



**The “early treatment”
per la prevenzione del
rischio cardiovascolare
nel diabete di tipo 2.**

Angelo Avogaro

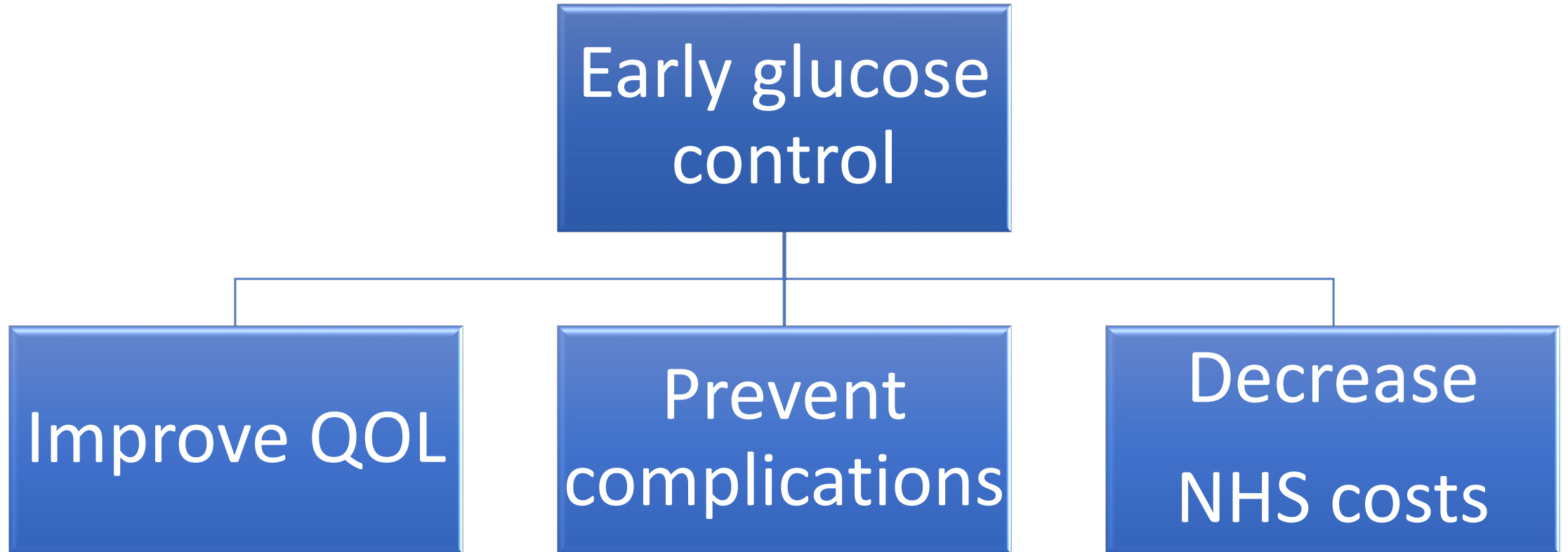
Società Italiana di
Diabetologia

Conflitti di interesse di Angelo Avogaro

Dichiaro di aver ricevuto negli ultimi 2 anni compensi dalle seguenti aziende:

Pharma International Company, AstraZeneca, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, Bruno Farmaceutici, Mundipharma, Neopharmed, Amgen, Servier, GlaxoSmithKline, Merck Sharp & Dohme, Novartis, Novo Nordisk, Sanofi, Takeda.

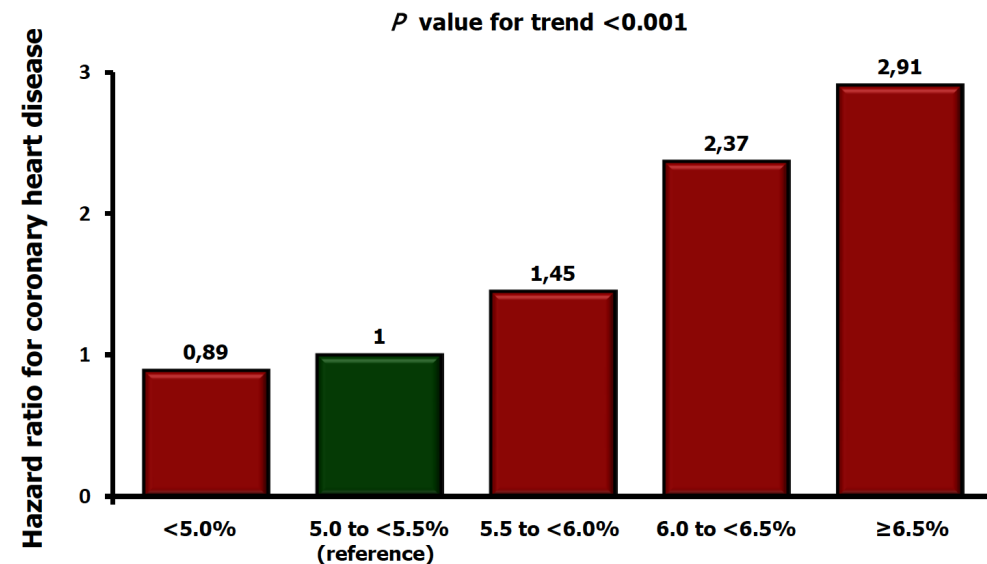
Why early treatment?



HbA_{1c} levels below the diagnostic threshold for Diabetes associate with an increased risk of cardiovascular disease

Selvin E, et al. *N Engl J Med* 2010;362:800–811

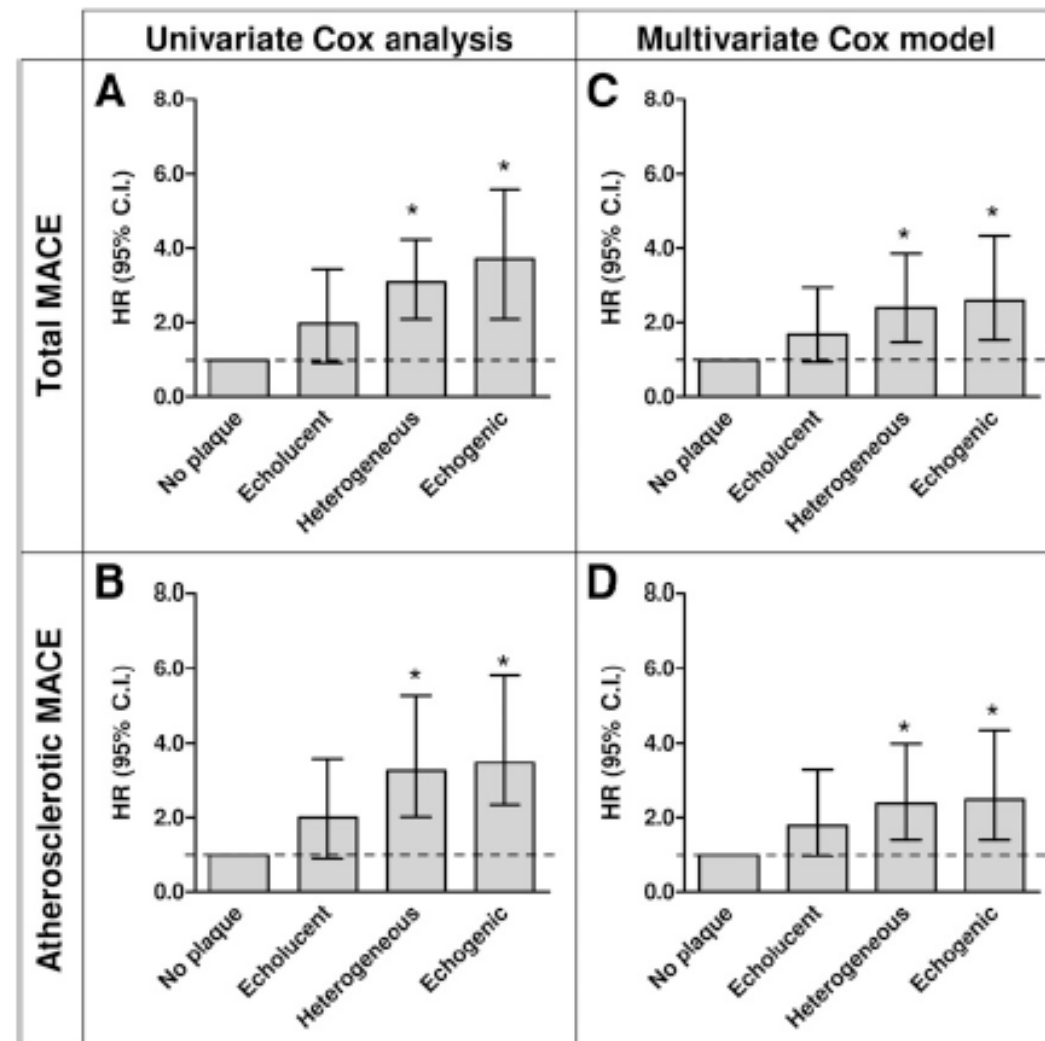
Hazard Ratios for coronary heart disease in the Atherosclerosis Risk in Communities (ARIC) population during the 15-Year study period according to HbA_{1c} category at baseline



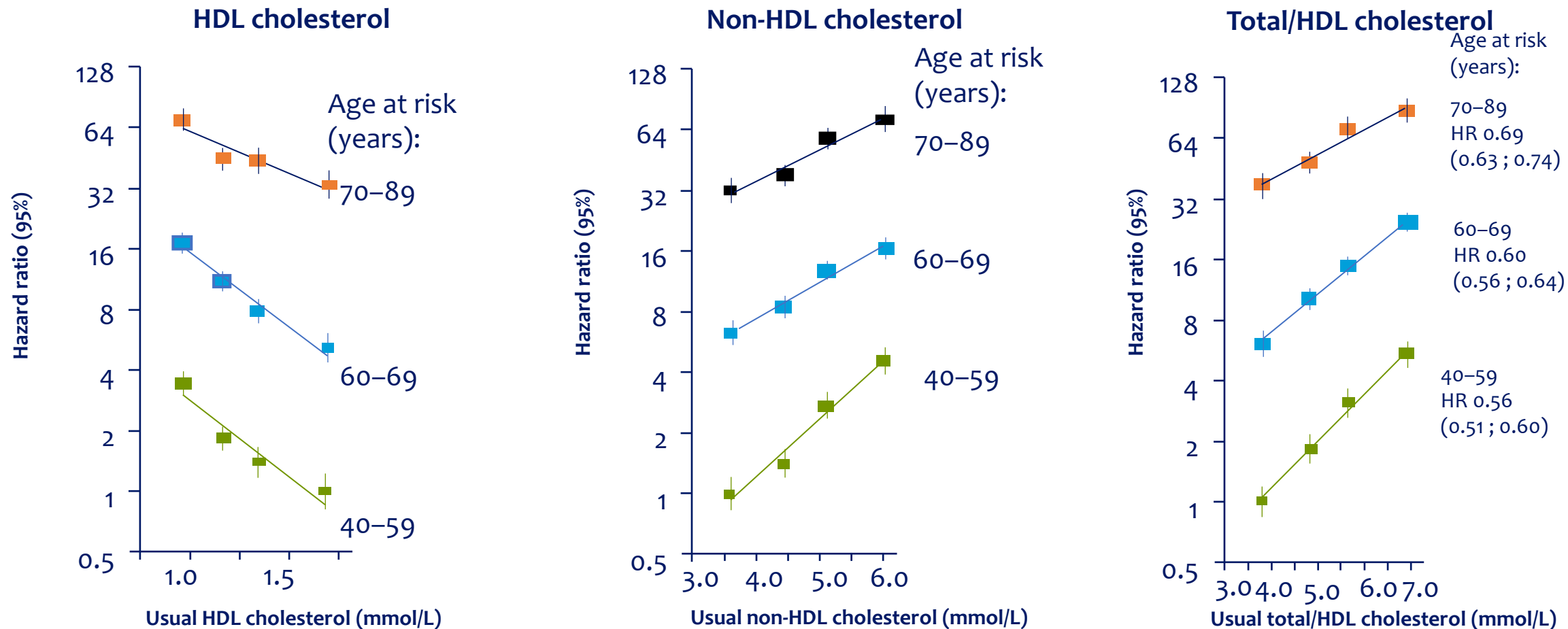
Carotid Plaque Calcification Predicts Future Cardiovascular Events in Type 2 Diabetes

Diabetes Care 2015;38:1937–1944 | DOI: 10.2337/dc15-0327

Saula Vigili de Kreutzenberg,¹
Gian Paolo Fadini,^{1,2} Stefano Guzzinati,³
Marta Mazzucato,¹ Antonio Volpi,⁴
Anna Coracina,⁴ and Angelo Avogaro^{1,2}



Ischaemic heart disease (IHD) mortality and cholesterol

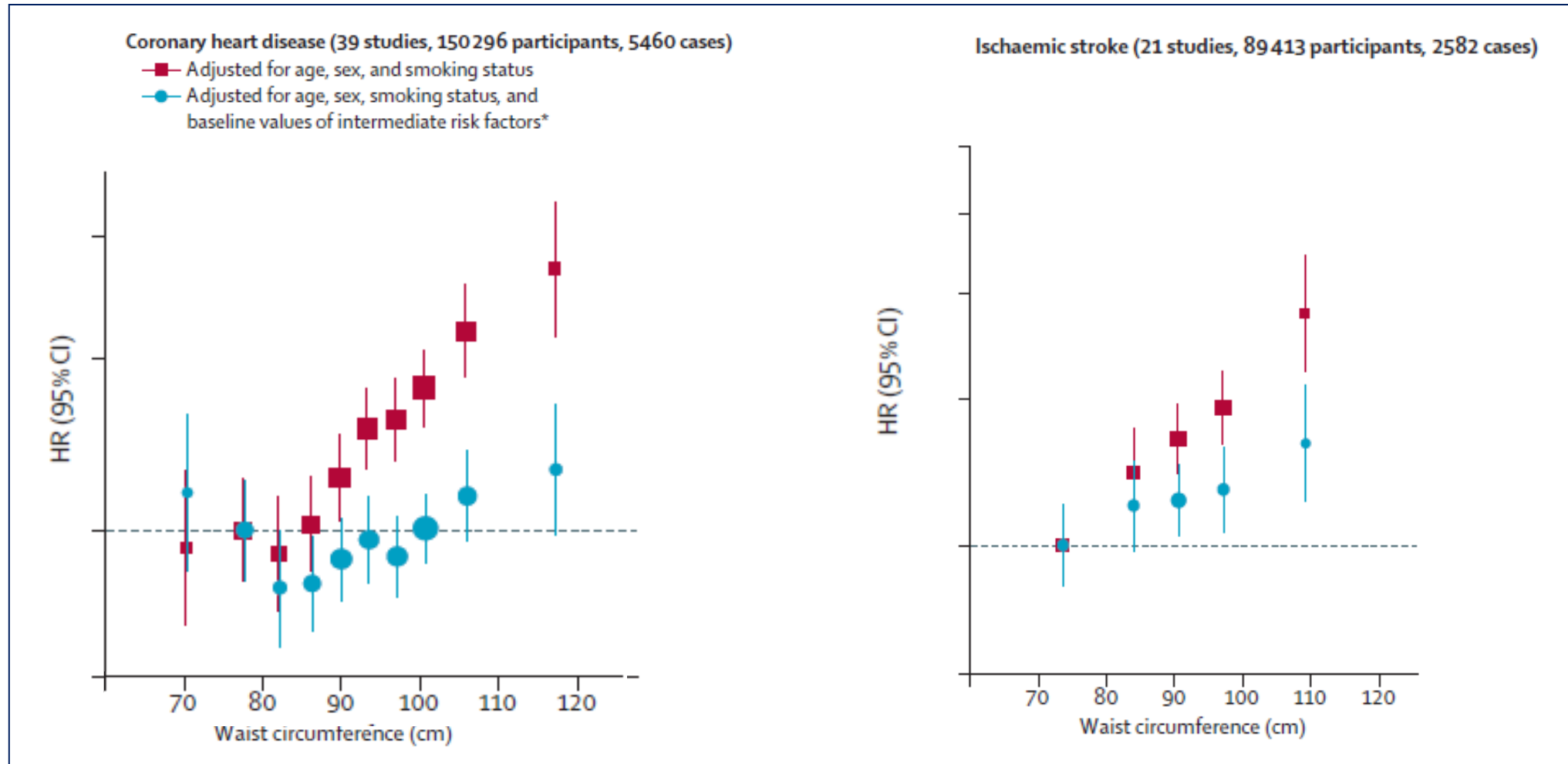


Hazard ratio (95% CI) per 1.33 lower total/HDL cholesterol; IHD mortality (3,020 deaths) vs. usual HDL cholesterol, HDL cholesterol and total/HDL cholesterol. Hazard ratios on the left are plotted on a floating absolute scale of risk (so each log hazard ratio has an appropriate variance assigned to it)

CI, confidence interval; HDL, high density lipoprotein; IHD, ischaemic heart disease

Lewington S et al. *Lancet* 2007; 370: 1829-39

The risk of for coronary heart disease and ischaemic stroke increase across quantiles of waist circumference

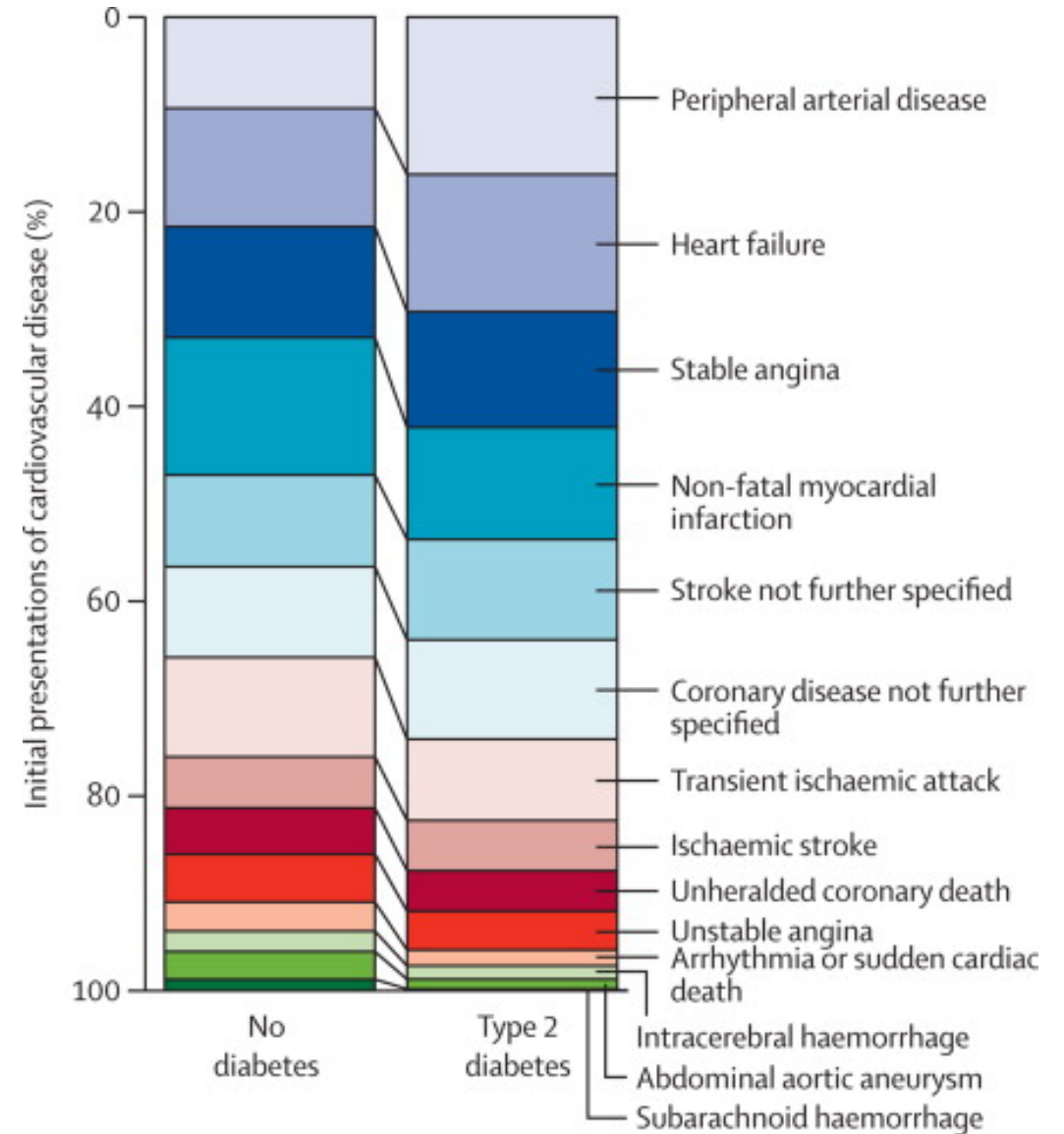


HR: Hazard ratio;

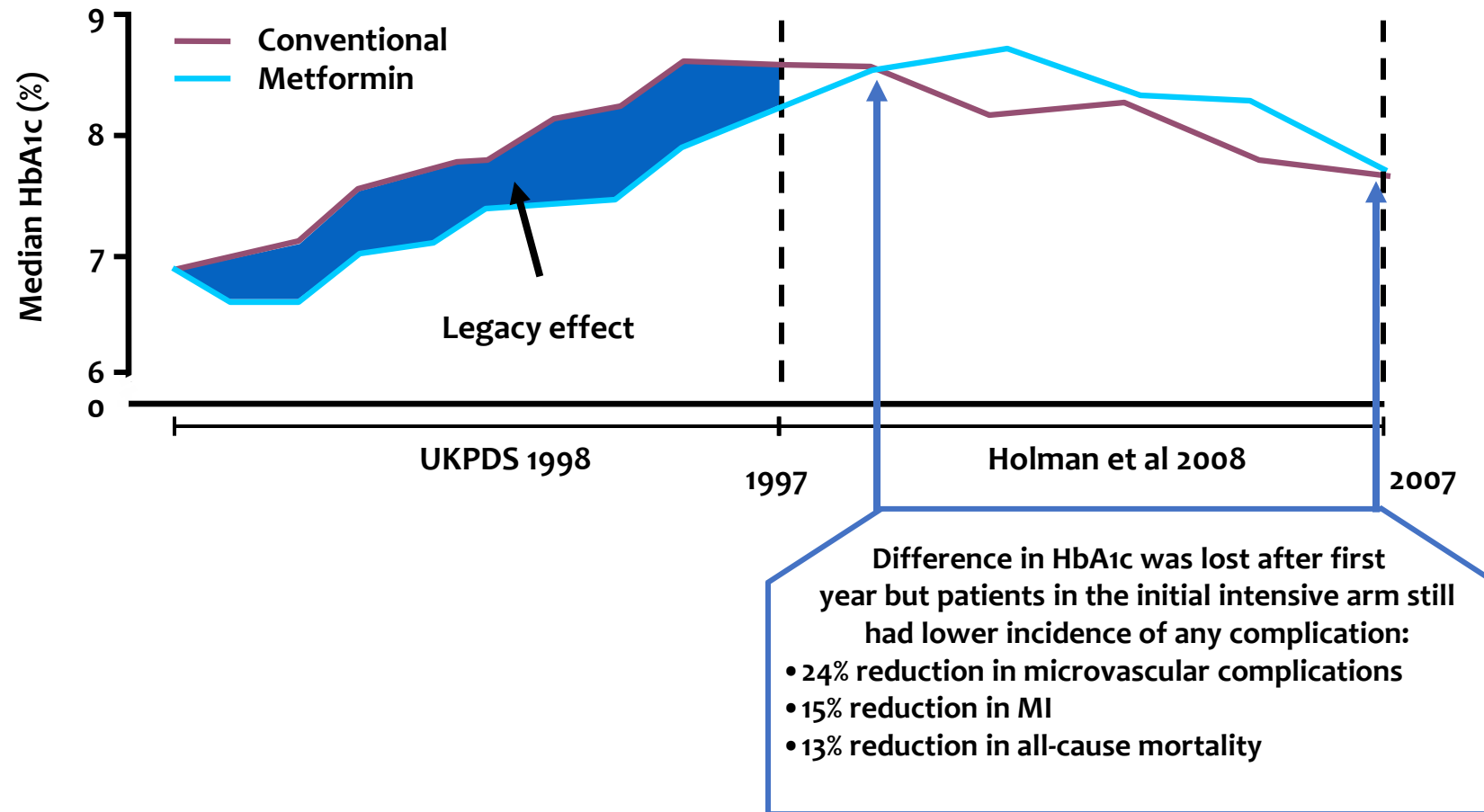
The Emerging Risk Factors Collaboration; Lancet 2011; 377: 1085–95

Shah AD et al. *Lancet Diabetes Endocrinol* 2015; 3(2): 105-13.

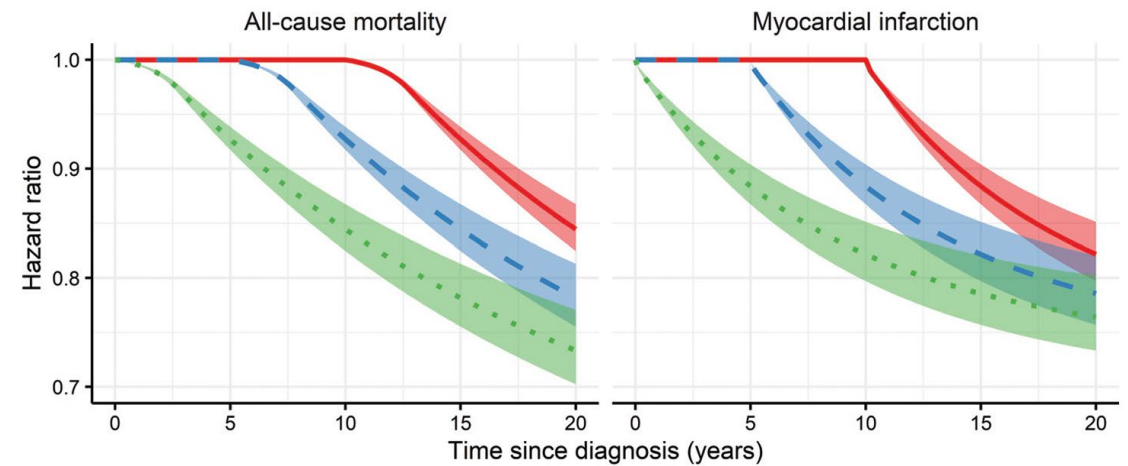
Peripheral artery disease is the most common long-term complication in newly onset diabetes



Targeting: Achieving early glycaemic control which may generate a good legacy effect

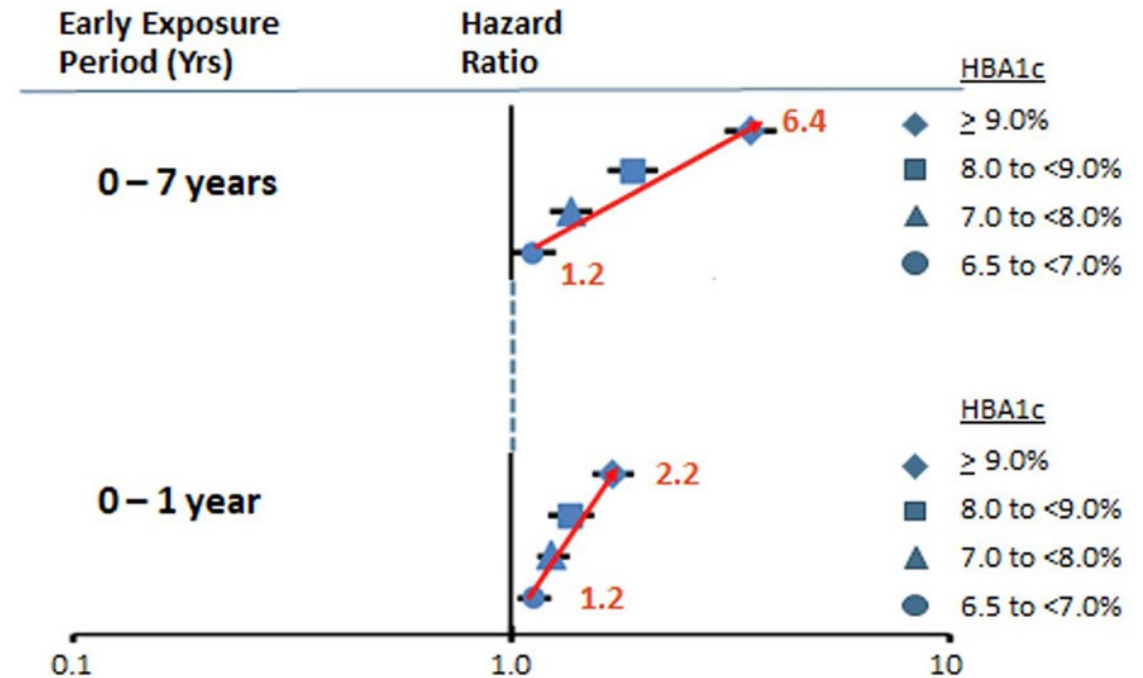


Time-dependent HRs for all cause-mortality and myocardial infarction from 0 to 20 years after diagnosis of type2 diabetes, assuming a one per centage unit lower HbA1c from diagnosis

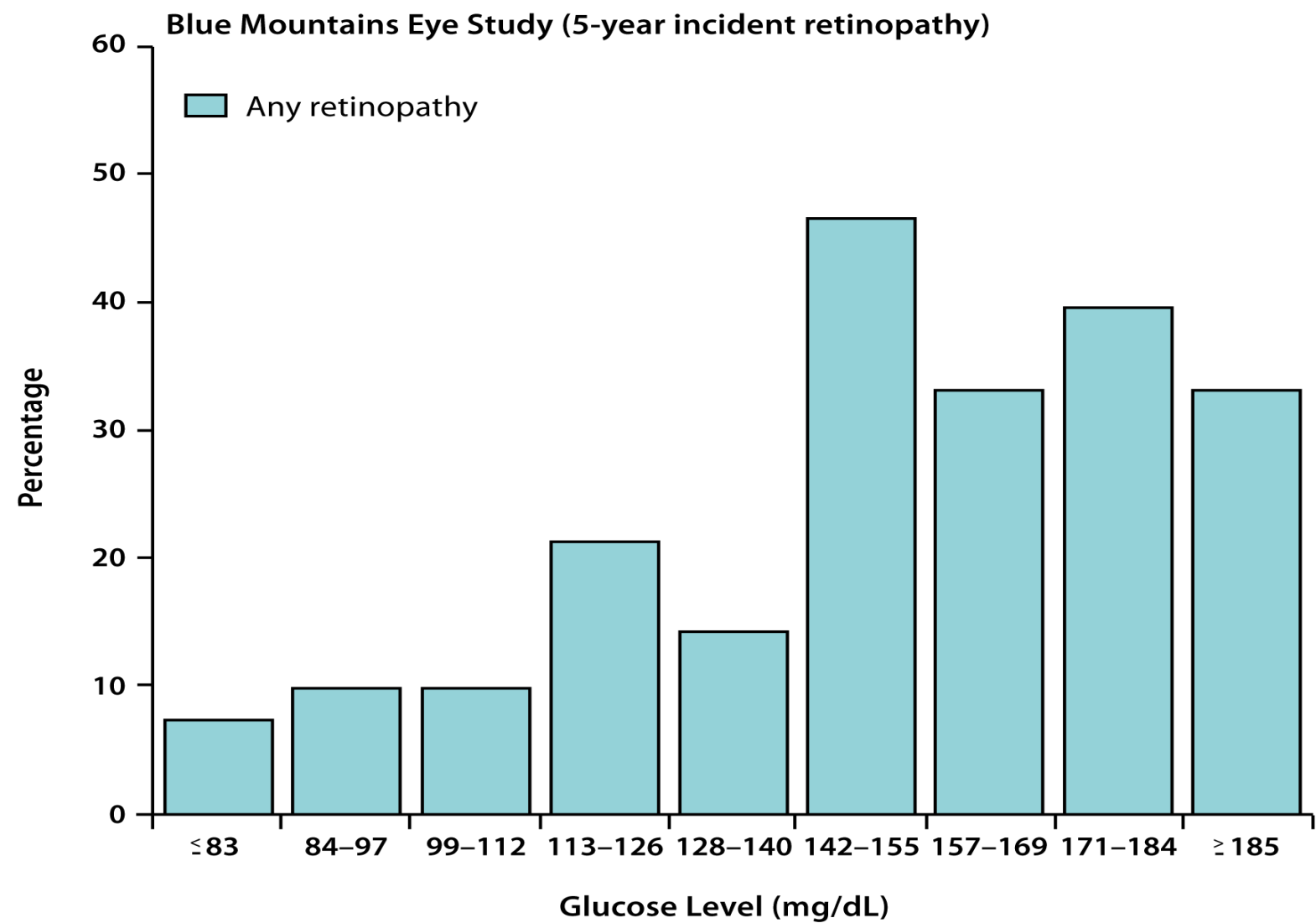


Impact of early glycaemic control in patients with type 2 diabetes on microvascular events

Laiteerapong et al. Diabetes Care 2019



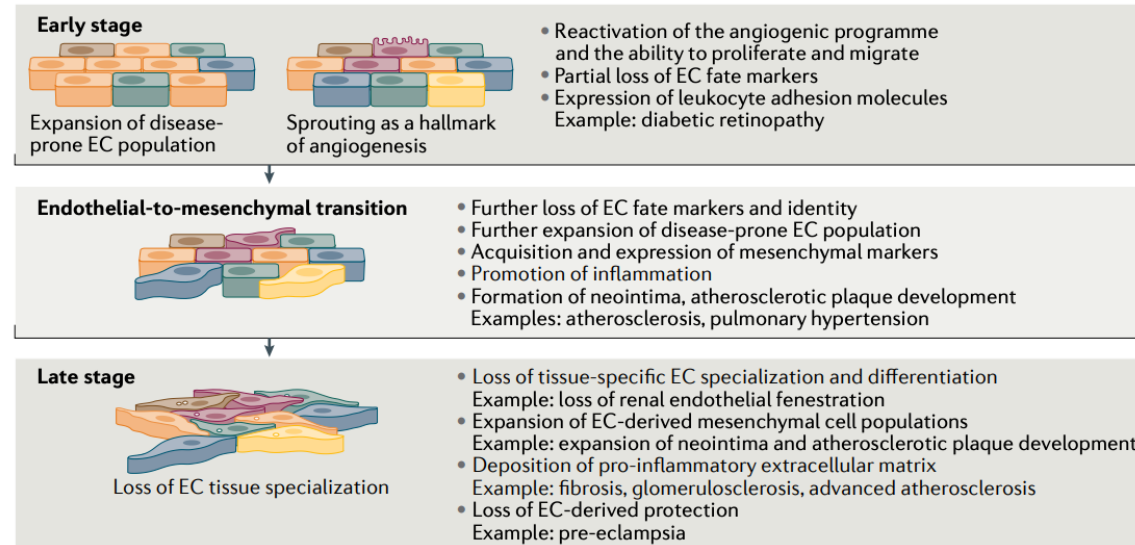
Relationship Between FPG and 5-Year Incident Retinopathy



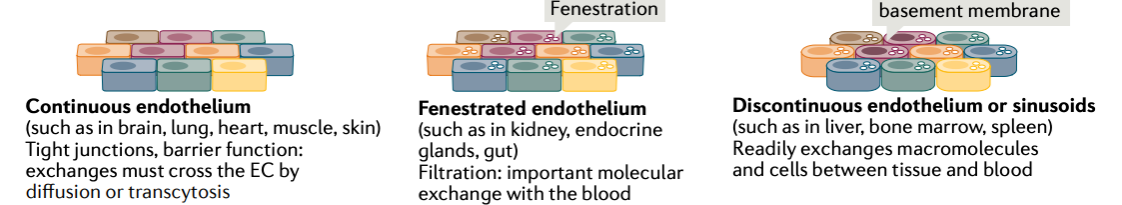
FPG, fasting plasma glucose.

Wong TY, et al. *Lancet*. 2008;371:736-743.

c Pathogenic endothelium

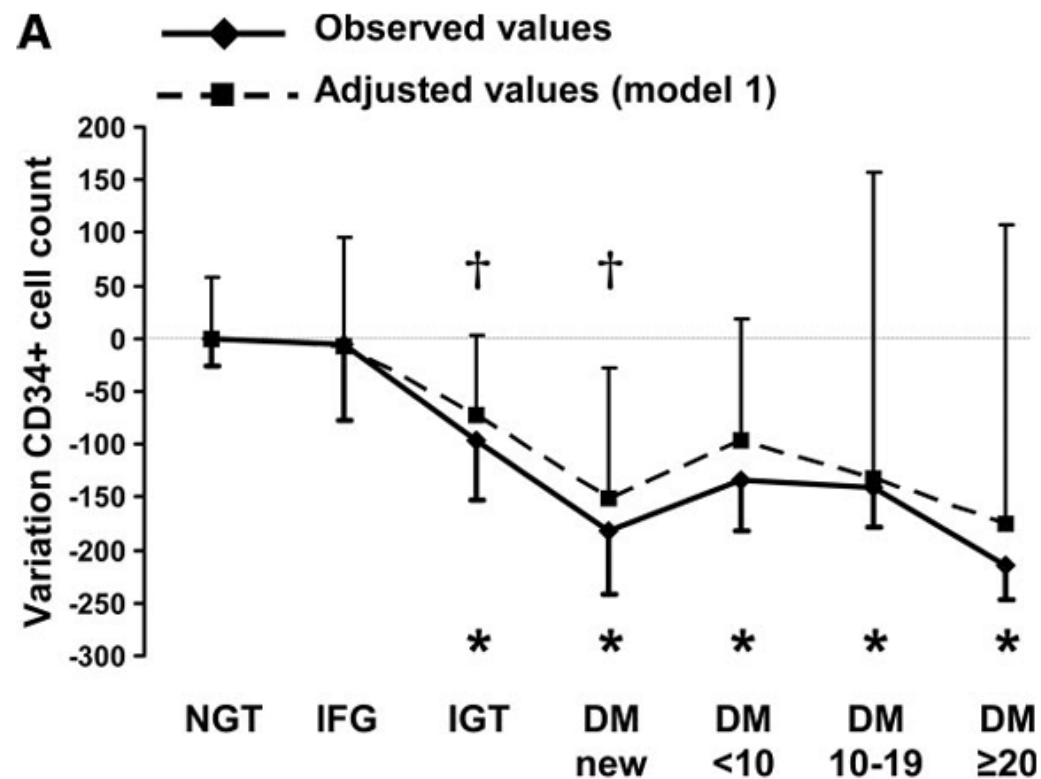


b Healthy endothelium



Hyperglycemia-induced endothelial damage

- Ricard et al. Nat Rev Cardiol 2021

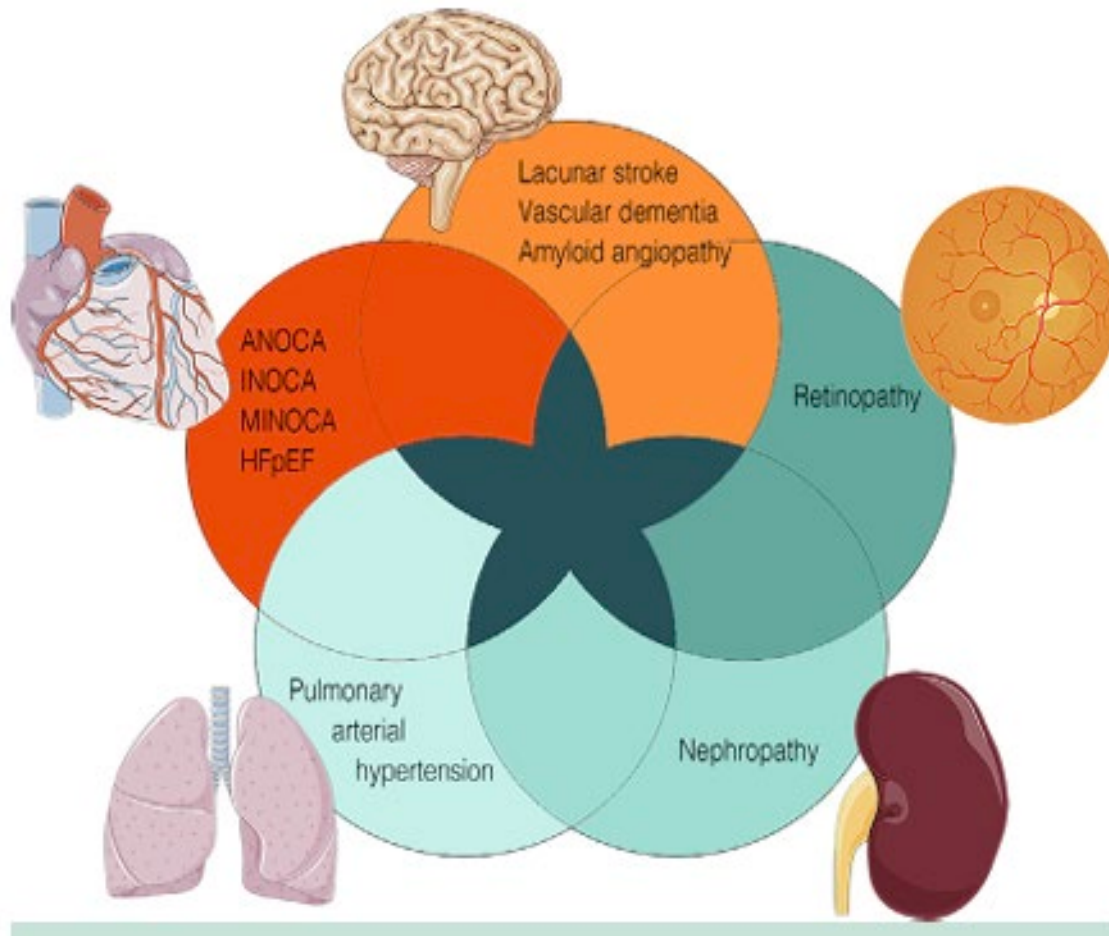


Time Course and Mechanisms of Circulating Progenitor Cell Reduction in the Natural History of Type 2 Diabetes

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 ELISA BOSCARO, BSC¹
 SAULA DE KREUTZENBERG, MD, PHD²
 CARLO AGOSTINI, MD¹
 FLORIAN SEEGER, MD²

STEFANIE DIMMELER, PHD²
 ANDREAS ZEIHNER, MD²
 ANTONIO TIENGO, MD¹
 ANGELO AVOGARO, MD, PHD¹

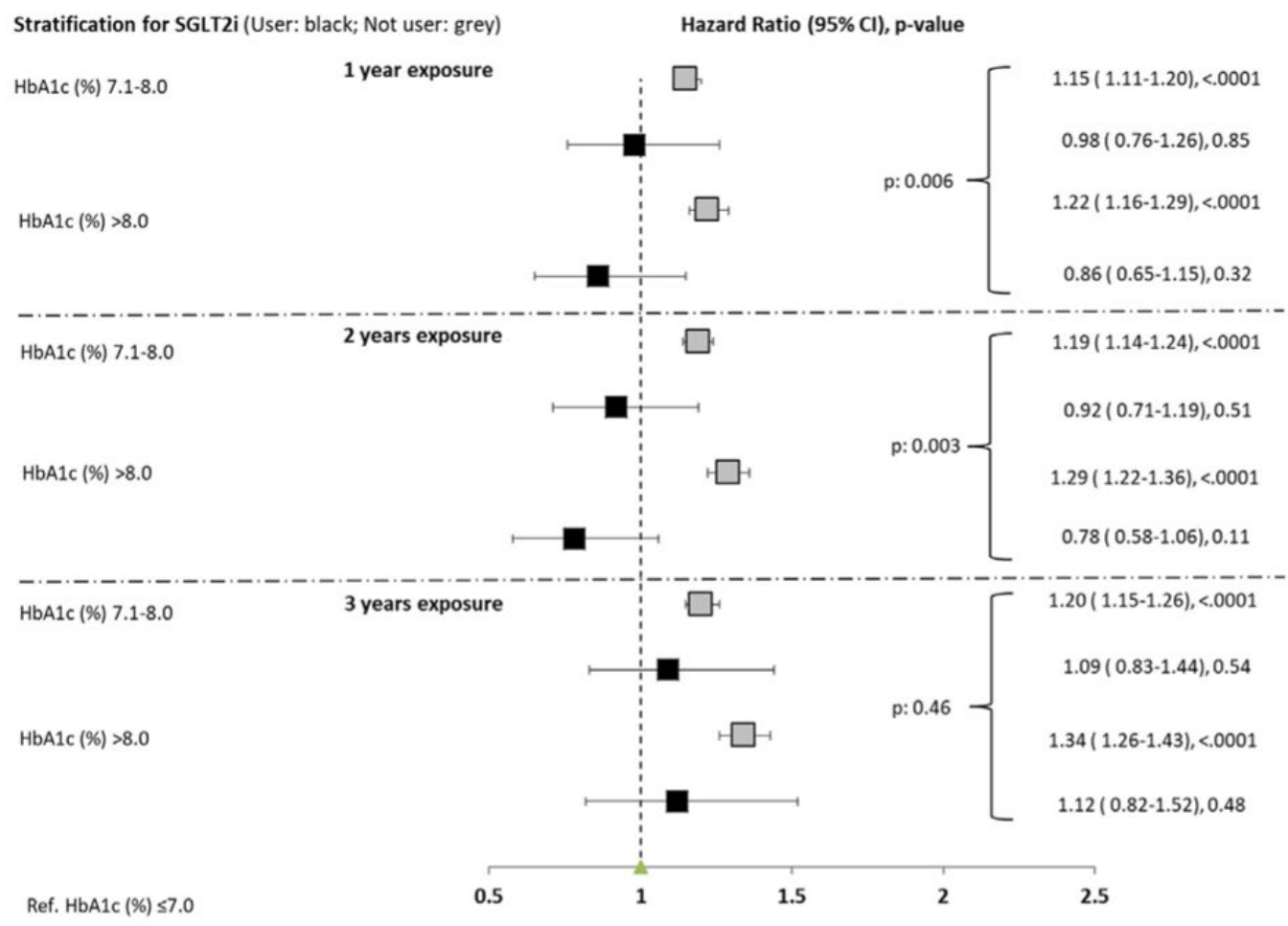
A relatively novel paradigm of CVD pathogenesis is the loss of normal endothelial turnover caused by a reduction of circulating endothelial progenitor cells (EPCs) (4). EPCs are mainly derived from



Microvascular dysfunction affecting the heart, brain, retina, lung, and kidney, representing different manifestations of small vessel disease. They share pathophysiologic mechanisms and can occur concomitantly.

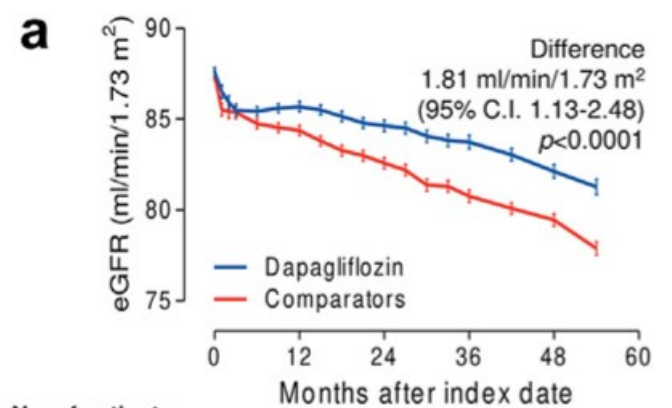
The legacy effect of hyperglycemia and early use of SGLT-2 inhibitors: a cohort study with newly-diagnosed people with type 2 diabetes

Antonio Ceriello,^{a,*} Giuseppe Lucisano,^b Francesco Prattichizzo,^{a,**} Rosalba La Grotta,^a Chiara Frigé,^a Salvatore De Cosmo,^c Paolo Di Bartolo,^d Graziano Di Cianni,^e Paola Fioretto,^f Carlo Bruno Giorda,^g Roberto Pontremoli,^h Giuseppina Russo,ⁱ Francesca Viazzi,^h and Antonio Nicolucci,^b *AMD Annals study group,^j*



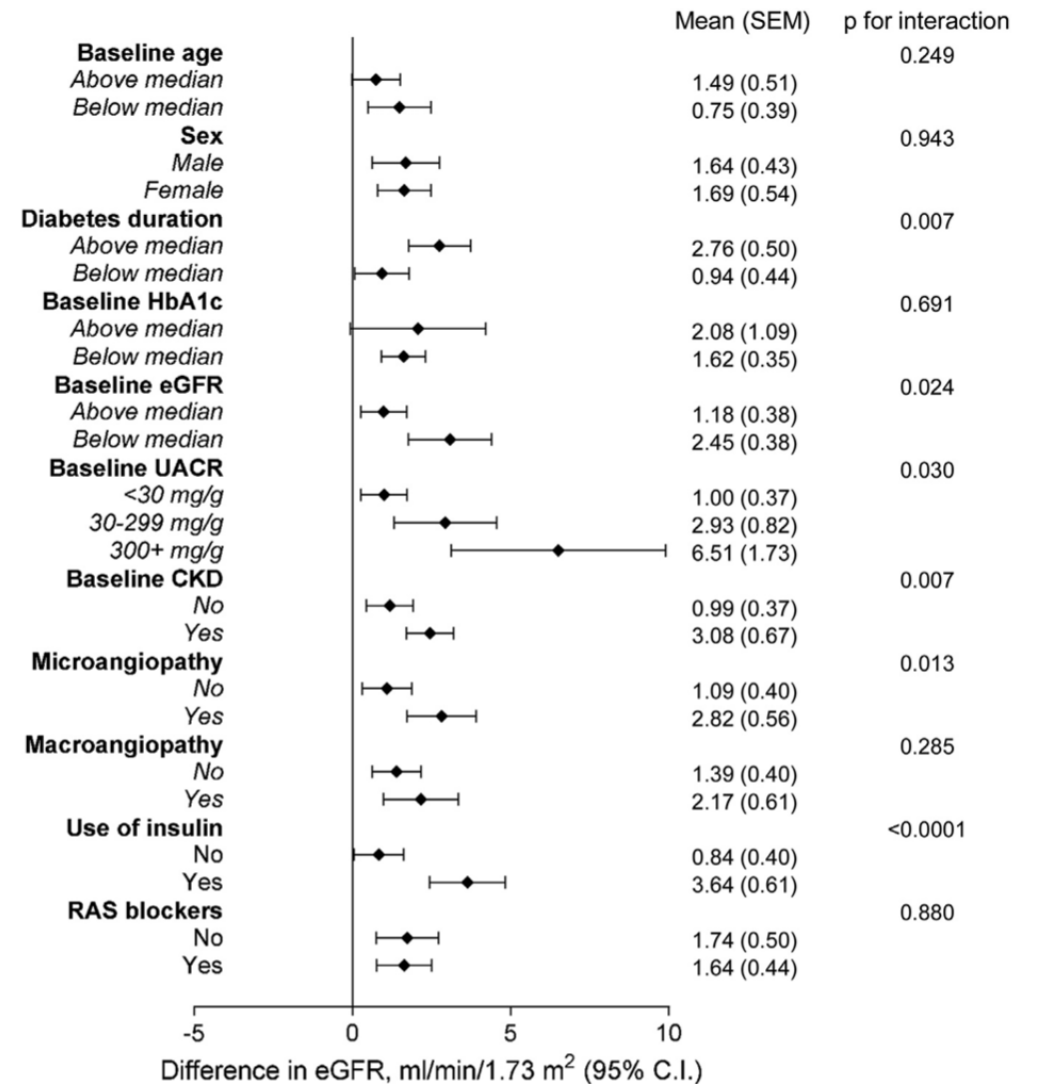
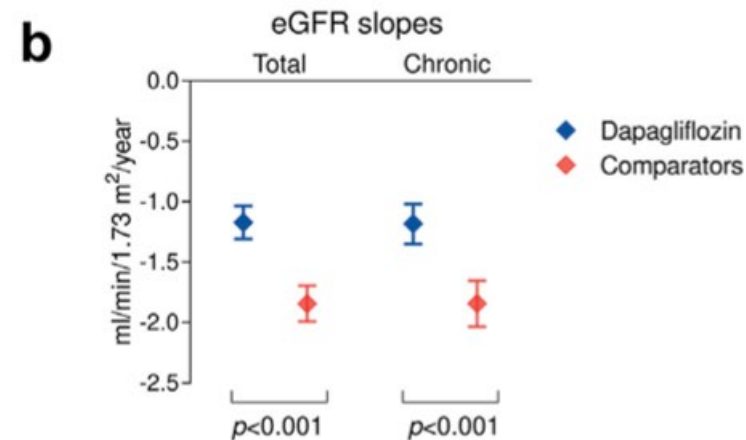
Long-term benefits of dapagliflozin on renal outcomes of type 2 diabetes under routine care: a comparative effectiveness study on propensity score matched cohorts at low renal risk

Gian Paolo Fadini,^{a,b,f,*} Enrico Longato,^{c,f} Mario Luca Morieri,^a Stefano Del Prato,^d Angelo Avogaro,^a and Anna Solini,^e
DARWIN-Renal Study Investigators



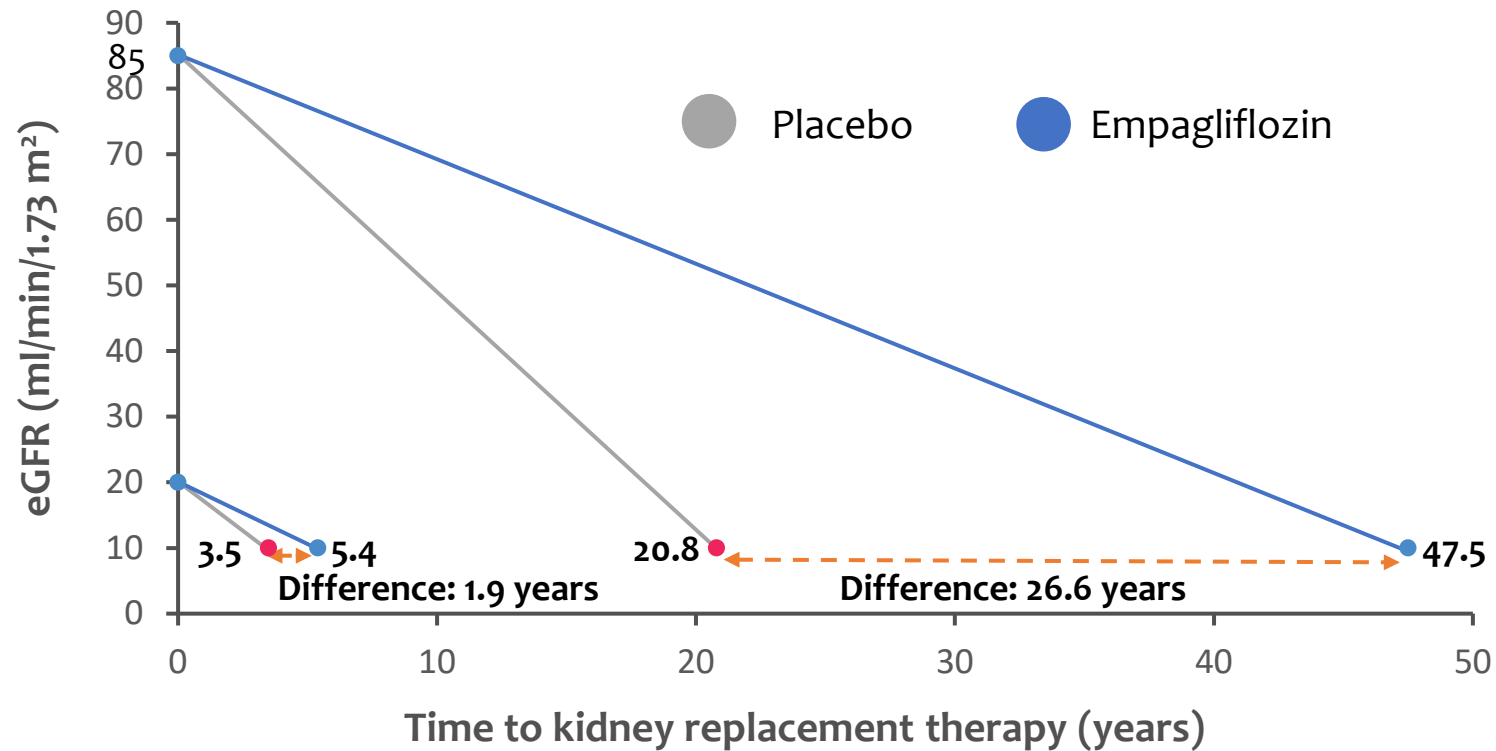
No. of patients						
Dapagliflozin	4547	1988	1418	919	1058	699*
Comparators	4241	1997	1530	1197	1486	1139*

*54 months



EMPA-KIDNEY: time to kidney replacement therapy

Potential impact on time to kidney replacement therapy of the different eGFR slopes on placebo and on empagliflozin*

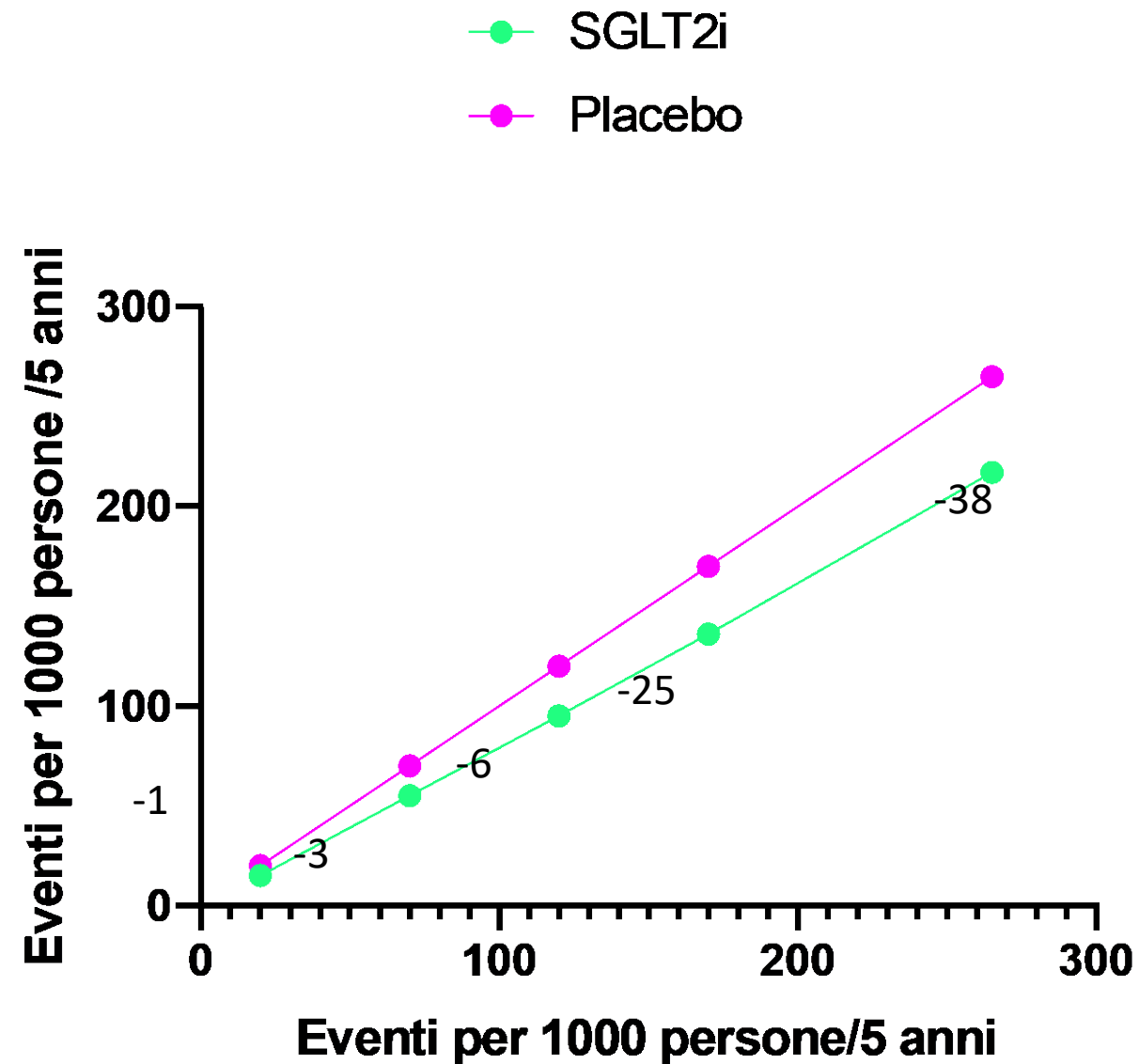


*The difference in the time to kidney failure corresponds to the values in the figure on the previous slide for baseline eGFR 20 and 85 ml/min/1.73m².

eGFR, estimated glomerular filtration rate

Fernández-Fernandez B et al. Clin Kidney J 2023;0:1

Sodium-glucose cotransporter protein-2 (SGLT-2) inhibitors and glucagon-like peptide-1 (GLP-1) receptor agonists for type 2 diabetes: systematic review and network meta-analysis of randomised controlled trials





ORIGINAL RESEARCH

The “Early Treatment” Approach Reducing Cardiovascular Risk in Patients with Type 2 Diabetes: A Consensus From an Expert Panel Using the Delphi Technique

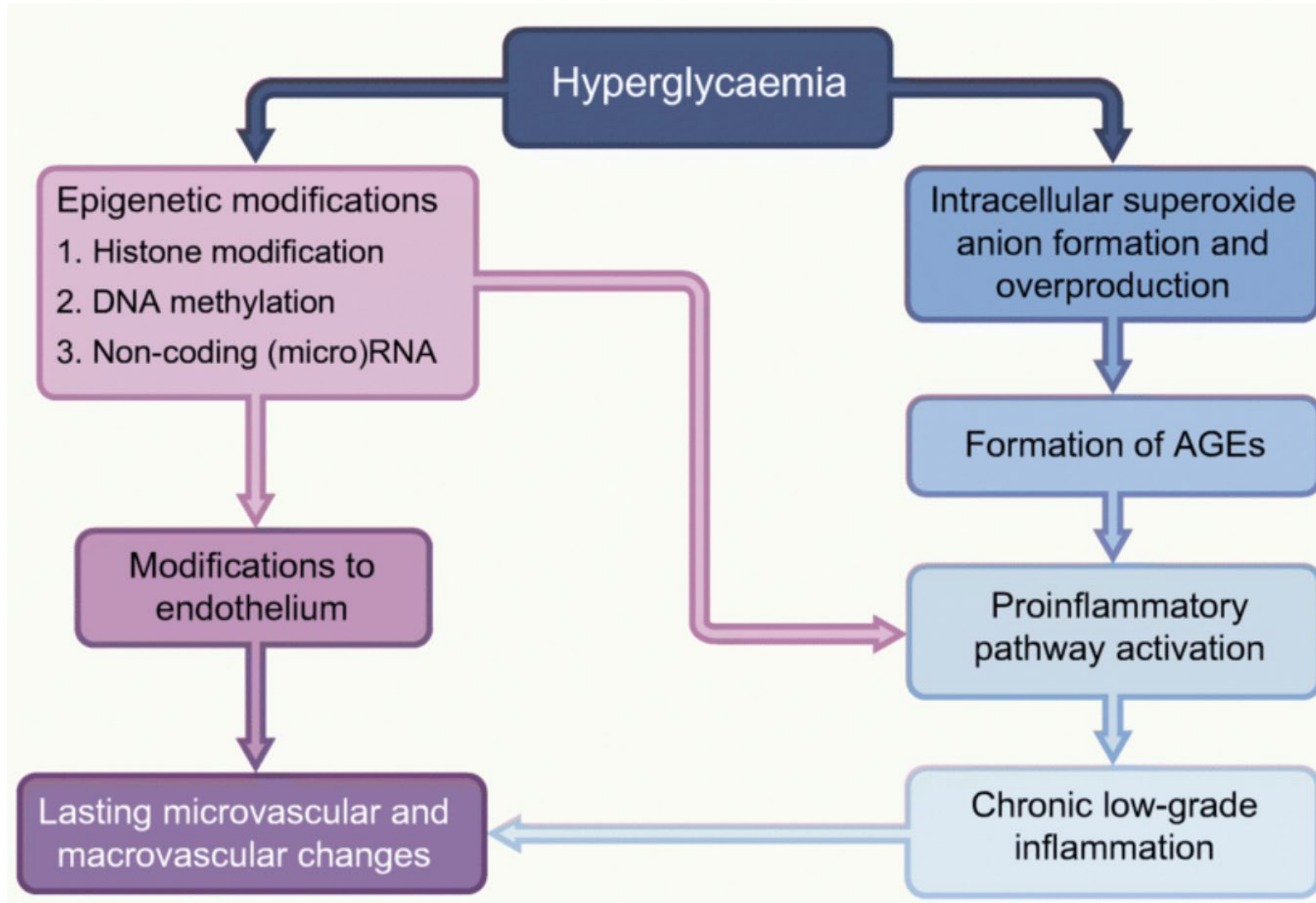
Giuseppina Russo  · Matteo Monami · Gianluca Perseghin ·
Angelo Avogaro · Pasquale Perrone Filardi · Michele Senni ·
Claudio Borghi · Aldo P. Maggioni

Received: December 30, 2020 / Accepted: March 2, 2021 / Published online: March 25, 2021
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1. Italian diabetologists consider the importance of adopting a personalized approach for patients with T2DM and CV risk factors.

2. GLP-1RAs and SGLT2 inhibitors were recognized as key strategies in the treat-to-benefit approach.

3. A paradigm shift should be implemented to focus clinicians' attention not only on metabolic control but also on the longterm CV benefits, even at early stages.



Post-trial monitoring of a randomised controlled trial of intensive glycaemic control in type 2 diabetes extended from 10 years to 24 years (UKPDS 91)



Amanda I Adler*, Ruth L Coleman*, Jose Leal, William N Whiteley, Philip Clarke, Rory R Holman

Interpretation Early intensive glycaemic control with sulfonylurea or insulin, or with metformin, compared with conventional glycaemic control, appears to confer a near-lifelong reduced risk of death and myocardial infarction. Achieving near normoglycaemia immediately following diagnosis might be essential to minimise the lifetime risk of diabetes-related complications to the greatest extent possible.

CARDIOVASCULAR CONTINUUM EARLY TREATMENT

LOW-to-MODERATE RISK

HIGH RISK

VERY HIGH RISK

**ENDOTHELIAL DYSFUNCTION
MICROVASCULAR DYSFUNCTION**

SUBCLINICAL ATHEROSCLEROSIS

TARGET ORGAN DAMAGE

