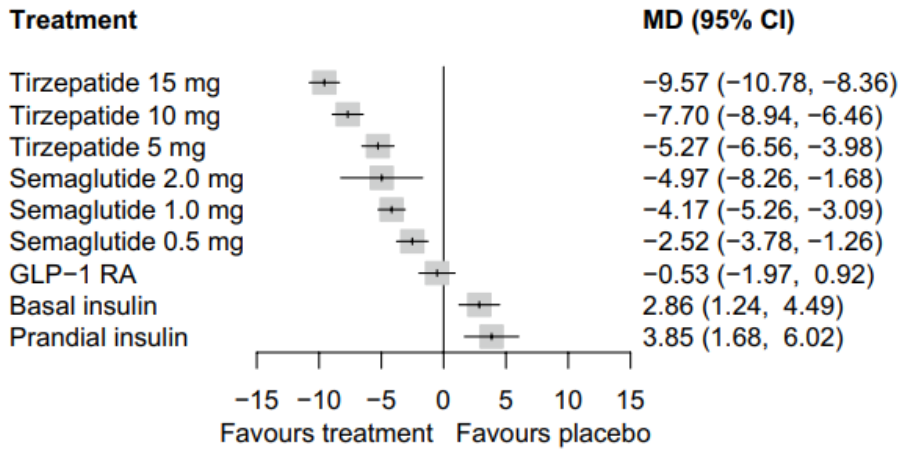
Diabetologia (2024) 67:1206–1222
https://doi.org/10.1007/s00125-024-06144-1

ARTICLE

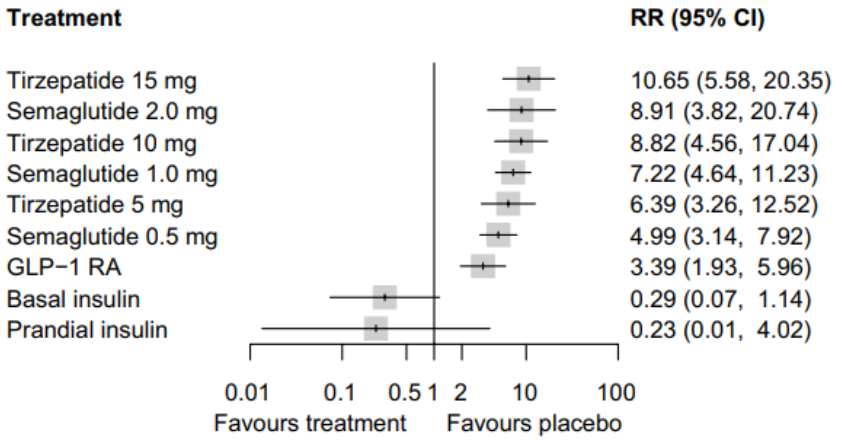
Subcutaneously administered tirzepatide vs semaglutide for adults with type 2 diabetes: a systematic review and network meta-analysis of randomised controlled trials

Thomas Karagiannis[1,2] · Konstantinos Malandris[1] · Ioannis Avgerinos[1,2] · Athina Stamati[3] · Panagiota Kakotrichi[1] · Aris Liakos[1,2] · Despoina Vasilakou[1,2] · Nikolaos Kakaletsis[1] · Apostolos Tsapas[1,2,4] · Eleni Bekiari[1,2]

Change in body weight (kg) compared with placebo



Discontinuation of treatment due to gastrointestinal adverse events compared with placebo



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Tirzepatide for Obesity Treatment and Diabetes Prevention

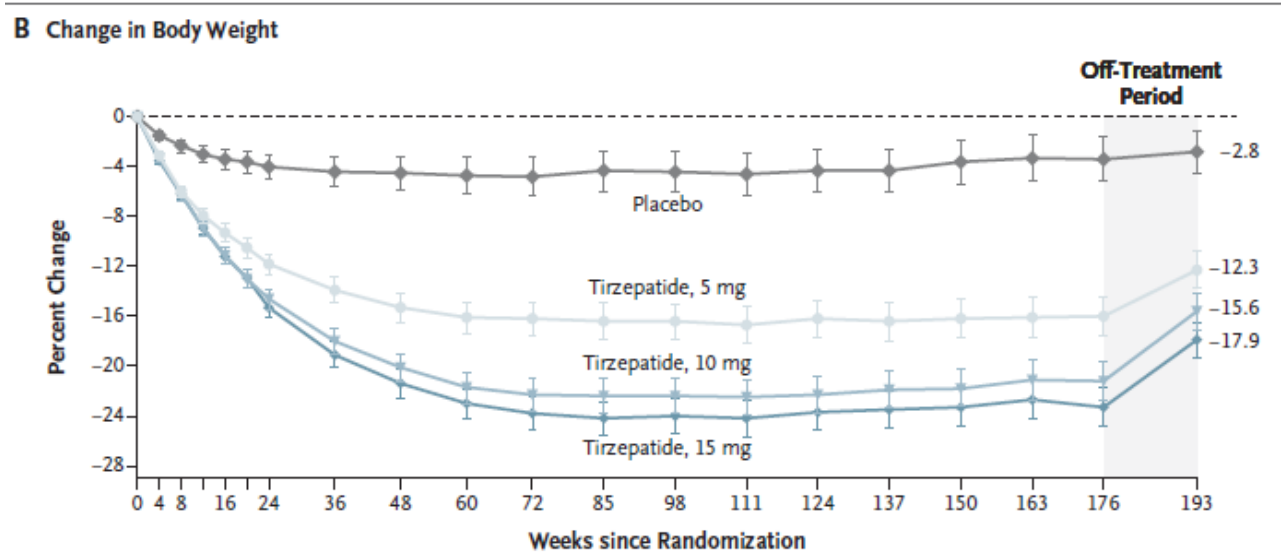
Ania M. Jastreboff, M.D., Ph.D.,[1,2] Carel W. le Roux, F.R.C.P., Ph.D.,[3] Adam Stefanski, M.D., Ph.D.,[4] Louis J. Aronne, M.D.,[5] Bruno Halpern, M.D., Ph.D.,[6] Sean Wharton, M.D., Pharm.D.,[7,8] John P.H. Wilding, D.M.,[9] Leigh Perreault, M.D.,[10] Shuyu Zhang, M.S.,[4] Ramakrishna Battula, M.S.,[4] Mathijs C. Bunck, M.D., Ph.D.,[4] Nadia N. Ahmad, M.D., M.P.H.,[4] and Irina Jouravskaya, M.D., Ph.D.,[4] for the SURMOUNT-1 Investigators*

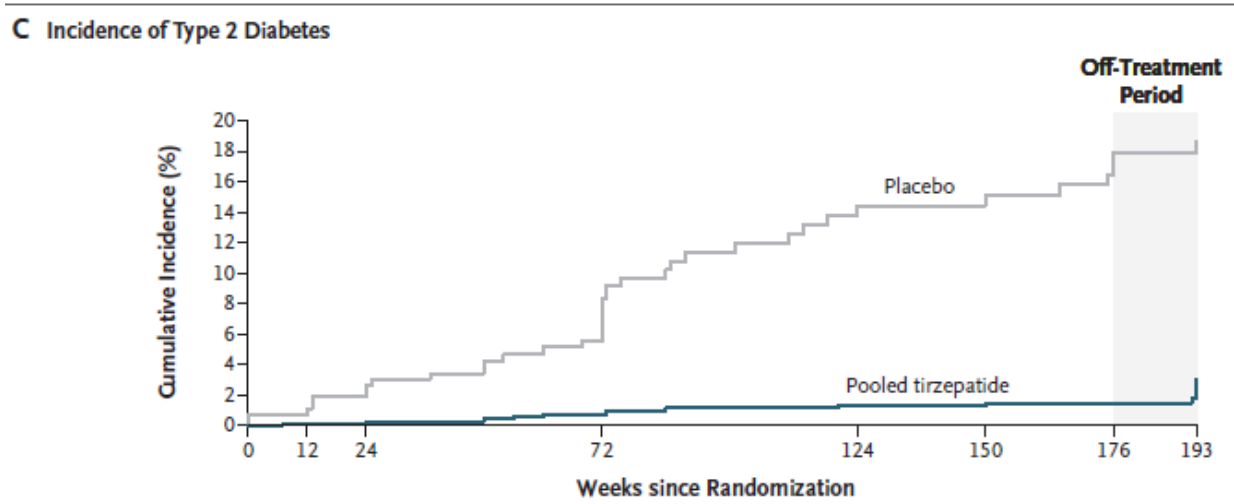
2539 patients (1032 with pre-diabetes)

- BMI > 30
- BMI >27 if prediabetes
- No history of diabetes

Primary end points:
Percent change in body weight
Percentage of participants with >5% weight reduction

Tirzepatide once-weekly dose of 5, 10 or 15 mg or placebo.
Follow-up 176 weeks.





No. at Risk								
Placebo	270	266	257	209	137	126	121	99
Pooled tirzepatide	762	751	742	700	581	570	557	494
No. of Participants with Diagnosis								
Placebo	2	3	7	20	31	32	36	37
Pooled tirzepatide	0	1	2	5	9	10	10	18

N Engl J Med 2025;392:958-71.

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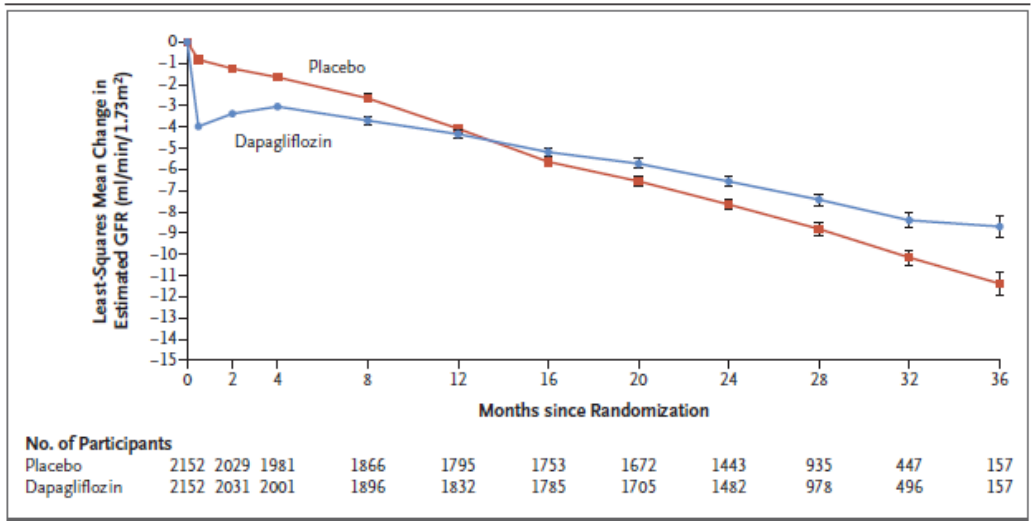
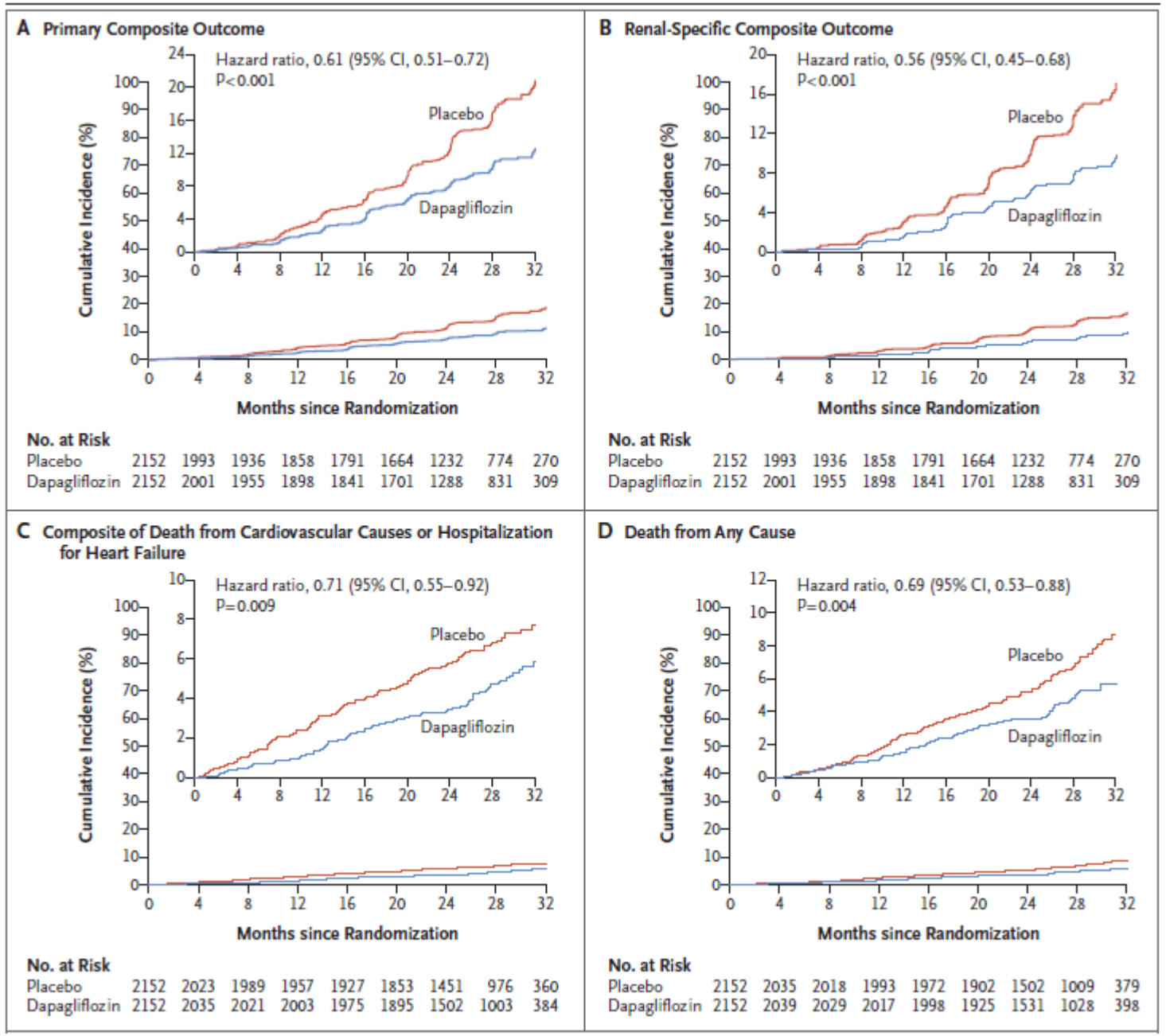
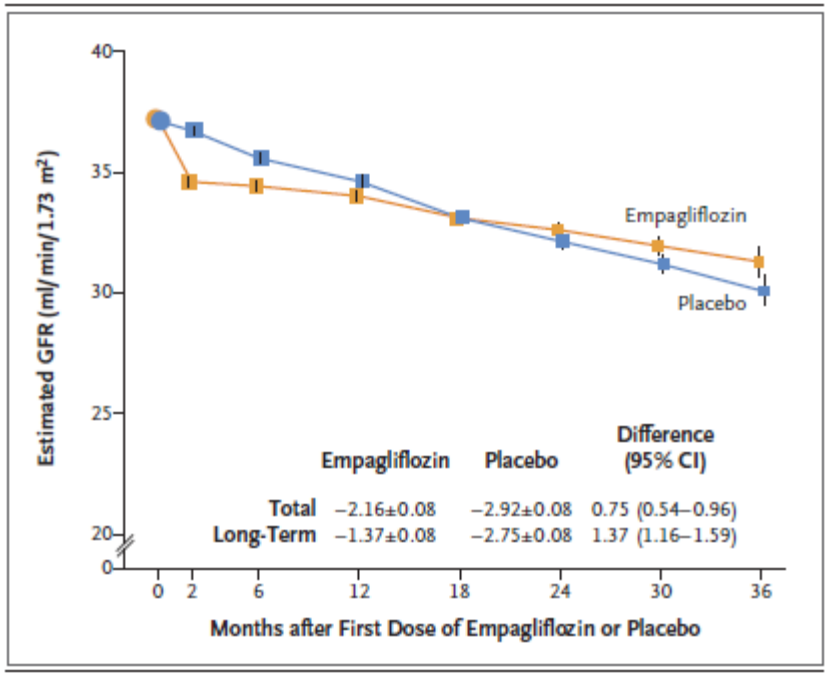
DAPA CKD
Trial results

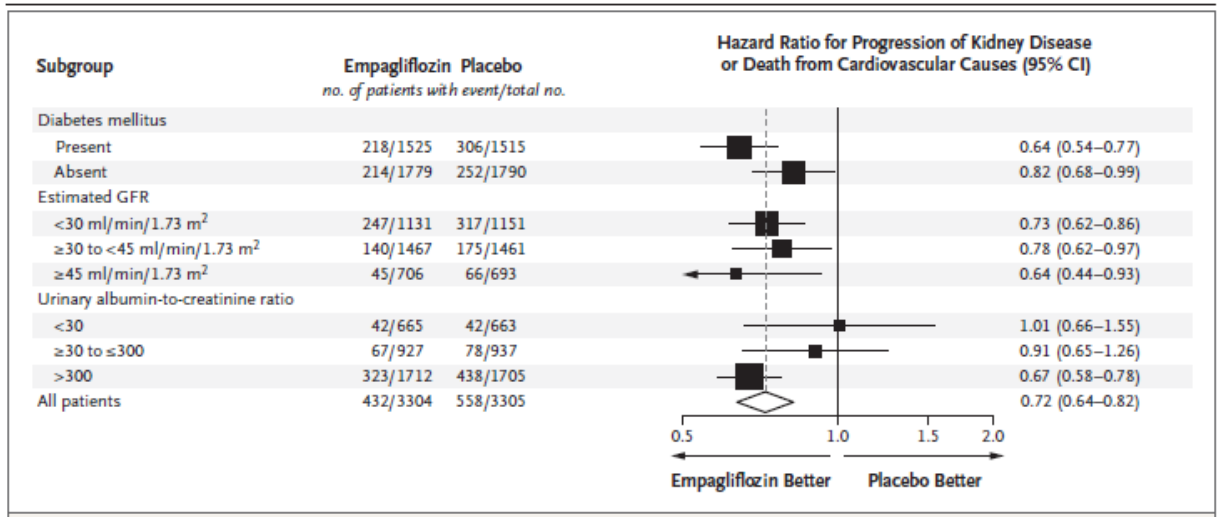


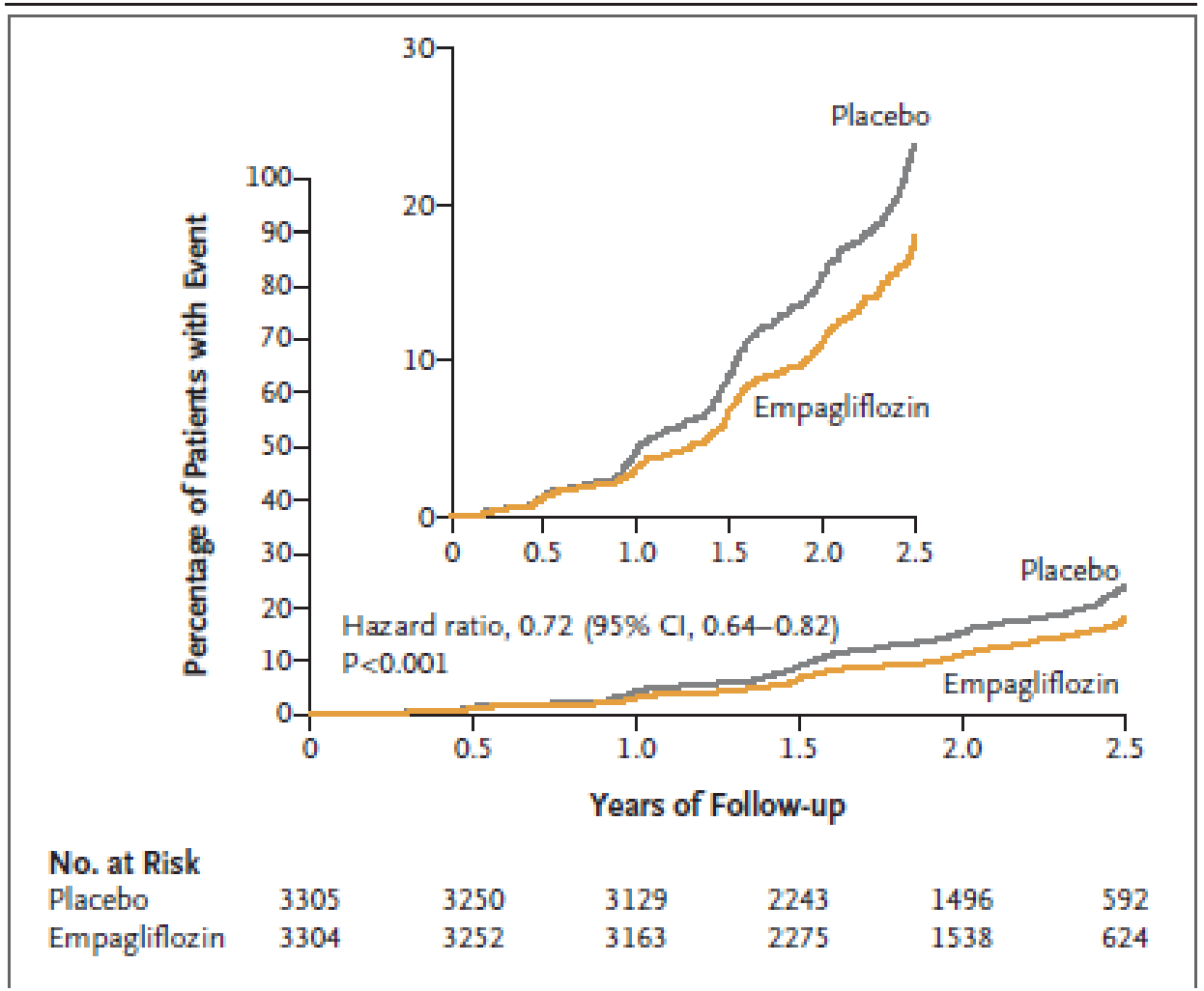


N Engl J Med. 2020 Oct 8;383(15):1436-1446.

EMPA Kidney Trial results







N Engl J Med. 2023 Jan 12;388(2):117-127.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Effects of Semaglutide on Chronic Kidney Disease in Patients with Type 2 Diabetes

Vlado Perkovic, M.B., B.S., Ph.D., Katherine R. Tuttle, M.D., Peter Rossing, M.D., D.M.Sc., Kenneth W. Mahaffey, M.D., Johannes F.E. Mann, M.D., George Bakris, M.D., Florian M.M. Baeres, M.D., Thomas Idorn, M.D., Ph.D., Heidrun Bosch-Traberg, M.D., Nanna Leonora Lausvig, M.Sc., and Richard Pratley, M.D., for the FLOW Trial Committees and Investigators*

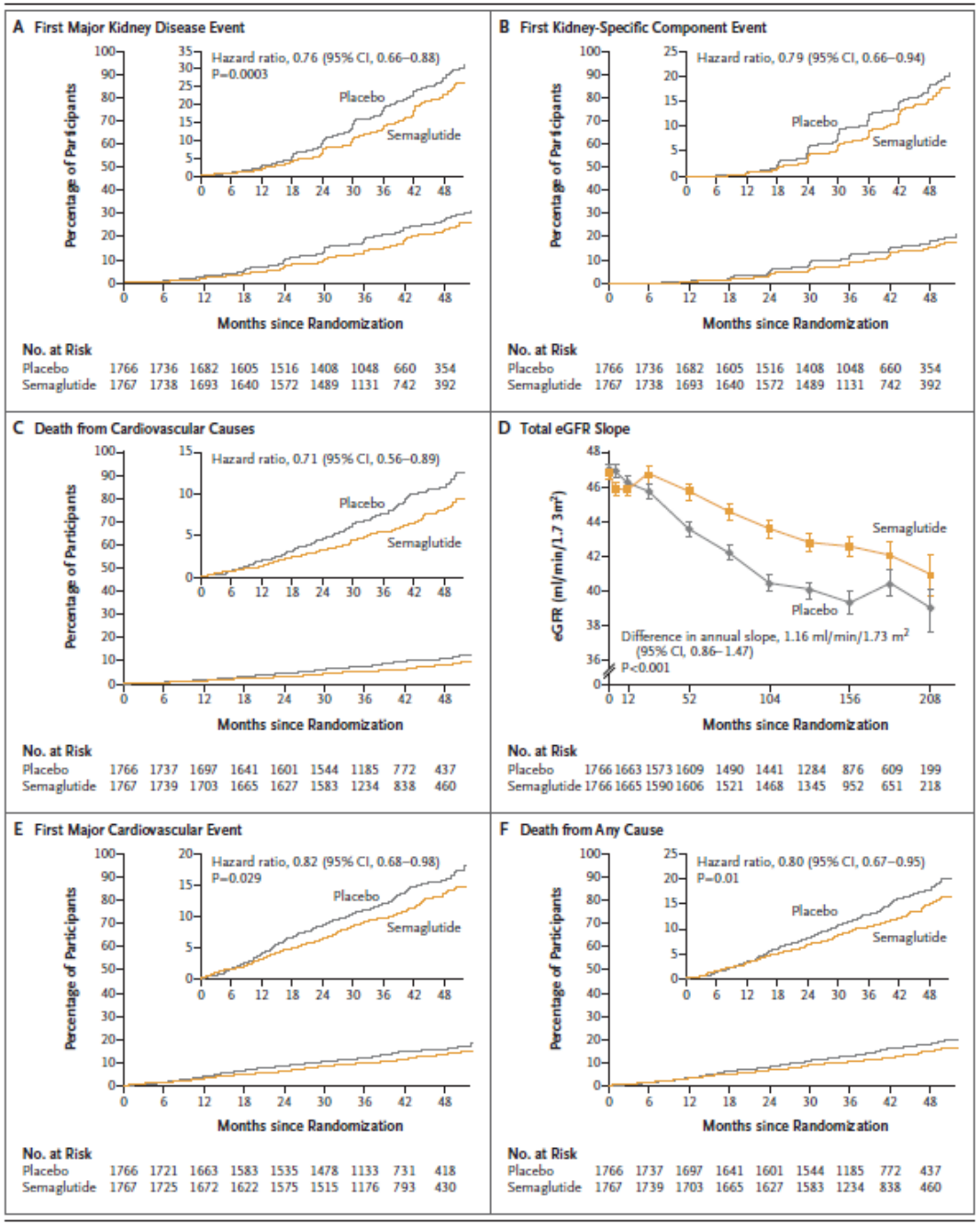
3533 patients

- History of diabetes (Hb1Ac <10)
- eGFR from 25 to 75
- urinary albumin-to-creatinine ratio from 300 to 5000 if eGFR from 50 to 75
- urinary albumin-to-creatinine ratio from 100 to 5000 if eGFR from 25 to 50

Primary end point:

Major kidney disease events (dialysis, renal transplant, eGFR <15 or ≥50% decrease) or death from kidney-related or CV causes

Subcut. **semaglutide** at 1.0 mg weekly or placebo.
Median **follow-up** was 3.4 years.



N Engl J Med. 2024;391:109-121

Un paio di informazioni finali

Valutazione EMA (PRAC) in corso su eventuali eventi avversi degli GLP1 RA

- Gastrointestinal Adverse Events (biliary disease, pancreatitis, bowel obstruction, and gastroparesis) in patients with T2DM.
- Nonarteritic Anterior Ischemic Optic Neuropathy Risk Among Patients With T2DM.
- Thyroid cancer in patients with T2DM.

JAMA Internal Medicine | Original Investigation

Comparative Bleeding Risk in Older Patients With HIV and Atrial Fibrillation Receiving Oral Anticoagulants

Claire M. Quinlan, MD; Jerry Avorn, MD; Aaron S. Kesselheim, MD, JD, MPH; Daniel E. Singer, MD; Yichi Zhang, MS; Alex Cervone, BA; Kueiyu Joshua Lin, MD, SCD

Patient population

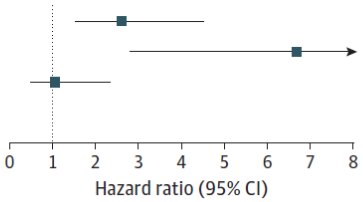
2683 new initiators of warfarin vs apixaban, rivaroxaban vs apixaban, and rivaroxaban vs warfarin aged 50 years or older with nonvalvular AF and HIV.

CONCLUSIONS AND RELEVANCE

This study found that in patients with HIV and AF, especially those treated with ART, warfarin and rivaroxaban were associated with higher rates of major bleeding compared with apixaban, suggesting a superior safety profile for apixaban in this high-risk population.

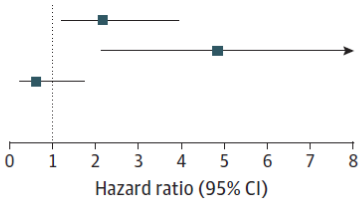
A Warfarin vs apixaban

Subgroup	No. of Warfarin events; IR per 1000 person-years	No. of Apixaban events; IR per 1000 person-years	Rate difference (95% CI)	Hazard ratio (95% CI)
Overall	53 (55.38)	27 (21.42)	33.96 (6.91 to 61.01)	2.60 (1.51 to 4.49)
ART use	40 (58.09)	9 (8.76)	49.33 (19.19 to 79.47)	6.68 (2.78 to 16.02)
No ART use	13 (50.08)	18 (52.29)	1.79 (-58.03 to 61.6)	1.04 (0.47 to 2.32)
P for heterogeneity			.16	<.01



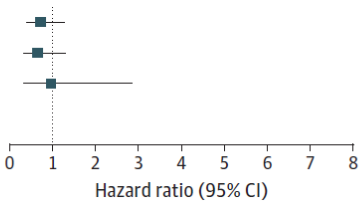
B Rivaroxaban vs apixaban

Subgroup	No. of Rivaroxaban events; IR per 1000 person-years	No. of Apixaban events; IR per 1000 person-years	Rate difference (95% CI)	Hazard ratio (95% CI)
Overall	21 (42.94)	30 (20.06)	22.89 (-3.83 to 49.62)	2.15 (1.18 to 3.94)
ART use	16 (46.88)	11 (9.74)	37.14 (7.43 to 66.85)	4.83 (2.11 to 11.08)
No ART use	5 (31.20)	19 (53.82)	-22.62 (-84.14 to 38.91)	0.59 (0.2 to 1.71)
P for heterogeneity			.09	<.01



C Rivaroxaban vs warfarin

Subgroup	No. of Rivaroxaban events; IR per 1000 person-years	No. of Warfarin events; IR per 1000 person-years	Rate difference (95% CI)	Hazard ratio (95% CI)
Overall	19 (35.79)	53 (49.55)	-13.76 (-47.06 to 19.53)	0.72 (0.41 to 1.27)
ART use	14 (34.89)	40 (53.53)	-18.65 (-59.82 to 22.51)	0.65 (0.33 to 1.29)
No ART use	5 (34.86)	13 (35.84)	-0.98 (-56.11 to 54.14)	0.96 (0.33 to 2.85)
P for heterogeneity			.61	.55



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Conclusioni: le novità nella gestione delle problematiche cardio-metaboliche

- Il controllo della **ipercolesterolemia** é possibile anche con l'utilizzo di trattamenti tradizionali a basso costo (statine+ezetimibe), lasciando i nuovi farmaci più costosi e potenti aun numero limitato di pazienti.
- Nei **pazienti diabetici** si è passati dal solo controllo del metabolismo glucidico alla prevenzione degli eventi cardiovascolari.
- L'**obesità**, considerata oggi come una vera e propria malattia, trova nuovi orizzonti terapeutici non solo in termini di riduzione del peso corporeo ma anche di prevenzione degli eventi cardiovascolari.
- La progressione della **malattia renale cronica** può essere rallentata da nuovi trattamenti quali SGLT2-i e probabilmente GLP1 RA.
- Una **gestione specifica** del rischio cardiometabolico può/deve essere pianificata **nel PLWH.**

Grazie infinite per l'attenzione

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