Il dr. ROBERTO TREVISAN dichiara di aver ricevuto negli ultimi due anni compensi o finanziamenti dalle seguenti Aziende Farmaceutiche e/o Diagnostiche:

- NOVO
- SANOFY
- LILLY
- NOVARTIS
- ASTRA ZENECA
- MEDTRONIC
- MERCK
- TAKEDA

SID
fondata nel 1964
Società Italiana di Diabetologia

MICROANGIOPATIA E MACROANGIOPATIA: DUE FACCE DELLA STESSA COMPLICANZA?

Roberto Trevisan
UOC Malattie Endocrine – Diabetologia
ASST Papa Giovanni XXIII, Bergamo


vildagliptin
SERVIER
Humalog 25
Apidra

TYPE 1 and TYPE 2 DIABETES ARE TWO DISEASES

- **MICROVASCULAR**
- **MACROVASCULAR**

WITH 2 DISTINCT PATHOGENIC SEQUENCES

LEADING TO 2 DISTINCT CLINICAL PRESENTATIONS

Diabetologia (1989) 32: 219–226

Diabetologia

© Springer-Verlag 1989

Reviews

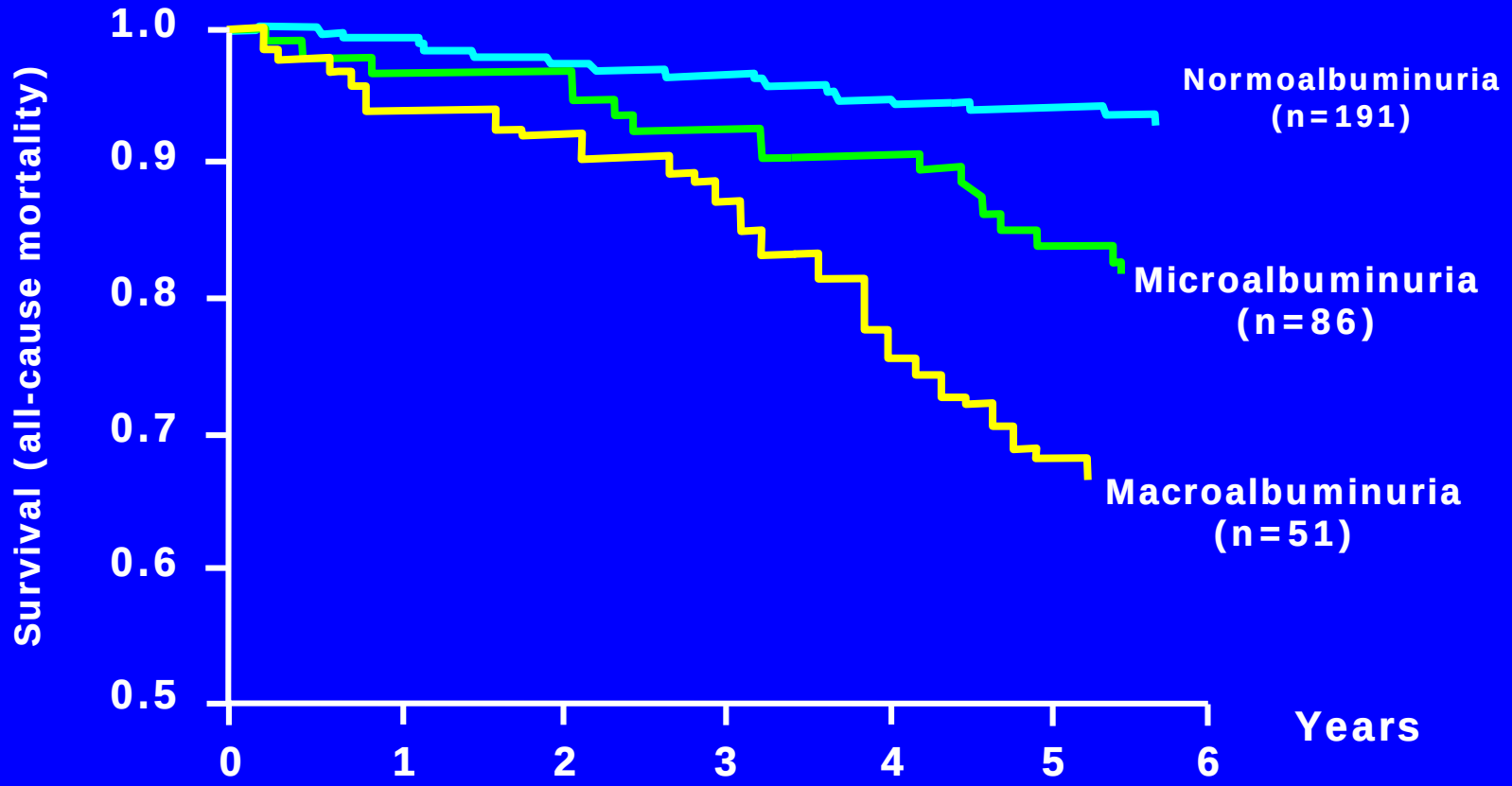
Albuminuria reflects widespread vascular damage*
The Steno hypothesis

T. Deckert, B. Feldt-Rasmussen, K. Borch-Johnsen, T. Jensen and A. Kofoed-Enevoldsen

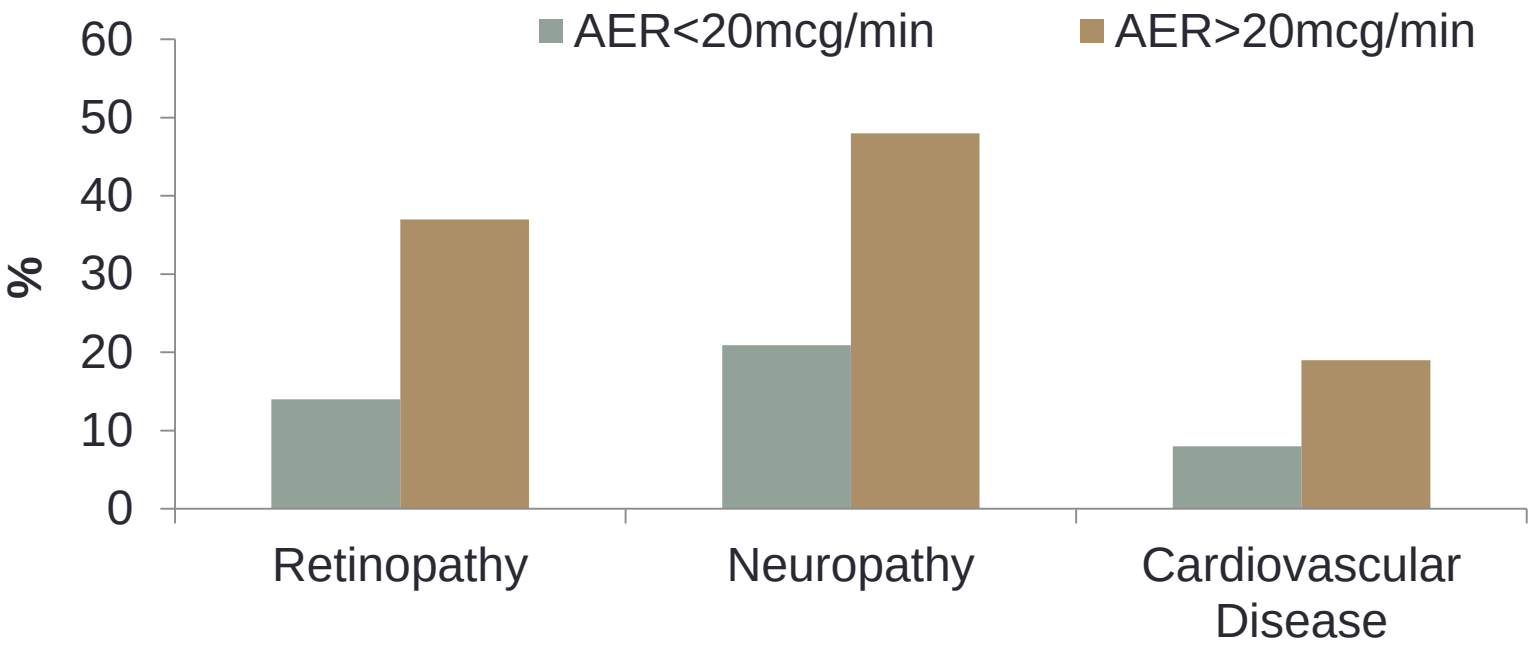
Steno Memorial Hospital, Gentofte, Denmark

Gall MA, et al. Diabetes. 1995;44:1303-1309.

Proteinuria as a Risk Factor for Mortality in Type 2 Diabetes

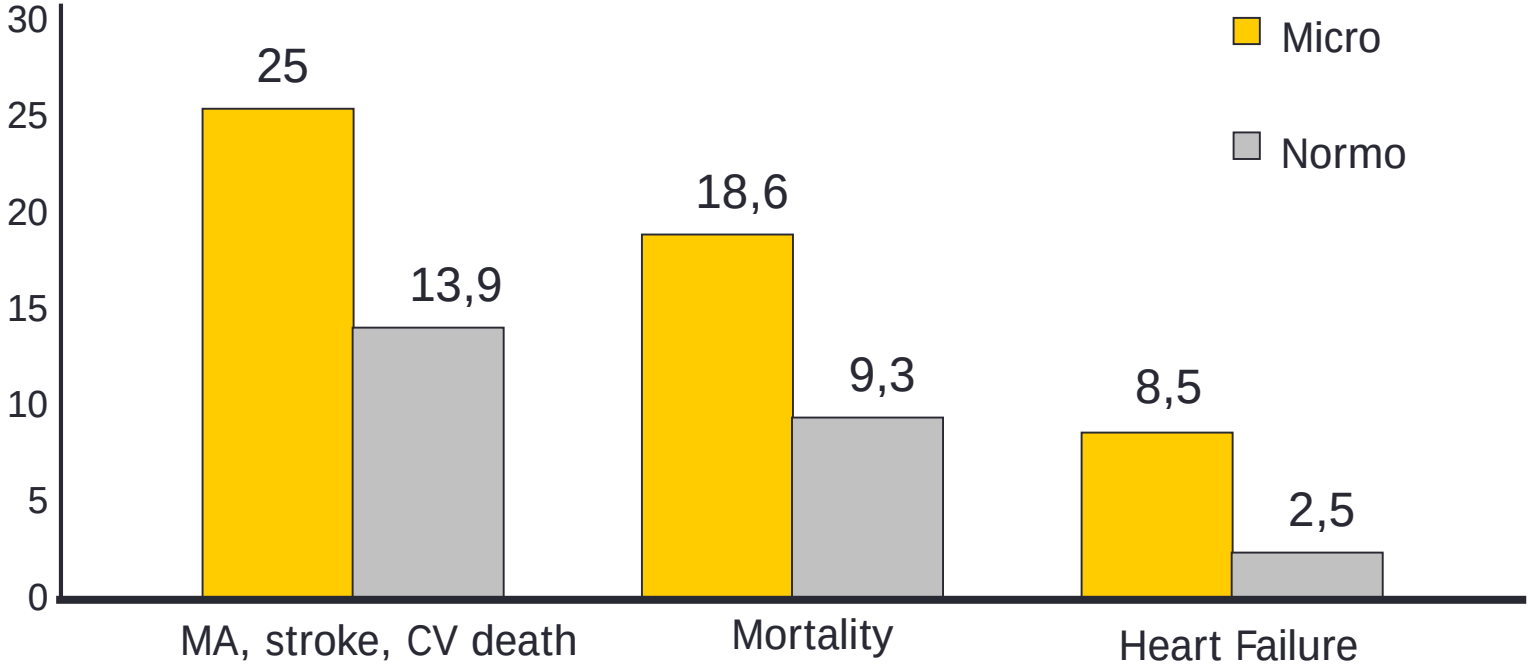


Prevalence of retinopathy, neuropathy and cardiovascular disease in type 2 diabetic patients with and without abnormal AER



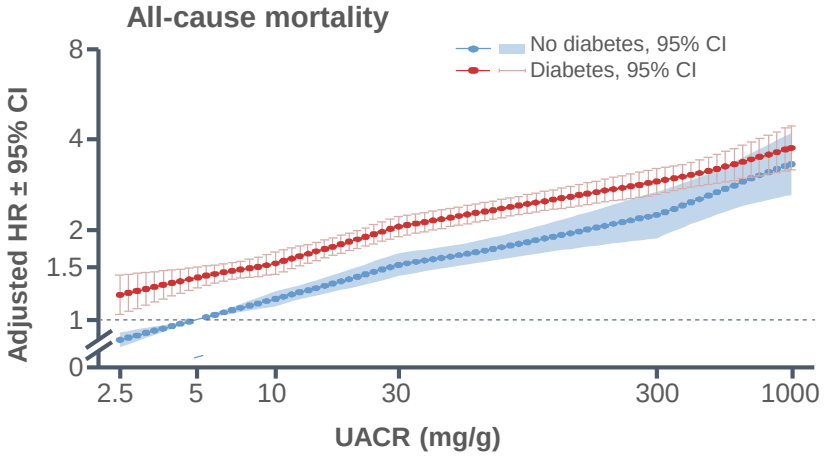
JAMA. 2001 Jul 25;286(4):421-6.

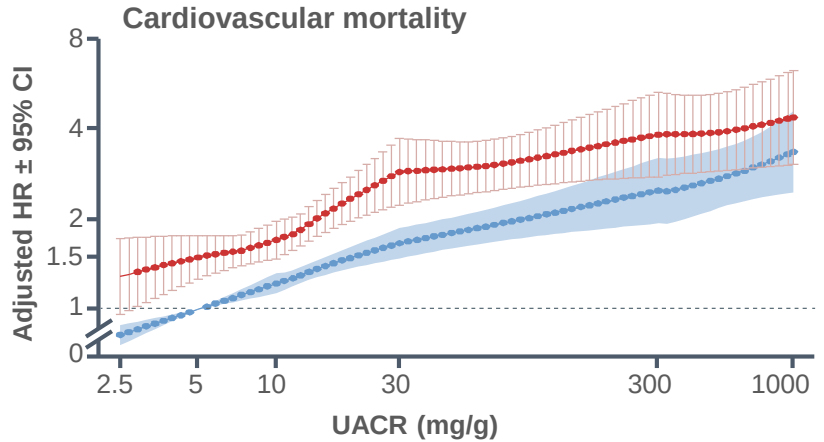
Incidence (%) of Cardiovascular events in the HOPE study in diabetic patients with and without microalbuminuria

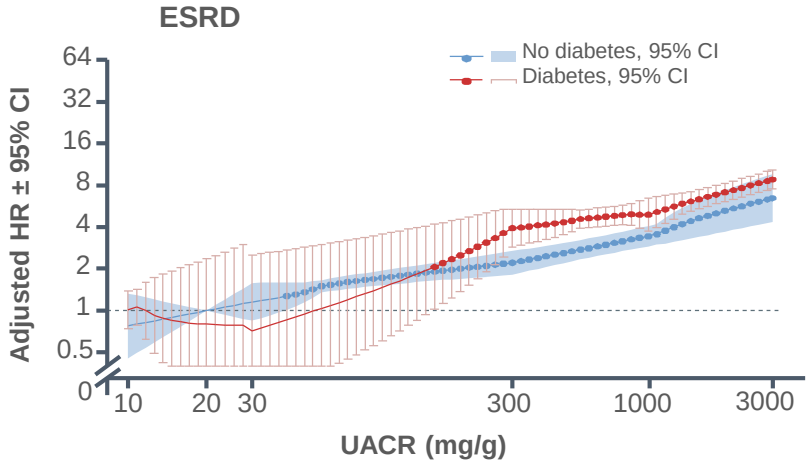


Increasing UACR is associated with mortality and ESRD in diabetes

1,024,977 participants (128,505 with diabetes)





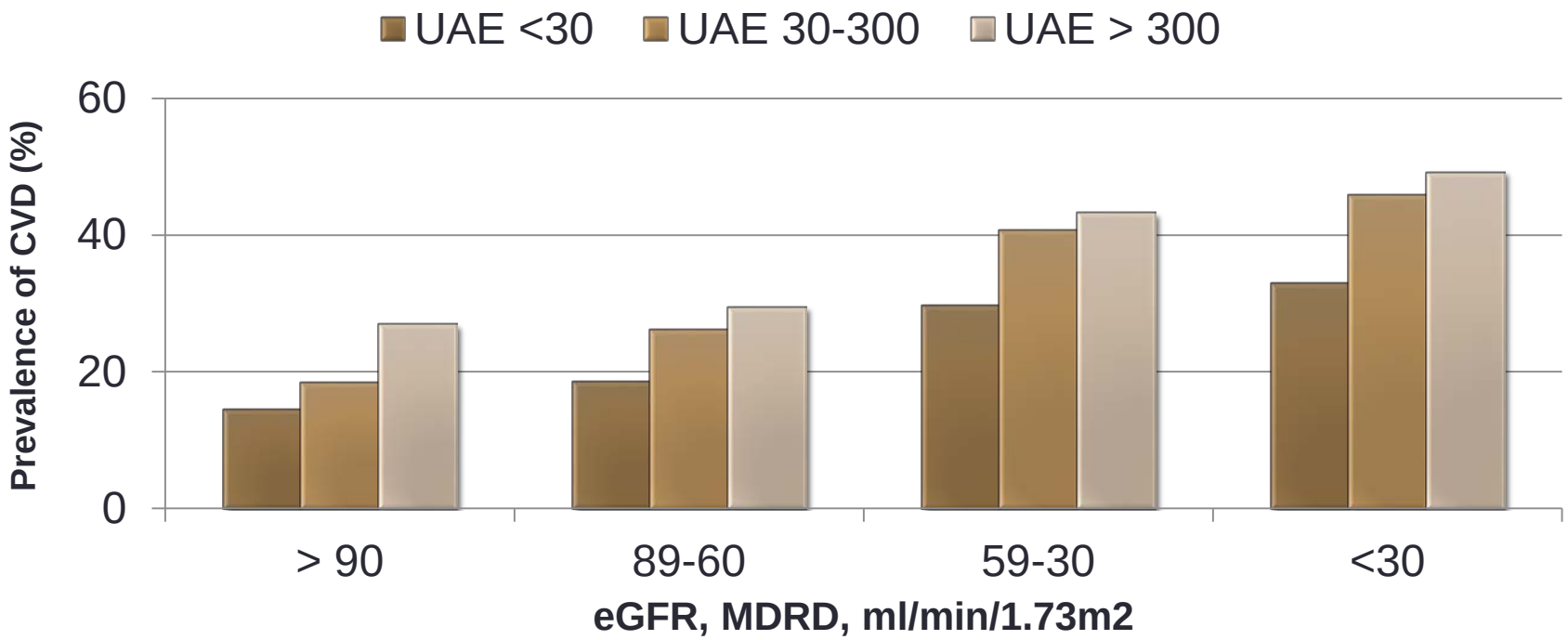


HRs adjusted for age, sex, race, smoking, history of cardiovascular disease, serum total cholesterol concentration, body-mass index and albuminuria

Includes data from participants with type 1 and type 2 diabetes

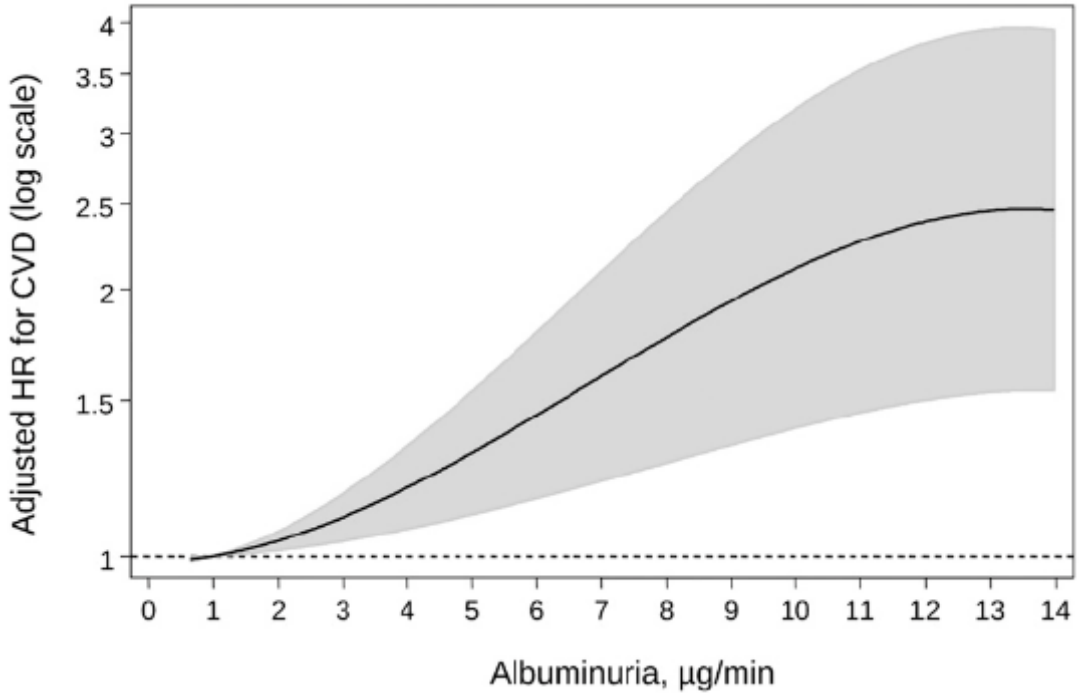
Nutr Metab Cardiovasc Dis. 2014 Aug;24(8):815-22.

The RIACE Study
CVD by eGFR and UAE

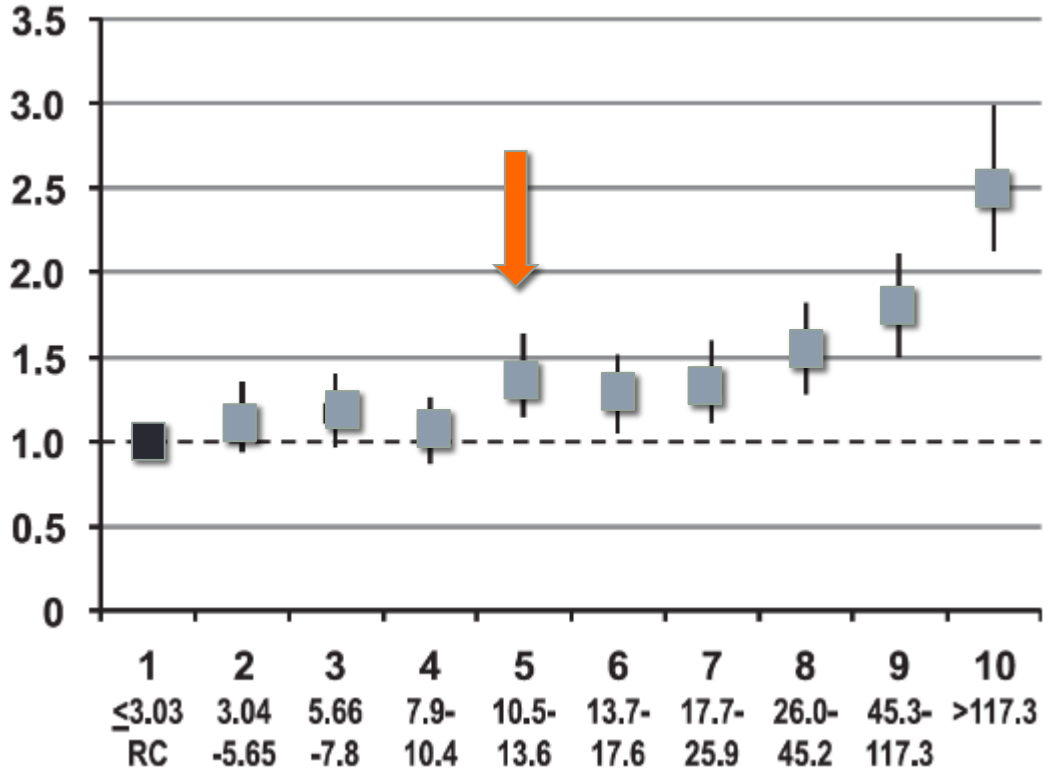


BENEDICT: Measurable urinary albumin predicts cardiovascular risk among 1208 normoalbuminuric patients with type 2 diabetes

Median follow-up 9.2 yrs



RIACE STUDY: Age- and sex-adjusted risk of major acute CVD events (OR [95% CI]) according to albuminuria deciles (mg/24 ore)

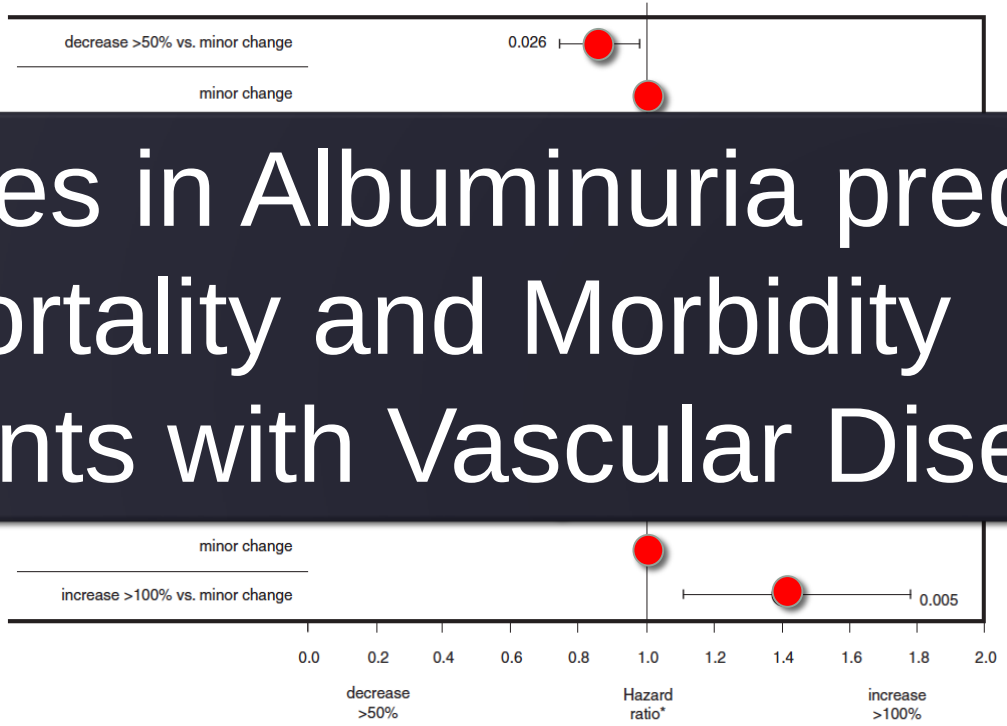


ONTARGET: Adjusted HR (95 CI %) of changes in UACR from baseline to 2-year visit for all-cause mortality, cardiovascular events and renal outcome after the 2-year visit with mean follow-up of 32 months in the whole study group (23480 pts)

All Cause mortality

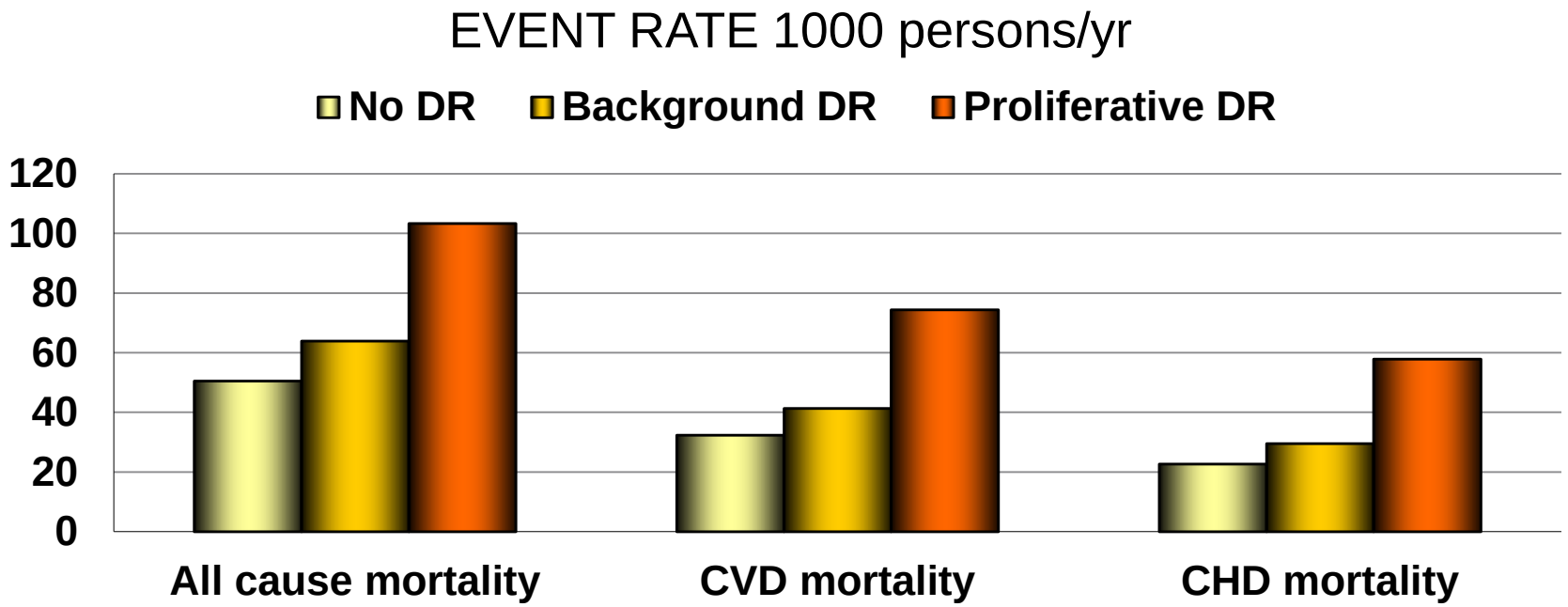
Car

Combined renal endpoints



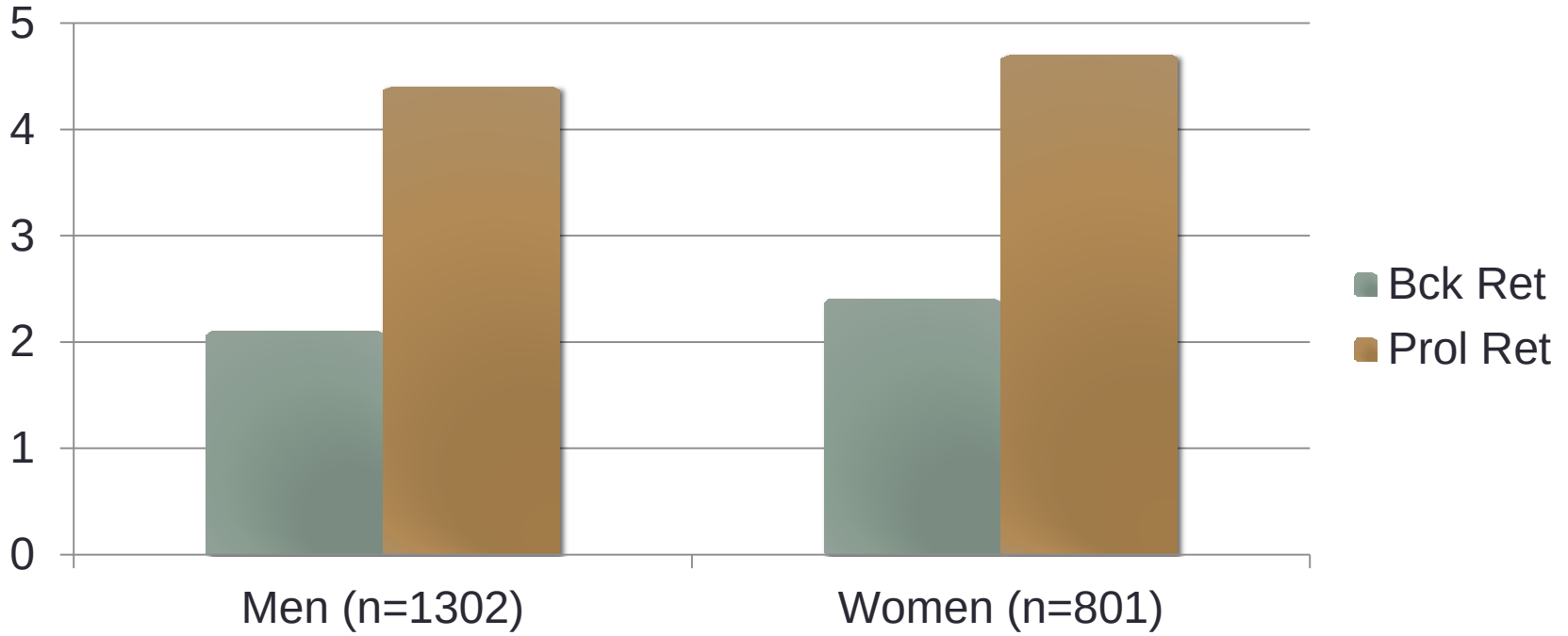
Changes in Albuminuria predict Mortality and Morbidity in patients with Vascular Disease

Retinopathy Predicts Cardiovascular Mortality in Type 2 Diabetic Men and Women

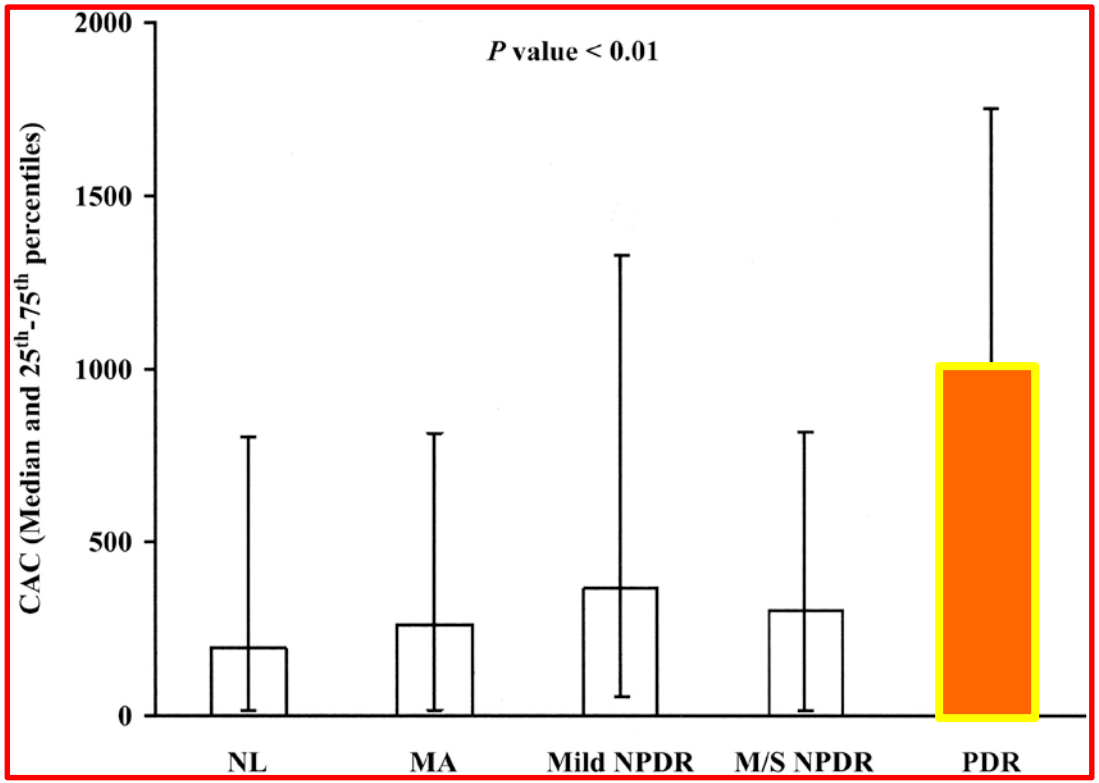


These associations were independent of current smoking, hypertension, total cholesterol, HDL cholesterol, glycemic control of diabetes, duration of diabetes, and proteinuria.

Hazard Ratio for incident cardiovascular disease events in Type 2 diabetic patients in relation to diabetic retinopathy status at baseline

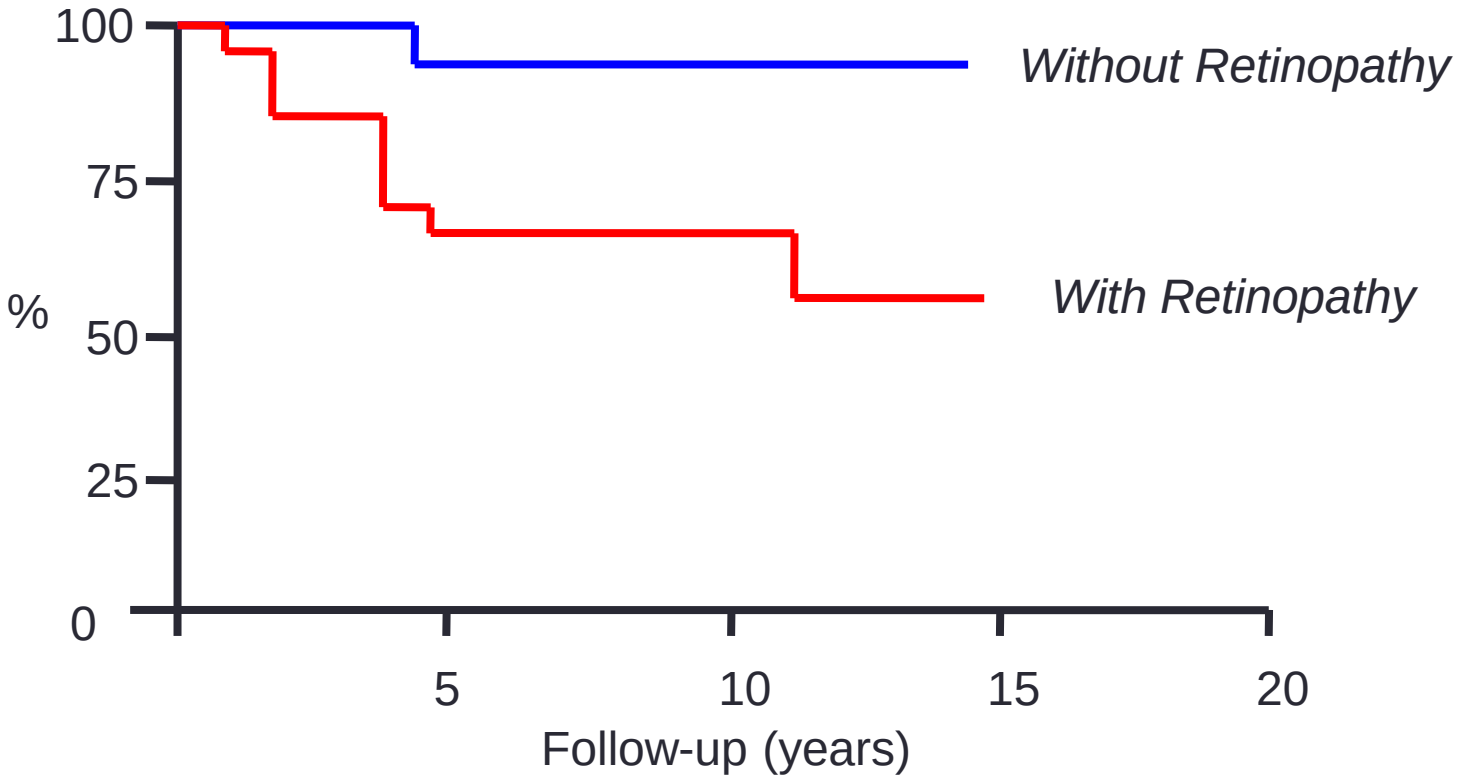


Proliferative Diabetic Retinopathy in Type 2 Diabetes is related to Coronary Artery Calcium in the VADT



R. Trevisan, Diabetes Care 2002; 25 : 2026-31.

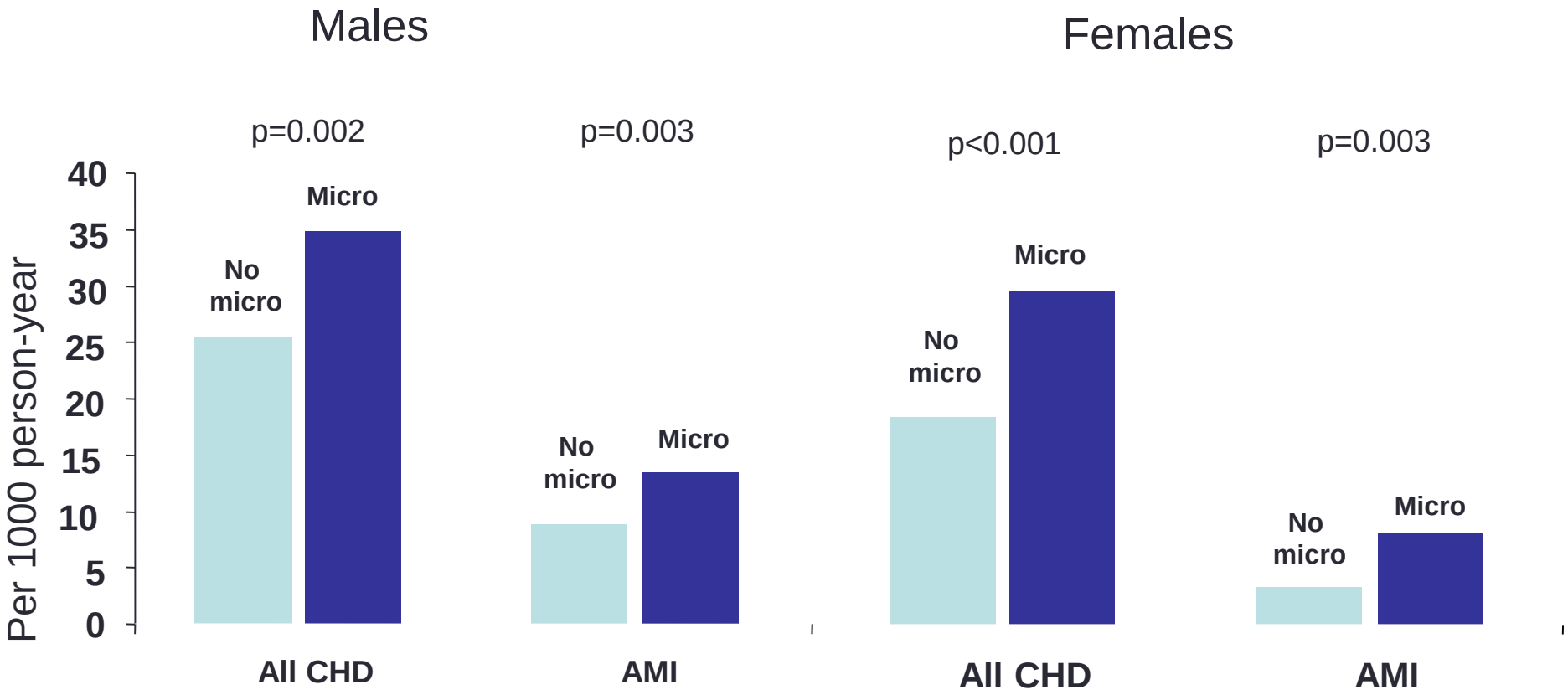
Survival curves of Type 2 diabetic patients with overt proteinuria In relation to retinopathy status



Association between retinal disease and risk of diabetes-related complications

	Risk with retinal disease vs no retinal disease
Cardiovascular disease	4.1-fold higher incidence (type 1 DM) 2.3-fold higher incidence (type 2 DM)
Heart failure	2.7-fold higher incicence (type 2 DM)
Macroalbuminuria	3.2-fold higher incidence (type 1 DM)
Chronic Kidney Disease	2.8-fold higher incidence (type 1 DM) 1.4-fold higher incidence (type 2 DM)
Neuropathy	1.8-fold higher incidence (type 2 DM)
Lower Limb amputations	25.0-fold higher incidence (type 1 DM) 5.0-fold higher incidence (type 2 DM)
Skeletal fractures	5.4-fold higher incidence (type 1 DM) 5.3-fold higher incidence (type 2 DM)
Non-alcoholic fatty liver disease	3.3-fold higher incidence (type 1 DM) 1.8-fold higher incidence (type 2 DM)

Incidence Rate of CHD Events: The role of microvascular complications

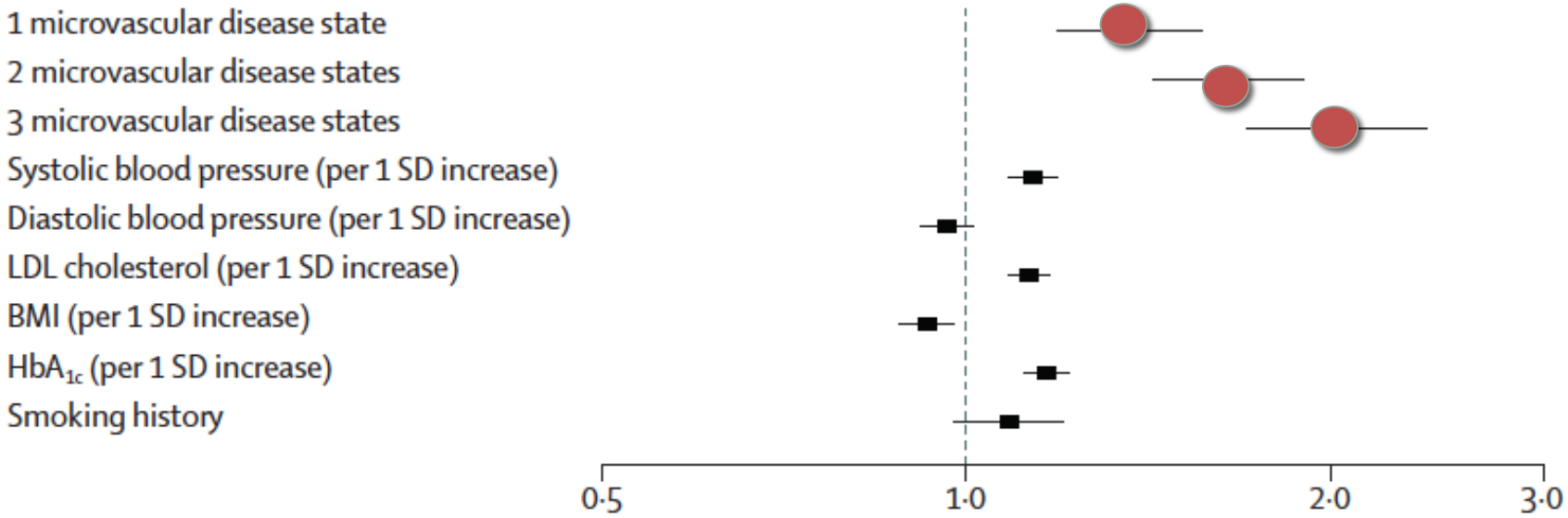


Microvascular disease and risk of cardiovascular events among individuals with type 2 diabetes: a population-level cohort study

Jack R W Brownrigg, Cian O Hughes, David Burleigh, Alan Karthikesalingam, Benjamin O Patterson, Peter J Holt, Matthew M Thompson, Simon de Lusignan, Kausik K Ray, Robert J Hinchliffe**

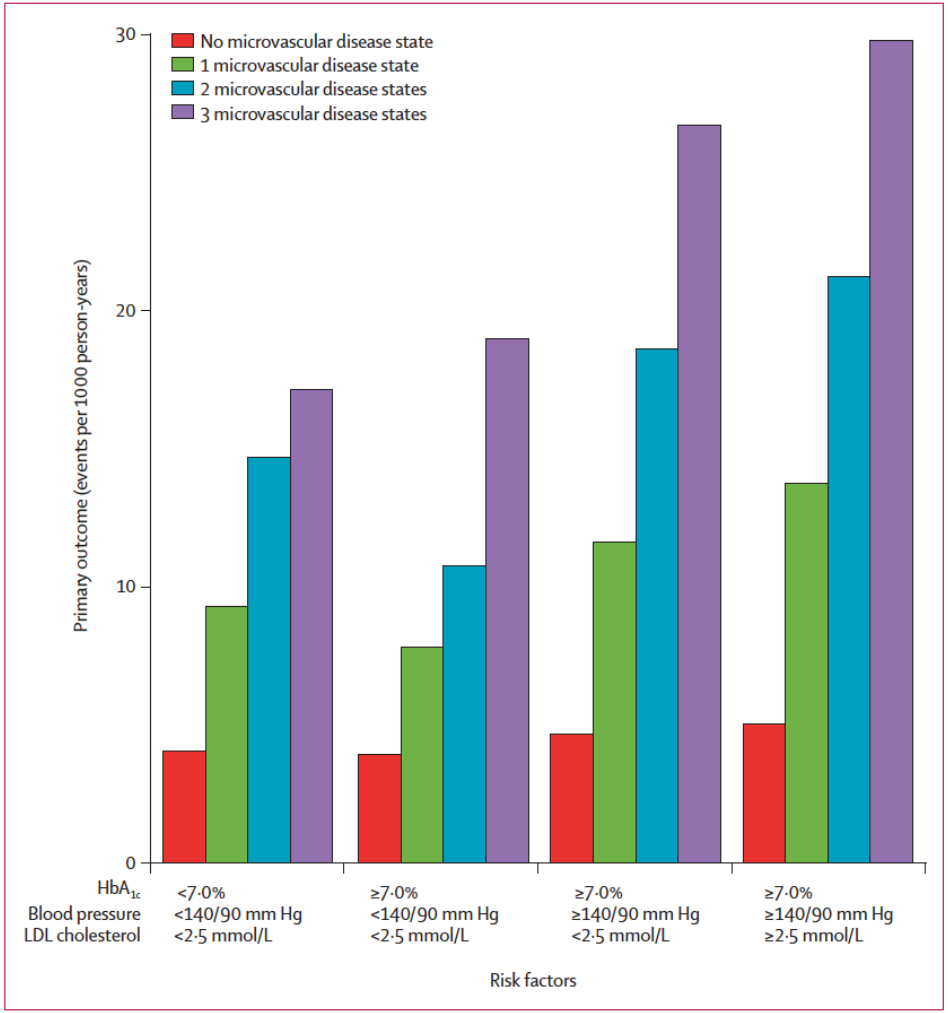
- *A population-based cohort of patients with type 2 diabetes from the UK Clinical Practice Research Datalink (n=49 027).*
- *Median follow-up of 5.5 years.*
- *2822 (5.8%) individuals experienced a primary outcome (a composite of cardiovascular death, non-fatal myocardial infarction, or non-fatal ischaemic stroke).*

Adjusted hazard ratio for the primary outcome (cardiovascular mortality, non-fatal myocardial infarction, or non-fatal ischaemic stroke) by cumulative burden of microvascular disease and per 1 SD difference in values for established risk factors*



1 SD of each established risk factor is:
blood pressure 13.5/8.4 mmHg ;
LDL cholesterol 0.9 mmol/L;
BMI 6.3 kg/m^2; HbA1c 1.3% .

Adjusted event rates for the primary outcome (cardiovascular mortality, non-fatal myocardial infarction, or non-fatal ischaemic stroke) by cumulative burden of microvascular disease and established risk factor goals



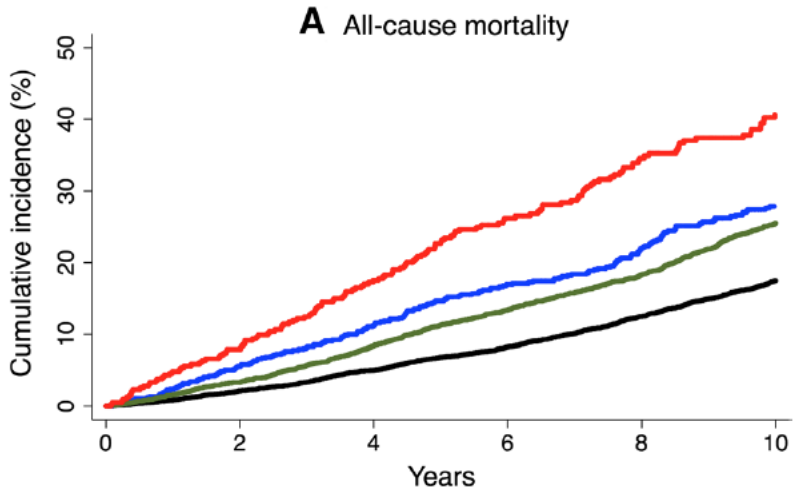
ADVANCE: Cumulative incidence of outcomes during follow-up according to status of microvascular and macrovascular disease at baseline.

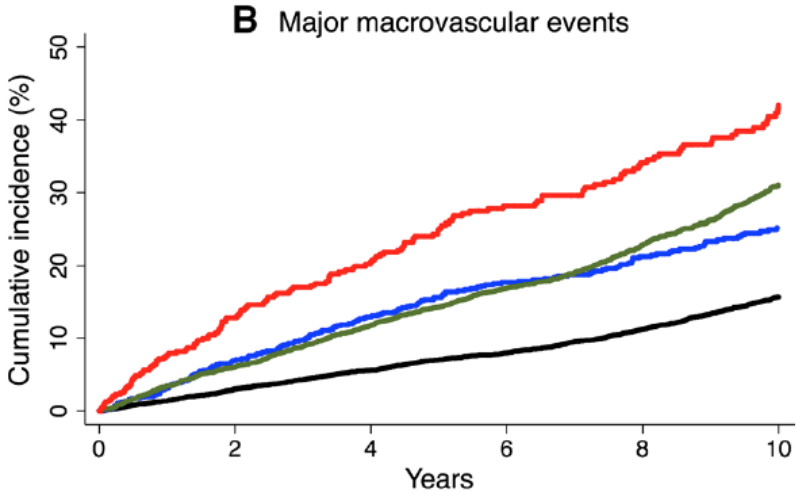
absence of both macrovascular and microvascular disease

presence of microvascular disease alone

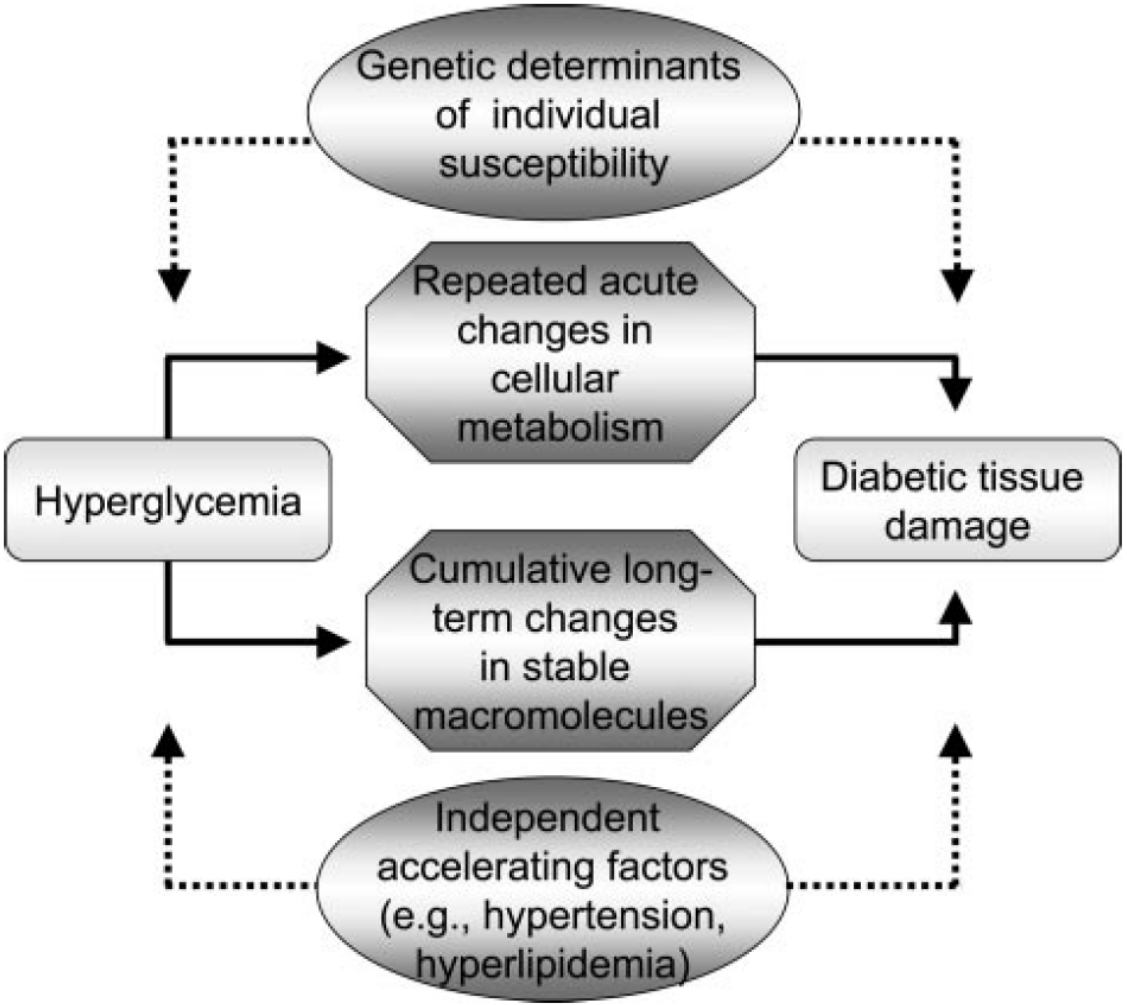
presence of macrovascular disease alone

presence of both macrovascular and microvascular disease





General features of hyperglycemia-induced tissue damage



La Microangiopatia Diabetica

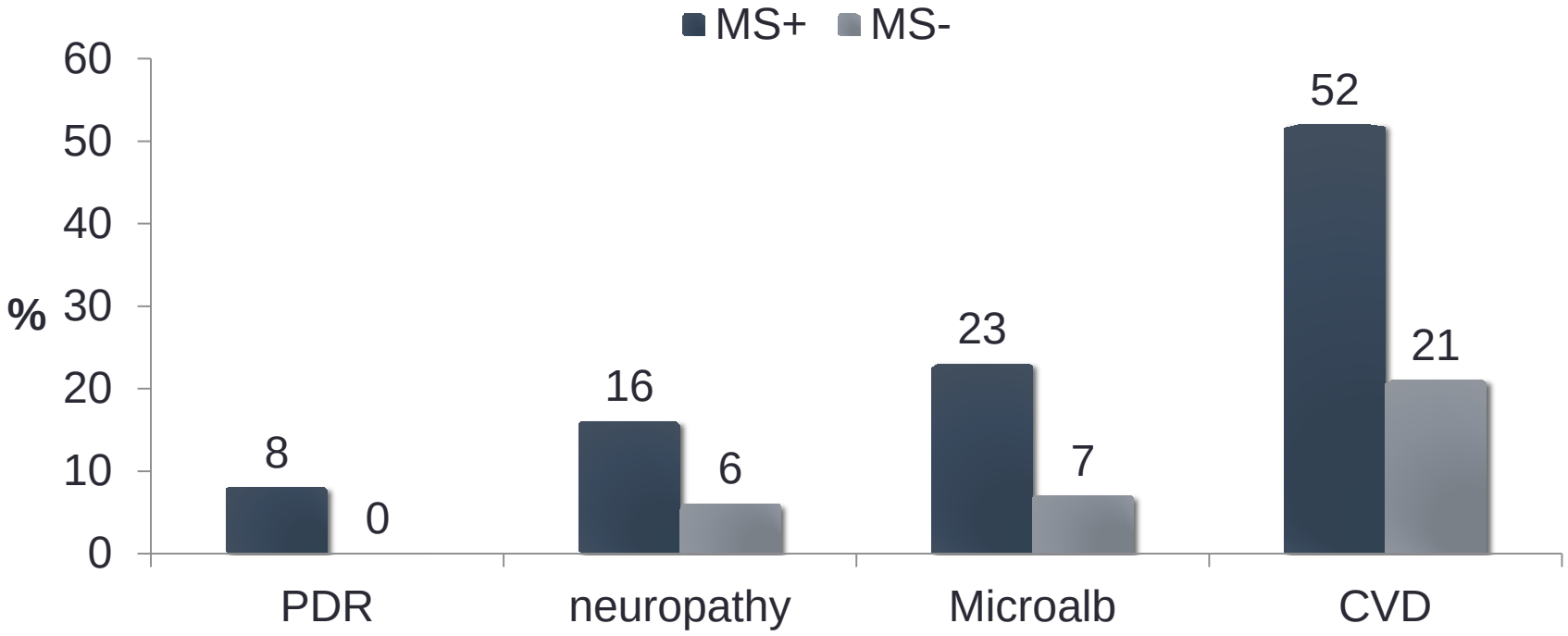
"Esposizione" al diabete e sue conseguenze

- The total glycemic exposure (A1c and duration of diabetes) explains only ~ 11% of the variation in retinopathy risk in the complete cohort of DCCT.
- Other factors explain the remaining 89% of the variation in risk among subjects independent of A1c.

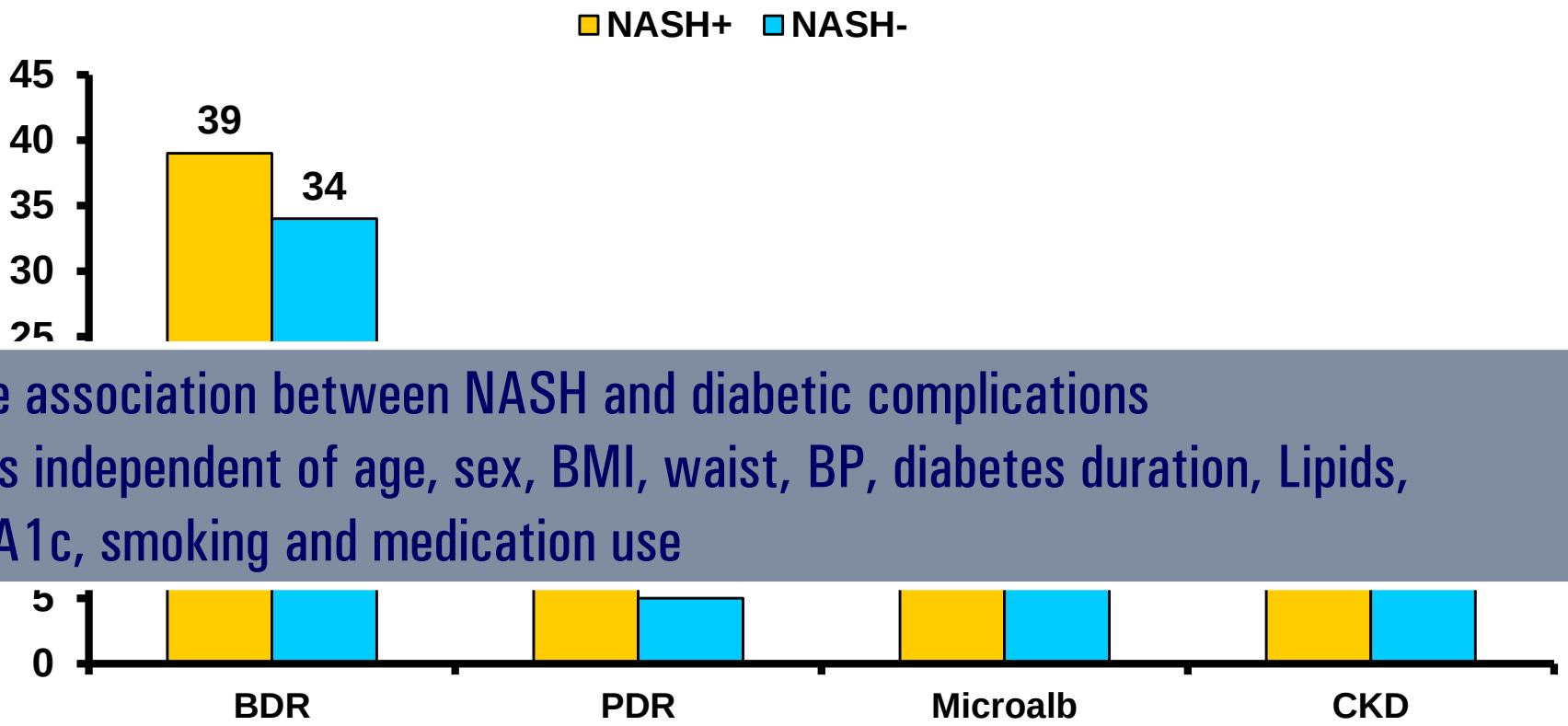
Fattori di rischio cardiovascolare = Fattori di rischio microangiopatico

- Iperglicemia
- Ipertensione
- Proteinuria
- Fumo
- Ridotta fuzione renale
- Dislipidemia
- Fattori genetici
- Disfunzione endoteliale
- Insulino-resistenza

The Metabolic Syndrome and Complications in Type 2 Diabetes

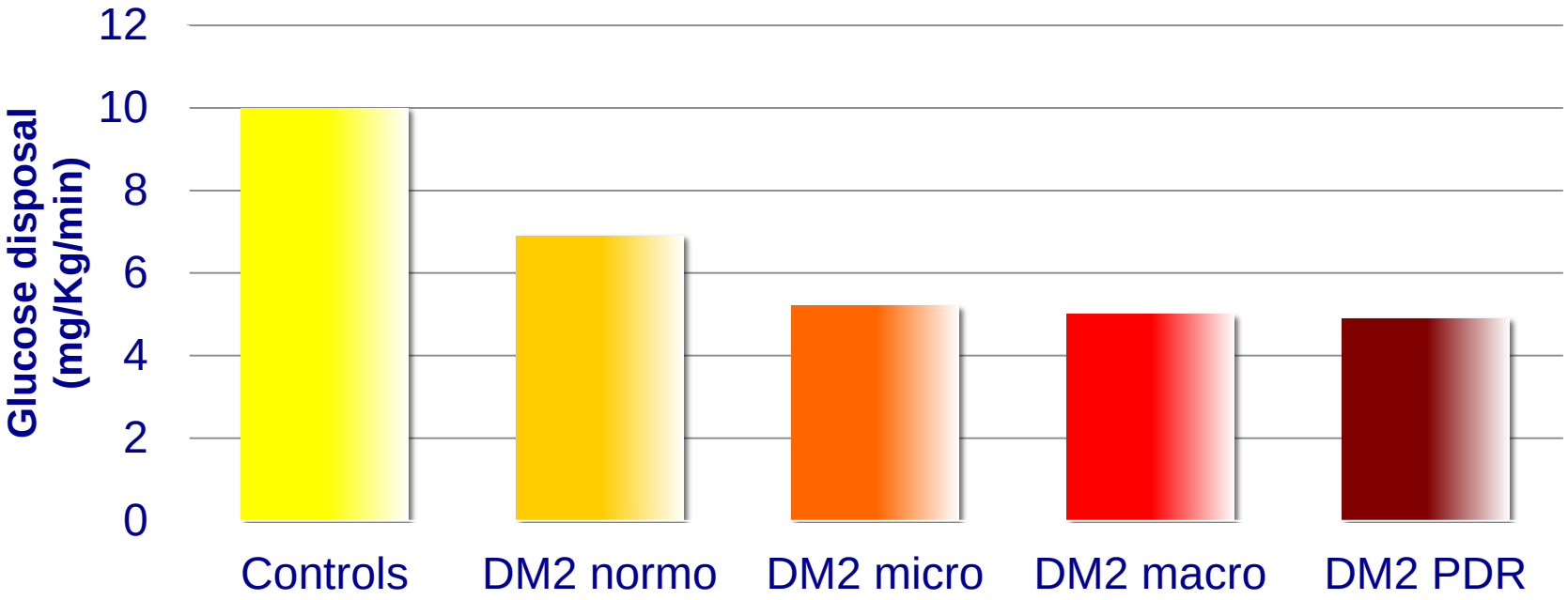


NASH and complications in Type 2 Diabetes

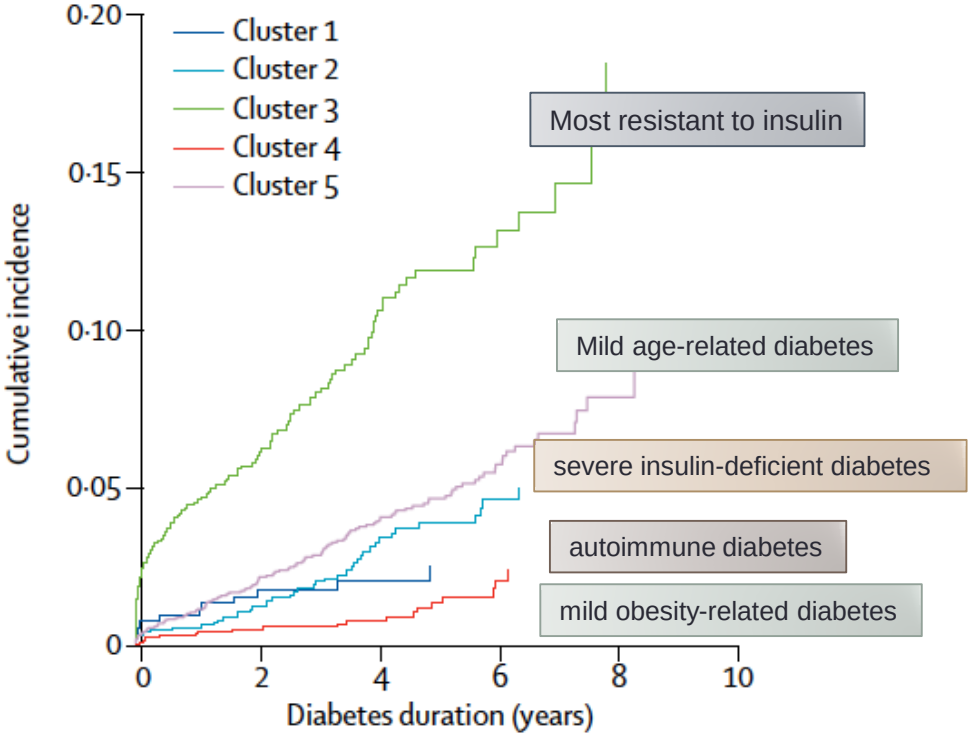


The association between NASH and diabetic complications was independent of age, sex, BMI, waist, BP, diabetes duration, Lipids, HbA1c, smoking and medication use

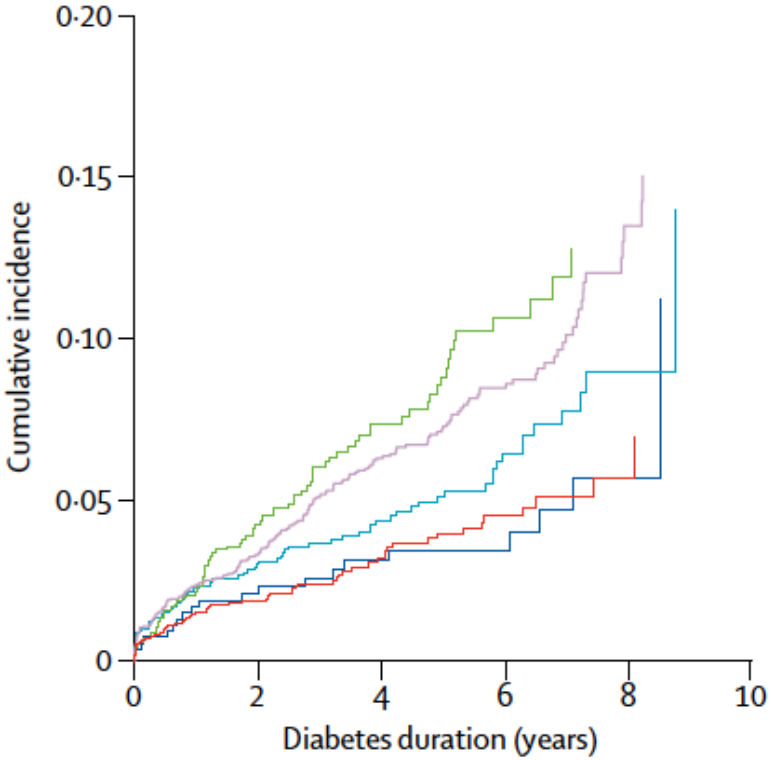
Type 2 diabetic patients with increased AER and PDR have a greater insulin resistance



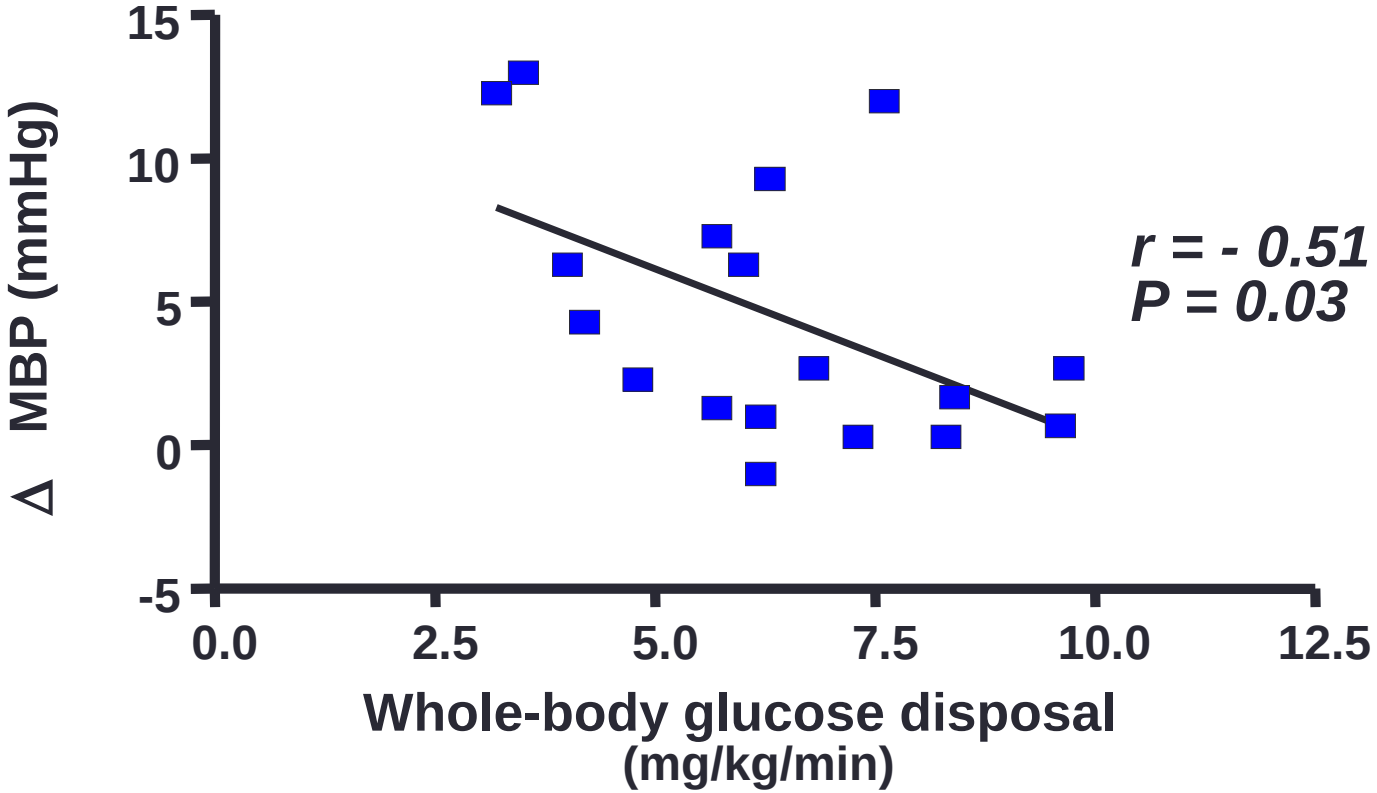
Time to chronic kidney disease (at least stage 3B) in the ANDIS cohort



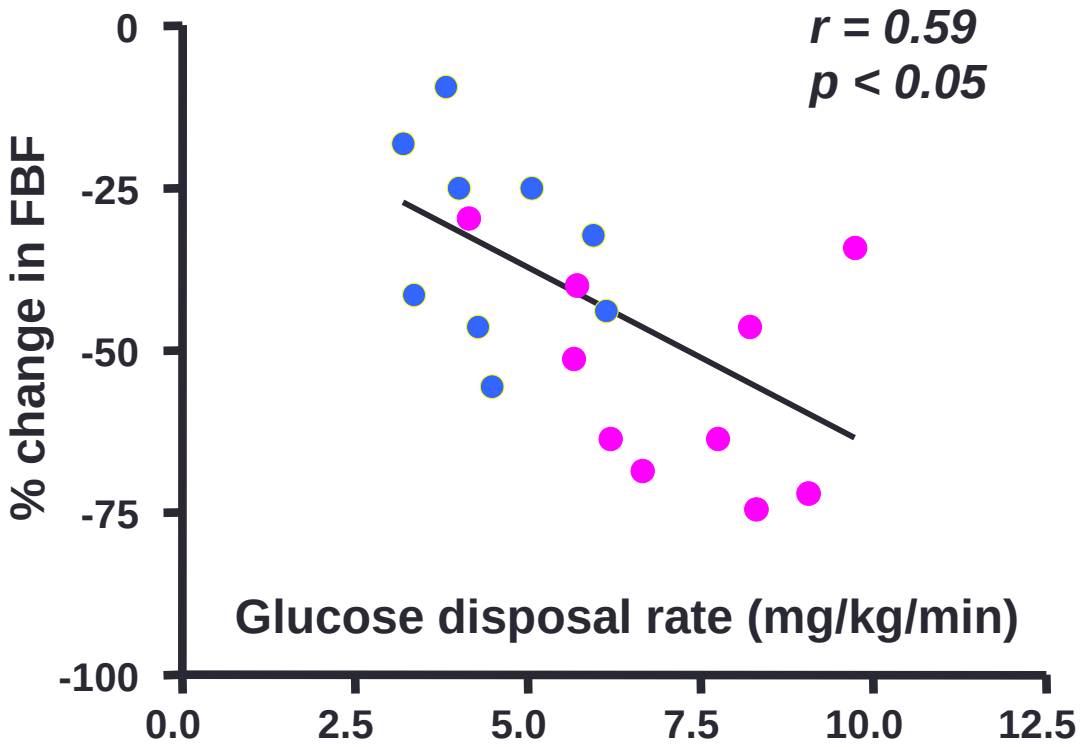
Time to coronary events in the ANDIS cohort



INSULIN RESISTANCE IS A MAJOR DETERMINANT OF BLOOD PRESSURE INCREASE AFTER A HIGH SODIUM DIET



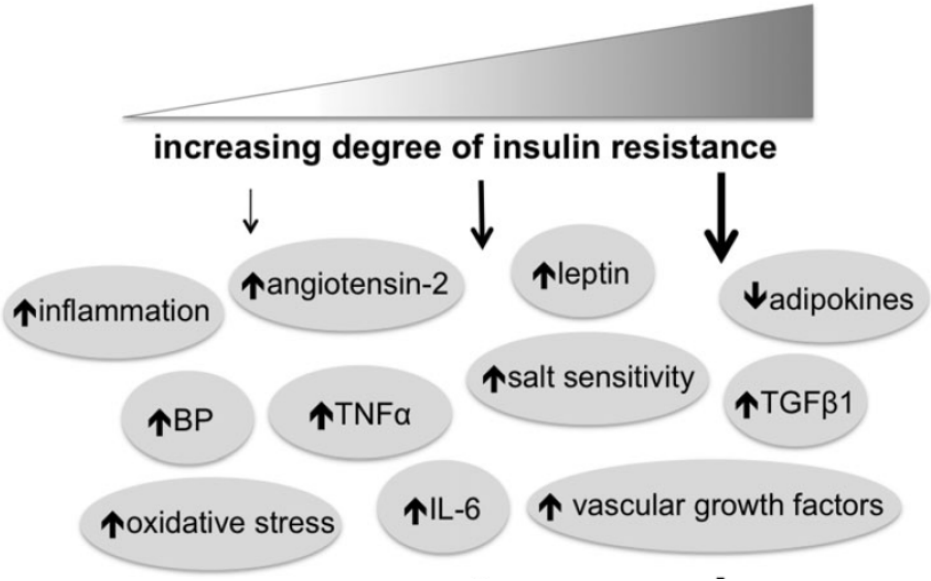
RELATIONSHIP BETWEEN TOTAL GLUCOSE DISPOSAL RATE AND PERCENT CHANGE IN FOREARM BLOOD FLOW AFTER L-NMMA INFUSION IN TYPE 2 DIABETIC PATIENTS



Insulin resistance is associated with a reduced NO availability

Insulin-resistance:
Mechanisms of Micro- and Macrovascular damage

- Abdominal adiposity
- ↓ Ch-HDL
- ↑ Trigliceride
- ↑ Blood Pressure
- Higher nocturnal BP
- Sodium sensitivity
- Endothelial dysfunction
- Reduced EPC
- Arterial stiffness
- Renal dysfunction
- High uric acid



CONCLUSIONS

- There is a cluster of micro/macroangioapthy in diabetes
- Microangiopathy predicts macroangiopathy
- Insulin resistance is associated with microangiopathy in both type 1 and type 2 diabetes.
- Insulin resistance (and endothelial dysfunction) is closely associated to microvascular disease and may represent the common risk factor/process underlying the association between microangiopathy and cardiovascular disease





Grazie per la vostra attenzione!