La terapia del diabete

Meglio tutto e subito

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Conflict of Interest
last 3 years

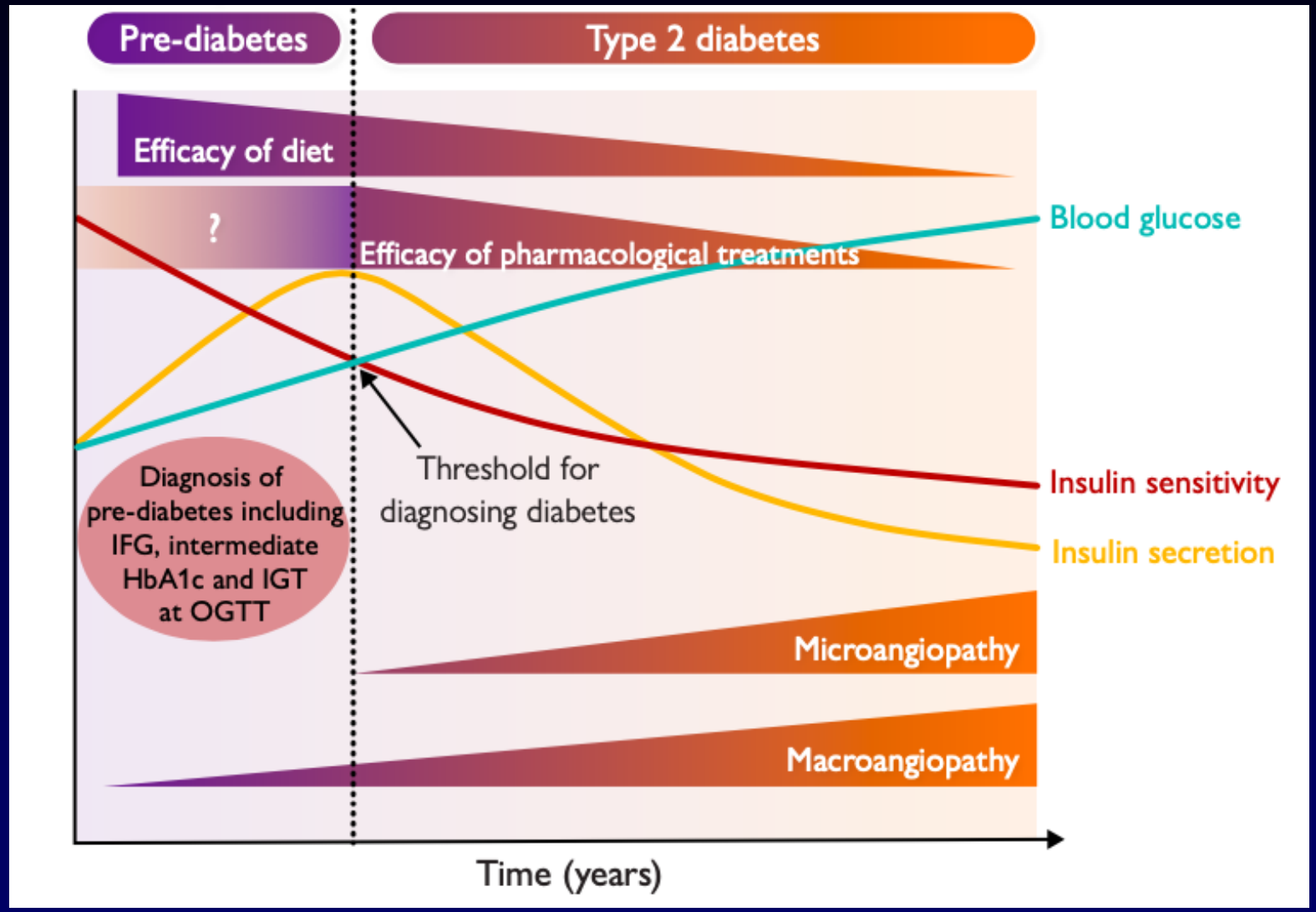
Speaker in Scientific Events

AstraZeneca
Amgen
Bayer
Boheringer Ingelheim
Daiichi Sankyo
Echosens
Lilly
Menarini Diag
Merck
Novartis
Novo Nordisk
Pfizer
PikDare
Roche Diag
Sanofi
Servier

Scientific AB

Amgen
Bruno Farmaceutici
EG
Lilly
Merck
Novartis
Novo Nordisk
Pfizer
PikDare
Sanofi

SUBITO è più efficace



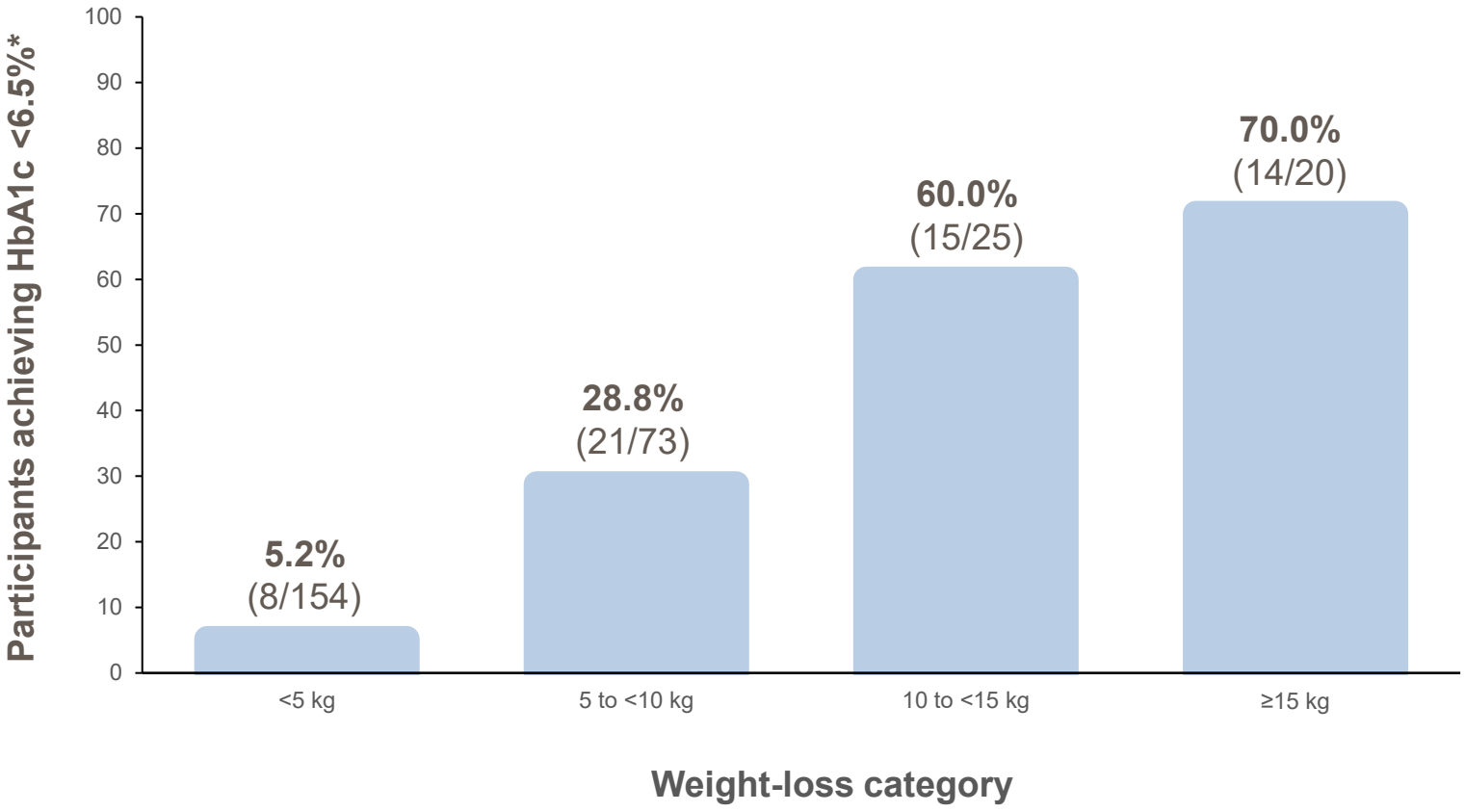
Marx N et al Eur Heart J, 2024

Alla diagnosi del DMT2 allo scopo di aver un buon controllo metabolico

non considerando la eterogeneità del DMT2, in particolare escludendo i pazienti SIDD

DiRECT Study

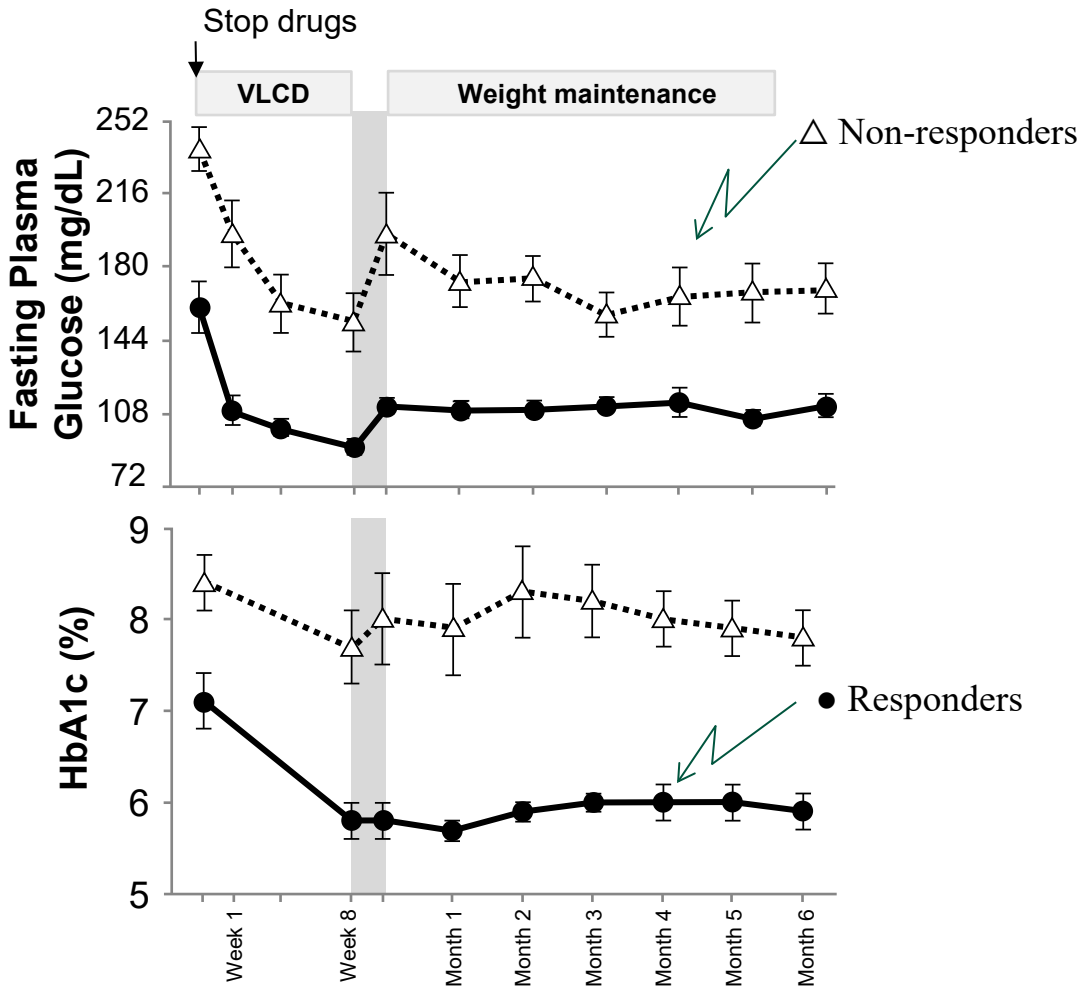
Improvement of HbA1c was proportional to body weight reduction

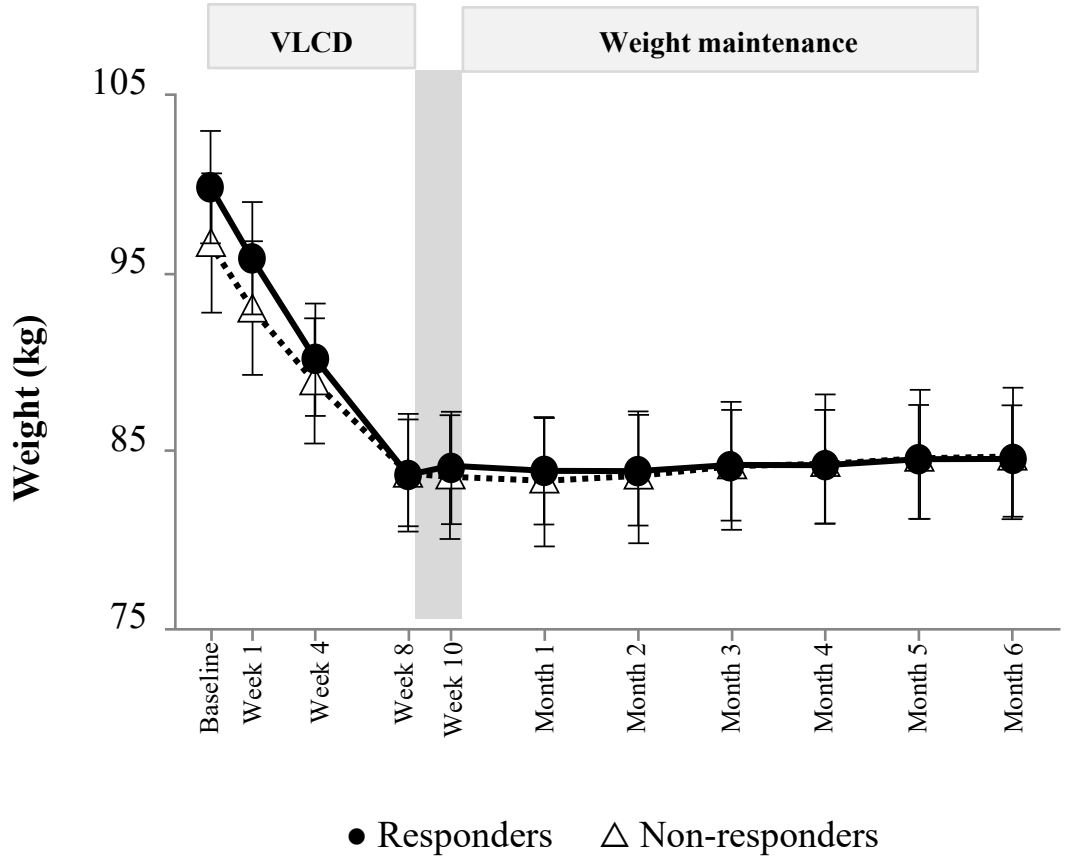


- 36% of the patients achieved HbA1c <6.5% without drugs
- 60% of the patients maintained the target without drugs up to 2 years
- For evey kg lost, 25% increment of the probability to achieve HbA1c <6.5%

Lean MEJ et al Lancet Diabetes Endocrinol, 2019

Remission depends on duration of the disease and baseline HbA1c

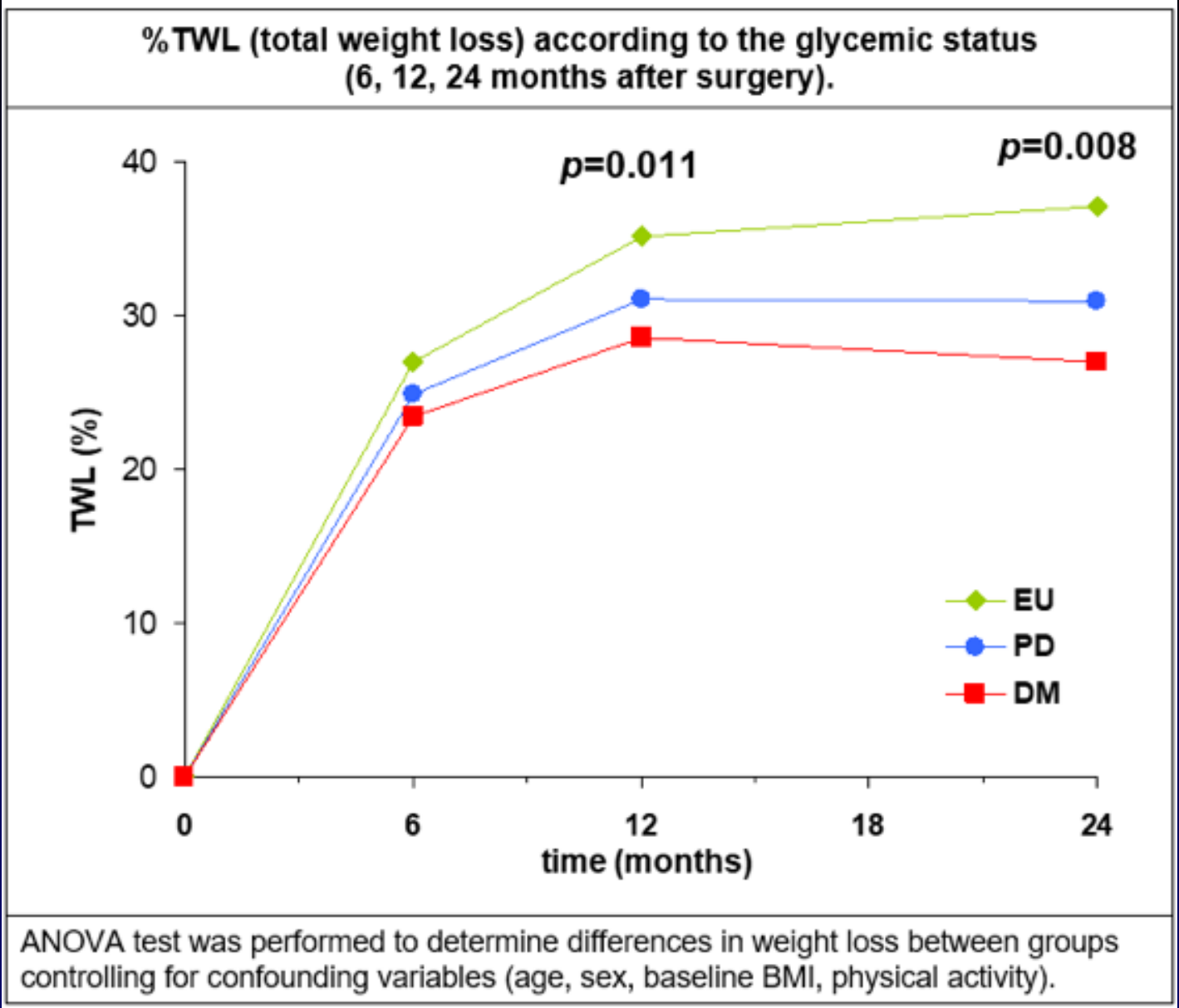




Steven S et al. Diabetes Care, 2016

Bariatric Surgery

Sleeve gastrectomy



Timing

Riduzione di efficacia non solo sull'outcome "glicemico"

Muraca E et al (in preparation)

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 SEPTEMBER 22, 2022 VOL. 387 NO. 12

Glycemia Reduction in Type 2 Diabetes — Glycemic Outcomes

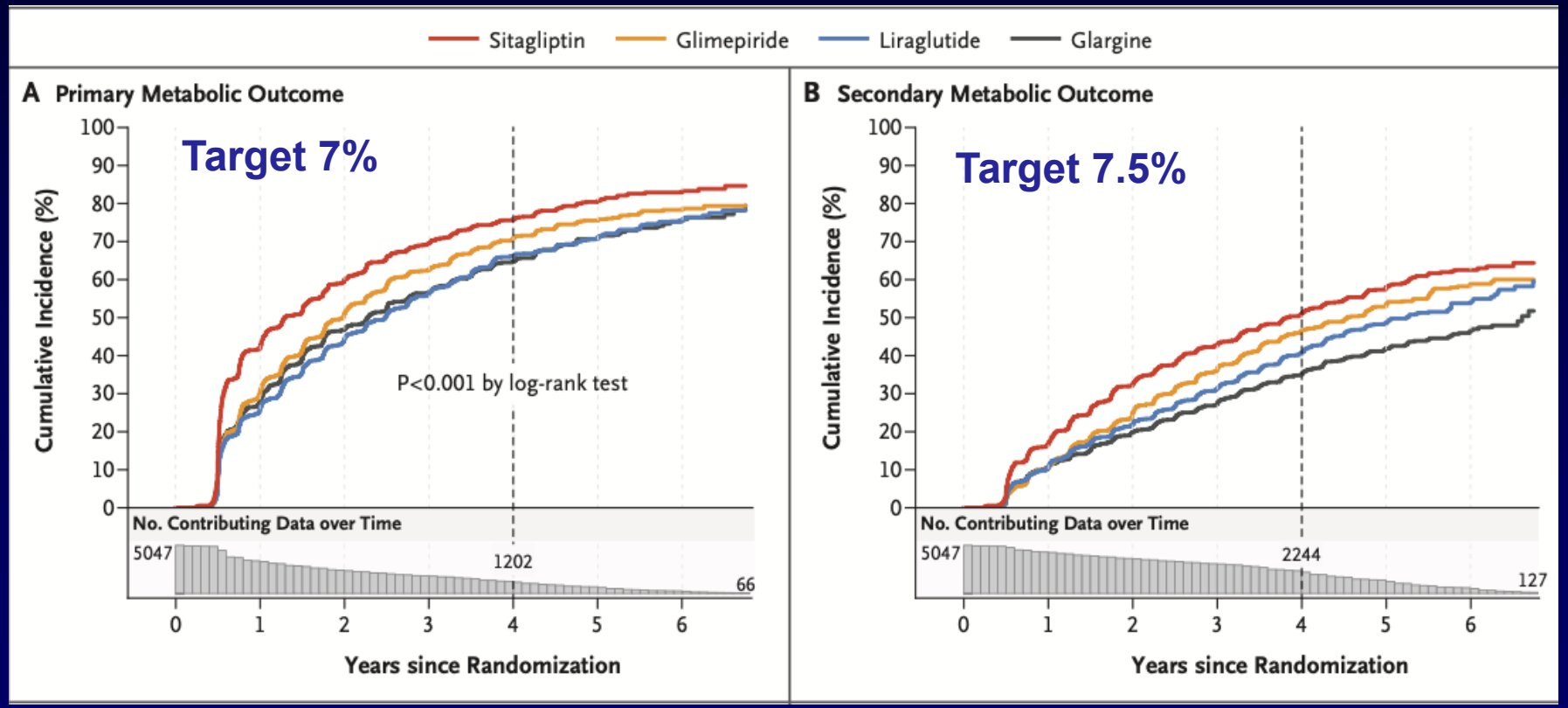
The GRADE Study Research Group*

Standard strategy

Short duration (4 years)

In metformina al basale

a 4 anni 71% dei pazienti con HbA1c > 7%



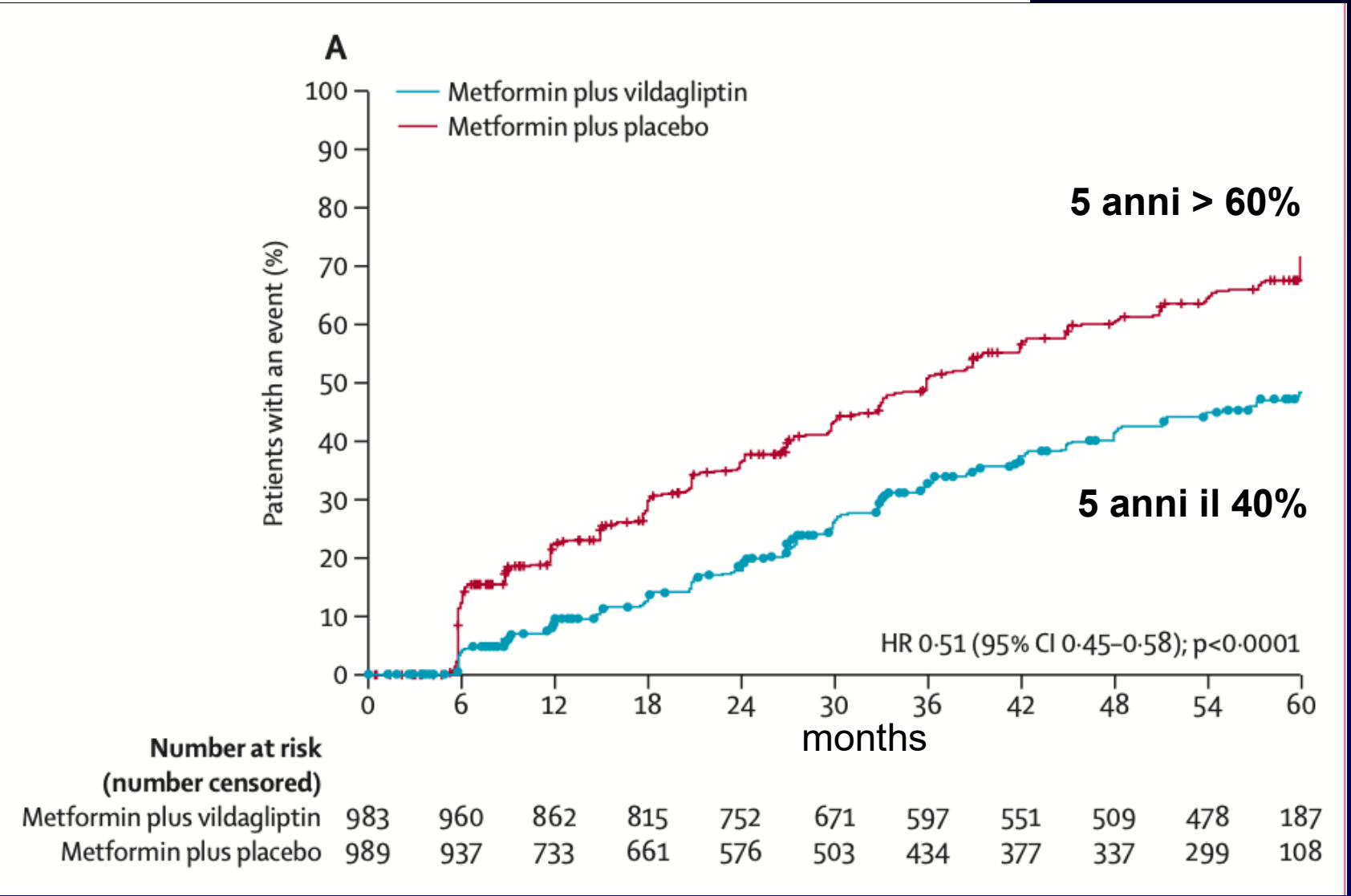
The GRADE Study Research Group N Engl J Med, 2022

Glycaemic durability of an early combination therapy with vildagliptin and metformin versus sequential metformin monotherapy in newly diagnosed type 2 diabetes (VERIFY): a 5-year, multicentre, randomised, double-blind trial

David R Matthews, Päivi M Paldánius, Pieter Proot, YannTong Chiang, Michael Stumvoll, Stefano Del Prato, for the VERIFY study group

SUBITO E TUTTO

WH: "Although initial combination therapy has been suggested to offer more opportunities than a traditional stepwise approach, its validity remains to be determined"



efficacy endpoint

time from randomisation to initial treatment failure

HbA1c measurement of at least 7·0% at two consecutive scheduled visits

Matthews DR et al Lancet, 2019

Prediabetes

STEP-10

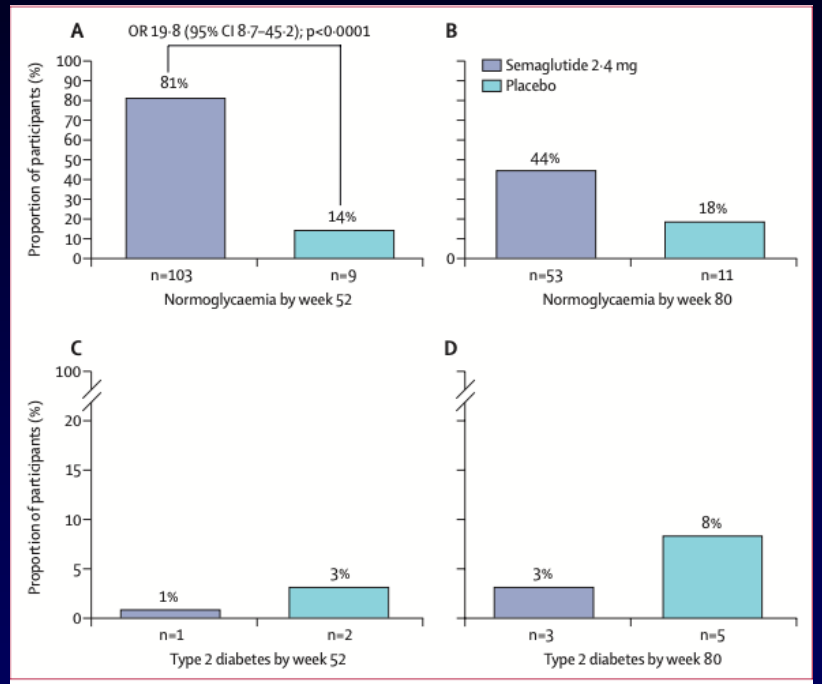
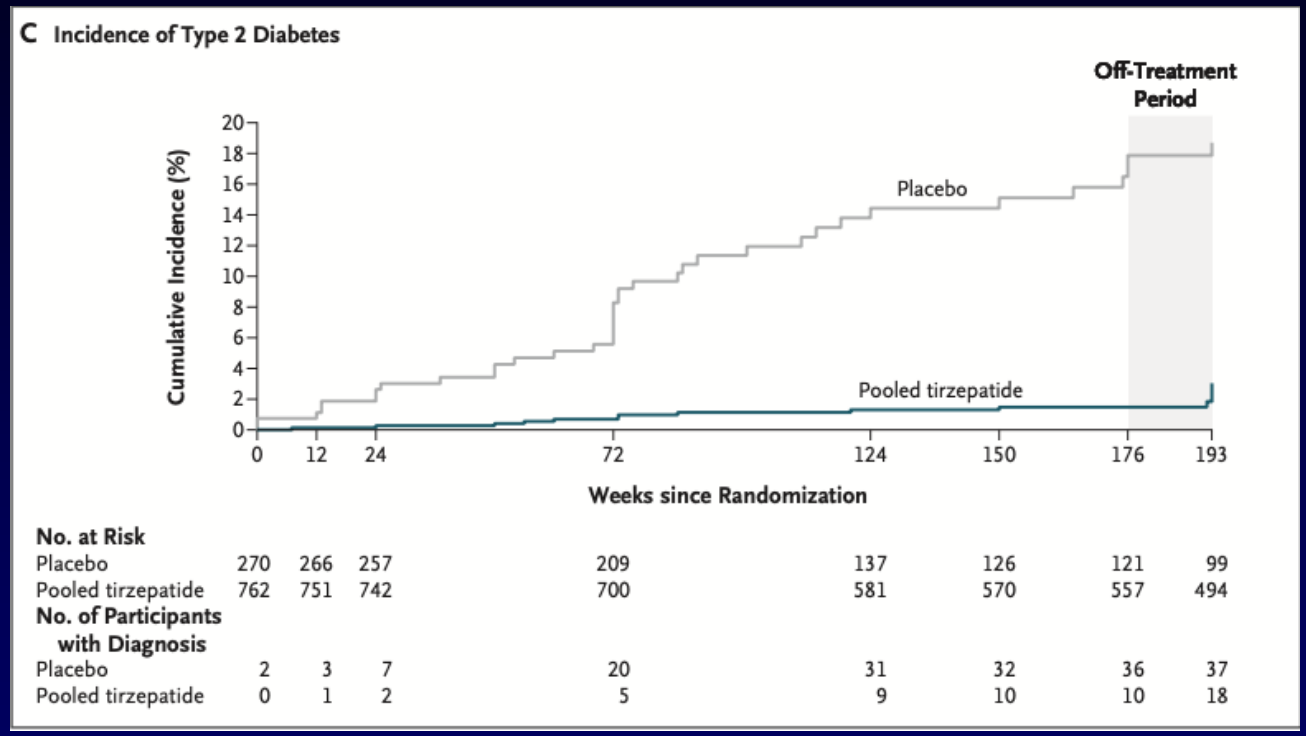


Figure 3: **Proportion of participants who reverted to normoglycaemia or progressed to type 2 diabetes with semaglutide 2·4 mg versus placebo in the full analysis set during the in-trial observation period**
Observed proportions of participants who reverted to normoglycaemia (HbA_{1c} <6·0% [<42 mmol/mol] and FPG <5·5 mmol/L) at week 52 (A; OR is for the treatment policy estimand) and week 80 (B). Observed proportions of who progressed to type 2 diabetes (HbA_{1c} ≥6·5% [≥48 mmol/mol] or FPG ≥7·0 mmol/L, verified with a repeated blood sample within 4 weeks from baseline) at week 52 (C) and week 80 (D). OR for panel A is for the treatment policy estimand. FPG=fasting plasma glucose. OR=odds ratio.

1% vs 3%
OR 19.8; 95% CI 8.7 to 45.2; p<0.0001

McGovan B et al Lancet Diabetol Endocrinol, 2024

SURMOUNT-1



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

1.3% vs. 13.3%
HR 0.07; 95% CI: 0.0-0.1; P<0.001

Jastreboff AM et al N Engl J Med, 2024

alla diagnosi del DMT2 per la prevenzione delle complicanze

(non considerando la eterogeneità del DMT2)

PREVALENCE OF COMPLICATIONS: DURATION < 5 YEARS (patients with hepatic steatosis at US)

DURATION OF DIABETES (years)	1.7±1.3
Age (years)	61±13
BMI (kg/m^2)	31.4±5.6
CVD (%)	**15.7%**
CKD (%)	**28.0%**
UACR > 30 mg/g (%)	**17.0%**
Motor and sensory neuropathy (%)	3.4%
Retinopathy (%)	5.6%
LSM > 8 KPa (%) (if FIB-4 > 1.3)	**31.0%**

GRADE
Short diabetes duration (4 years)
High rate of CVD complications

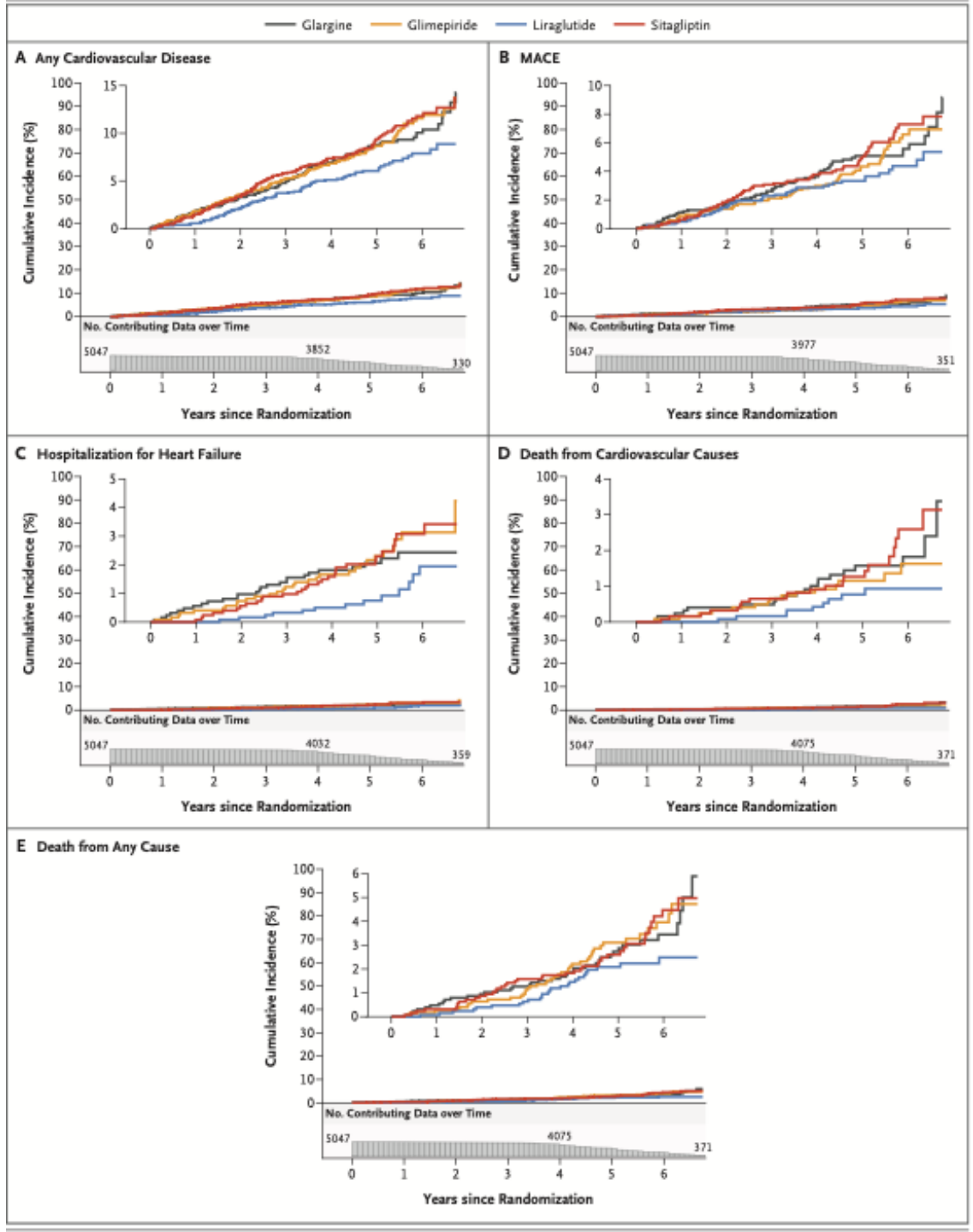
On top of metformin

Glargine
Glimepiride
Liraglutide
Sitagliptin

6-7% with previous stroke or AMI

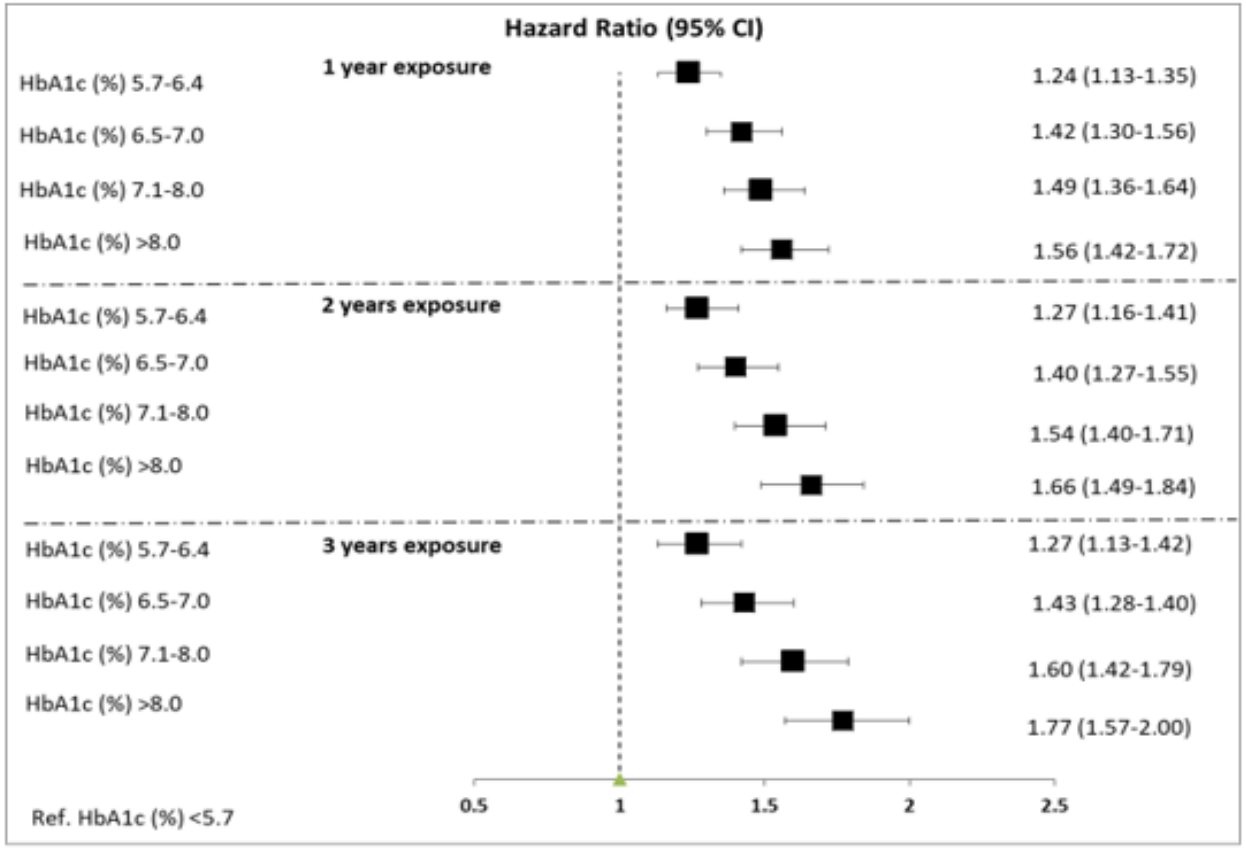
Any CVD
~ 10% in 6 years

Death
~ 4-5% in 6 years



The GRADE Study Research Group N Engl J Med, 2022

Controllo glicemico precoce e successivo rischio di CVD con HbA1c <5,7% come valore di riferimento



Pseudo-forest plot showing the adjusted hazard ratios (HR) with the relative 95% confidence interval (CI), derived from the Cox regression analyses exploring the associations between glycemic control and the risk of the CVD at follow-up to the degree of glycemic control in the three exposure periods assessed

Neda Laiterapong, The Diabetes Aging Study
Diabetes Care, 2019

- **Complessivamente, il 5.7% dei pazienti con DT2 aveva valori medi di HbA1c <5.7% nel primo anno dopo la diagnosi.**
- **Durante un follow-up medio di 4.6±2.9 years, 13,822 pazienti (5.5%) hanno sviluppato un evento cardiovascolare maggiore.**
- **Rispetto ai pazienti con HbA1c media <5.7%, quelli al di sopra di questa soglia avevano un aumentato rischio di malattie cardiovascolari al follow-up per tutti e tre i periodi di esposizione precoce e per tutti gli intervalli di controllo glicemico considerati**
- **Rispetto ad una HbA1c media <5.7% durante il primo anno dopo la diagnosi, i pazienti con HbA1c media compresa tra il 5.7% e il 6.4% avevano un rischio aumentato del 24% di malattie cardiovascolari (HR=1.24; 95%CI 1.13-1.35)**

Russo G et al. Diabetes 2025

Historical HbA_{1c} Values May Explain the Type 2 Diabetes Legacy Effect: UKPDS 88

Marcus Lind,[1,2] Henrik Imberg,[3] Ruth L. Coleman,[4] Olle Nerman,[3] and Rury R. Holman[4]

Diabetes Care 2021;44:2231–2237 | https://doi.org/10.2337/dc20-2439

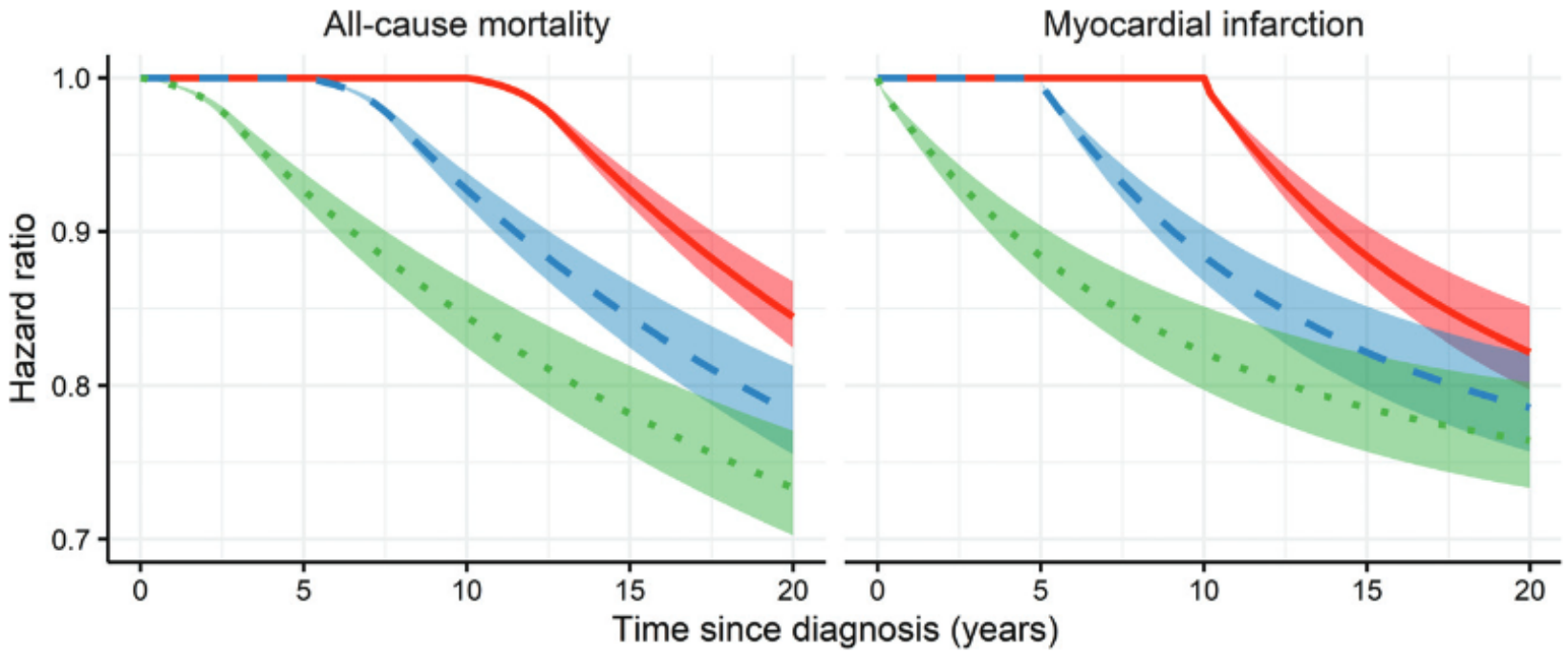


Figure 1—Time-dependent HRs for all cause-mortality (left) and myocardial infarction (right) from 0 to 20 years after diagnosis of type 2 diabetes, assuming a one percentage unit lower HbA_{1c} from diagnosis (green dotted lines), and when the same degree of HbA_{1c} lowering was imposed from 5 years (blue dashed lines), and from 10 years (red solid lines) after diagnosis. The shaded regions represent 95% confidence limits. HRs were calculated according to Eq. 6 in the Supplementary Material.

The glycemic legacy effects seen in T2DM are explained largely by historical HbA 1c values having a greater impact than recent values on clinical outcomes

Early detection of diabetes and intensive glucose control from the time of diagnosis is essential to maximize reduction of the long-term risk of glycemic complications

Lind M et al. Diabetes Care 2021

Look-ahead and remission (CVD & CKD)

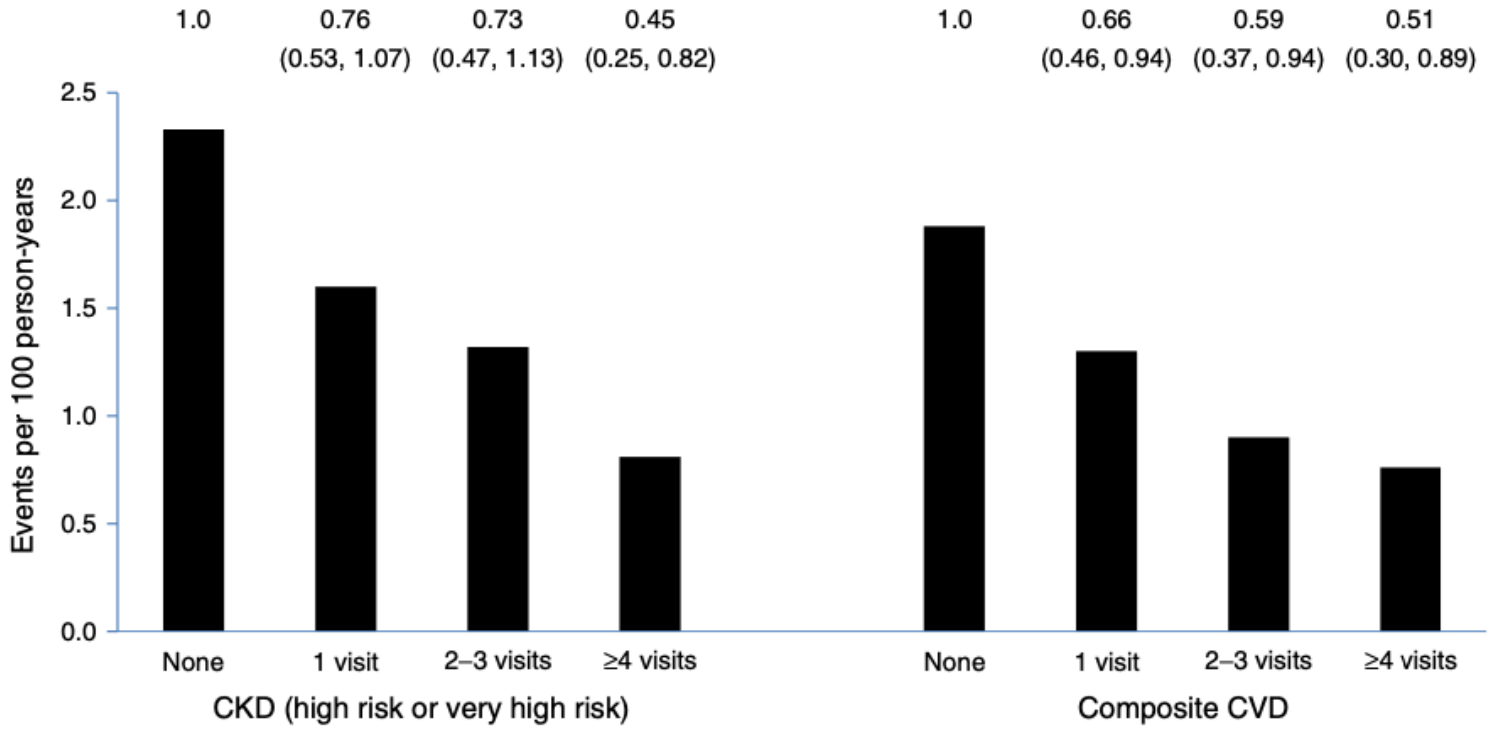


Fig. 2 Incidence of CKD and CVD based on number of visits with remission. The HR and 95% CI values are shown at the top

Metabolic memory

Number of visits in remission

Gregg EW et al Diabetologia, 2024

At diagnosis in Lombardy - 2012

Within the first year?

1) HbA1c
2) lipid profile
3) AER
4) creatinine

3 categories of adherence

1) 0-1	low	43%
2) 2	intermediate	36%
3) 3-4	high	21%

End-points

Complications of diabetes (time to hosp admission for short term and long term complications) - Costs for the health care system (€)

Clinical outcome

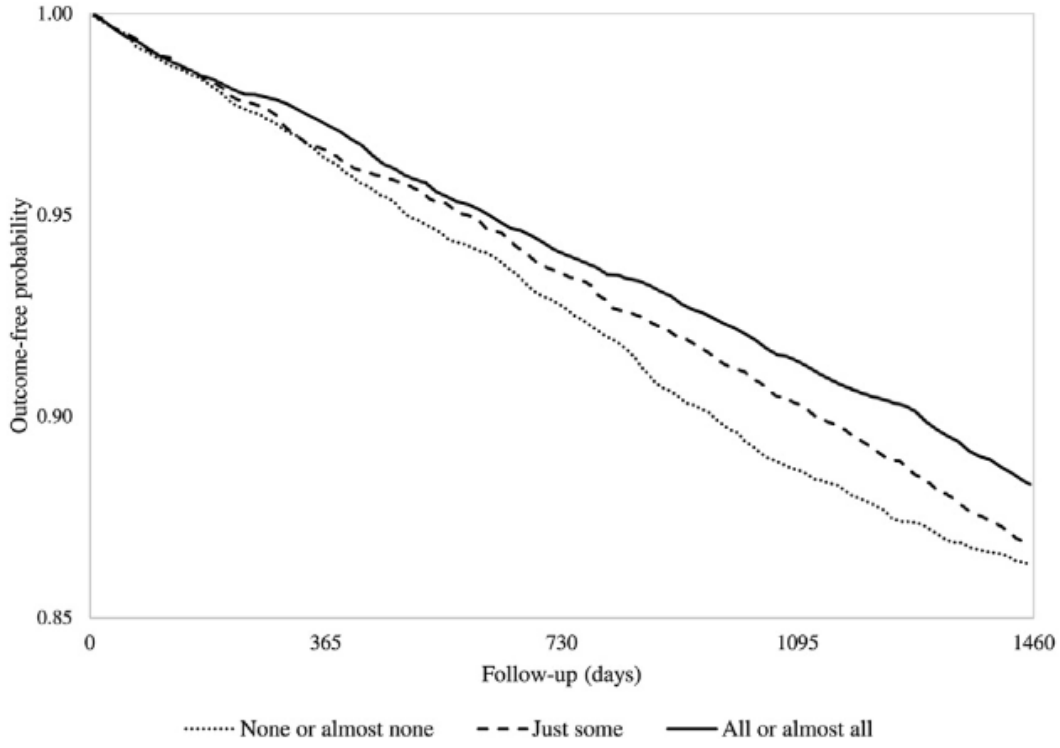


Figure 1 Time-free-to-complications among matched cohorts differentiated according to whether none or almost none, just some or all or almost all recommendations were followed. Footnote. A score of

Corrao G et al. Nutr Metab Cardiovasc Dis, 2021

Prediabetes remission and cardiovascular morbidity and mortality: post-hoc analyses from the Diabetes Prevention Program Outcome study and the DaQing Diabetes Prevention Outcome study

Elsa Vazquez Arreola, Qiuhong Gong*, Robert L Hanson, Jinping Wang, Leontine Sandforth, Siyao He, Arvid Sandforth, Xin Qian, Mauro Giacca, Stefan R Bornstein, Andreas Fritsche, Norbert Stefan, Hubert Preissl, Edward W Gregg, Nikolaus Marx, Reiner Jumpertz-von Schwartzenberg*, Guangwei Li*, Andreas L Birkenfeld**

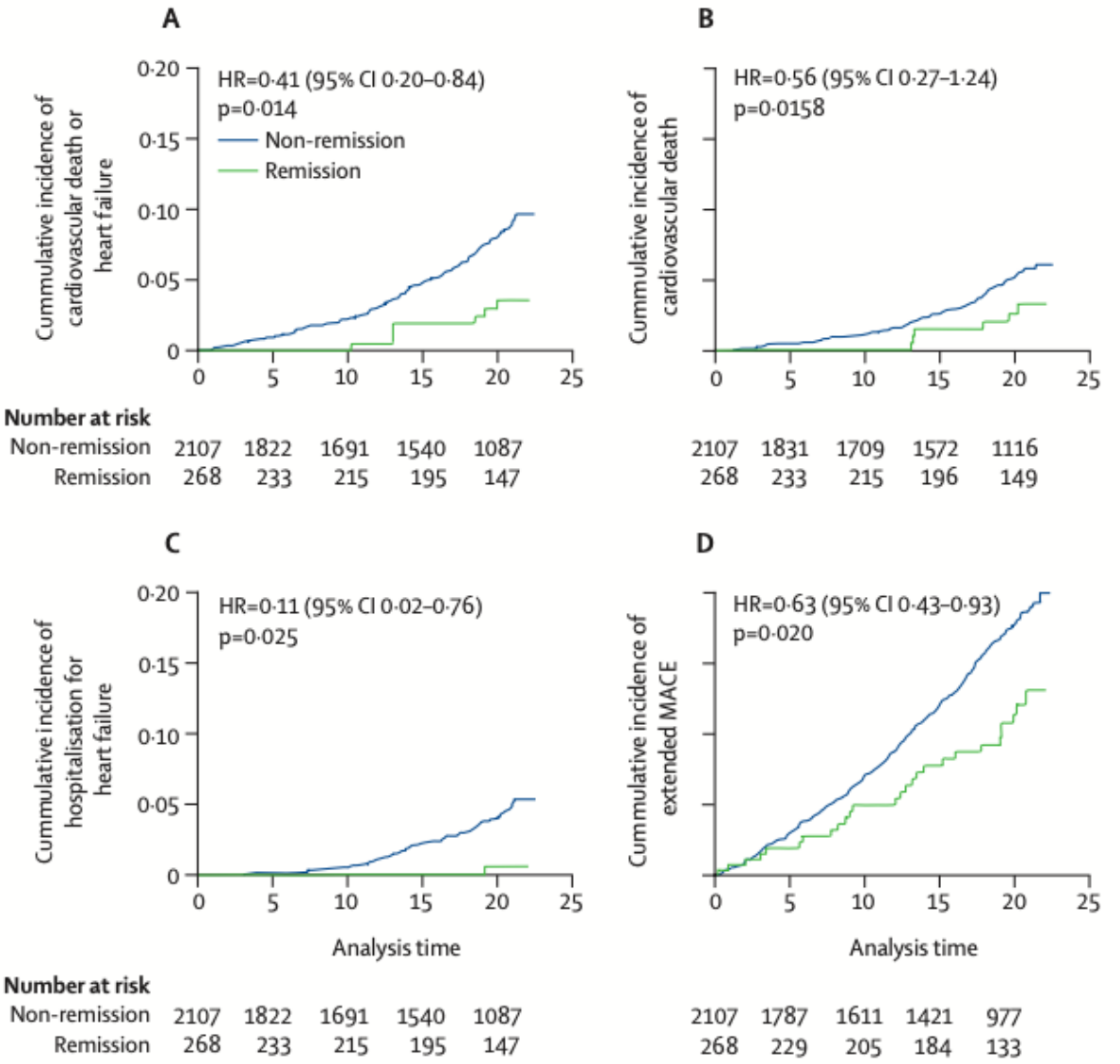
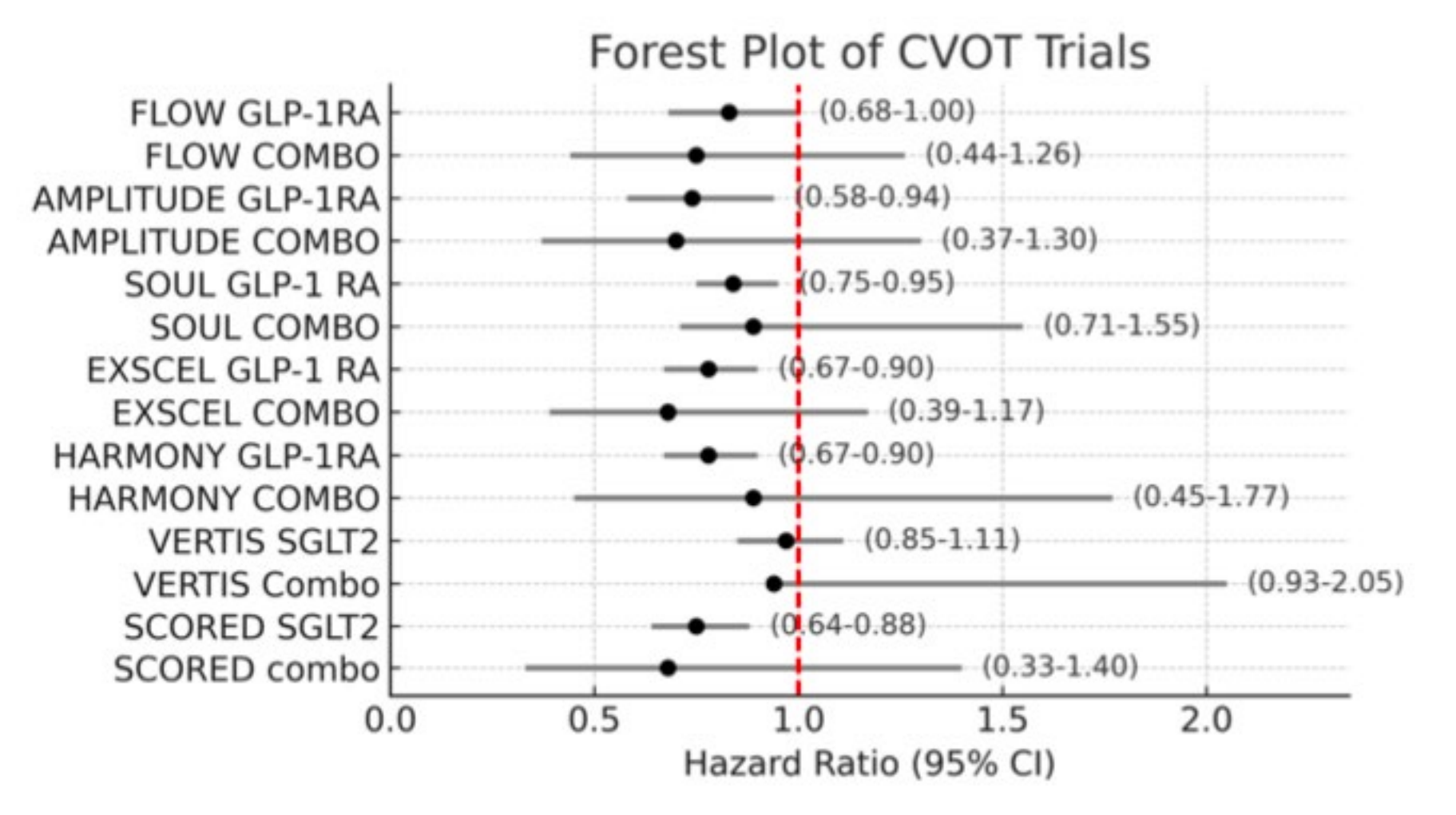


Figure 1: **DPPOS: Kaplan–Meier curves for risk of composite endpoint cardiovascular death or hospitalisation for heart failure (A), cardiovascular death (B), hospitalisation for heart failure (C), and extended MACE (D) by remission status after 1 year of lifestyle intervention and over up to 20 years of follow-up**
Remission status was determined according to ADA criteria. Extended MACE included cardiovascular death, non-fatal myocardial infarction, non-fatal stroke, coronary or peripheral revascularisation, hospitalisation for heart failure or unstable angina, new diagnosis of coronary heart disease, or silent myocardial infarction. DPPOS=Diabetes Prevention Program Outcomes Study. MACE=major adverse cardiovascular event.

Vazquez Arreola E et al
Lancet Diabetes Endocrinol, 2026

nel paziente con malattia CVD

Benefit of combination therapy: GLP1-RA & SGLT2-i



Avogaro A et al Acta Diabetol, 2026

SOUL: Oral Semaglutide CV Outcomes by SGLT2i Use

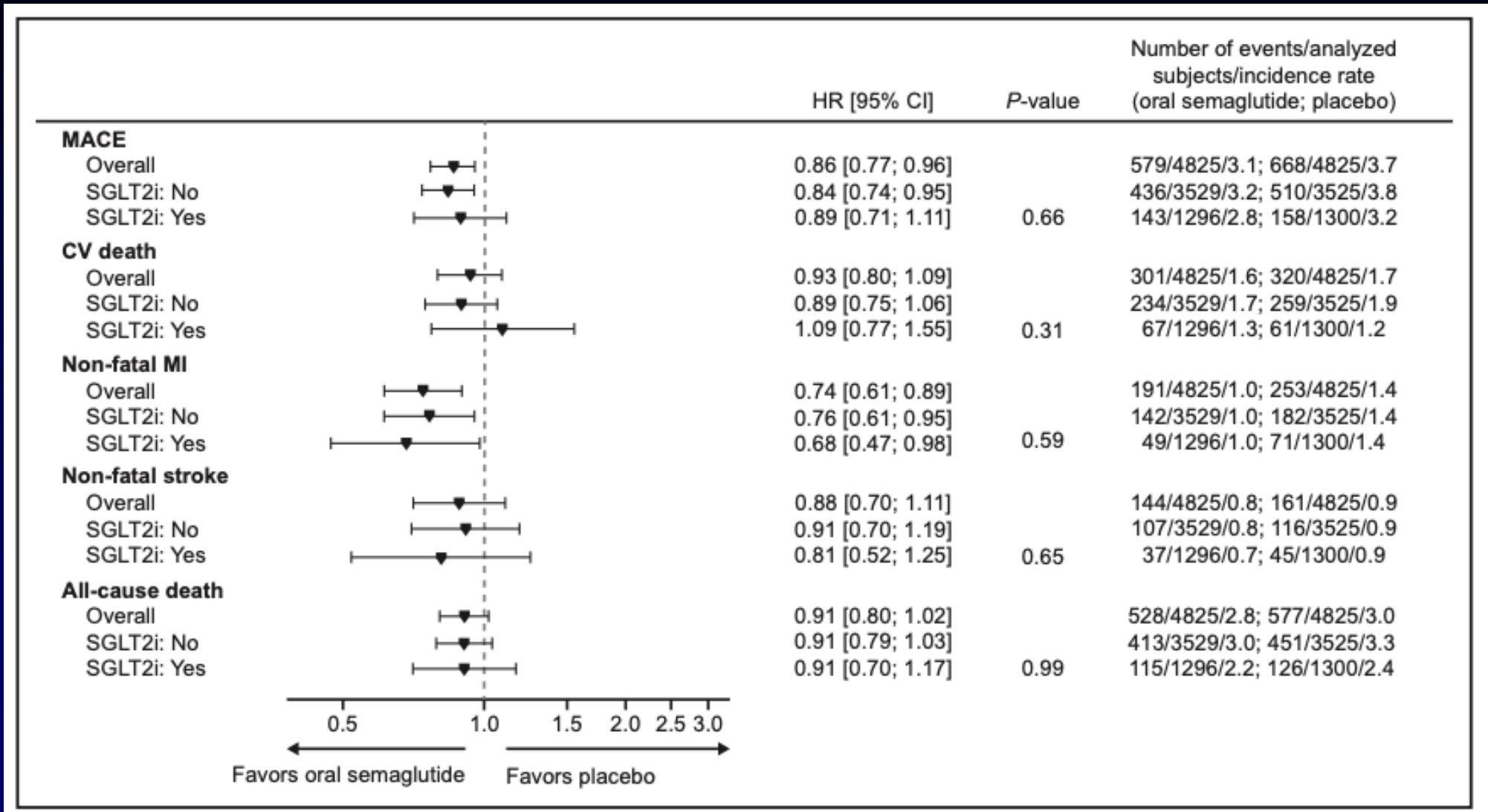
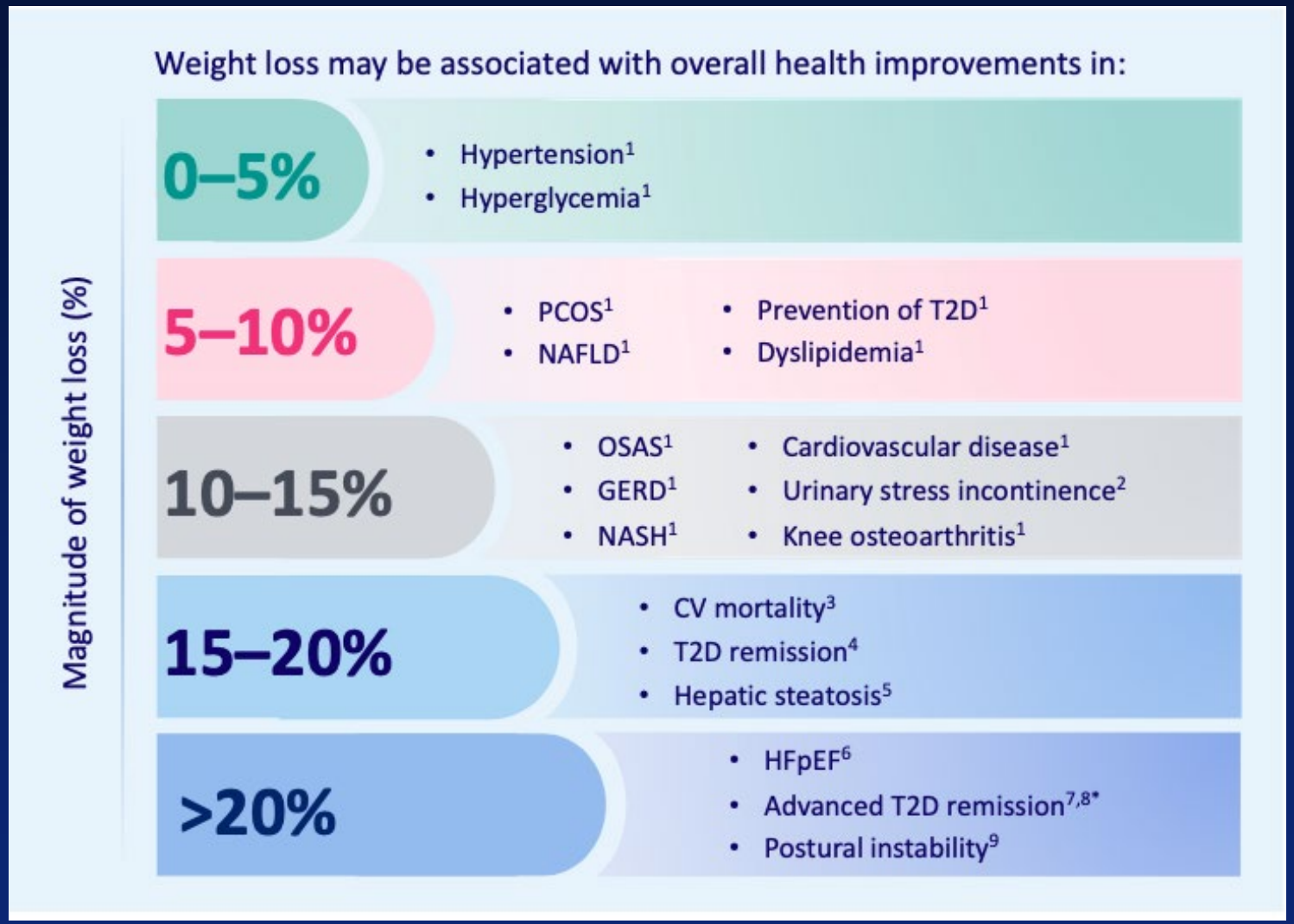


Figure 2. Forest plot: primary outcomes, components and all-cause death according to SGLT2i use at baseline.

Marx N et al. Circulation, 2025

Conclusion, the new paradigm



Greater weight loss = better health outcomes

*T2D remission rates have been found to plateau at 20–25% total weight loss where 25% total weight loss did not confer additional benefits;

BP, blood pressure; CV, cardiovascular; GERD, gastro-oesophageal reflux disease; HbA1c, glycated hemoglobin; HFpEF, heart failure with preserved ejection fraction; NAFLD; non-alcoholic fatty liver disease; NASH, non-alcoholic steatohepatitis; OSAS, obstructive sleep apnoea syndrome; PCOS, polycystic ovary syndrome; PwO, people with obesity; T2D, type 2 diabetes; TG, triglycerides. 1. Horn D et al. Postgrad Med. 2022;134:359–75; 2. Garvey WT et al. Endocr Pract. 2016;22(Suppl. 3):1–203; 3. Look AHEAD Research Group, Gregg EW et al. Lancet Diabetes Endocrinol. 2016;4:913–21; 4. Lean ME et al. Lancet. 2018;391:541–51; 5. Sundström J et al. Circulation. 2017;135:1577–85;
6. Benraoune F & Litwin SE. Curr Opin Cardiol. 2011;26:555–61; 7. Meerasa A & Dash S. Diabetes Care 2022;45:28–30; 8. Teasdale, N et al. Int J Obes 2007;31:153–160; 9. Ryan DH and Yockey SR. Curr Obes Rep 2017;6:187–94.

TUTTO & SUBITO: it works …. but it's a challenge

Life-style intervention: very restrictive and difficult to maintain over the long term (in DiRECT at 5 years remission dropped to 13%)

Intensive drug treatment: probably rapidly diminishes when the drug is discontinued and level of patients' acceptability may be low

Bariatric surgery: level of patients' acceptability is low and there is time-dependent loss of efficiency

Also, consider you need to achieve the target of LDL-cholesterol and blood pressure "***early***" and using ***"combination therapy approaches"***

Patients must be informed and very well motivated

Metabolic Memory

Cultural change

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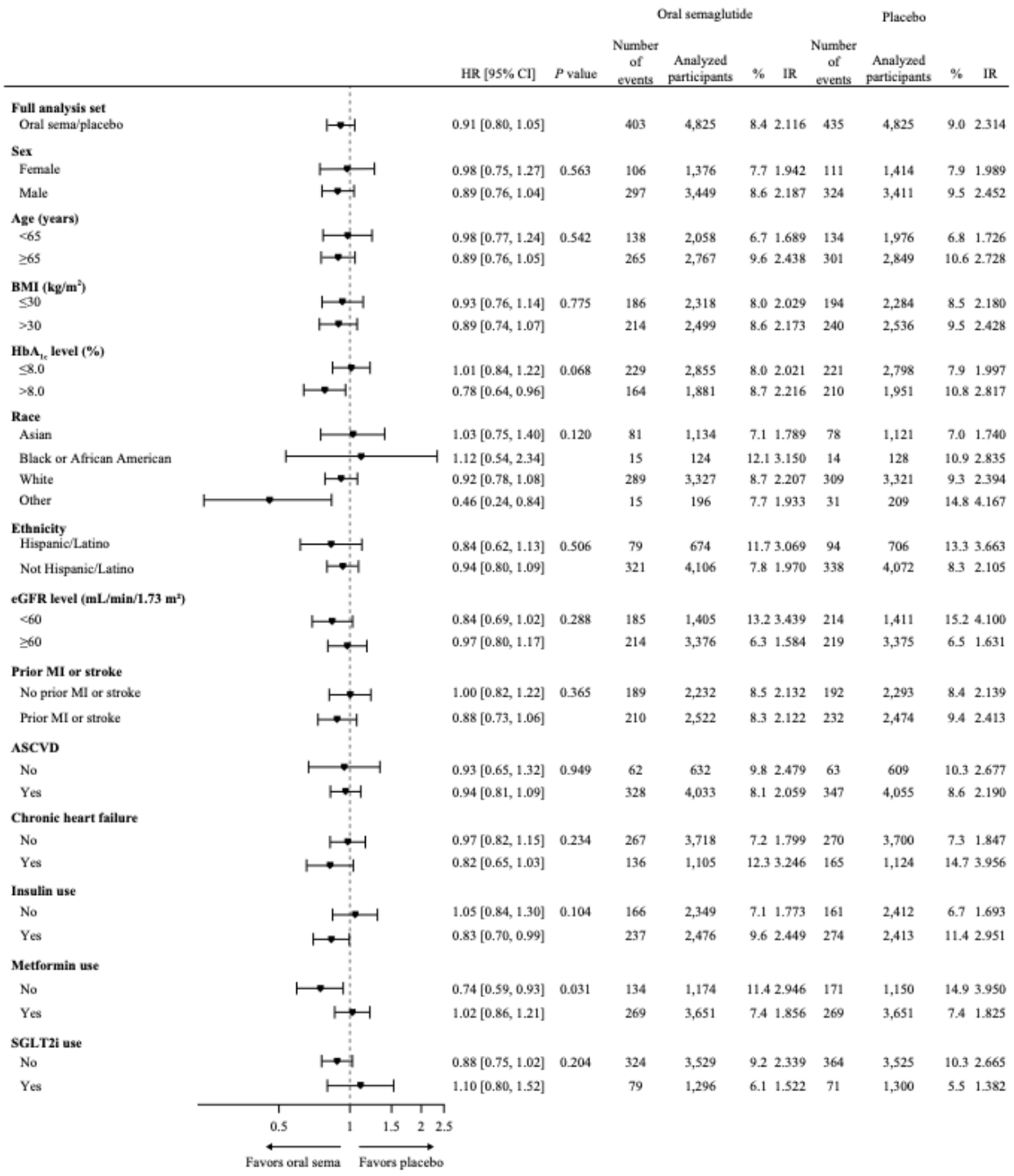
SOUL: Oral Semaglutide kidney outcomes by SGLT2i Use



	HR [95% CI]	*P* value	Oral semaglutide: Number of events	Oral semaglutide: Analyzed participants	Oral semaglutide: %	Oral semaglutide: IR	Placebo: Number of events	Placebo: Analyzed participants	Placebo: %	Placebo: IR
Full analysis set										
Oral sema/placebo	0.91 [0.80, 1.05]		403	4,825	8.4	2.116	435	4,825	9.0	2.314
Sex										
Female	0.98 [0.75, 1.27]	0.563	106	1,376	7.7	1.942	111	1,414	7.9	1.989
Male	0.89 [0.76, 1.04]		297	3,449	8.6	2.187	324	3,411	9.5	2.452
Age (years)										
<65	0.98 [0.77, 1.24]	0.542	138	2,058	6.7	1.689	134	1,976	6.8	1.726
≥65	0.89 [0.76, 1.05]		265	2,767	9.6	2.438	301	2,849	10.6	2.728
BMI (kg/m^2)										
≤30	0.93 [0.76, 1.14]	0.775	186	2,318	8.0	2.029	194	2,284	8.5	2.180
>30	0.89 [0.74, 1.07]		214	2,499	8.6	2.173	240	2,536	9.5	2.428
HbA_{1c} level (%)										
≤8.0	1.01 [0.84, 1.22]	0.068	229	2,855	8.0	2.021	221	2,798	7.9	1.997
>8.0	0.78 [0.64, 0.96]		164	1,881	8.7	2.216	210	1,951	10.8	2.817
Race										
Asian	1.03 [0.75, 1.40]	0.120	81	1,134	7.1	1.789	78	1,121	7.0	1.740
Black or African American	1.12 [0.54, 2.34]		15	124	12.1	3.150	14	128	10.9	2.835
White	0.92 [0.78, 1.08]		289	3,327	8.7	2.207	309	3,321	9.3	2.394
Other	0.46 [0.24, 0.84]		15	196	7.7	1.933	31	209	14.8	4.167
Ethnicity										
Hispanic/Latino	0.84 [0.62, 1.13]	0.506	79	674	11.7	3.069	94	706	13.3	3.663
Not Hispanic/Latino	0.94 [0.80, 1.09]		321	4,106	7.8	1.970	338	4,072	8.3	2.105
eGFR level (mL/min/1.73 m^2)										
<60	0.84 [0.69, 1.02]	0.288	185	1,405	13.2	3.439	214	1,411	15.2	4.100
≥60	0.97 [0.80, 1.17]		214	3,376	6.3	1.584	219	3,375	6.5	1.631
Prior MI or stroke										
No prior MI or stroke	1.00 [0.82, 1.22]	0.365	189	2,232	8.5	2.132	192	2,293	8.4	2.139
Prior MI or stroke	0.88 [0.73, 1.06]		210	2,522	8.3	2.122	232	2,474	9.4	2.413
ASCVD										
No	0.93 [0.65, 1.32]	0.949	62	632	9.8	2.479	63	609	10.3	2.677
Yes	0.94 [0.81, 1.09]		328	4,033	8.1	2.059	347	4,055	8.6	2.190
Chronic heart failure										
No	0.97 [0.82, 1.15]	0.234	267	3,718	7.2	1.799	270	3,700	7.3	1.847
Yes	0.82 [0.65, 1.03]		136	1,105	12.3	3.246	165	1,124	14.7	3.956
Insulin use										
No	1.05 [0.84, 1.30]	0.104	166	2,349	7.1	1.773	161	2,412	6.7	1.693
Yes	0.83 [0.70, 0.99]		237	2,476	9.6	2.449	274	2,413	11.4	2.951
Metformin use										
No	0.74 [0.59, 0.93]	0.031	134	1,174	11.4	2.946	171	1,150	14.9	3.950
Yes	1.02 [0.86, 1.21]		269	3,651	7.4	1.856	269	3,651	7.4	1.825
SGLT2i use										
No	0.88 [0.75, 1.02]	0.204	324	3,529	9.2	2.339	364	3,525	10.3	2.665
Yes	1.10 [0.80, 1.52]		79	1,296	6.1	1.522	71	1,300	5.5	1.382

Mann JFE et al. Diabetes Care, 2026

Comparative effectiveness of combination therapy with SGLT-2 inhibitors and GLP-1 RAs compared with SGLT-2 inhibitors in individuals with type 2 diabetes: A prevalent new-user cohort study

RWD

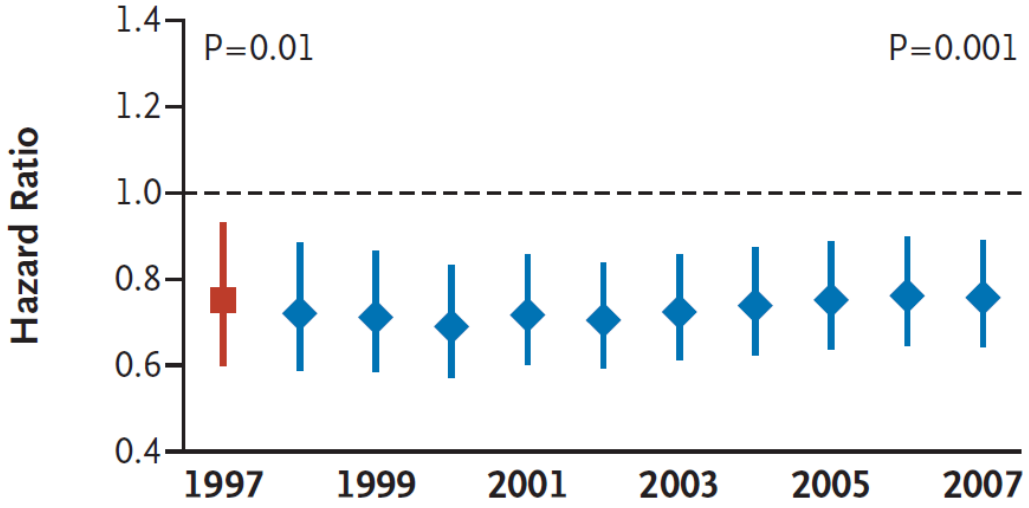
TABLE 2 Results for the primary and secondary outcomes for combination therapy with SGLT-2 inhibitors and GLP-1 RAs compared with continued SGLT-2 inhibitor therapy after matching on hybrid exposure set and time-conditional propensity scores.

Outcome	Individuals, *n*	Events	Person-years	IR[a] (95% CI)	HR[b] (95% CI)
Primary outcome					
All-cause mortality					
Combination therapy (SGLT-2 inhibitors and GLP-1 RAs)	21 664	410	30 660	13.4 (12.1–14.7)	0.71 (0.63–0.80)
Continued SGLT-2 inhibitor therapy	21 664	868	46 626	18.6 (17.4–19.9)	Reference
Secondary outcomes					
Modified cardiovascular composite					
Combination therapy (SGLT-2 inhibitors and GLP-1 RAs)	21 664	740	30 279	24.4 (22.7–26.3)	0.81 (0.74–0.88)
Continued SGLT-2 inhibitor therapy	21 664	1372	45 877	29.9 (28.3–31.5)	Reference
Myocardial infarction					
Combination therapy (SGLT-2 inhibitors and GLP-1 RAs)	21 664	190	30 447	6.2 (5.4–7.2)	0.95 (0.79–1.14)
Continued SGLT-2 inhibitor therapy	21 664	302	46 264	6.5 (5.8–7.3)	Reference
Stroke					
Combination therapy (SGLT-2 inhibitors and GLP-1 RAs)	21 664	187	30 488	6.1 (5.3–7.1)	0.86 (0.72–1.04)
Continued SGLT-2 inhibitor therapy	21 664	319	46 234	6.9 (6.2–7.7)	Reference
Heart failure					
Combination therapy (SGLT-2 inhibitors and GLP-1 RAs)	21 664	304	30 421	10.0 (8.9–11.2)	0.78 (0.68–0.89)
Continued SGLT-2 inhibitor therapy	21 664	562	46 073	12.2 (11.2–13.2)	Reference
Nephropathy					
Combination therapy (SGLT-2 inhibitors and GLP-1 RAs)	21 664	32	30 629	1.0 (0.7–1.5)	1.23 (0.76–1.99)
Continued SGLT-2 inhibitor therapy	21 664	36	46 600	0.8 (0.5–1.1)	Reference

Maier JA et al. Diabetes Obes Metab, 2026

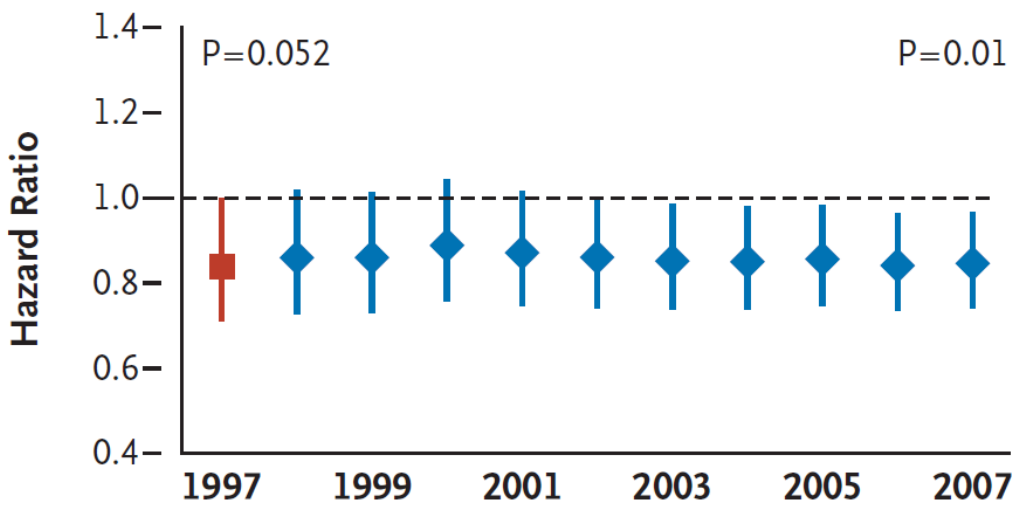
UKPDS: un controllo glicemico precoce ed intensivo riduce il rischio di complicanze croniche a lungo termine nel DMT2 Effetto legacy

E Microvascular Disease



No. of Events	1997	1999	2001	2003	2005	2007
Conventional therapy	121	155	187	205	212	222
Sulfonylurea–insulin	225	277	338	378	406	429

C Myocardial Infarction



No. of Events	1997	1999	2001	2003	2005	2007
Conventional therapy	186	212	239	271	296	319
Sulfonylurea–insulin	387	450	513	573	636	678

Holman RR.et al. N Engl J Med 2008

Timing of cardiovascular protection

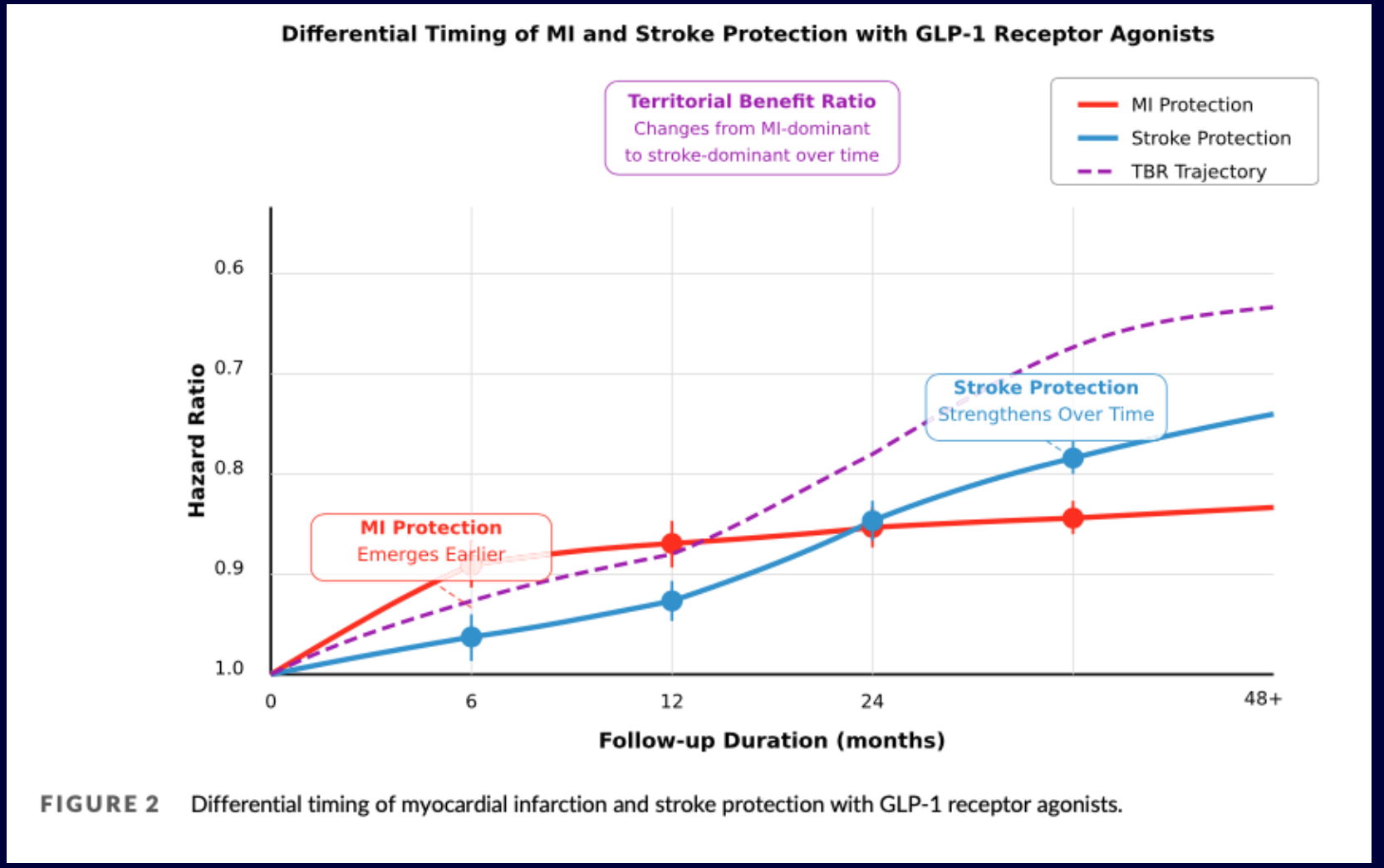


FIGURE 2 Differential timing of myocardial infarction and stroke protection with GLP-1 receptor agonists.

Alammari N et al Diabetes Obes Metab, 2025

Definition of prediabetes

Diabetologia

Table 1 Definitions of prediabetes

Definition	ADA Prediabetes	WHO Intermediate hyperglycaemia	IDF IFG, IGT
IFG			
FPG in mmol/l	5.6–6.9	6.1–6.9	6.1–6.9
FPG in mg/dl	100–125	110–125	110–125
IGT			
2 h PG in mmol/l	7.8–11.0	7.8–11.0	7.8–11.0
2 h PG in mg/dl	140–199	140–199	140–199
HbA_{1c}			–
mmol/mol	39–47		–
%	5.7–6.4		–

2 h PG, 2 h plasma glucose during 75 g OGTT; FPG, fasting plasma glucose

What is the key question?

- Is prediabetes associated with health outcomes, and how strong is the certainty of evidence?

Schlesinger S et al Diabetologia, 2021

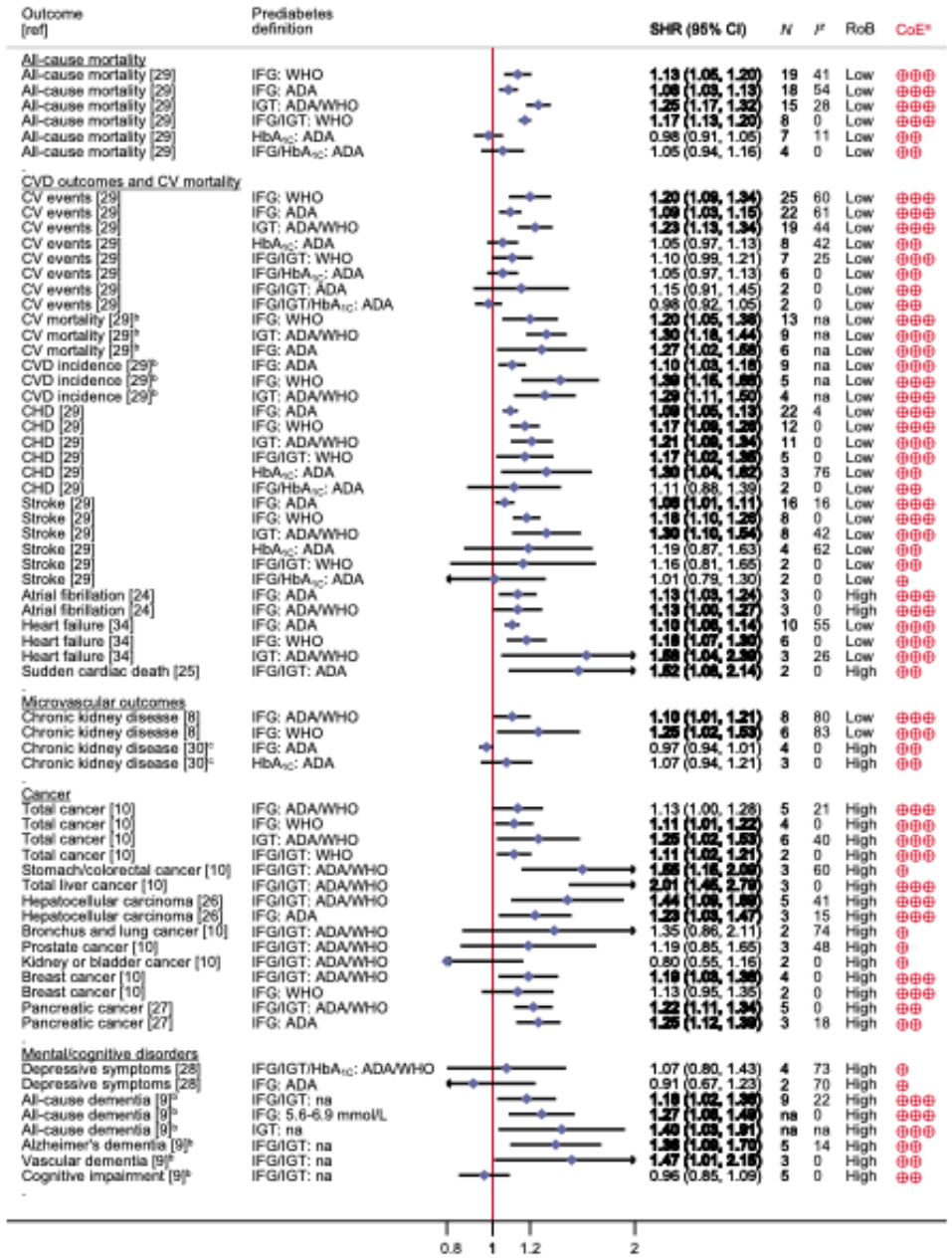


Fig. 2 Associations between prediabetes and risk of diabetes-related complications, comorbidities and mortality among the general population. [a]Interpretation of the certainty of evidence is denoted by crossed circles: four symbols, high; three symbols, moderate; two symbols, low; and one symbol, very low. [b]Could not be recalculated because of missing information. [c]Individuals with diabetes at follow-up were excluded. Boldface indicates that the 95% CI does not include the null value and findings are precisely estimated. CoE, certainty of evidence; CV, cardiovascular; *N*, number of primary studies; na, not available; RoB, risk of bias

Prediabetes and risk of mortality, diabetes-related complications and comorbidities: umbrella review of meta-analyses of prospective studies

Sabrina Schlesinger[1,2] · Manuela Neuenschwander[1,2] · Janett Barbaresko[1] · Alexander Lang[1] · Haifa Maalmi[2,3] · Wolfgang Rathmann[1,2] · Michael Roden[2,3,4] · Christian Herder[2,3,4]

Conclusions Prediabetes was associated with a higher relative risk of all-cause mortality and higher incidences of CV events, CHD, stroke, heart failure, atrial fibrillation, chronic kidney disease, total cancer, liver cancer, hepatocellular carcinoma, breast cancer and all-cause dementia with moderate certainty of evidence. Effect estimates were lower than comparable effect estimates for type 2 diabetes as exposure, suggesting a dose–response gradient in the relationship with complications.

Schlesinger S et al Diabetologia, 2021

Glycated Hemoglobin, Prediabetes, and the Links to Cardiovascular Disease: Data From UK Biobank

Diabetes Care 2020;43:440–445 | https://doi.org/10.2337/dc19-1683

Claire Welsh,[1] Paul Welsh,[1] Carlos A. Celis-Morales,[1] Patrick B. Mark,[1] Daniel Mackay,[2] Nazim Ghouri,[1] Fredrick K. Ho,[2] Lyn D. Ferguson,[1] Rosemary Brown,[1] James Lewsey,[2] John G. Cleland,[2] Stuart R. Gray,[1] Donald M. Lyall,[2] Jana J. Anderson,[2] Pardeep S. Jhund,[1] Jill P. Pell,[2] Darren K. McGuire,[3] Jason M.R. Gill,[1] and Naveed Sattar[1]

RESEARCH DESIGN AND METHODS

UK Biobank participants without baseline CVD or known diabetes (n = 357,833) were included. Associations of HbA1c with CVD was assessed using Cox models adjusting for classical risk factors. Predictive utility was determined by the C-index and net reclassification index (NRI). A separate analysis was conducted in 16,596 participants with known baseline diabetes.

In conclusion, in this very large well-phenotyped cohort with central laboratory assessment of HbA_{1c}, we show that HbA_{1c} minimally improves CVD risk prediction in patients without diabetes. The same is also true for the subset with prediabetes. The near twofold higher unadjusted risk for CVD in prediabetes is driven mainly by abnormal levels of conventional CVD risk factors. As such, and as recommended (14), this group would benefit from lifestyle advice to prevent diabetes and from having all conventional CVD risk factors assessed and, where relevant, treated.

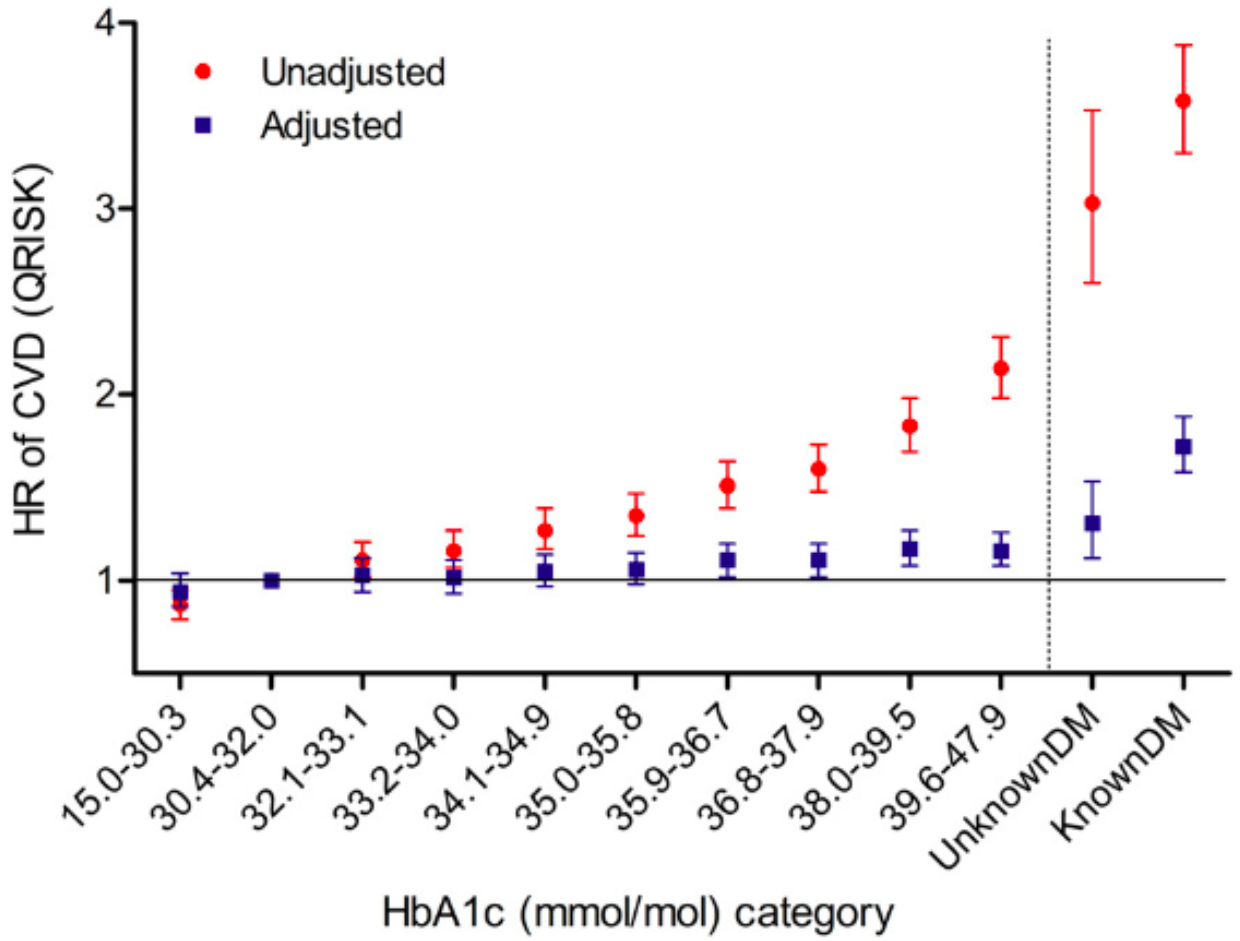
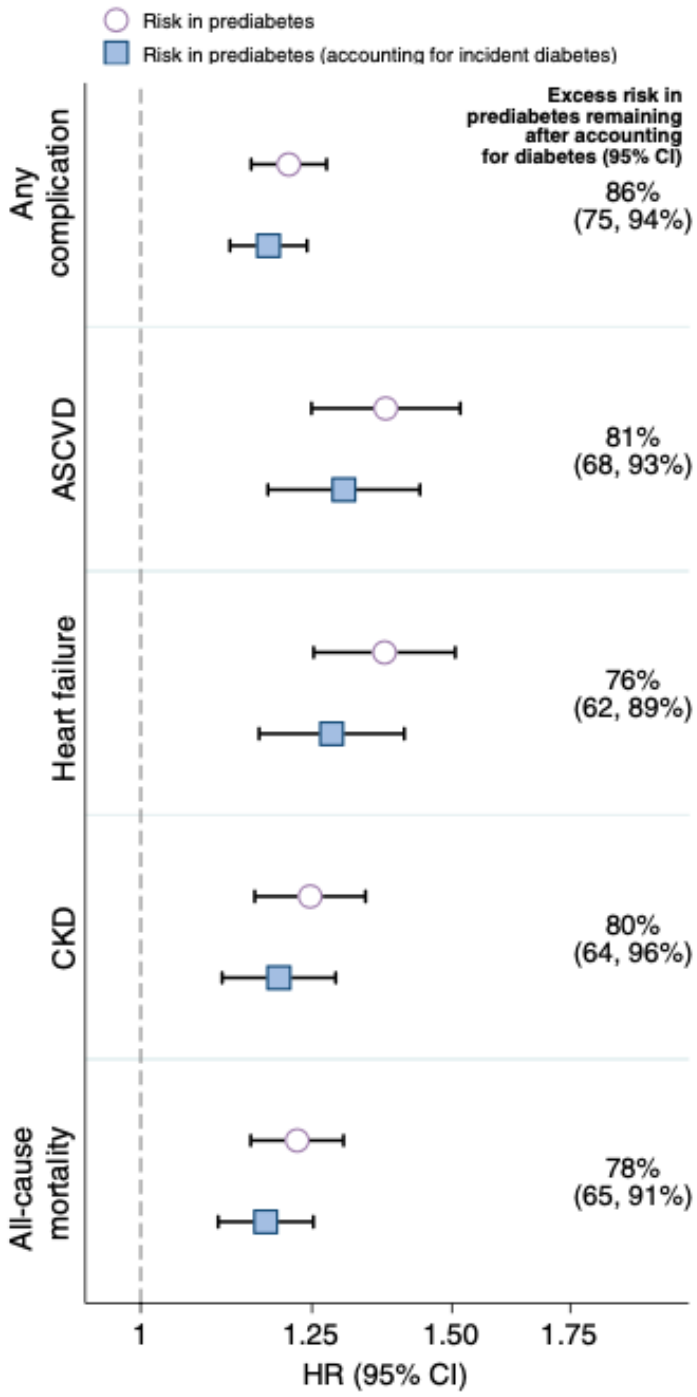


Figure 1—Unadjusted and adjusted (for QRISK3 risk factors) HRs of composite fatal/nonfatal CVD by deciles of baseline HbA_{1c} in those without baseline diabetes (n = 355,260) and in participants with undiagnosed diabetes (n = 2,573) or diagnosed diabetes (n = 16,596). For simplicity, categories are depicted only as mmol/mol. The dashed line represents ≥48 mmol/mol (6.5%). Please note all results referent to decile 2 (30.4–32.0 mmol/mol).

Welsh C et al Diabetes Care, 2020



Prediabetes is associated with elevated risk of clinical outcomes even without progression to diabetes

Mary R. Rooney[1,2] · Amelia S. Wallace[1,2] · Justin B. Echouffo Tcheugui[2,3] · Michael Fang[1,2] · Jiaqi Hu[1,2,4] · Pamela L. Lutsey[5] · Morgan E. Grams[6] · Josef Coresh[7] · Elizabeth Selvin[1,2]

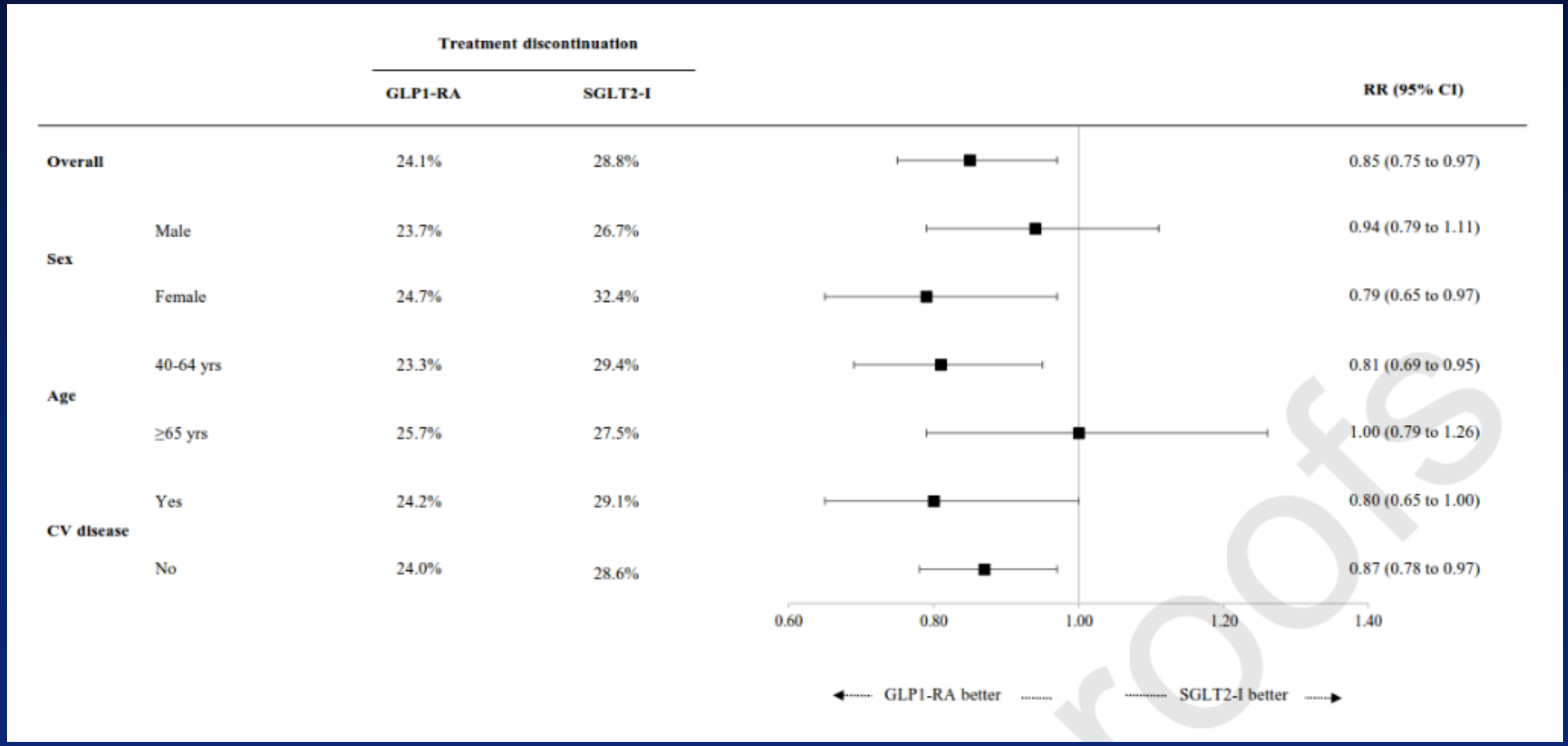
10310 participants from the Atherosclerosis Risk in Communities (ARIC) Study without diabetes at baseline (1990–1992)

Follow-up: 30 years

For the first time analysis was adjusted for incident diabetes

Rooney MR al Diabetologia, 2025

High discontinuation rate



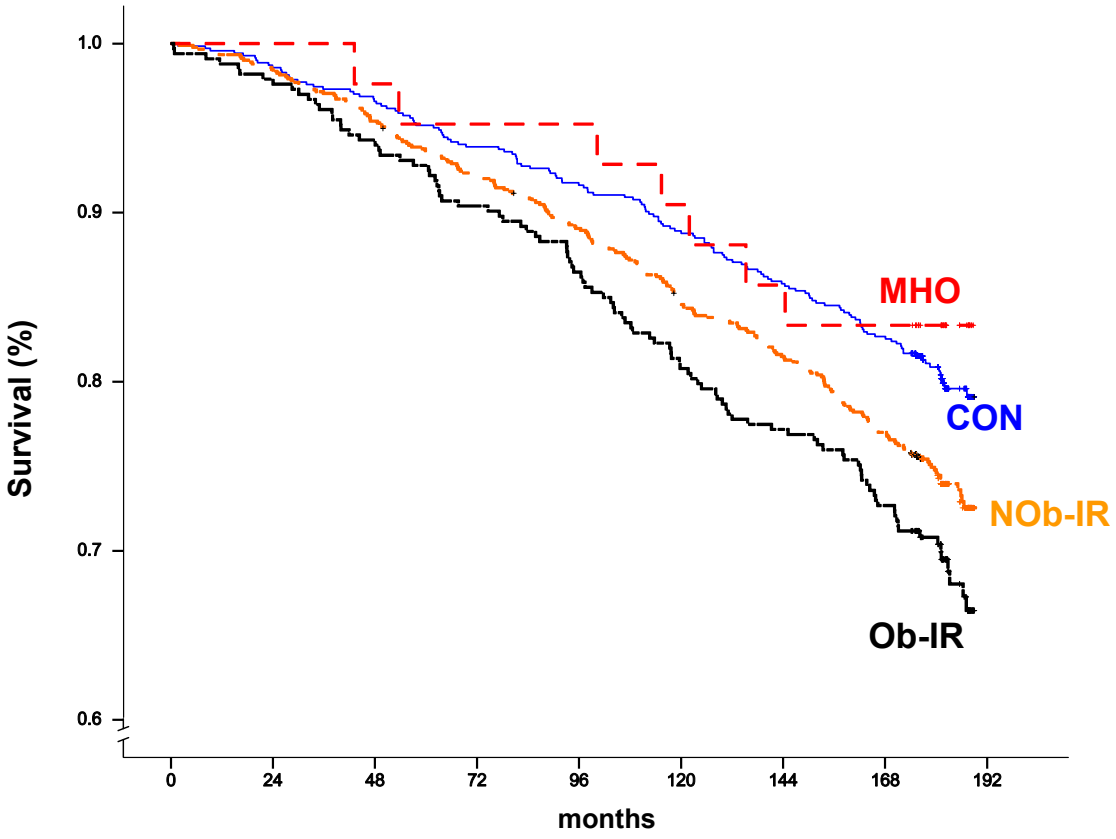
Rea F, Ciardullo S et al Diabetes Res Clin Pract, 2021

Prognosis of obese metabolically-healthy individuals the Cremona Study

All–cause mortality

The total number of deaths after 15 years was 495

CVD: 221
cancer: 180



Non-obese insulin sensitive **(CON)**	708	693	679	662	645	625	603	581	366
Non-obese insulin resistant **(NOb-IR)**	923	899	872	841	812	769	741	699	462
Metabolically healthy obese **(MHO)**	43	43	41	40	40	38	35	35	27
Obese insulin resistant **(Ob-IR)**	337	325	313	301	288	269	257	242	171

obese insulin-resistant (HR: 1.37; 95% CI: 1.09-1.72; P=0.01)
obese metabolically healthy (HR: 0.98; 95% CI: 0.46-2.07; P=0.95)

Calori G et al Diabetes Care, 2011

Relationship of DM Duration and HR for CVD Events with Intensive Therapy