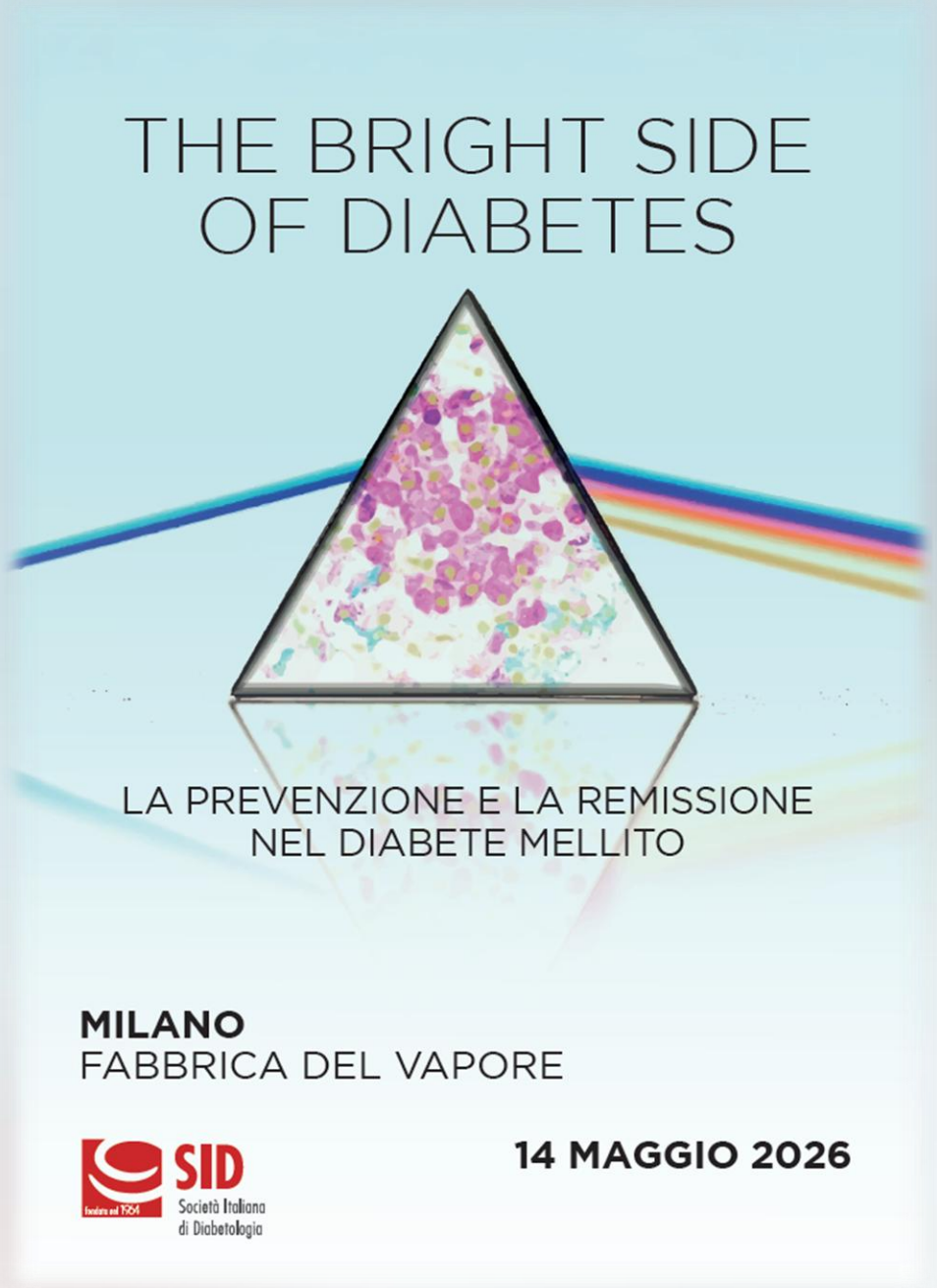


SGLT2i nel pre-diabete

Dott.ssa Irene Cogliati

2° SESSIONE - PREVENZIONE NEL DIABETE TIPO 2 OLTRE IL LIFESTYLE

Moderatori: Federico Giacchetti, Yana Pigotskaya

11.20	GLP1-RA e Dual Agonist-Tirzepatide nel pre-diabete ***Stefano Ciardullo***
11.40	SGLT2-i nel pre-diabete ***Irene Cogliati***
12.00	Discussione

Fondazione IRCCS Ca' Granda
Ospedale Maggiore Policlinico
Sistema Socio Sanitario
Regione Lombardia
UNIVERSITÀ DEGLI STUDI DI MILANO

La sottoscritta dichiara di NON aver ricevuto negli ultimi due anni compensi o finanziamenti da Aziende Farmaceutiche e/o Diagnostiche

Dichiara altresì il proprio impegno ad astenersi, nell'ambito dell'evento, dal nominare, in qualsivoglia modo o forma, aziende farmaceutiche e/o denominazione commerciale e di non fare pubblicità di qualsiasi tipo relativamente a specifici prodotti di interesse sanitario (farmaci, strumenti, dispositivi medico-chirurgici, ecc.).

Agenda

1

Prediabete: perché dobbiamo occuparcene?
Epidemiologia, definizioni e rischio di progressione a T2DM

2

SGLT2i: potenziali meccanismi nel prediabete
Razionale fisiopatologico e dati preclinici

3

Esperienze cliniche: SGLT2i e prediabete
Evidenze dai trial

4

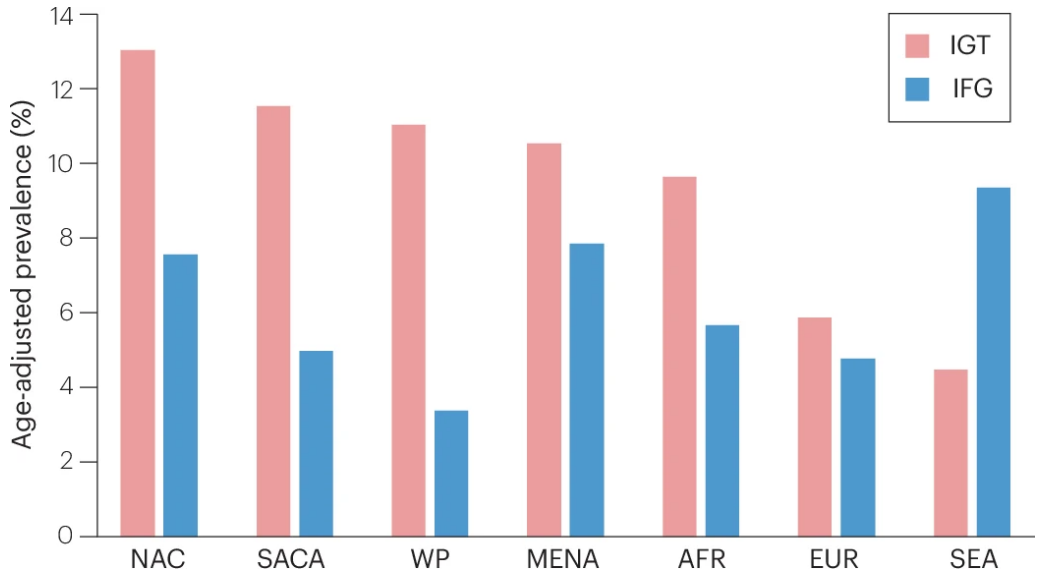
A che punto siamo oggi?
Trial in corso e prospettive future

Prediabete

Table 1 | Definitions of prediabetes

Organization	IFG based on fasting plasma glucose	IGT based on 2-h glucose value during an OGTT	At risk of diabetes based on HbA1c	Ref.
ADA	5.6–6.9 mmol/l (100–125 mg/dl)	7.8–11.0 mmol/l (140–199 mg/dl)	5.7–6.4% (39–46 mmol/mol)	2
WHO	6.1–6.9 mmol/l (110–125 mg/dl)	7.8–11.0 mmol/l (140–199 mg/dl)	NA	208
IEC	NA	NA	6.0–6.4% (42–46 mmol/mol)	209

ADA, American Diabetes Association; HbA1c, glycated haemoglobin; IEC, International Expert Committee; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; NA, not applicable; OGTT, oral glucose tolerance test.



634M

Adulti con IGT
12% della popolazione adulta mondiale (2024)

488M

Adulti con IFG
9.2% della popolazione adulta mondiale (2024)

Unnikrishnan et al. Prediabetes. Nat Rev Dis Primers, 2025

Prediabete

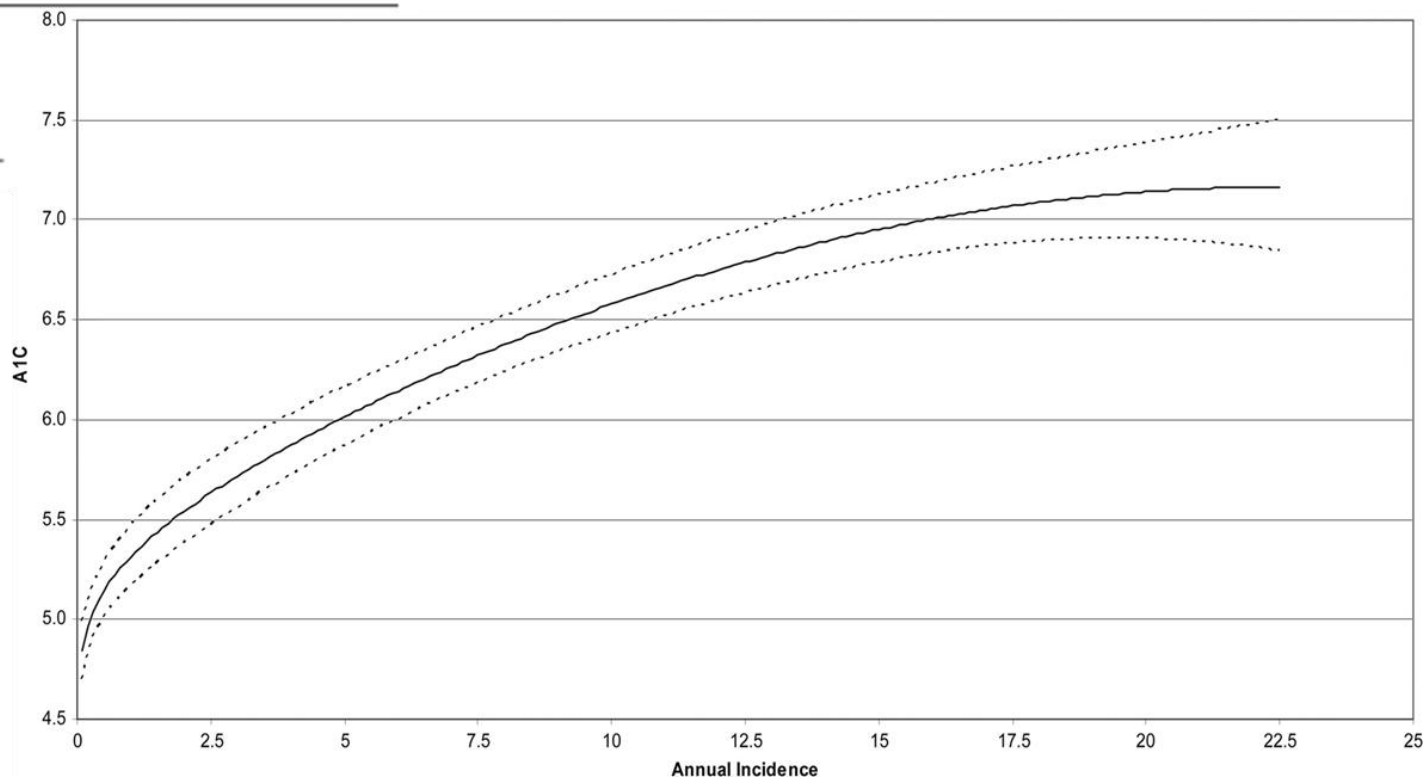
Prediabete

Reviews/Commentaries/ADA Statements
REVIEW ARTICLE

A1C Level and Future Risk of Diabetes: A Systematic Review

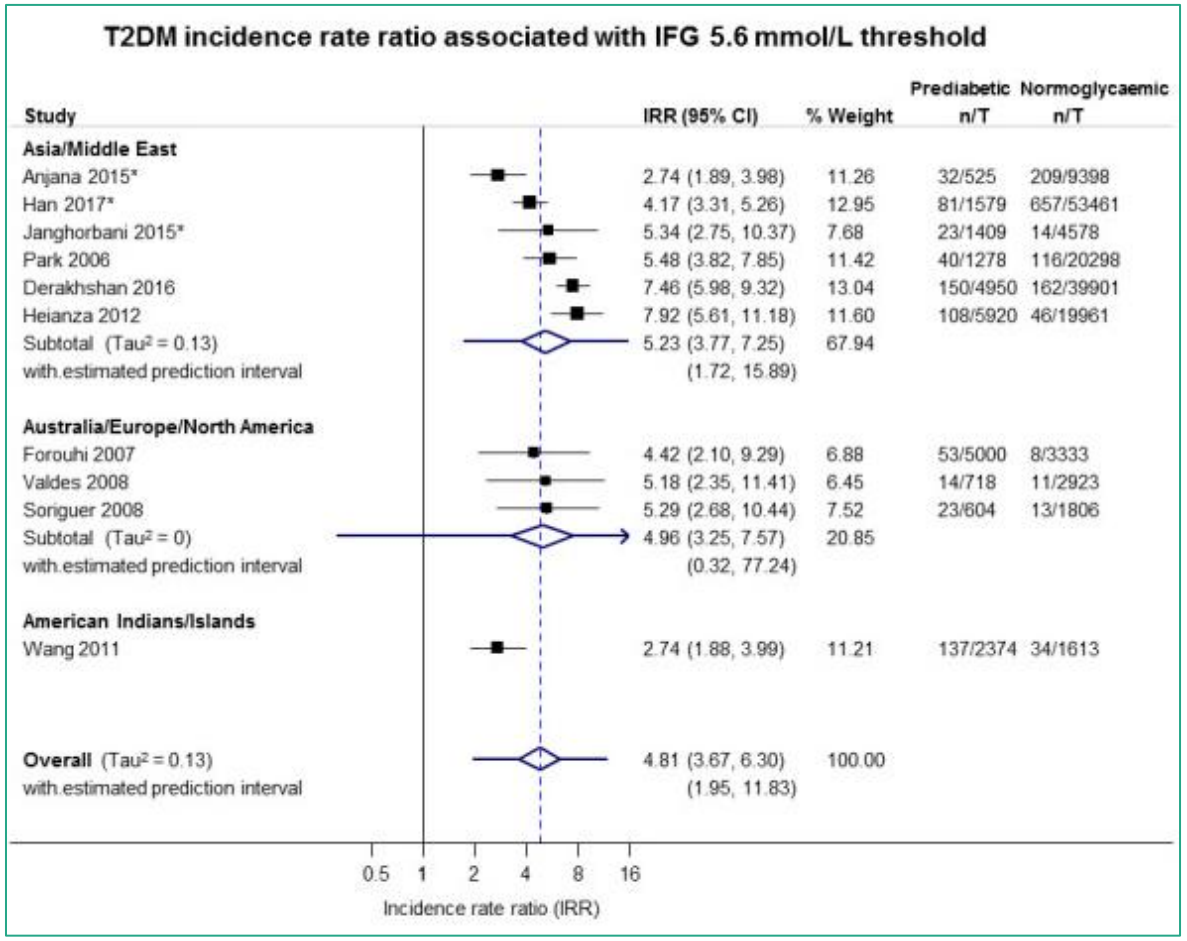
XUANPING ZHANG, PHD[1]
EDWARD W. GREGG, PHD[1]
DAVID F. WILLIAMSON, PHD[2]
LAWRENCE E. BARKER, PHD[1]
WILLIAM THOMAS, MLIS[1]
KAI MCKEEVER BULLARD, PHD[1]
GIUSEPPINA IMPERATORE, MD, PHD[1]
DESMOND E. WILLIAMS, MD, PHD[1]
ANN L. ALBRIGHT, PHD, RD[1]

A1C modeled as a function of annualized incidence.



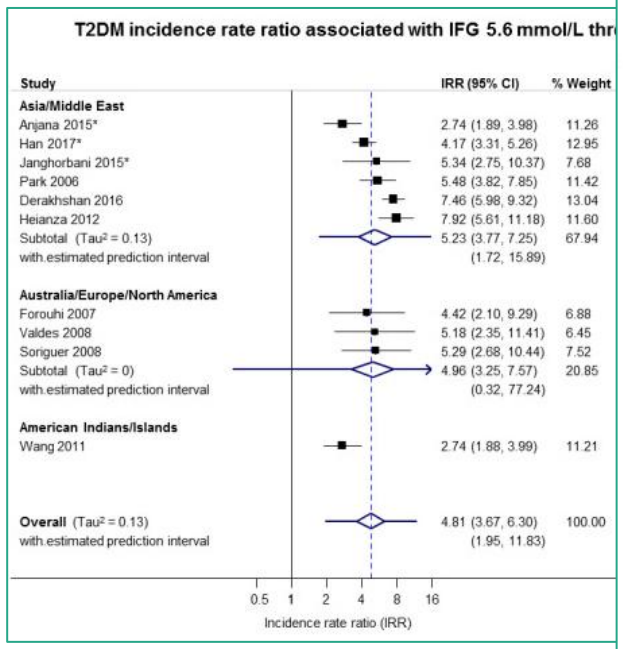
Zhang et al. A1C Level and Future Risk of Diabetes: A Systematic Review. Diabetes Care 2010

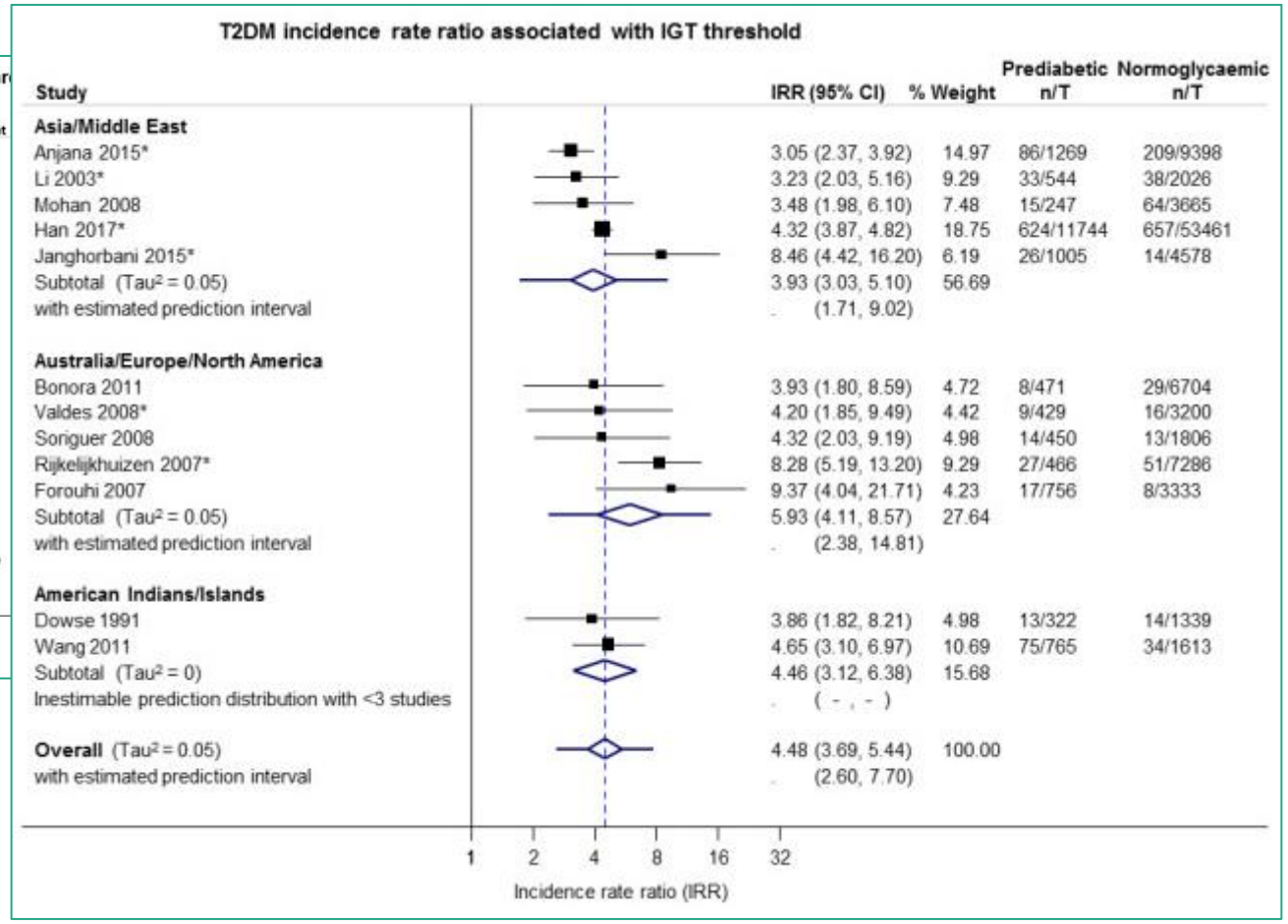
Rischio di progressione a diabete



Richter et al. Development of type 2 diabetes mellitus in people with intermediate hyperglycaemia. Cochrane Database Syst Rev. 2018

Rischio di progressione a diabete





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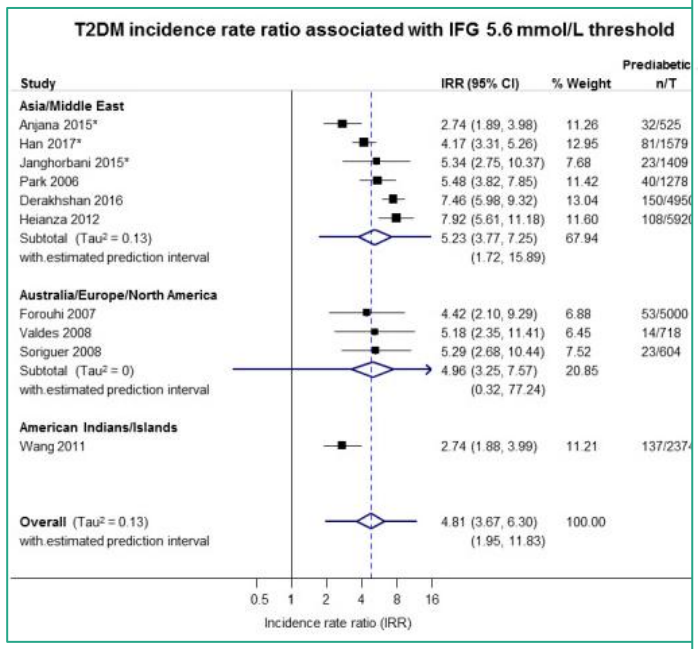

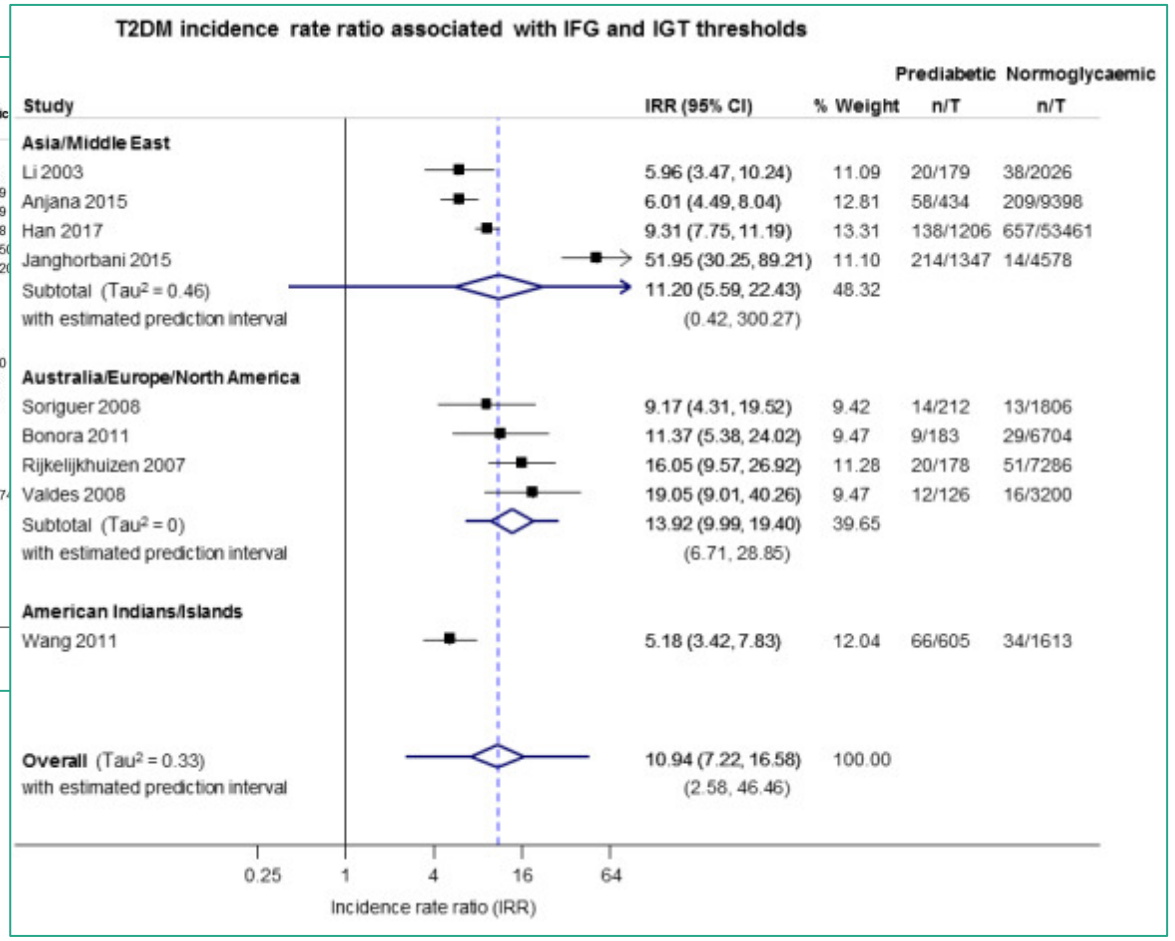

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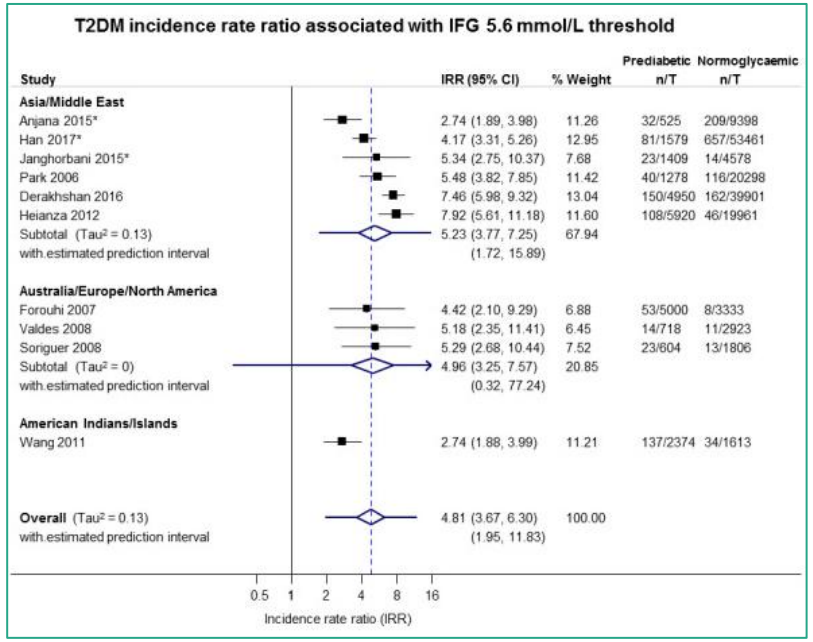
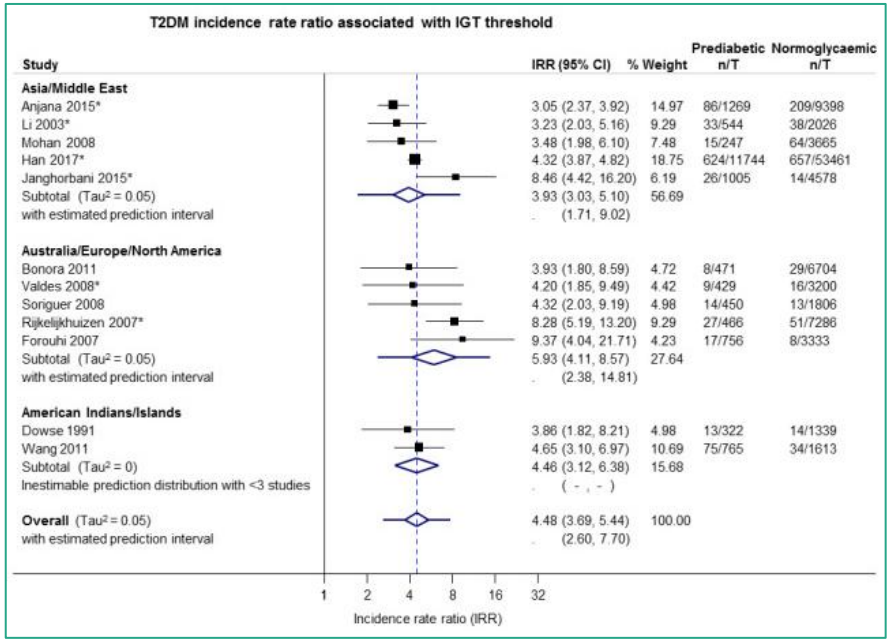
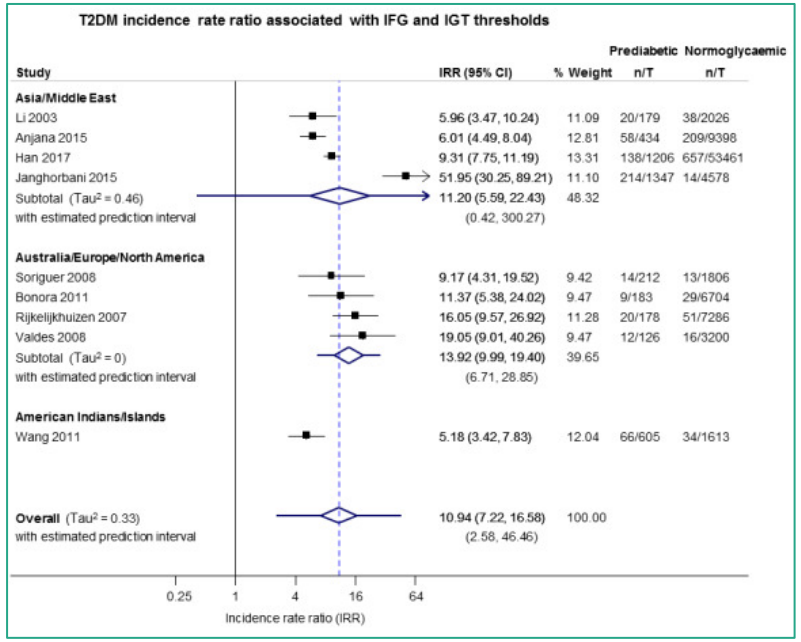
Rischio di progressione a diabete







IFG 5,6 mmol/L

IRR complessivo: **4,81** (95% CI 3,67–6,30) per T2DM vs normoglicemia

IGT

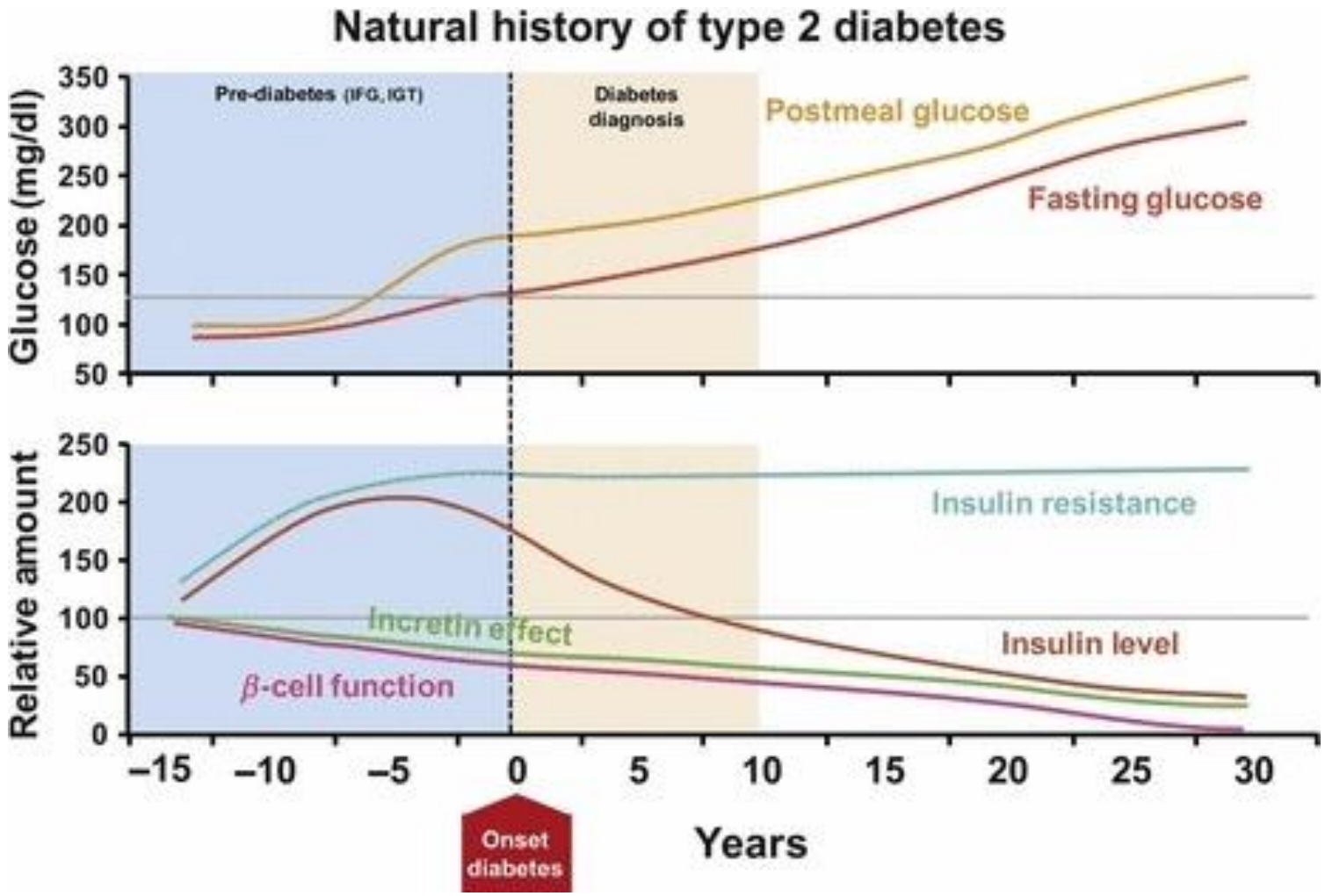
IRR complessivo: **4,48** (95% CI 3,69–5,44) per T2DM vs normoglicemia

IFG+IGT

IRR complessivo: **10,94** (95% CI 7,22-16,58) per T2DM vs normoglicemia

Richter et al. Development of type 2 diabetes mellitus in people with intermediate hyperglycaemia. Cochrane Database Syst Rev. 2018

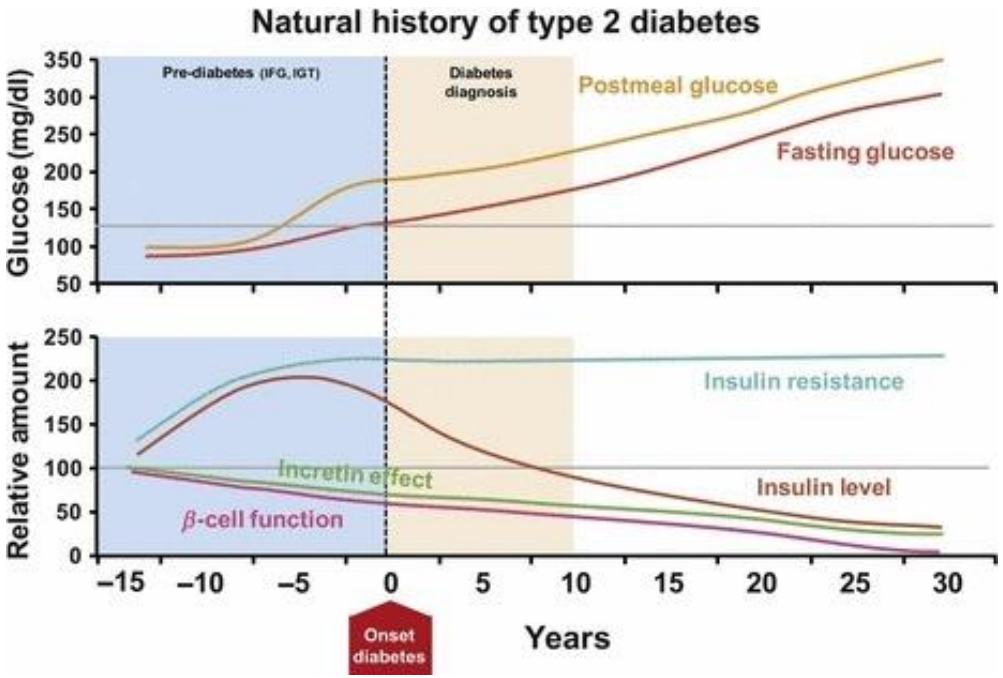
Storia naturale del T2DM

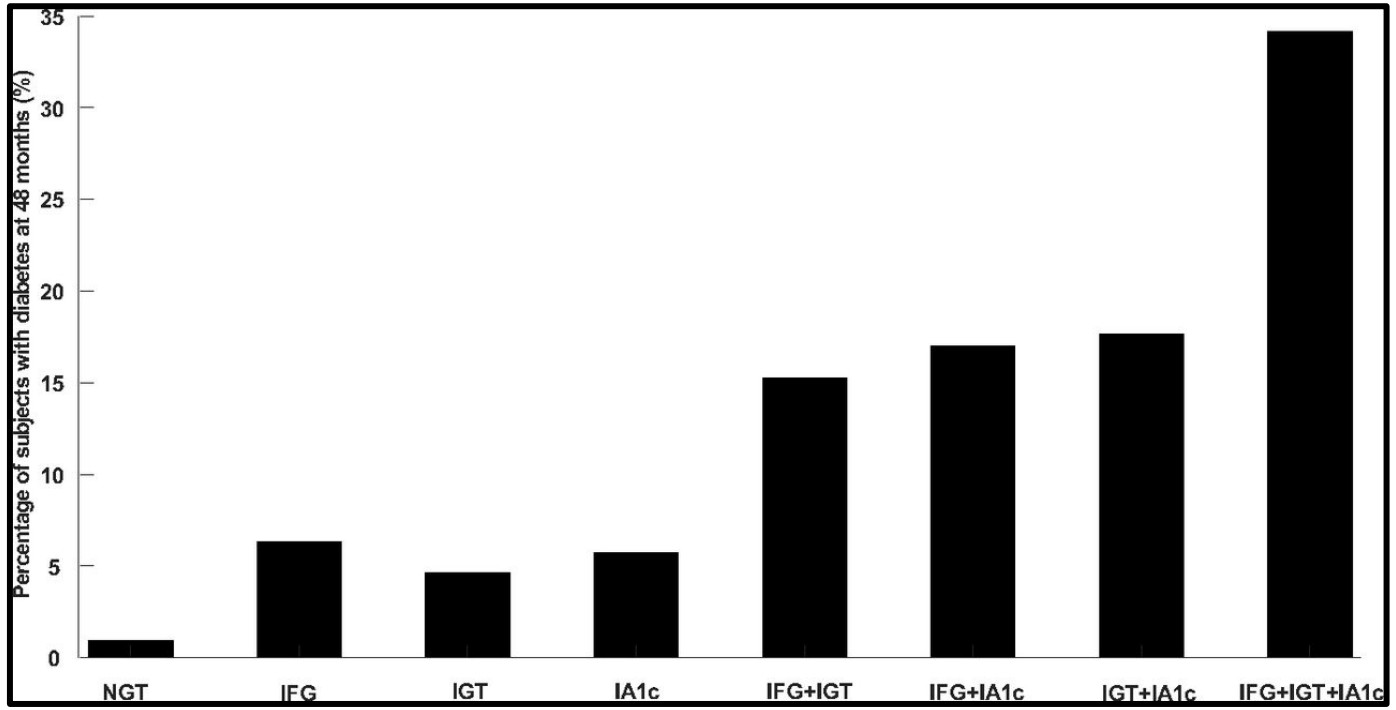


Tobin et al. Addition of exenatide twice daily to basal insulin for the treatment of type 2 diabetes: clinical studies and practical approaches to therapy. Int J Clin Pract. 2012

Tura et al. Profiles of Glucose Metabolism in Different Prediabetes Phenotypes, Classified by Fasting Glycemia, 2-Hour OGTT, Glycated Hemoglobin, and 1-Hour OGTT: An IMI DIRECT Study. Diabetes. 2021

Storia naturale del T2DM





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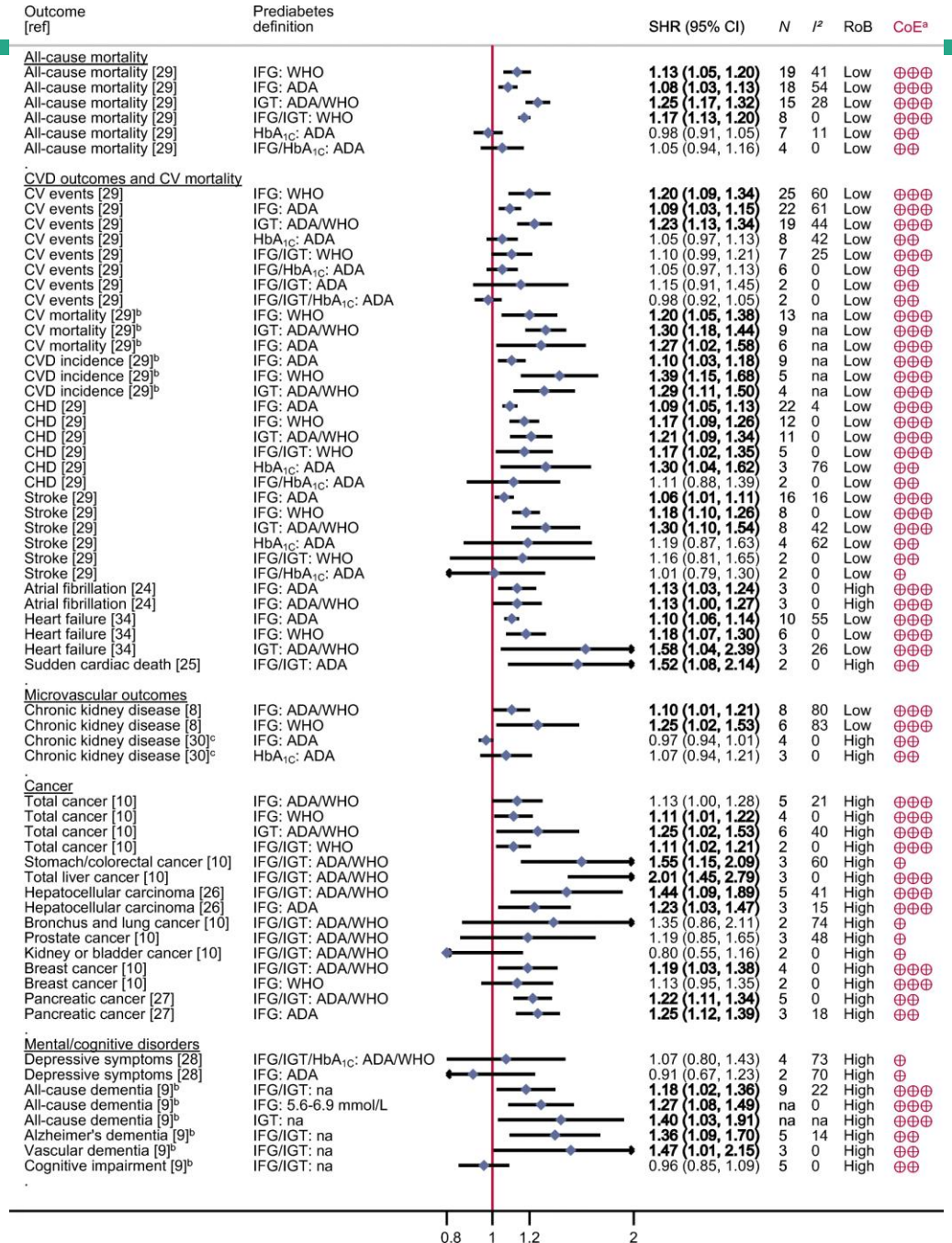
Prediabete e comorbidità



Outcome [ref]	Prediabetes definition	SHR (95% CI)	N	I^2	RoB	CoE[a]
All-cause mortality						
All-cause mortality [29]	IFG: WHO	**1.13 (1.05, 1.20)**	19	41	Low	⊕⊕⊕
All-cause mortality [29]	IFG: ADA	**1.08 (1.03, 1.13)**	18	54	Low	⊕⊕⊕
All-cause mortality [29]	IGT: ADA/WHO	**1.25 (1.17, 1.32)**	15	28	Low	⊕⊕⊕
All-cause mortality [29]	IFG/IGT: WHO	**1.17 (1.13, 1.20)**	8	0	Low	⊕⊕⊕
All-cause mortality [29]	HbA_{1c}: ADA	0.98 (0.91, 1.05)	7	11	Low	⊕⊕
All-cause mortality [29]	IFG/HbA_{1c}: ADA	1.05 (0.94, 1.16)	4	0	Low	⊕⊕
CVD outcomes and CV mortality						
CV events [29]	IFG: WHO	**1.20 (1.09, 1.34)**	25	60	Low	⊕⊕⊕
CV events [29]	IFG: ADA	**1.09 (1.03, 1.15)**	22	61	Low	⊕⊕⊕
CV events [29]	IGT: ADA/WHO	**1.23 (1.13, 1.34)**	19	44	Low	⊕⊕⊕
CV events [29]	HbA_{1c}: ADA	1.05 (0.97, 1.13)	8	42	Low	⊕⊕
CV events [29]	IFG/IGT: WHO	1.10 (0.99, 1.21)	7	25	Low	⊕⊕⊕
CV events [29]	IFG/HbA_{1c}: ADA	1.05 (0.97, 1.13)	6	0	Low	⊕⊕
CV events [29]	IFG/IGT: ADA	1.15 (0.91, 1.45)	2	0	Low	⊕⊕
CV events [29]	IFG/IGT/HbA_{1c}: ADA	0.98 (0.92, 1.05)	2	0	Low	⊕⊕
CV mortality [29][b]	IFG: WHO	**1.20 (1.05, 1.38)**	13	na	Low	⊕⊕⊕
CV mortality [29][b]	IGT: ADA/WHO	**1.30 (1.18, 1.44)**	9	na	Low	⊕⊕⊕
CV mortality [29][b]	IFG: ADA	**1.27 (1.02, 1.58)**	6	na	Low	⊕⊕⊕
CVD incidence [29][b]	IFG: ADA	**1.10 (1.03, 1.18)**	9	na	Low	⊕⊕⊕
CVD incidence [29][b]	IFG: WHO	**1.39 (1.15, 1.68)**	5	na	Low	⊕⊕⊕
CVD incidence [29][b]	IGT: ADA/WHO	**1.29 (1.11, 1.50)**	4	na	Low	⊕⊕⊕
CHD [29]	IFG: ADA	**1.09 (1.05, 1.13)**	22	4	Low	⊕⊕⊕
CHD [29]	IFG: WHO	**1.17 (1.09, 1.26)**	12	0	Low	⊕⊕⊕
CHD [29]	IGT: ADA/WHO	**1.21 (1.09, 1.34)**	11	0	Low	⊕⊕⊕
CHD [29]	IFG/IGT: WHO	**1.17 (1.02, 1.35)**	5	0	Low	⊕⊕⊕
CHD [29]	HbA_{1c}: ADA	**1.30 (1.04, 1.62)**	3	76	Low	⊕⊕
CHD [29]	IFG/HbA_{1c}: ADA	1.11 (0.88, 1.39)	2	0	Low	⊕⊕
Stroke [29]	IFG: ADA	**1.06 (1.01, 1.11)**	16	16	Low	⊕⊕⊕
Stroke [29]	IFG: WHO	**1.18 (1.10, 1.26)**	8	0	Low	⊕⊕⊕
Stroke [29]	IGT: ADA/WHO	**1.30 (1.10, 1.54)**	8	42	Low	⊕⊕⊕
Stroke [29]	HbA_{1c}: ADA	1.19 (0.87, 1.63)	4	62	Low	⊕⊕
Stroke [29]	IFG/IGT: WHO	1.16 (0.81, 1.65)	2	0	Low	⊕⊕
Stroke [29]	IFG/HbA_{1c}: ADA	1.01 (0.79, 1.30)	2	0	Low	⊕
Atrial fibrillation [24]	IFG: ADA	**1.13 (1.03, 1.24)**	3	0	High	⊕⊕⊕
Atrial fibrillation [24]	IFG: ADA/WHO	**1.13 (1.00, 1.27)**	3	0	High	⊕⊕⊕
Heart failure [34]	IFG: ADA	**1.10 (1.06, 1.14)**	10	55	Low	⊕⊕⊕
Heart failure [34]	IFG: WHO	**1.18 (1.07, 1.30)**	6	0	Low	⊕⊕⊕
Heart failure [34]	IGT: ADA/WHO	**1.58 (1.04, 2.39)**	3	26	Low	⊕⊕⊕
Sudden cardiac death [25]	IFG/IGT: ADA	**1.52 (1.08, 2.14)**	2	0	High	⊕⊕
Microvascular outcomes						
Chronic kidney disease [8]	IFG: ADA/WHO	**1.10 (1.01, 1.21)**	8	80	Low	⊕⊕⊕
Chronic kidney disease [8]	IFG: WHO	**1.25 (1.02, 1.53)**	6	83	Low	⊕⊕⊕
Chronic kidney disease [30][c]	IFG: ADA	0.97 (0.94, 1.01)	4	0	High	⊕⊕
Chronic kidney disease [30][c]	HbA_{1c}: ADA	1.07 (0.94, 1.21)	3	0	High	⊕⊕
Cancer						
Total cancer [10]	IFG: ADA/WHO	1.13 (1.00, 1.28)	5	21	High	⊕⊕⊕
Total cancer [10]	IFG: WHO	**1.11 (1.01, 1.22)**	4	0	High	⊕⊕⊕
Total cancer [10]	IGT: ADA/WHO	**1.25 (1.02, 1.53)**	6	40	High	⊕⊕⊕
Total cancer [10]	IFG/IGT: WHO	**1.11 (1.02, 1.21)**	2	0	High	⊕⊕⊕
Stomach/colorectal cancer [10]	IFG/IGT: ADA/WHO	**1.55 (1.15, 2.09)**	3	60	High	⊕
Total liver cancer [10]	IFG/IGT: ADA/WHO	**2.01 (1.45, 2.79)**	3	0	High	⊕⊕⊕
Hepatocellular carcinoma [26]	IFG/IGT: ADA/WHO	**1.44 (1.09, 1.89)**	5	41	High	⊕⊕⊕
Hepatocellular carcinoma [26]	IFG: ADA	**1.23 (1.03, 1.47)**	3	15	High	⊕⊕⊕
Bronchus and lung cancer [10]	IFG/IGT: ADA/WHO	1.35 (0.86, 2.11)	2	74	High	⊕
Prostate cancer [10]	IFG/IGT: ADA/WHO	1.19 (0.85, 1.65)	3	48	High	⊕
Kidney or bladder cancer [10]	IFG/IGT: ADA/WHO	0.80 (0.55, 1.16)	2	0	High	⊕
Breast cancer [10]	IFG/IGT: ADA/WHO	**1.19 (1.03, 1.38)**	4	0	High	⊕⊕⊕
Breast cancer [10]	IFG: WHO	1.13 (0.95, 1.35)	2	0	High	⊕⊕⊕
Pancreatic cancer [27]	IFG/IGT: ADA/WHO	**1.22 (1.11, 1.34)**	5	0	High	⊕⊕
Pancreatic cancer [27]	IFG: ADA	**1.25 (1.12, 1.39)**	3	18	High	⊕⊕
Mental/cognitive disorders						
Depressive symptoms [28]	IFG/IGT/HbA_{1c}: ADA/WHO	1.07 (0.80, 1.43)	4	73	High	⊕
Depressive symptoms [28]	IFG: ADA	0.91 (0.67, 1.23)	2	70	High	⊕
All-cause dementia [9][b]	IFG/IGT: na	**1.18 (1.02, 1.36)**	9	22	High	⊕⊕⊕
All-cause dementia [9][b]	IFG: 5.6-6.9 mmol/L	**1.27 (1.08, 1.49)**	na	0	High	⊕⊕⊕
All-cause dementia [9][b]	IGT: na	**1.40 (1.03, 1.91)**	na	na	High	⊕⊕⊕
Alzheimer's dementia [9][b]	IFG/IGT: na	**1.36 (1.09, 1.70)**	5	14	High	⊕⊕
Vascular dementia [9][b]	IFG/IGT: na	**1.47 (1.01, 2.15)**	3	0	High	⊕⊕
Cognitive impairment [9][b]	IFG/IGT: na	0.96 (0.85, 1.09)	5	0	High	⊕⊕

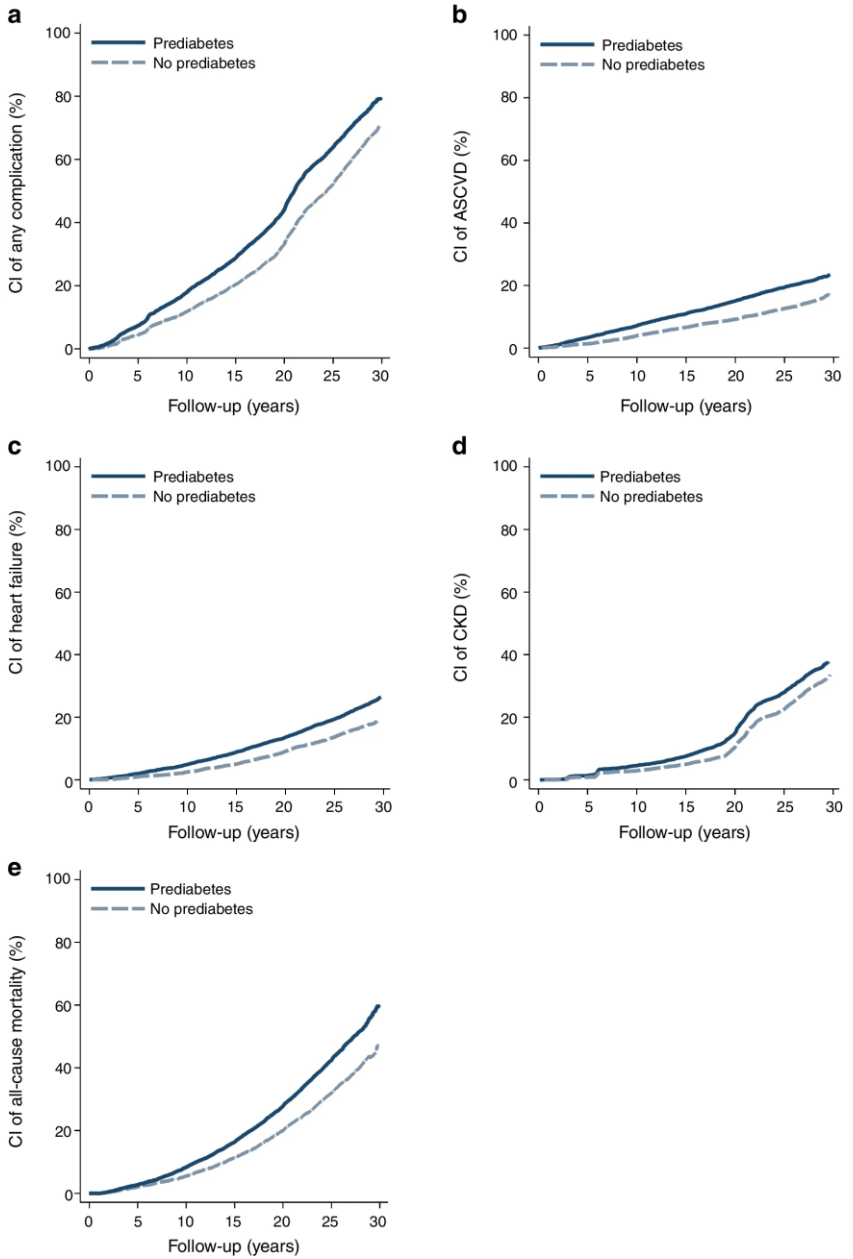
Prediabete = fattore di rischio indipendente per mortalità per tutte le cause, eventi cardiovascolari maggiori e mortalità cardiovascolare e malattia renale cronica.

8–25%

increased risk of all-cause mortality

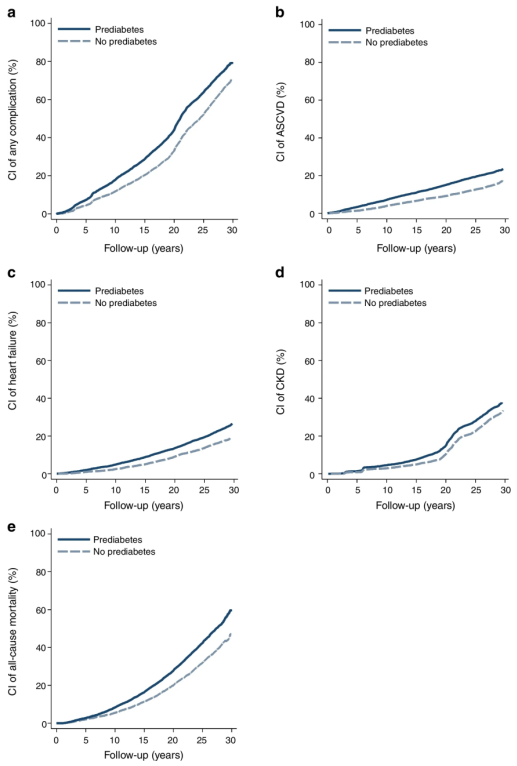
Schlesinger et al. Diabetologia 2022

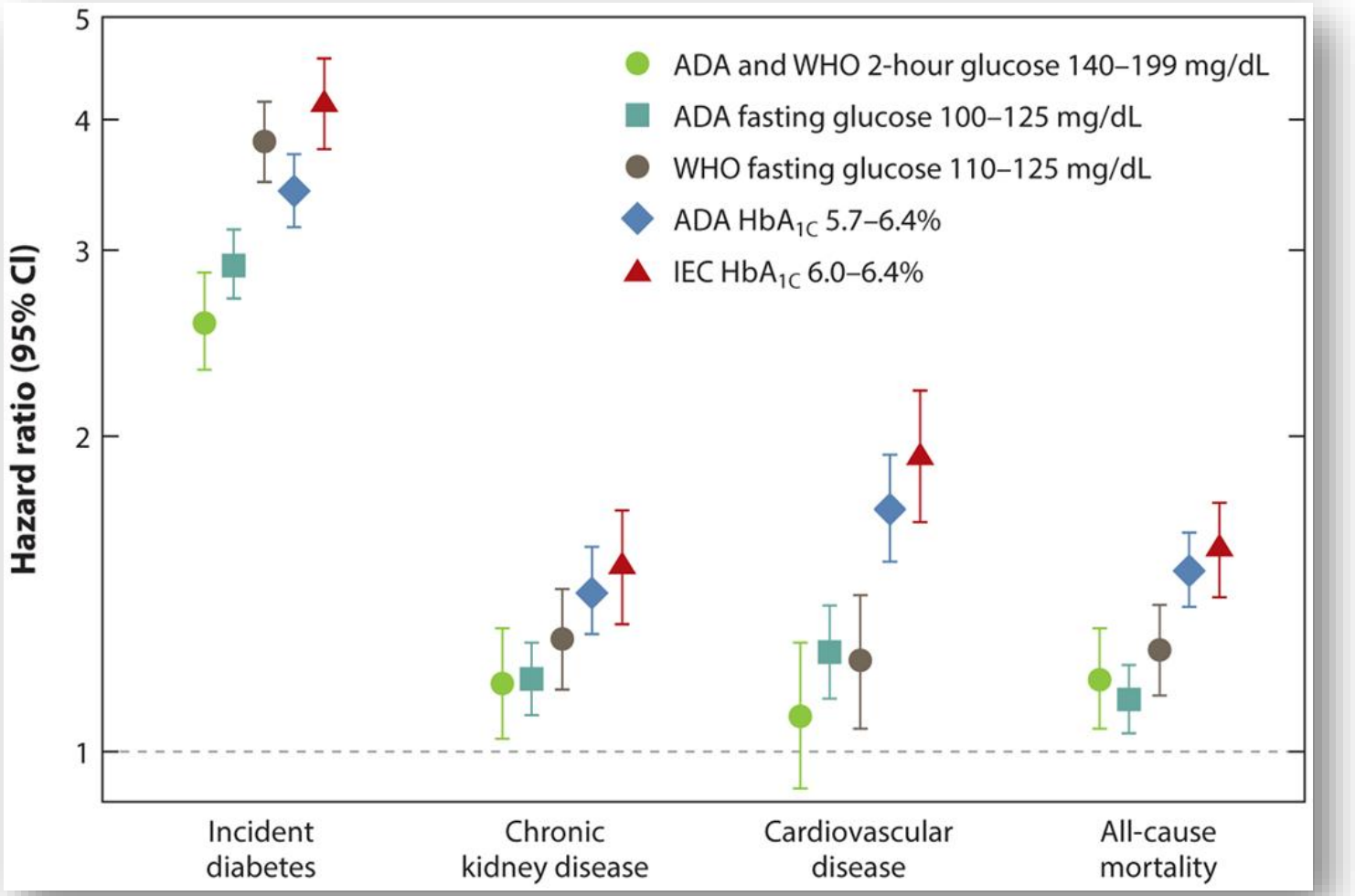
Prediabete e comorbidità



Rooney et al. Diabetologia 2025

Prediabete e comorbidità





Rooney et al. Diabetologia 2025
Echouffo-Tcheugui et al. Prediabetes and What It Means: The Epidemiological Evidence. Annu Rev Public Health. 2021

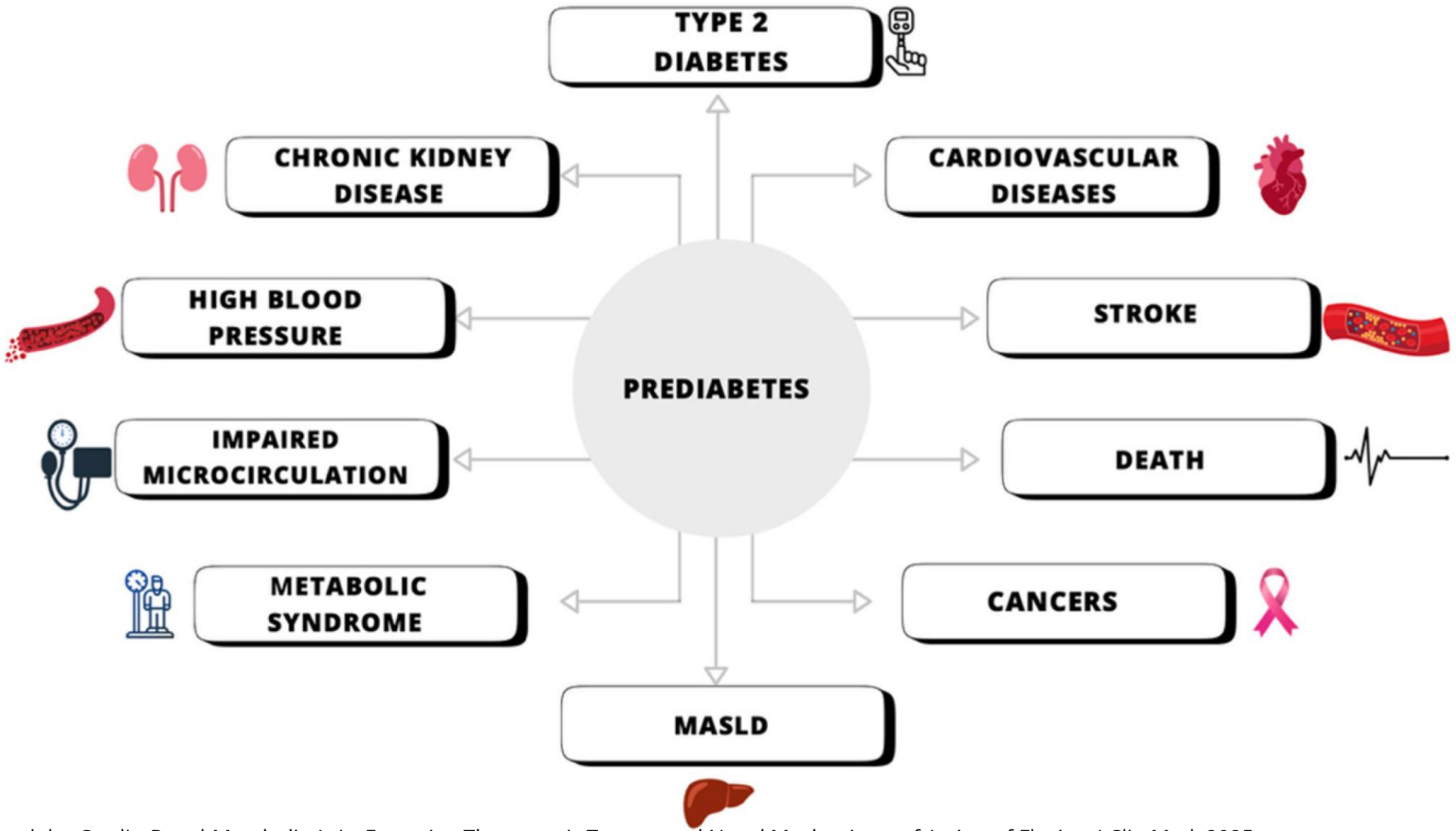
Prediabete

↑ rischio di DM2

↑ rischio cardio-nefro-vascolare

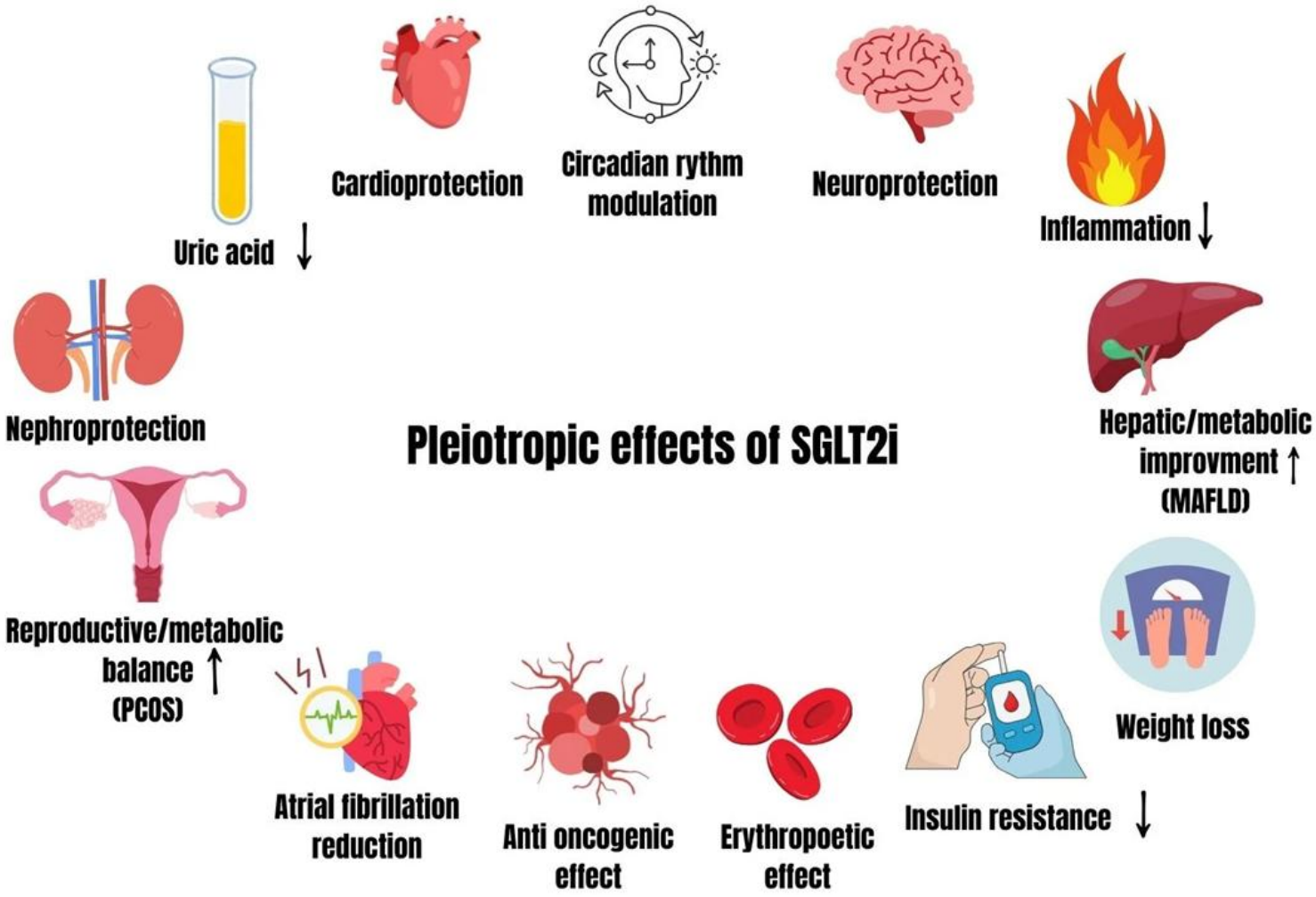
↑ rischio di mortalità

Prediabete



Matuszewski et al. Beyond the Cardio-Renal-Metabolic Axis: Emerging Therapeutic Targets and Novel Mechanisms of Action of Flozins. J Clin Med. 2025

Prediabete



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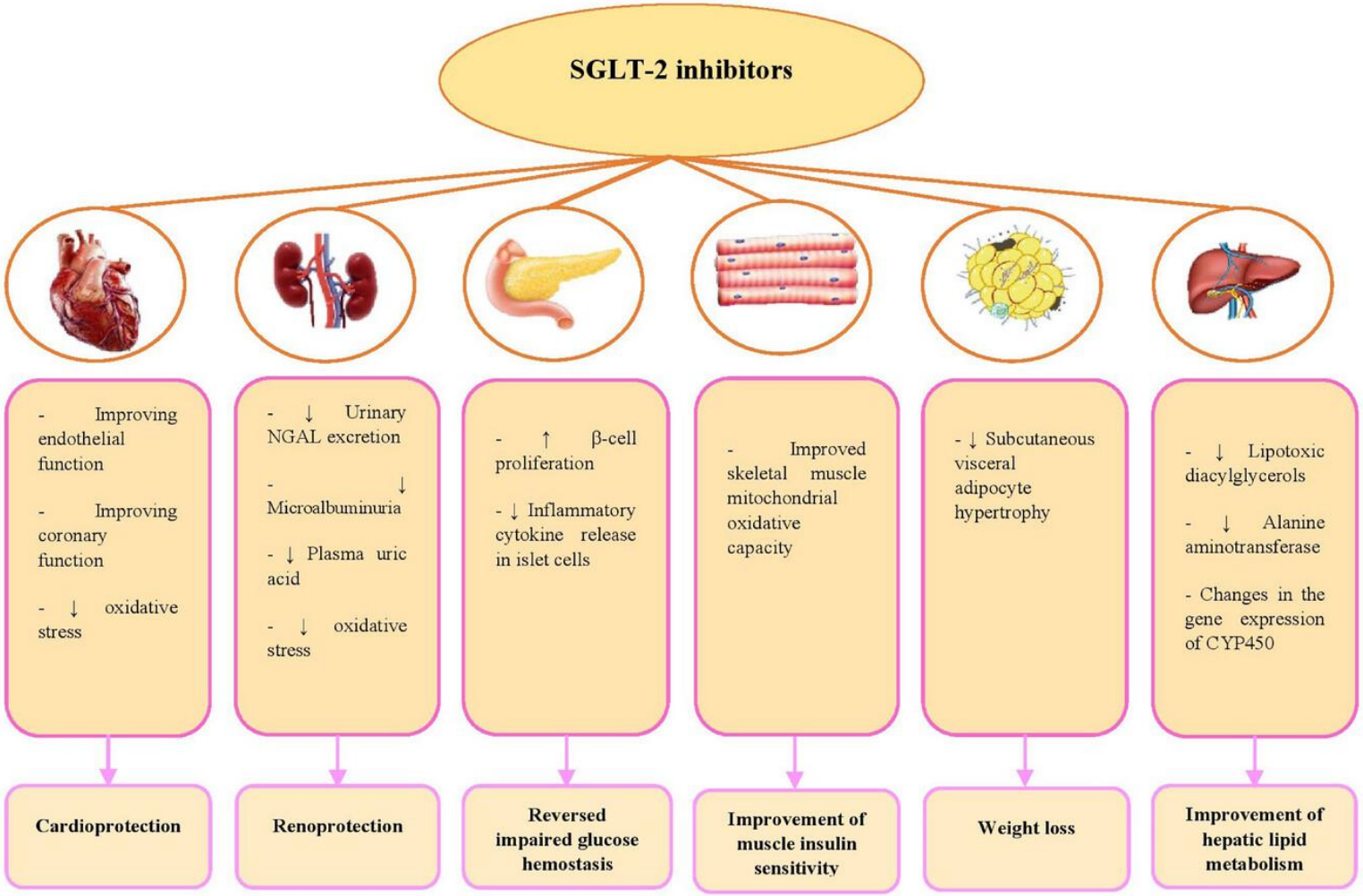
SGLT2i e prediabete



Pourkarim et al. Current Evidence on SGLT-2 Inhibitors in Prediabetes: A Review of Preclinical and Clinical Data. J Clin Pharmacol. 2025

SGLT2i e prediabete

New-onset diabetes with sodium-glucose cotransporter-2 inhibitors in prediabetes: An updated meta-analysis and possible mechanisms

Awadhesh Kumar Singh [a, b, c, *], Akriti Singh [d], Ritu Singh [a, c]

[a] G. D Hospital & Diabetes Institute, Kolkata, West Bengal, India
[b] Sun Valley Hospital & Diabetes Research Center, Guwahati, Assam, India
[c] Horizon Life Line Multispecialty Hospital, Kolkata, West Bengal, India
[d] Jawaharlal Nehru Medical College & Hospital, Kalyani, West Bengal, India

SGLT2i e prediabete

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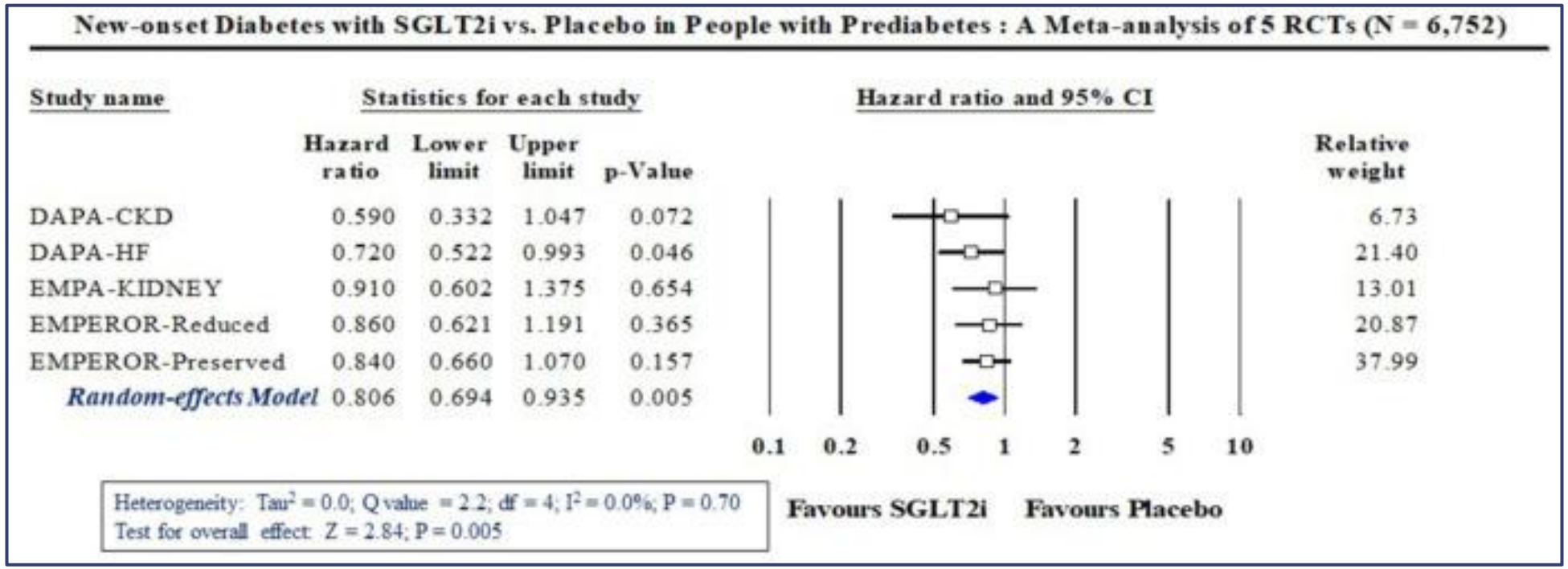

SGLT2i e prediabete

The effects of dapagliflozin, metformin or exercise on glycaemic variability in overweight or obese individuals with prediabetes (the PRE-D Trial): a multi-arm, randomised, controlled trial

Kristine Færch[1] · Martin B. Blond[1] · Lea Bruhn[1] · Hanan Amadid[1] · Dorte Vistisen[1] · Kim K. B. Clemmensen[1] · Camilla T. R. Vainø[1] · Camilla Pedersen[1] · Maria Tvermosegaard[1,2] · Thomas F. Dejgaard[1] · Kristian Karstoft[3] · Mathias Ried-Larsen[3,4] · Frederik Persson[1] · Marit E. Jørgensen[1,2]

120 pazienti inclusi
randomizzazione 1:1:1:1 →

- placebo
- metformina 1700 mg/die
- dapagliflozin 10 mg
- esercizio fisico (30 min/die per 5 gg/sett)

26 settimane di studio

Endpoint primario: variazione del **MAGE**

Table 2 Pairwise comparisons of the change in the primary outcome (MAGE) and other measures of glycaemic variability from baseline to 6, 13 and 26 weeks

Measure	Week 6		Week 13		Week 26	
	Difference	*p* value	Difference	*p* value	Difference	*p* value
MAGE						
DAP vs CON	−16.6 (−30.3, −0.2)	0.047	−17.1 (−30.8, −0.7)	0.042	−18.0 (−31.7, −1.7)	0.032
MET vs CON	−7.6 (−22.4, 10.2)	0.379	0.1 (−16.1, 19.4)	0.991	−9.1 (−23.9, 8.5)	0.291
EXE vs CON	−15.7 (−29.3, 0.6)	0.059	−15.3 (−29.1, 1.2)	0.067	−21.4 (−34.5, −5.7)	0.009
DAP vs MET	−9.8 (−24.5, 7.8)	0.257	−17.2 (−30.9, −0.8)	0.041	−9.8 (−24.6, 7.8)	0.256
EXE vs DAP	1.1 (−15.5, 20.9)	0.903	2.2 (−14.8, 22.5)	0.815	−4.1 (−20.2, 15.1)	0.651
EXE vs MET	−8.8 (−23.4, 8.7)	0.305	−15.4 (−29.1, 1.1)	0.065	−13.6 (−27.7, 3.4)	0.110
SD						
DAP vs CON	−13.3 (−26.2, 1.9)	0.083	−15.8 (−28.4, −0.9)	0.039	−12.1 (−25.4, 3.6)	0.124
MET vs CON	−7.6 (−21.1, 8.2)	0.324	−0.3 (−15.0, 16.8)	0.966	−7.2 (−20.9, 8.9)	0.362
EXE vs CON	−9.6 (−22.9, 6.0)	0.215	−9.1 (−22.5, 6.7)	0.245	−12.5 (−25.7, 3.1)	0.111
DAP vs MET	−6.1 (−20.0, 10.2)	0.438	−15.5 (−28.2, −0.5)	0.043	−5.3 (−19.3, 11.3)	0.509
EXE vs DAP	4.4 (−11.2, 22.5)	0.607	8.0 (−8.3, 27.2)	0.360	−0.5 (−15.6, 17.4)	0.956
EXE vs MET	−2.1 (−16.4, 14.7)	0.794	−8.8 (−22.2, 7.1)	0.262	−5.7 (−19.7, 10.7)	0.474
CV						
DAP vs CON	−10.0 (−22.8, 4.8)	0.176	−13.4 (−25.7, 1.1)	0.068	−11.5 (−24.2, 3.3)	0.121
MET vs CON	−4.6 (−17.9, 10.7)	0.534	−1.2 (−15.0, 14.8)	0.870	−7.3 (−20.3, 7.9)	0.329
EXE vs CON	−8.2 (−21.0, 6.7)	0.267	−6.1 (−19.3, 9.2)	0.414	−11.1 (−23.8, 3.9)	0.139
DAP vs MET	−5.6 (−18.9, 9.8)	0.454	−12.3 (−24.8, 2.3)	0.096	−4.6 (−18.1, 11.1)	0.543
EXE vs DAP	2.0 (−12.4, 18.9)	0.795	8.3 (−7.2, 26.6)	0.310	0.5 (−14.0, 17.5)	0.946
EXE vs MET	−3.7 (−17.1, 11.9)	0.621	−4.9 (−18.3, 10.6)	0.512	−4.1 (−17.6, 11.7)	0.590

Data were $\log_e$-transformed for analysis and back-transformed for presentation. Results are presented as relative changes and were calculated as the ratio of mean (95% CI) change from baseline in one group vs the other in percentage term (i.e. if group A changed 20% between visit 1 and 2 [A2/A1 = 1.2] and group B changed 10% [B2/B1 = 1.1], then the relative change between group A and B is 1.2/1.1 = 9.1%)

CON, control; DAP, dapagliflozin; EXE, exercise; MET, metformin

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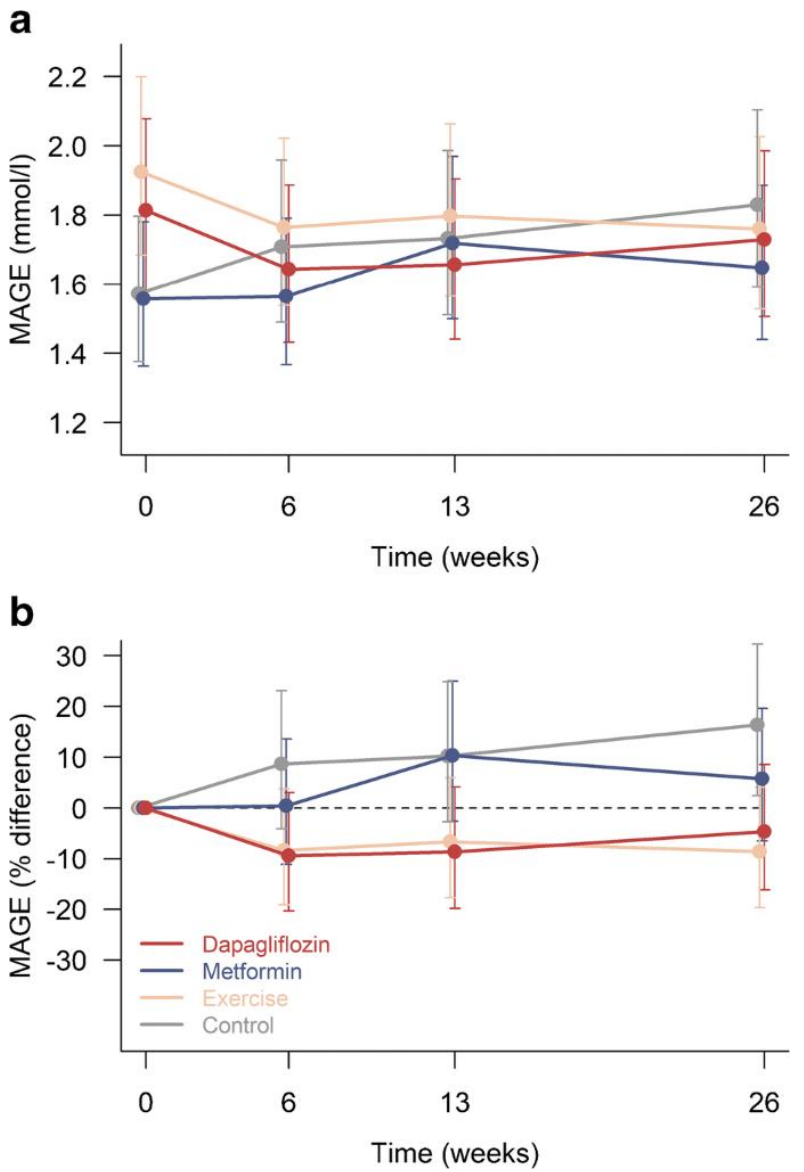

SGLT2i e prediabete

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Pazienti inclusi:
8 con NGT
8 con IFG

→ empagliflozin 25 mg/die per 14 gg

Clamp iperglicemico al:
- Baseline
- Dopo 48 ore
- Dopo 14 giorni

Table 2—Effect of empagliflozin on the FPG concentration and insulin secretion during the stepped hyperglycemic clamp

	NFG	IFG	*P* value
FPG (mg/dL)			
Baseline	95 ± 2 (96)	110 ± 2 (113)	<0.0001
48 h	94 ± 3 (97)	103 ± 3* (102)	0.07
Day 14	100 ± 3 (97)	103 ± 3* (103)	0.06
FP C-peptide (ng/mL)			
Baseline	2.1 ± 0.3 (2.0)	4.0 ± 0.4 (4.1)	0.002
48 h	2.0 ± 0.3 (2.0)	3.7 ± 0.5 (3.4)	0.008
Day 14	2.5 ± 0.4 (2.9)	3.7 ± 0.5 (3.8)	0.02
Fasting FFA (mmol)			
Baseline	0.54 ± 0.07 (0.48)	0.46 ± 0.04 (0.44)	NS
48 h	0.65 ± 0.09 (0.57)	0.62 ± 0.09* (0.61)	NS
Day 14	0.42 ± 0.05 (0.43)	0.49 ± 0.04 (0.46)	NS
ΔC-Pep$_{(0–10)}$ (ng/mL/min)			
Baseline	15 ± 4 (14)	26 ± 5 (18)	NS
48 h	14 ± 4 (13)	34 ± 4 (27)	0.05
Day 14	16 ± 4 (10)	32 ± 4 (30)	NS
ΔC-Pep$_{(10–360)}$ (ng/mL/min)			
Baseline	98 ± 11 (81)	116 ± 10 (94)	NS
48 h	107 ± 11 (105)	141 ± 8* (141)	0.07
Day 14	96 ± 9 (91)	141 ± 8* (138)	<0.05
Slope (C-Pep/PG)			
Baseline	0.10 ± 0.01 (0.08)	0.10 ± 0.01 (0.11)	NS
48 h	0.10 ± 0.01 (0.09)	0.11 ± 0.01 (0.11)	NS
Day 14	0.09 ± 0.01 (0.10)	0.12 ± 0.01 (0.12)	NS
TGU (mg/kg/min)			
Baseline	15.7 ± 1.2 (15.3)	12.4 ± 0.8 (12.2)	0.2
48 h	16.3 ± 1.5 (17.3)	12.8 ± 0.5 (12.9)	0.01
Day 14	16.3 ± 1.2 (17.0)	12.9 ± 0.9 (12.7)	0.02
TGU/MPI			
Baseline	48 ± 10 (49)	17.2 ± 2 (16.3)	0.01
48 h	44 ± 7 (47)	21 ± 3 (20.1)	0.01
Day 14	50 ± 10 (48)	20 ± 3 (17.4)	0.01
IS/IR index			
Baseline	4,324 ± 1,004 (3,854)	1,784 ± 160 (1,879)	<0.05
48 h	4,410 ± 927 (4,138)	2,863 ± 497* (2,898)	NS
Day 14	4,322 ± 810 (3,575)	2,697 ± 391* (2,623)	NS

Data are mean ± SEM (median) unless otherwise indicated. FFA, free fatty acid; FP, fasting plasma. *P < 0.05 versus baseline.

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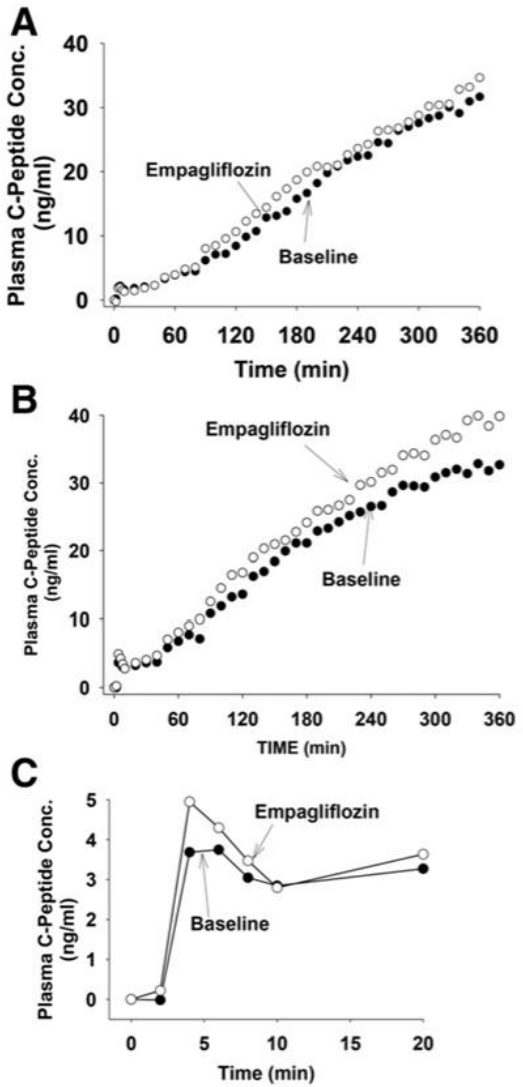

Figure 3—Increment above fasting in plasma C-peptide concentration during the hyperglycemic clamp in subjects with NFG (*A*) and IFG (*B*) at baseline and at 48 h after starting empagliflozin treatment. *C*: First-phase insulin secretion in subjects with IFG before and 48 h after starting empagliflozin.

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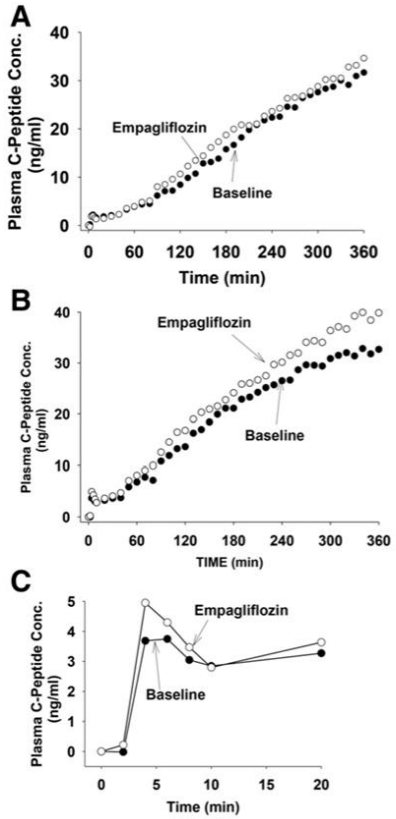

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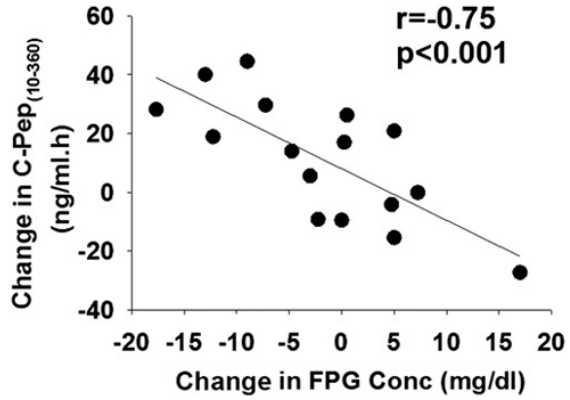

Figure 4—Relationship between the change in $\Delta C\text{-}Pep_{(10-360)}$ 48 h after the start of empagliflozin relative to baseline and the change in the FPG concentration after 48 h of empagliflozin treatment.

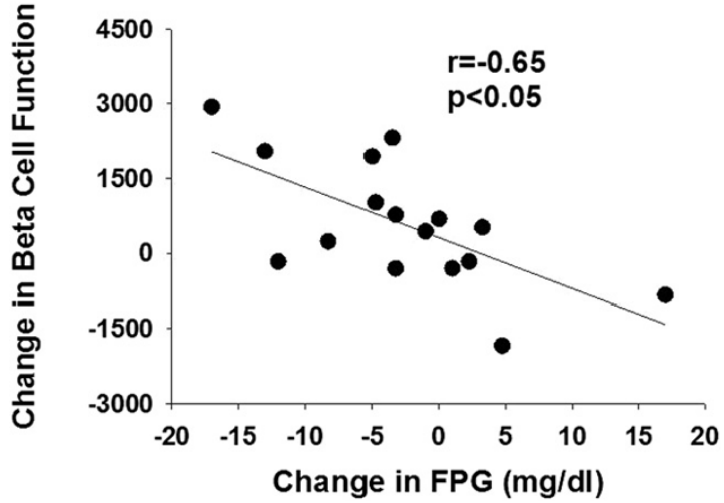

Figure 5—Correlation between the change in β-cell function (IS/IR index) and the change in FPG concentration after 48 h of empagliflozin treatment.

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Day 14	0.42 ± 0.05 (0.43		
ΔC-Pep$_{(0–10)}$ (ng/mL/min)			
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TGU (mg/kg/min)			
Baseline	15.7 ± 1.2 (15.3)	12.4 ± 0.8 (12.2)	0.2
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Day 14	4,322 ± 810 (3,575)	2,697 ± 391* (2,623)	NS

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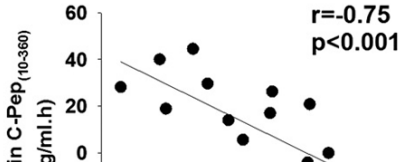


Table 3—Linear regression analysis with the increase in insulin secretion (ΔC-Pep$_{[10–360]}$) and increase in IS/IR index on days 2 and 14 as the dependent variable and the decrease in FPG concentration as the independent variable

Independent variable	Dependent variable	Covariates	Standardized β	*P* value	R^2
ΔFPG$_{(BL→day2)}$	ΔC-Pep$_{(10–360)}$	Age, sex, BMI, FPG	0.26	NS	0.17
ΔFPG$_{(BL→day2)}$	IS/IS index	Age, sex, BMI, FPG	0.52	0.03	0.28
ΔFPG$_{(BL→day14)}$	ΔC-Pep$_{(10–360)}$	Age, sex, BMI, FPG	0.59	0.01	0.13
ΔFPG$_{(BL→day14)}$	IS/IS index	Age, sex, BMI, FPG	0.43	0.05	0.21

BL, baseline.

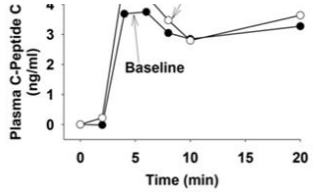


Figure 3—Increment above fasting in plasma C-peptide concentration during the hyperglycemic clamp in subjects with NFG (*A*) and IFG (*B*) at baseline and at 48 h after starting empagliflozin treatment. *C*: First-phase insulin secretion in subjects with IFG before and 48 h after starting empagliflozin.

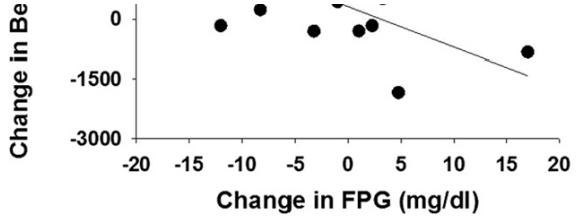
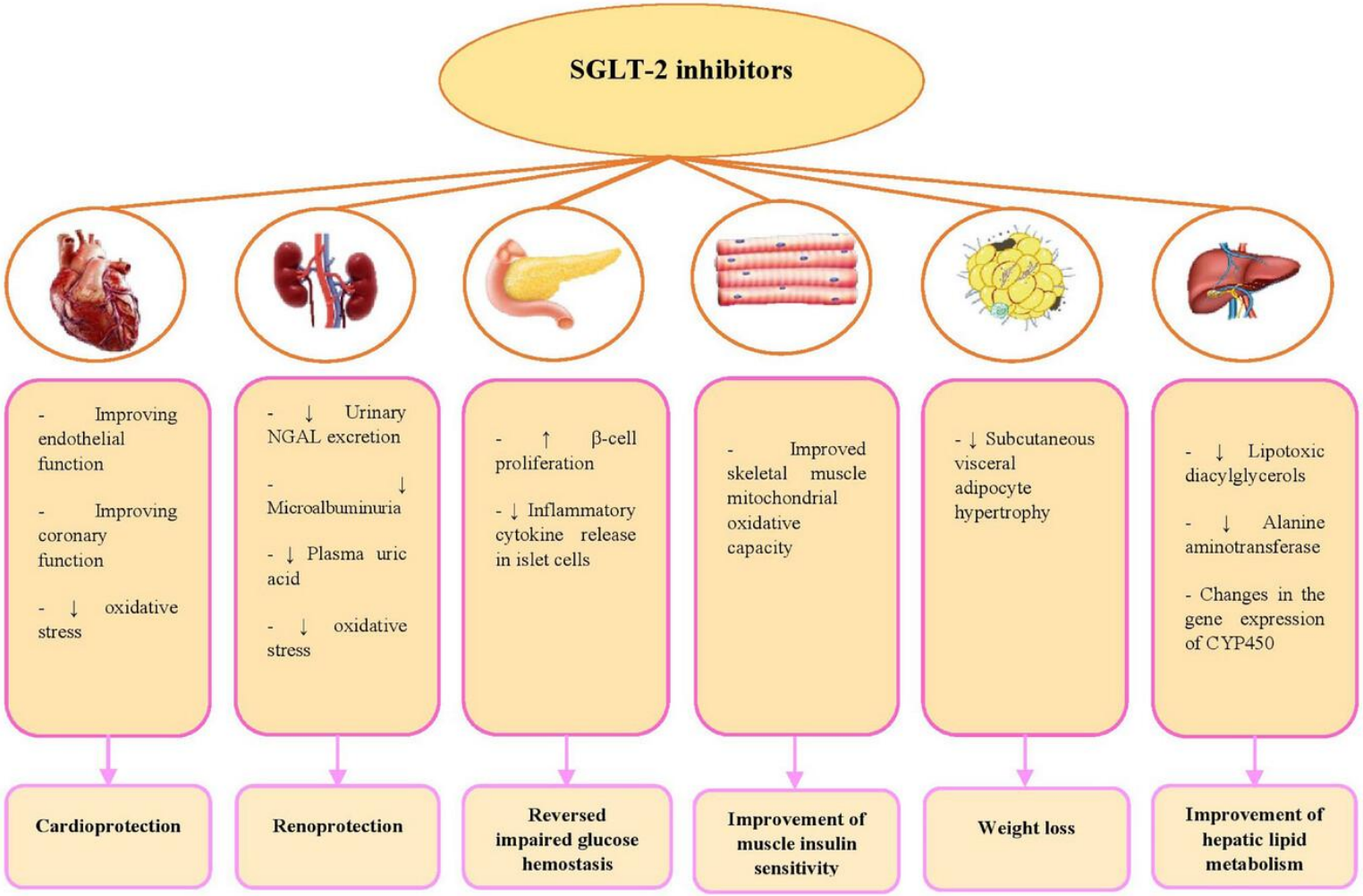
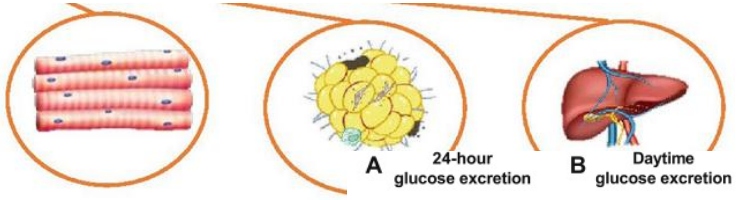


Figure 5—Correlation between the change in β-cell function (IS/IR index) and the change in FPG concentration after 48 h of empagliflozin treatment.

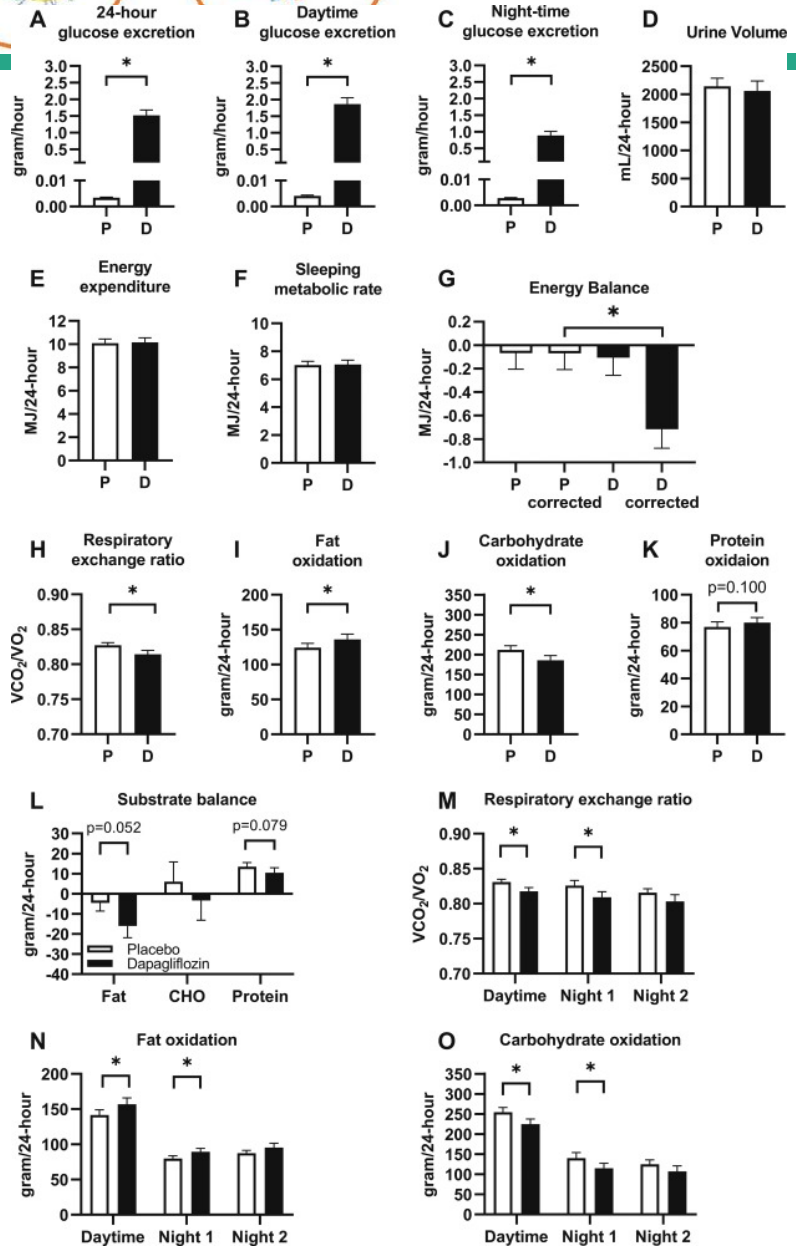
SGLT2i e prediabete



Pourkarim et al. Current Evidence on SGLT-2 Inhibitors in Prediabetes: A Review of Preclinical and Clinical Data. J Clin Pharmacol. 2025



SGLT2i e prediabete



Effects of the sodium-glucose cotransporter 2 inhibitor dapagliflozin on substrate metabolism in prediabetic insulin resistant individuals: A randomized, double-blind crossover trial

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14 pazienti inclusi, randomizzati a:
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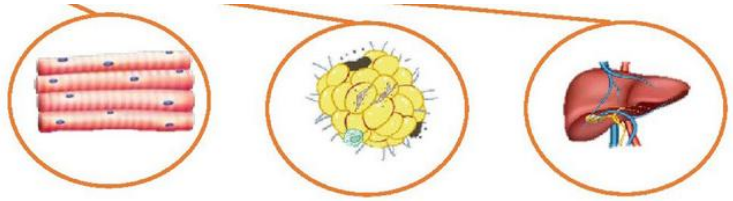
12°-14° valutazione con calorimetria indiretta

Veelen et al. Effects of the sodium-glucose cotransporter 2 inhibitor dapagliflozin on substrate metabolism in prediabetic insulin resistant individuals: A randomized, double-blind crossover trial. Metabolism. 2023



SGLT2i e prediabete

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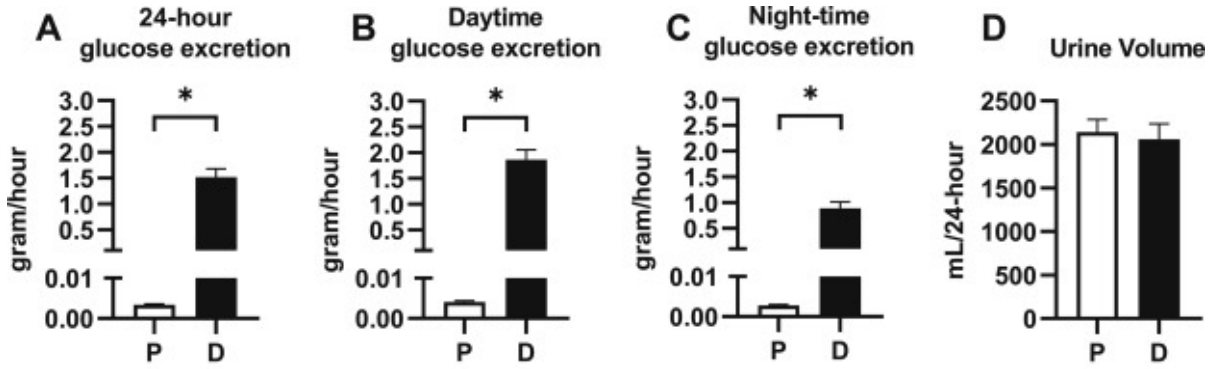

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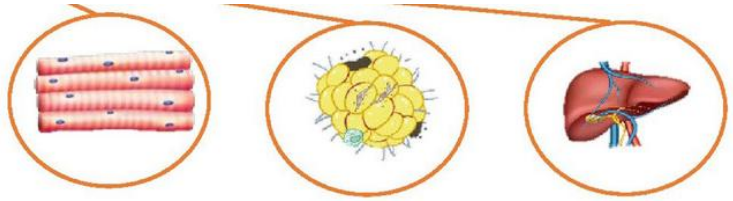

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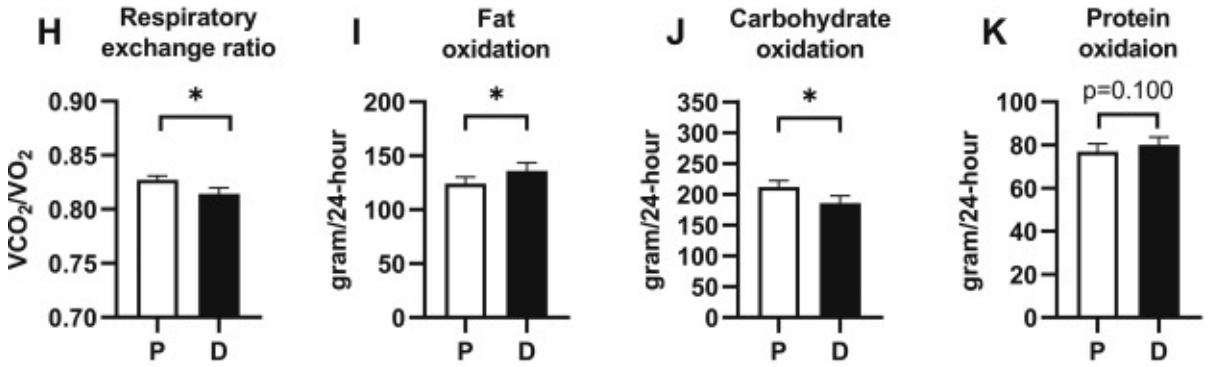

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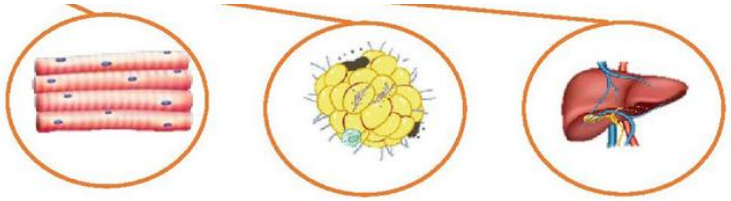
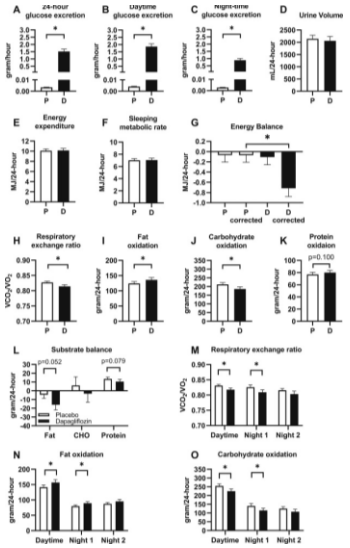
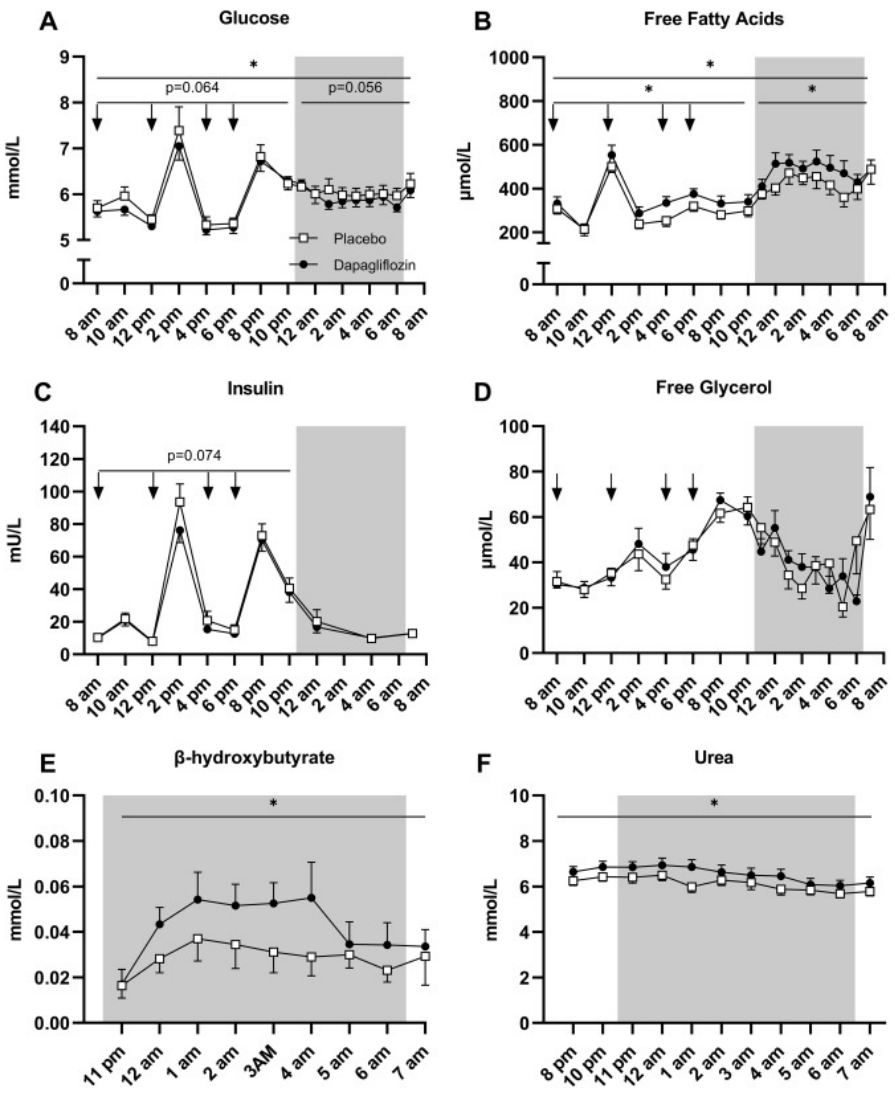


SGLT2i e prediabete





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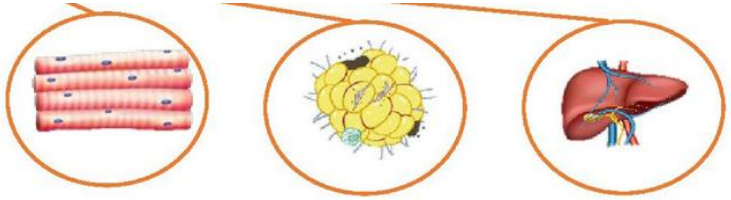
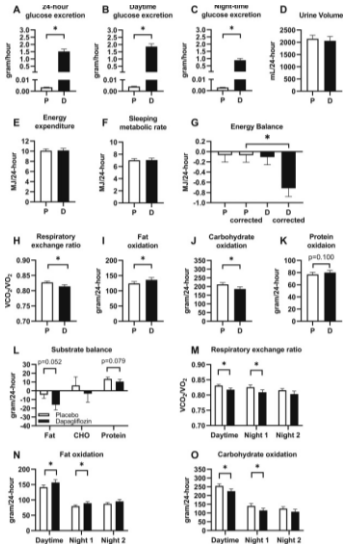
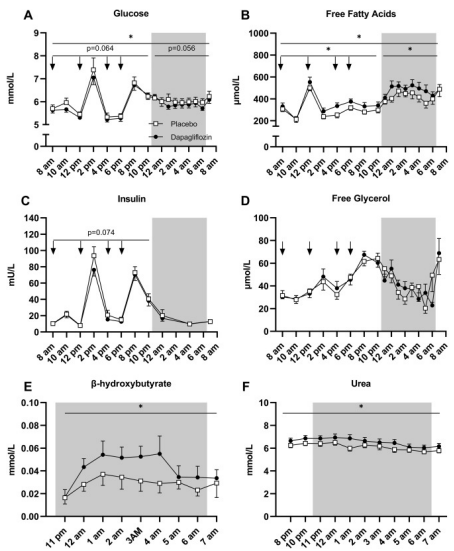


SGLT2i e prediabete





Highlights

- SGLT2i treatment results in beneficial metabolic adaptations in non-diabetic, insulin resistant individuals
- SGLT2i treatment led to lower 24-h glucose levels and higher free fatty acid and ß-hydroxybutyrate levels
- SGLT2i treatment improved skeletal muscle mitochondrial oxidative capacity
- SGLT2i treatment did not significantly affect hepatic glycogen levels, but seemed to affect muscle glycogen levels

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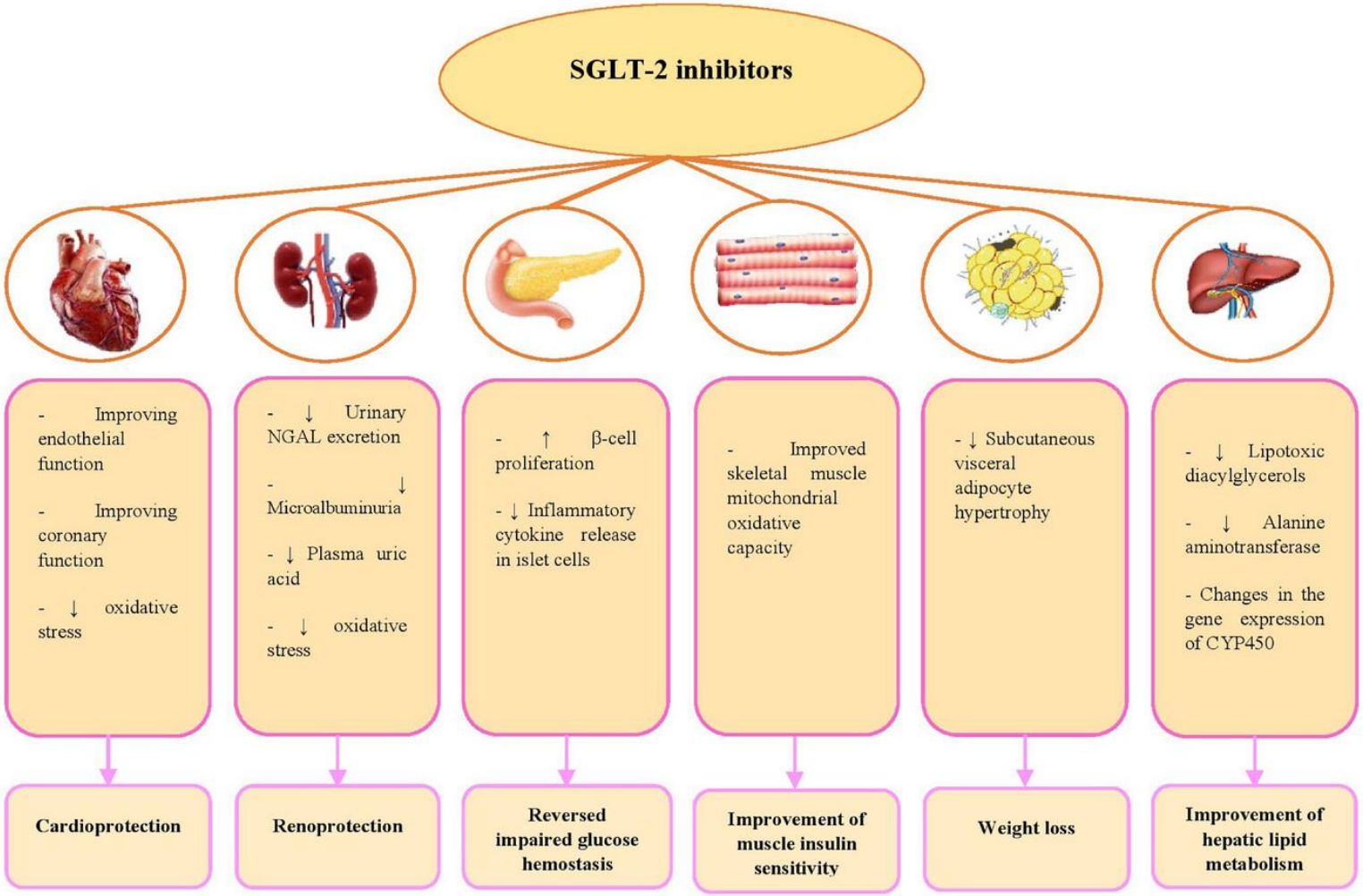
SGLT2i e prediabete



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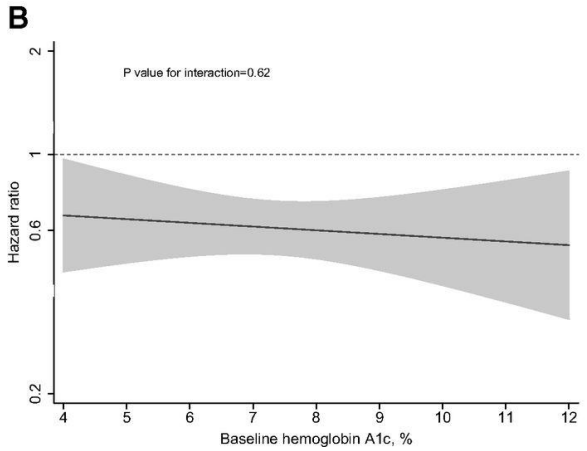
SGLT2i e prediabete

DAPA-CKD

A

	Dapagliflozin n/N	Placebo n/N	Dapagliflozin Events/100 patient-years	Placebo Events/100 patient-years	Hazard Ratio (95% CI)	P Value for Interaction	Absolute Risk Difference, % (95% CI)	P Value for Interaction
Primary outcome: eGFR decline ≥50%, ESKD, or kidney or CV death								
Overall	197/2152	312/2152	4.6	7.5	0.61 (0.51, 0.72)		5.3 (3.4, 7.3)	
Normal glucose	28/368	41/370	4.1	6.1	0.62 (0.39, 1.01)	0.19	3.5 (-0.7, 7.7)	0.42
Pre-diabetes	17/329	42/331	2.6	6.5	0.37 (0.21, 0.66)		7.5 (3.2, 11.8)	
Diabetes	152/1455	229/1451	5.2	8.0	0.64 (0.52, 0.79)		5.3 (2.9, 7.8)	
ESKD								
Overall	109/2152	161/2152	2.5	3.8	0.64 (0.50, 0.82)		2.4 (1.0, 3.9)	
Normal glucose	19/368	32/370	2.8	4.7	0.54 (0.30, 0.95)	0.72	3.5 (-0.2, 7.1)	0.81
Pre-diabetes	13/329	20/331	2.0	3.1	0.57 (0.28, 1.15)		2.1 (-1.2, 5.4)	
Diabetes	77/1455	109/1451	2.6	3.7	0.69 (0.51, 0.92)		2.2 (0.4, 4.0)	
eGFR decline ≥50%								
Overall	112/2152	201/2152	2.6	4.8	0.53 (0.42, 0.67)		4.1 (2.6, 5.7)	
Normal glucose	20/368	31/370	2.9	4.6	0.58 (0.33, 1.01)	0.60	2.9 (-0.7, 6.6)	0.71
Pre-diabetes	13/329	30/331	2.0	4.6	0.39 (0.20, 0.74)		5.1 (1.4, 8.9)	
Diabetes	79/1455	140/1451	2.7	4.9	0.55 (0.42, 0.72)		4.2 (2.3, 6.1)	

B



Persson F, et al. DAPA-CKD Trial Committees and Investigators. Efficacy and Safety of Dapagliflozin by Baseline Glycemic Status: A Prespecified Analysis From the DAPA-CKD Trial. Diabetes Care. 2021

SGLT2i e prediabete

DAPA-CKD

A

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Pre-diabetes	17/329	42/331	2.6	6.5	0.37 (0.21, 0.66)		7.5 (3.2, 11.8)	
Diabetes	152/1455	229/1451	5.2	8.0	0.64 (0.52, 0.79)		5.3 (2.9, 7.8)	
ESKD								
Overall	109/2152	161/2152	2.5	3.8	0.64 (0.50, 0.82)		2.4 (1.0, 3.9)	
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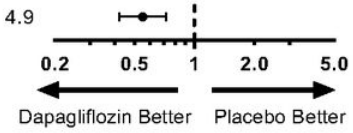
Diabetes	77/1455	109/1451	2.6	3.7	0.69 (0.51, 0.92)		2.2 (0.4, 4.0)	
eGFR decline ≥50%								
Overall	112/2152	201/2152	2.6	4.8	0.53 (0.42, 0.67)		4.1 (2.6, 5.7)	
Normal glucose	20/368	31/370	2.9	4.6	0.58 (0.33, 1.01)	0.60	2.9 (-0.7, 6.6)	0.71
Pre-diabetes	13/329	30/331	2.0	4.6	0.39 (0.20, 0.74)		5.1 (1.4, 8.9)	
Diabetes	79/1455	140/1451	2.7	4.9	0.55 (0.42, 0.72)		4.2 (2.3, 6.1)	



↓ endpoint primario composito

↓ insufficienza renale terminale

↓ decline del eGFR

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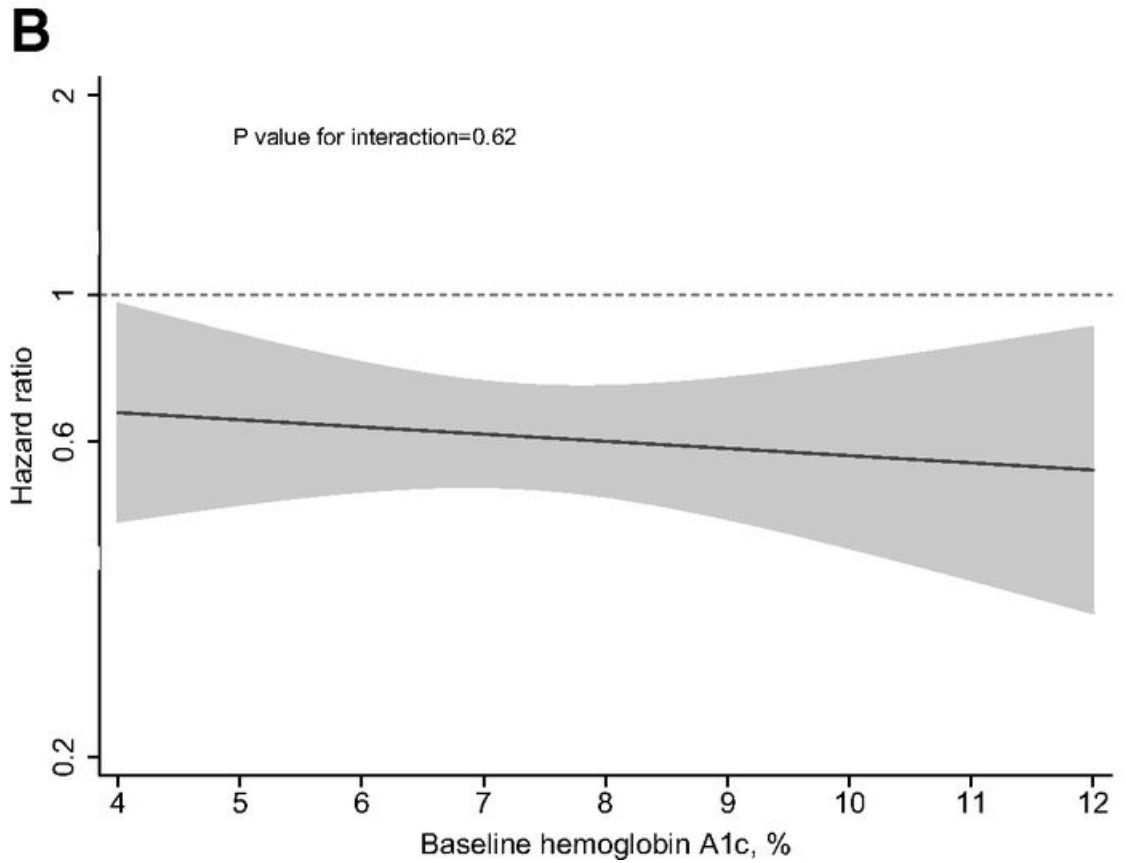
SGLT2i e prediabete

DAPA-CKD

- ↓ endpoint primario composito
- ↓ insufficienza renale terminale
- ↓ decline del eGFR



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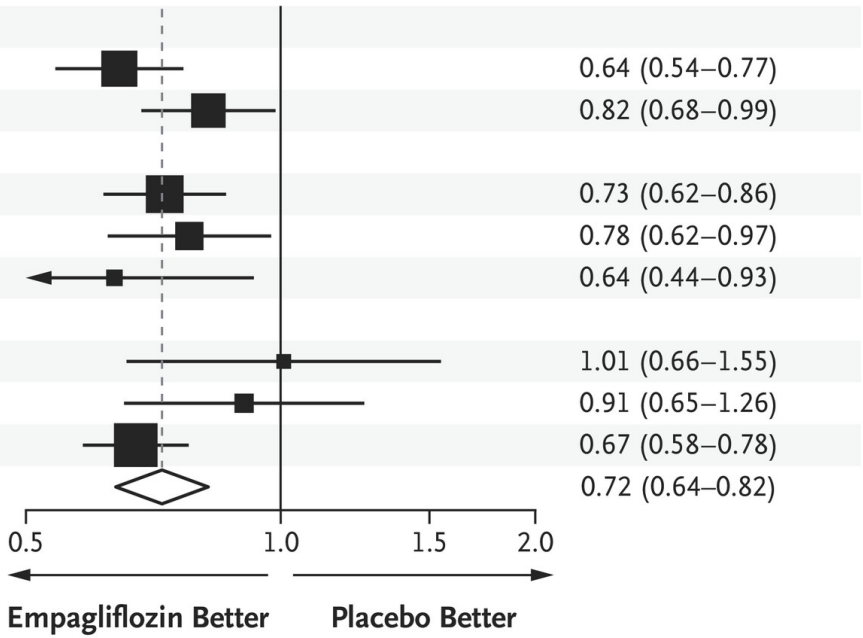
SGLT2i e prediabete

EMPA-KIDNEY

Subgroup	Empagliflozin	Placebo
	no. of patients with event/total no.	
Diabetes mellitus		
Present	218/1525	306/1515
Absent	214/1779	252/1790
Estimated GFR		
<30 ml/min/1.73 m^2	247/1131	317/1151
≥30 to <45 ml/min/1.73 m^2	140/1467	175/1461
≥45 ml/min/1.73 m^2	45/706	66/693
Urinary albumin-to-creatinine ratio		
<30	42/665	42/663
≥30 to ≤300	67/927	78/937
>300	323/1712	438/1705
All patients	432/3304	558/3305



Herrington et al. Empagliflozin in Patients with Chronic Kidney Disease. N Engl J Med. 2023

SGLT2i e prediabete

EMPA-KIDNEY

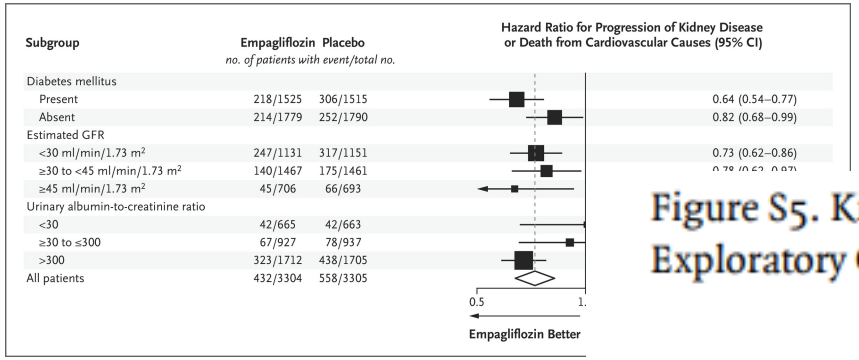
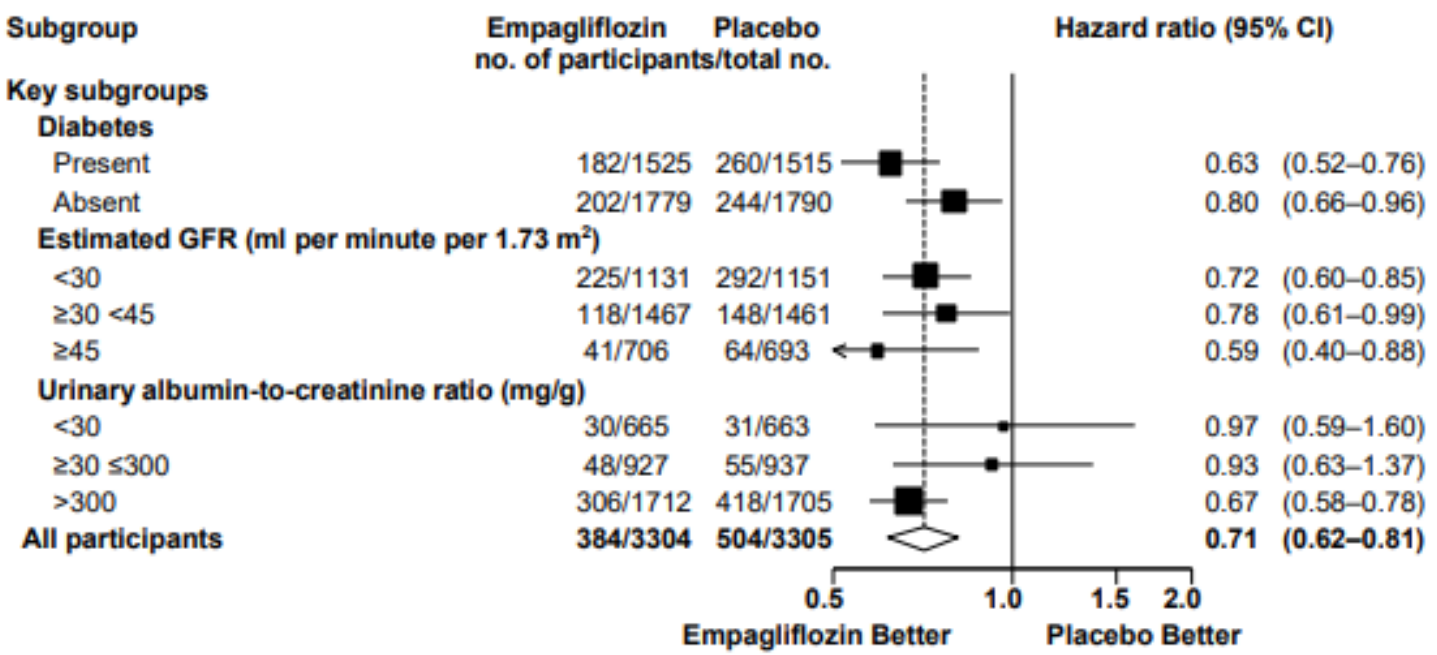
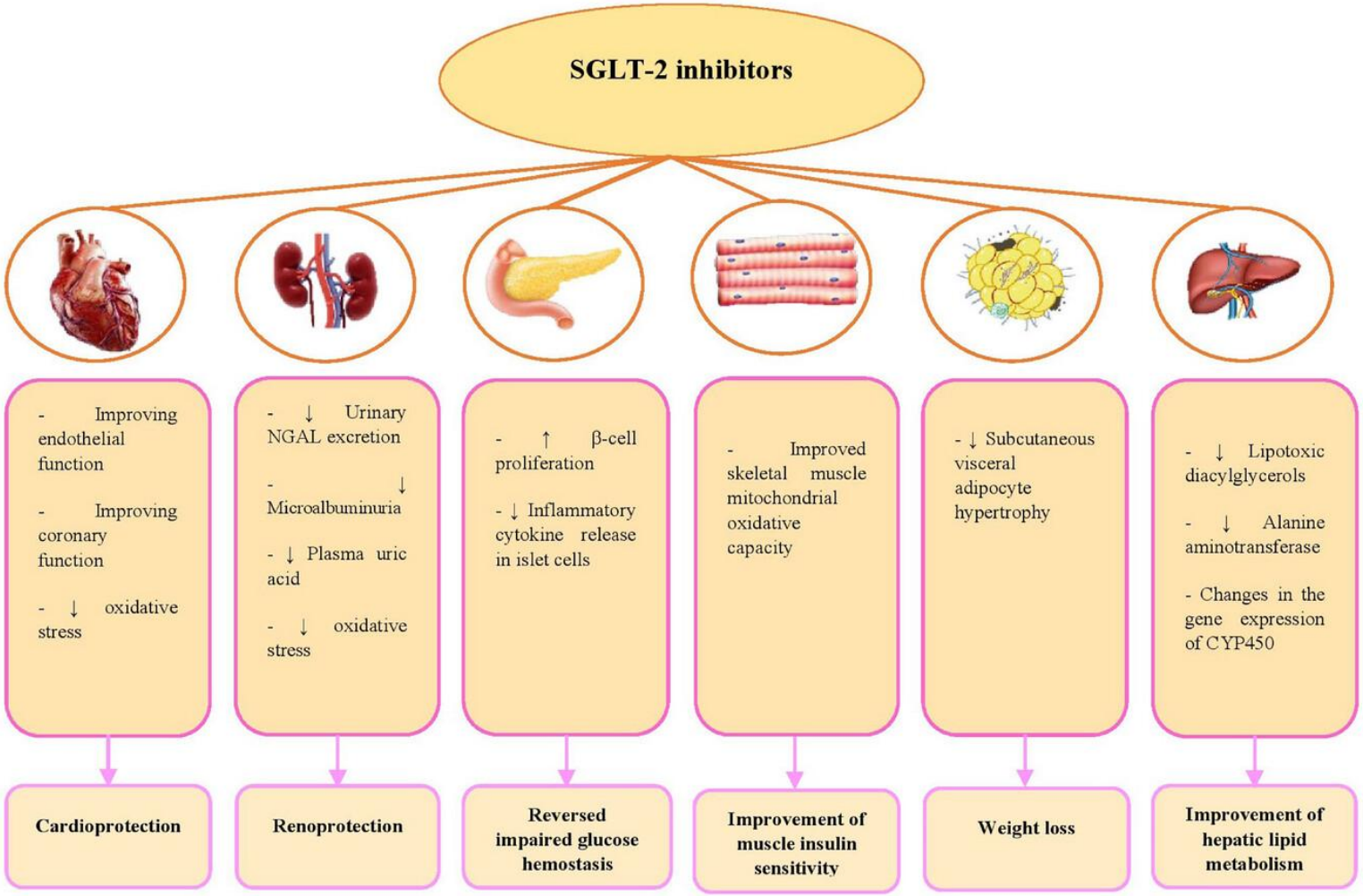


Figure S5. Kidney Disease Progression by Key Prespecified Subgroups (Prespecified Exploratory Outcome)



Herrington et al. Empagliflozin in Patients with Chronic Kidney Disease. N Engl J Med. 2023

SGLT2i e prediabete



Pourkarim et al. Current Evidence on SGLT-2 Inhibitors in Prediabetes: A Review of Preclinical and Clinical Data. J Clin Pharmacol. 2025

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DELIVER

DAPA-HF

Figure 2 (facing page). Primary Outcome in Prespecified Subgroups.

The primary outcome was a composite of worsening heart failure, which was defined as either an unplanned hospitalization for heart failure or an urgent visit for heart failure, or cardiovascular death. Race was reported by the investigators. The body-mass index is the weight in kilograms divided by the square of the height in meters. The size of the boxes is proportional to the number of patients in the subgroup, and arrows on the confidence interval bars indicate that the upper or lower boundary of the confidence interval is off the scale. One patient in the placebo group who had New York Heart Association (NYHA) class I disease at baseline was not included in the analysis of NYHA class at enrollment. ECG denotes electrocardiography, GFR glomerular filtration rate, LVEF left ventricular ejection fraction, and NT-proBNP N-terminal pro–B-type natriuretic peptide.

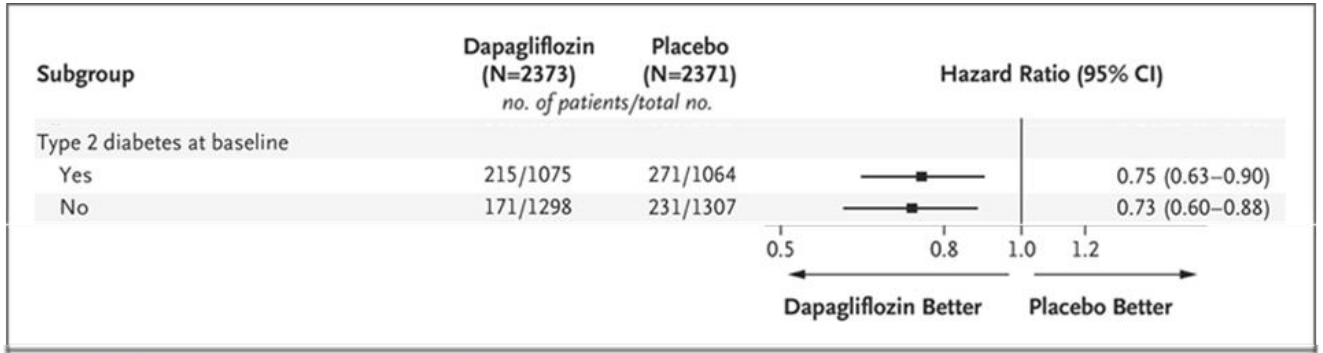
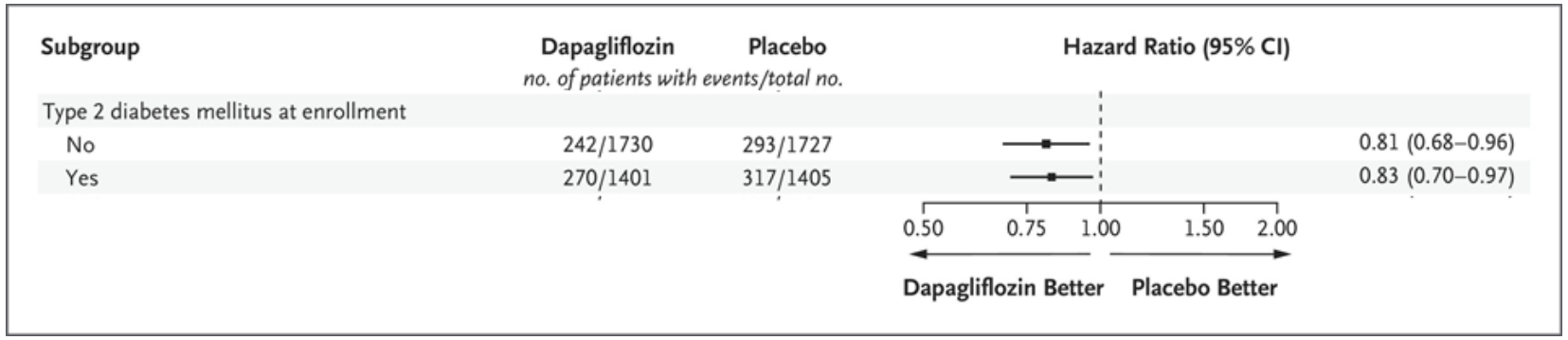


Figure 3. Primary Composite Outcome, According to Prespecified Subgroup.

Shown is the primary outcome of the trial — a composite of hospitalization for heart failure, an urgent visit resulting in intravenous therapy for heart failure, or death from cardiovascular causes — according to subgroups that were prespecified in the protocol. Race was reported by the investigators. The body-mass index is the weight in kilograms divided by the square of the height in meters. ECG denotes electrocardiography, eGFR estimated glomerular filtration rate, LVEF left ventricular ejection fraction, MRA mineralocorticoid receptor antagonist, NT-proBNP N-terminal pro–B-type natriuretic peptide, and NYHA New York Heart Association.



McMurray et al. DAPA-HF Trial Committees and Investigators. Dapagliflozin in Patients with Heart Failure and Reduced Ejection Fraction. N Engl J Med. 2019
Solomon et al. DELIVER Trial Committees and Investigators. Dapagliflozin in Heart Failure with Mildly Reduced or Preserved Ejection Fraction. N Engl J Med. 2022

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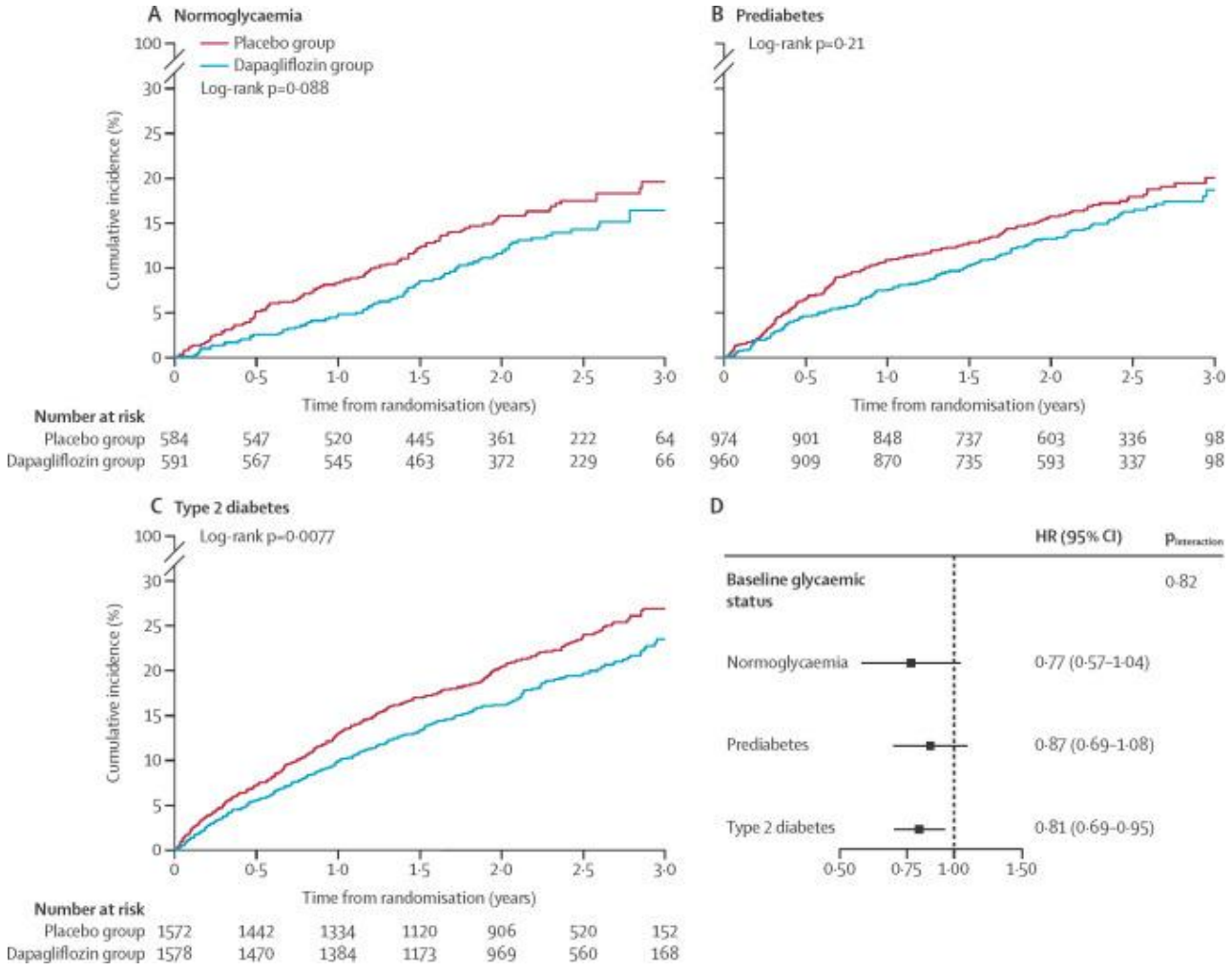

Inzucchi et al. Efficacy and safety of dapagliflozin in patients with heart failure with mildly reduced or preserved ejection fraction by baseline glycaemic status (DELIVER): a subgroup analysis from an international, multicentre, double-blind, randomised, placebo-controlled trial. Lancet Diabetes Endocrinol. 2022

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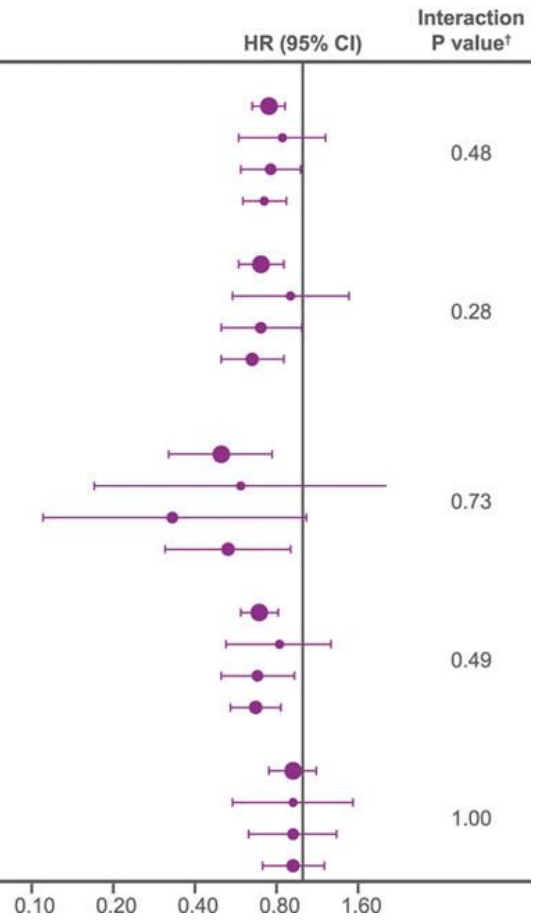
EMPEROR-r

	Empagliflozin (N=1863)			Placebo (N=1867)				Interaction P value†
	n*/N	%	Rate/100 PY	n*/N	%	Rate/100 PY	HR (95% CI)	
Primary outcome - Time to first event of cardiovascular death or HHF								
All patients	361/1863	19.4	15.77	462/1867	24.7	21.00	0.75 (0.65, 0.86)	
Normoglycemia	53/304	17.4	13.88	61/302	20.2	16.55	0.84 (0.58, 1.21)	0.48
Prediabetes	108/632	17.1	13.95	136/636	21.4	18.1	0.76 (0.59, 0.98)	
Diabetes	200/297	21.6	17.66	265/929	28.5	24.55	0.72 (0.60, 0.87)	
Key secondary outcome - First and recurrent HHF								
All patients	388/1863	-	-	553/1867	-	-	0.70 (0.58, 0.85)	
Normoglycemia	57/304	-	-	68/302	-	-	0.90 (0.55, 1.48)	0.28
Prediabetes	110/632	-	-	148/636	-	-	0.70 (0.50, 0.99)	
Diabetes	221/927	-	-	337/929	-	-	0.65 (0.50, 0.85)	
Secondary outcomes								
Time to first renal composite outcome‡								
All patients	30/1863	1.6	1.56	58/1867	3.1	3.07	0.50 (0.32, 0.77)	
Normoglycemia	4/304	1.3	1.29	7/302	2.3	2.20	0.59 (0.17, 2.03)	0.73
Prediabetes	4/632	0.6	0.62	12/636	1.9	1.89	0.33 (0.11, 1.03)	
Diabetes	22/297	2.4	2.30	39/929	4.2	4.17	0.53 (0.31, 0.90)	
First HHF								
All patients	246/1863	13.2	10.75	342/1867	18.3	15.55	0.69 (0.59, 0.81)	
Normoglycemia	36/304	11.8	9.43	43/302	14.2	11.66	0.82 (0.52, 1.27)	0.49
Prediabetes	70/632	11.1	9.04	98/636	15.4	13.04	0.68 (0.50, 0.93)	
Diabetes	140/927	15.1	12.36	201/929	21.6	18.62	0.67 (0.54, 0.83)	
Time to cardiovascular death								
All patients	187/1863	10.0	7.55	202/1867	10.8	8.13	0.92 (0.75, 1.12)	
Normoglycemia	29/304	9.5	7.10	30/302	9.9	7.46	0.92 (0.55, 1.53)	1.00
Prediabetes	54/632	8.5	6.49	59/636	9.3	7.08	0.92 (0.63, 1.33)	
Diabetes	104/297	11.2	8.42	113/929	12.2	9.06	0.92 (0.71, 1.20)	



Anker et al. Effect of Empagliflozin on Cardiovascular and Renal Outcomes in Patients With Heart Failure by Baseline Diabetes Status: Results From the EMPEROR-Reduced Trial. Circulation. 2021

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EMPEROR-r

	Empagliflozin (N=1863)			Placebo (N=1867)				Interaction P value‡
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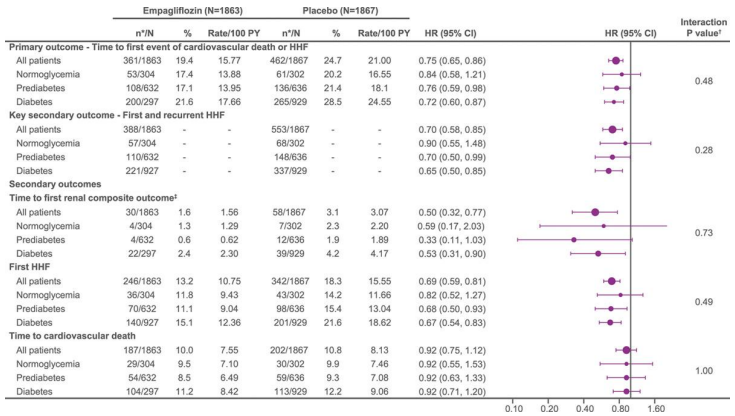

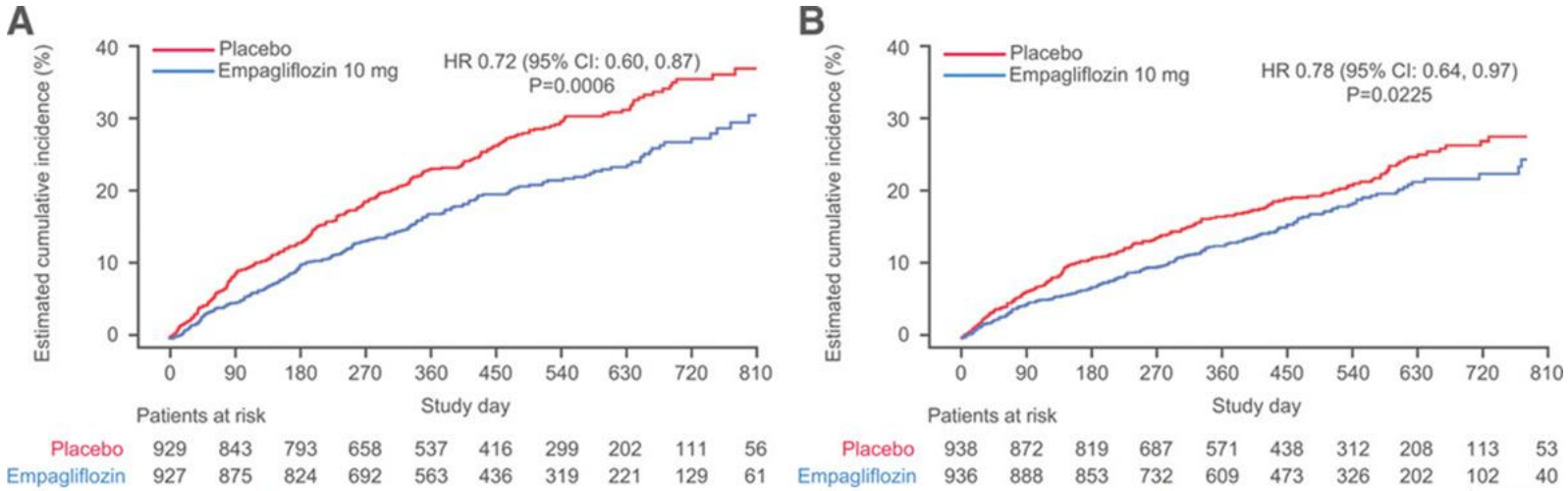

Figure 1. Effect of empagliflozin on the primary end point of EMPEROR-Reduced (Empagliflozin Outcome Trial in Patients With Chronic Heart Failure With Reduced Ejection Fraction). Time to first event of either cardiovascular death or heart failure hospitalization in (**A**) patients with diabetes and (**B**) patients without diabetes. HR indicates hazard ratio.

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EMPEROR-r

	Empagliflozin (N=1863)			Placebo (N=1867)				Interaction P value[†]
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Time to first renal composite outcome[‡]								
All patients	30/1863	1.6	1.56	58/1867	3.1	3.07	0.50 (0.32, 0.77)	
Normoglycemia	4/304	1.3	1.29	7/302	2.3	2.20	0.59 (0.17, 2.03)	0.73
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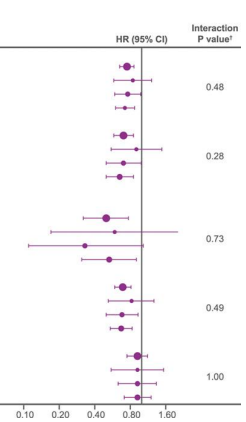


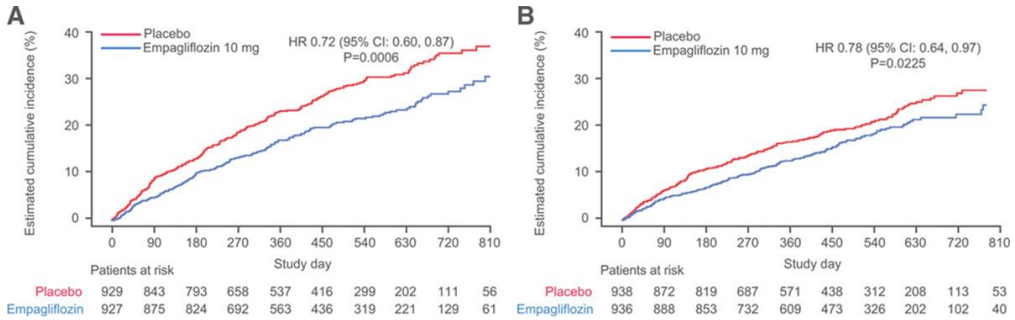
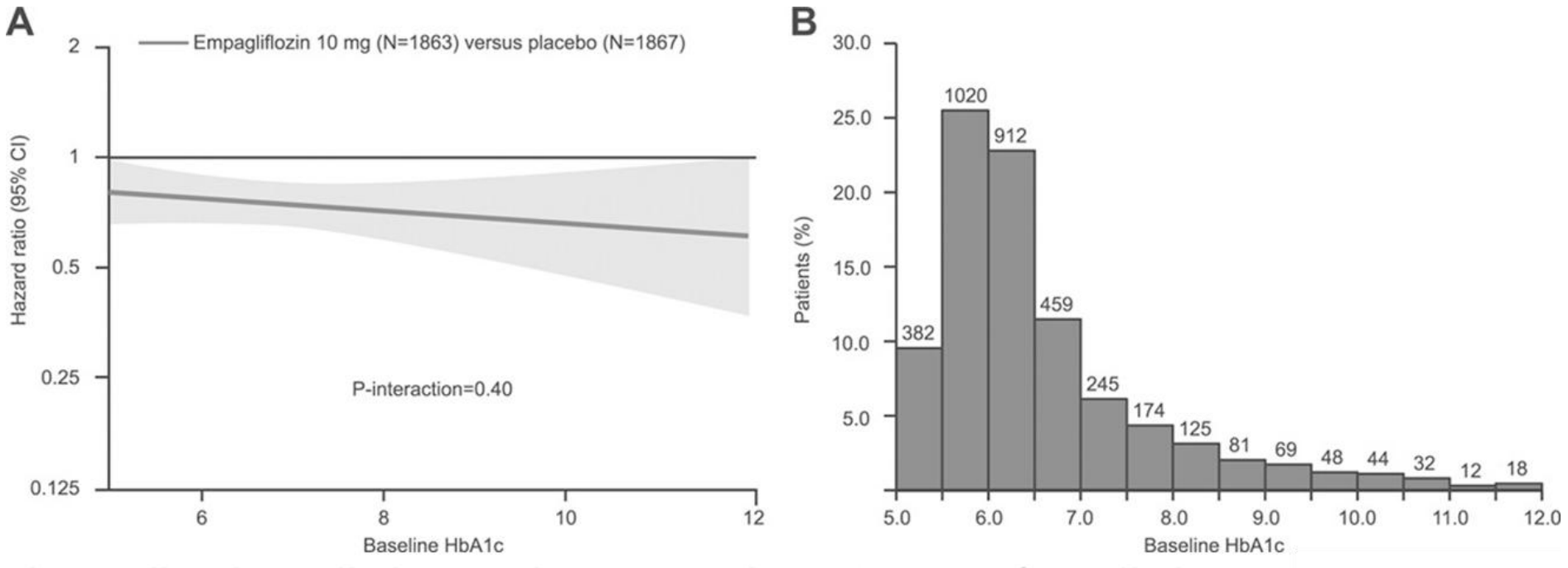


Figure 1. Effect of empagliflozin on the primary end point of EMPEROR-Reduced (Empagliflozin Outcome Trial in Patients With Chronic Heart Failure With Reduced Ejection Fraction). Time to first event of either cardiovascular death or heart failure hospitalization in (**A**) patients with diabetes and (**B**) patients without diabetes. HR indicates hazard ratio.



Anker et al. Effect of Empagliflozin on Cardiovascular and Renal Outcomes in Patients With Heart Failure by Baseline Diabetes Status: Results From the EMPEROR-Reduced Trial. Circulation. 2021

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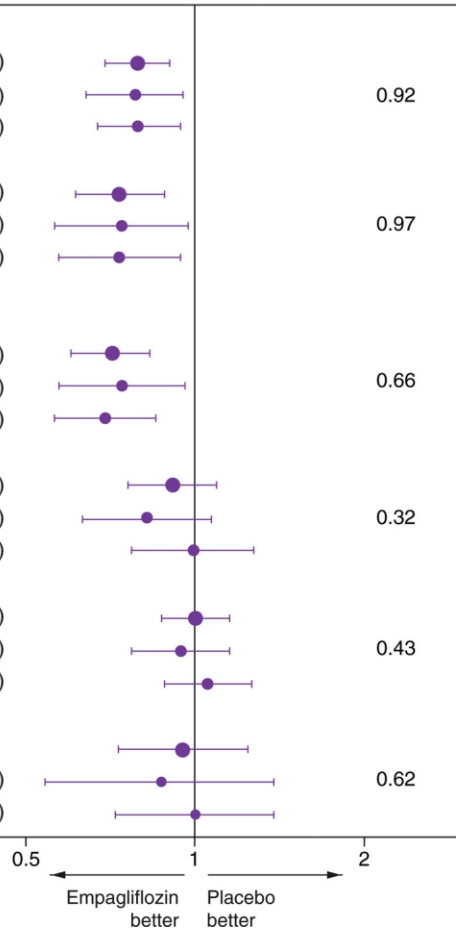
EMPEROR-p

	Empagliflozin (N=2997)			Placebo (N=2991)				Interaction
	n/N	%	Rate/100 PY	n/N	%	Rate/100 PY	HR (95% CI)	P value
Primary outcome: Time to first event of CV death or HHF								
All patients	415/2997	13.8	6.86	511/2991	17.1	8.67	0.79 (0.69, 0.90)	
No diabetes	176/1531	11.5	5.56	220/1519	14.5	7.21	0.78 (0.64, 0.95)	0.92
Diabetes	239/1466	16.3	8.30	291/1472	19.8	10.25	0.79 (0.67, 0.94)	
Key secondary outcome: First and recurrent HHF*								
All patients	407/2997	–	6.46	541/2991	–	8.60	0.73 (0.61, 0.88)	
No diabetes	157/1531	–	4.83	206/1519	–	6.44	0.74 (0.56, 0.97)	0.97
Diabetes	250/1466	–	8.19	335/1472	–	10.82	0.73 (0.57, 0.94)	
Secondary outcomes								
Time to first HHF								
All patients	259/2997	8.6	4.28	352/2991	11.8	5.97	0.71 (0.60, 0.83)	
No diabetes	104/1531	6.8	3.29	137/1519	9.0	4.49	0.74 (0.57, 0.96)	0.66
Diabetes	155/1466	10.6	5.38	215/1472	14.6	7.57	0.69 (0.56, 0.85)	
Time to CV death								
All patients	219/2997	7.3	3.42	244/2991	8.2	3.81	0.91 (0.76, 1.09)	
No diabetes	99/1531	6.5	3.00	121/1519	8.0	3.74	0.82 (0.63, 1.07)	0.32
Diabetes	120/1466	8.2	3.87	123/1472	8.4	3.89	0.99 (0.77, 1.27)	
Time to all-cause mortality								
All patients	422/2997	14.1	6.60	427/2991	14.3	6.67	1.00 (0.87, 1.15)	
No diabetes	188/1531	12.3	5.71	201/1519	13.2	6.21	0.94 (0.77, 1.15)	0.43
Diabetes	234/1466	16.0	7.54	226/1472	15.4	7.14	1.05 (0.88, 1.26)	
Composite renal end point†								
All patients	108/2997	3.6	2.13	112/2991	3.7	2.23	0.95 (0.73,1.24)	
No diabetes	33/1531	2.2	1.24	38/1519	2.5	1.47	0.87 (0.54, 1.38)	0.62
Diabetes	75/1466	5.1	3.09	74/1472	5.0	3.04	1.00 (0.72, 1.38)	



Filippatos et al. EMPEROR-Preserved Trial Committees and Investigators. Empagliflozin for Heart Failure With Preserved Left Ventricular Ejection Fraction With and Without Diabetes. Circulation. 2022

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EMPEROR-p

	Empagliflozin (N=2997)			Placebo (N=2991)				Interaction
	n/N	%	Rate/100 PY	n/N	%	Rate/100 PY	HR (95% CI)	P value
Primary outcome: Time to first event of CV death or HHF								
All patients	415/2997	13.8	6.86	511/2991	17.1	8.67	0.79 (0.69, 0.90)	
No diabetes	176/1531	11.5	5.56	220/1519	14.5	7.21	0.78 (0.64, 0.95)	0.92
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Key secondary outcome: First and recurrent HHF*								
All patients	407/2997	–	6.46	541/2991	–	8.60	0.73 (0.61, 0.88)	
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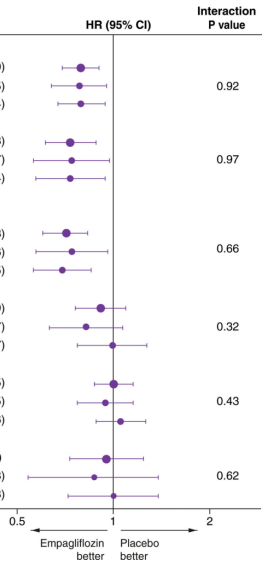

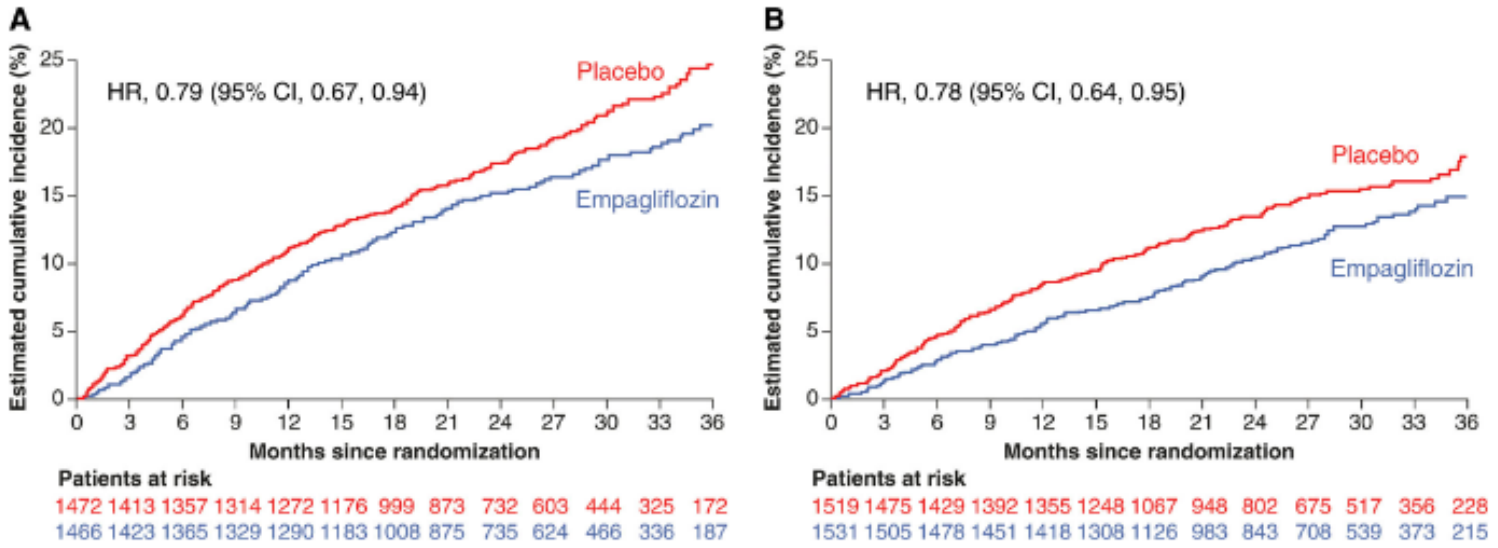

Figure 2. Effect of empagliflozin vs placebo on the primary end point of cardiovascular death or first hospitalization for heart failure in patients with and without diabetes. Effect of empagliflozin vs placebo on the primary end point of cardiovascular death or first hospitalization for heart failure in (**A**) patients with diabetes at baseline and (**B**) patients without diabetes. HR indicates hazard ratio.

Filippatos et al. EMPEROR-Preserved Trial Committees and Investigators. Empagliflozin for Heart Failure With Preserved Left Ventricular Ejection Fraction With and Without Diabetes. Circulation. 2022

SGLT2i e prediabete

EMPEROR-p

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All patients	259/2997	8.6	4.28	352/2991	11.8	5.97	0.71 (0.60, 0.83)	
No diabetes	104/1531	6.8	3.29	137/1519	9.0	4.49	0.74 (0.57, 0.96)	0.66
Diabetes	155/1466	10.6	5.38	215/1472	14.6	7.57	0.69 (0.56, 0.85)	
Time to CV death								
All patients	219/2997	7.3	3.42	244/2991	8.2	3.81	0.91 (0.76, 1.09)	
No diabetes	99/1531	6.5	3.00	121/1519	8.0	3.74	0.82 (0.63, 1.07)	0.32
Diabetes	120/1466	8.2	3.87	123/1472	8.4	3.89	0.99 (0.77, 1.27)	
Time to all-cause mortality								
All patients	422/2997	14.1	6.60	427/2991	14.3	6.67	1.00 (0.87, 1.15)	
No diabetes	188/1531	12.3	5.71	201/1519	13.2	6.21	0.94 (0.77, 1.15)	0.43
Diabetes	234/1466	16.0	7.54	226/1472	15.4	7.14	1.05 (0.88, 1.26)	
Composite renal end point†								
All patients	108/2997	3.6	2.13	112/2991	3.7	2.23	0.95 (0.73,1.24)	
No diabetes	33/1531	2.2	1.24	38/1519	2.5	1.47	0.87 (0.54, 1.38)	0.62
Diabetes	75/1466	5.1	3.09	74/1472	5.0	3.04	1.00 (0.72, 1.38)	

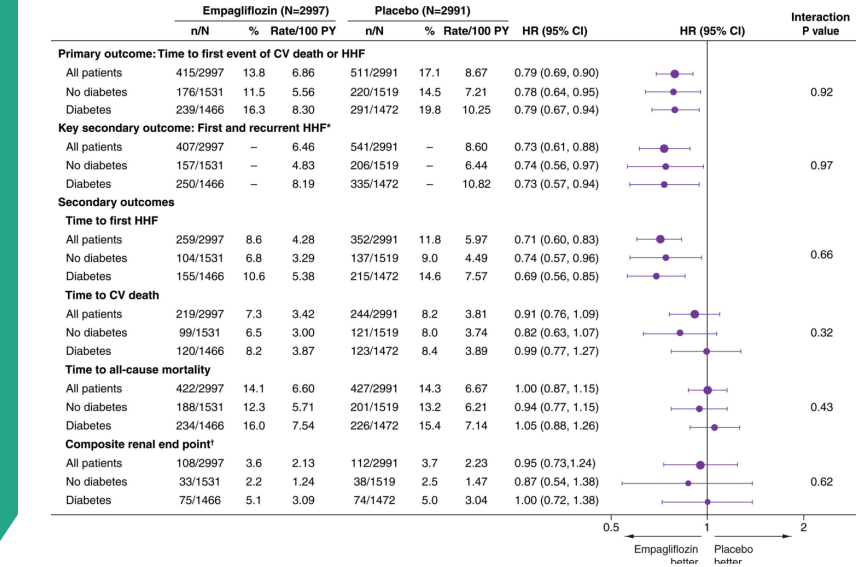
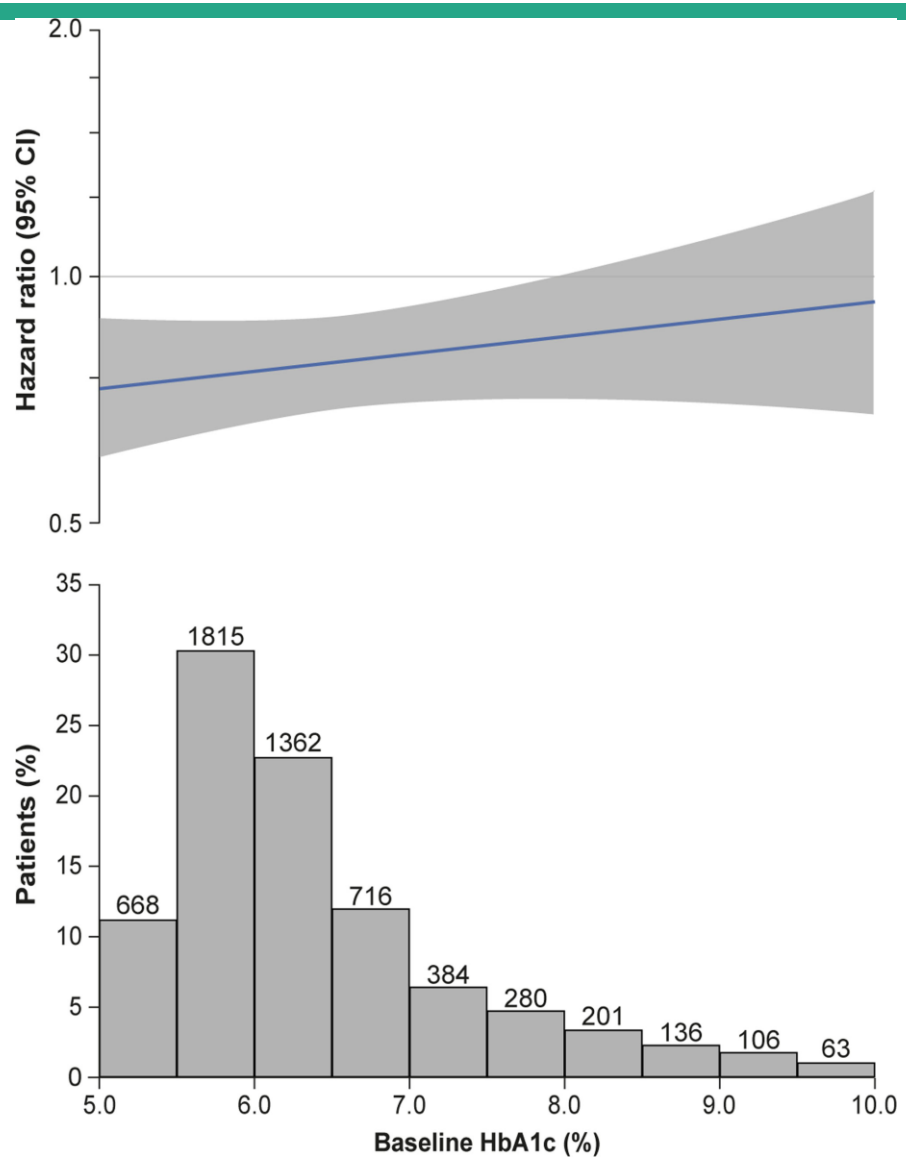


Figure 2. Effect of empagliflozin vs placebo on the primary end point of cardiovascular death or first hospitalization for heart failure in patients with and without diabetes. Effect of empagliflozin vs placebo on the primary end point of cardiovascular death or first hospitalization for heart failure in (**A**) patients with diabetes at baseline and (**B**) patients without diabetes. HR indicates hazard ratio.



Filippatos et al. EMPEROR-Preserved Trial Committees and Investigators. Empagliflozin for Heart Failure With Preserved Left Ventricular Ejection Fraction With and Without Diabetes. Circulation. 2022

Prediabete

Prediabete

3. Prevention or Delay of Diabetes and Associated Comorbidities: Standards of Care in Diabetes—2026

*American Diabetes Association Professional Practice Committee for Diabetes**

Diabetes Care 2026;49(Suppl. 1):S50–S60 | https://doi.org/10.2337/dc26-S003

PHARMACOLOGIC INTERVENTIONS TO DELAY TYPE 2 DIABETES

Recommendations

3.7 Metformin for the prevention of type 2 diabetes should be considered in adults at high risk of type 2 diabetes, as typified by the Diabetes Prevention Program, especially those aged 25–59 years with BMI ≥35 kg/m^2, higher fasting plasma glucose (e.g., ≥110 mg/dL [≥6 mmol/L]), and higher A1C (e.g., ≥6.0% [≥42 mmol/mol]), and in individuals with prior gestational diabetes mellitus. **A**

3.8 Consider using metformin to prevent hyperglycemia in high-risk individuals treated with a phosphatidylinositol 3-kinase α (PI3Kα) inhibitor (e.g., alpelisib and inavolisib). **B**

3.9 Consider using metformin to prevent hyperglycemia in high-risk individuals treated with high-dose glucocorticoids. **B**

PREVENTION OF VASCULAR DISEASE AND MORTALITY

Recommendations

3.11 Prediabetes is associated with heightened cardiovascular risk; therefore, screening for and treatment of modifiable risk factors for cardiovascular disease are suggested. **B**

3.12 Statin therapy may increase the risk of type 2 diabetes in people at high risk of developing type 2 diabetes. In such individuals, glucose status should be monitored regularly and diabetes prevention approaches reinforced. It is not recommended that statins be avoided or discontinued for this adverse effect. **B**

3.13 In people with a history of stroke and evidence of insulin resistance and prediabetes, pioglitazone may be considered to lower the risk of stroke or myocardial infarction. However, this benefit needs to be balanced with the increased risk of weight gain, edema, and fractures. **A** Lower doses may mitigate the risk of adverse effects but may be less effective. **C**

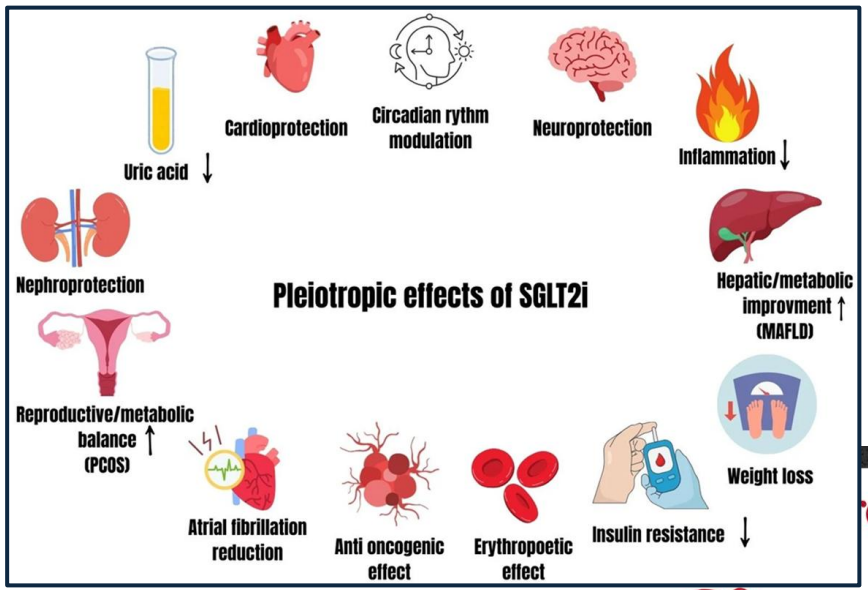
PERSON-CENTERED CARE GOALS

Recommendations

3.14 In adults with overweight or obesity at high risk of type 2 diabetes, care goals should include weight loss and maintenance, minimizing the progression of hyperglycemia, and attention to cardiovascular risk. **B**

3.15 Pharmacotherapy (e.g., for weight management, minimizing the progression of hyperglycemia, and cardiovascular risk reduction) should be considered to support person-centered care goals. **A**

3.16 More intensive preventive approaches should be considered in individuals who are at particularly high risk of progression to diabetes, including individuals with BMI ≥35 kg/m^2, those with higher glucose levels (e.g., fasting plasma glucose 110–125 mg/dL [6.1–6.9 mmol/L], 2-h postchallenge glucose 173–199 mg/dL [9.6–11.0 mmol/L], and A1C ≥6.0% [≥42 mmol/mol]), and individuals with a history of gestational diabetes mellitus. **A**



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American Diabetes Association.
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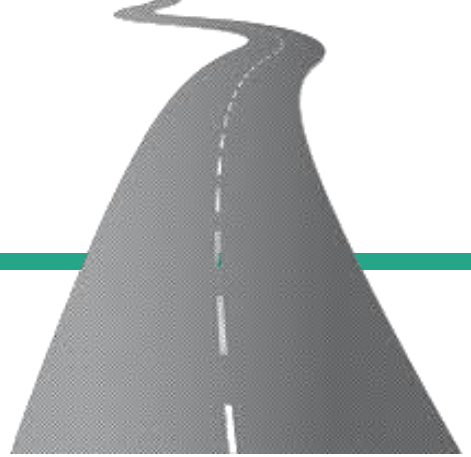
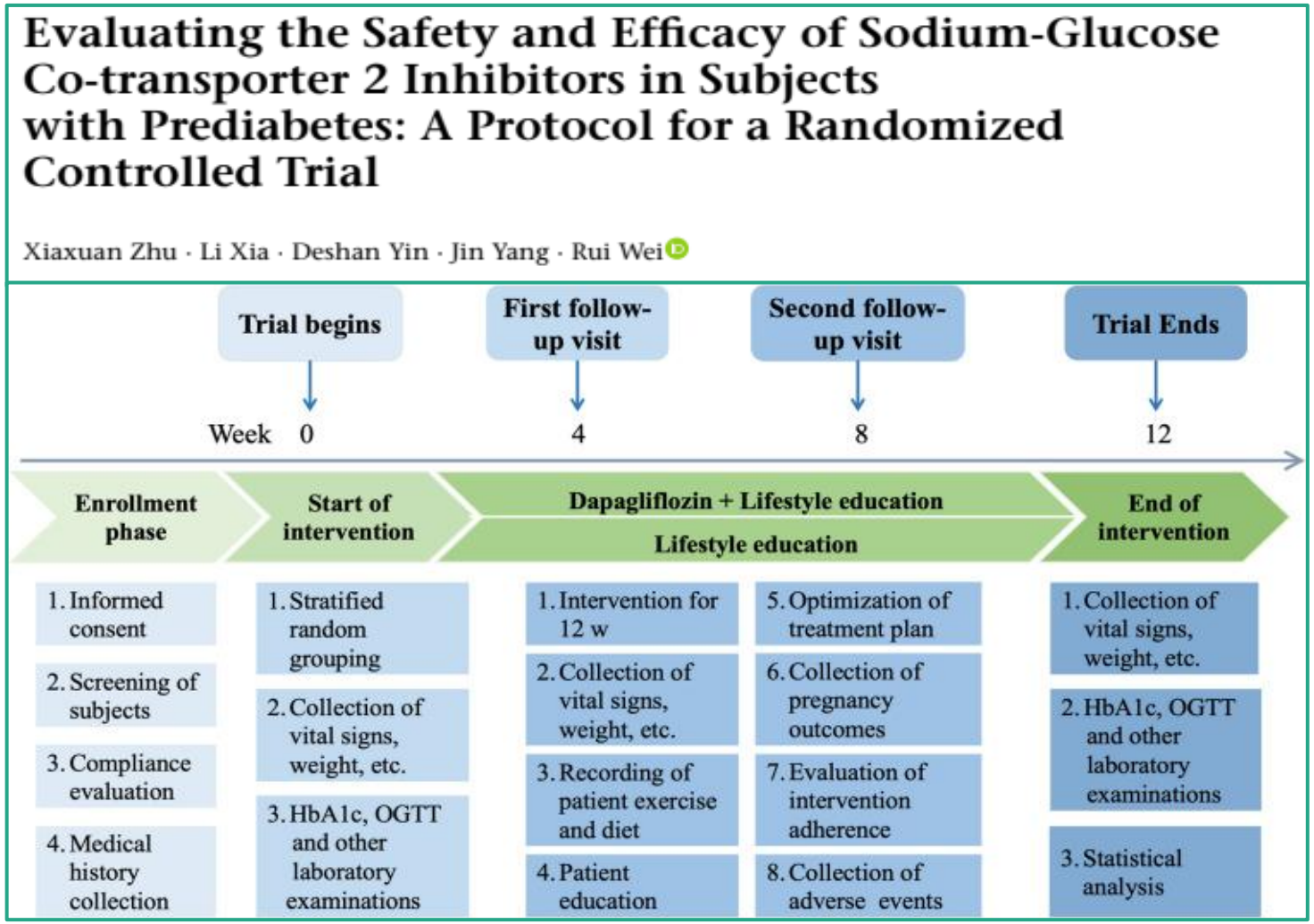


SGLT-2 Inhibitors in Prediabetes; Ongoing Clinical Trials

Based on the clinicaltrials.gov database, 12 ongoing clinical trials were conducted to evaluate the efficacy and safety of SGLT-2 inhibitors in prediabetes including dapagliflozin (six trials), empagliflozin (five trials), and canagliflozin (one trial). Study sample sizes range from 34 to 700, with a cumulative sample size of 2100 including dapagliflozin (1620), empagliflozin (262), and canagliflozin (218). The route of administration of SGLT-2 inhibitors is oral. The dose range, duration of



Pourkarim et al. Current Evidence on SGLT-2 Inhibitors in Prediabetes: A Review of Preclinical and Clinical Data. J Clin Pharmacol. 2025

THE BRIGHT SIDE OF DIABETES

LA PREVENZIONE E LA REMISSIONE
NEL DIABETE MELLITO

MILANO
FABBRICA DEL VAPORE

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Società Italiana di Diabetologia

14 MAGGIO 2026

Grazie!