La dr.ssa CHIARA GOTTARDI 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.).*

La terapia ipoglicemizzante nel paziente diabetico arteriopatico

Chiara Gottardi
SS Centro Diabetologico D4
ASUGI -Trieste-

La terapia ipoglicemizzante nel paziente diabetico arteriopatico

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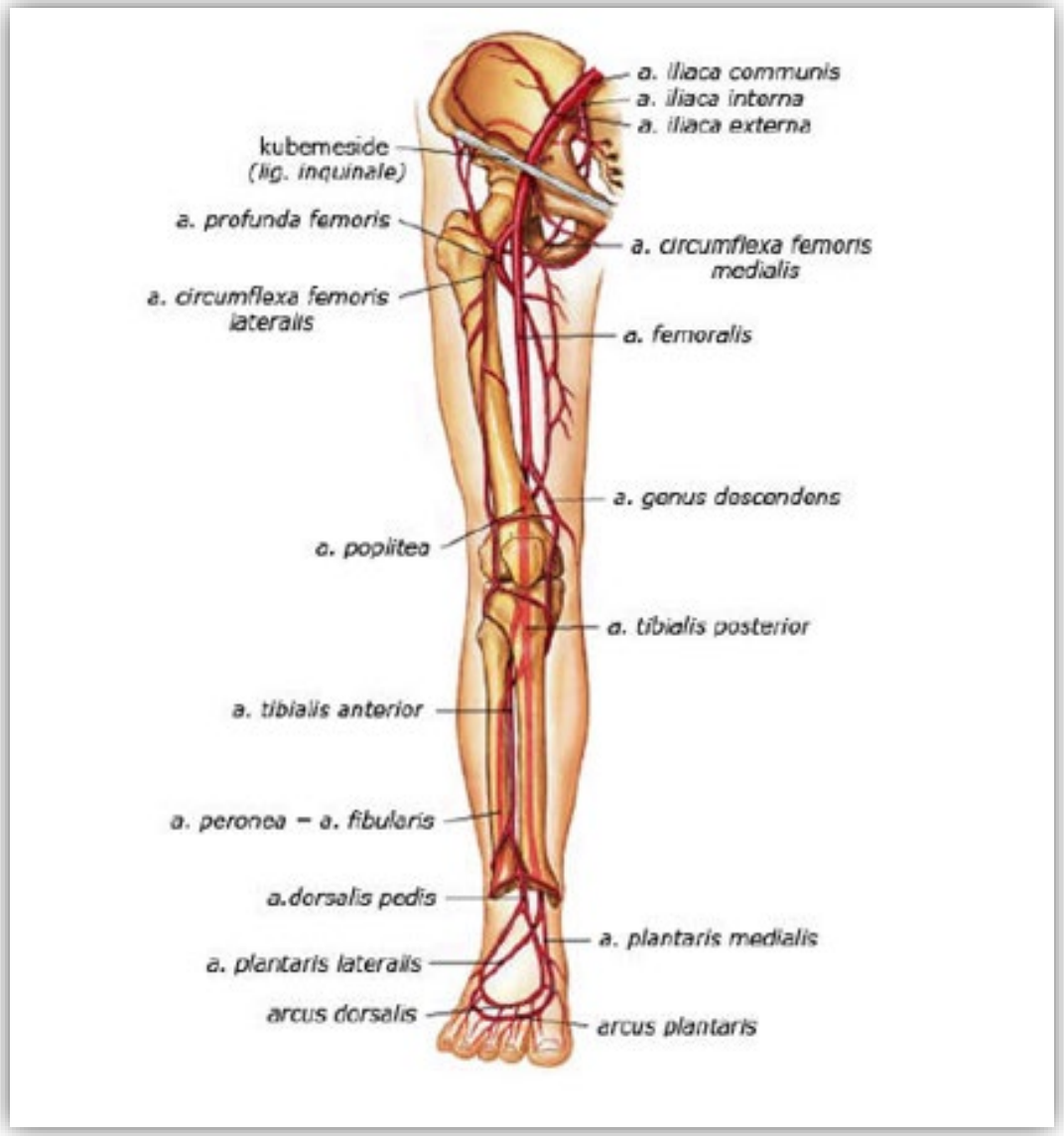
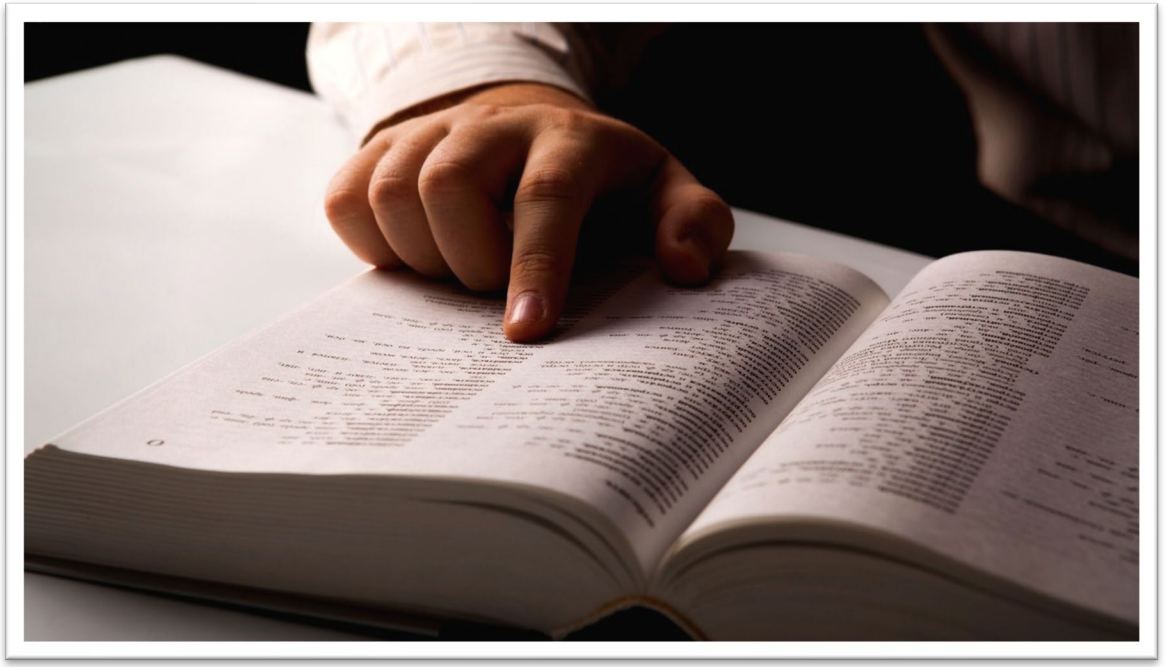
Di cosa stiamo parlando?





Oggi la PAD è definita la "lower extremity PAD"

Ostruzione aterosclerotica dei segmenti vascolari da sede aortoiliaca a rami delle arterie pedidee

PAD

come

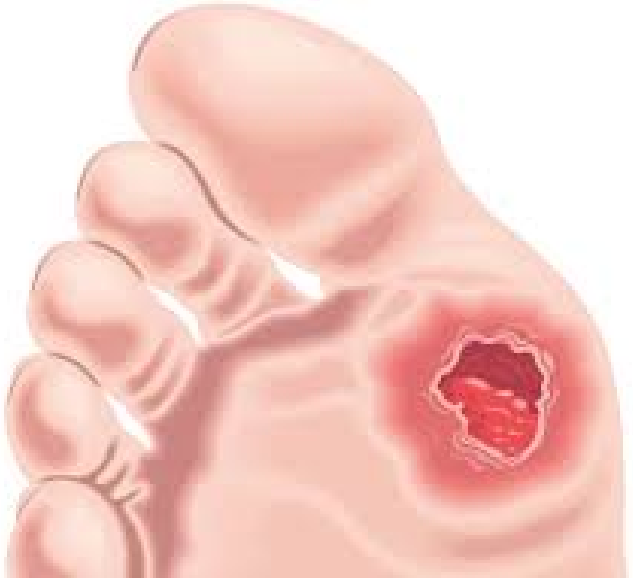
CAUSA ED EFFETTO

Mettiamo a fuoco… **“EFFETTO”…**

PAD è COMPLICANZA

La lower extremity peripheral artery disease (PAD) è stata studiata meno ed è spesso non riconosciuta rispetto ad altri quadri di patologia aterosclerotica come l'infarto e lo stroke

Perché???



1-percezione che PAD non sia una condizione **fatale** (come cpt ischemica…)

2- spesso non è riconosciuta come una condizione **disabilitante** (come invece lo è lo stroke)

3- le difficoltà deambulatorie a volte vengono **confuse** con la perdita di autonomia legata all'età

4- i **sintomi** talvolta possono essere confusi con altri disordini degenerativi (artritici, spinali..)

5-sotto utilizzo dell' **ABI e TBI**

Ulcera come manifestazione iniziale di vasculopatia misconosciuta

Scarsa percezione nel paziente

Can J Cardiol. 2009 Jan;25(1):39-45. doi: 10.1016/s0828-282x(09)70021-2.

Peripheral arterial disease: lack of awareness in Canada

Marge Lovell [1], Kenneth Harris, Thomas Forbes, Gwen Twillman, Beth Abramson, Michael H Criqui, Paul Schroeder, Emile R Mohler 3rd, Alan T Hirsch, Peripheral Arterial Disease Coalition

Sondaggio telefonico trasversale, condotto in Canada

501 adulti di età sup o uguale ai 50 aa

Nonostante molti di loro avessero ipertensione (43%), iperlipidemia (37%), diabete (12%) e un passato da fumatori (tutti fattori di rischio cardiovascolare noti)

solo il 36% sapeva qualcosa della PAD

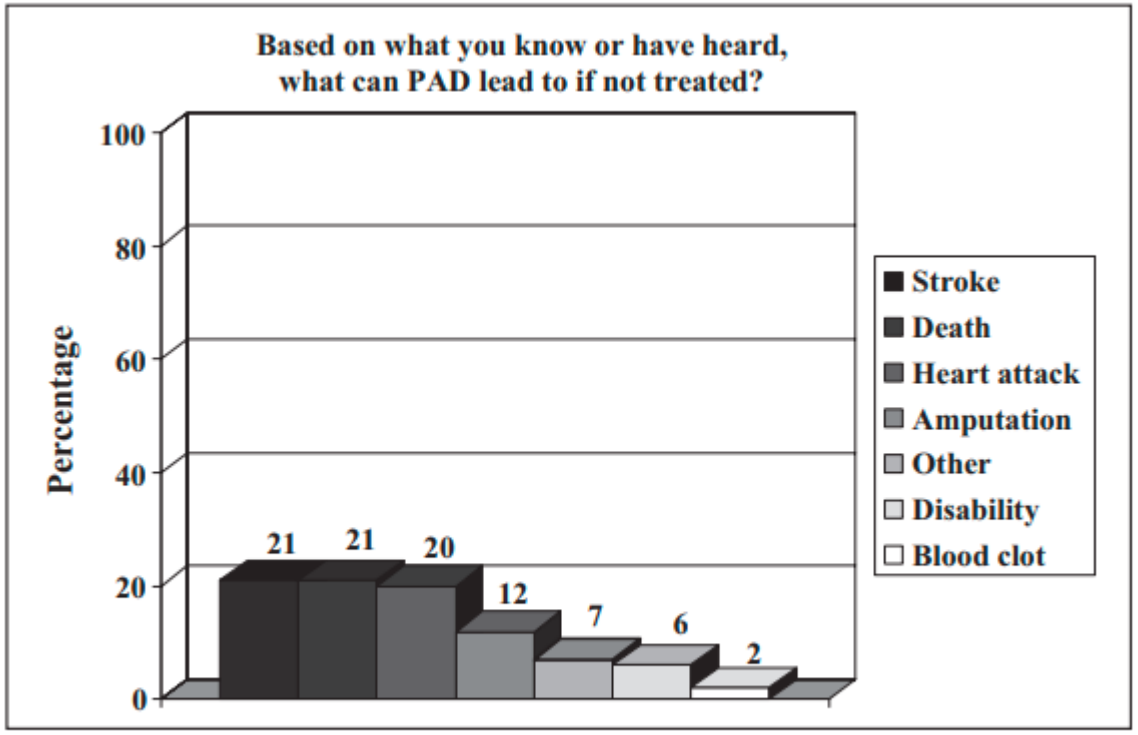


Figure 1) *Perceived consequences of peripheral arterial disease (PAD) among those who are 'PAD aware'*

«EFFETTO» SFUMATO

Mettiamo a fuoco…**“CAUSA”…**

PAD

E’

FATTORE DI RISCHIO CV

RICONOSCERE LA PRESENZA DI PAD E' IMPORTANTE

- E' correlata ad elevato rischio di morbilità e mortalità CV

Criqui MH, Langer RD, Fronek A, Feigelson HS, Klauber MR, McCann TJ, Browner D. Mortali
over a period of 10 years in patients with peripheral arterial disease. N Engl J Med

- E' un forte predittore di IMA

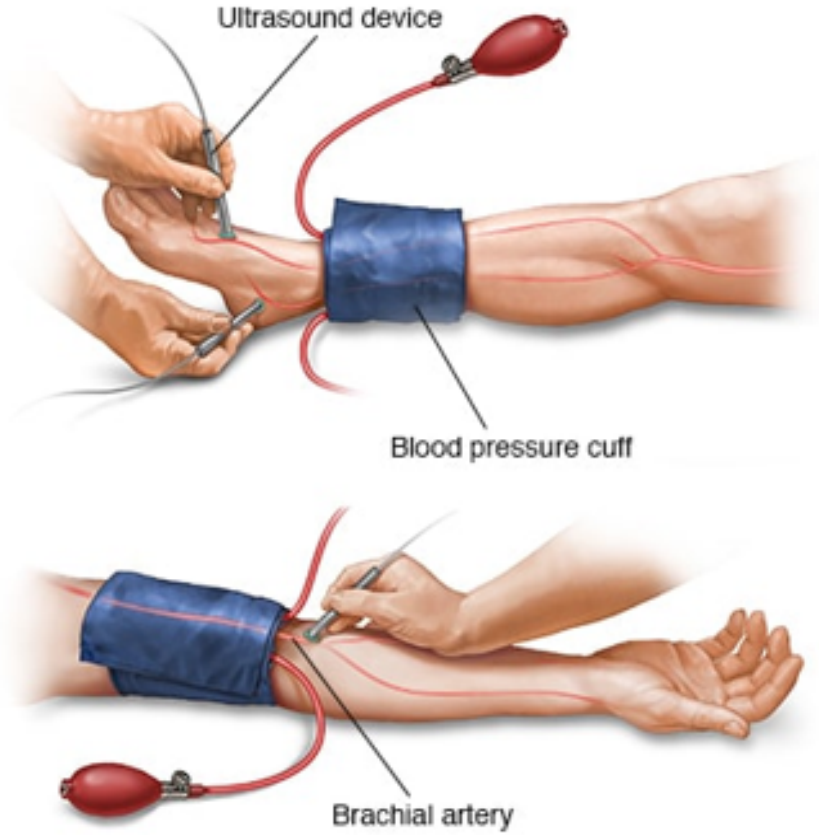
Gerhard-Herman MD, Gornik HL, Barrett
Fowkes FG, Hamburg NM, Kinla
patients with lower ext
Cardiology/ Am
2017;1

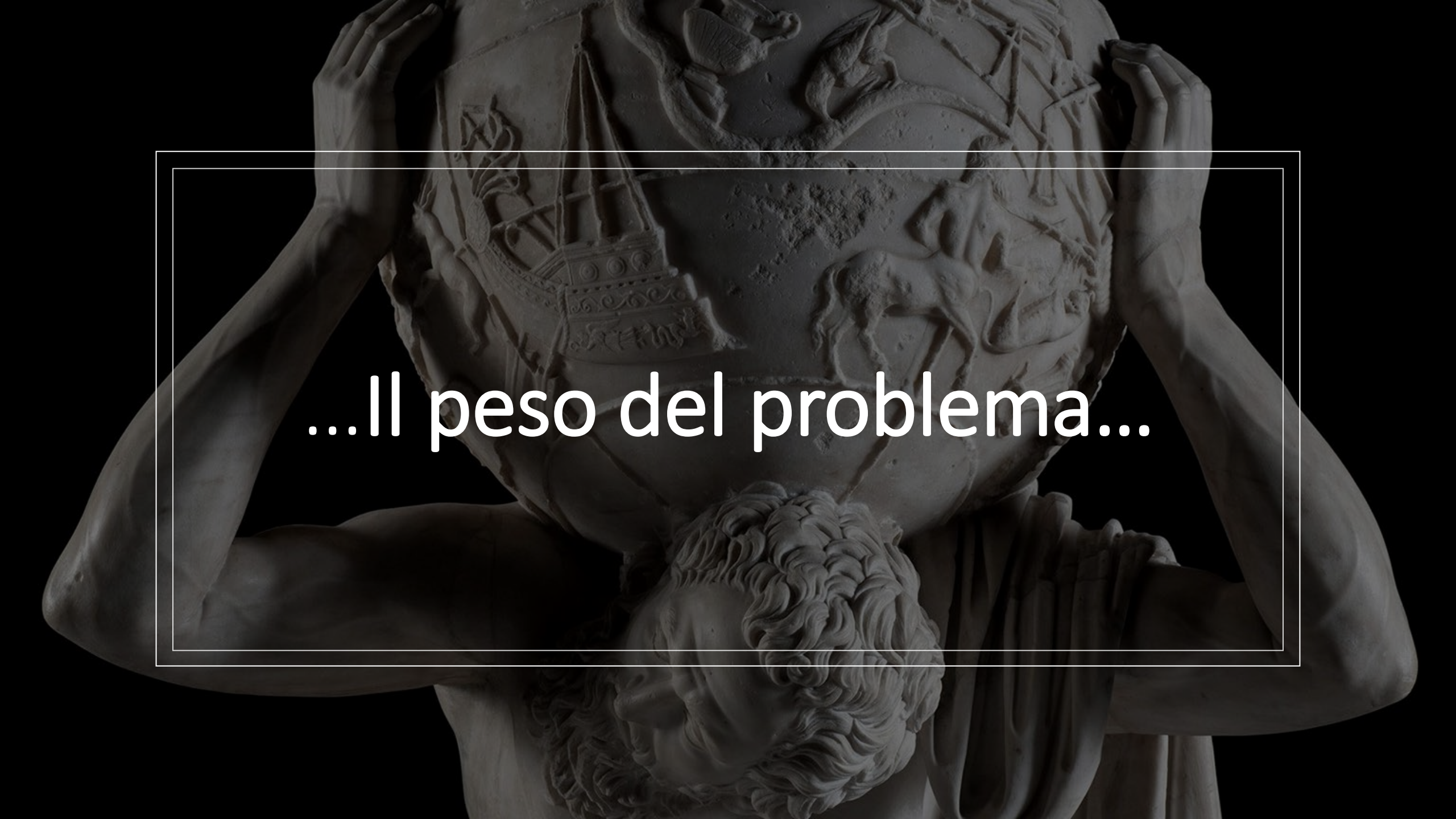
ege of
elines. Circulation.

Necessità di screening precoce!

(Anamnesi, EO, ABI/TBI)

- ome ischemia acuta ed hanno un forte impatto
tario
- Le cause di PAD e di altre patologie aterosclerotiche non sono le stesse, ad indicare la necessità di approccio specifico



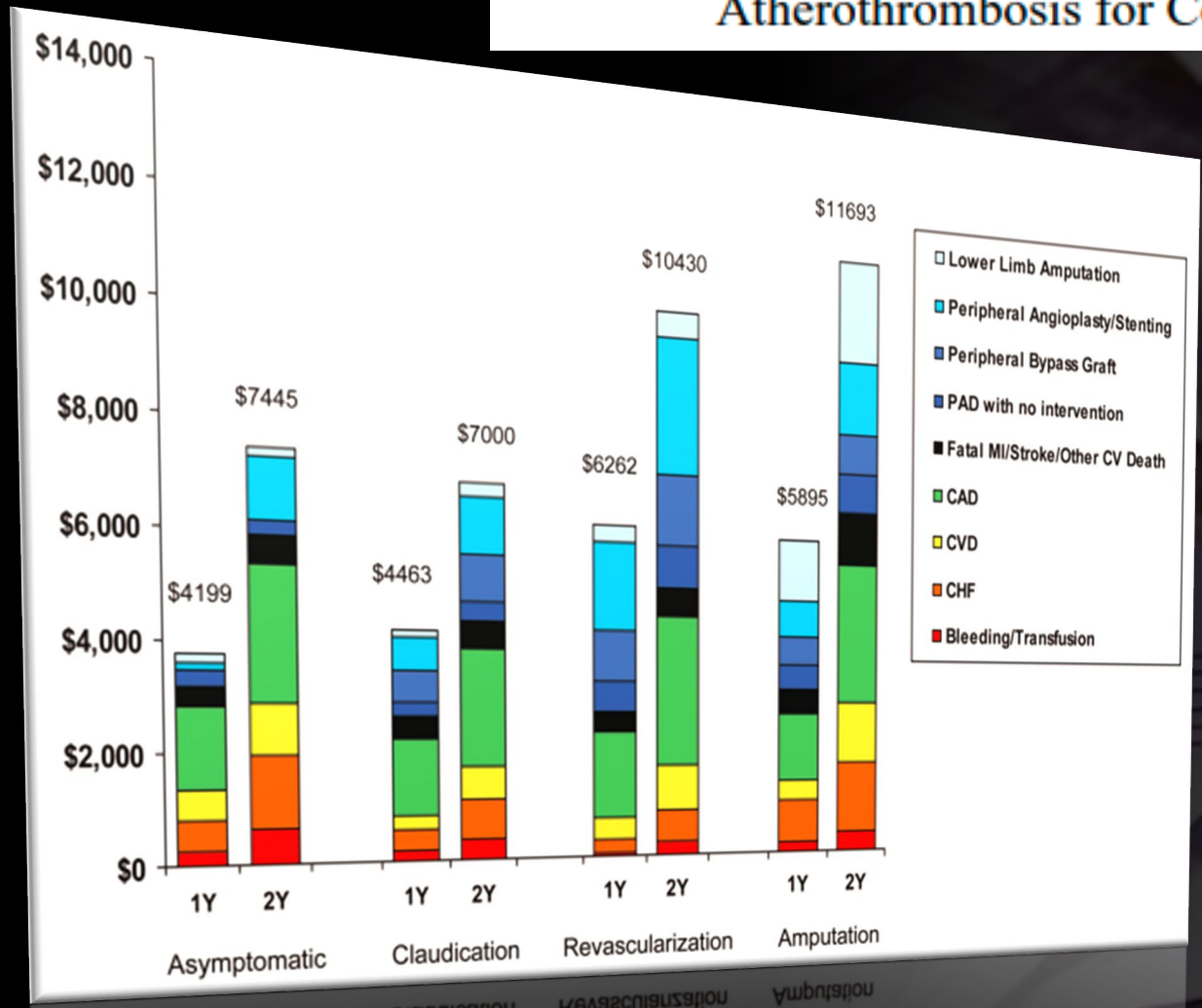

…Il peso del problema…

- Rappresenta **25.6% del global burden** della pt CV e **1.7% del global burden of disease**
- **Terza** principale causa di morte di morbidità CV dopo Cpt ischemica & stroke
- Prevalenza relata **all'età** (20% a 80 aa in US)
- Aumentata prevalenza nei **low & middle-income countries**
- Elevate **mortalità**, **morbidità** e **disabilità** dovuta alle amputazioni

Costi

Vascular Hospitalization Rates and Costs in Patients With Peripheral Artery Disease in the United States

Elizabeth M. Mahoney, Kaijun Wang, Hong H. Keo, Sue Duval, Kim G. Smolderen, David J. Cohen, Gabriel Steg, Deepak L. Bhatt, Alan T. Hirsch and on behalf of the Reduction of Atherothrombosis for Continued Health (REACH) Registry Investigators



- This study provides an in-depth examination of long-term rates of vascular events, hospitalizations, and revascularization procedures in different PAD subgroups categorized according to symptomatic status and prior diagnostic/treatment history.
- This study documents the existence of an iterative pattern of cost accrual related to high rates of recurrent rehospitalizations and repeat revascularization procedures in patients with symptomatic PAD.
- The high rates of recurring rehospitalizations and revascularization procedures suggest that neither patients, physicians, nor healthcare systems should assume that an initial lower extremity PAD procedure serves as a permanent resolution of the underlying condition.

Mahoney et al Circ Cardiovasc Qual Outcomes 2010

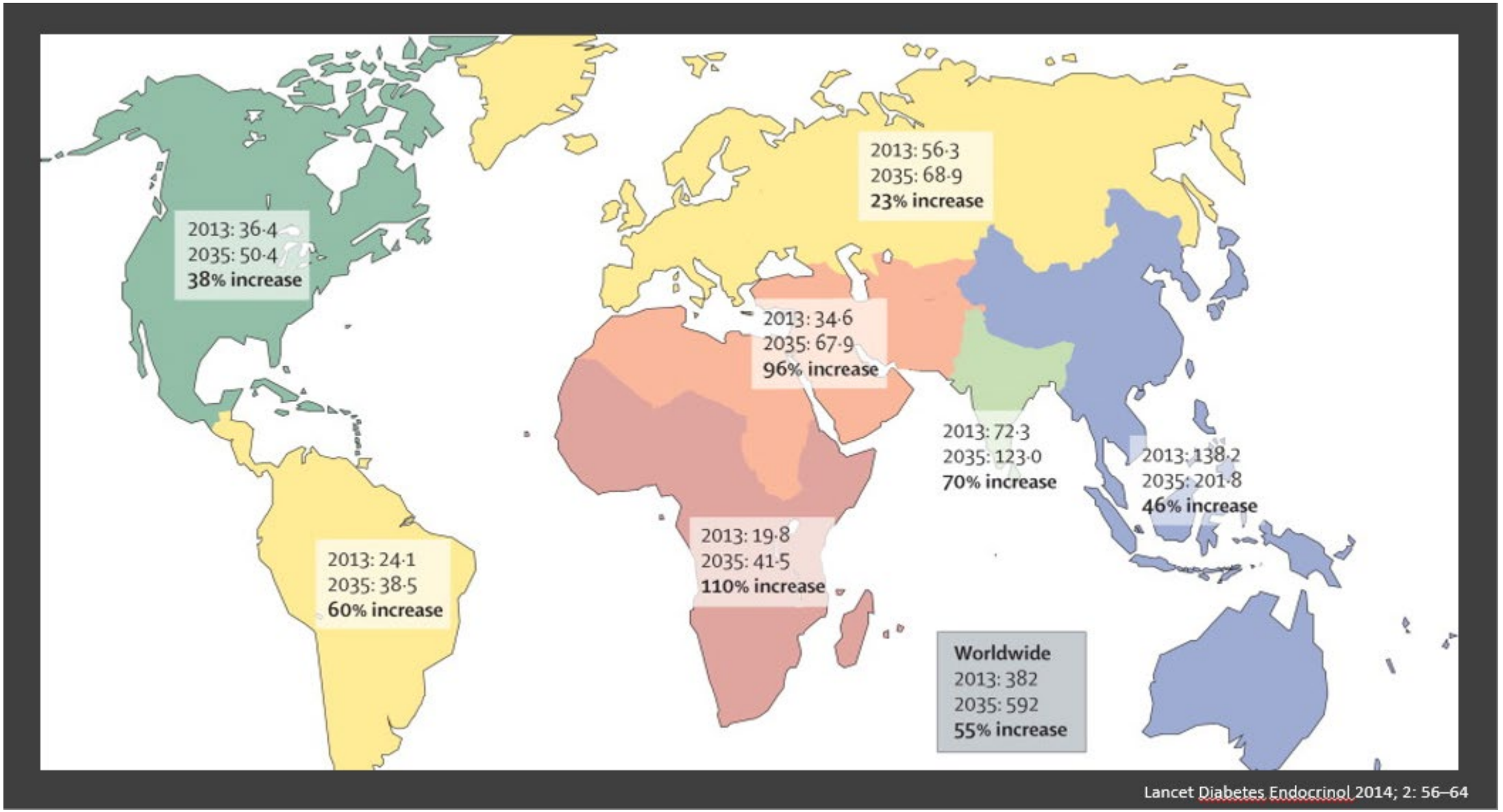
…mettiamo a fuoco la PAD nel Diabete…

Caratteristiche nel Diabete

- Più giovani
- BMI maggiore
- Neuropatici
- Maggiore comorbidità CV

- Patologia ostruttiva su base aterosclerotica con maggiore incidenza di **calcificazioni vascolari**
- Rapida **progressione**
- Prevalentemente **distale** (meno passibile di rivascolarizzazione) e bilaterale
- Prevalgono le **occlusioni** rispetto alle stenosi
- Minor **neoangiogenesi** con minor capacità di compenso

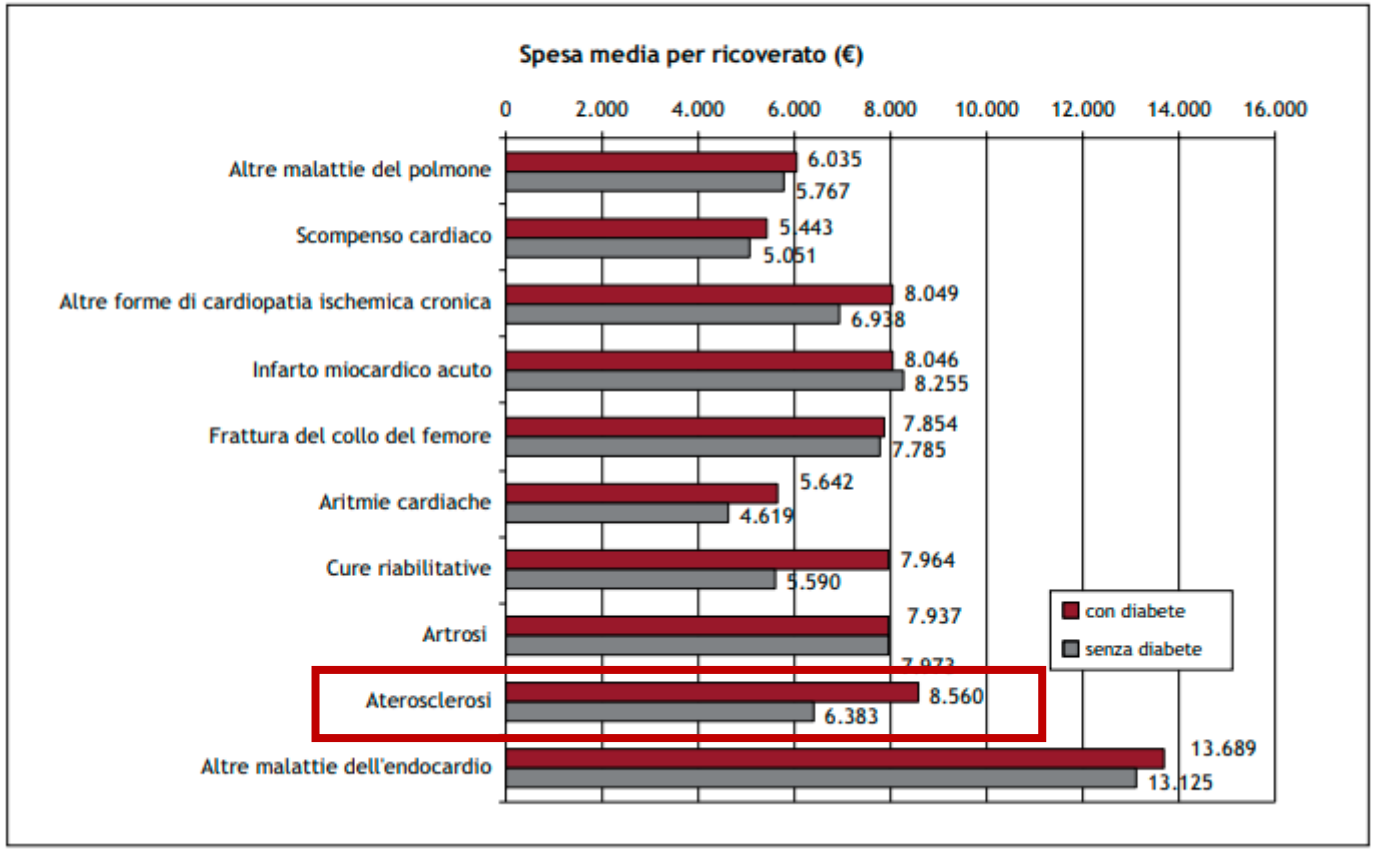
Considerando la prevalenza del Diabete...**GRANDI NUMERI!**



Costi

Grafico 25

Spesa media per le prime 10 diagnosi principali in caso di ricovero ordinario nei soggetti con e senza diabete (sono considerati i casi che assorbono la maggior parte di spesa)



… il peso dell'associazione è noto da tempo…

Large population-based studies have shown that the prevalence of PAD is higher in patients with DM

Lo Studio Framingham ha dimostrato un rischio di **3.5- e di 8,6** vv rispettivamente in uomini e donne di sviluppare PAD in presenza di DM. Kannel WB, McGee DL. Update on some epidemiologic features of intermittent claudication: the Framingham Study. J Am Geriatr Soc 1985; 33: 13–18

Nel Rochester Study la prevalenza di PAD al momento della diagnosi di DM era **8%** tra il 1945 and 1969, mentre era **10.5%** in 1970 . Melton LJ III, Macken KM, Palumbo PJ, Elveback LR. Incidence and prevalence of clinical peripheral vascular disease in a populationbased cohort of diabetic patients. Diabetes Care 1980; 3: 650–654

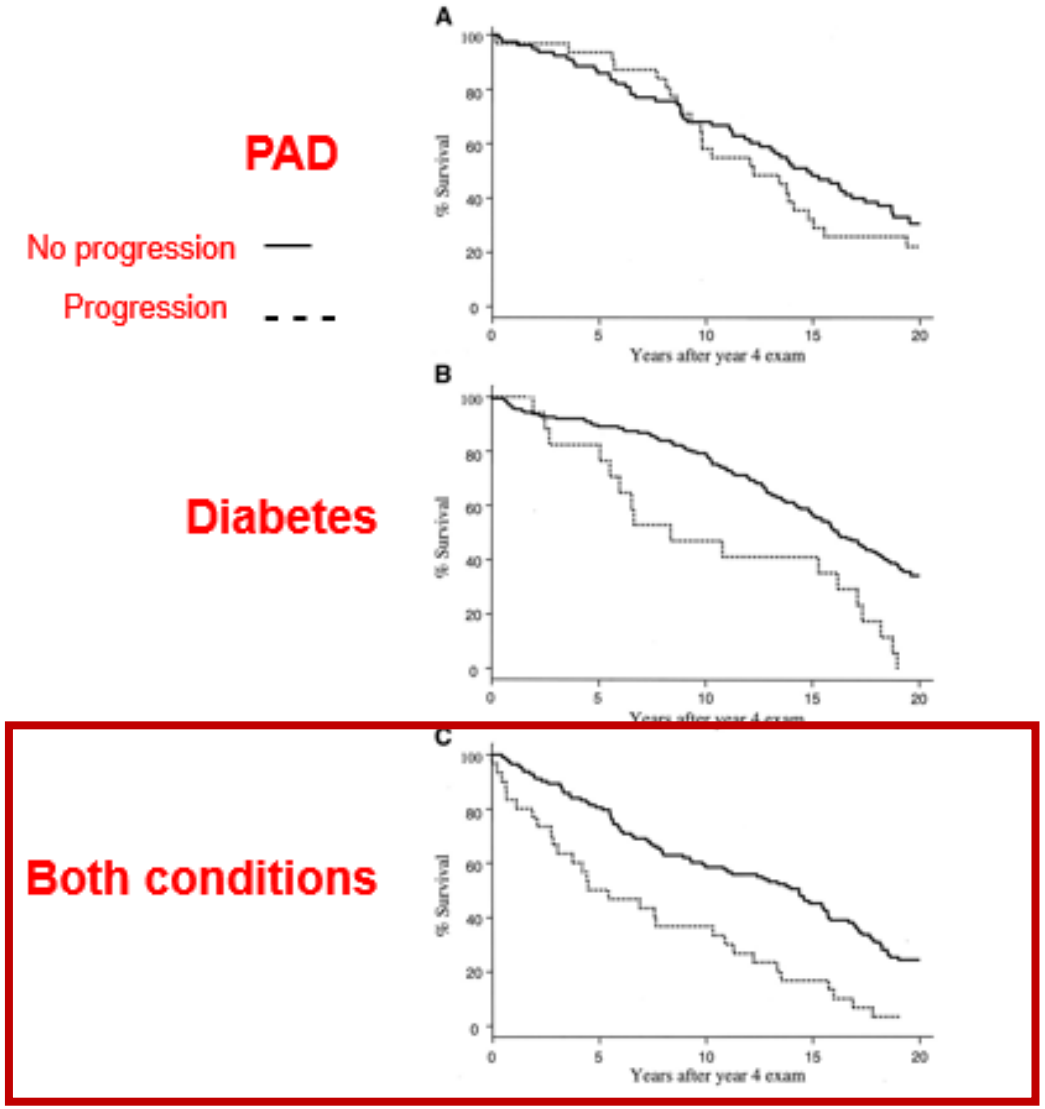
Lo Studio Hoorn ha documentato che la prevalenza di ABI < 0.9 in soggetti con normale tolleranza glucidica era **7%** per arrivare al **20.9%** in soggetti con diabete Beks PJ, Mackaay AJ, de Neeling JN, de Vries H, Bouter LM, Heine RJ. Peripheral arterial disease in relation to glycaemic level in an elderly Caucasian population: the Hoorn study. Diabetologia 1995; 38: 86–96

Uno studio pilota ha documentato una prevalenza di asymptomatic PAD del **33%** Elhadd T, Robb R, Jung R, Stonebridge P, Belch J. Pilot study of prevalence of asymptomatic peripheral arterial occlusive disease in patients with diabetes attending a hospital clinic. Pract Diabetes Int 1999; 16: 163–166.

…ed oggi…

È come se questa evidenza ci appartenesse poco….

PAD progression at year 4 was a significant predictor of mortality in DM



Cynthia L. Leibson et al. Dia Care 2004;27:2843-2849

PAD+T2DM

Maggiore progressione di danno:

PAD+T2D sviluppano quadro sintomatico che si manifesta ad uno stadio più severo rispetto ai non diabetici

Poorer outcomes

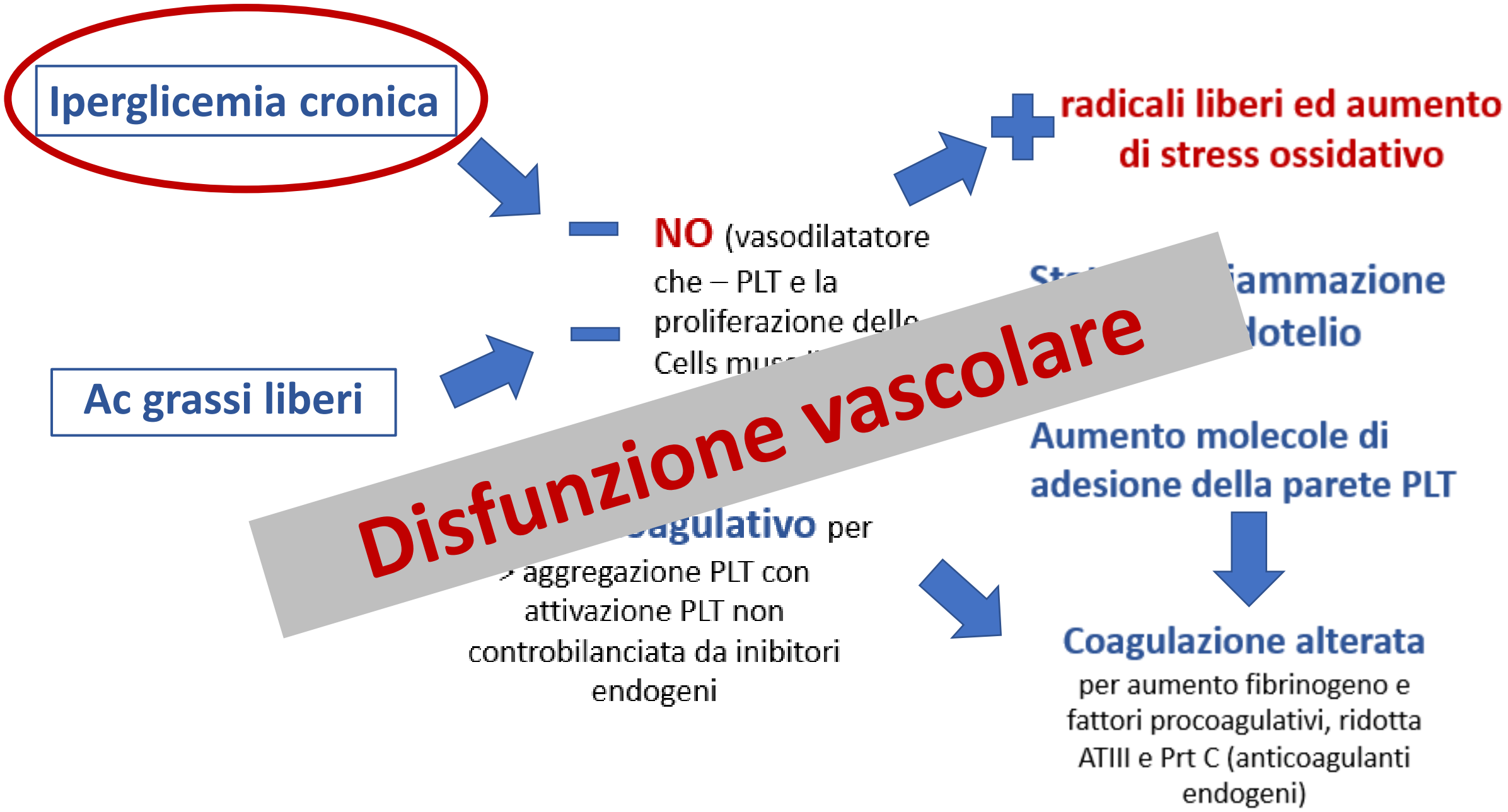
PAD+T2D: probabilità raddoppiata di sviluppare ulcere ai piedi ed amputazioni rispetto a PAD senza T2D

PAD + T2D hanno un rischio quasi TRIPLICATO di stroke e SCC rispetto al singolo quadro

Thiruvoipati T et al. World J Diabetes 2015;6:961–9


Stringere l’obiettivo

Patogenesi nel Diabete




IL CONTROLLO GLICEMICO
E’ FONDAMENTALE

2016 AHA/ACC Guideline on the Management of Patients With Lower Extremity Peripheral Artery Disease: Executive Summary

A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines

5.3. Glycemic Control

Recommendations for Glycemic Control

COR	LOE	Recommendations
I	C-EO	Management of diabetes mellitus in the patient with PAD should be coordinated between members of the healthcare team.
IIa	B-NR	Glycemic control can be beneficial for patients with CLI to reduce limb-related outcomes[161,162]

LEVEL (QUALITY) OF EVIDENCE‡

LEVEL C-EO (Expert Opinion)

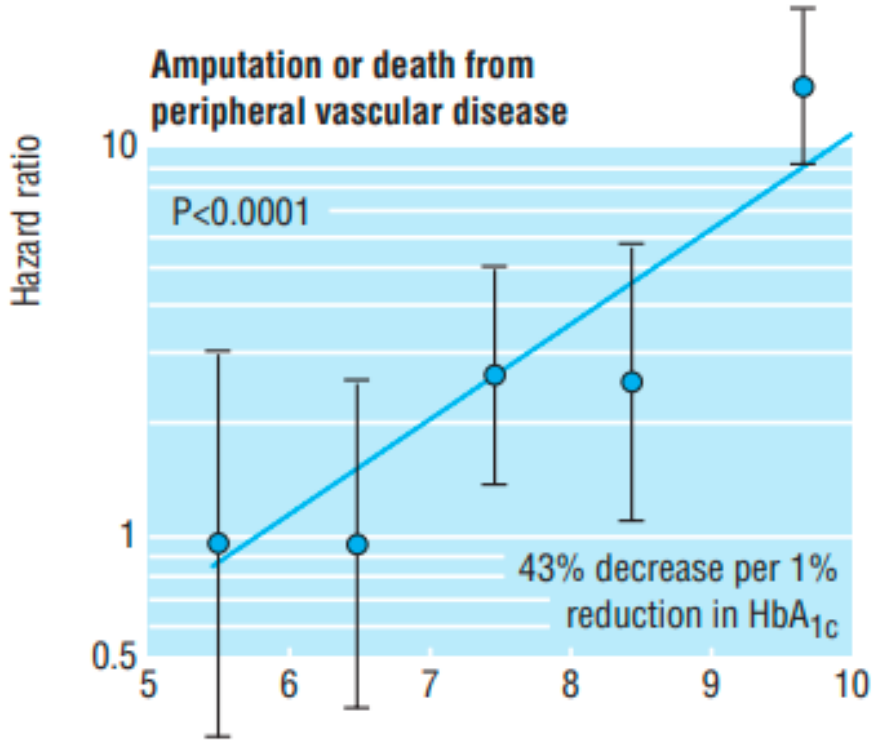
Consensus of expert opinion based on clinical experience

LEVEL B-NR (Nonrandomized)

- Moderate-quality evidence‡ from 1 or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies
- Meta-analyses of such studies

Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study

Irene M Stratton, Amanda I Adler, H Andrew W Neil, David R Matthews, Susan E Manley, Carole A Cull, David Hadden, Robert C Turner, Rury R Holman on behalf of the UK Prospective Diabetes Study Group



Conclusions In patients with type 2 diabetes the risk of diabetic complications was strongly associated with previous hyperglycaemia. Any reduction in HbA1c is likely to reduce the risk of complications, with the lowest risk being in those with HbA1c values in the normal range (< 6.0%).

SGLT2 inhibitors for primary and secondary prevention of cardiovascular and renal outcomes in type 2 diabetes: a systematic review and meta-analysis of cardiovascular outcome trials

Thomas A Zelniker, Stephen D Wiviott, Itamar Raz, Kyungah Im, Erica L Goodrich, Marc P Bonaca, Ofri Mosenzon, Eri T Kato, Avivit Cahn, Remo H M Furtado, Deepak L Bhatt, Lawrence A Leiter, Darren K McGuire, John P H Wilding, Marc S Sabatine

Composite of myocardial infarction, stroke, and cardiovascular death (major adverse cardiovascular events)

MACE – 10%

	Patients		Events	Events per 1000 patient-years		Weight (%	HR	HR (95% CI)
	Treatment (n/N)	Placebo (n/N)		Treatment	Placebo			
Patients with atherosclerotic cardiovascular disease								
EMPA-REG OUTCOME	4687/7020	2333/7020	772	37·4	43·9	29		
CANVAS Program	3756/6656	2900/6656	796	34·1	41·3	32		
DECLARE-TIMI 58	3474/6974	3500/6974	1020	36·8	41·0	38		
Fixed effects model for atherosclerotic cardiovascular disease (p=0·0002)								
Patients with multiple risk factors								
CANVAS Program	2039/3486	1447/3486	215	15·8	15·5	25		
DECLARE-TIMI 58	5108/10 186	5078/10 186	539	13·4	13·3	74		
Fixed effects model for multiple risk factors (p=0·98)								

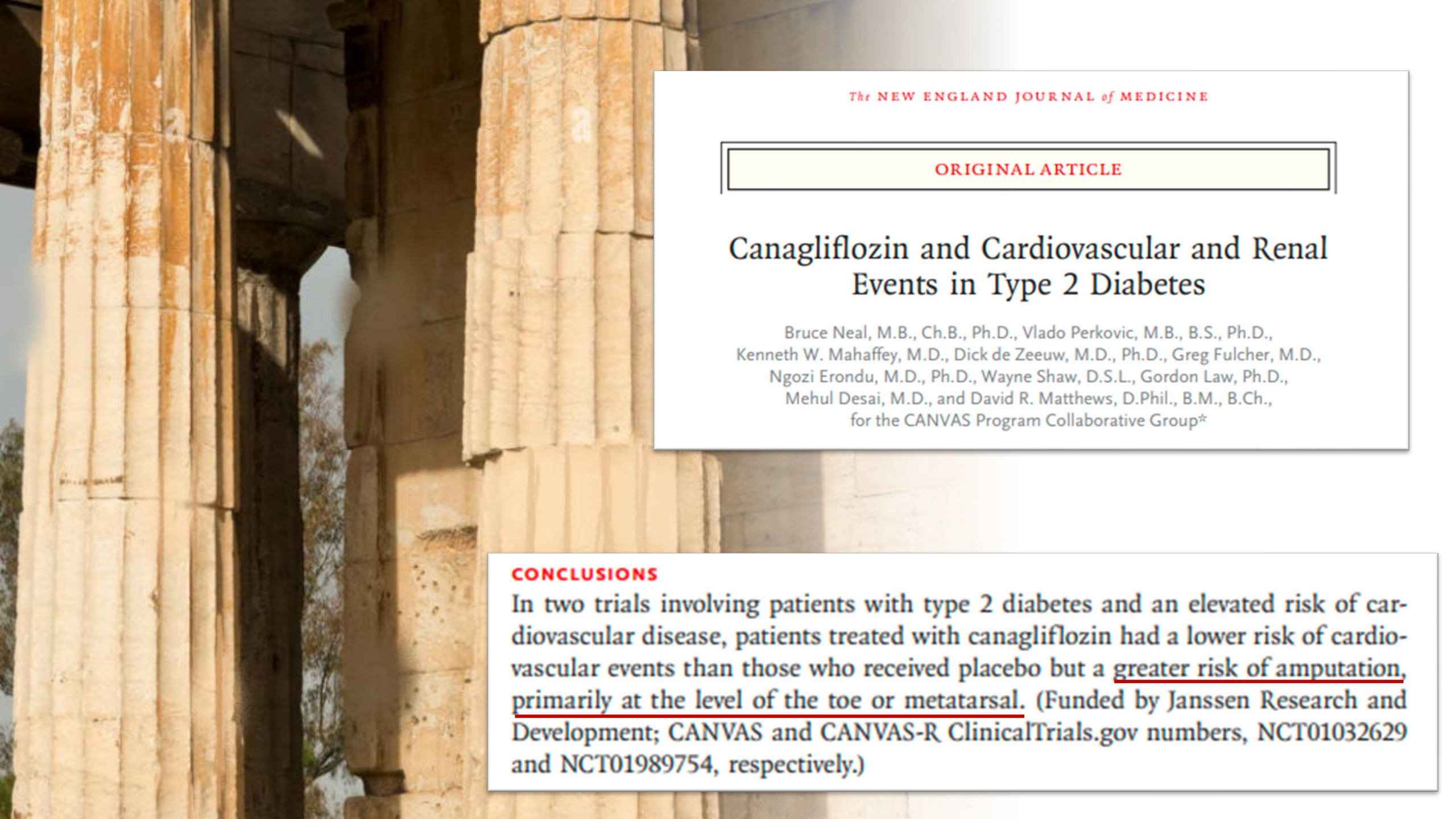
Cardiovascular, mortality, and kidney outcomes with GLP-1 receptor agonists in patients with type 2 diabetes: a systematic review and meta-analysis of cardiovascular outcome trials

Søren L Kristensen, Rasmus Rørth, Pardeep S Jhund, Kieran F Docherty, Naveed Sattar, David Preiss, Lars Køber, Mark C Petrie, John J V McMurray

Lancet Diabetes Endocrinol 14 Agust 2019

MACE – 12%

	GLP-1 receptor agonist n/N (%)	Placebo n/N (%)	Hazard ratio (95% CI)	NNT (95% CI)	p value
Three-component 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)		0·015
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)		<0·0001
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
Overall (I^2=40·9%, p=0·118)	**2948/27 977 (11%)**	**3304/28 027 (12%)**	**0·88 (0·82–0·94)**	**75 (50–151)**	**<0·0001**



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Canagliflozin and Cardiovascular and Renal Events in Type 2 Diabetes

Bruce Neal, M.B., Ch.B., Ph.D., Vlado Perkovic, M.B., B.S., Ph.D., Kenneth W. Mahaffey, M.D., Dick de Zeeuw, M.D., Ph.D., Greg Fulcher, M.D., Ngozi Erondu, M.D., Ph.D., Wayne Shaw, D.S.L., Gordon Law, Ph.D., Mehul Desai, M.D., and David R. Matthews, D.Phil., B.M., B.Ch., for the CANVAS Program Collaborative Group*

CONCLUSIONS

In two trials involving patients with type 2 diabetes and an elevated risk of cardiovascular disease, patients treated with canagliflozin had a lower risk of cardiovascular events than those who received placebo but a greater risk of amputation, primarily at the level of the toe or metatarsal. (Funded by Janssen Research and Development; CANVAS and CANVAS-R ClinicalTrials.gov numbers, NCT01032629 and NCT01989754, respectively.)

U.S. Food and Drug Administration
Protecting and Promoting *Your* Health

Drug Safety Communications

FDA confirms increased risk of leg and foot amputations with the diabetes medicine canagliflozin

This information is an update to the FDA Drug Safety Communication: Interim clinical trial results find increased risk of leg and foot amputations, mostly affecting the toes, with the diabetes medicine canagliflozin
May 18, 2016.

Table 2. Adverse Events.*

Event	Canagliflozin	Placebo	P Value†
	event rate per 1000 patient-yr		
All serious adverse events	104.3	120.0	0.04
Adverse events leading to discontinuation	35.5	32.8	0.07
Serious and nonserious adverse events of interest recorded in the CANVAS Program			
Acute pancreatitis (adjudicated)	0.5	0.4	0.63
Cancer			
Renal cell	0.6	0.2	0.17
Bladder	1.0	1.1	0.74
Breast	3.1	2.6	0.65
Photosensitivity	1.0	0.3	0.07
Diabetic ketoacidosis (adjudicated)	0.6	0.3	0.14
Amputation	6.3	3.4	<0.001
Fracture (adjudicated)‡			
All	15.4	11.9	0.02
Low-trauma	11.6	9.2	0.06
Venous thromboembolic events	1.7	1.7	0.63
Infection of male genitalia§	34.9	10.8	<0.001
Serious and nonserious adverse events of interest collected in CANVAS alone¶			
Osmotic diuresis	34.5	13.3	<0.001
Volume depletion	26.0	18.5	0.009
Hypoglycemia	50.0	46.4	0.20
Acute kidney injury	3.0	4.1	0.33
Hyperkalemia	6.9	4.4	0.10
Urinary tract infection	40.0	37.0	0.38
Mycotic genital infection in women	68.8	17.5	<0.001
Severe hypersensitivity or cutaneous reaction	8.5	6.1	0.17
Hepatic injury	7.4	9.1	0.35
Renal-related (including acute kidney injury)	19.7	17.4	0.32

The association of amputations and peripheral artery disease in patients with type 2 diabetes mellitus receiving sodium-glucose cotransporter type-2 inhibitors: real-world study

Sanjoy K. Paul [1]*, Deepak L. Bhatt [2], and Olga Montvida[1]

[1]Melbourne EpiCentre, University of Melbourne, The Royal Melbourne Hospital – City Campus, 7 East, Main Building, Grattan Street, Parkville Victoria 3050, Australia; and [2]Brigham and Women's Hospital Heart & Vascular Center and Harvard Medical School, 75 Francis Street, Boston, MA 02115, USA

Received 8 July 2020; revised 18 August 2020; editorial decision 4 November 2020; accepted 12 November 2020

3 293 983 pz con DM2

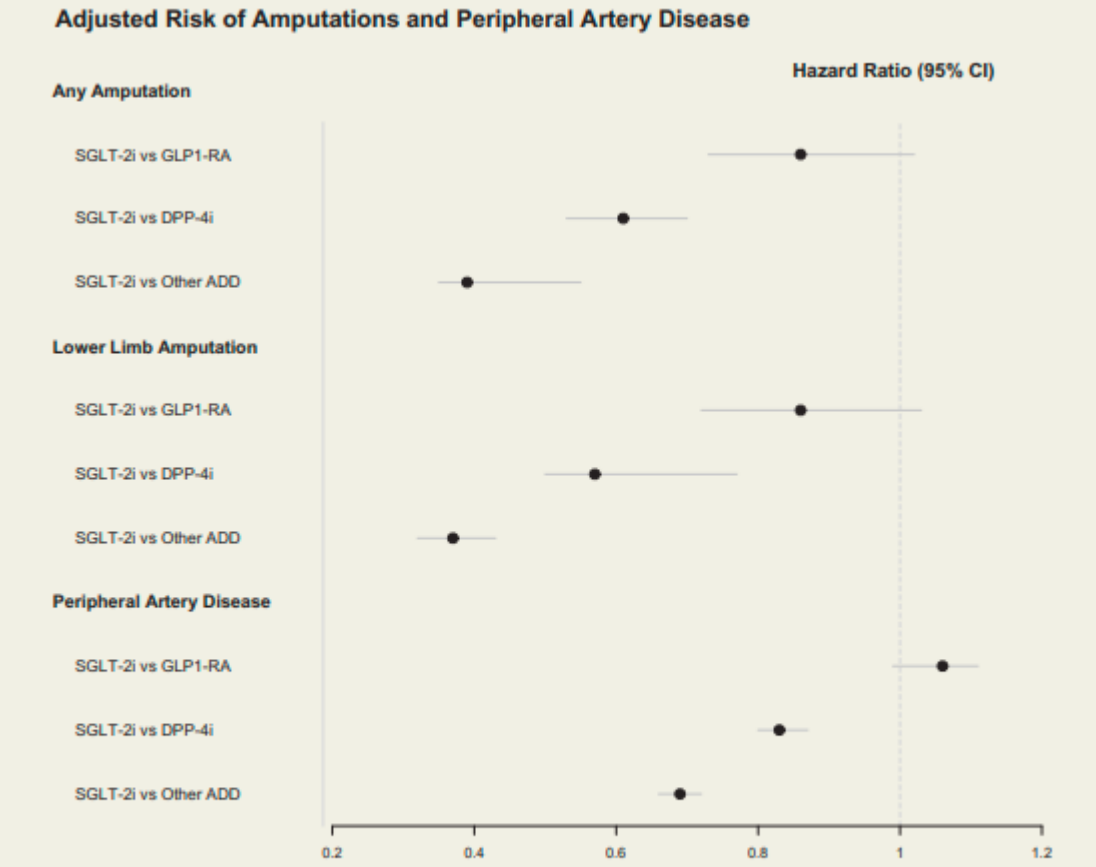
169 739 in SGLT-2i (no incretine)

149 826 in GLP-1RA (no SGLT-2i o DPP4i)

448 225 in DPP-4i (no GLP-1RA o SGLT-2i)

1 954 353 other ADDs

Graphical Abstract

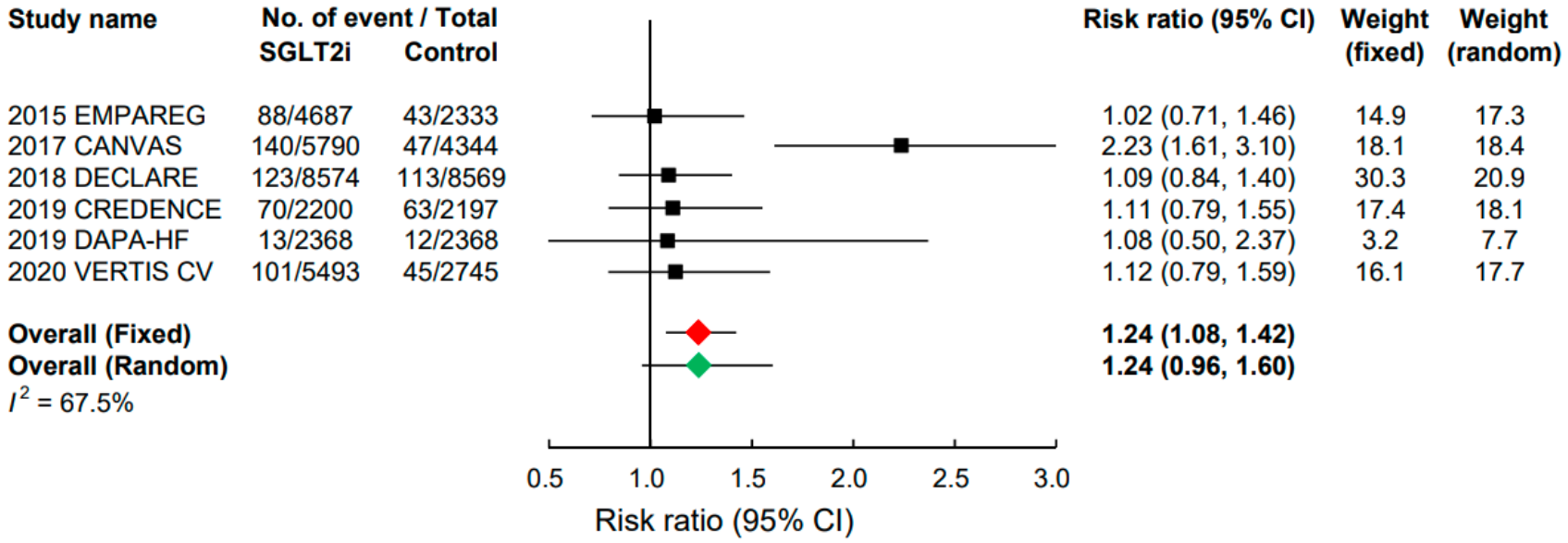


Keywords Amputation • Type 2 diabetes mellitus • Anti-diabetic drug • Sodium-glucose cotransporter-2 inhibitor • SGLT-2i • Canagliflozin • Incretins • Peripheral artery disease • Peripheral vascular disease

Conclusion The risk of amputation in patients treated with SGLT-2i and incretins was not higher compared with other ADDs. Pre-existing PAD was the greatest driver of amputation risk.

Sodium-glucose co-transporter-2 inhibitors and major adverse limb events: A trial-level meta-analysis including 51 713 individuals

Chen-Yu Huang MD, Jen-Kuang Lee MD, PhD



The amputation events primarily arise **from critical limb ischaemia** and **infection** instead of acute limb ischaemia.

"SGLT-2 inhibitors **are not** associated with increased risks of amputation operations even among various high-risk subgroups, including patients with PAD"

Diabetes Obes Metab 2020 Dec;22(12):2348-2355.

Lin et al. Cardiovasc Diabetol (2021) 20:91
https://doi.org/10.1186/s12933-021-01276-9

Cardiovascular Diabetology

ORIGINAL INVESTIGATION Open Access

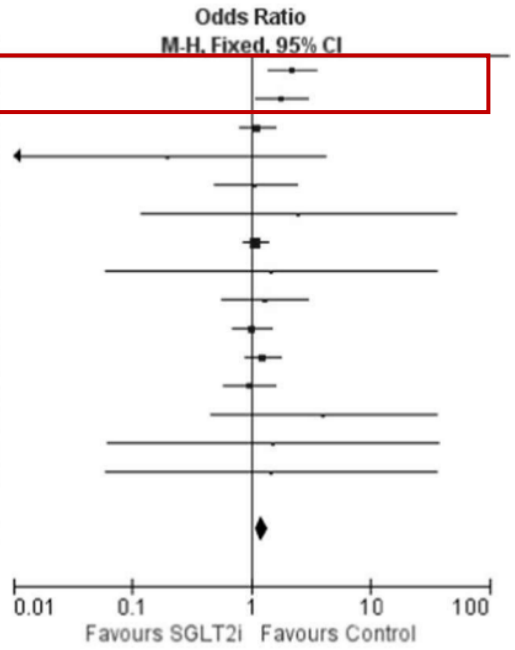
SGLT2 inhibitors and lower limb complications: an updated meta-analysis

Chu Lin[1†], Xingyun Zhu[1†], Xiaoling Cai[1*], Wenjia Yang[1], Fang Lv[1], Lin Nie[2] and Linong Ji[1*]

a

Study or Subgroup	SGLT2i Events	SGLT2i Total	Control Events	Control Total	Weight	Odds Ratio M-H, Fixed, 95% CI
CANA Neal 2017(CANVAS)	95	2886	22	1441	7.1%	2.20 [1.37, 3.51]
CANA Neal 2017(CANVAS-R)	45	2904	25	2903	6.1%	1.81 [1.11, 2.96]
CANA Perkovic 2019(CREDENCE)	70	2202	63	2199	15.2%	1.11 [0.79, 1.57]
DAPA Herspink 2020(DAPA-CKD)	0	2152	2	2151	0.6%	0.20 [0.01, 4.16]
DAPA McMurray 2019(DAPA-HF)	13	2368	12	2368	3.0%	1.08 [0.49, 2.38]
DAPA Pollock 2019(DELIGHT)	2	300	0	148	0.2%	2.49 [0.12, 52.14]
DAPA Wiviott 2019(DECLARE-TIMI 58)	123	8574	113	8569	27.8%	1.09 [0.84, 1.41]
EMPA Lewin & Defronzo 2015	1	551	0	267	0.2%	1.46 [0.06, 35.90]
EMPA Packer 2020(EMPEROR)	13	1863	10	1867	2.5%	1.30 [0.57, 2.98]
EMPA Zinman 2015(EMPA-REG)	88	4687	43	2333	14.0%	1.02 [0.71, 1.47]
ERTU Cannon 2020(VERTIS CV)	111	5493	45	2745	14.6%	1.24 [0.87, 1.76]
SOTA Bhatt 2020(SCORED)	32	5291	33	5286	8.2%	0.97 [0.59, 1.58]
SOTA Bhatt 2020(SOLOIST-WHF)	4	605	1	611	0.2%	4.06 [0.45, 36.43]
SOTA Buse 2018	1	525	0	268	0.2%	1.54 [0.06, 37.83]
SOTA Danne 2018	1	524	0	258	0.2%	1.48 [0.06, 36.49]
Total (95% CI)		**40925**		**33414**	**100.0%**	**1.23 [1.08, 1.40]**
Total events	599		369			

Heterogeneity: Chi² = 14.25, df = 14 (P = 0.43); I² = 2%
Test for overall effect: Z = 3.04 (P = 0.002)



Compared with nonSGLT2i users, the risks of amputation and PAD were **slightly increased** in patients with canaglifozin treatment.

Greater reductions in **body weight** and **blood pressure** might be associated with the increased risk of lower limb complications in SGLT2i users.

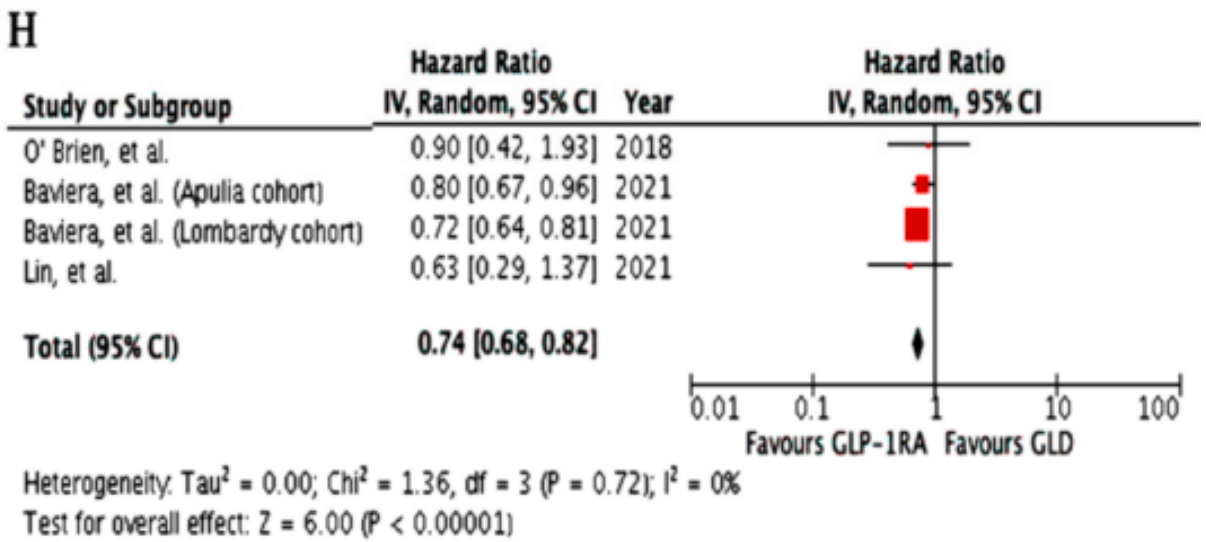
Monitoring body weight and blood pressure reduction might be an important risk **precaution** action for patients at high risk of lower limb complications during the SGLT2i treatment course.

Systematic Review

Cardiovascular and Renal Effectiveness of GLP-1 Receptor Agonists vs. Other Glucose-Lowering Drugs in Type 2 Diabetes: A Systematic Review and Meta-Analysis of Real-World Studies

Irene Caruso, Angelo Cignarelli, Gian Pio Sorice, Annalisa Natalicchio, Sebastio Perrini, Luigi Laviola and Francesco Giorgino *

Meta-analysis of the CV effects in RWS comparing GLP-1RA vs. other GLD (except SGLT-2i)



Peripheral artery disease occurrence showed a significant 25% risk reduction of this particular outcome (HR 0.74, 95% CI 0.68–0.82, I2 = 0%)

The Impact of Liraglutide on Diabetes-Related Foot Ulceration and Associated Complications in Patients With Type 2 Diabetes at High Risk for Cardiovascular Events: Results From the LEADER Trial

Ketan Dhatariya,[1,2] Stephen C. Bain,[3] John B. Buse,[4] Richard Simpson,[5] Lise Tarnow,[6] Margit Staum Kaltoft,[7] Michael Stellfeld,[7] Karen Tornøe,[7] Richard E. Pratley,[8] and the LEADER Publication Committee on behalf of the LEADER Trial Investigators

Diabetes Care 2018;41:2229–2235 | https://doi.org/10.2337/dc18-1094

CONCLUSIONS

Treatment with liraglutide in patients with type 2 diabetes and at high risk of CV events in the LEADER trial did not increase the risk of DFU events and was associated with a significantly lower risk of DFU-related amputations compared with placebo. This association, possibly due to chance, needs further investigation.

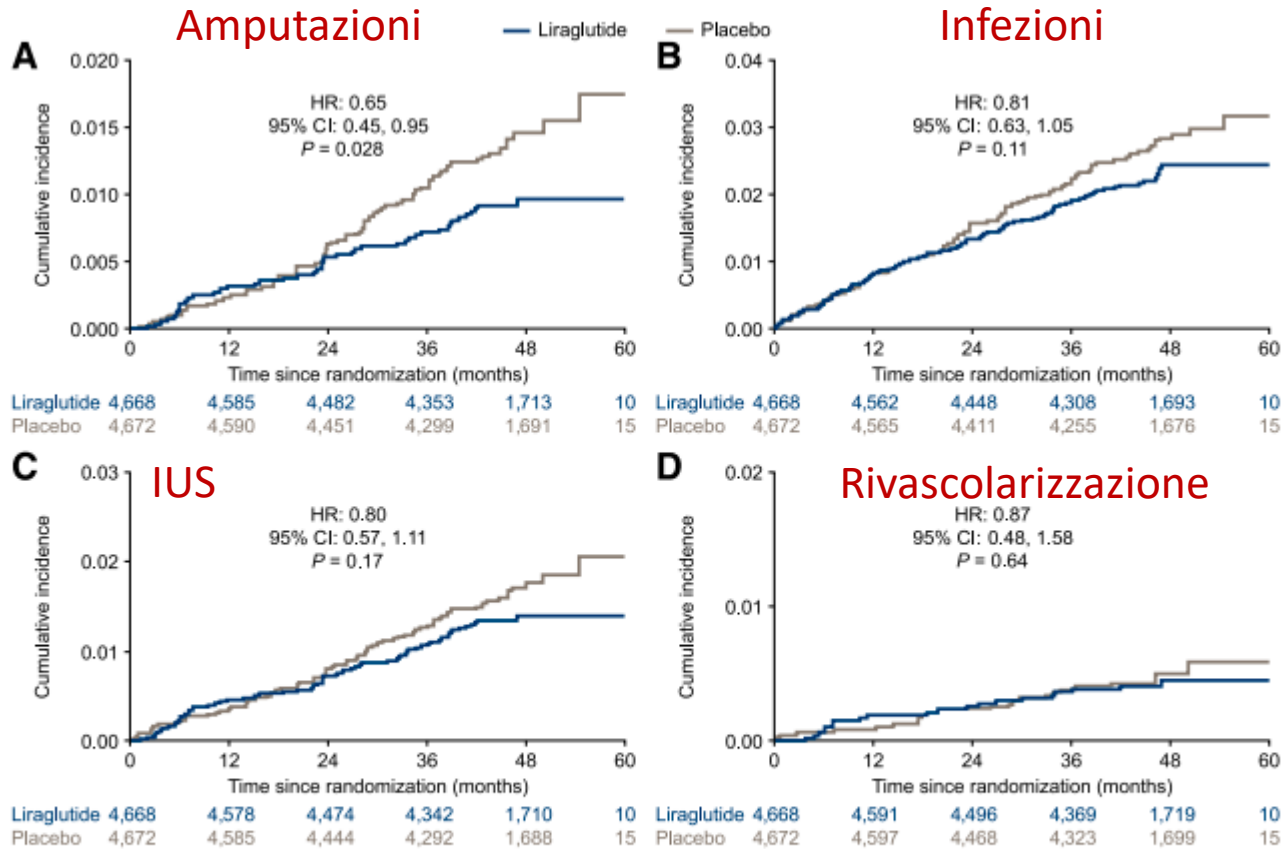


Figure 2—Cumulative incidence plot of time to first DFU-related complication among patients treated with liraglutide vs. placebo in the LEADER trial. *A*: Amputation (44 first DFU events in the liraglutide group and 67 first DFU events in the placebo group). *B*: Infection (107 and 131 first DFU events in liraglutide and placebo groups, respectively). *C*: Involvement of underlying structures (64 and 80 first DFU events in liraglutide and placebo groups, respectively). *D*: Peripheral revascularization (20 and 23 first DFU events in liraglutide and placebo groups, respectively).

The GLP-1 receptor agonist liraglutide inhibits progression of vascular disease via effects on atherogenesis, plaque stability and endothelial function in an ApoE$^{-/-}$ mouse model

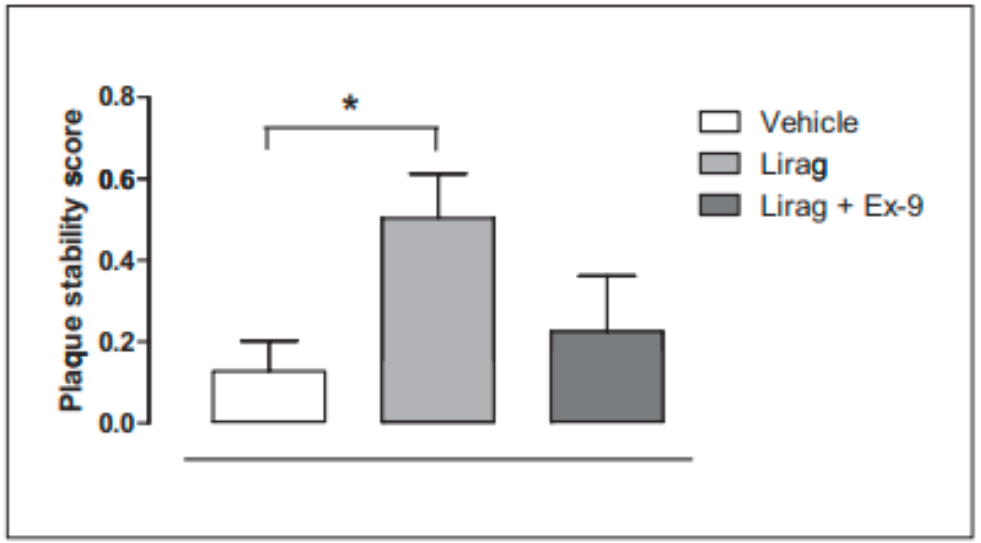
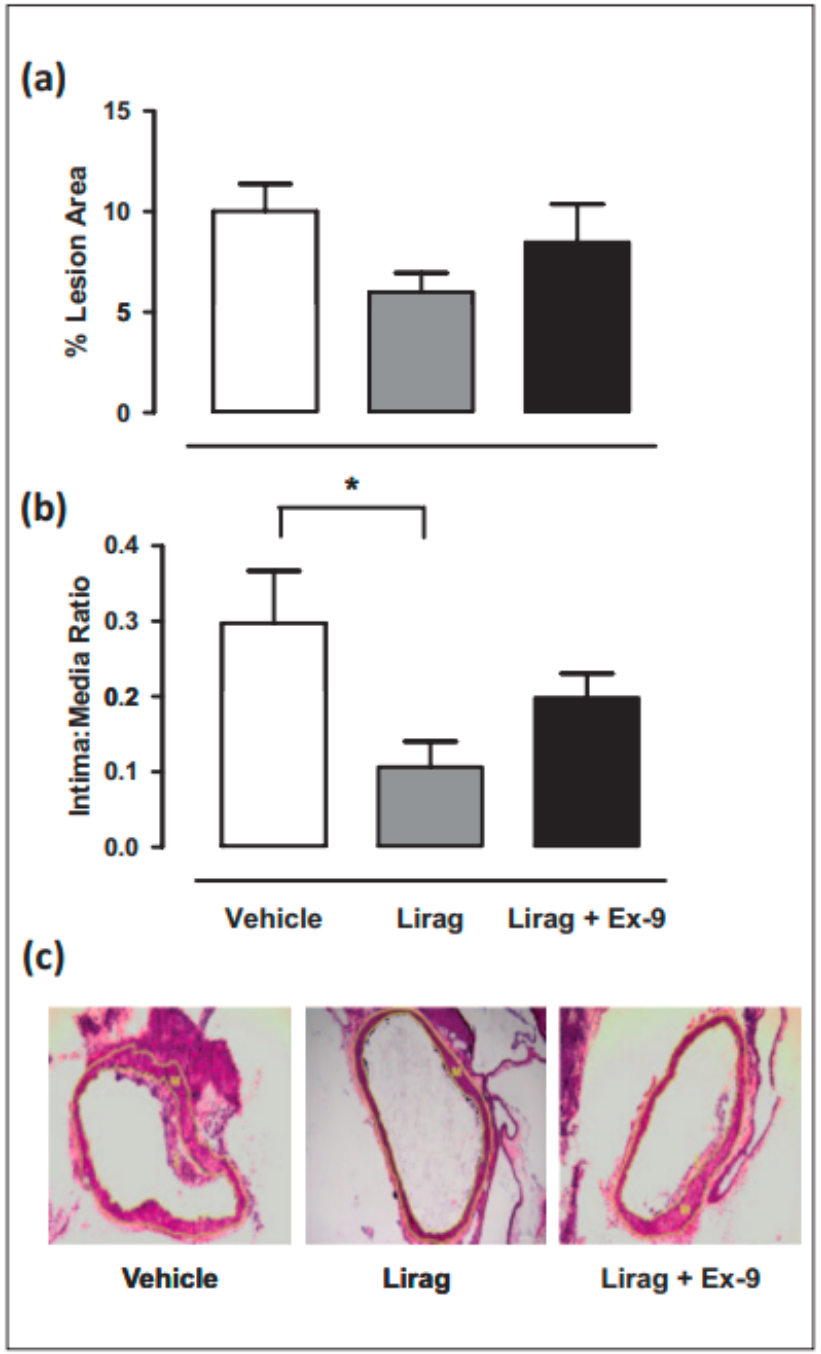
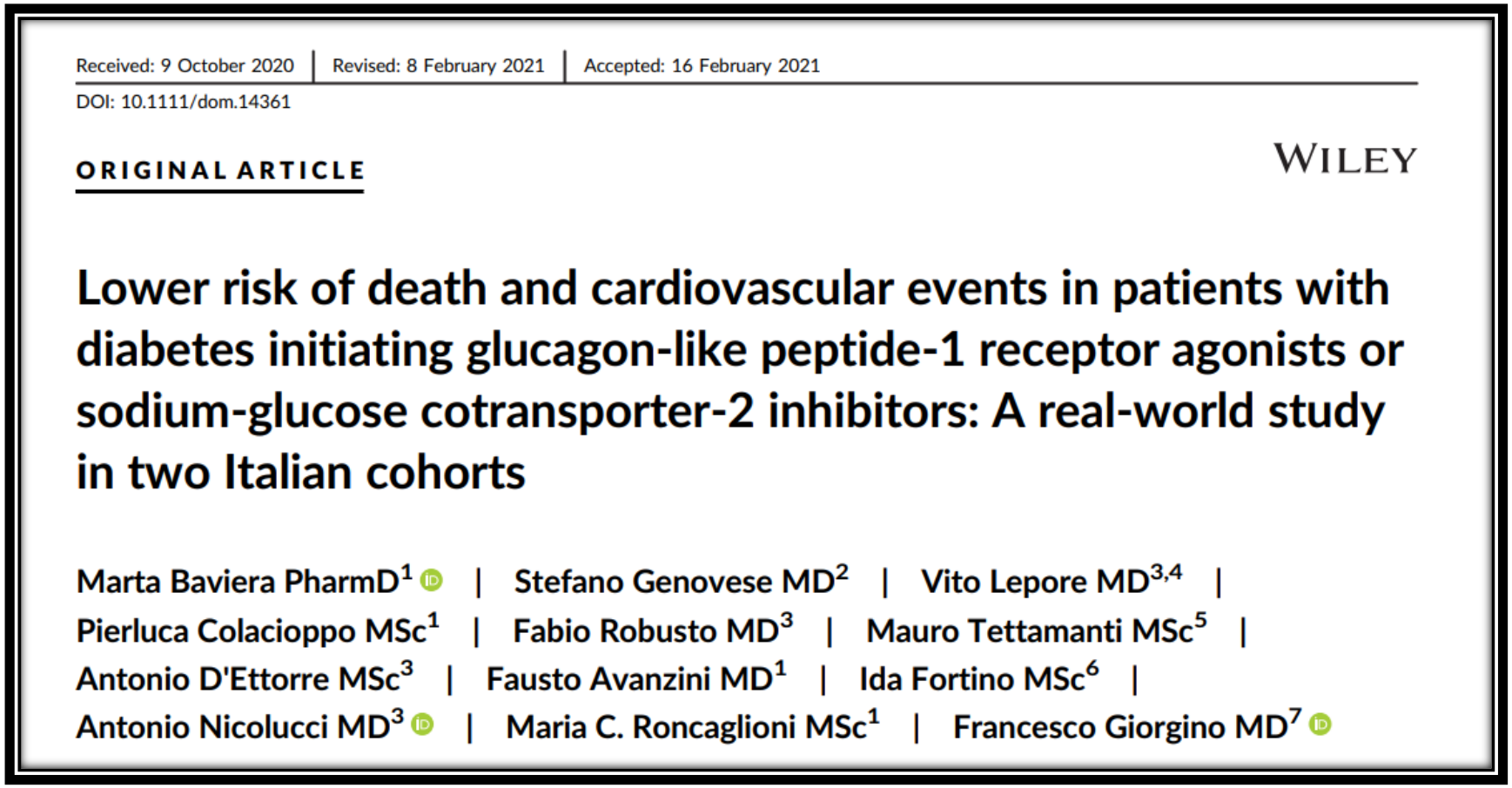


Figure 4. Liraglutide treatment significantly improves plaque stability score in early, low-burden atherosclerotic disease in ApoE$^{-/-}$ mice. Plaque stability calculated as described in methods.
ApoE$^{-/-}$: apolipoprotein E-deficient; ANOVA: analysis of variance.
*p< 0.05 versus vehicle, one-way ANOVA with Dunnett's post hoc test (n = 5–7).





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ORIGINAL ARTICLE

WILEY

Lower risk of death and cardiovascular events in patients with diabetes initiating glucagon-like peptide-1 receptor agonists or sodium-glucose cotransporter-2 inhibitors: A real-world study in two Italian cohorts

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Studio osservazionale di coorte in **18716 pazienti lombardi** e **11683 pazienti pugliesi**

- pazienti first users con GLP1RA vs altri AHAs
- pz first users con SGLT2i vs altri AHAs

Esaminato il rischio di morte e gli eventi cv dal 2010 al 2018.

Obiettivo: valutare efficacia e sicurezza GLP1RA e SGLT2i vs altri AHAs in ampia casistica real life

Lombardia: 18716 pz trattati con GLP1RA, 11683 trattati con sglt2i

Risultati coorte lombarda:

- l'inizio di un GLP1RA è risultato associato a un più basso rischio di morte x tutte le cause (-39%), malattia cerebrovascolare (-30%), stroke ischemico (-28%), **PAD (-28%) e complicanze arti inferiori (--33%) rispetto agli altri AHA**
- Inizio sglt2i era associato con più basso rischio di morte (-53%), malattia cerebrovascolare (-25%), HF (-44%) rispetto agli altri AHA

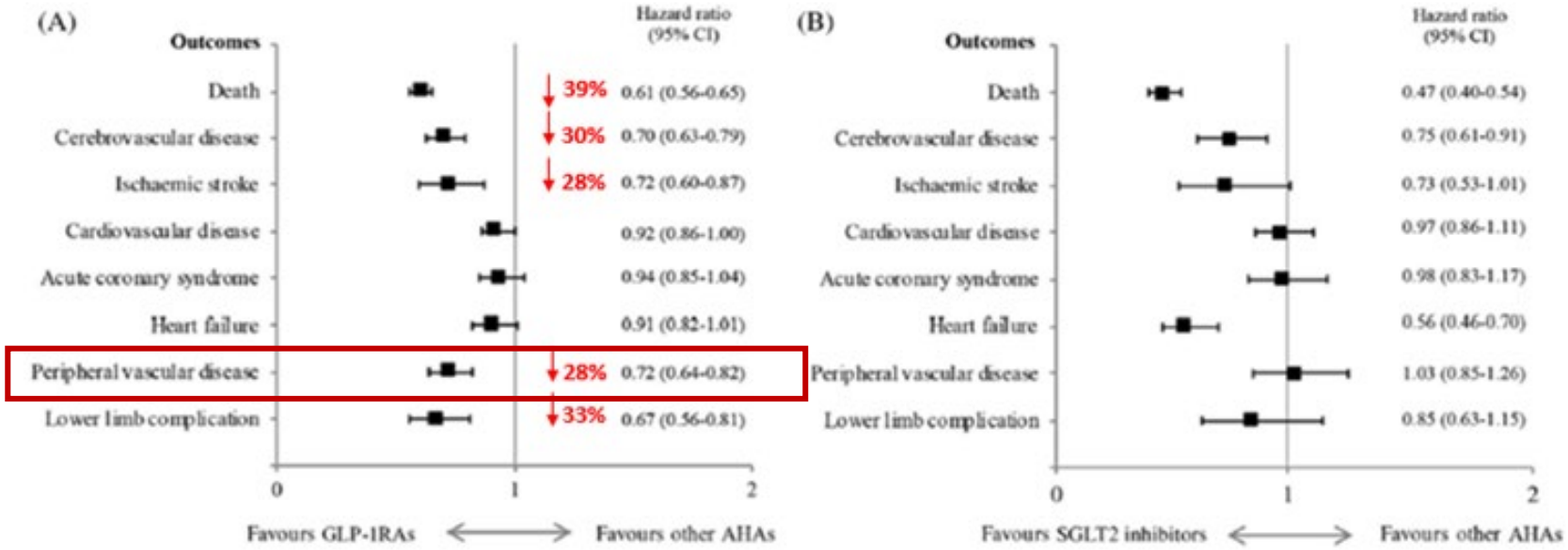


FIGURE 1 A, B, Hazard ratios (95% confidence interval [CI]) for death and clinical events in matched populations according to treatment status in Lombardy. GLP-1RA, glucagon-like peptide-1 receptor agonist; SGLT2, sodium-glucose cotransporter-2; AHA, antihyperglycaemic agent Baviera M. et al., 2021

Baviera M. et al, 2021

Puglia: 9772 pz trattati con GLP1RA, 6046 trattati con sglt2i

Risultati coorte pugliese:

- l'inizio di un GLP1RA è risultato associato a un più basso rischio di morte (-37%), **PAD (-20%) e complicanze arti inferiori (-31%) rispetto agli altri AHA**
- Inizio sglt2i era associato con più basso rischio di morte (-57%), malattia cerebrovascolare (-28%), HF (-43%) rispetto agli altri AHA

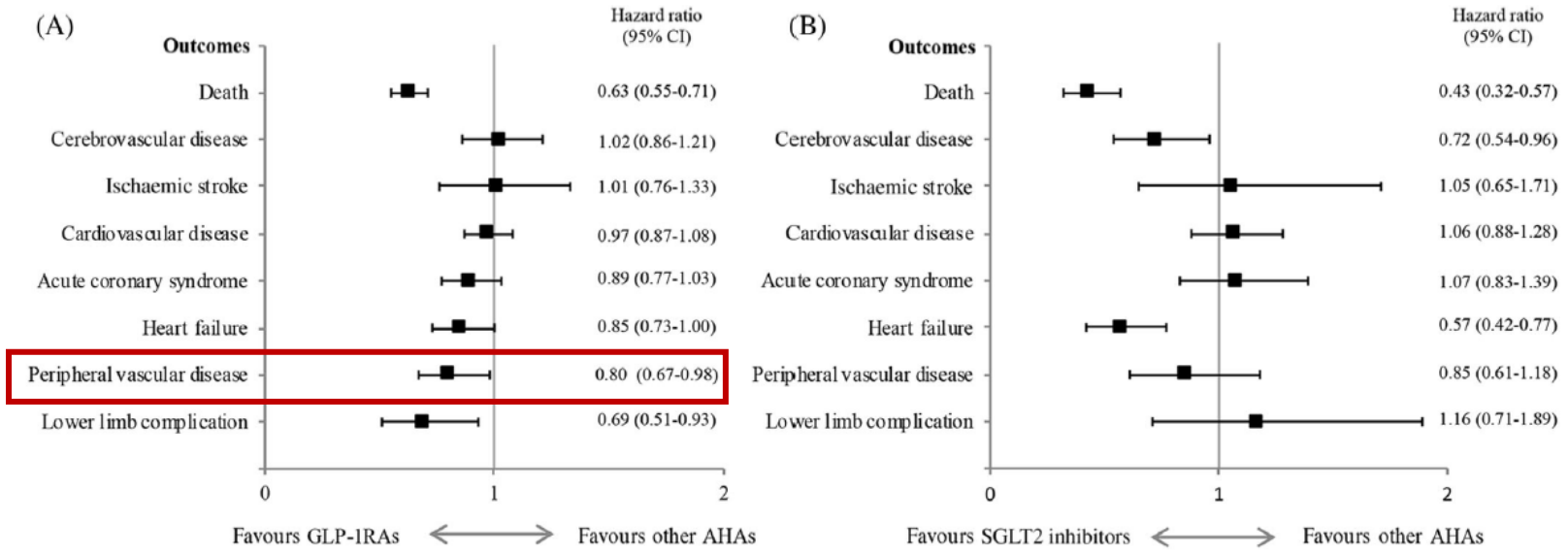
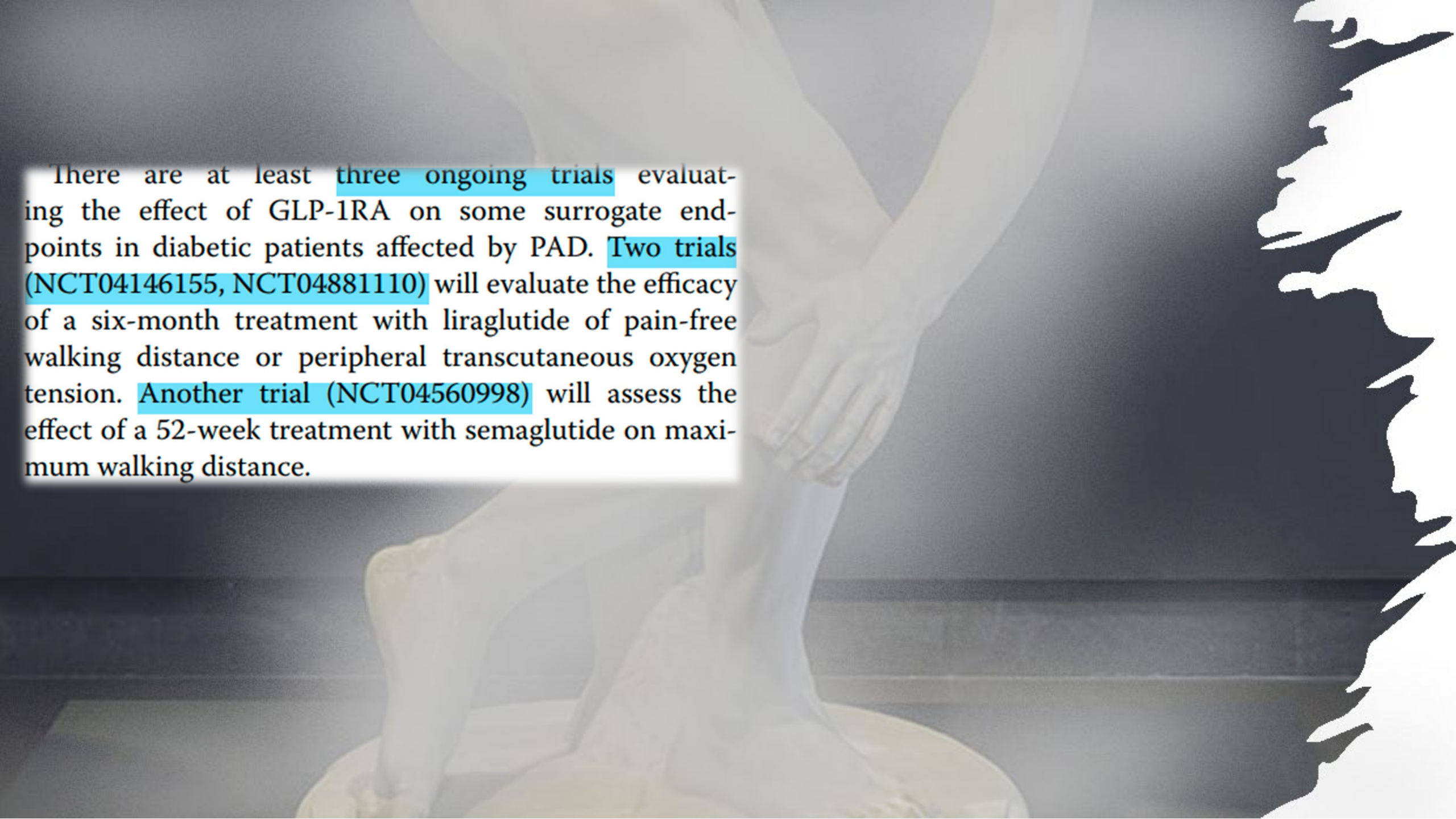


FIGURE 2 A, B, Hazard ratios (95% confidence interval [CI]) for death and clinical events in matched populations according to treatment status in Apulia. GLP-1RA, glucagon-like peptide-1 receptor agonist; SGLT2, sodium-glucose cotransporter-2; AHA, antihyperglycaemic agent

Baviera M. et al, 2021



There are at least three ongoing trials evaluating the effect of GLP-1RA on some surrogate endpoints in diabetic patients affected by PAD. Two trials (NCT04146155, NCT04881110) will evaluate the efficacy of a six-month treatment with liraglutide of pain-free walking distance or peripheral transcutaneous oxygen tension. Another trial (NCT04560998) will assess the effect of a 52-week treatment with semaglutide on maximum walking distance.

….Grazie per l’attenzione