



VIII CONGRESSO
NAZIONALE
PIEDE DIABETICO
INTERASSOCIATIVO SID-AMD

*Focus sul piede nella
gestione del diabete*

ROMA, 18-20 GIUGNO 2026
HOTEL NH VILLA CARPEGNA

Il ruolo dei GLP1 e GLP1-GIP RA nella protezione vascolare del piede diabetico

Dott.ssa Silvia Acquati

UOC Endocrinologia e Malattie Metaboliche Romagna

AUSL Romagna

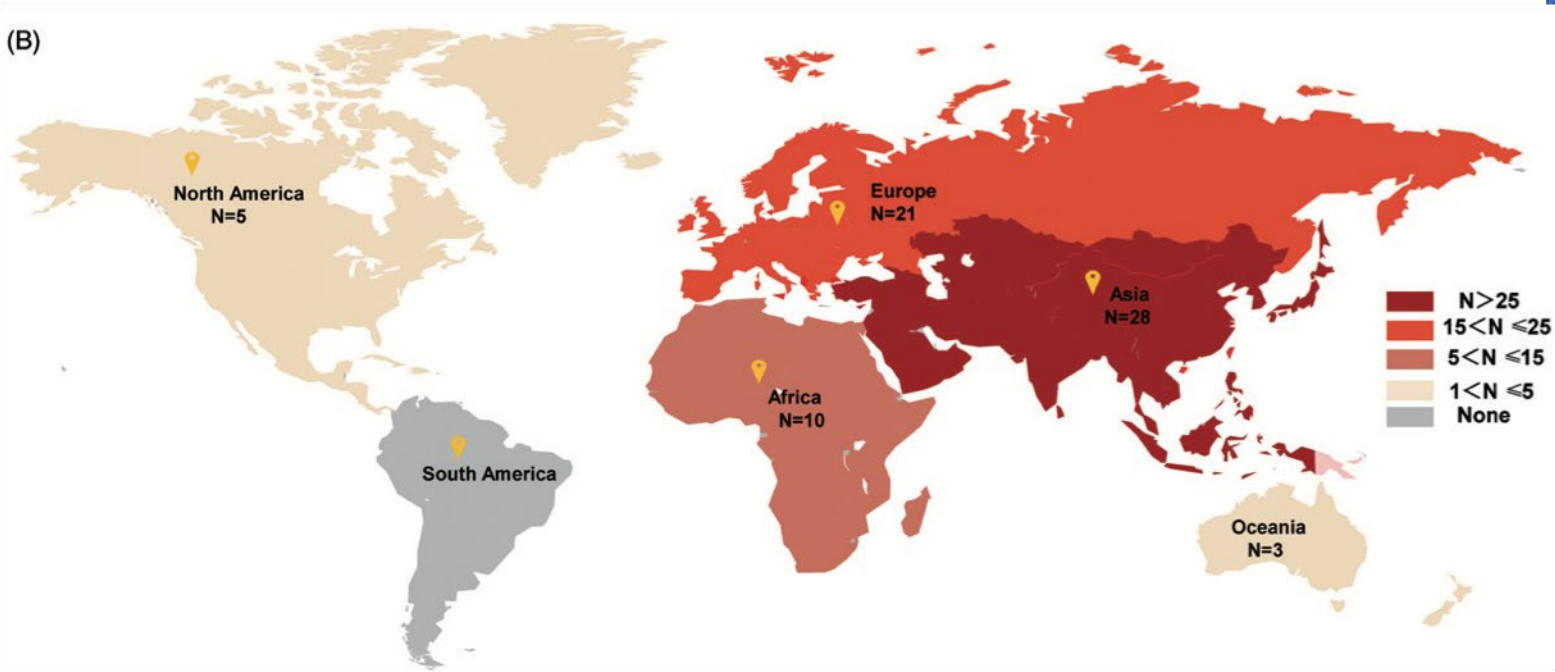
La sottoscritta dichiara di NON aver ricevuto negli ultimi due anni compensi o finanziamenti da Aziende Farmaceutiche e/o Diagnostiche

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.).

Global epidemiology of diabetic foot ulceration: a systematic review and meta-analysis

Pengzi Zhang, Jng Lu, Yali Jng, Sunyinyan Tang, Dalong Zhu & Yan Bi

WHO mortality database → 7 milioni di decessi nei diabetici
27% dei decessi dovuto a complicanze macrovascolari



Prevalenza alta North America (13.0%),
Prevalenza bassa in Oceania (3.0%) and Europe (5.1%).

Table 1. Prevalence of diabetic foot ulcer in each country.

Country	No. of studies	Prevalence	95%CI	I ²
Belgium	1	16.6	10.7–22.4	NA
Canada	1	14.8	9.4–20.1	NA
USA	3	13	8.3–17.7	98
Trinidad	1	12.2	10.8–13.6	NA
India	2	11.6	6.4–16.8	90.8
Norway	1	10.4	8.8–11.9	NA
Cameroon	3	9.9	6.3–13.5	86.6
Italy	1	9.7	7.8–11.6	NA
Thailand	2	8.8	1.7–15.9	95
Iran	2	8.1	0.1–16.1	94.9
Denmark	1	7.8	5.6–10.1	NA
Pakistan	4	7.4	0.5–14.3	99
Tanzania	2	7.3	2.1–12.6	83.4
Pacific island countries	1	6.8	4.5–9.0	NA
UK	4	6.3	4.6–8.0	79.8
Egypt	2	6.2	4.1–8.2	49.8
Bahrain	1	5.9	4.7–7.1	NA
South Africa	2	5.8	3.8–7.9	0
France	1	5.6	2.4–8.7	NA
Greece	1	4.8	3.3–6.2	NA
Jordan	2	4.2	3.4–5.1	0
China	10	4.1	3.1–5.2	97.4
Uganda	1	4	1.6–6.4	NA
Ireland	1	3.9	2.3–5.5	NA
Turkey	1	3.1	1.9–4.3	NA
Spain	5	3	1.9–4.4	97
Germany	2	2.8	2.4–3.3	0
Saudi Arabia	1	2.3	2.2–2.4	NA
Japan	1	2	1.4–2.6	NA
Netherland	2	1.8	1.0–2.6	0
Korea	2	1.7	0.6–2.9	85.1
Poland	1	1.7	1.1–2.3	NA
Australia	2	1.5	0.7–2.4	58.1

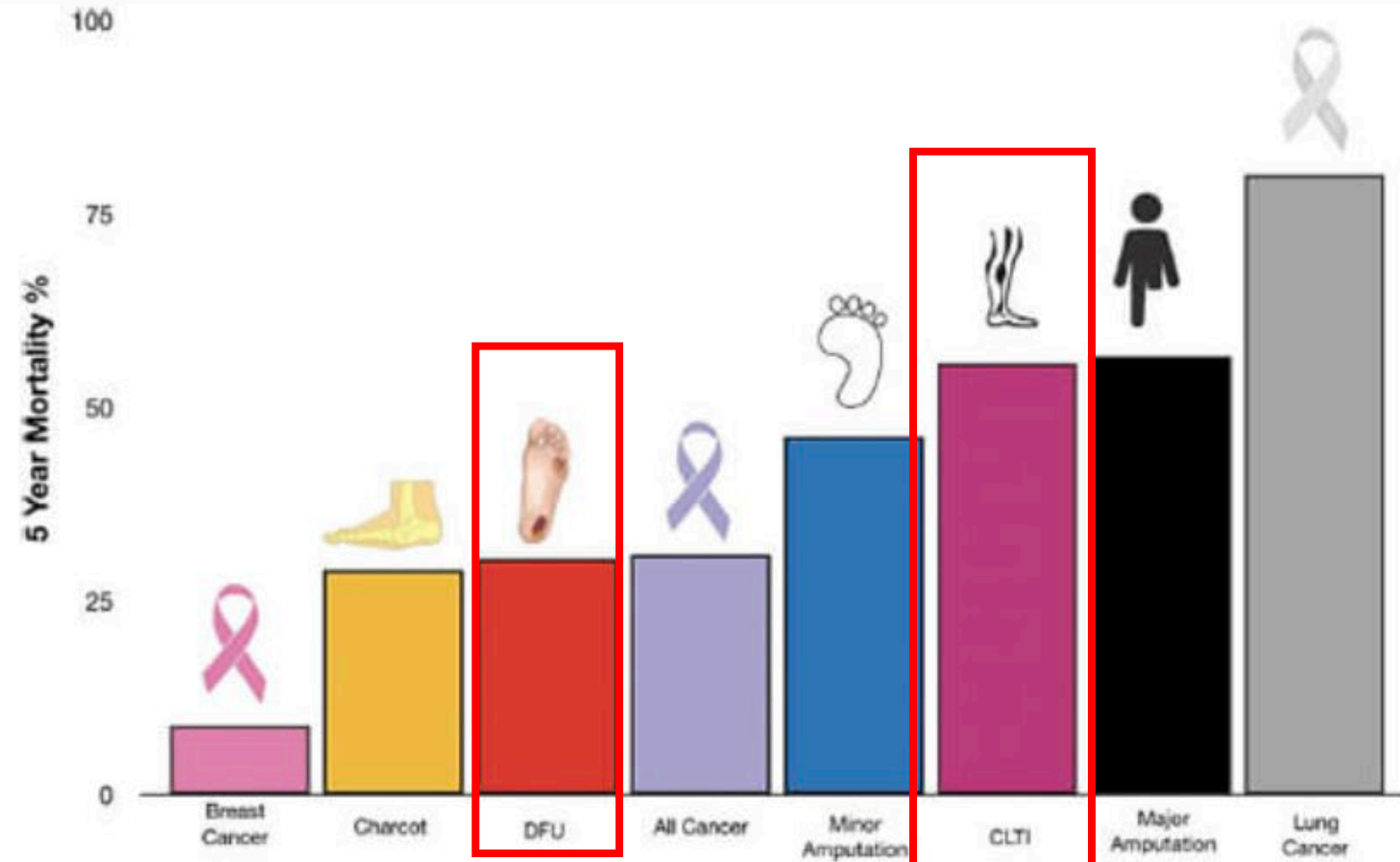
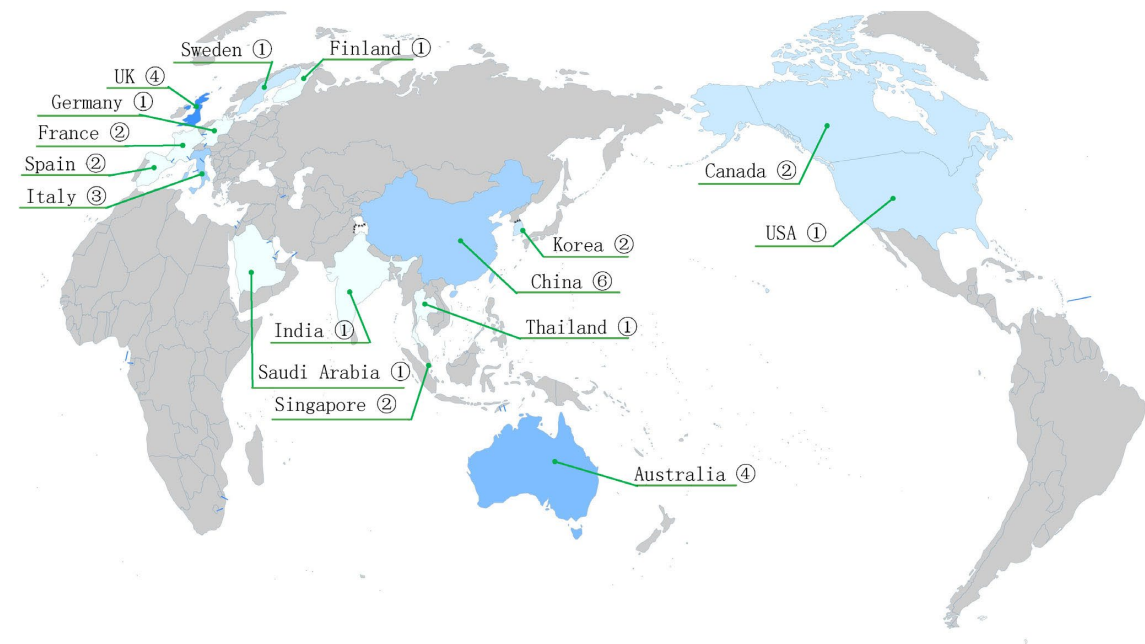
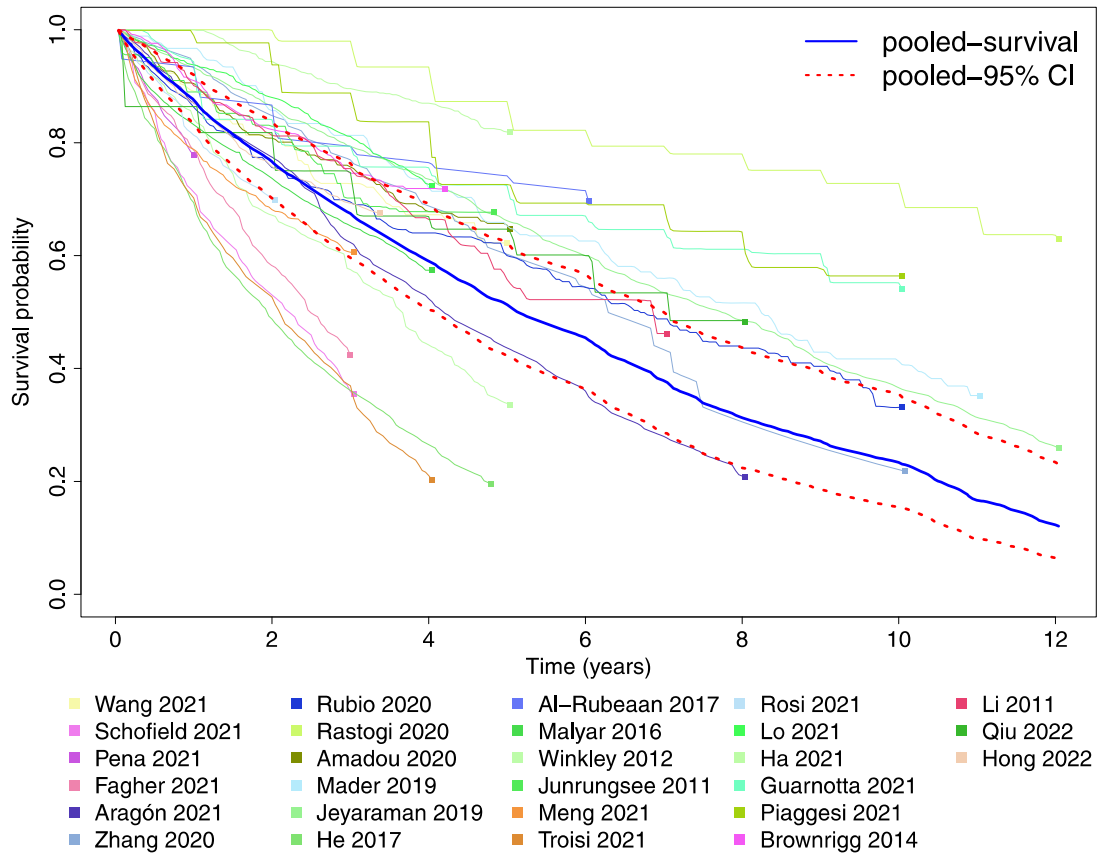


Fig. 1 Five Year Mortality of Diabetic Foot Complications and Cancer. Diabetic foot complications compared to cancer. DFU = diabetic foot ulcers [11] = 30.5%. Charcot = Charcot neuroarthropathy of the foot [14]. All Cancer = pooled 5 year survival of all cancers [11]. CLTI = chronic limb threatening ischemia [28, 29]. Major Amputation = above foot amputation [20–22, 26, 27]. Minor Amputation = foot level amputation [17, 27]

Global mortality of diabetic foot ulcer: A systematic review and meta-analysis of observational studies

Lihong Chen MD¹ | Shiyi Sun MD¹ | Yunyi Gao MD² | Xingwu Ran MD¹ 



I TASSI DI SOPRAVVIVENZA:

A 1 ANNO 86.9%

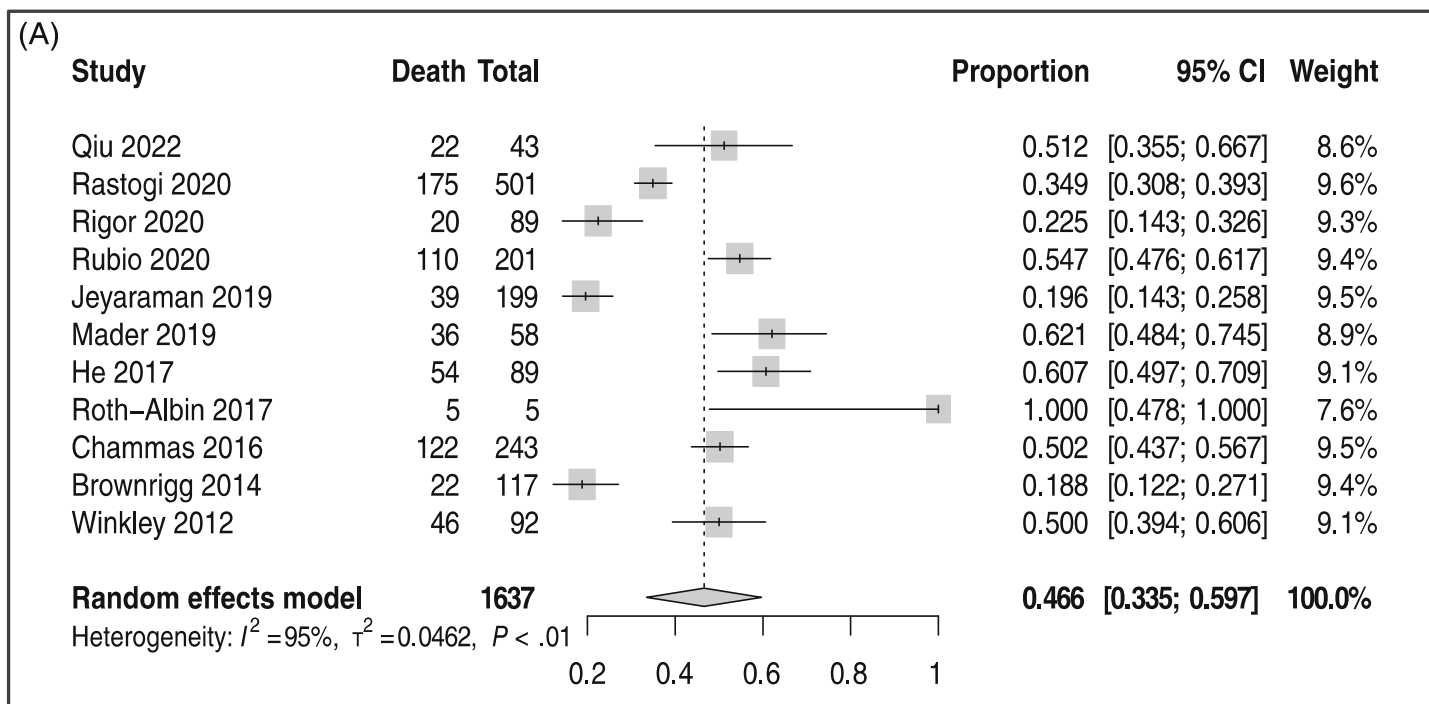
A 3 ANNI 66.9%

A 5 ANNI 50.9%

Diabetes Obes Metab. 2023;25:36–45.

PRINCIPALI CAUSE DI MORTALITA' IN DFU

MORTALITA' PER CAUSE CARDIOVASCOLARI



1° CAD (46.6%)
2° INFEZIONI (24.8%)

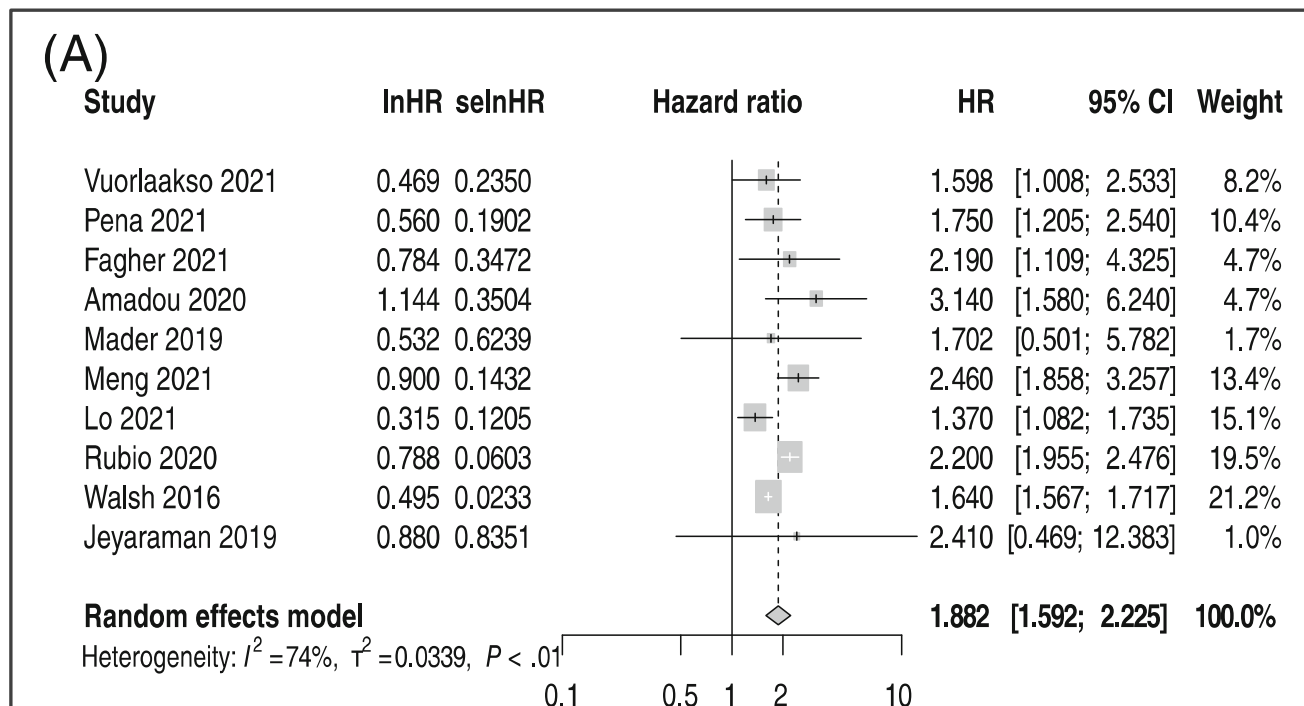
Diabetes Obes Metab. 2023;25:36–45.

FATTORI DI RISCHIO

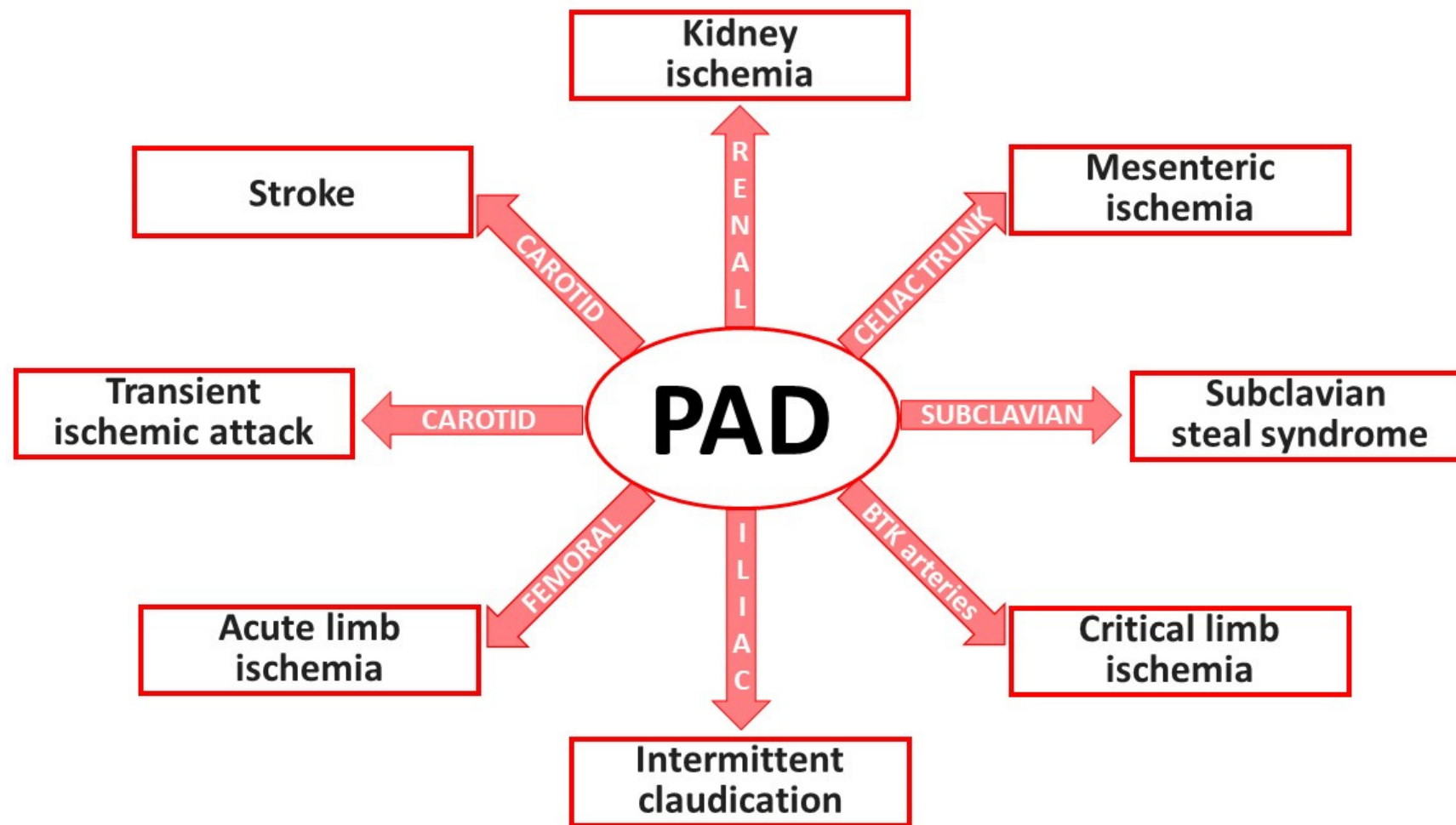
AUMENTATA MORTALITA':

- ✓ PAD
- ✓ CKD
- ✓ ESRD
- ✓ AMPUTAZIONE
- ✓ PREGRESSO EVENTO CARDIOVASCOLARE

PAD → 88%



TRATTARE IN MODO AGGRESSIVO I FDR CARDIOVASCOLARI



Biomedicines **2023**, *11*, 3131

Quadri di PAD sempre piu' complessi in pazienti sempre più fragili

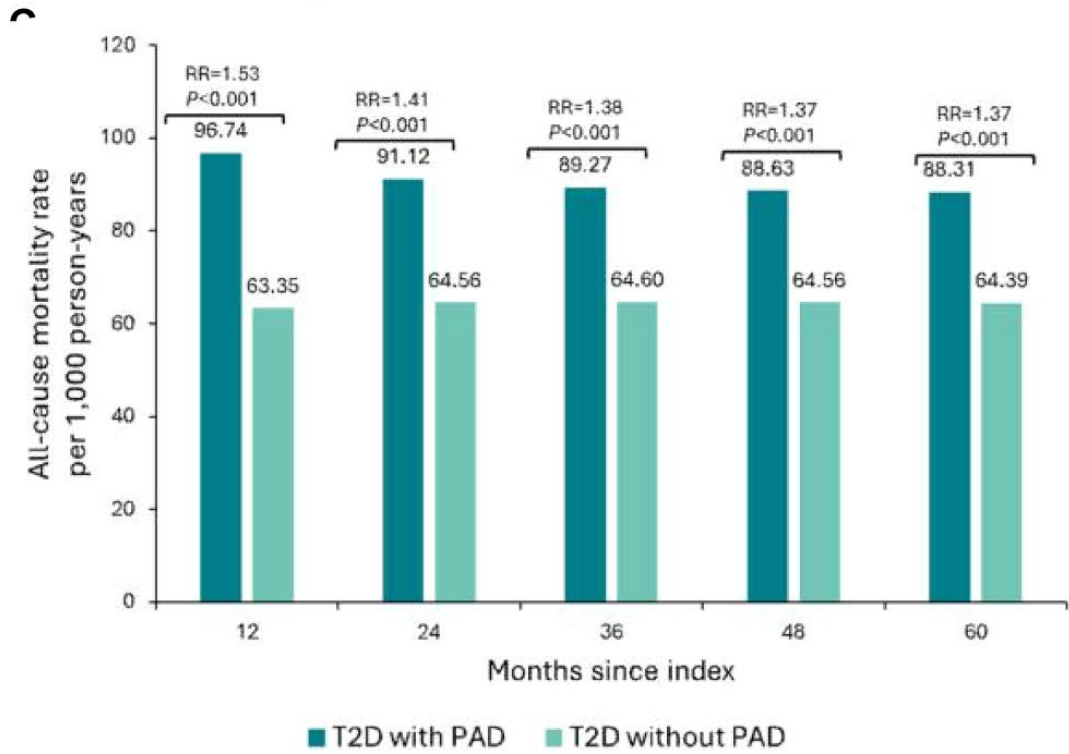




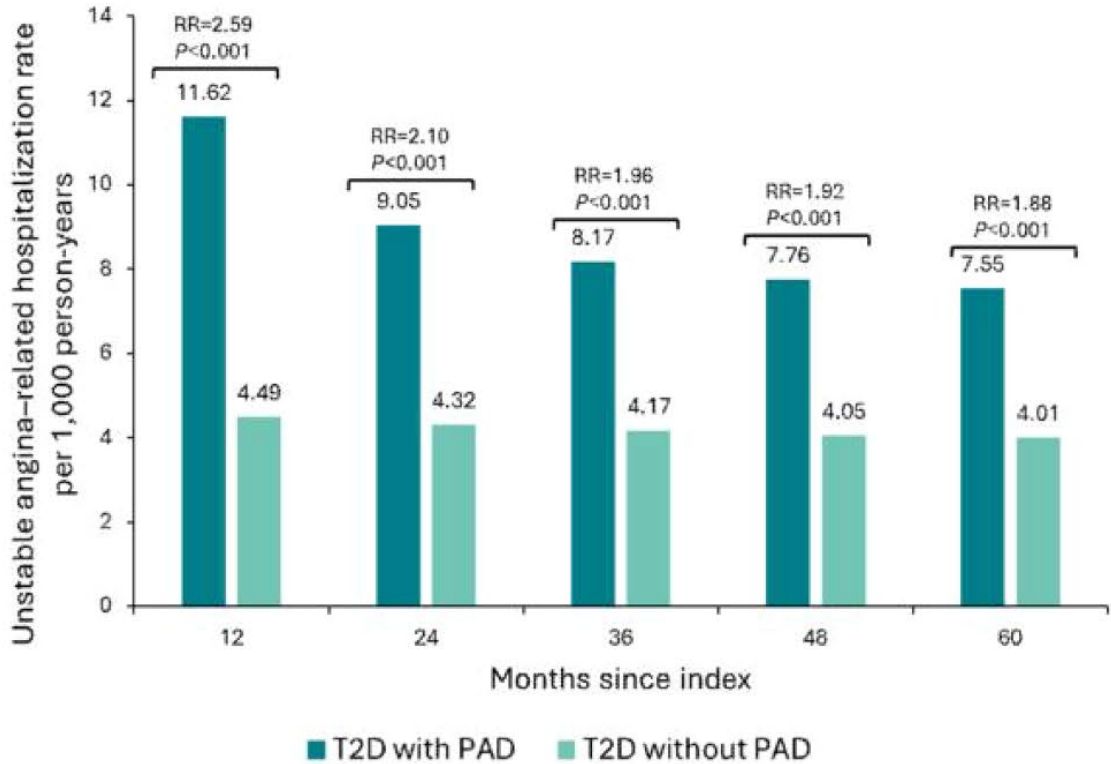
Impact of peripheral artery disease (PAD) on risk of major adverse cardiovascular events (MACE) in patients with type 2 diabetes

James Amamoo^a, Lin Xie^{a,*}, Andrea Steffens^b, Erin Buysman^b, Caroline Swift^a, Sherif Mehanna^a, Noelle N. Gronroos^b, Marc P. Bonaca^{c,d}

INFARTO MIOCARDICO

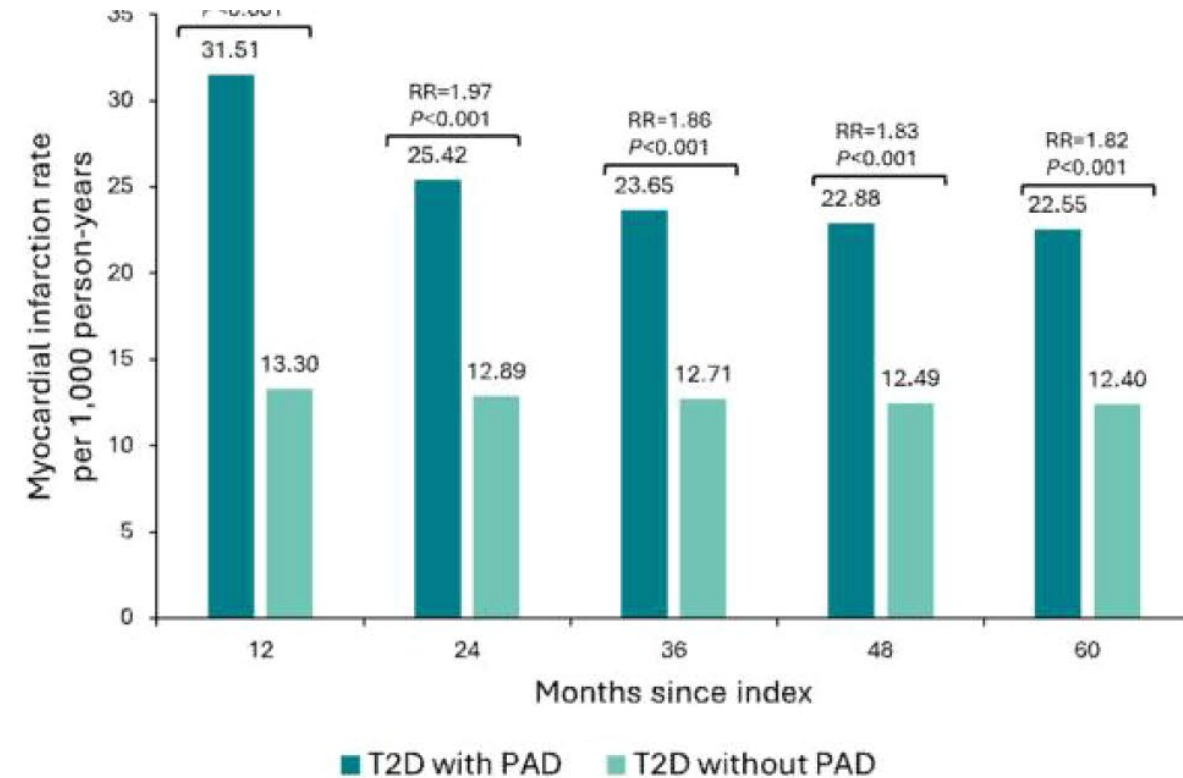


ICTUS ISCHEMICO

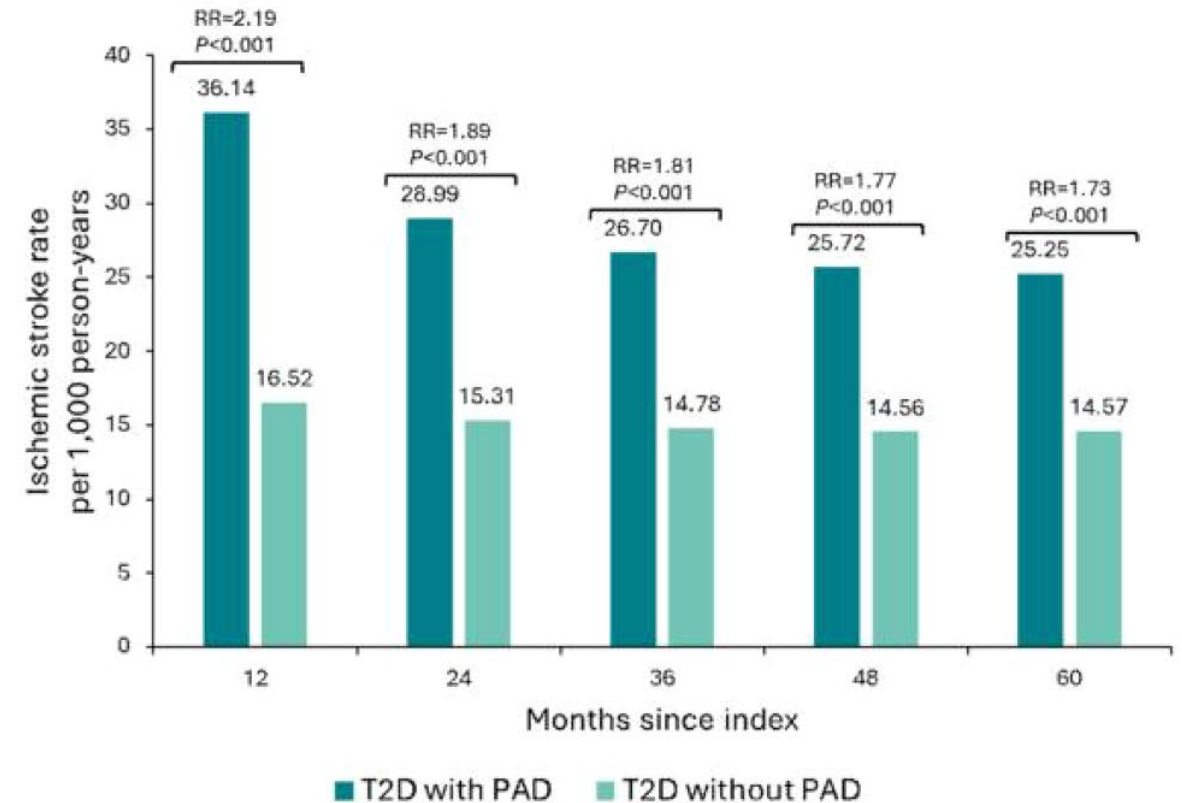


Mortalità nel piede diabetico vascolare

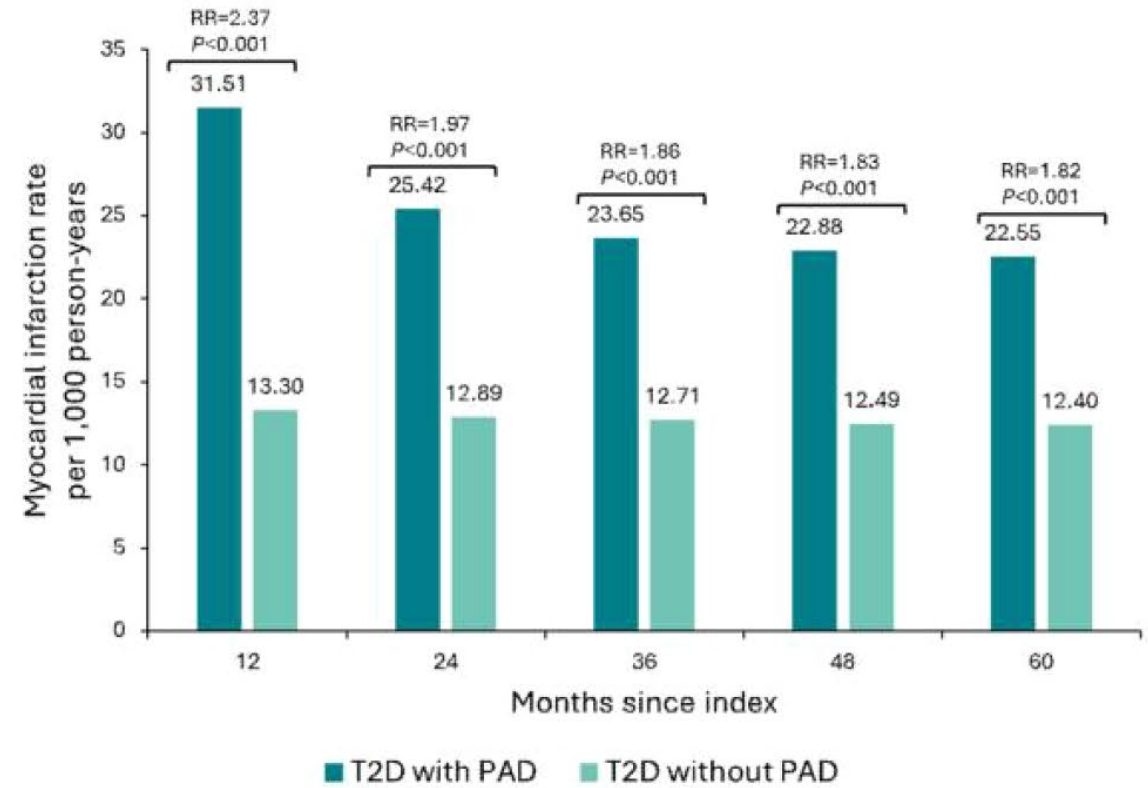
MORTALITA' PER TUTTE LE CAUSE



OSPEDALIZZAZIONI PER ANGINA INSTABILE



OSPEDALIZZAZIONI PER SCOMPENSO CARDIACO



B.

T2D with PAD vs T2D without PAD, incidence per 1000 person-years

	Overall		Patients aged ≥65 years		Widespread atherosclerosis	
	Ratio	P value	Ratio	P value	Ratio	P value
Ischemic stroke	2.19	<0.001	2.12	<0.001	2.08	<0.001
MI	2.37	<0.001	2.27	<0.001	2.29	<0.001
Unstable angina-related hospitalization	2.59	<0.001	2.52	<0.001	2.56	<0.001
Heart failure-related hospitalization	2.05	<0.001	1.98	<0.001	2.00	<0.001
All-cause mortality	1.53	<0.001	1.50	<0.001	1.45	<0.001
MACE						
2-point MACE ^a	2.27	<0.001	2.19	<0.001	2.19	<0.001
3-point MACE ^b	1.74	<0.001	1.69	<0.001	1.68	<0.001
5-point MACE ^c	1.83	<0.001	1.77	<0.001	1.81	<0.001

D.



Table 2. Microvascular and Macrovascular related complications, and concomitant comorbidities.

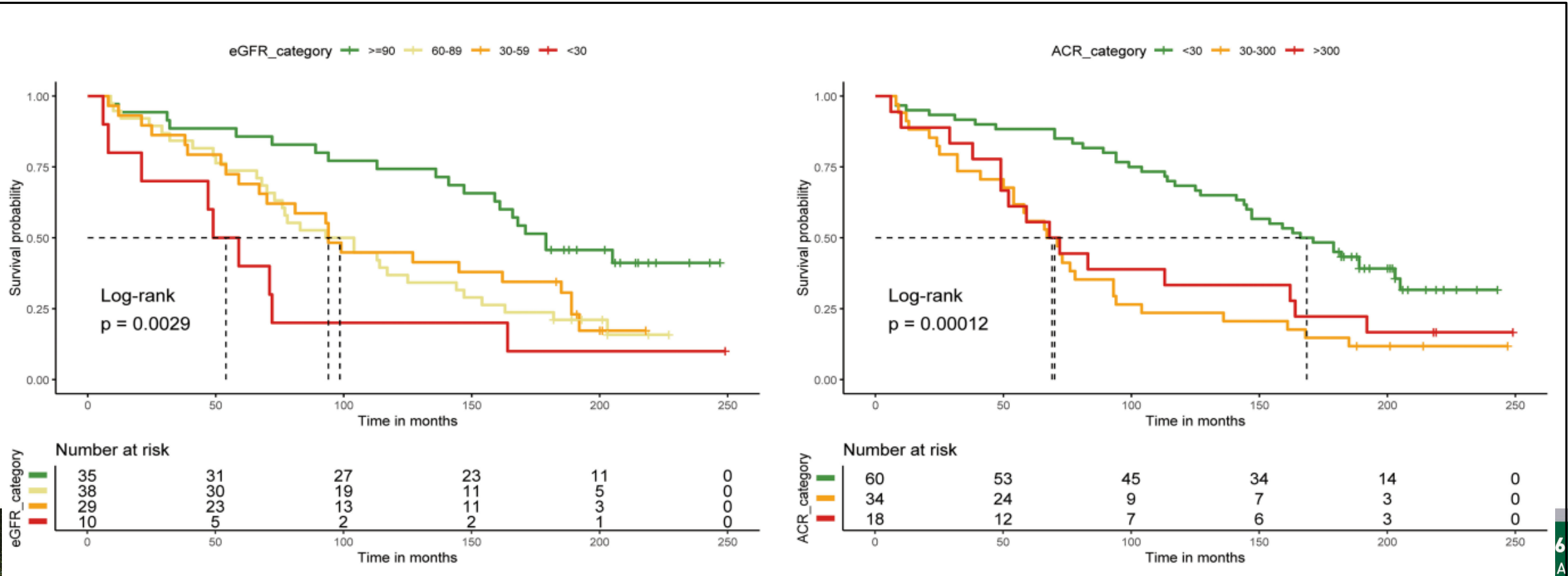
Microvas. Complications	<i>n</i> = 1198	Neuropathic DF (<i>n</i> = 386)	Ischemic DF (<i>n</i> = 812)	<i>p</i> -Value
Retinopathy	612 (51.2%)	194 (50.2%)	420 (51.7%)	0.7
Nephropathy	410 (34.2%)	88 (22.8%)	321 (39.6%)	<0.0001
Peripheral neuropathy	1102 (92%)	386 (100%)	716 (88.2)	0.0002
Macrovas. Complications				
Ischemic heart disease	388 (32.4%)	88 (22.8%)	(299) 36.9%	0.0004
Cerebrovascular disease	192 (14.3%)	8.3%	(140) 17.2%	0.002
Peripheral arterial disease	812 (67.8%)	—	812 (100%)	
Comorbidities				
Hypertension	950 (79.3%)	284 (73.6%)	666 (82%)	0.01
Dyslipidemia	482 (40.2%)	168 (43.5%)	314 (38.7%)	0.2
Heart failure	269 (22.4%)	68 (10.1%)	201 (24.7%)	0.0002
ESRD	240 (20%)	21 (5.4%)	219 (27%)	0.0001
Anemia	226 (18.8%)	31 (8%)	195 (24%)	0.0003
Smoke	90 (7.5%)	24 (6.2%)	66 (8.1%)	0.4

Microvasc.: microvascular; macrovasc.: macrovascular; ESRD: end-stage-renal-disease.

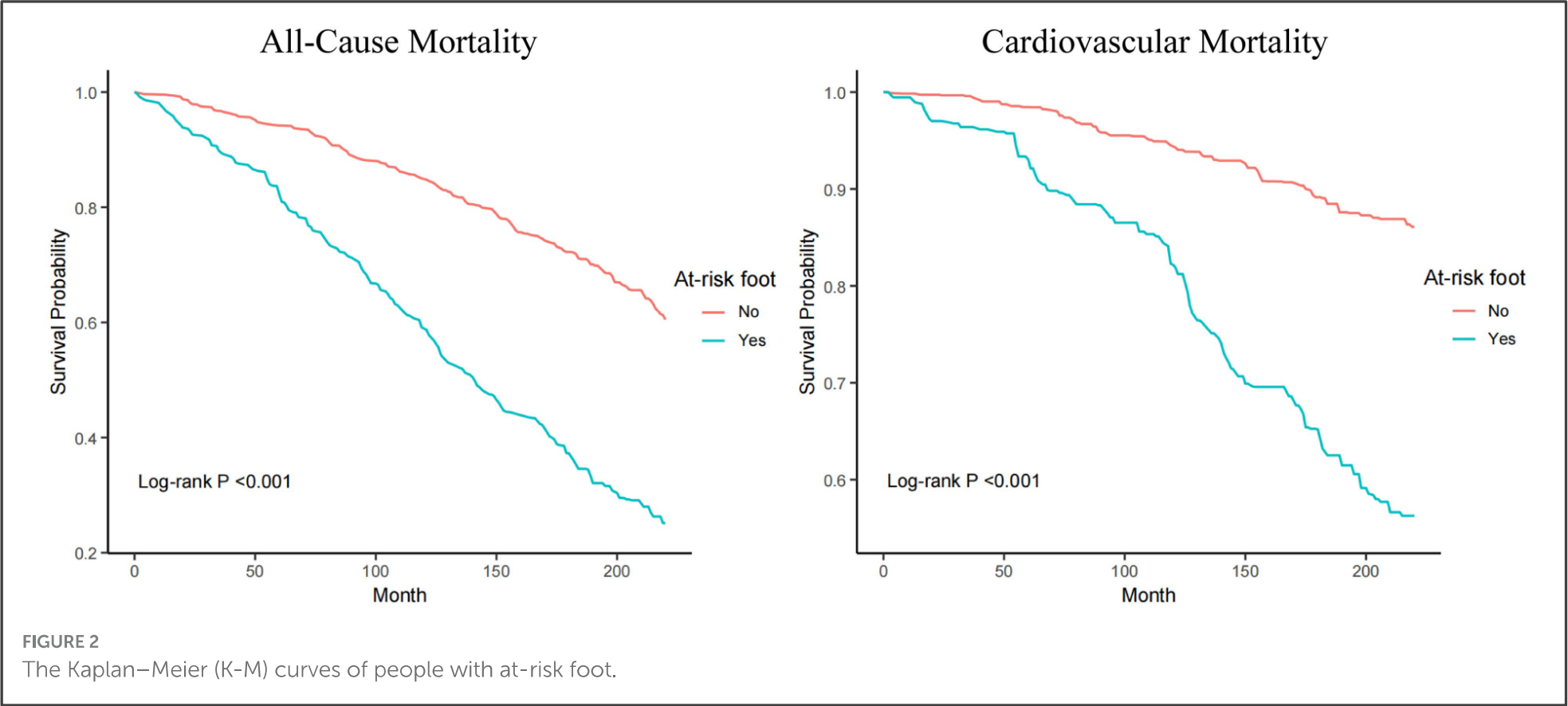
Correlation between chronic kidney disease and all-cause mortality in diabetic foot ulcers: evidence from the 1999-2004 national health and nutrition examination survey (NHANES)

Jiaru Liang^{1,2}, Hang An², Xuyang Hu², Yuling Gao¹, Jiaqi Zhou Xiaoyang Gong^{1*}, Junwei Zong^{3*} and Yong Liu^{1,2,4*}

DFU + DKD E MORTALITA'



PIEDE AD ALTO RISCHIO:
PAD and/or PN,



DIAGNOSI PRECOCE ED INTERVENTO PRECOCE DI PAD E PN NEI DIABETICI PER RIDURRE IL RISCHIO DI MORTALITA'

RIASSUMENDO...

- I pazienti con sindrome del piede diabetico sono ad alto rischio cardiovascolare
- Presentano mortalità aumentata soprattutto per cause cardiovascolari

- La mortalità

QUALE STRATEGIE TERAPEUTICHE ?

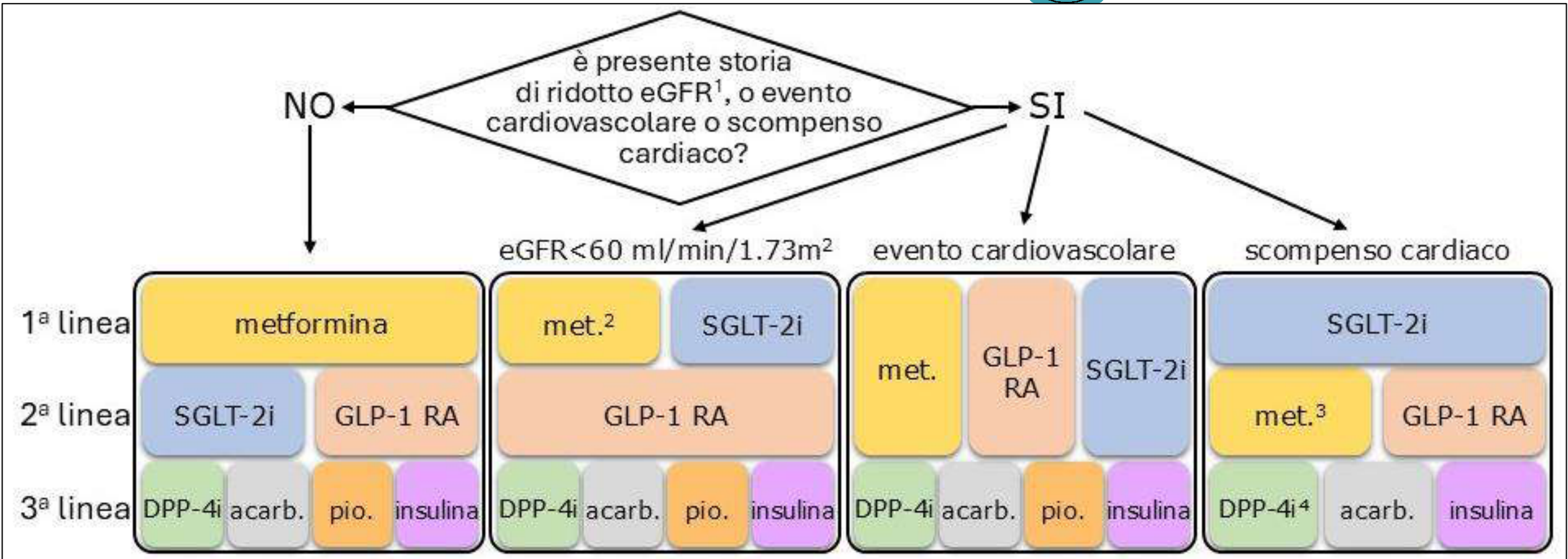
- Trattare precocemente l'FDR cardiovascolare è fondamentale per ridurre i tassi di morbilità e mortalità
- Necessario un approccio terapeutico cardio-renale e il trattamento multifattoriale di tutti i fattori di rischio cardiovascolari



Use of glucose-lowering medications in the management of type 2 diabetes
(For recommendations for specific conditions, including non-glucose-lowering medications, refer to pertinent sections)

Healthy lifestyle behaviors; diabetes self-management education and support; social determinants of health

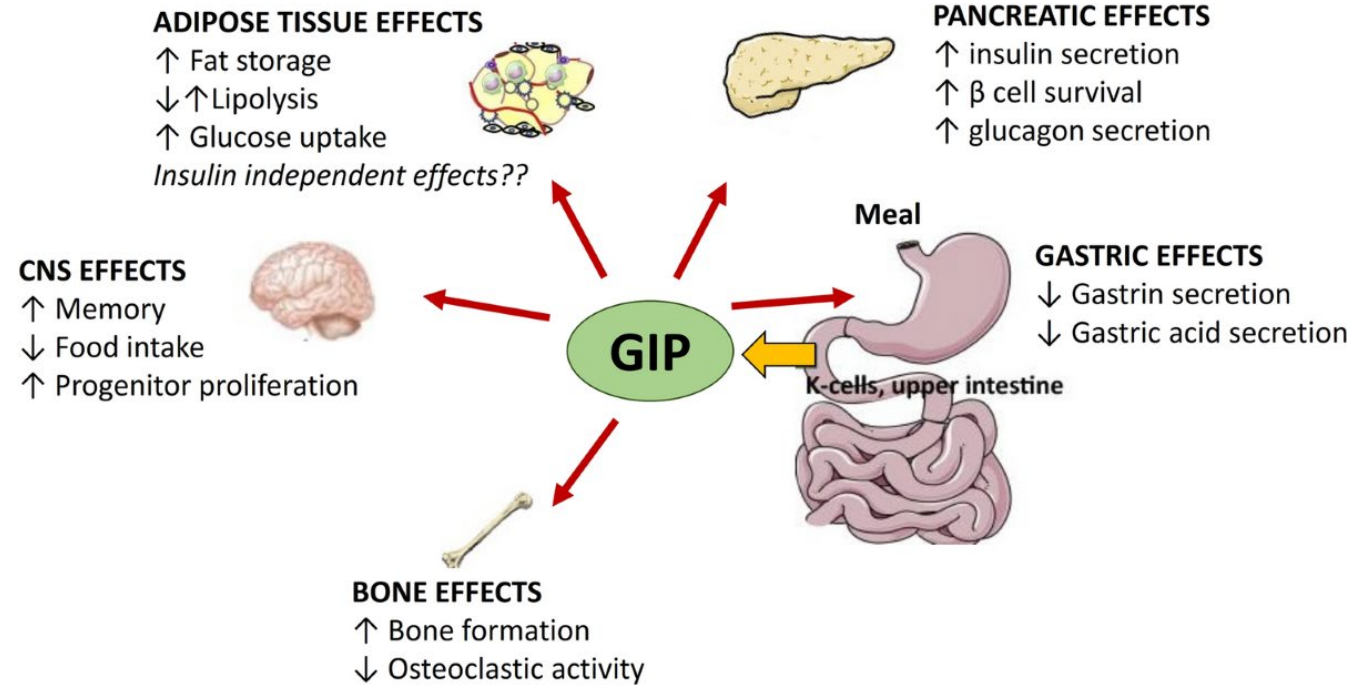
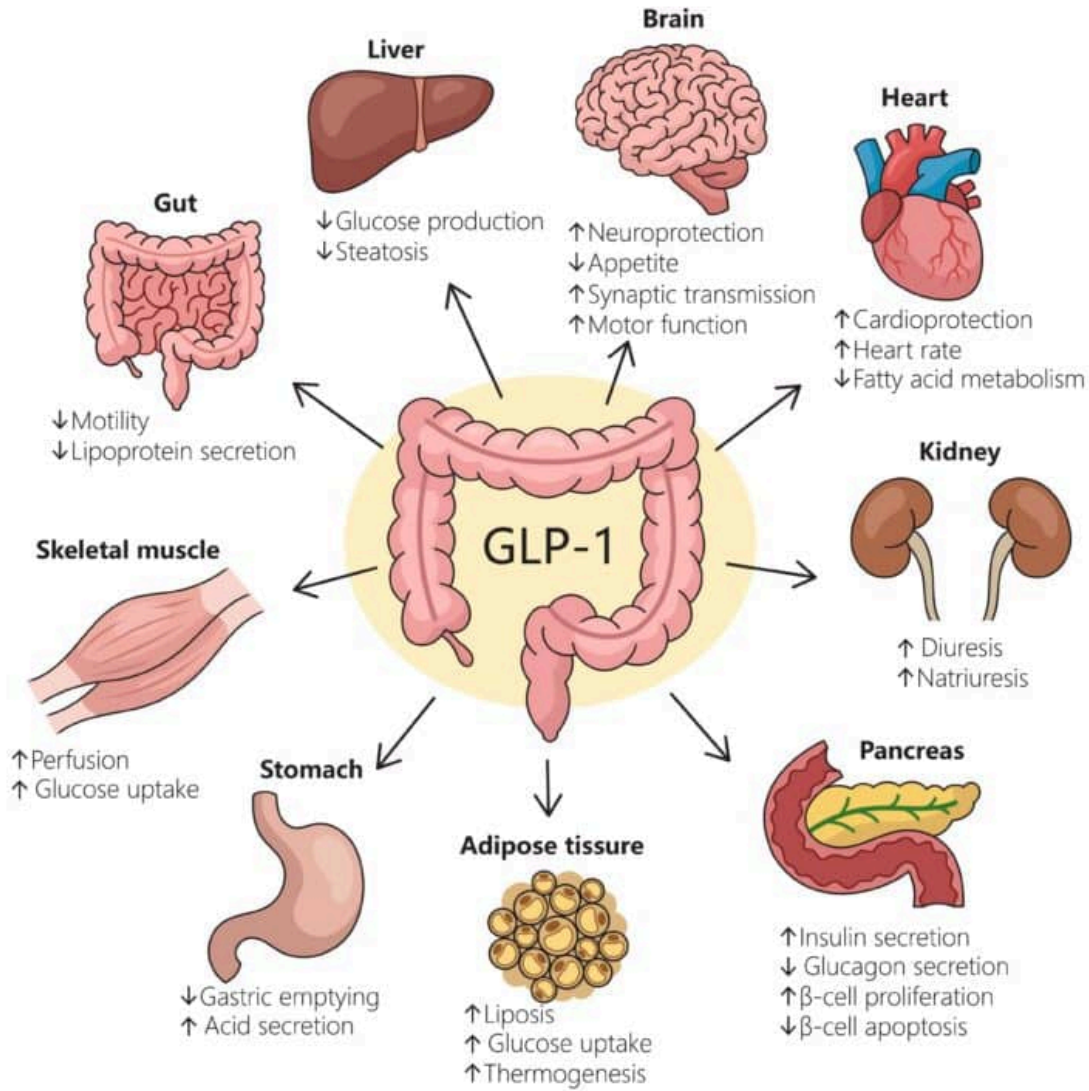
To avoid therapeutic inertia, reassess and modify treatment regularly (3-6 months)



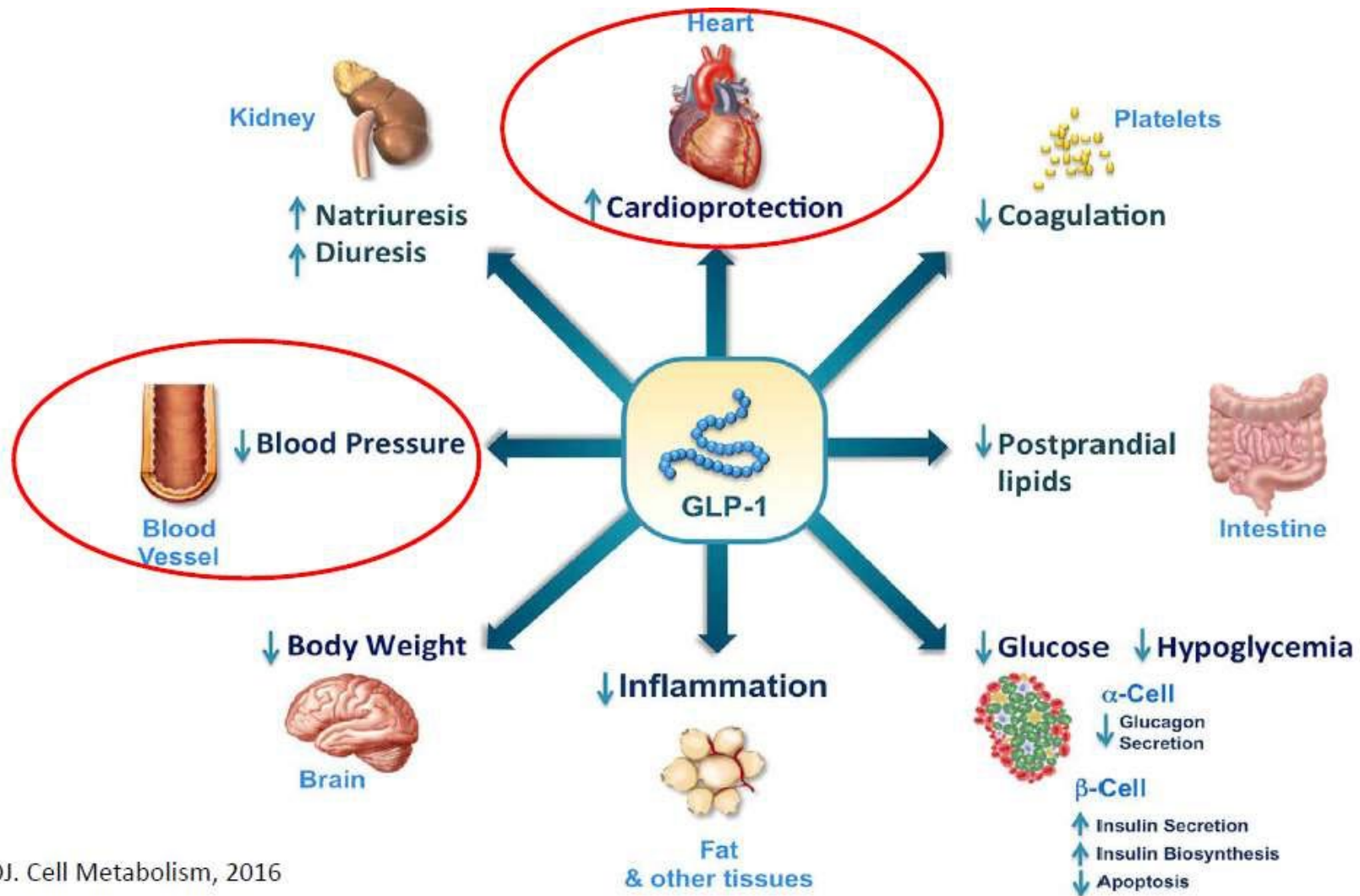
+Mitigating risk of MASLD or MASH

- Refer to DSMES to support self-efficacy in achievement of treatment goal
- Consider technology (e.g., diagnostic or personal CGM) to identify therapeutic gaps and tailor therapy
- Identify and address SDOH that affect achievement of treatment goals

GLP1 RA e GLP1-GIP RA

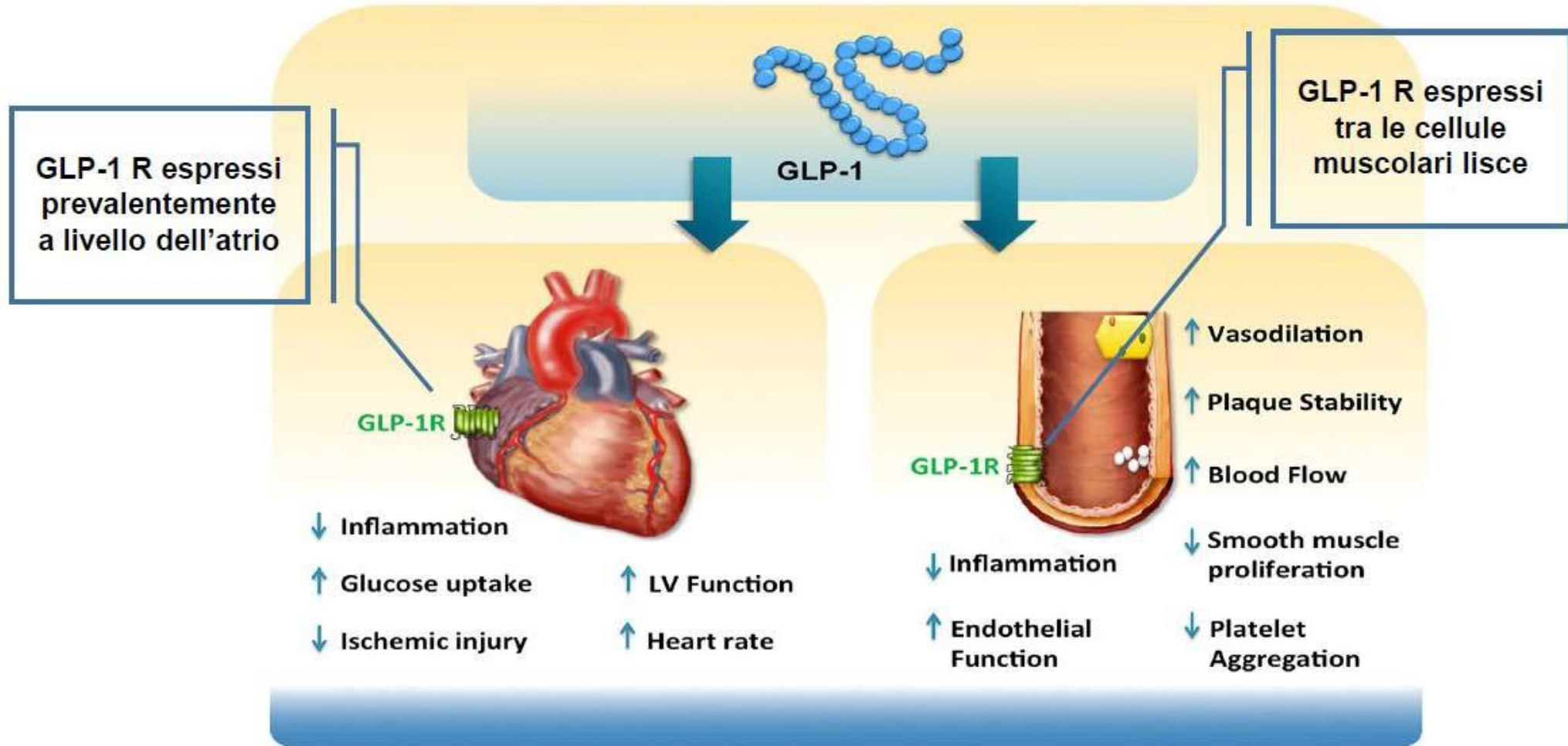


GLP1 RA OLTRE IL CONTROLLO GLICEMICO



Drucker DJ. Cell Metabolism, 2016

EFFETTI CARDIOVASCOLARI GLP1

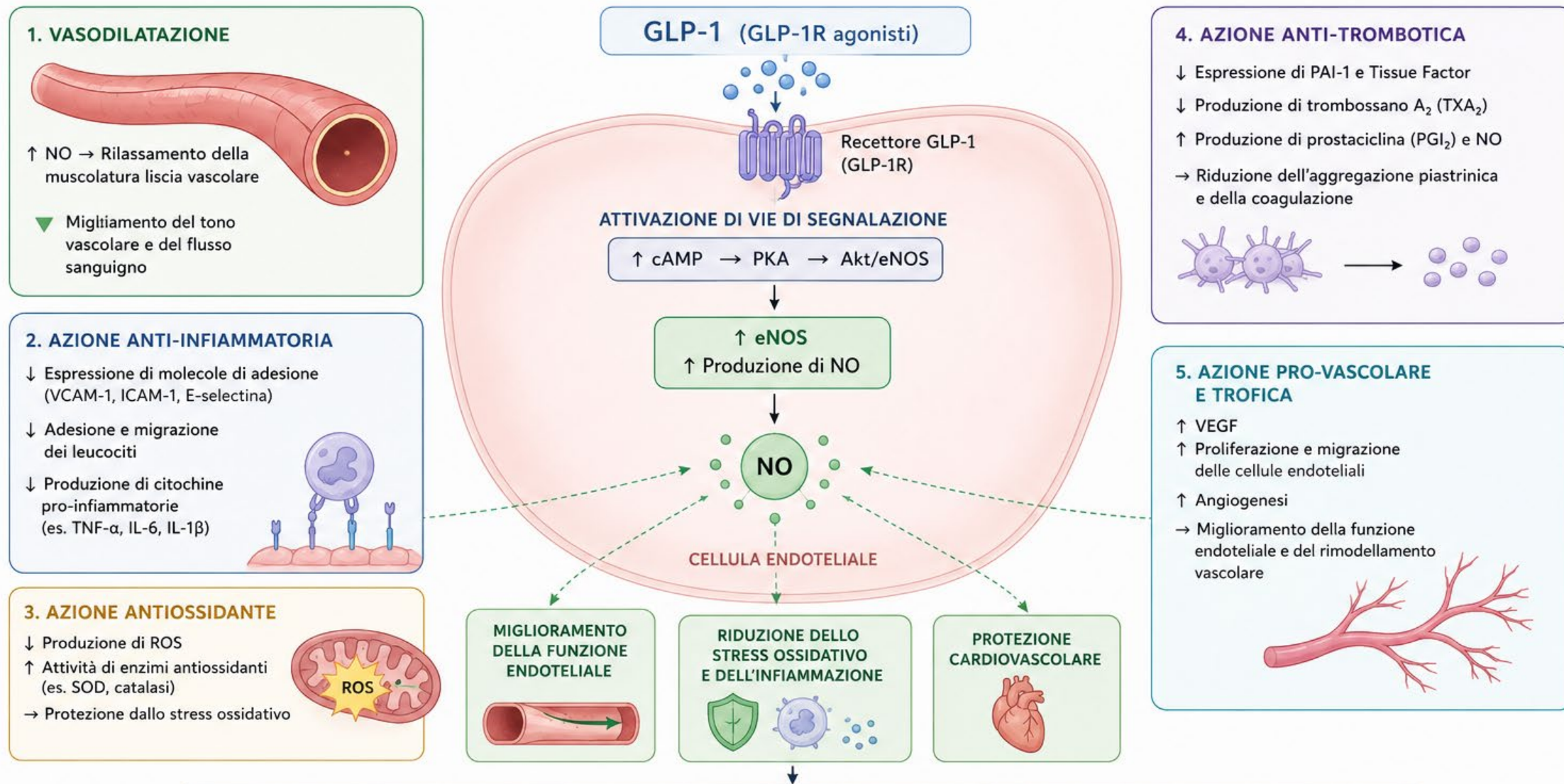


Drucker DJ. Cell Metabolism, 2016

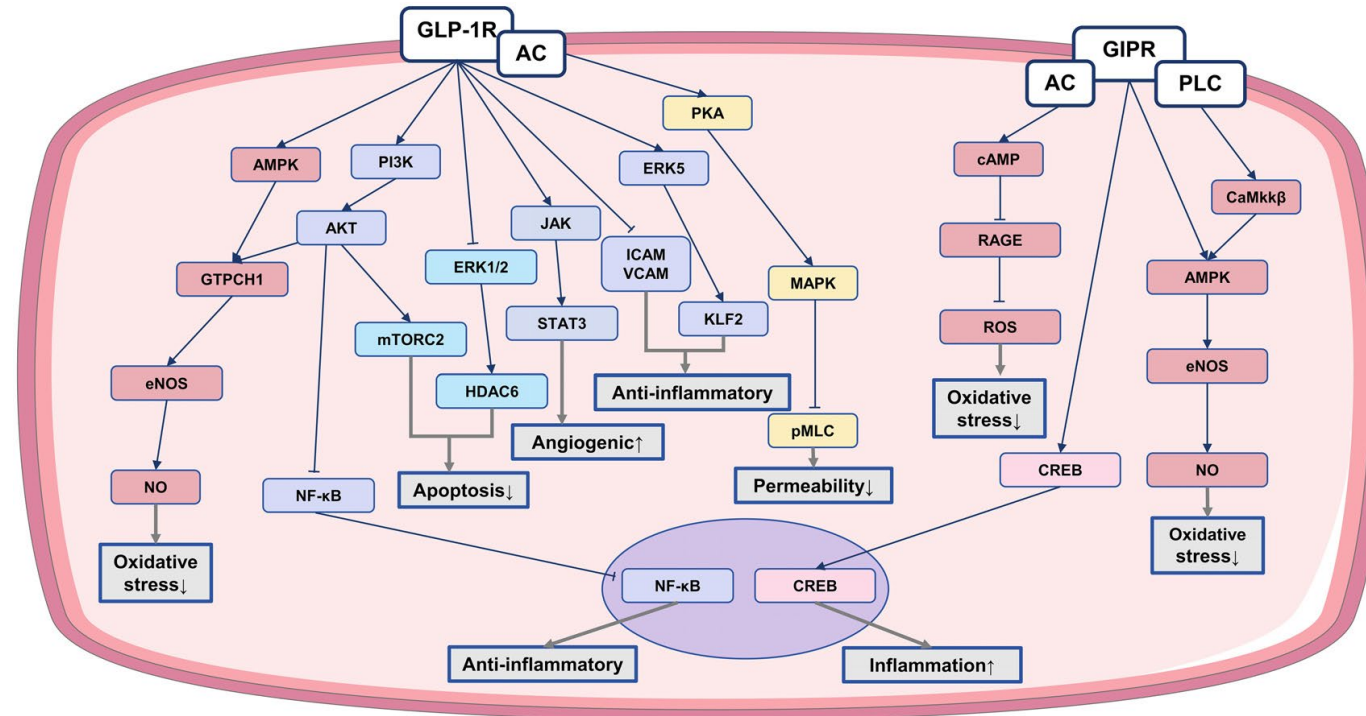


EFFETTI DEL GLP-1

Azione a livello vascolare endoteliale



EFFETTI ANTI ATEROSCLEROTICI DI GIPRA e GLP1RA



- ✓ Riduzione stress ossidativo
- ✓ Aumento di produzione di NO
- ✓ Riduzione infiammazione endoteliale
- ✓ Riduzione permeabilità vascolare
- ✓ Riduzione formazione di cellule schiumose
- ✓ Regolazione dell'apoptosi e della proliferazione cell endoteliali
- ✓ Polarizzazione dei macrofagi a fenotipo M2
- ✓ ...

Frontiers in Endocrinology, Wung et al. 15: 1436, 2024



Cardiovascular, mortality, and kidney outcomes with GLP-1 receptor agonists in patients with type 2 diabetes:
a systematic review and meta-analysis of randomised trials

GLP1 RA E CVOT

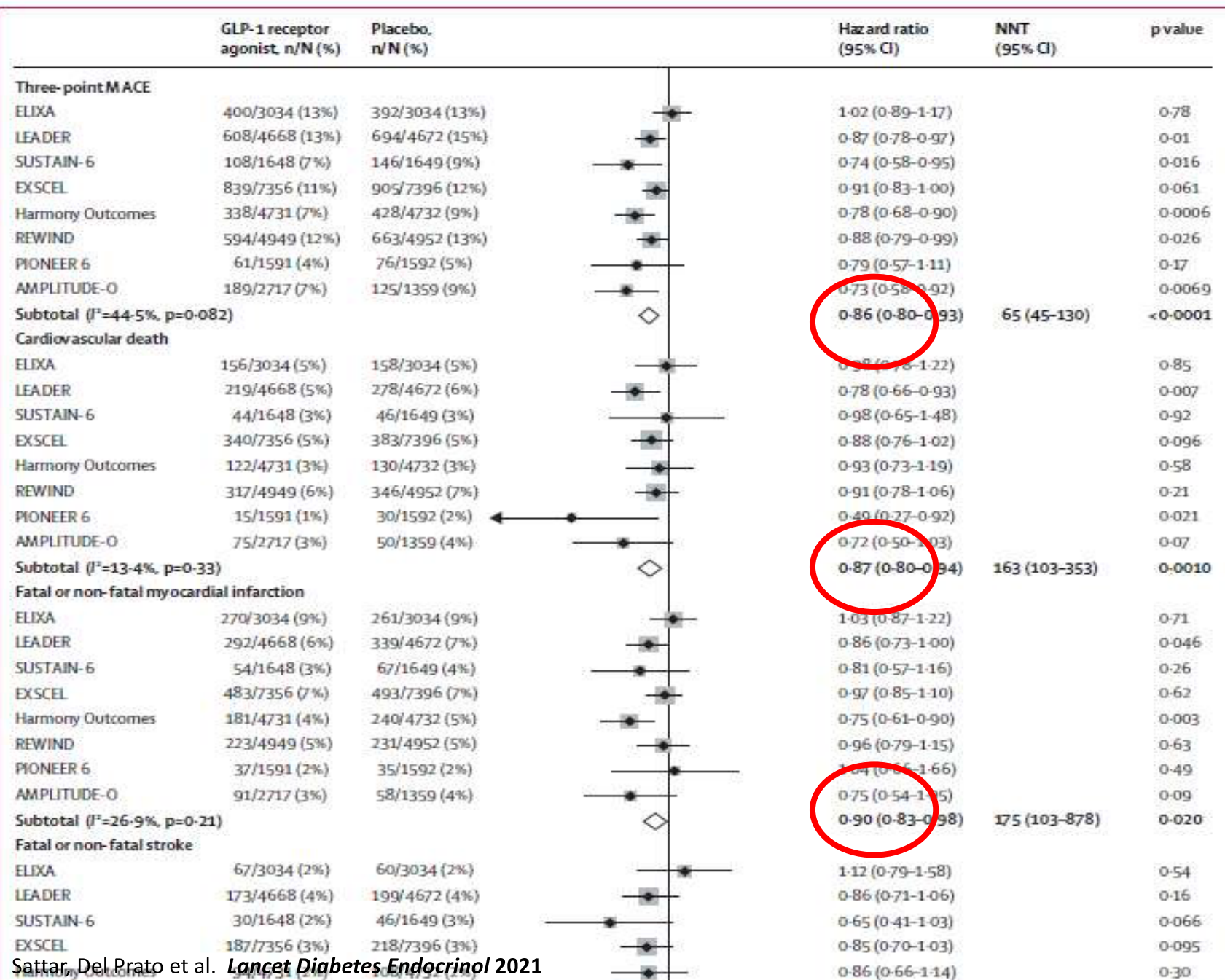
	GLP-1 receptor agonist, n/N (%)	Placebo, n/N (%)		Hazard ratio (95% CI)	NNT (95% CI)	p value
Three-point MACE						
ELIXA	400/3034 (13%)	392/3034 (13%)		1.02 (0.89-1.17)		0.78
LEADER	608/4668 (13%)	694/4672 (15%)		0.87 (0.78-0.97)		0.01
SUSTAIN-6	108/1648 (7%)	146/1649 (9%)		0.74 (0.58-0.95)		0.016
EXSCEL	839/7356 (11%)	905/7396 (12%)		0.91 (0.83-1.00)		0.061
Harmony Outcomes	338/4731 (7%)	428/4732 (9%)		0.78 (0.68-0.90)		0.0006
REWIND	594/4949 (12%)	663/4952 (13%)		0.88 (0.79-0.99)		0.026
PIONEER 6	61/1591 (4%)	76/1592 (5%)		0.79 (0.57-1.11)		0.17
AMPLITUDE-O	189/2717 (7%)	125/1359 (9%)		0.73 (0.58-0.92)		0.0069
Subtotal (I ² =44.5%, p=0.082)				0.86 (0.80-0.93)	65 (45-130)	<0.0001

↓ rischio MACE a 3 punti del 14%

(HR=0.86, 95% CI, 0.89–0.93, P <0.0001).

- Morte CV
- IMA non fatale
- Ictus non fatale

60.080 pazienti



↓
Rischio di morte
cardiovascolare
13%

↓
Rischio di IMA fatale o
non fatale
10%

↓
Rischio **stroke** fatale o
non fatale
-17%

**2024 ACC/AHA/AACVPR/APMA/ABC/SCAI/SVM/SVN/SVS/SIR/
VESS Guideline for the Management of Lower Extremity
Peripheral Artery Disease: A Report of the American College
of Cardiology/American Heart Association Joint Committee on
Clinical Practice Guidelines**

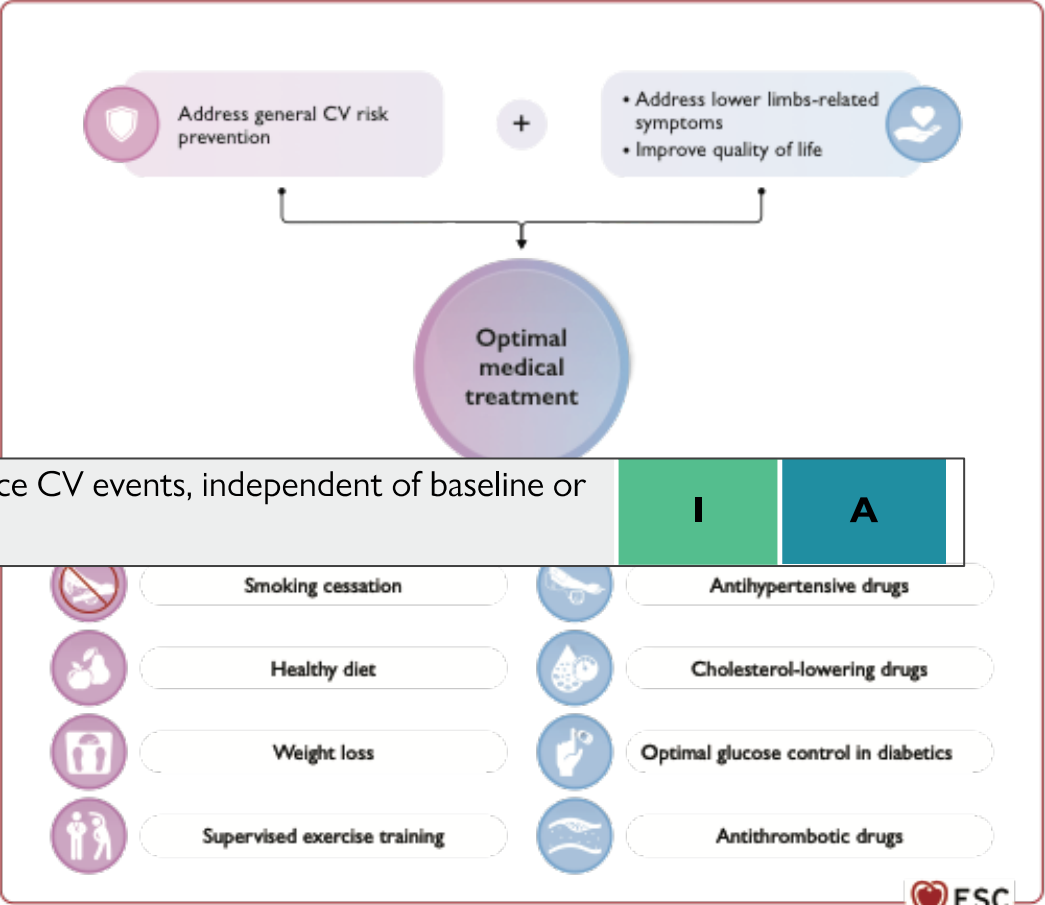
COR	LOE	Recommendations
1	A	1. In patients with PAD and type 2 diabetes, use of glucagon-like peptide–1 agonists (liraglutide and semaglutide) and sodium-glucose cotransporter-2 (SGLT-2) inhibitors (canagliflozin, dapagliflozin, and empagliflozin) are effective to reduce the risk of MACE. ^{1–12}

Linee guida ESC ADA e AHA inseriscono GLP 1 RA nel trattamento della PAD

ESC GUIDELINES

2024 ESC Guidelines for the management of peripheral arterial and aortic diseases

GLP-1RAs with proven CV benefit are recommended in patients with T2DM and PAAD to reduce CV events, independent of baseline or target HbA1c and concomitant glucose-lowering medication.



TRIAL SURPASS-CVOT

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

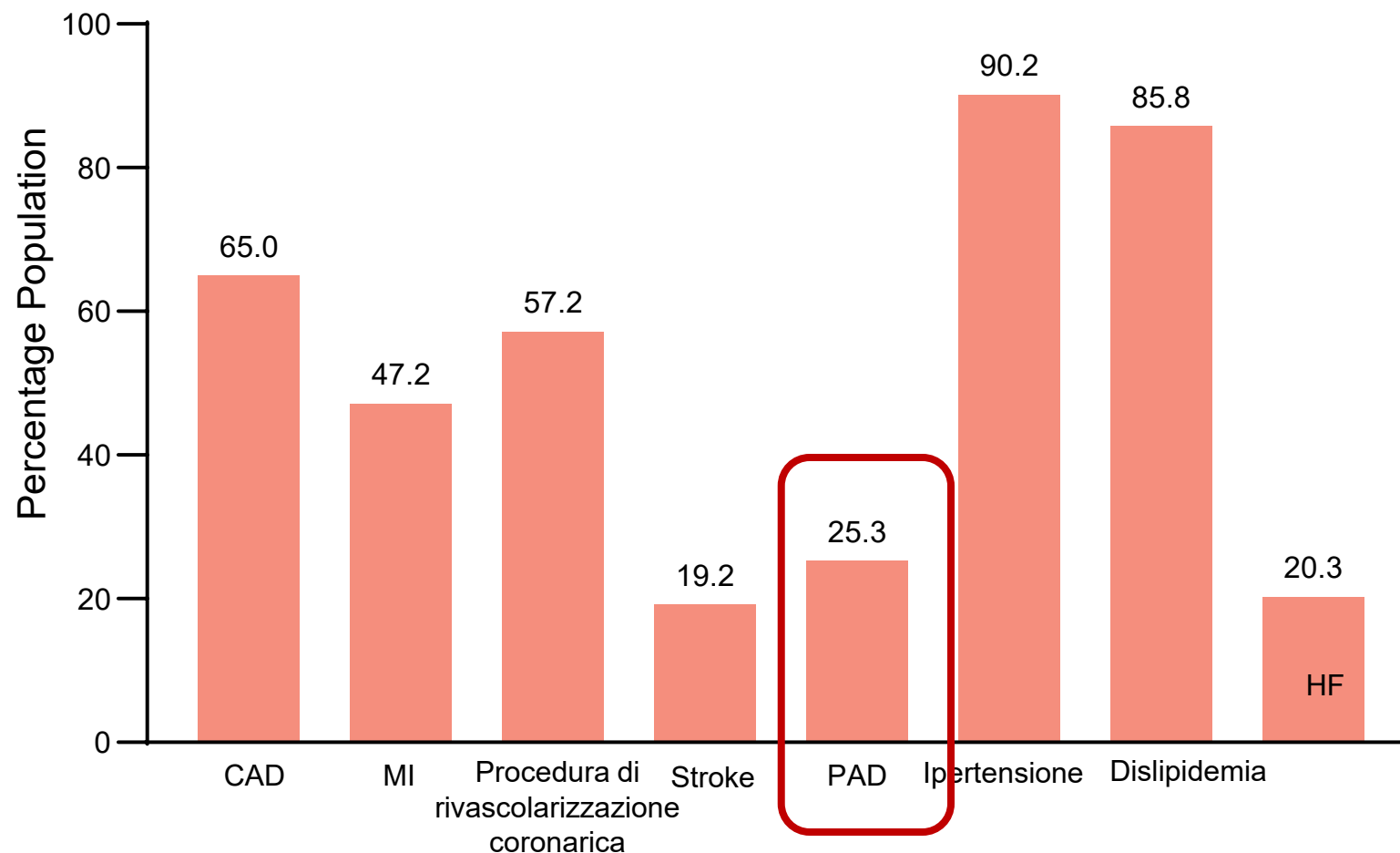
Cardiovascular Outcomes with Tirzepatide versus Dulaglutide in Type 2 Diabetes

S.J. Nicholls,¹ I. Pavo,² D.L. Bhatt,³ J.B. Buse,⁴ S. Del Prato,⁵ S.E. Kahn,⁶
A.M. Lincoff,⁷ D.K. McGuire,^{8,9} D. Miller,² M.A. Nauck,^{10,11} H. Nishiyama,²
S.E. Nissen,^{12,13} N. Sattar,¹⁴ G. Weerakkody,² R.J. Wiese,² B. Zinman,^{15,16}
S. Zoungas,^{1,17} J. Basile,^{18,19} M.J. Davies,^{20,21} F. Giorgino,²² M. Kellerer,^{23,24} L. Ji,²⁵
T. Varkonyi,²⁶ V. Menon,^{12,13} J.C. Broder,^{17,27} A. Herschtal,²⁷ and D. D'Alessio,²⁸
for the SURPASS-CVOT Investigators*

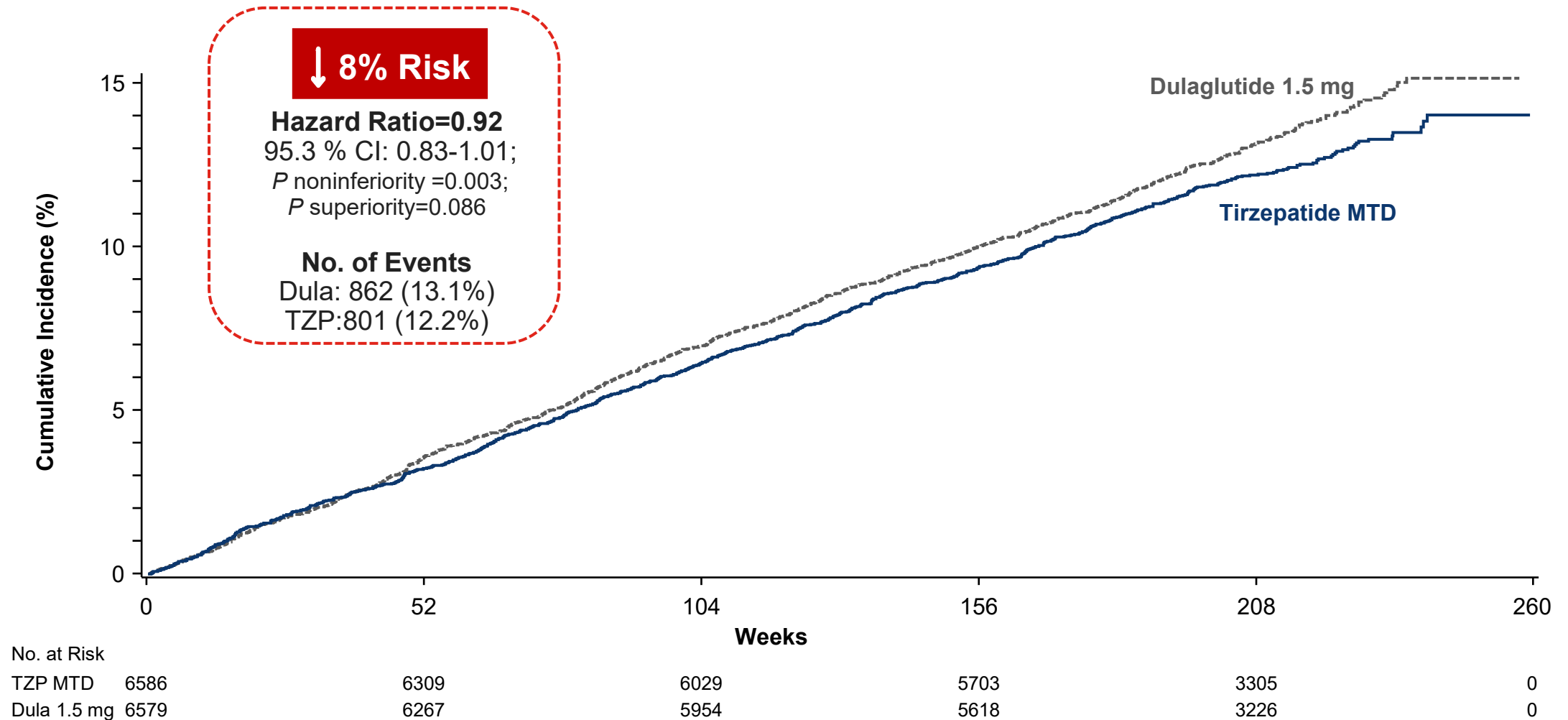
Storia Medica al Baseline

Pazienti **T2D con ASCVD** ad alto rischio residuo (25% **PAD**)

Mediana di follow-up è **4 anni**, arruolando **13.299** pazienti



Endpoint Primario: Morte CV, Infarto Miocardio o Ictus



Endpoint Secondari di Interesse

Time to all-cause death¹

↓ 16% Risk

Tirzepatide vs. dulaglutide

HR=0.84
95.0% CI: 0.75-0.94; p=0.002^a

MACE-4

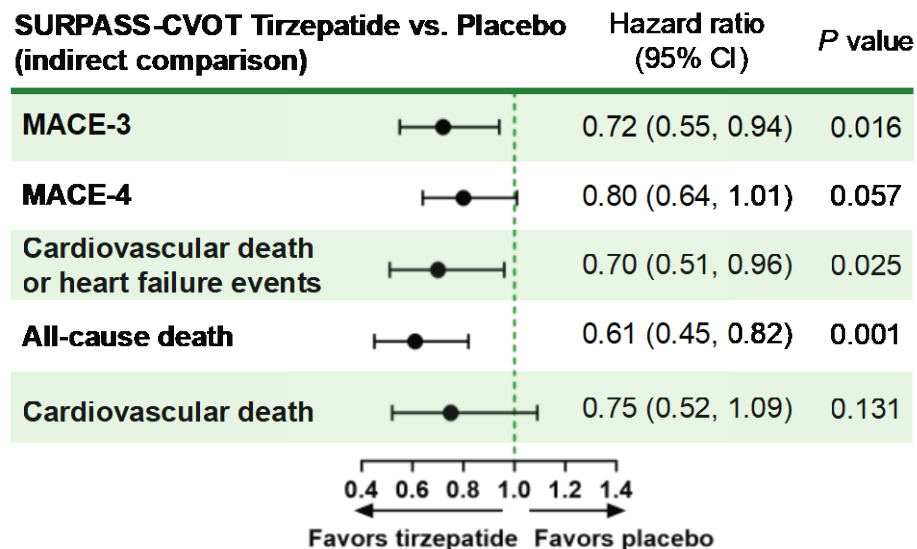
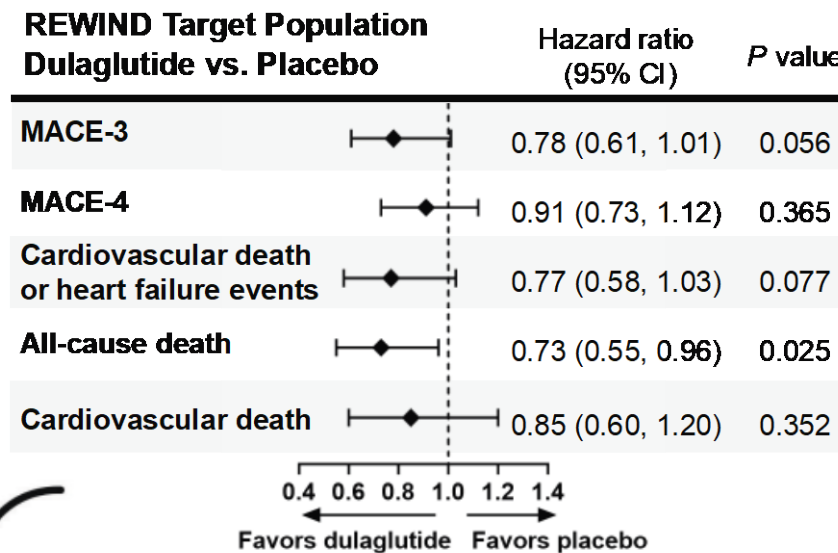
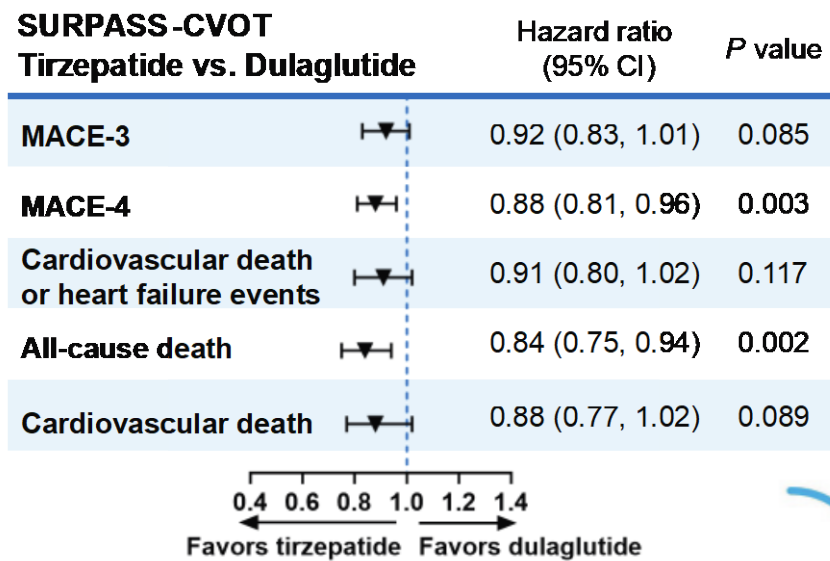
↓ 12% Risk

Tirzepatide vs. dulaglutide

HR= 0.88
95% CI: 0.81-0.96 p=0.002^a



Du



abo

)

Dulaglutide 4949

4810

4070

4021

4309

3080

741

CI SONO EVIDENZE SUL RUOLO DI GLP1-RA e GLP1-GIP RA IN PAZIENTI CON PIEDE DIABETICO E/O PAD?



PAZIENTI CON PAD NEI GRANDI TRIAL

Studio	Farmaco	N pazienti	PAD (%)
LEADER	Liraglutide	9.340	12,7
SUSTAIN-6	Semaglutide s.c.	3.297	14,0
EXSCEL	Exenatide	14.752	19
REWIND	Dulaglutide	9.901	5,1
FLOW	Semaglutide s.c.	3.533	20,3
SOUL	Semaglutide orale	9.650	15,7
SURPASS-CVOT	Tirzepatide	13.299	25,3

CVOT non sono stati disegnati per studiare MACE nella popolazione diabetica con PAD e/o con piede diabetico né per valutare i MALE

..... IN SINTESI

LEA e MALE sono stati valutati in post hoc analisi o come eventi di safety

Non ci sono RCT che abbiano come endpoint primari MALE, LEA o DFU in pazienti in trattamento con GLP1 RA -BST

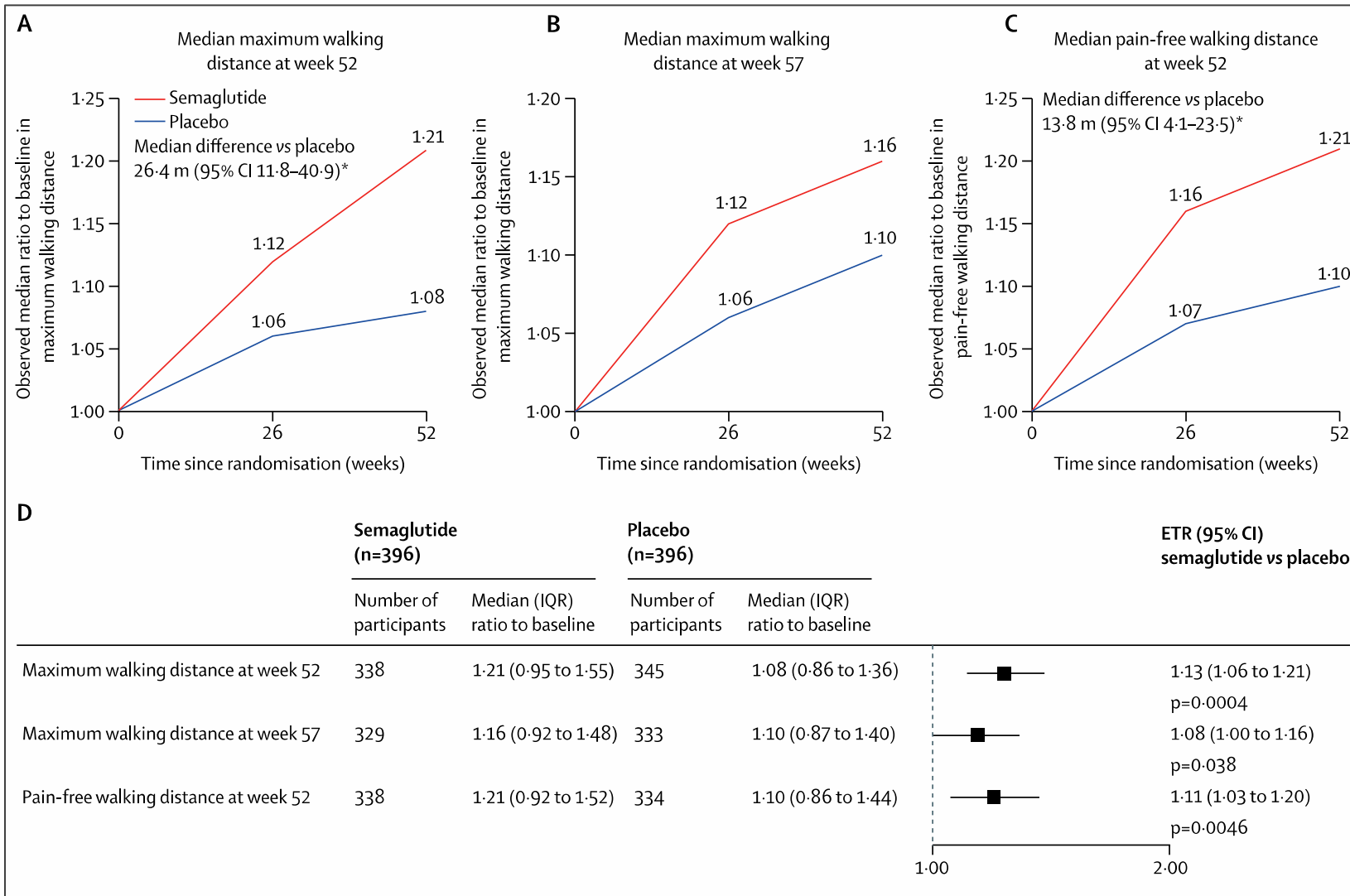
MACE in PAD sempre in post-hoc analysis

Solo 2 RCT hanno valutato paziente con PAD ma outcome funzionali



Semaglutide and walking capacity in people with symptomatic peripheral artery disease and type 2 diabetes (STRIDE): a phase 3b, double-blind, randomised, placebo-controlled trial

*Marc P Bonaca, Andrei-Mircea Catarig, Kim Houliand, Bernhard Ludvik, Joakim Nordanstig, Chethana Kalmady Ramesh, Neda Rasouli, Harald Sourij, Alex Videmark, Subodh Verma, for the STRIDE Trial Investigators**



Miglioramento medio MWD di **39.9 m**

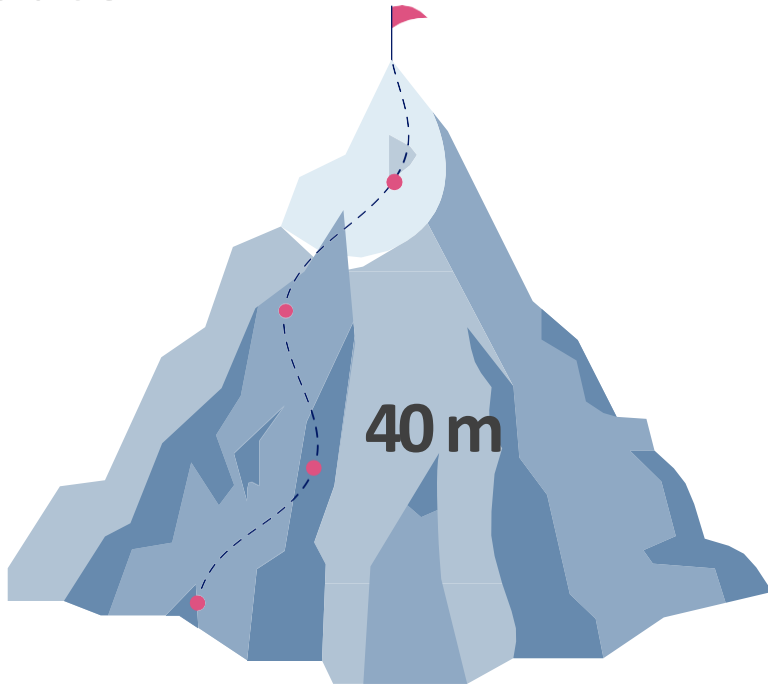
Miglioramento score vascuQoL -6

SEMAGLUTIDE HA MIGLIORATO IN MODO SIGNIFICATIVO FUNZIONE, SINTOMI E QUALITA' DI VITA NEI PAZIENTI AFFETTI DA D2 E PAD CON CLAUDICATIO.

Lancet, 405: 1508-93, 2025

Quali implicazioni cliniche?

Un incremento di 40 m in MWD si traduce in:



Un miglioramento nella capacità funzionale migliora le performance del paziente



Andare alla casetta della posta

Andare al supermercato



Passeggiare con il cane

Svolgere attività quotidiane con minori pause e disagio



Miglioramento della qualità di vita

Original Investigation | Diabetes and Endocrinology

Liraglutide for Lower Limb Perfusion in People With Type 2 Diabetes and Peripheral Artery Disease

The STARDUST Randomized Clinical Trial

Paola Caruso, PhD; Maria Ida Maiorino, PhD; Miriam Longo, MD; Chiara Porcellini, MD; Rita Matrone, MD; Lucia Digitale Selvaggio, MD; Maurizio Gicchino, PhD; Carla Carbone, MD; Lorenzo Scappaticcio, PhD; Giuseppe Bellastella, PhD; Dario Giugliano, MD; Katherine Esposito, PhD

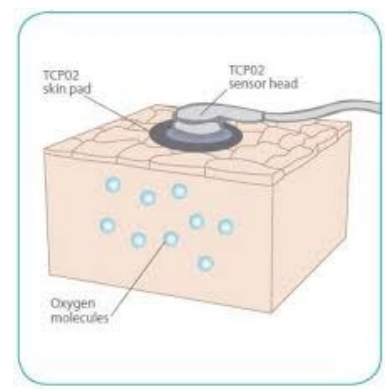
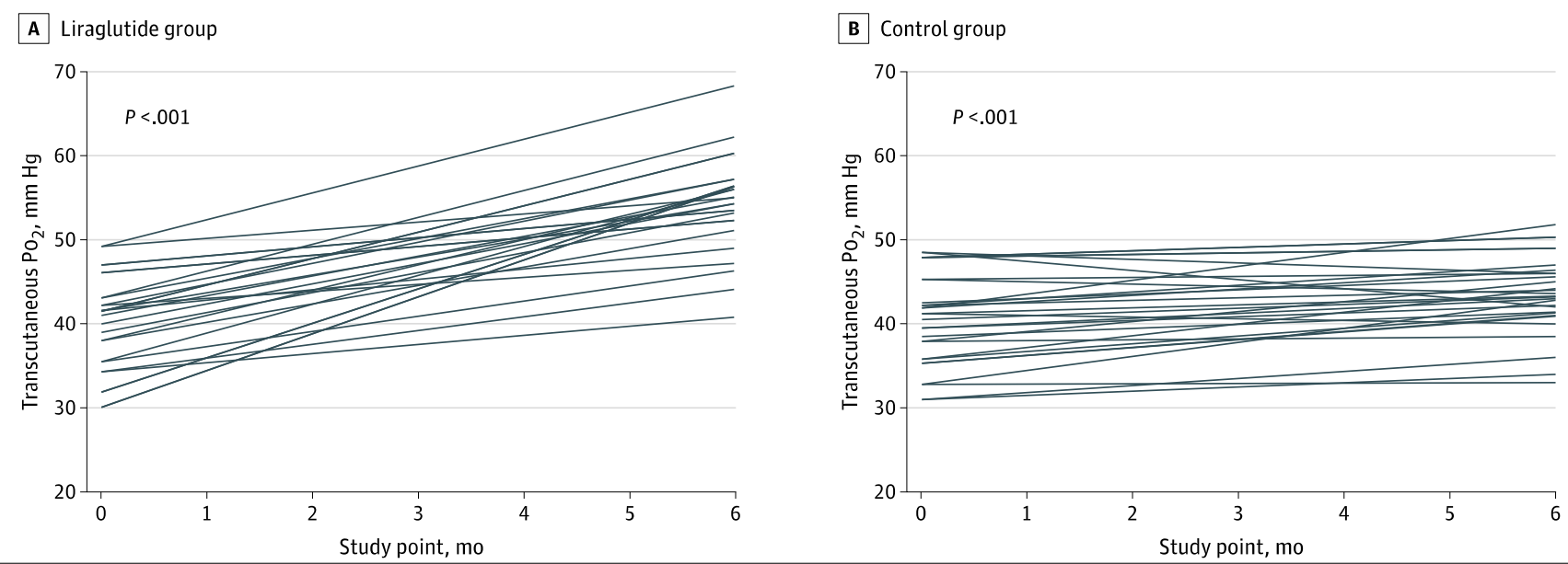


Figure 2. Individual Changes in Transcutaneous Oxygen Pressure



↑ TCPO2

↓ Citochine infiammatorie

Impact of glucagon-like peptide-1 receptor agonism-based therapies on limb outcomes in peripheral artery disease and type 2 diabetes: An updated systematic review and meta-analysis

Deep Dutta DM ¹ | Kunal Mahajan DM ² |

Diabetes Obes Metab. 2026;28:2075–2084.
5 RCT ; 7 OS

COORTE PAD	OR (favors to GLP1 RA -BTs)	95% CI
MALE	0.66	0.44-1.00
MORTALITA' PER TUTTE LE CAUSE	0.55	0.38-0.78
RIVASCOLARIZZAZIONI	0.85	0.8-0.9
AMPUTAZIONI	0.74	0.54-1.02
MACE	0.68	0.52-0.88
MORTALITA' CARDIOVASCOLARE	0.87	0.69-1.11

GLP1RA- BTs sono associati a riduzioni degli eventi cardiovascolari nei pazienti affetti da diabete e PAD.

COORTE DT2 (PAD <15%)	OR (favors to GLP1 RA -BTs)	95% CI
MALE	0.70	0.57-0.85
MORTALITA' PER TUTTE LE CAUSE	0.55	0.43-0.69
STROKE	0.85	0.6-1.2
AMPUTAZIONI	0.58	0.48-0.69
MORTALITA' CARDIOVASCOLARE	0.44	0.21-0.45

Il beneficio sembra maggiore quando la terapia e' iniziata precocemente suggerendo un effetto protettivo vascolare oltre il controllo glicemico

Major adverse cardiovascular and limb events caused by tirzepatide in patients with type 2 diabetes at high cardiovascular risk: A comparison with sitagliptin

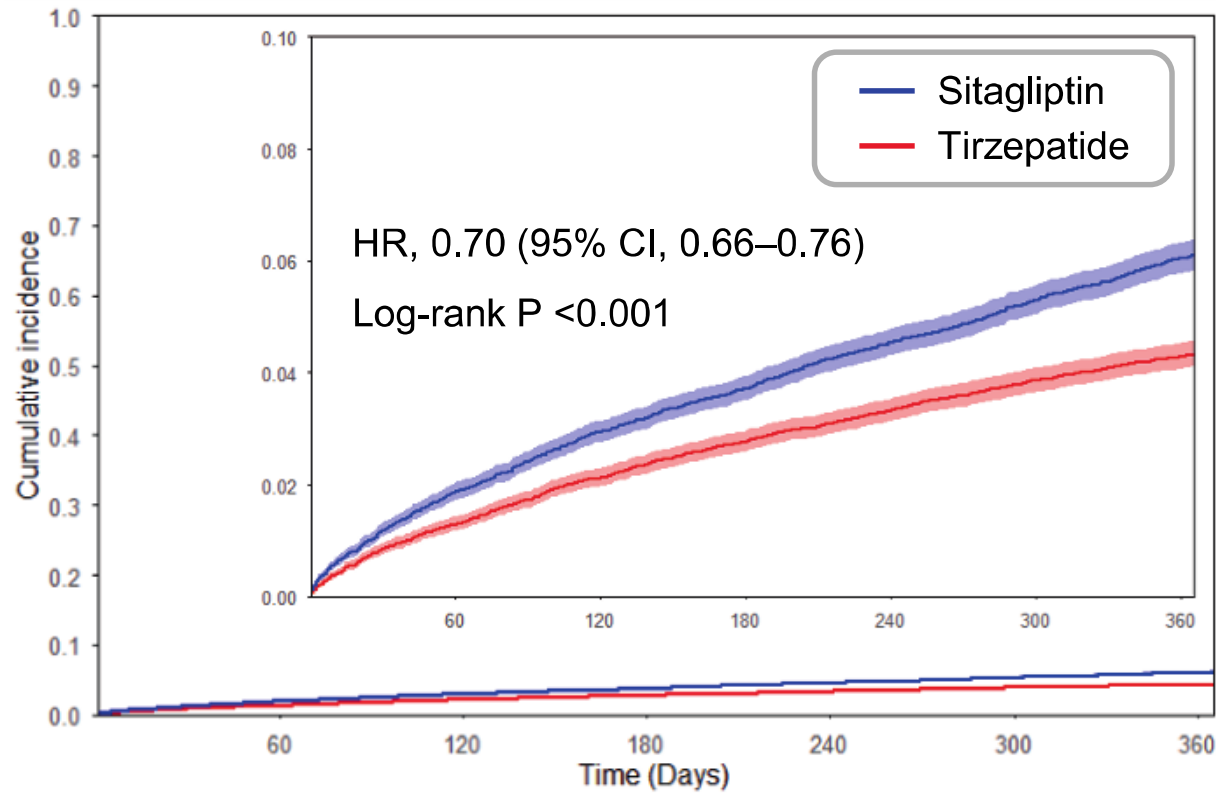
Yoshihiro Iwasaki ^a, Takenobu Shimada ^b, Takefumi Kishimori ^{a,*}, Takao Kato ^c, Jumpei Koike ^a, Takehiro Matsumoto ^a, Takafumi Yagi ^a, Masaharu Okada ^a

Clinical outcomes.

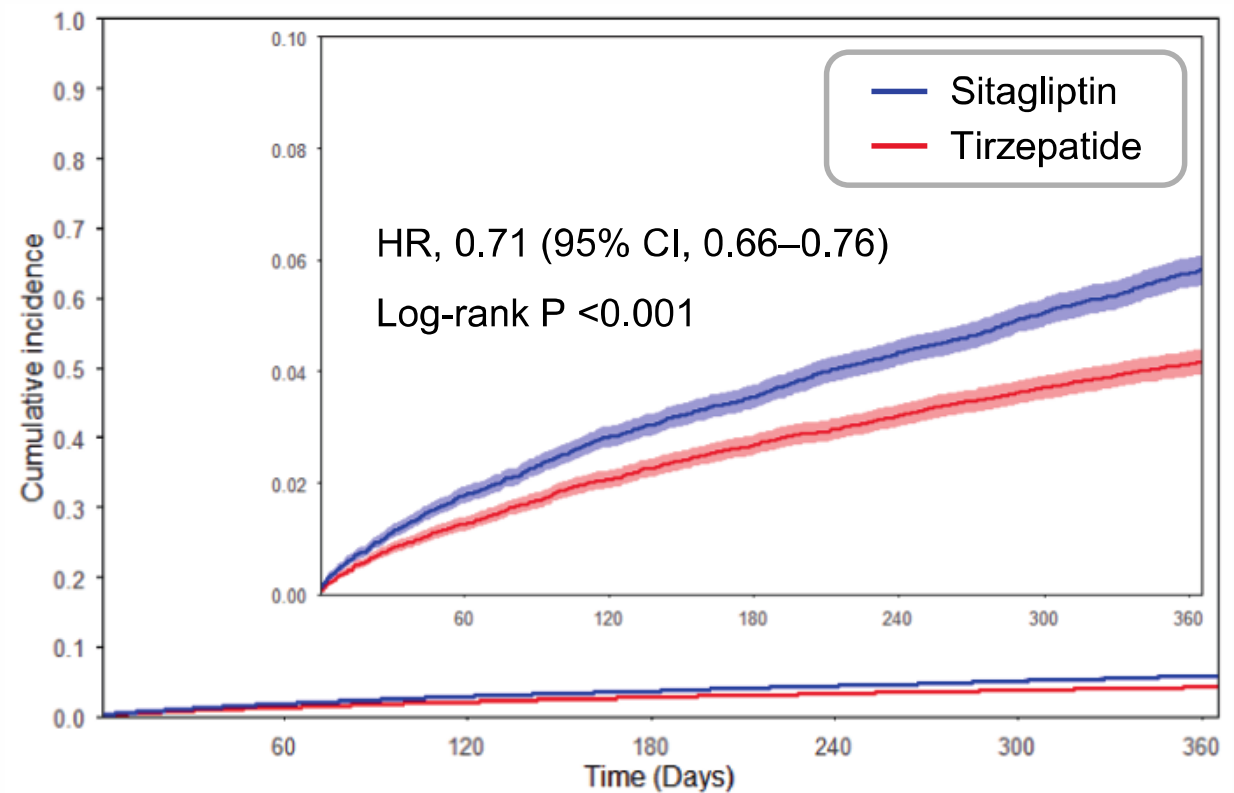
	Events with tirzepatide		Events with sitagliptin		HR	95 % CI
	1-year cumulative incidence		1-year cumulative incidence			
	(n = 31,751)		(n = 31,751)			
All-cause death (n, %)	187	(0.6 %)	505	(1.7 %)	0.35	0.30–0.42
Acute myocardial infarction (n, %)	491	(1.6 %)	581	(2.0 %)	0.81	0.72–0.92
Stroke (n, %)	673	(2.2 %)	782	(2.7 %)	0.83	0.75–0.92
Major lower limb amputation (n, %)	60	(0.2 %)	95	(0.3 %)	0.61	0.44–0.84

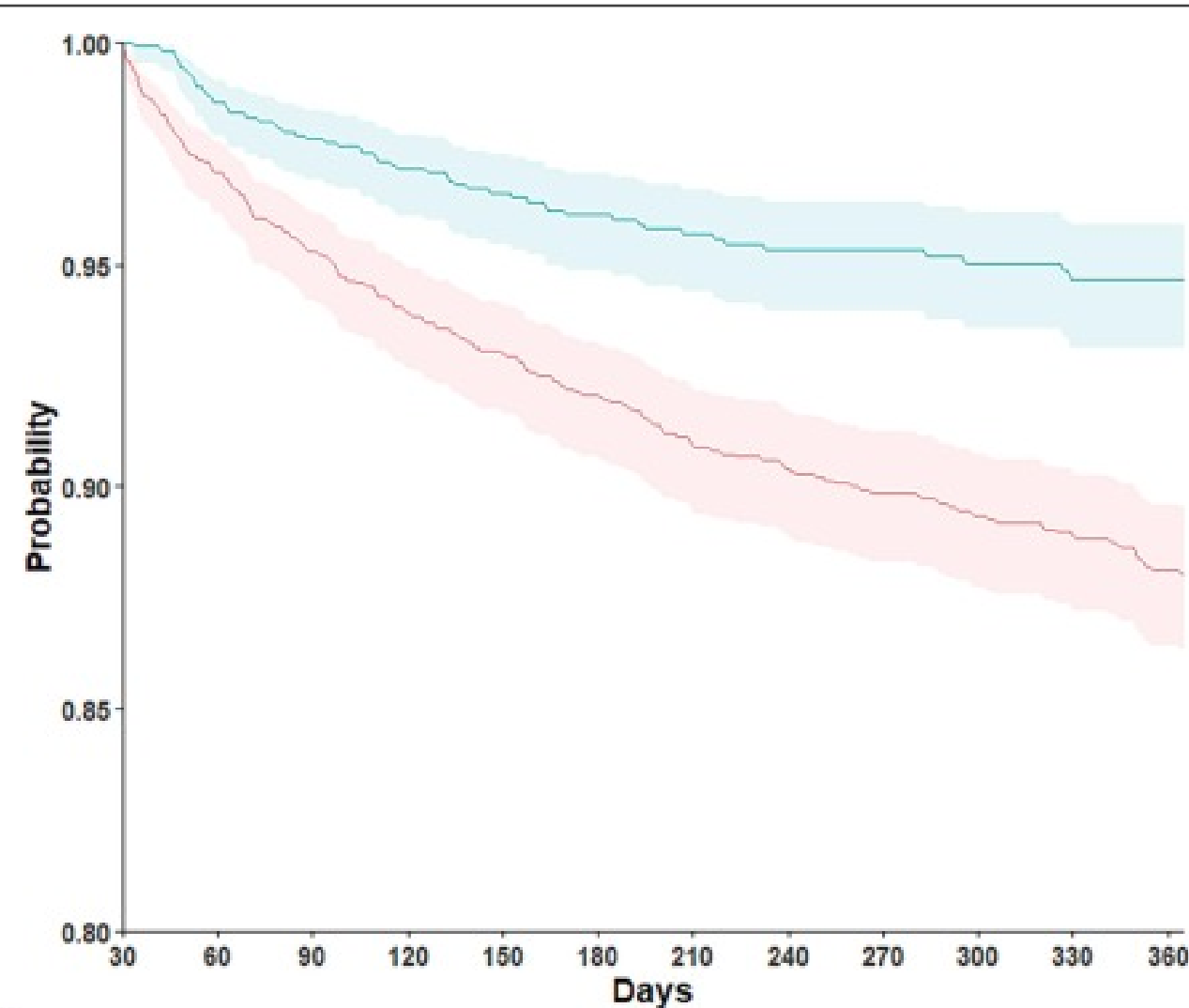
HR, hazard ratio; CI, confidence interval.

(A) MACLE



(B) MACE





-56% rischio

Subgroup	Tirzepatide, n(%)	Control, n(%)	Hazard Ratio (95% CI)	p-value
Overall	60 (1.49)	196 (4.87)	0.44 (0.33, 0.59)	<.001
Obesity				
(+)	41 (1.36)	110 (3.66)	0.55 (0.38, 0.79)	0.001
(-)	19 (1.76)	52 (4.81)	0.49 (0.29, 0.84)	0.007
CAD				
(+)	44 (1.84)	106 (4.44)	0.65 (0.46, 0.93)	0.016
(-)	17 (1.02)	54 (3.24)	0.37 (0.21, 0.64)	<.001
Stroke				
(+)	10 (2.04)	19 (3.89)	0.96 (0.40, 2.29)	0.923
(-)	56 (1.51)	160 (4.31)	0.49 (0.36, 0.66)	<.001

324,622 pts con PAD e diabete
4,028 tirzepatide,
320,594 no tirzepatide

Kaplan-Meier time-to-event free curves of the major adverse limb events comparison to tirzepatide and control groups.

Diabetes Res and Clin Prac, vol 222, 2025

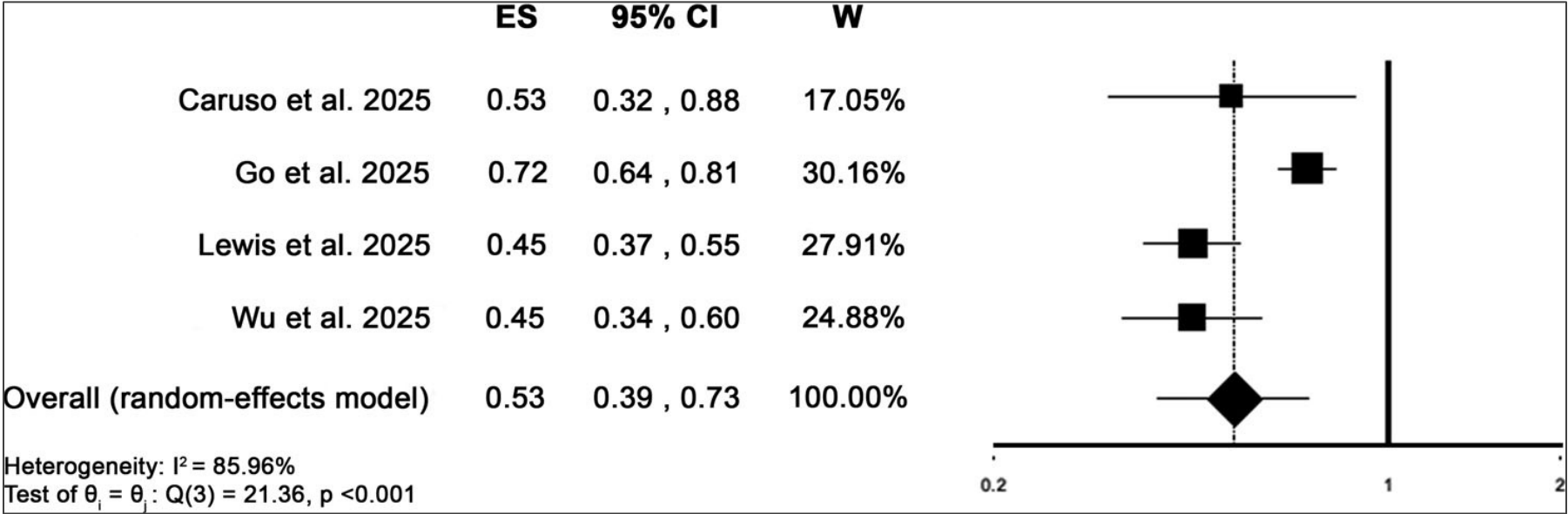
GLP1-1RAs improve walking distance and reduce amputation in people with type 2 diabetes and peripheral artery disease: A systematic review and meta-analysis of randomised controlled trials and cohort studies

Dario Giugliano MD¹ | Miriam Longo PhD^{1,2} | Nicole Di Martino PhD³ |

Diabetes Obes Metab. 2026;28:2775–2783.

3 RCT (STRIDE STURDUST e EXSCEL)

4 studi osservazionali



LEA: Riduzione del 47%

GLP-1 Receptor Agonists Are Associated With Reduced Mortality Following Diabetic Foot Ulcers: A Nationwide Observational Study

Objective: identifying factors associated with 1-year mortality following a first diabetic foot ulcer (DFU)

French National Health Insurance Database (SNDS)
2017–2018: 133,791 incident DFUs



Death within 1 year post-DFU:
19,521 (14.6%)

Major amputation within 1 year
post-DFU: 4,733 (3.5%)



Death within 1 year post major
amputation: 1,360 (28.7%)



↑Risk:

Male sex, older age, major amputation, comorbidities, insulin

Protective:

GLP-1-RA, statins, multidisciplinary care

Effects of Sodium/Glucose Cotransporter-2 Inhibitor Use on Mortality, Amputation, and Healing in Patients With Diabetic Foot Ulcer

Clothilde Dumortier, Serge Aho Glele, Alexia Rouland, Lina Houbachi, Coralie Fourmont, Bruno Vergès, Jean Michel Petit, and Benjamin Bouillet

Diabetes Care 2026;49(4):1–8 | <https://doi.org/10.2337/dg25-2001>

The use of SGLT2i inhibitors does not negatively affect the 1-year amputation rate or 6-month healing rate of DFU. The 1-year mortality rate was lower in patients treated with SGLT2is.

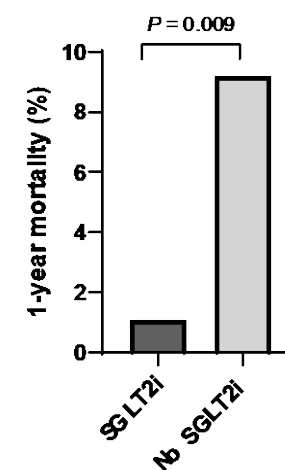
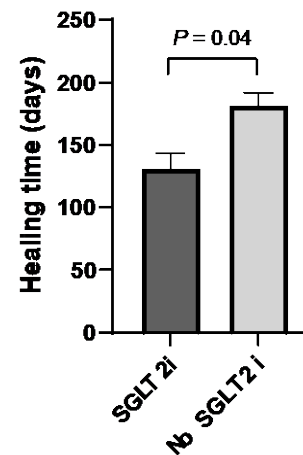
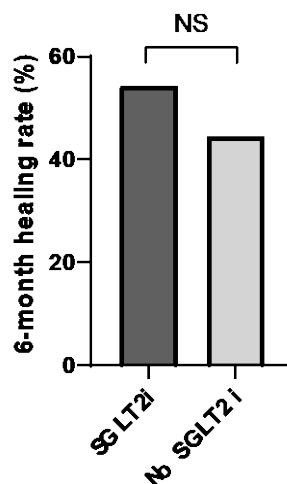
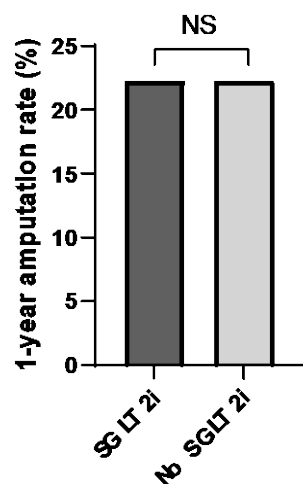


Table 1—Characteristics of the study population (N = 452)

Characteristic	Total study population	Patients not treated with SGLT2i (n = 358)	Patients treated with SGLT2i (n = 94)	P value for treated vs. not treated with SGLT2i
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Diabetes complications

Neuropathy	239 (64.1)	179 (62.2)	60 (70.6)	0.465
PAD	187 (44.1)	152 (45.8)	35 (38.0)	0.186
Severe PAD	35 (8.2)	32 (9.6)	3 (3.3)	0.054
History of revascularization	95 (22.3)	75 (22.5)	20 (21.7)	0.873
Ischemic heart disease	161 (41.5)	117 (38.7)	44 (51.2)	0.039
Retinopathy	167 (48.0)	129 (48.0)	38 (48.1)	0.982
Nephropathy	239 (64.1)	179 (62.2)	60 (70.6)	0.154
Hemodialysis	21 (4.6)	21 (5.9)	0 (0)	0.016

Treatment

Metformin	247 (54.8)	201 (56.3)	46 (48.9)	0.202
Insulin	247 (54.8)	193 (54.1)	54 (57.4)	0.557
GLP-1 analogs	145 (32.2)	102 (28.6)	43 (45.7)	0.002
Sulfamides	47 (10.4)	36 (10.1)	11 (11.7)	0.648
Glinides	106 (23.5)	83 (23.2)	23 (24.5)	0.804
DDP4 inhibitors	61 (13.9)	50 (14.5)	11 (11.7)	0.489
Aspirin	218 (50.2)	168 (49.1)	50 (54.8)	0.329
Clopidogrel	79 (18.1)	57 (16.7)	22 (23.7)	0.122
Rivaroxaban/apixaban	90 (20.1)	63 (18.4)	27 (29.0)	0.025

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VI

Focus sul piede nella gestione del diabete

MA, 18-20 GIUGNO 2026
HOTEL NH VILLA CARPEGNA



12. Retinopathy, Neuropathy, and Foot Care: Standards of Care in Diabetes—2026

Diabetes Care 2026;49(Suppl. 1):S261–S276 | <https://doi.org/10.2337/dc26-S012>

Emerging glucose-lowering therapies with PAD (and other cardiovascular disease) benefits include GLP-1 RA agents. Treatment with GLP-1 RAs may reduce risk of lower-extremity amputations, DFUs, and all-cause mortality compared with sodium–glucose cotransporter 2 (SGLT2)



CONCLUSIONI

- ❑ GLP-1 RA e GLP-1/GIP RA hanno effetti favorevoli sulla riduzione dell'infiammazione e sul miglioramento della funzione endoteliale.
- ❑ Sono farmaci che riducono i MACE nella popolazione ad alto rischio cardiovascolare come quella affetta da piede diabetico
- ❑ Recenti evidenze mostrano che i GLP1 RA sono in grado di migliorare gli outcome funzionali nei pazienti diabetici affetti da PAD
- ❑ GLP-1 RA e GLP-1/GIP RA sono da considerare terapie di prima linea nei pazienti diabetici con DFU e/o con PAD per migliorare la protezione vascolare e la prognosi globale del paziente in un approccio multifattoriale precoce
- ❑ Nonostante i risultati incoraggianti, le evidenze dirette sull'effetto di GLP-1 RA e GLP-1/GIP RA sugli esiti clinici del piede diabetico anche rispetto ad altre classe di farmaci, rimangono ancora limitate.



Grazie per
la vostra attenzione



VIII CONGRESSO NAZIONALE **PIEDE DIABETICO**
Focus sul piede nella gestione del diabete

INTERASSOCIATIVO SID-AMD

ROMA, 18-20 GIUGNO 2026
HOTEL NH VILLA CARPEGNA



VIII CONGRESSO NAZIONALE **PIEDE DIABETICO**
Focus sul piede nella gestione del diabete

INTERASSOCIATIVO SID-AMD

ROMA, 18-20 GIUGNO 2026
HOTEL NH VILLA CARPEGNA

- **Entrambi aumentano la produzione di ossido nitrico (NO)**, migliorando la funzione endoteliale e la vasodilatazione.
 - **Entrambi riducono infiammazione e stress ossidativo**, contribuendo alla protezione cardiovascolare.
 - Il **GLP-1** ha effetti cardiovascolari ben consolidati e dimostrati da numerosi studi clinici.
 - Il **GIP**, oltre a condividere alcune azioni del GLP-1, sembra potenziare gli effetti metabolici e vascolari quando i due recettori vengono attivati contemporaneamente. Questo concetto è alla base dei farmaci **agonisti duali GIP/GLP-1**, come Tirzepatide. Studi sperimentali e clinici suggeriscono che l'attivazione combinata dei due recettori può determinare:
 - maggiore miglioramento della funzione endoteliale;
 - riduzione più marcata dell'infiammazione e dello stress ossidativo;
 - migliori effetti su glicemia e peso corporeo;
 - potenzialmente una protezione cardiovascolare superiore rispetto all'attivazione del solo recettore GLP-1 (aspetto ancora oggetto di studio).
- Quindi, **si può dire che il GIP non sostituisce il GLP-1, ma ne potenzia e completa l'azione**, producendo un effetto sinergico piuttosto che una semplice amplificazione quantitativa.



VascuQoL-6 total score at week 52

Diab

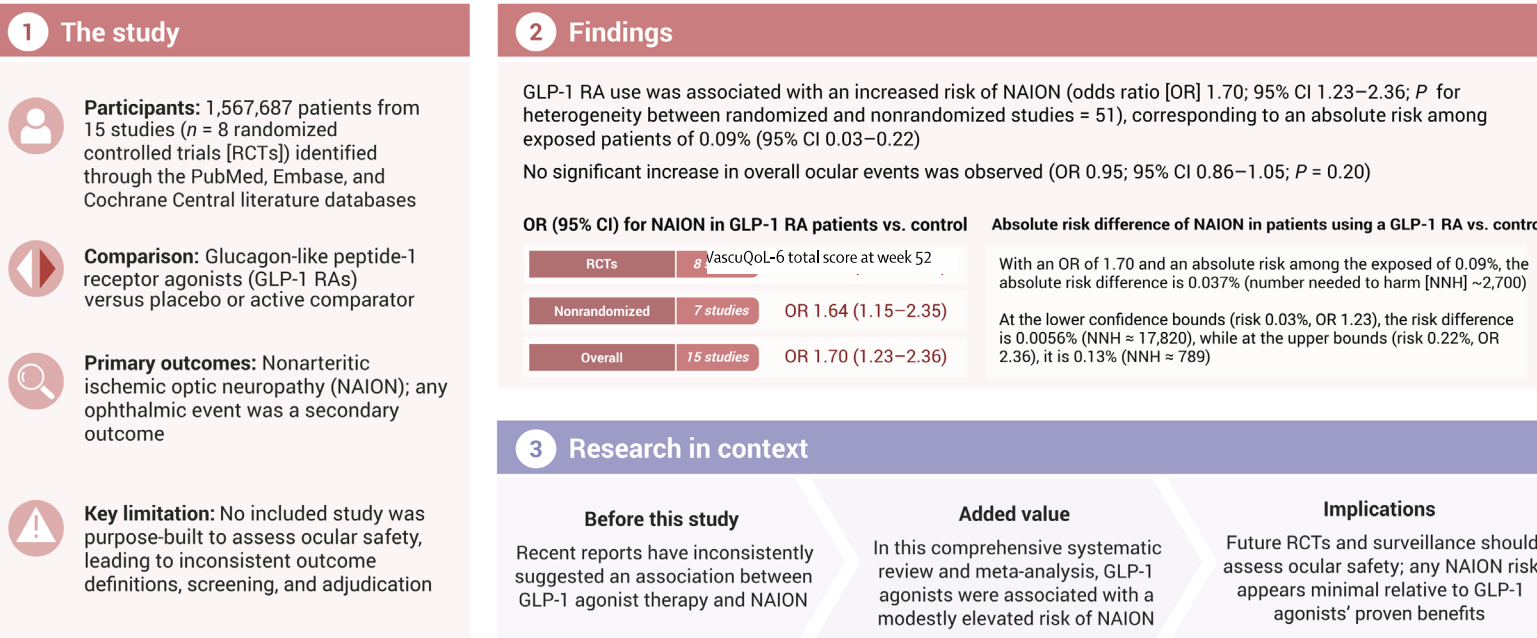
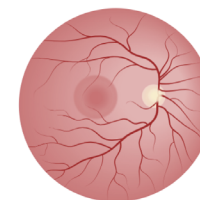
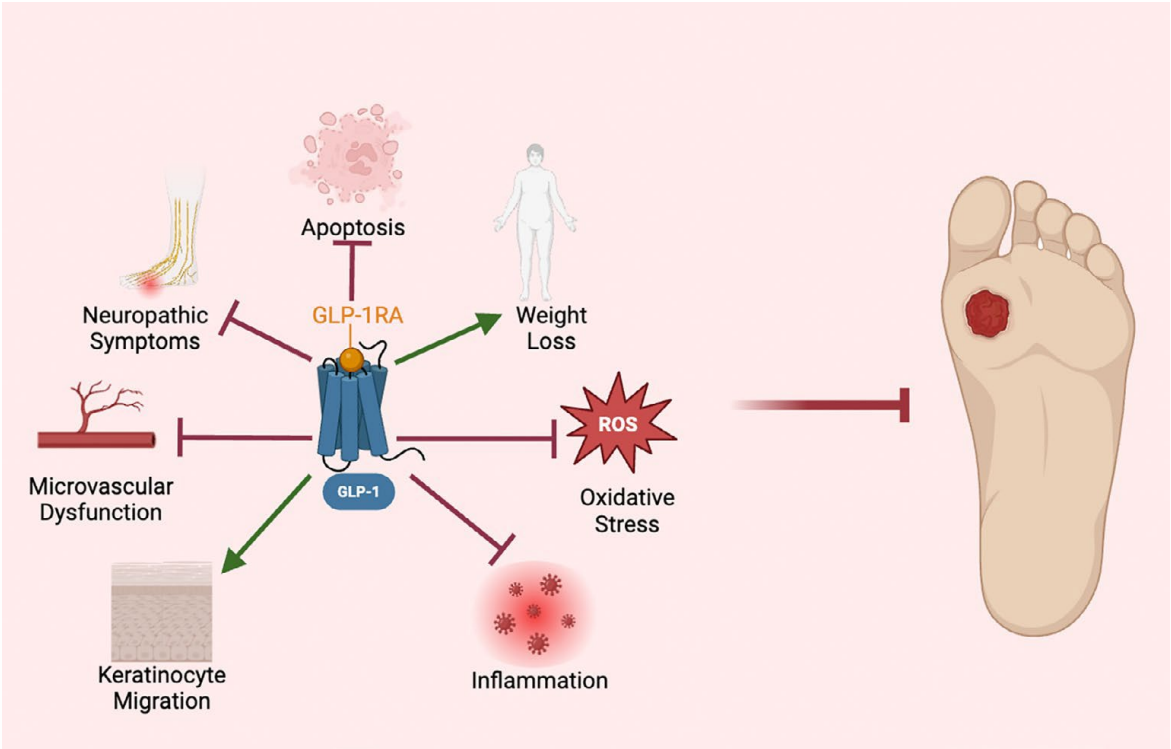


Figure Legend:

Exploring the Role of GLP-1 Agents in Managing Diabetic Foot Ulcers: A Narrative and Systematic Review

Fiona S. Gruzmark | Gabriela E. Beraja | Ivan Jozic | Hadar A. Lev-Tov



282-OR: Major Adverse Limb Events with Tirzepatide vs. Injectable Semaglutide in Adults with Type 2 Diabetes and Peripheral Artery Disease

Introduction and Objective: Peripheral artery disease (PAD) increases the risk for amputations and limb-threatening events in people with type 2 diabetes (T2D). Tirzepatide and injectable semaglutide are associated with improved limb outcomes. However, real-world comparative outcomes are unknown.

Methods: This retrospective cohort study used the TriNetX real-world global database across 112 healthcare organizations over 130 million patients. Adults 18 years or older with T2D and PAD initiating tirzepatide or injectable semaglutide were included. Propensity score matching (1:1) was performed on 54 covariates across demographics, cardiovascular risk factors, relevant medications, and laboratory measures. The study was conducted from May 13, 2022-December 10, 2025, with 12-month look-back for inclusion of baseline characteristics. Outcomes were evaluated following the index date where inclusion criteria were met. The primary outcome was a composite of major adverse limb events consisting of critical limb ischemia, amputation, or percutaneous transluminal angioplasty (PTA) or peripheral bypass. Kaplan-Meier analysis was performed for calculation of risk ratios and 95% confidence intervals for outcomes.

Results: After matching, 24,274 people were included (N=12,137 in each cohort). Cohorts were well-balanced after matching. Tirzepatide was associated with a significantly lower risk of major adverse limb events versus injectable semaglutide (RR: 0.50, 95% CI: 0.46-0.65, P <0.001). Individual endpoints including CLI (RR: 0.50, 95% CI: 0.39-0.63, P <0.001), amputation (RR: 0.45, 95% CI: 0.45-0.92, P=0.015), and PTA or peripheral bypass (RR: 0.53, 95% CI: 0.43-0.64, P <0.001) all favored tirzepatide.

Conclusion: In the real-world, among adults with T2D and PAD, tirzepatide was associated with significantly lower risks of major adverse limb events compared with injectable semaglutide. These findings suggest tirzepatide may offer improved limb protection in this high-risk population.



THERAPEUTIC STRATEGIES OF PERIPHERAL ARTERY DISEASE

- **Risk factors modification**
 - Quitting tobacco
 - Treating obesity
 - Diabetes: GLP1-RA/ SGLT2i
- **Background therapy: ASA and/or thienopyridines**
- **ACE-I and ARBs**
- **Hypocholesterolemic drugs:**
 - Statins, ezetimibe, PCSK9-I, inclisiran and bempedoic acid
- **Exercise therapy**
- **Rivaroxaban 2.5 mg twice/day + ASA**
- **Percutaneous revascularization**
 - Stenting
 - Balloon angioplasty
 - POBA
 - Drug-eluting balloon
- **Surgical revascularization**
 - Venous by-pass graft

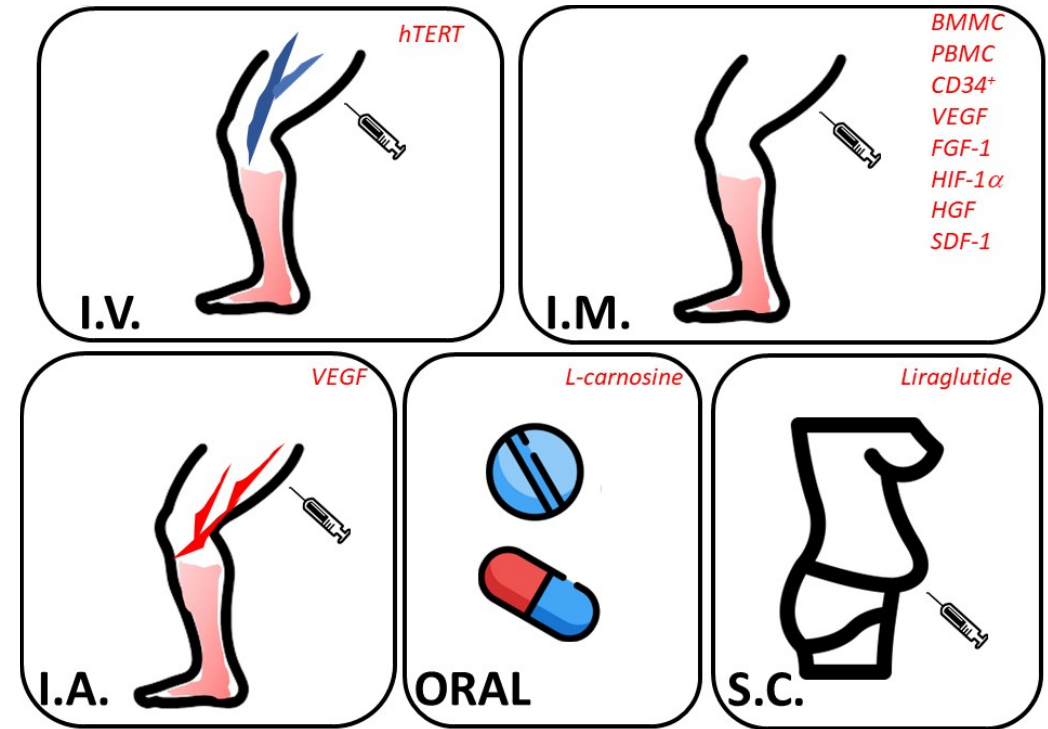


Figure 4. Providing alternative therapies for PAD. The figure represents the routes of a

