24 settembre 2022

Percorsi Clinici In Medicina Generale

Messina

Early treatment nel Diabete tipo 2

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U.O.C. Medicina Interna iGR

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PROMISE

C.R.E.A.M.

Università degli Studi di Palermo

Il sottoscritto Salvatore Corrao
ai sensi dell'art. 3.3 sul Conflitto di Interessi, pag. 17 del Reg. Applicativo dell'Accordo Stato - Regione del 5 novembre 2009

dichiara

che negli ultimi due anni ha avuto i seguenti rapporti anche di finanziamento con soggetti portatori di interessi commerciali in campo sanitario:

Novartis, Boehringer, Abbvie, Lilly, Galapagos, Almirall

Agenda

- *Che ruolo riveste il controllo glicemico precoce?*
- *Quale Approccio Clinico?*
- *Con quali farmaci?*

Early Glycemic Control and Magnitude of HbA_{1c} Reduction Predict Cardiovascular Events and Mortality: Population-Based Cohort Study of 24,752 Metformin Initiators

Elisabeth Svensson,[1] Lisbeth M. Baggesen,[1] Søren P. Johnsen,[1] Lars Pedersen,[1] Helene Nørrelund,[1] Esben S. Buhl,[2] Christiane L. Haase,[2] and Reimar W. Thomsen[1]

Diabetes Care 2017;40:800–807 | https://doi.org/10.2337/dc16-2271

RESEARCH DESIGN AND METHODS

This was a population-based cohort study including all metformin initiators with HbA_{1c} tests in Northern Denmark, 2000–2012. Six months after metformin initiation, we classified patients by HbA_{1c} achieved (<6.5% or higher) and by magnitude of HbA_{1c} change from the pretreatment baseline. We used Cox regression to examine subsequent rates of acute myocardial infarction, stroke, or death, controlling for baseline HbA_{1c} and other confounding factors.

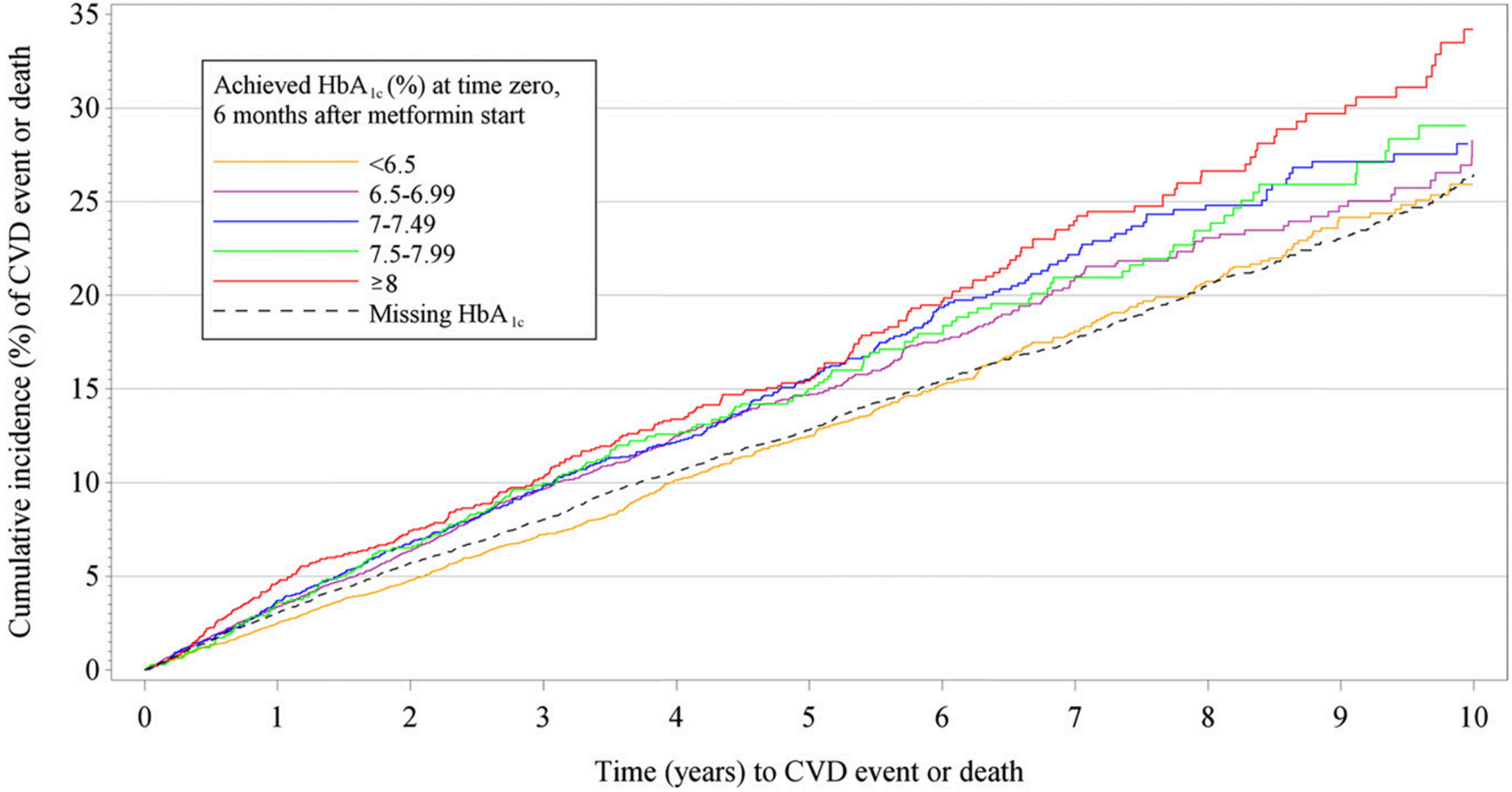


Figure 1—Combined outcome event (acute myocardial infarction, stroke, or death) by achieved early glycemic level. The cumulative incidences of a combined outcome event by achieved HbA_{1c} level 6 months after metformin start are shown among 24,752 metformin initiators in Northern Denmark during 2000–2012. As a point of comparison, the black stippled line shows the event rate among 17,134 metformin initiators in whom an HbA_{1c} measurement was missing before and after metformin initiation. Time (years) to cardiovascular disease (CVD) or death was from 6 months (180 days) after metformin initiation.

The Legacy Effect in Type 2 Diabetes: Impact of Early Glycemic Control on Future Complications (The Diabetes & Aging Study)

Neda Laiteerapong,[1] Sandra A. Ham,[2] Yue Gao,[1] Howard H. Moffet,[3] Jennifer Y. Liu,[3] Elbert S. Huang,[1] and Andrew J. Karter[3]

Diabetes Care 2019;42:416–426 | https://doi.org/10.2337/dc17-1144

the Kaiser Permanente Northern California (KPNC) Diabetes Registry

OBJECTIVE

To examine for a legacy effect of early glycemic control on diabetic complications and death.

RESEARCH DESIGN AND METHODS

This cohort study of managed care patients with newly diagnosed type 2 diabetes and 10 years of survival (1997–2013, average follow-up 13.0 years, *N* = 34,737) examined associations between HbA_{1c} <6.5% (<48 mmol/mol), 6.5% to <7.0% (48 to <53 mmol/mol), 7.0% to <8.0% (53 to <64 mmol/mol), 8.0% to <9.0% (64 to <75 mmol/mol), or ≥9.0% (≥75 mmol/mol) for various periods of early exposure (0–1, 0–2, 0–3, 0–4, 0–5, 0–6, and 0–7 years) and incident future microvascular (end-stage renal disease, advanced eye disease, amputation) and macrovascular (stroke, heart disease/failure, vascular disease) events and death, adjusting for demographics, risk factors, comorbidities, and later HbA_{1c}.

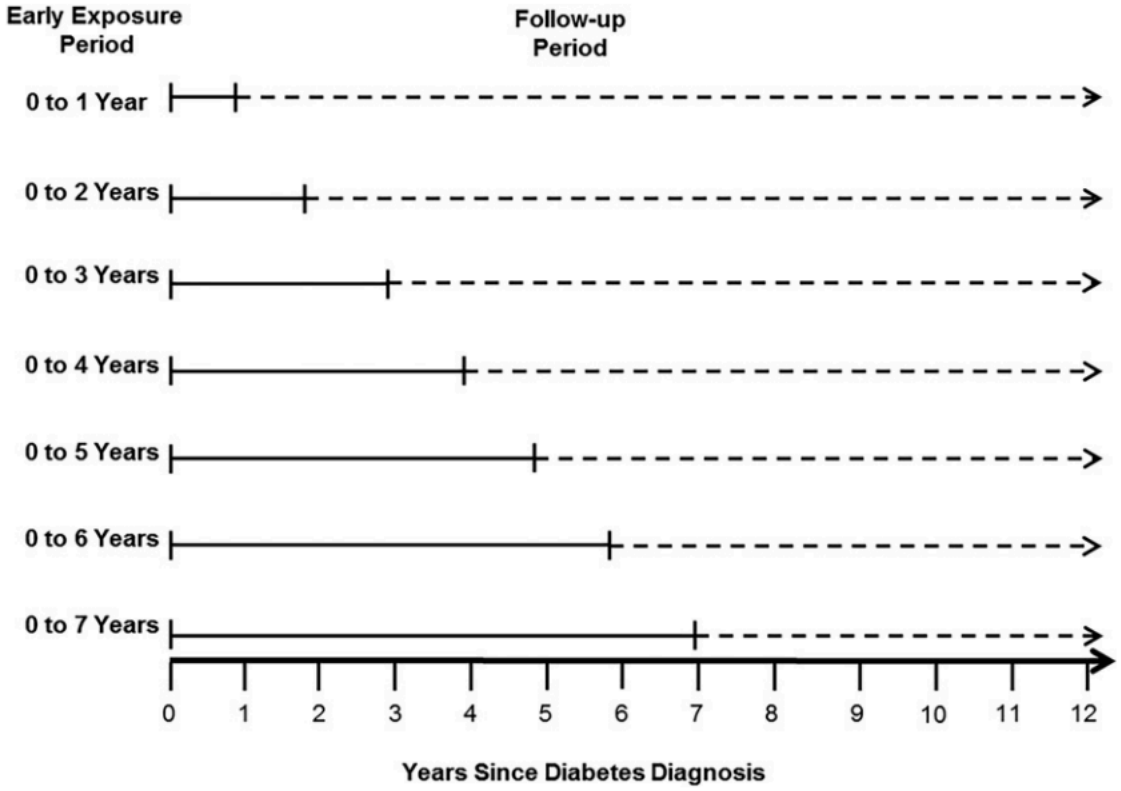
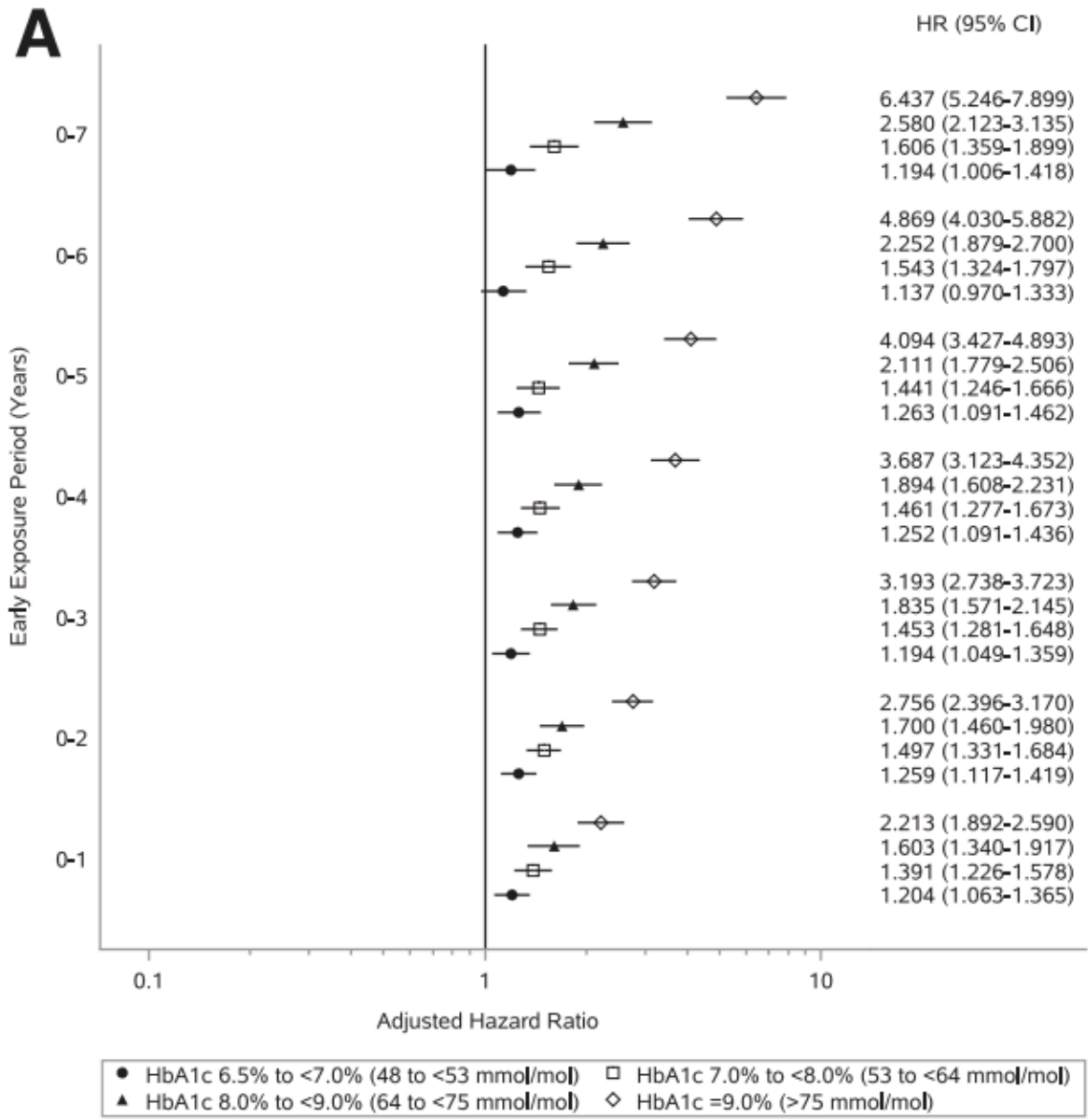


Figure 1—Definitions of early exposure periods and subsequent follow-up periods for the research design.

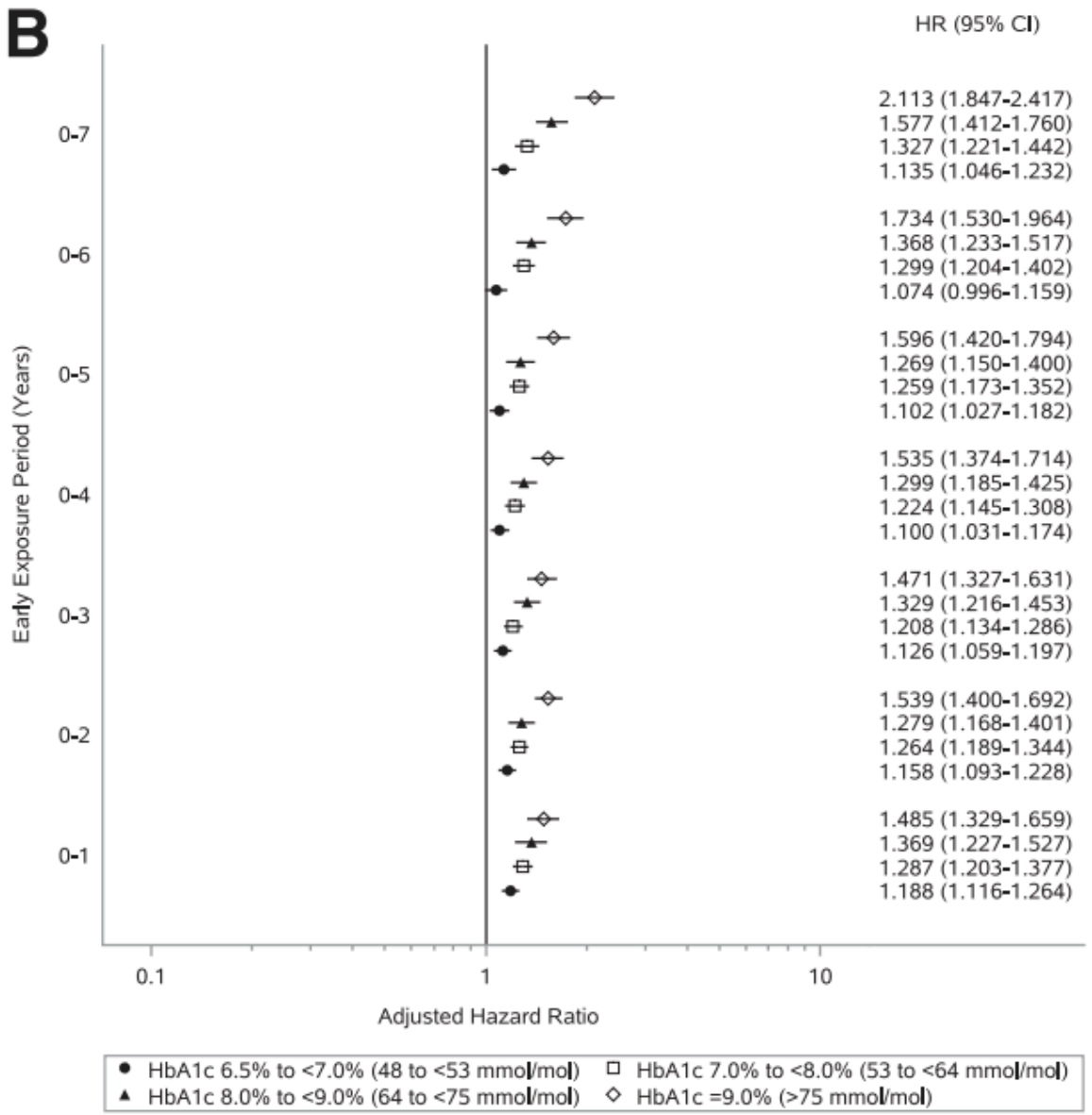
A: Microvascular events (vs. HbA1c ,6.5% [,48 mmol/mol]).

HRs adjusted for year of diagnosis, age at diagnosis, sex, race/ethnicity, BMI, systolic and diastolic blood pressure, total cholesterol, HDL cholesterol, smoking status, HbA1c after each early exposure period, and comorbidity.



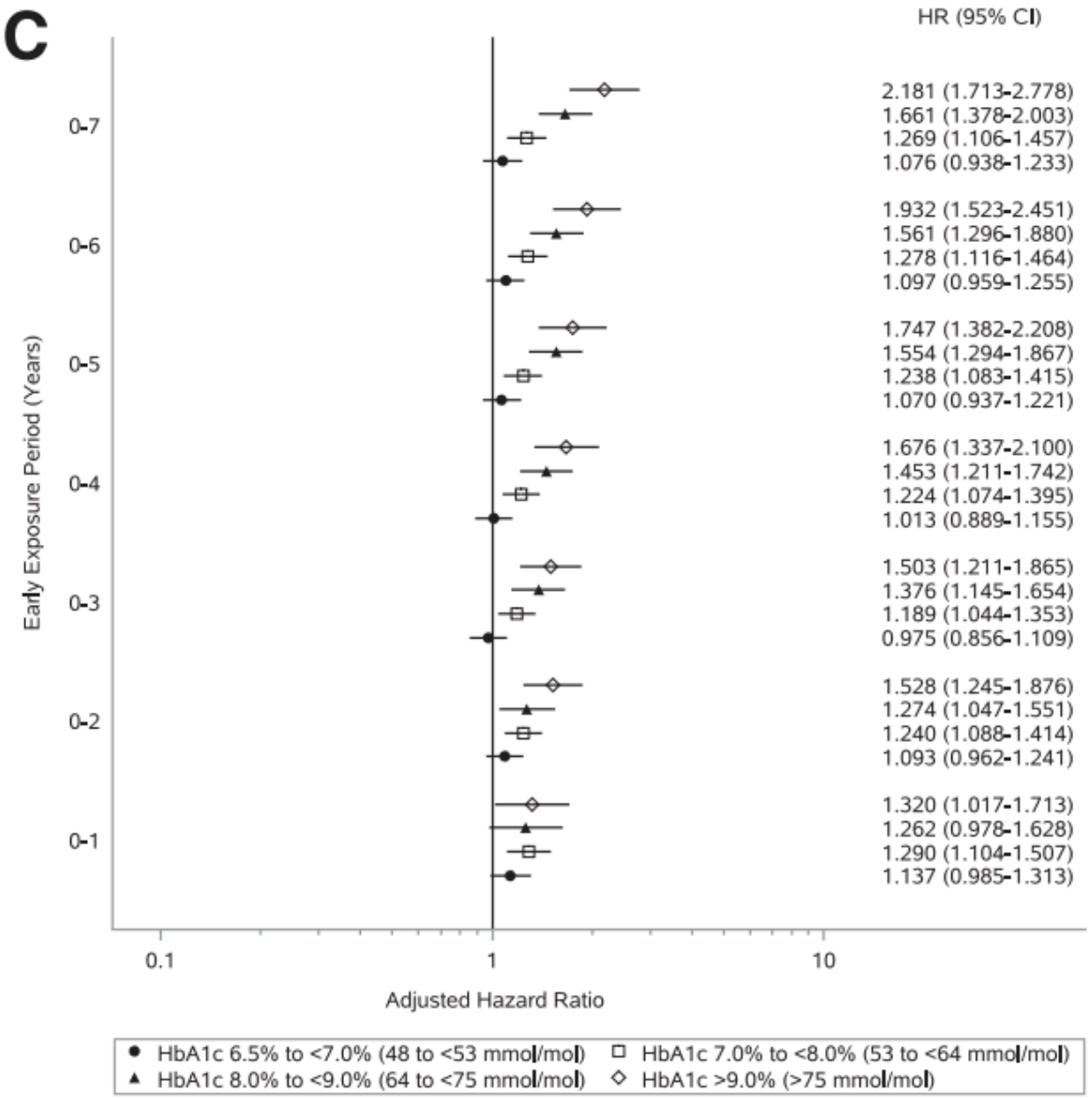
B: Macrovascular events (vs. HbA1c ,6.5% [,48 mmol/mol]).

HRs adjusted for year of diagnosis, age at diagnosis, sex, race/ethnicity, BMI, systolic and diastolic blood pressure, total cholesterol, HDL cholesterol, smoking status, HbA1c after each early exposure period, and comorbidity.



C: Mortality (vs. HbA1c ,6.5% [,48 mmol/mol]).

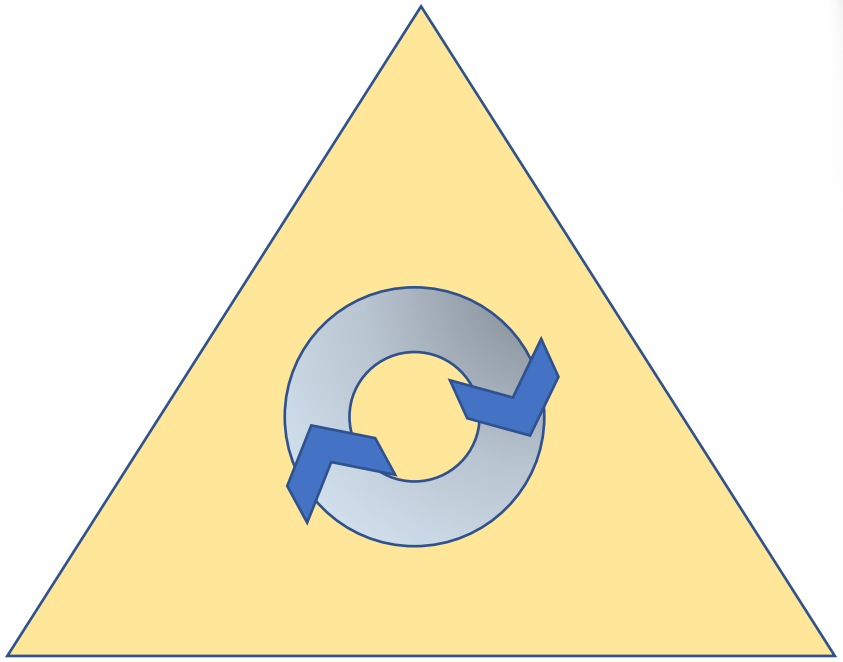
HRs adjusted for year of diagnosis, age at diagnosis, sex, race/ethnicity, BMI, systolic and diastolic blood pressure, total cholesterol, HDL cholesterol, smoking status, HbA1c after each early exposure period, and comorbidity.



Agenda

- *Che ruolo riveste il controllo glicemico precoce?*
- *Quale Approccio Clinico?*
- *Con quali farmaci?*

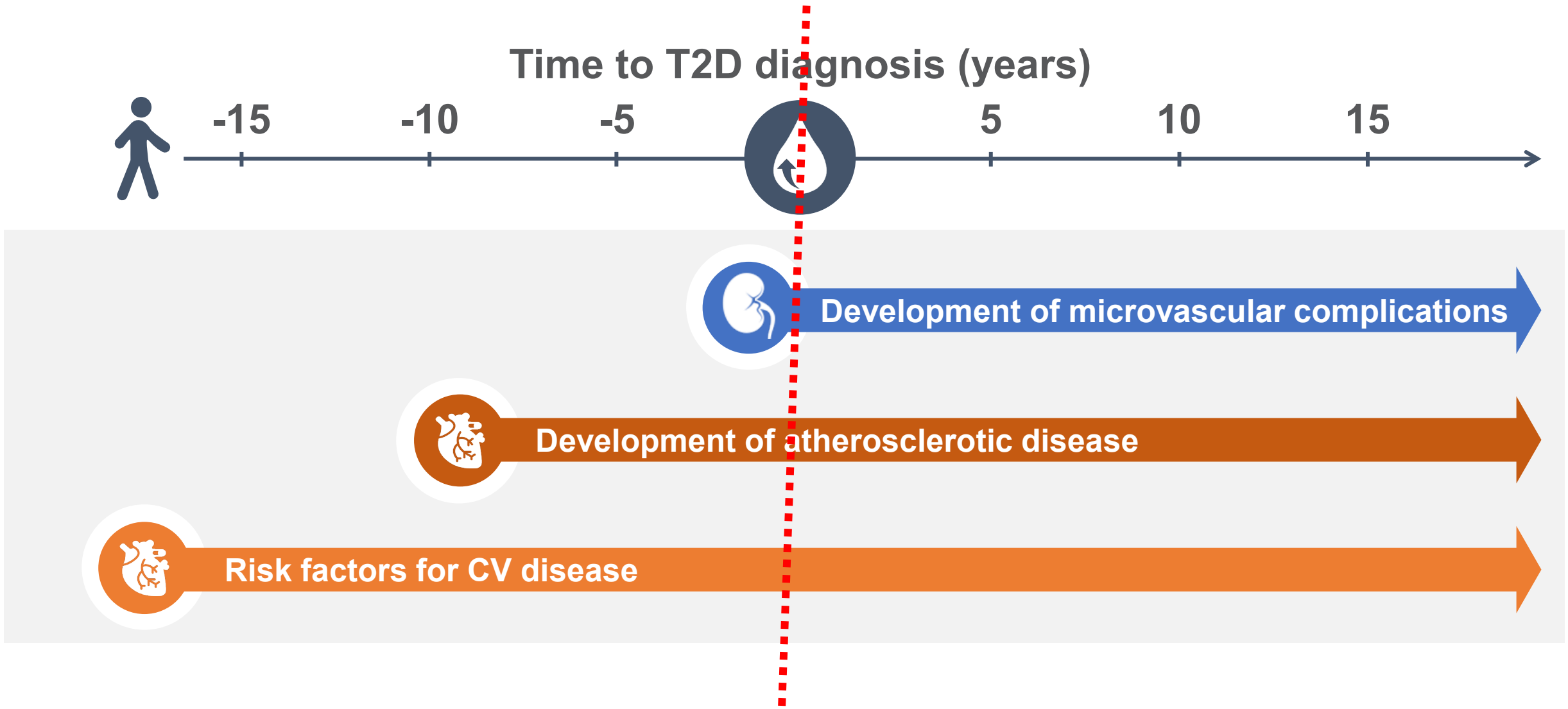
Early treatment



Early Diagnosis

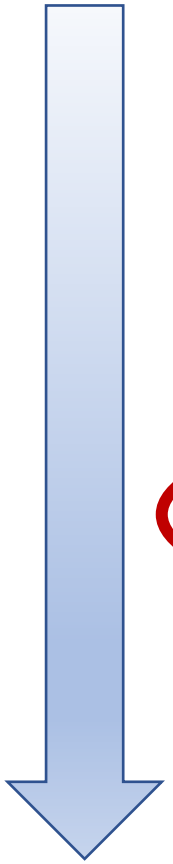
Early Organ Damage Recognition

CV disease can occur even before diagnosis of T2D



Adapted from Ramlo-Halsted BA & Edelman SV. Prim Care 1999;26:771; Nathan DM. N Engl J Med 2002;347:1342; UKPDS Group. Diabetes 1995;44:1249

Il Paziente diabetico
Dalla prevenzione alla gestione della complessità



Prevenzione primaria del diabete

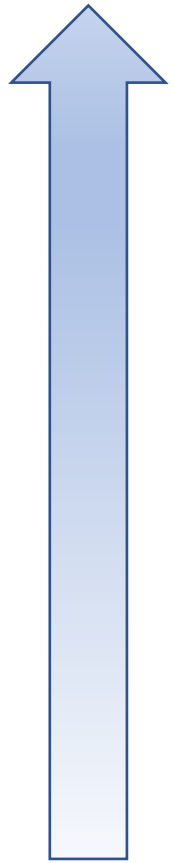
- MMG
- Cure primarie

Prevenzione secondaria e terziaria

- **MMG – Diabetologo**
- Aggregazioni funzionali territoriali (… Case della Salute?)

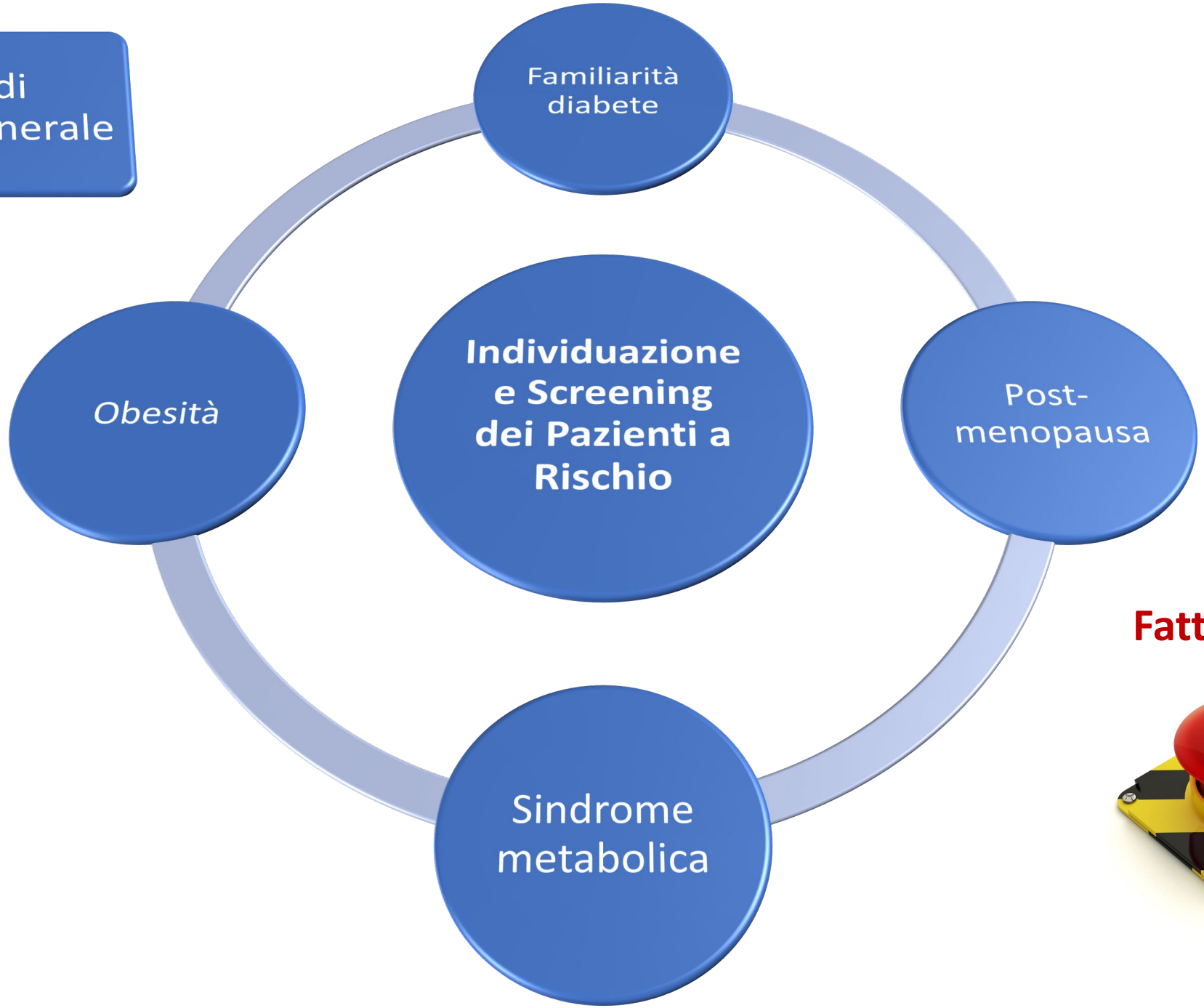
Valutazione dei pazienti complessi

- Struttura Ospedaliera di alta Specialità



Corrao S et al Nutrition, Metabolism & Cardiovascular Diseases sept 2022

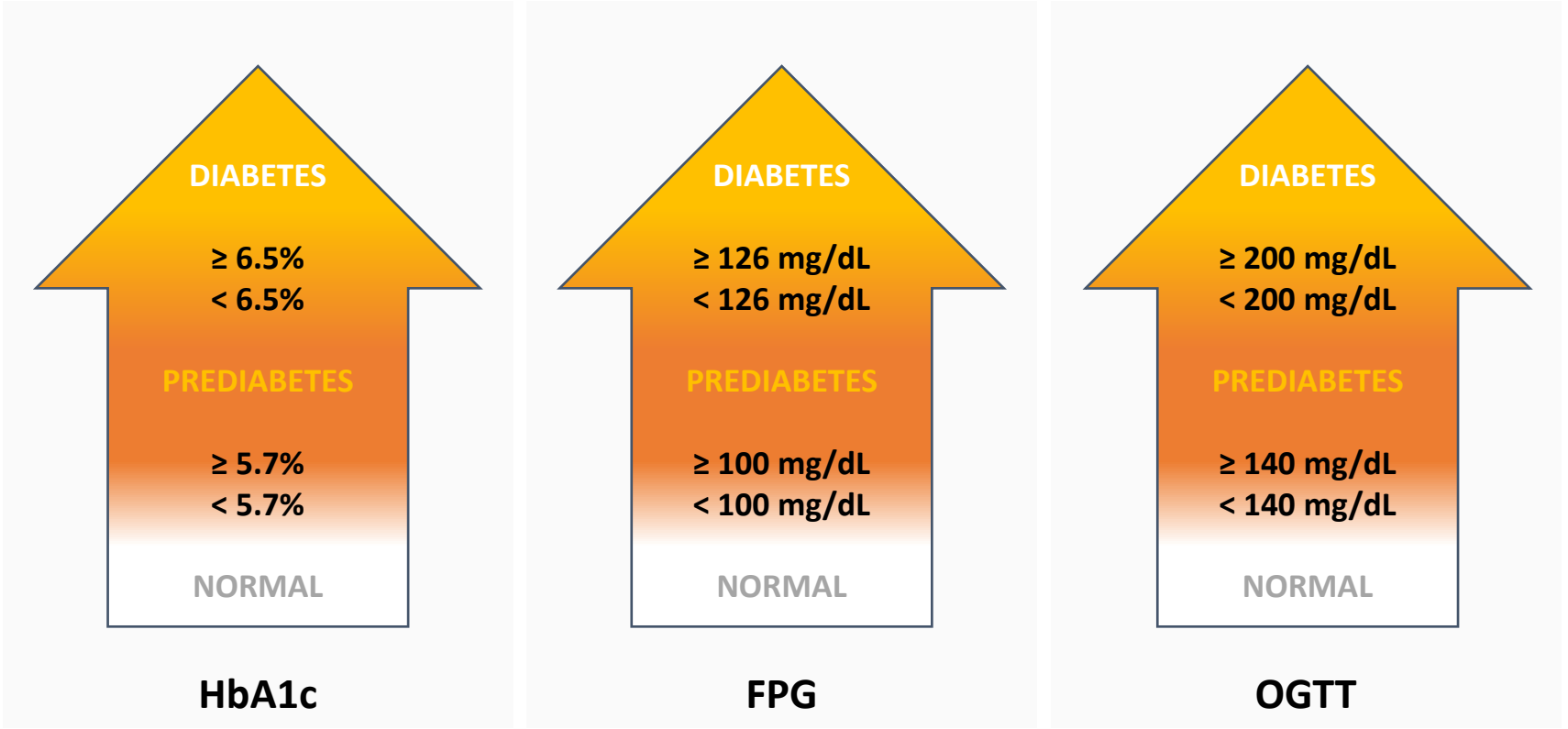
Medico di Medicina Generale



Fattore Età !!!

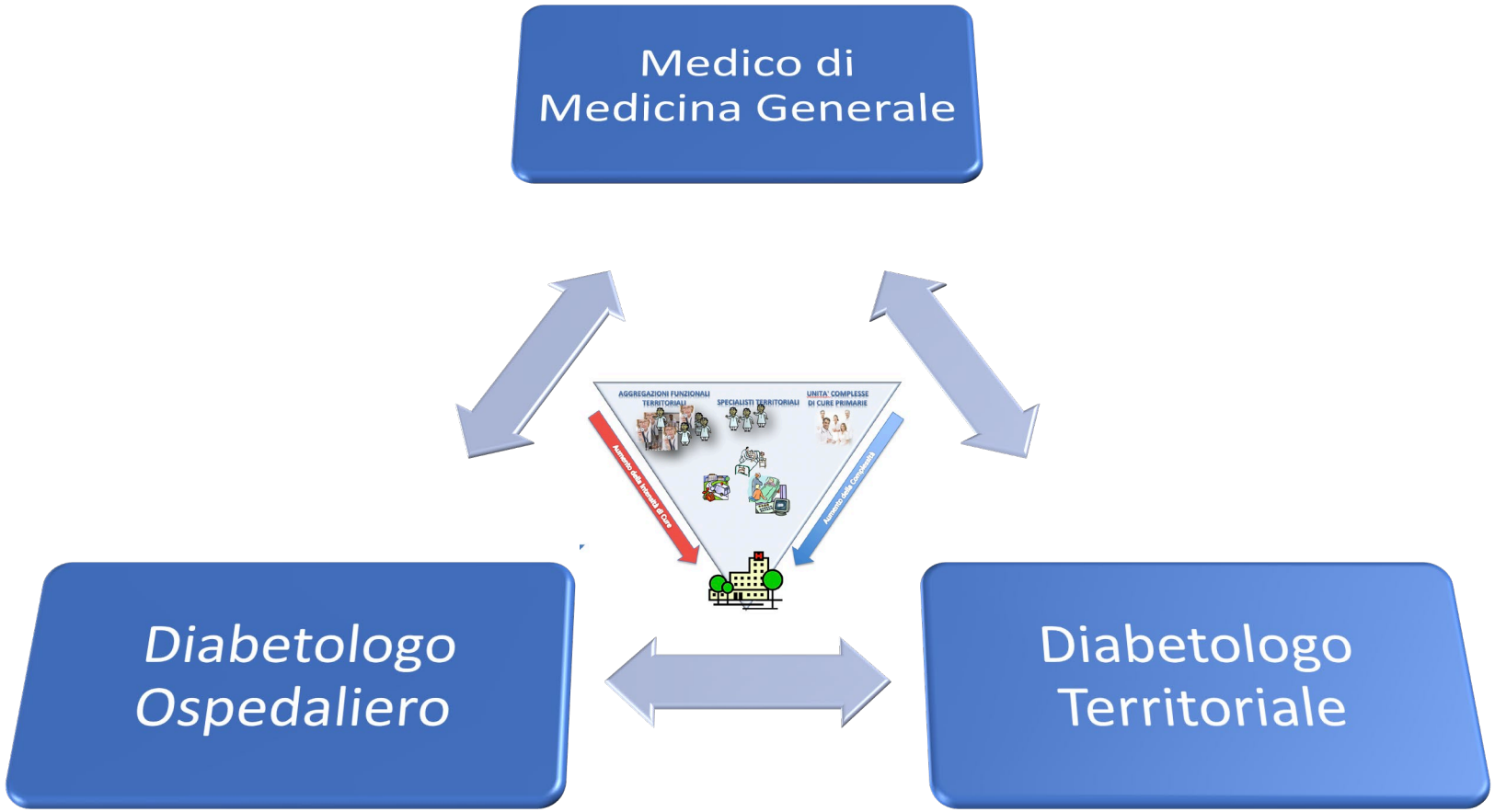
Diagnostic Criteria for T2DM and Prediabetes

Blood glucose levels span a continuum of increasing T2DM risk



OGTT refers to the measurement of 2-hour prandial glucose during a 75-g OGTT.
HbA1c = glycated hemoglobin; DM = diabetes mellitus; FPG = fasting plasma glucose;
OGTT = oral glucose tolerance test; T2DM = type 2 diabetes mellitus.
American Diabetes Association. *Diabetes Care*. 2017;40(Suppl 1):S11-S24.

Re-ingegnerizzazione del sistema per l'early treatment del DMT2



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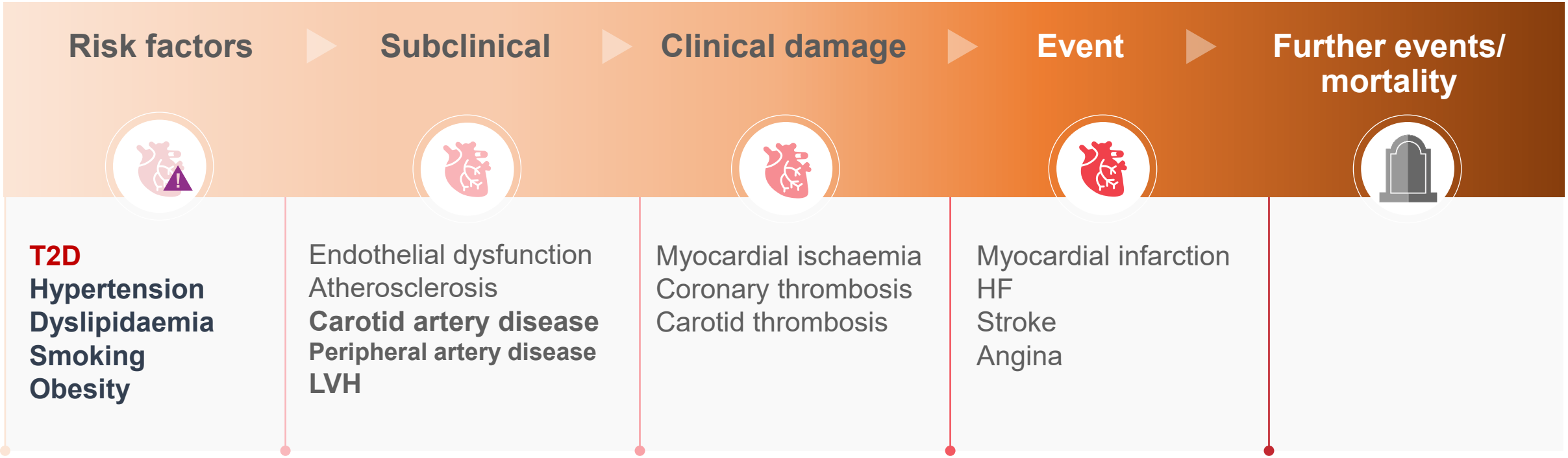
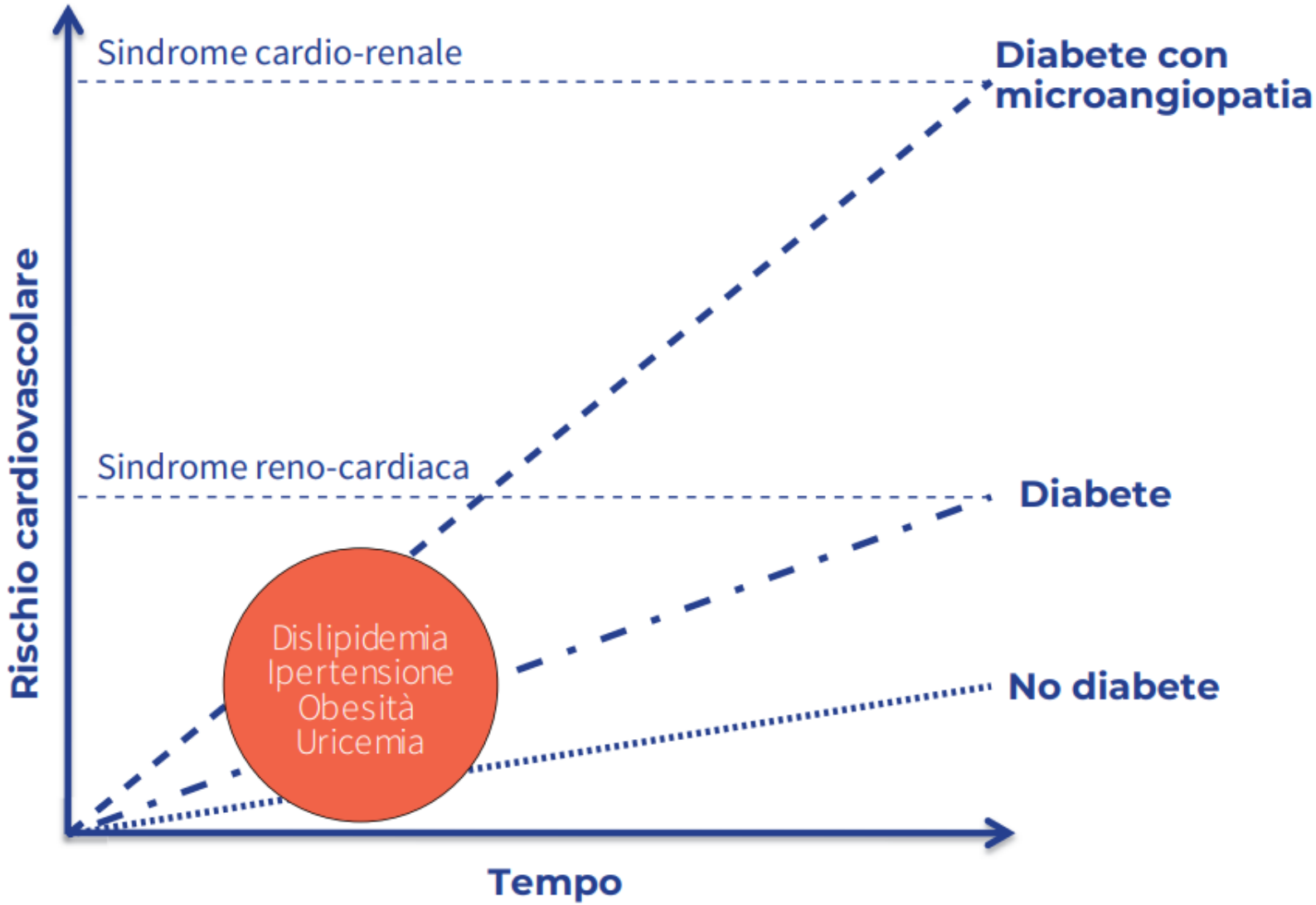
CV disease exists as a continuum



LVH, left ventricular hypertrophy

Adapted from: Dzau VJ et al. Circulation 2006;114:2850; Franklin BA & Cushman M Circulation 2011;123:2274; Ingelsson E et al. Diabetes 2007;56:1718



Corrao S et al. JAMD 2020

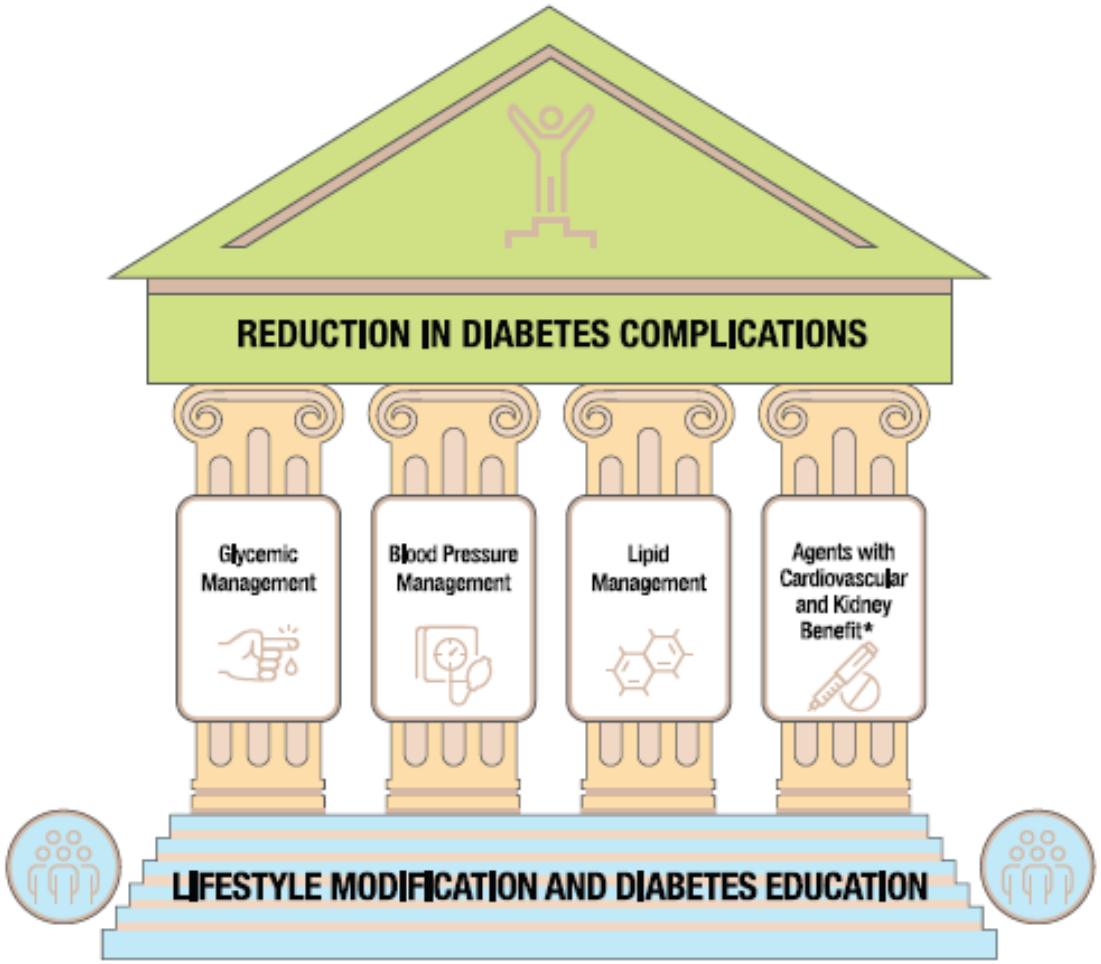


Figure 10.1—Multifactorial approach to reduction in risk of diabetes complications. *Risk reduction interventions to be applied as individually appropriate.

Cardiovascular Disease and Risk Management:
Standards of Medical Care in Diabetes - 2022. Diabetes Care 2022;45(Suppl. 1):S144-S174

Agenda

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- ***Con quali farmaci?***

SISTEMA NAZIONALE LINEE GUIDA DELL'ISTITUTO SUPERIORE DI SANITÀ

Linea Guida della Società Italiana di Diabetologia (SID) e dell'Associazione dei Medici Diabetologi (AMD)

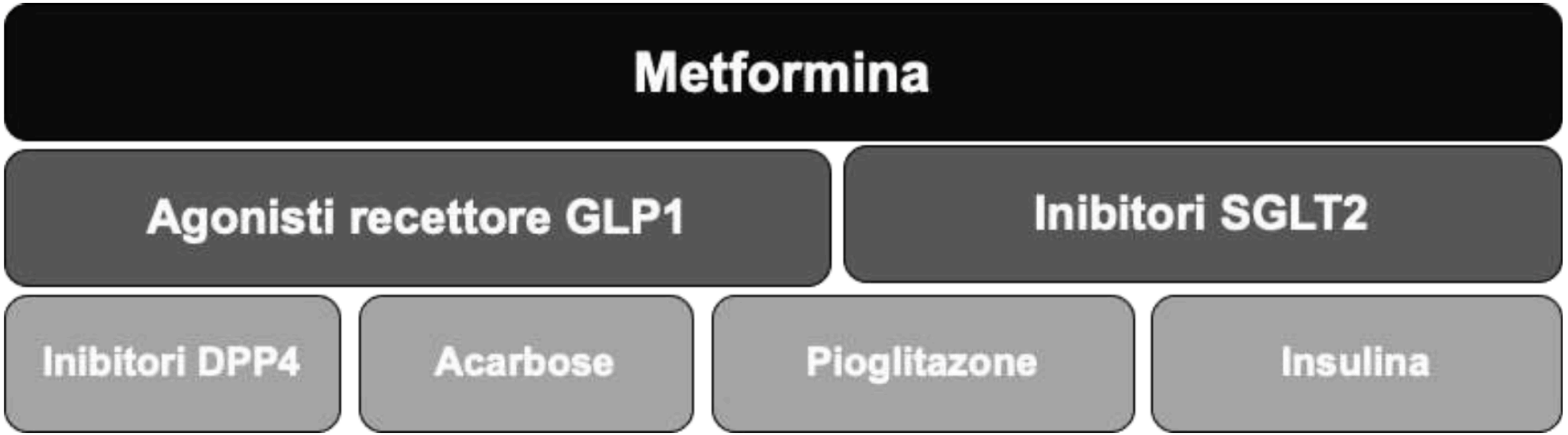
La terapia del diabete mellito di tipo 2

Linea guida pubblicata nel Sistema Nazionale Linee Guida

Roma, 26 luglio 2021

5.1 Si raccomanda l'uso di metformina come farmaco di prima scelta per il trattamento a lungo termine in pazienti con diabete di tipo 2 senza pregressi eventi cardiovascolari: SGLT-2i e i GLP-1 RA sono raccomandati come farmaci di seconda scelta. Pioglitazone, DPP-4i, acarbosio ed insulina dovrebbero essere considerati farmaci di terza scelta.

Forza della raccomandazione: forte. Qualità delle prove: moderata.



5.2.1. Si raccomanda l'uso di metformina, SGLT-2i e GLP-1 RA come farmaci di prima scelta per il trattamento a lungo termine in pazienti con diabete di tipo 2 con pregressi eventi cardiovascolari e senza scompenso cardiaco. Pioglitazone, DPP-4i, acarbosio ed insulina dovrebbero essere considerati farmaci di seconda scelta.

Forza della raccomandazione: forte. Qualità delle prove: moderata.

Le associazioni tra più farmaci devono essere prescritte secondo le indicazioni delle rispettive schede tecniche.

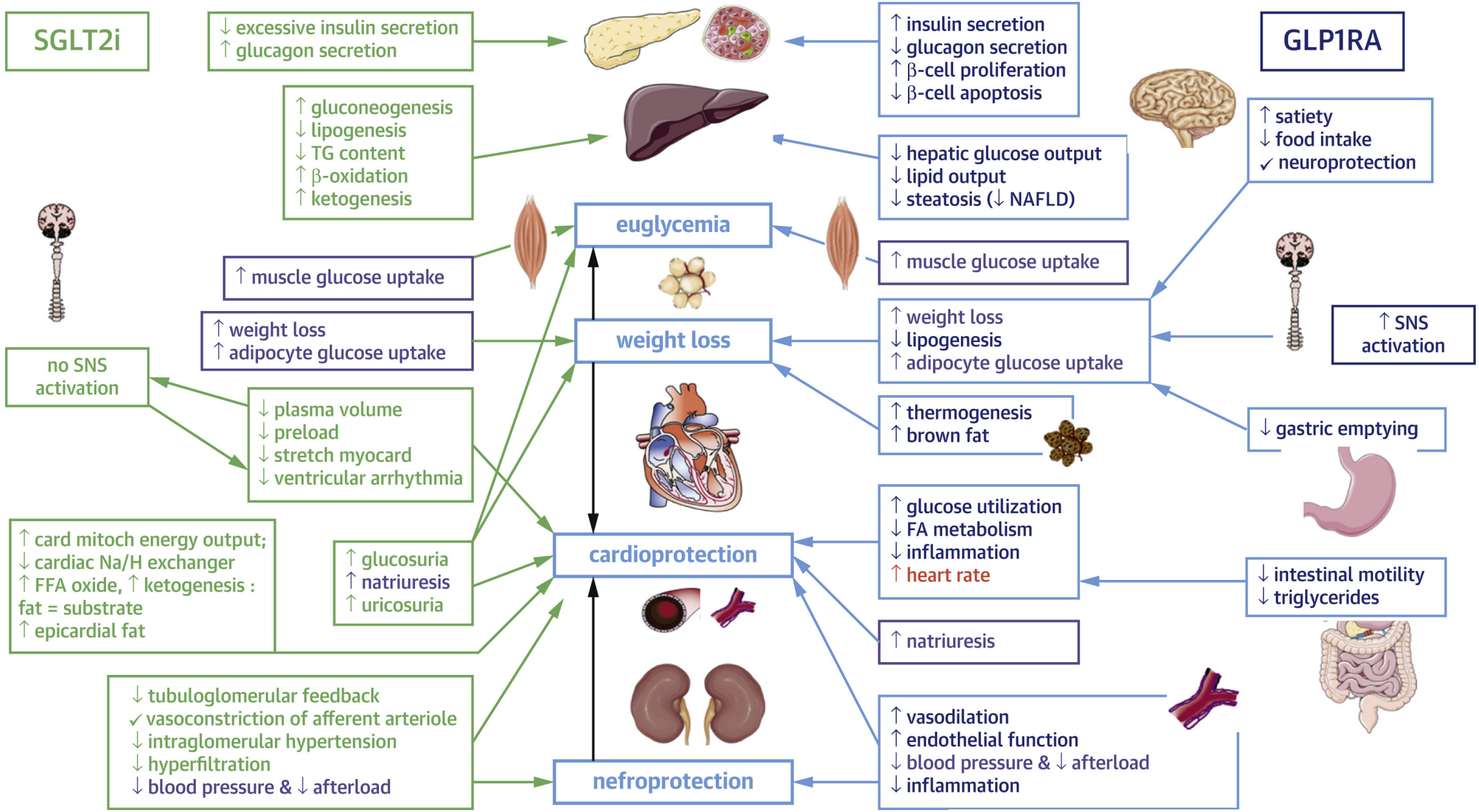
5.2.2. Si raccomanda l'uso di SGLT-2i come farmaci di prima scelta per il trattamento a lungo termine di pazienti con diabete di tipo 2 con scompenso cardiaco. I GLP-1 RA e metformina dovrebbero essere considerati come farmaci di seconda scelta, mentre DPP-4i, acarbosio ed insulina come farmaci di terza scelta.

Forza della raccomandazione: forte. Qualità delle prove: moderata.

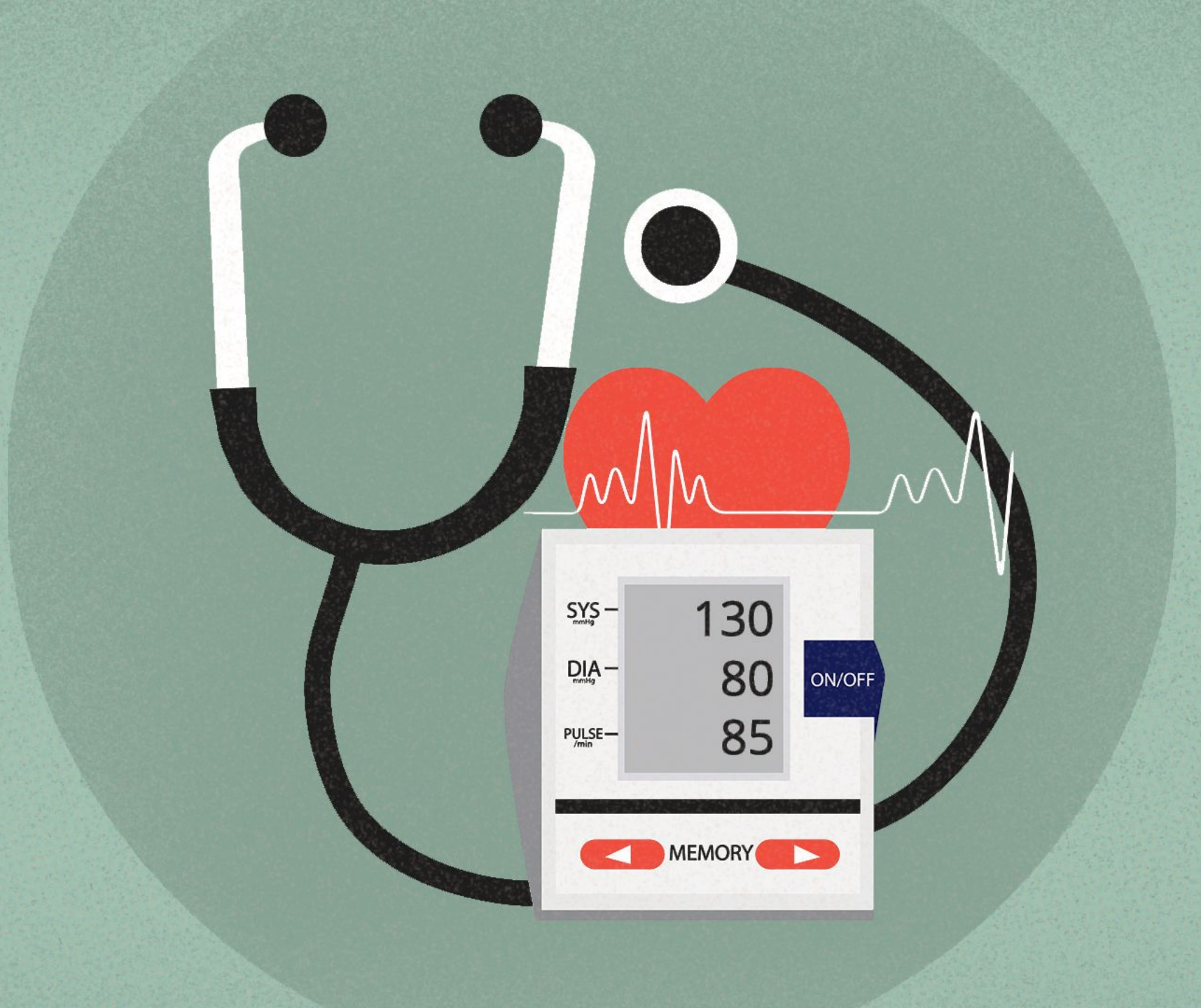
Le associazioni tra più farmaci devono essere prescritte secondo le indicazioni delle rispettive schede tecniche.
** La metformina è controindicata in classe III e IV NYHA; ** Saxagliptin è associato ad un aumento di ricoveri per scompenso cardiaco*

GLP-1 RA

SGLT2-I



Wilcox, T. et al. J Am Coll Cardiol. 2020;75(16):1956-74.


SYS
mmHg
130
DIA
mmHg
80
PULSE
/min
85
ON/OFF
MEMORY

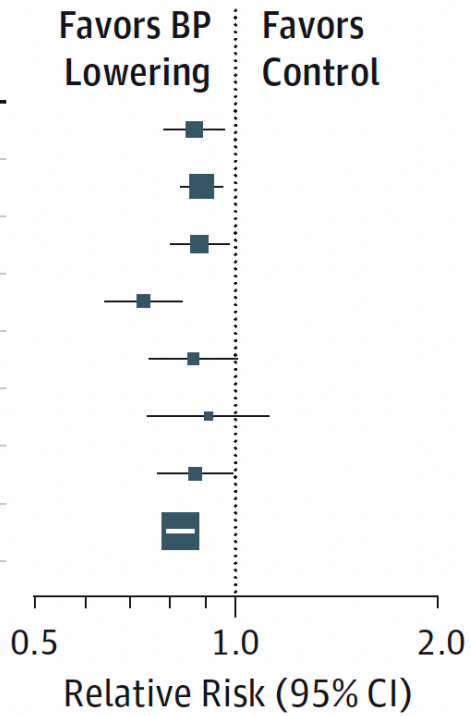
Original Investigation

Blood Pressure Lowering in Type 2 Diabetes
A Systematic Review and Meta-analysis

Connor A. Emdin, HBSc; Kazem Rahimi, DM, MSc; Bruce Neal, PhD; Thomas Callender, MBChB; Vlado Perkovic, PhD; Anushka Patel, PhD

Figure 2. Standardized Associations Between 10-mm Hg Lower Systolic BP and All-Cause Mortality, Macrovascular Outcomes, and Microvascular Outcomes in Diabetic Patients

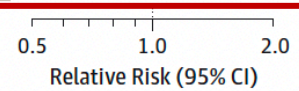
Outcome	No. of Studies	BP Lowering		Control		Relative Risk (95% CI)
		Events	Participants	Events	Participants	
Mortality	20	2334	27 693	2319	25 864	0.87 (0.78-0.96)
Cardiovascular disease	17	3230	25 756	3280	24 862	0.89 (0.83-0.95)
Coronary heart disease	17	1390	26 150	1449	24 761	0.88 (0.80-0.98)
Stroke	19	1350	27 614	1475	26 447	0.73 (0.64-0.83)
Heart failure	13	1235	21 684	1348	20 791	0.86 (0.74-1.00)
Renal failure	9	596	19 835	560	18 912	0.91 (0.74-1.12)
Retinopathy	7	844	9781	905	9566	0.87 (0.76-0.99)
Albuminuria	7	2799	13 804	3163	12 821	0.83 (0.79-0.87)



JAMA. 2015;313(6):603-615.

Figure 3. Standardized Associations Between 10-mm Hg Lower Systolic BP and All-Cause Mortality, Macrovascular Outcomes, and Microvascular Outcomes Stratified by Mean Systolic BP of Trial Participants at Entry

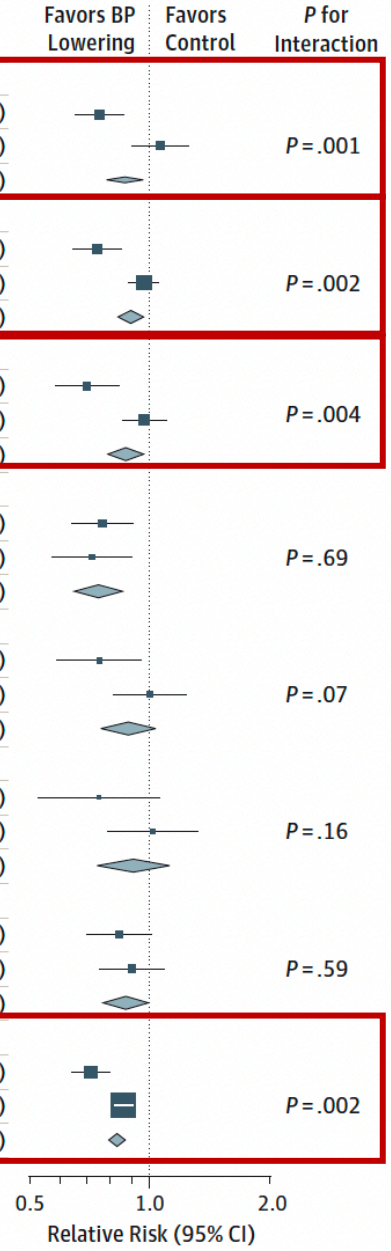
Outcome	No. of Studies	Baseline SBP, Mean, mm Hg	BP Lowering, No. Events	BP Lowering, No. Participants	Control, No. Events	Control, No. Participants	Relative Risk (95% CI)	*P* for Interaction
Mortality, mm Hg								
≥140[16, 18, 19, 27-30, 35, 39-41, 51, 55, 56, 64, 65, 77-80]	13	149	1614	16418	1626	14580	0.73 (0.64-0.84)	
<140[17, 31, 36-38, 58-60, 80, 81]	7	137	720	1275	693	11284	1.07 (0.92-1.26)	*P*<.001
Overall							0.87 (0.78-0.96)	
Cardiovascular disease, mm Hg								
≥140[16, 18, 19, 27-30, 35, 39-41, 46, 47, 51-53]	11	148	1861	14976	1918	14068	0.74 (0.65-0.85)	
<140[17, 31, 36-38, 58-60, 80, 81]	6	137	1369	10780	1362	10794	0.96 (0.88-1.05)	*P* = .001
Overall							0.89 (0.83-0.95)	
Coronary heart disease, mm Hg								
≥140[16, 18, 27, 29, 30, 35, 39-41, 47, 51, 64, 65]	10	148	858	14875	931	13477	0.73 (0.61-0.87)	
<140[17, 31, 36-38, 43, 58-60, 80, 81]	7	137	532	11275	518	11284	0.97 (0.86-1.10)	*P* = .01
Overall							0.88 (0.80-0.98)	
Stroke, mm Hg								
≥140[16, 18, 19, 27, 29, 30, 35, 39-41, 45-47, 51, 55, 56, 63-65]	14	148	1129	19066	1245	17868	0.74 (0.64-0.86)	
<140[31, 36-38, 58-60, 80, 81]	5	137	221	8548	230	8579	0.69 (0.52-0.92)	*P* = .70
Overall							0.73 (0.64-0.83)	
Heart failure, mm Hg								
≥140[16, 18, 29, 30, 35, 39-41, 46, 47, 64, 65]	8	146	774	13592	814	12676	0.75 (0.59-0.94)	
<140[31, 42, 43, 58-60, 80, 81]	5	137	461	8092	534	8115	0.97 (0.79-1.19)	*P* = .09
Overall							0.86 (0.74-1.00)	
Renal failure, mm Hg								
≥140[16, 18, 29, 30, 35, 40, 41, 64, 65]	6	147	389	12475	346	11530	0.75 (0.52-1.08)	
<140[31, 58-60]	3	138	207	7360	214	7382	1.00 (0.77-1.29)	*P* = .21
Overall							0.91 (0.74-1.12)	
Retinopathy, mm Hg								
≥140[16, 29, 30, 64, 65, 77-80]	4	146	564	7946	586	7753	0.86 (0.70-1.04)	
<140[36-38, 59, 60, 80, 81]	3	137	280	1835	319	1813	0.88 (0.74-1.05)	*P* = .85
Overall							0.87 (0.76-0.99)	
Albuminuria, mm Hg								
≥140[16, 28-30, 64, 65]	4	146	1681	8447	1898	7647	0.71 (0.63-0.79)	
<140[17, 36-38, 59, 60]	3	137	1118	5357	1265	5174	0.86 (0.81-0.90)	*P* = .002
Overall							0.83 (0.79-0.87)	



JAMA. 2015;313(6):603-615.

Figure 4. Standardized Associations Between 10-mm Hg Lower Systolic BP and All-Cause Mortality, Macrovascular Outcomes, and Microvascular Outcomes, Stratified by Mean Achieved Systolic BP in the Active Group of Each Trial

Outcome	No. of Studies	Achieved SBP, Mean, mm Hg	BP Lowering, No. Events	BP Lowering, No. Participants	Control, No. Events	Control, No. Participants	Relative Risk (95% CI)	*P* for Interaction
Mortality, mm Hg								
≥130[16, 18, 19, 27-31, 35-41, 51, 55, 56, 58, 64, 65, 77-80]	16	138	2090	22367	2079	20545	0.75 (0.65-0.86)	
<130[17, 42, 43, 59, 60, 80, 81]	4	123	244	5326	240	5319	1.06 (0.90-1.25)	*P* = .001
Overall							0.87 (0.78-0.96)	
Cardiovascular disease, mm Hg								
≥130[16, 18, 19, 27, 29, 30, 32, 35-41, 51-53, 58]	13	138	2551	20529	2558	19668	0.74 (0.64-0.85)	
<130[17, 59, 60, 80, 81]	3	123	597	4831	631	4829	0.96 (0.88-1.05)	*P* = .002
Overall							0.89 (0.83-0.96)	
Coronary heart disease, mm Hg								
≥130[16, 18, 27, 29, 30, 32, 35-41, 51, 58, 64, 65]	12	138	1055	20428	1126	19077	0.70 (0.58-0.83)	
<130[17, 42, 43, 59, 60, 80, 81]	4	123	305	5326	302	5319	0.97 (0.85-1.10)	*P* = .004
Overall							0.87 (0.78-0.96)	
Stroke, mm Hg								
≥130[16, 18, 19, 27, 29, 30, 32, 35-41, 45, 51, 55, 56, 58, 64, 65]	15	138	1196	24066	1261	22915	0.76 (0.64-0.90)	
<130[59, 60, 63, 80, 81]	3	121	106	3152	149	3167	0.72 (0.57-0.90)	*P* = .69
Overall							0.74 (0.65-0.85)	
Heart failure, mm Hg								
≥130[16, 18, 29, 30, 32, 35, 38-41, 58, 64, 65]	9	138	1043	18194	1106	17322	0.75 (0.59-0.95)	
<130[42, 43, 59, 60, 80, 81]	3	121	167	3094	209	3104	1.00 (0.81-1.23)	*P* = .07
Overall							0.88 (0.75-1.03)	
Renal failure, mm Hg								
≥130[16, 18, 29, 30, 32, 35, 40, 41, 58, 64, 65]	8	139	537	17473	502	16541	0.74 (0.52-1.06)	
<130[59, 60]	1	119	59	2362	58	2371	1.01 (0.78-1.32)	*P* = .16
Overall							0.91 (0.74-1.12)	
Retinopathy, mm Hg								
≥130[16, 29, 30, 36-38, 64, 65, 77-80]	5	137	694	8897	736	8707	0.84 (0.70-1.01)	
<130[59, 60, 80, 81]	2	120	150	884	169	859	0.90 (0.75-1.08)	*P* = .59
Overall							0.87 (0.76-0.99)	
Albuminuria, mm Hg								
≥130[16, 28-30, 36-38, 64, 65]	5	137	1822	9398	2049	8601	0.71 (0.64-0.79)	
<130[17, 59, 60]	2	122	977	4406	1114	4220	0.86 (0.81-0.90)	*P* = .002
Overall							0.83 (0.79-0.87)	



JAMA. 2015;313(6):603-615.

Efficacia di perindopril/indapamide

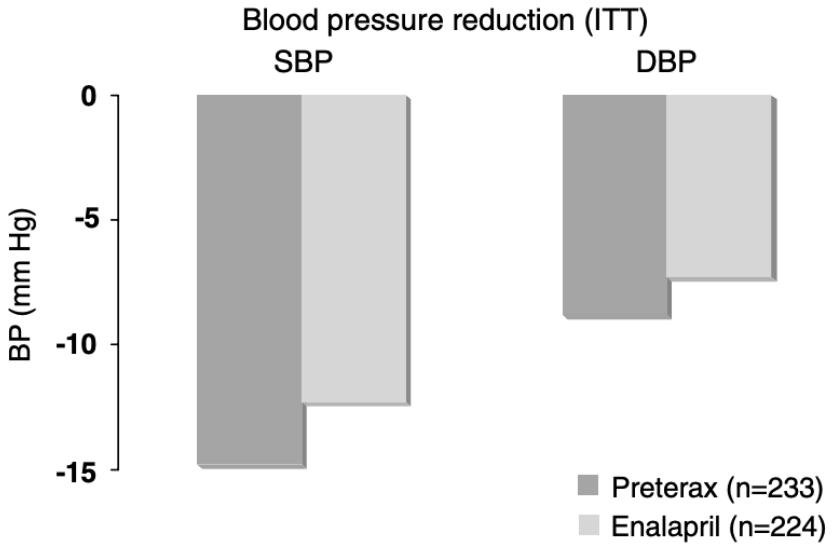


Figure 1 Reduction in the blood pressure in the intention-to-treat (ITT) population in the PREterax in microalbuMInurIa rEgRession (PREMIER) study. DBP, diastolic blood pressure; SBP, systolic blood pressure. Based on data from Mogensen *et al.*[7]

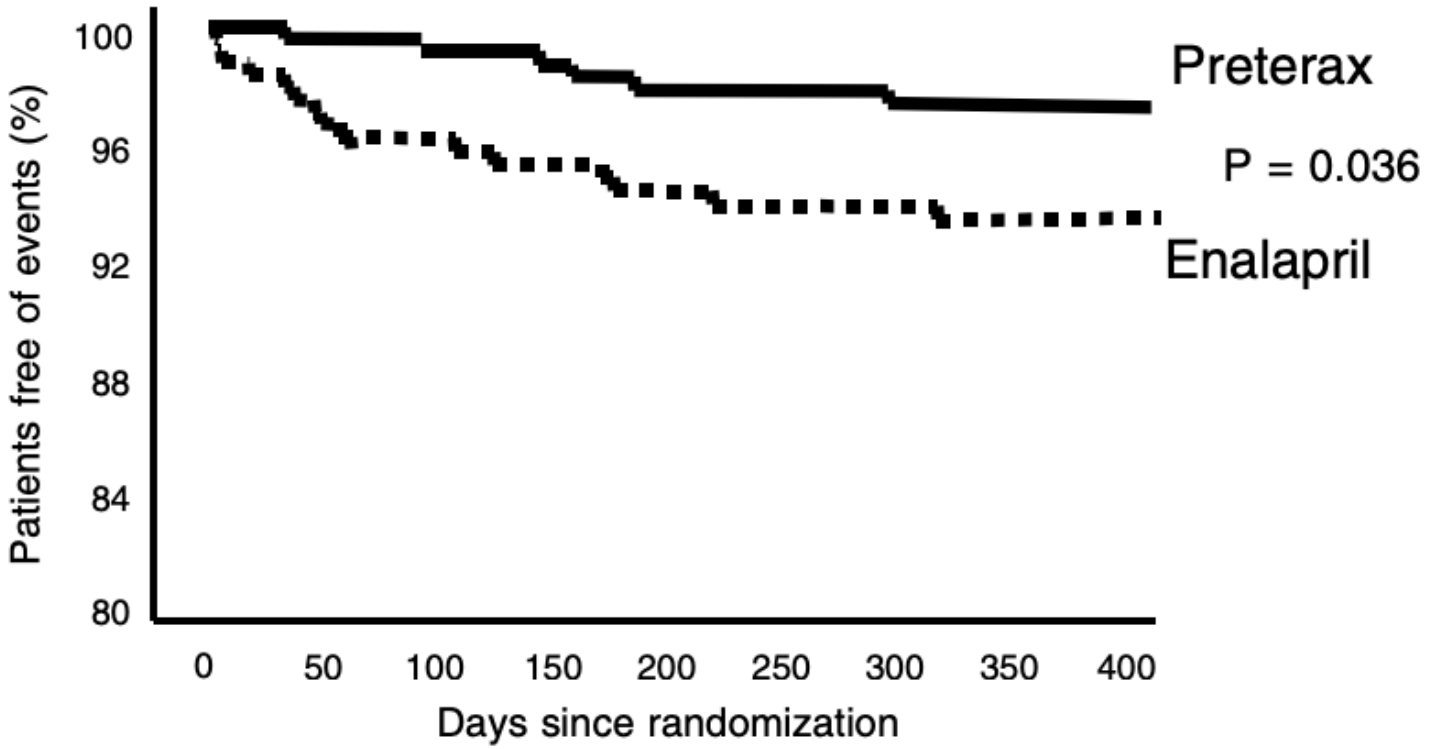
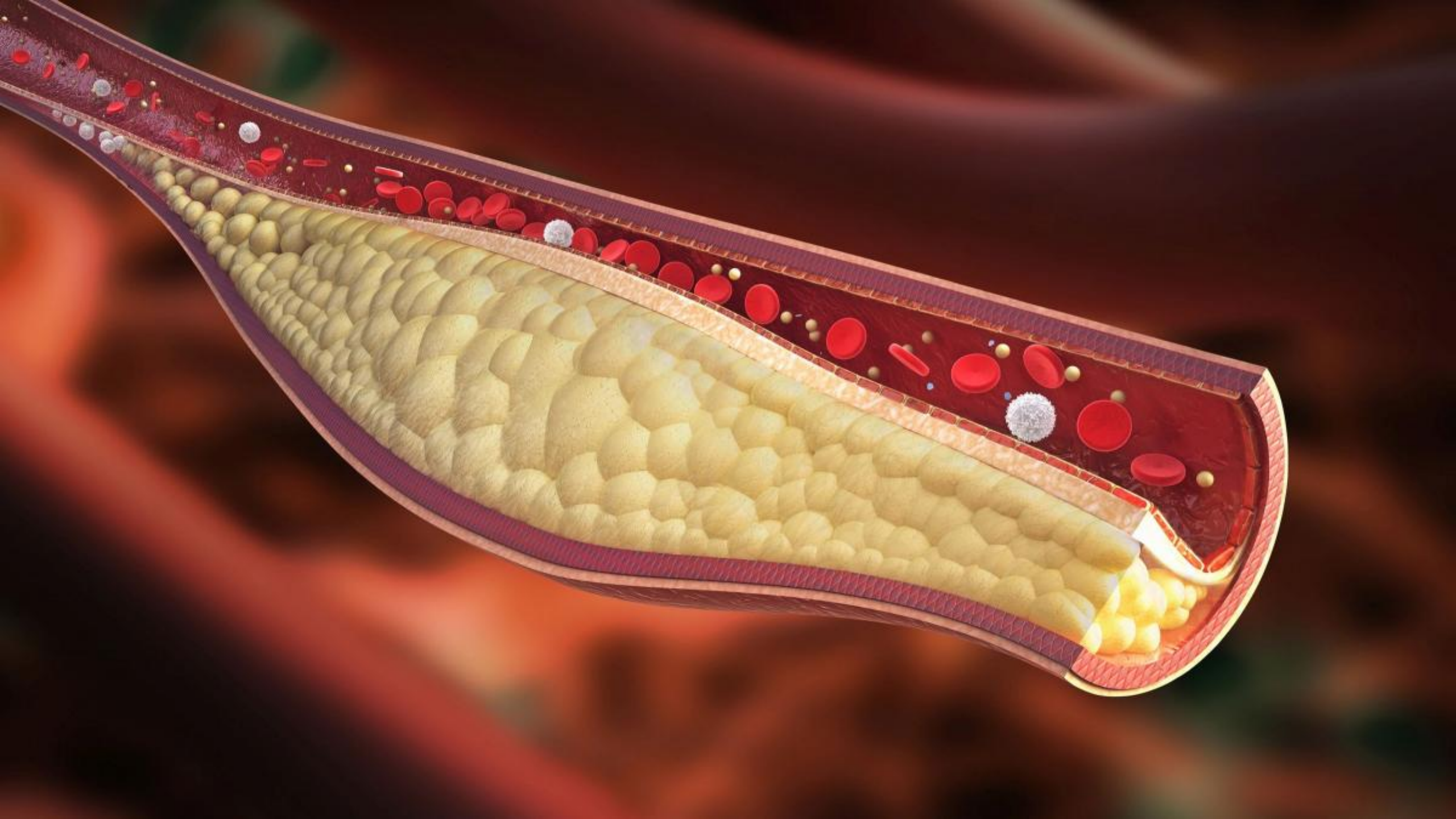


Figure 2 Occurrence of serious cardiovascular events in the PREterax in albuMInuria rEgRession (PREMIER) study. From Mogensen *et al.*[7]

Mogensen CE et al. Effect of low-dose perindopril/ indapamide on albuminuria in diabetes: Preterax in albuminuria regression: PREMIER. Hypertension 2003; 41: 1063–1071



Intensive LDL cholesterol-lowering treatment beyond current recommendations for the prevention of major vascular events: a systematic review and meta-analysis of randomised trials including 327 037 participants

Nelson Wang, Jordan Fulcher, Nishan Abeysuriya, Laura Park, Shejil Kumar, Gian Luca Di Tanna, Ian Wilcox, Anthony Keech, Anthony Rodgers, Sean Lal

A

Baseline LDL-cholesterol (mmol/L)	Studies	Patients	Events (% per year)		RR (95% CI)
			More intensive or some LDL cholesterol-lowering therapy	Less intensive or no LDL cholesterol-lowering therapy	
≤ 2·60	8	116 895	7025 (3·4)	7958 (3·9)	0·83 (0·75–0·90)
2·61–3·40	19	115 211	5476 (2·5)	6759 (3·2)	0·77 (0·71–0·83)
3·41–4·10	16	77 277	5023 (3·2)	5912 (3·8)	0·84 (0·79–0·88)
4·10	9	17 654	1133 (2·9)	1595 (4·1)	0·79 (0·73–0·84)
Overall	**52**	**327 037**	**18 657 (3·0)**	**22 224 (3·6)**	**0·81 (0·78–0·84)**

Test for heterogeneity I^2=60%, p=0·232

B

Studies	Baseline LDL-cholesterol (mmol/L)	Patients	Events (% per year)		RR (95% CI)
			More intensive or some LDL cholesterol-lowering therapy	Less intensive or no LDL cholesterol-lowering therapy	
CTTC	<2·00	9120	923 (4·1)	1020 (4·6)	0·79 (0·65–0·96)
IMPROVE-IT	<2·04	4542	123 (5·4)	129 (5·7)	0·90 (0·73–1·11)
FOURIER	<1·81	2034	86 (3·8)	106 (4·8)	0·81 (0·62–1·06)
ODYSSEY OUTCOMES	<2·07	7164	106 (3·0)	122 (3·4)	0·82 (0·66–1·01)
Overall	**<2·07**	**22 860**	**1238**	**1377**	**0·83 (0·75–0·92)**

Test for heterogeneity I^2=0%, p=0·820

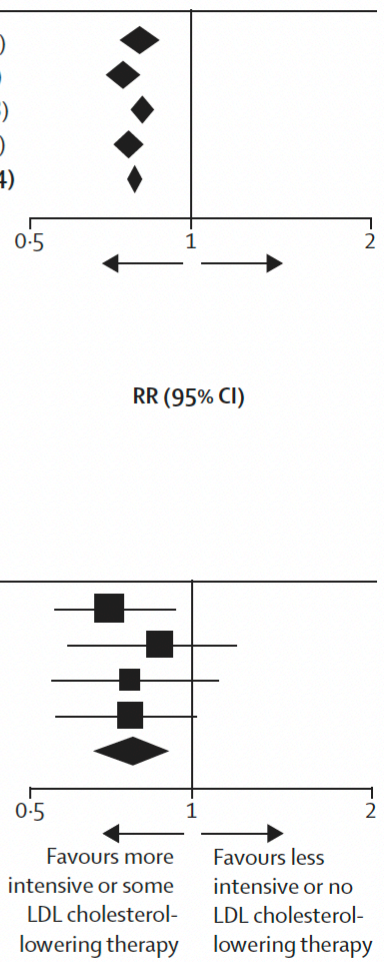


Figure 2: **Relative risk of major vascular events per 1 mmol/L reduction in LDL cholesterol, by baseline LDL-cholesterol concentration**
(A) Meta-analysis according to baseline LDL cholesterol concentration. (B) Meta-analysis of subgroups of patients with LDL cholesterol less than 2·07 mmol/L (80 mg/dL). Squares represent individual studies, with the size proportional to the weight in the meta-analysis. Diamonds represent pooled results. RR=relative risk.

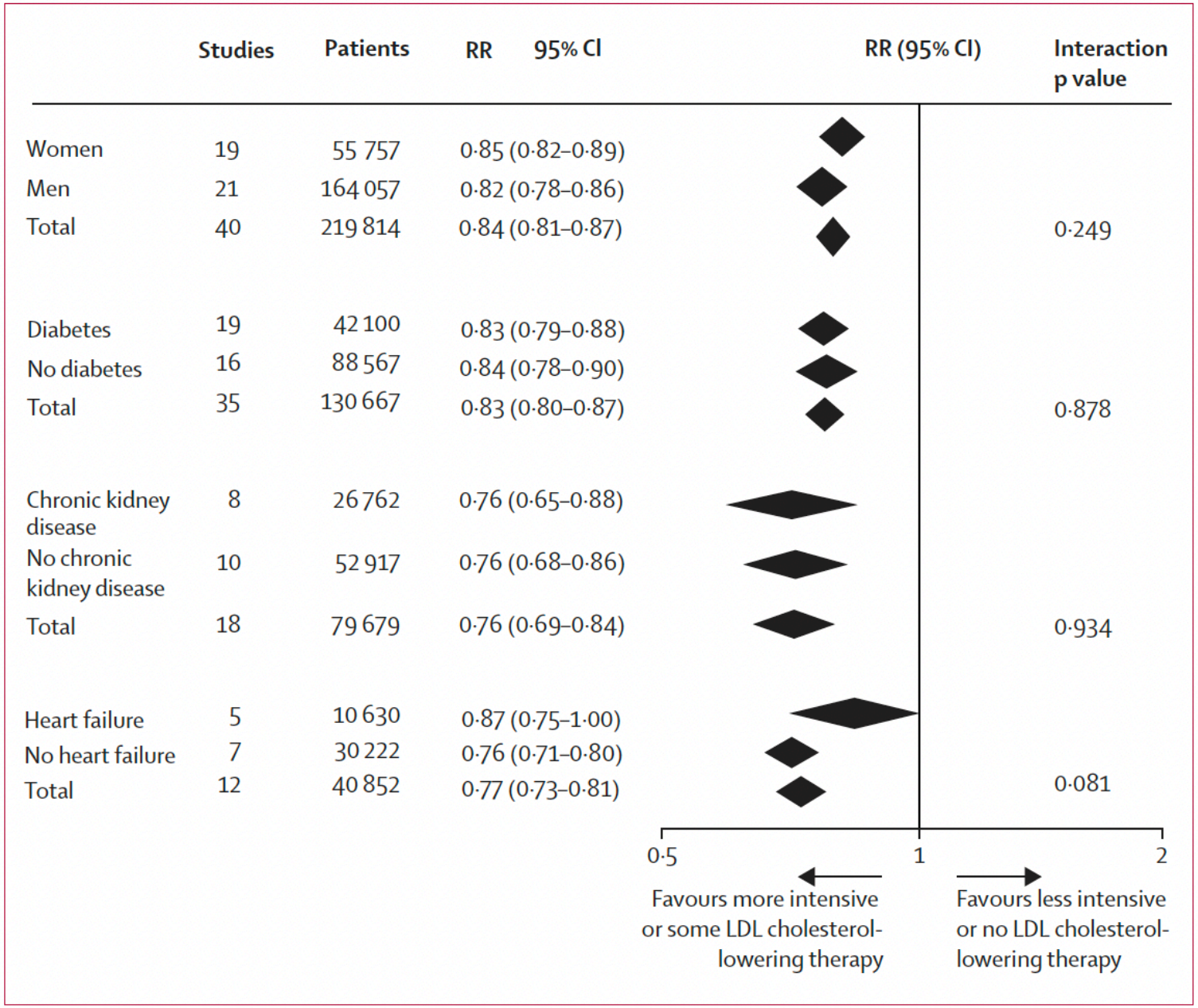
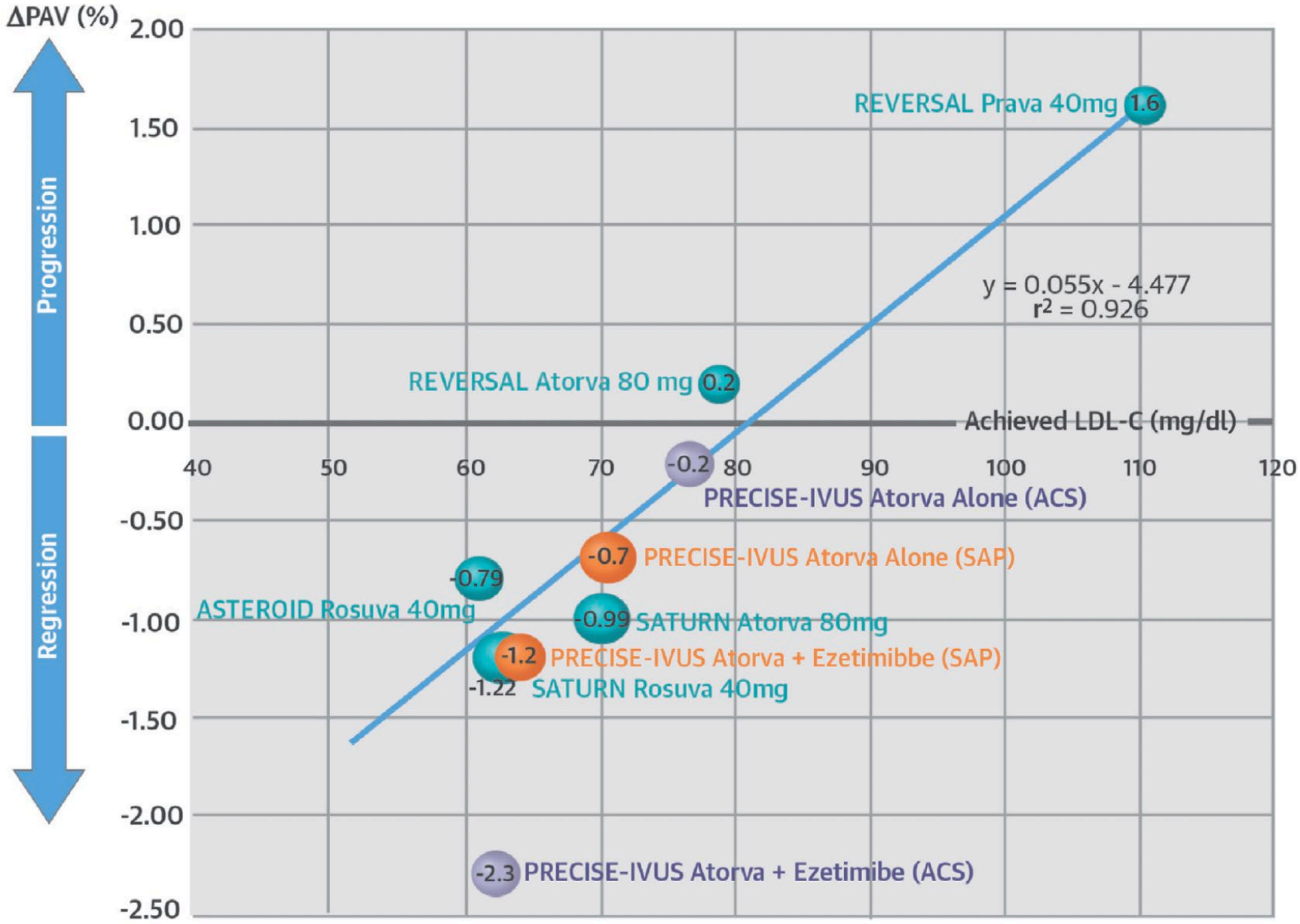


Figure 4: **Effect of LDL cholesterol reduction on the relative risk of major vascular events, by subgroup**
Data are pooled results for each subgroup. Totals within each subgroup represent only those trials that reported the outcomes of patients with each characteristic. RR=relative risk.

CENTRAL ILLUSTRATION **Relationship Between Achieved Low-Density Lipoprotein Cholesterol Levels and the Median Change in Percent Atheroma Volume for Previous Intravascular Ultrasound Trials and the PRECISE-IVUS Trial**



Tsujita, K. et al. J Am Coll Cardiol. 2015; 66(5):495-507.


Triglyceride - Test

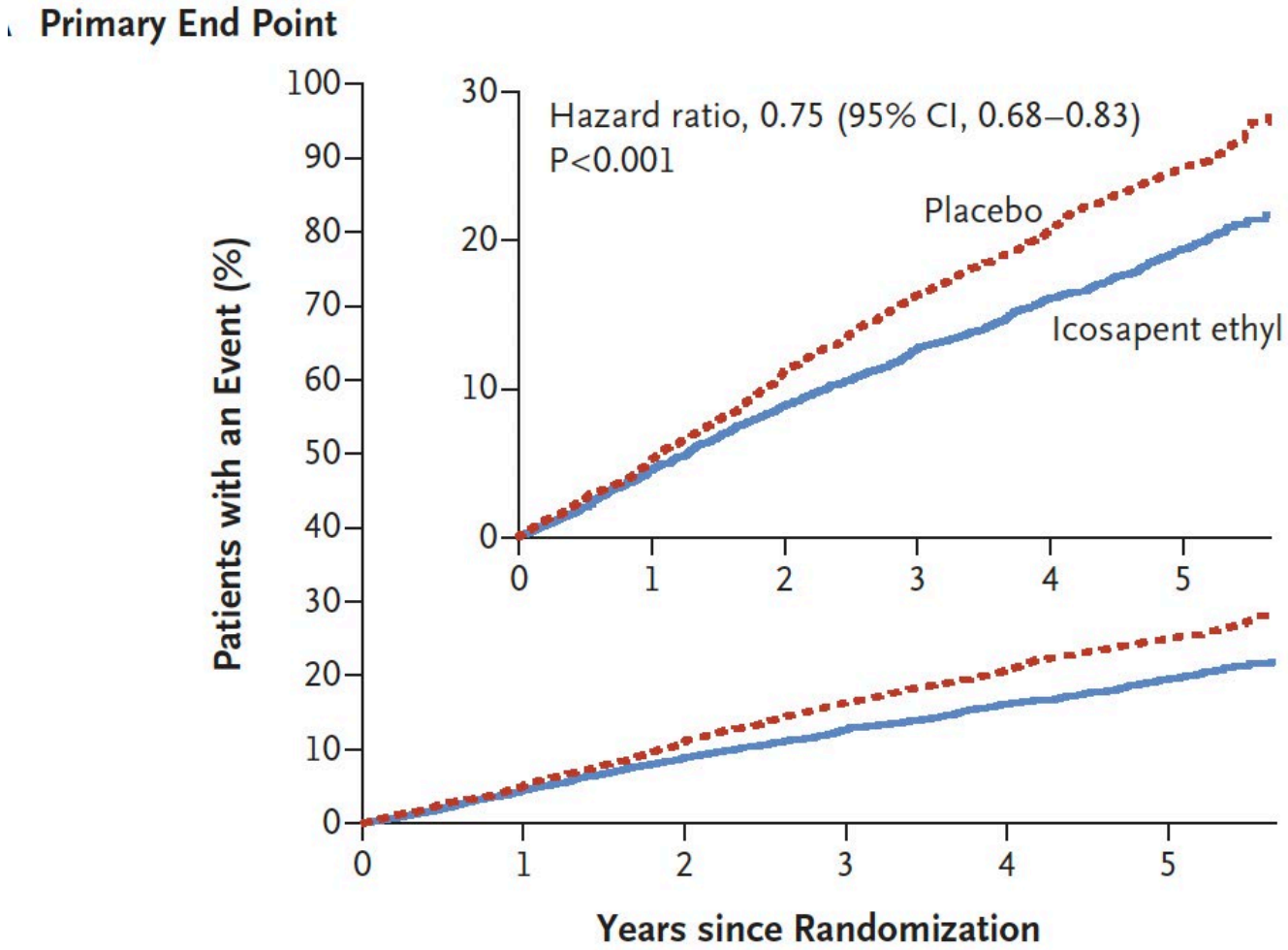
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Cardiovascular Risk Reduction with Icosapent Ethyl for Hypertriglyceridemia

Deepak L. Bhatt, M.D., M.P.H., P. Gabriel Steg, M.D., Michael Miller, M.D., Eliot A. Brinton, M.D., Terry A. Jacobson, M.D., Steven B. Ketchum, Ph.D., Ralph T. Doyle, Jr., B.A., Rebecca A. Juliano, Ph.D., Lixia Jiao, Ph.D., Craig Granowitz, M.D., Ph.D., Jean-Claude Tardif, M.D., and Christie M. Ballantyne, M.D., for the REDUCE-IT Investigators*

Primary efficacy composite end point: cardiovascular death, nonfatal myocardial infarction, nonfatal stroke, coronary revascularization, or unstable angina.



NEJM 2018

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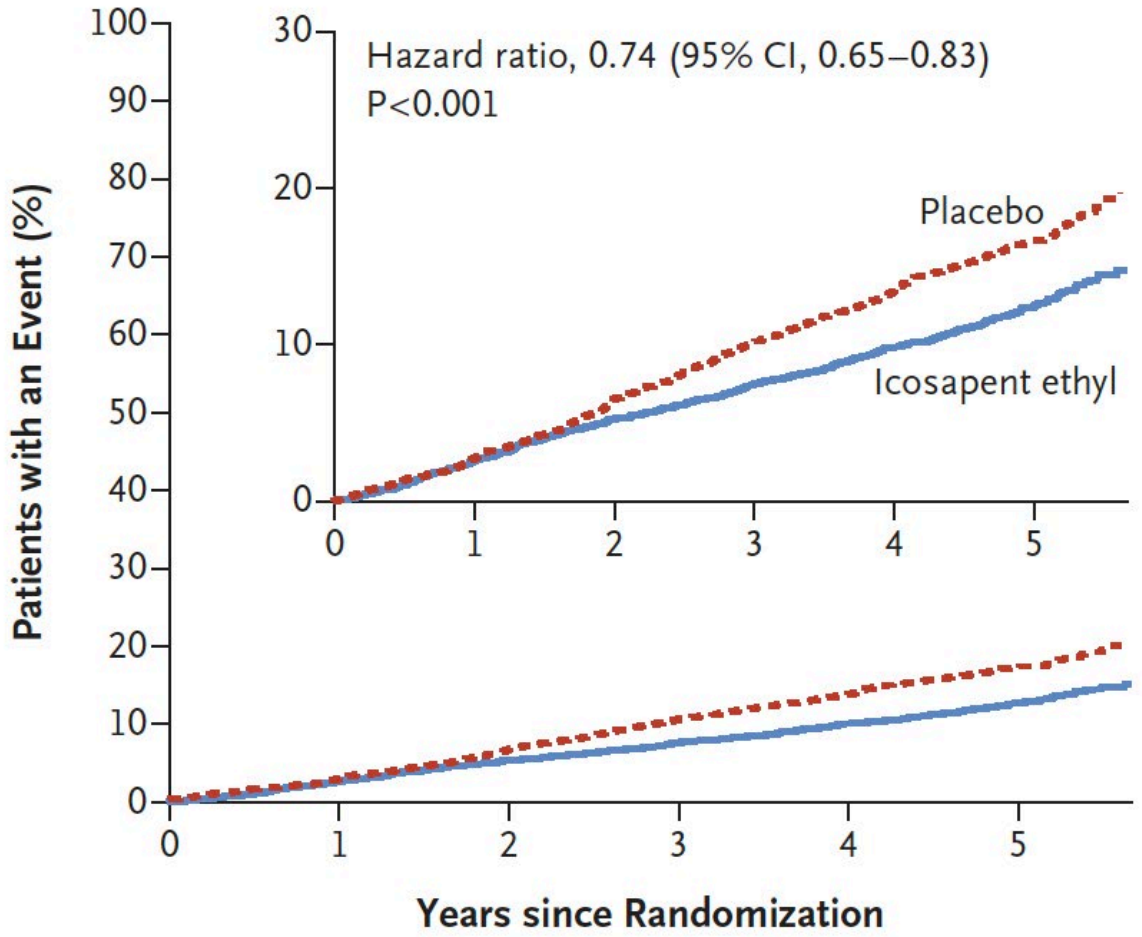
Secondary efficacy composite end point: cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke

Key Secondary End Point



No. at Risk

Placebo	4090	3837	3500	3002	2542	1487
Icosapent ethyl	4089	3861	3565	3115	2681	1562

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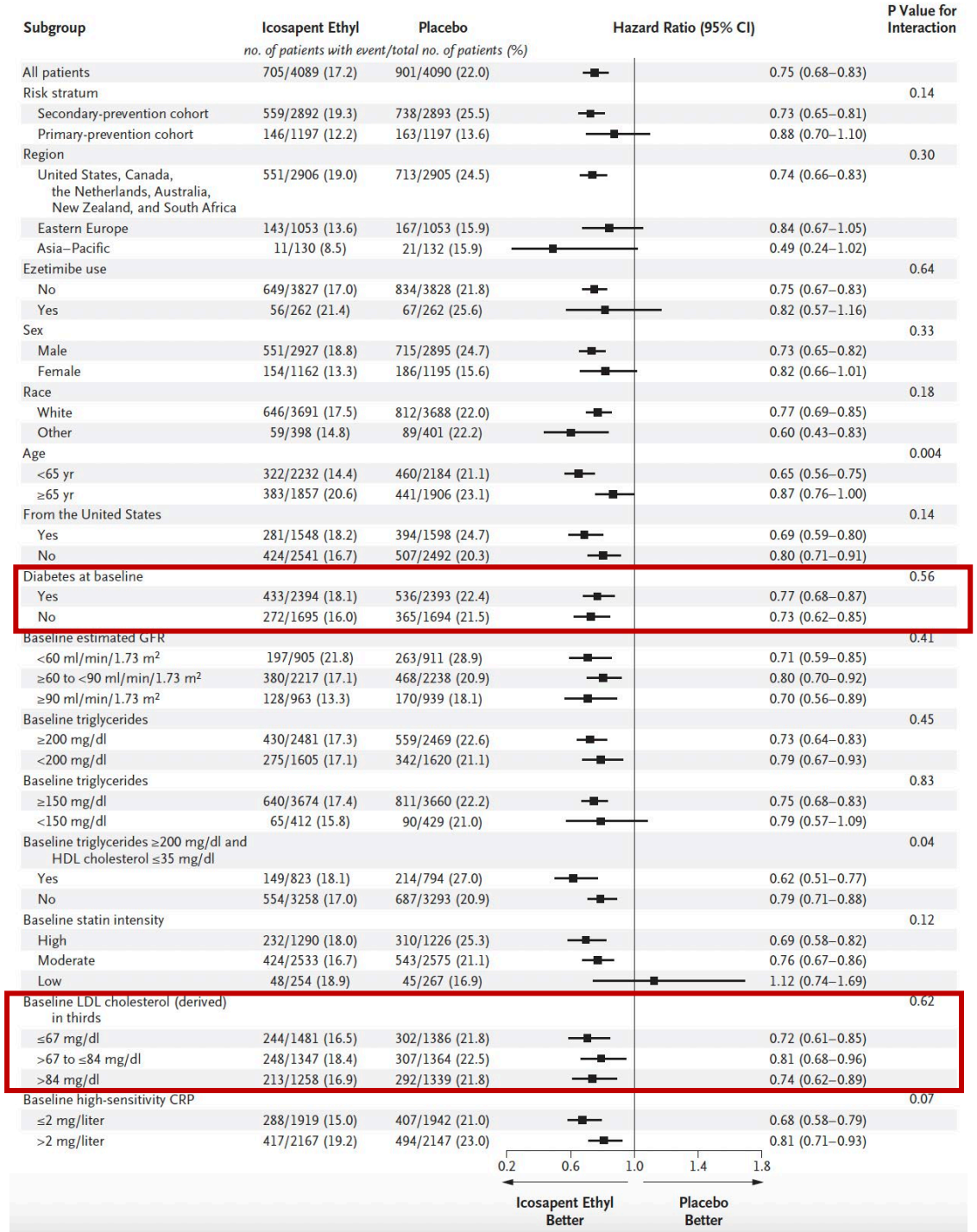
Subgroup
Icosapent Ethyl
Placebo
Hazard Ratio (95% CI)
P Value for Interaction
no. of patients with event/total no. of patients (%)
All patients 705/4089 (17.2) 901/4090 (22.0) 0.75 (0.68–0.83)
Risk stratum 0.14
Secondary-prevention cohort 559/2892 (19.3) 738/2893 (25.5) 0.73 (0.65–0.81)
Primary-prevention cohort 146/1197 (12.2) 163/1197 (13.6) 0.88 (0.70–1.10)
Region 0.30
United States, Canada, the Netherlands, Australia, New Zealand, and South Africa 551/2906 (19.0) 713/2905 (24.5) 0.74 (0.66–0.83)
Eastern Europe 143/1053 (13.6) 167/1053 (15.9) 0.84 (0.67–1.05)
Asia–Pacific 11/130 (8.5) 21/132 (15.9) 0.49 (0.24–1.02)
Ezetimibe use 0.64
No 649/3827 (17.0) 834/3828 (21.8) 0.75 (0.67–0.83)
Yes 56/262 (21.4) 67/262 (25.6) 0.82 (0.57–1.16)
Sex 0.33
Male 551/2927 (18.8) 715/2895 (24.7) 0.73 (0.65–0.82)
Female 154/1162 (13.3) 186/1195 (15.6) 0.82 (0.66–1.01)
Race 0.18
White 646/3691 (17.5) 812/3688 (22.0) 0.77 (0.69–0.85)
Other 59/398 (14.8) 89/401 (22.2) 0.60 (0.43–0.83)
Age 0.004
<65 yr 322/2232 (14.4) 460/2184 (21.1) 0.65 (0.56–0.75)
≥65 yr 383/1857 (20.6) 441/1906 (23.1) 0.87 (0.76–1.00)
From the United States 0.14
Yes 281/1548 (18.2) 394/1598 (24.7) 0.69 (0.59–0.80)
No 424/2541 (16.7) 507/2492 (20.3) 0.80 (0.71–0.91)
Diabetes at baseline 0.56
Yes 433/2394 (18.1) 536/2393 (22.4) 0.77 (0.68–0.87)
No 272/1695 (16.0) 365/1694 (21.5) 0.73 (0.62–0.85)
Baseline estimated GFR 0.41
<60 ml/min/1.73 m² 197/905 (21.8) 263/911 (28.9) 0.71 (0.59–0.85)
≥60 to <90 ml/min/1.73 m² 380/2217 (17.1) 468/2238 (20.9) 0.80 (0.70–0.92)
≥90 ml/min/1.73 m² 128/963 (13.3) 170/939 (18.1) 0.70 (0.56–0.89)
Baseline triglycerides 0.45
≥200 mg/dl 430/2481 (17.3) 559/2469 (22.6) 0.73 (0.64–0.83)
<200 mg/dl 275/1605 (17.1) 342/1620 (21.1) 0.79 (0.67–0.93)
Baseline triglycerides 0.83
≥150 mg/dl 640/3674 (17.4) 811/3660 (22.2) 0.75 (0.68–0.83)
<150 mg/dl 65/412 (15.8) 90/429 (21.0) 0.79 (0.57–1.09)
Baseline triglycerides ≥200 mg/dl and HDL cholesterol ≤35 mg/dl 0.04
Yes 149/823 (18.1) 214/794 (27.0) 0.62 (0.51–0.77)
No 554/3258 (17.0) 687/3293 (20.9) 0.79 (0.71–0.88)
Baseline statin intensity 0.12
High 232/1290 (18.0) 310/1226 (25.3) 0.69 (0.58–0.82)
Moderate 424/2533 (16.7) 543/2575 (21.1) 0.76 (0.67–0.86)
Low 48/254 (18.9) 45/267 (16.9) 1.12 (0.74–1.69)
Baseline LDL cholesterol (derived) in thirds 0.62
≤67 mg/dl 244/1481 (16.5) 302/1386 (21.8) 0.72 (0.61–0.85)
>67 to ≤84 mg/dl 248/1347 (18.4) 307/1364 (22.5) 0.81 (0.68–0.96)
>84 mg/dl 213/1258 (16.9) 292/1339 (21.8) 0.74 (0.62–0.89)
Baseline high-sensitivity CRP 0.07
≤2 mg/liter 288/1919 (15.0) 407/1942 (21.0) 0.68 (0.58–0.79)
>2 mg/liter 417/2167 (19.2) 494/2147 (23.0) 0.81 (0.71–0.93)
0.2
0.6
1.0
1.4
1.8
Icosapent Ethyl Better
Placebo Better

NEJM 2018

Conclusioni

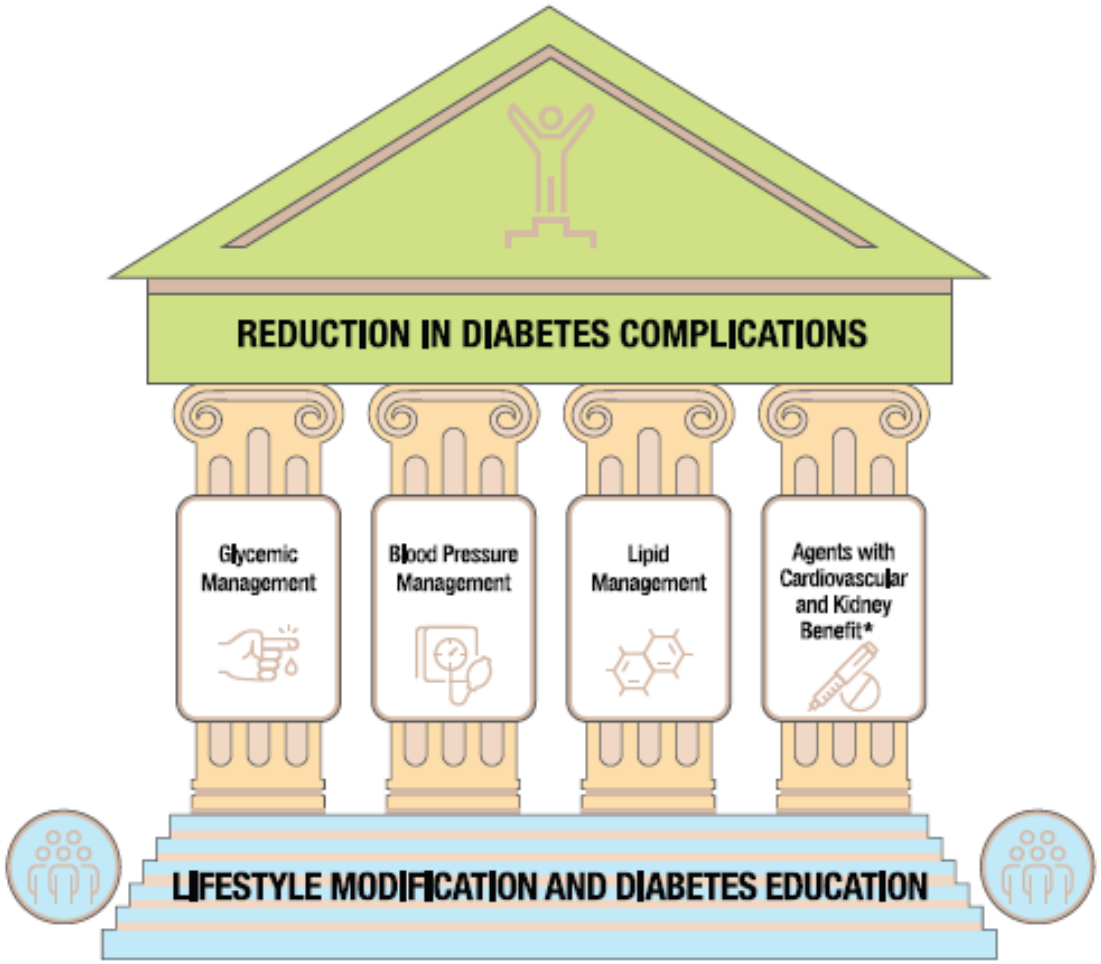

Figure 10.1—Multifactorial approach to reduction in risk of diabetes complications. *Risk reduction interventions to be applied as individually appropriate.

Cardiovascular Disease and Risk Management:
Standards of Medical Care in Diabetes - 2022. Diabetes Care 2022;45(Suppl. 1):S144-S174

Take-Home Messages

- ✓ Il controllo glicemico precoce e constante nel tempo può ridurre la mortalità generale e l'incidenza degli eventi micro e macro vascolari
- ✓ GLP1-AR e SGLT2-I sono farmaci in grado di modificare la storia naturale del diabete mellito tipo 2 indipendentemente dai livelli di HbA1c
- ✓ La riduzione dei livelli pressori al di sotto di 140 mmHg di sistolica porta a degli indubbi benefici (ma non al di sotto di 130 mmHg!) e il trattamento con perindopril/indapamide è superiore al solo ace-inibitore con maggiori benefici sugli outcome clinici
- ✓ Il controllo dei livelli di colesterolo-LDL con un trattamento intensivo porta ad una riduzione degli eventi cardiovascolari
- ✓ Il trattamento dell'ipertrigliceridemia con esteri etilici di ac. eiosapentanoico porta ad una riduzione degli eventi cardiovascolari con un effetto indipendente dai livelli di colesterolo LDL