“Il paziente diabetico: una gestione complessa"

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Case: Sig. Esposito

65 y/o man referred to the Diabetes Clinic for care.

Past Medical History

- **T2DM × 14 yrs**, with an HbA1c ranging during the last 5 yrs between 7.7 and 8.0%
- **HTN × 16 yrs**, with a systolic BP ranging during the last 5 yrs between 135 and 150 mm Hg
- **Obesity for > 25 yrs**, BMI more or less stable during the 5 last yrs
- Background diabetic retinopathy known for ~5 yrs

Case: Sig. Esposito

Current Clinical and Labs Features

- **BP = 140/88 mm Hg** *on ACE-inhibitor + BB + CCB*
- **BMI = 34.6 kg/m^2**
- **HbA1c = 8.1%**
- **Lipids: WNL**
- **eGFR = 58 mL/min, ACR = 925 mg/g creatinine**

Case: Sig. Esposito

Current Medications

- **Metformin 850 mg BID, glimepiride 2 mg QD**
- **4 antihypertensive agents for BP control**

“What should we consider for the treatment choice of this patient?”

- T2DM duration
- Glycemic control
- Age
- Gender
- Concomitant diseases and treatments
  - Potential drug-drug interaction
  - Hepatic and renal function
  - CV risk (risk factors like hypertension, hyperlipidemia, smoke, CHD,…)

Hepatic function

- In Italy, the frequency of HCV infection in the general population is variable (from 3 to 15%, depending on geographical areas)

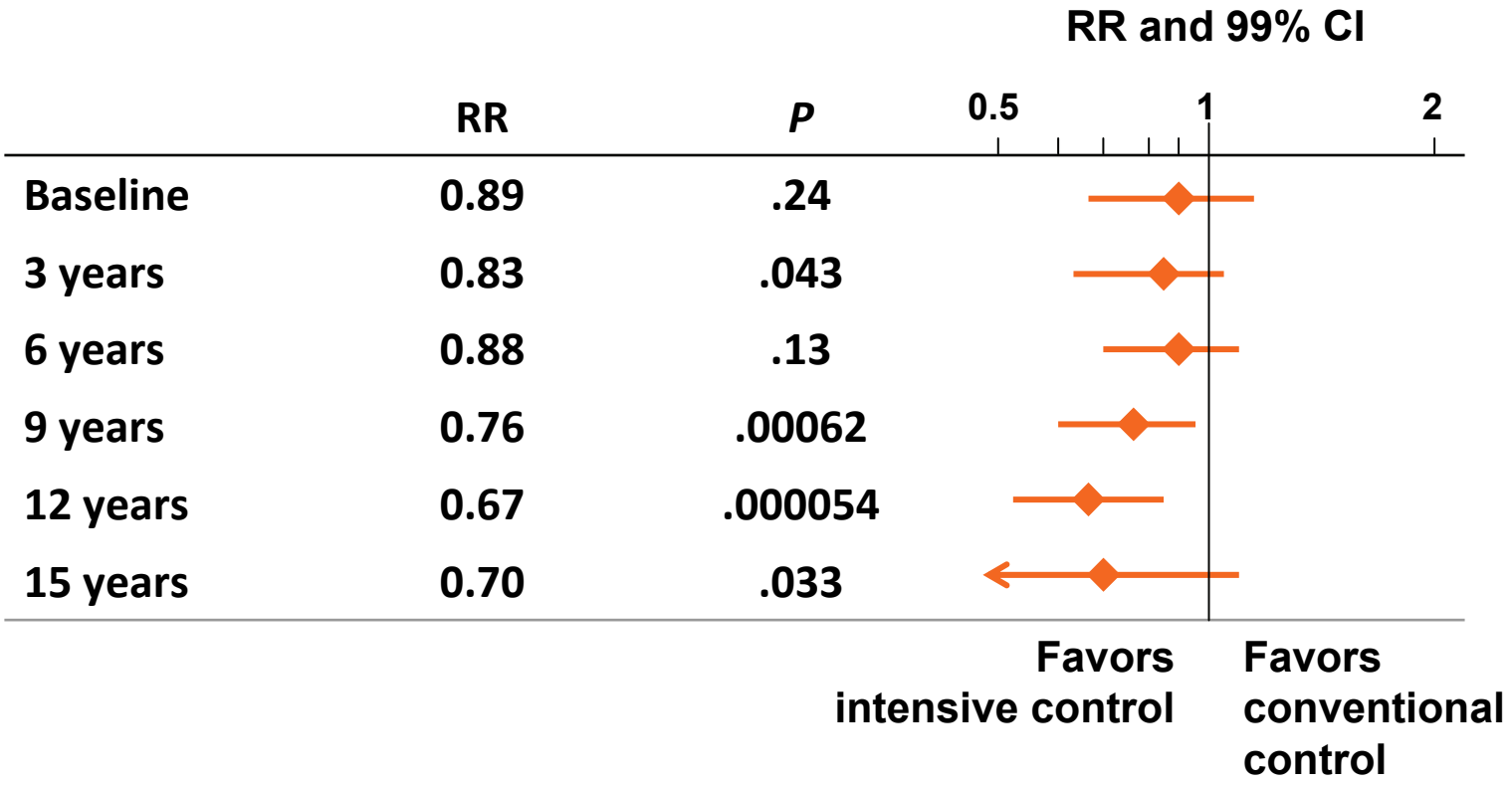
- Elevated liver enzymes may be clinically disregarded and considered features of nonalcoholic fatty liver disease (NAFLD), not signs of a possible underlying viral infection.

Soverini et al Acta Diabetol (2011) 48:337–343

“What evidence do we have for the benefit of glycemic control in a diabetes patient like this, with moderate CKD?”

- Strong evidence exists for the benefit of glycemic control in diabetes patients with **relatively preserved kidney function (reduced microvascular outcomes, including new-onset albuminuria)**

UKPDS: Intensive Glucose Control Prevented Microalbuminuria* Over Time



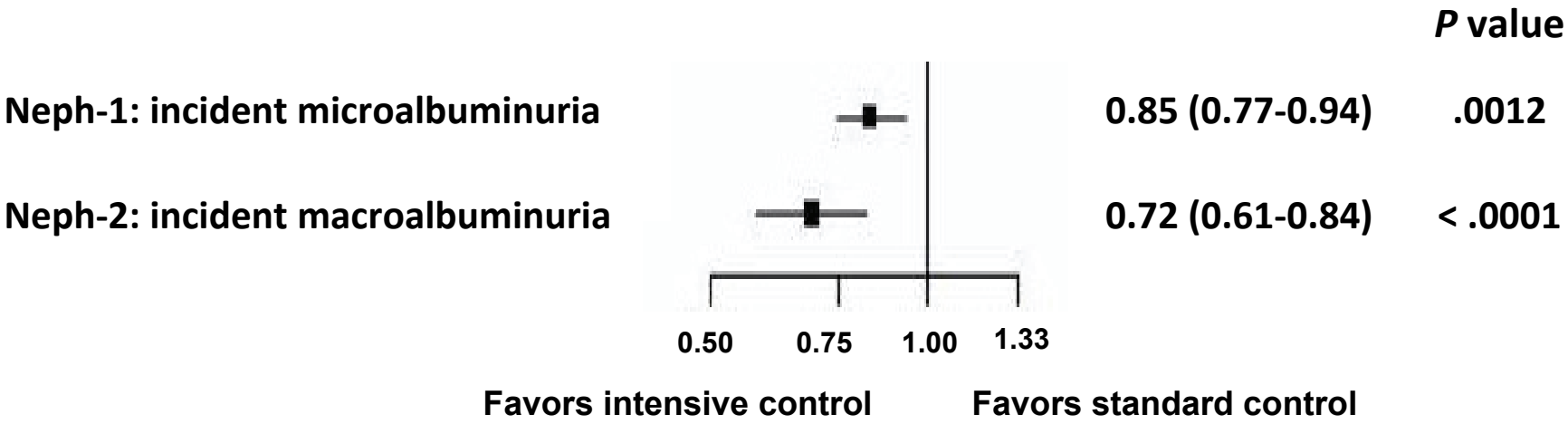
***Microalbuminuria defined as urine albumin > 50 mg/L**

CI = confidence interval; RR = relative risk

Adapted from UKPDS Group 33. *Lancet*. 1998;352(9131):837-853.

Intensive Glycemic Treatment Reduces Albuminuria: Results of the ACCORD Study

- **In 10,251 patients with T2DM, intensive glycemic treatment (HbA1c < 6.0%) reduced the risk for microalbuminuria by 15% and the risk for macroalbuminuria by 28% compared with standard glycemic therapy (HbA1c 7.0%-7.9%)**

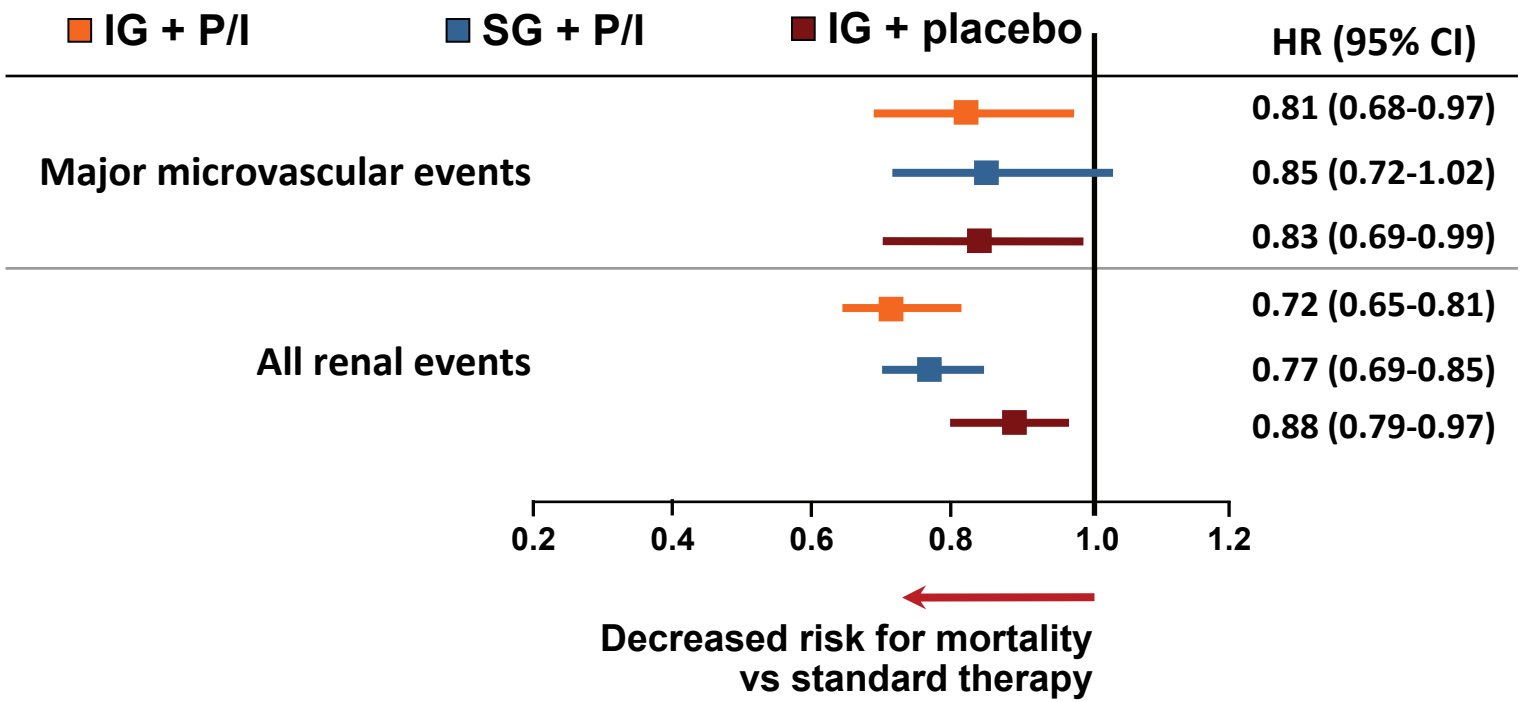


Intensive glucose control reduced albuminuria

ACCORD = Action to Control Cardiovascular Risk in Diabetes

Adapted from Ismail-Beigi F, et al. *Lancet*. 2010;376:419-430.

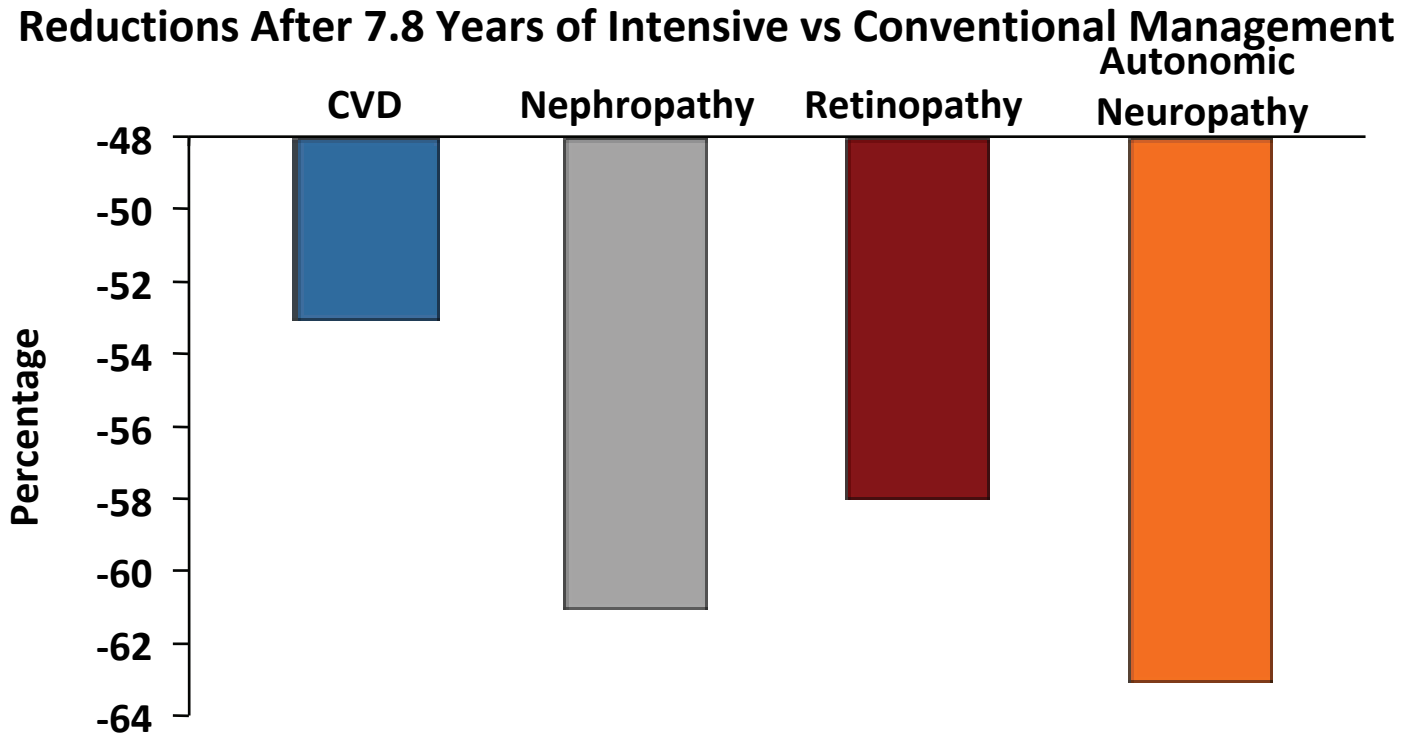
ADVANCE: Greatest Benefits Achieved with Combined Intensive Glucose Control and BP Reduction



BP = blood pressure; IG = intensive glucose control; P/I = BP treatment with perindopril/indapamide;
SG = standard glucose control

Adapted from Zoungas S, et al. *Diabetes Care*. 2009;32(11):2068-2074.

Steno-2: Intensive, Multifactorial Management* Reduces the Risk for Microvascular Complications in T2DM Patients



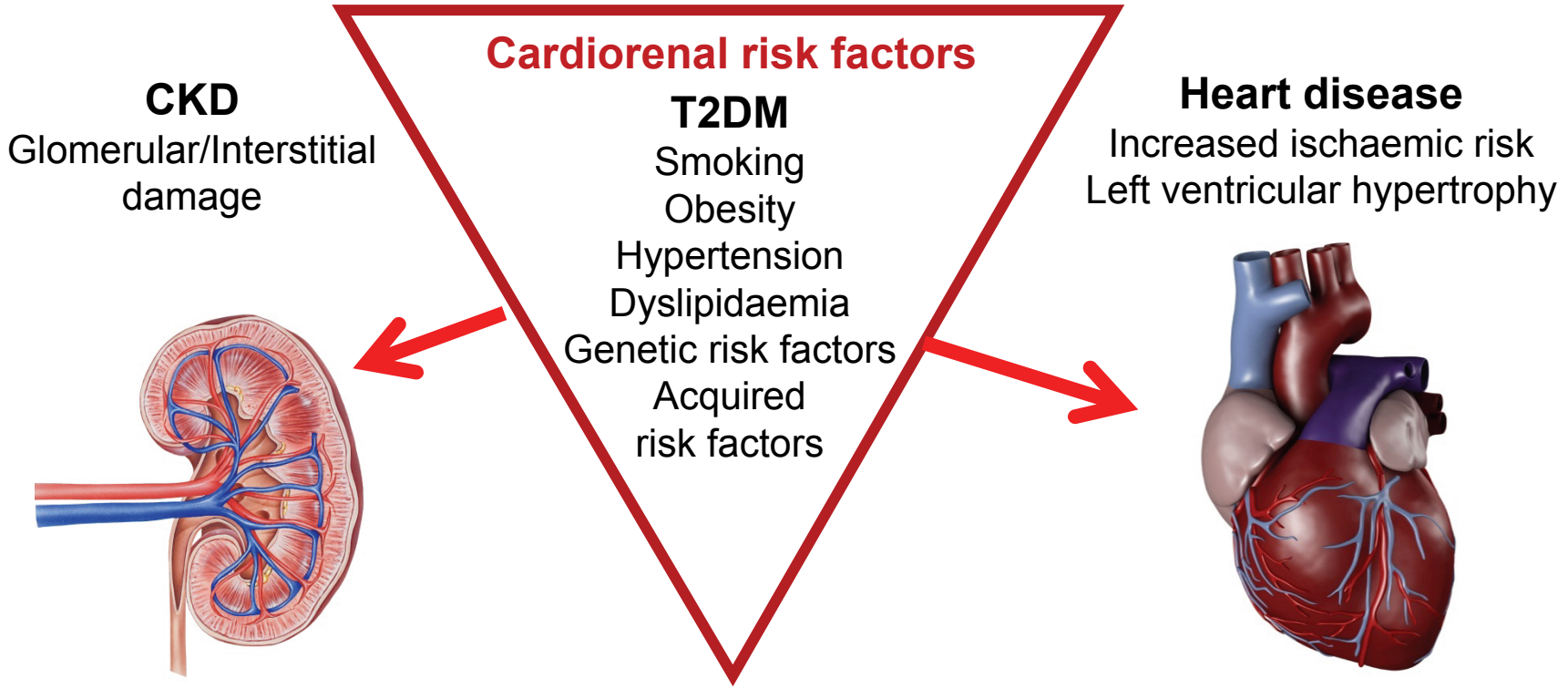
***Intensive, multifactorial management included CV risk factor reduction with behavior modification and pharmacologic therapy that targeted hyperglycemia, hypertension, dyslipidemia, and microalbuminuria along with secondary prevention of CVD with aspirin.**

Adapted from Gaede P, et al. *N Engl J Med.* 2003;348(5):383-393.

- Adequate control of hyperglycemia remains important
  - Renal outcomes are clearly linked to CV outcomes

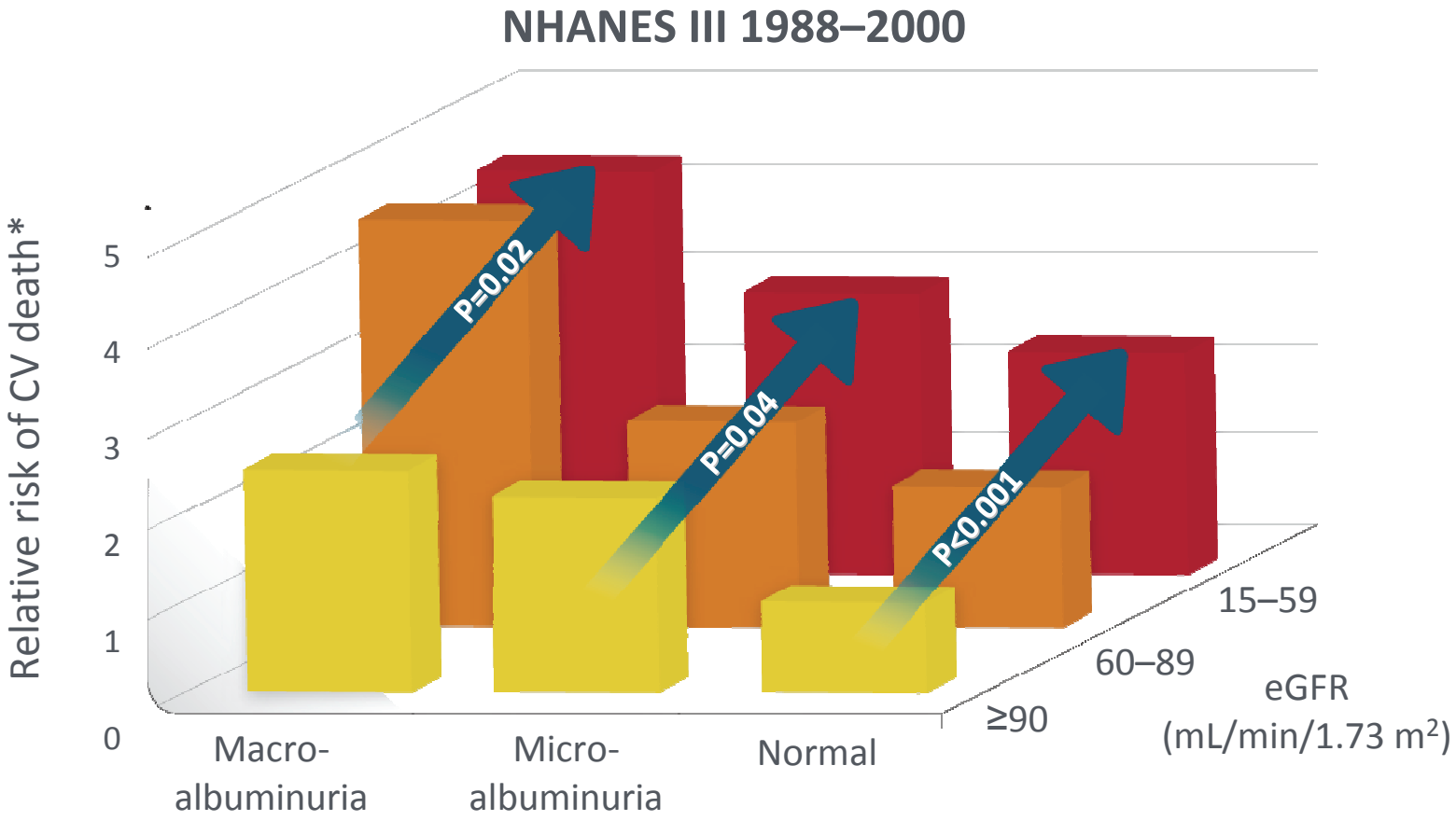
The coexistence of T2D and CKD markedly elevates risk of cardiovascular disease

A Close Relationship Exists Between Cardiac and Renal Pathophysiology in T2DM



Afghahi H, *et al. Nephrol Dial Transplant*. 2011;26:1236-1243;
Ronco C, *et al. J Am Coll Cardiol*. 2008;52:1527-1539;

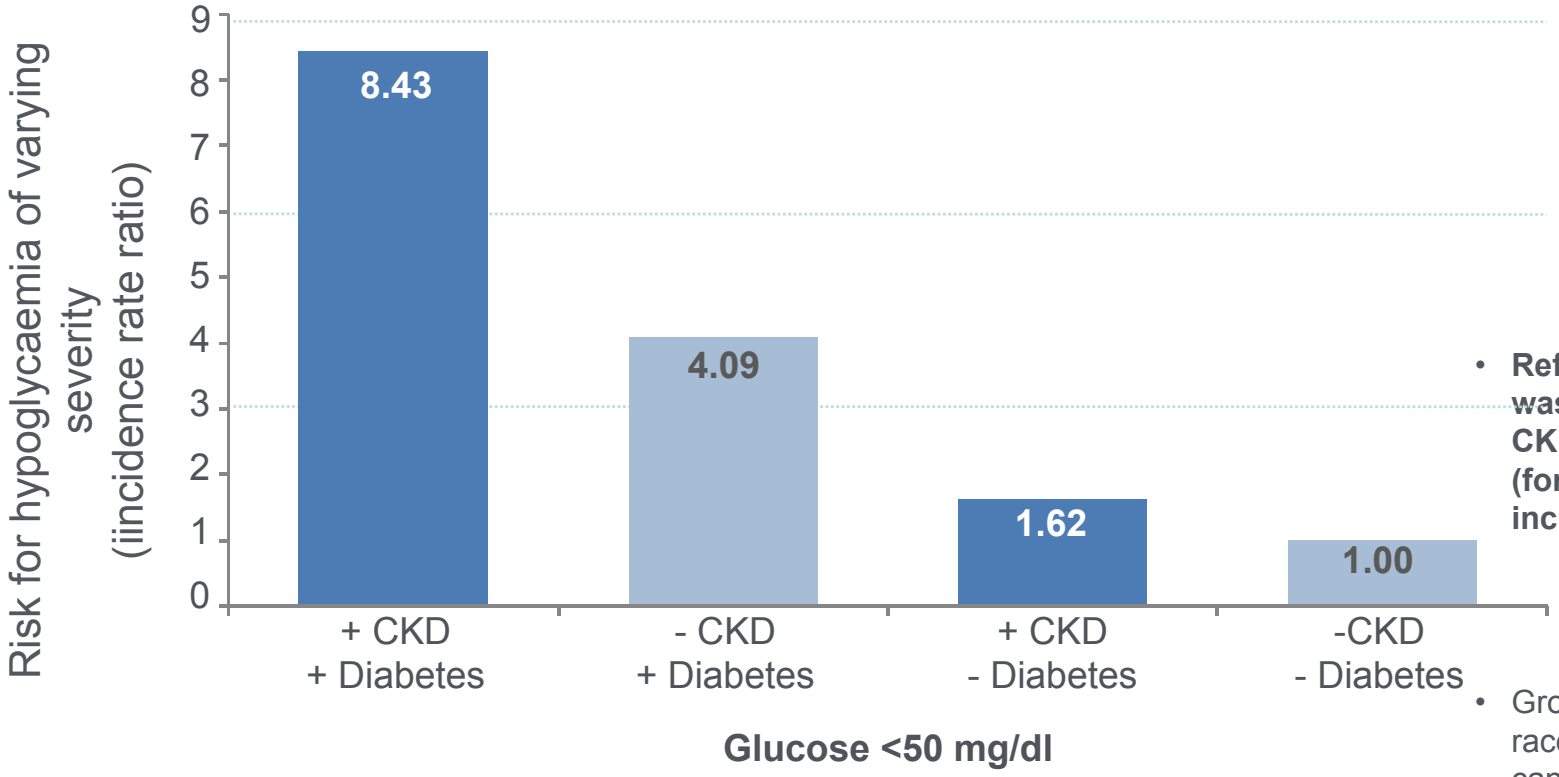
Cardiovascular (CV) mortality risk increases with declining renal function[1]



*Adjusted for age, sex, race/ethnicity, previous CV disease, blood pressure category, use of antihypertensive medication, diabetes mellitus, smoking status, body mass index, physical activity level, low density lipoprotein and high density lipoprotein cholesterol, log triglyceride level, and C-reactive protein category.

1. Astor BC, *et al*. *Am J Epidemiol* 2008;167:1226–34.

Declining renal function also increases risk of hypoglycaemia of varying severity



- **Reference group was adults without CKD or diabetes (for whom the incident ratio =1)**
- Groups adjusted for race, gender, age, cancer, diabetes and CV disease (all rate ratios p<0.0001)

Adapted from 1. Moen MF, et al. *Clin J Am Soc Nephrol*. 2009;4(6):1121–1127

What are the treatment consequences?

- Patients with CKD are more likely to have poor glucose control and have an increased risk for hypoglycemia[1]
- Most antidiabetic medications are either contraindicated or have critical side-effects in renal patients with type 2 diabetes patients
  - Fluid retention, edema, and hypoglycemia are the most common[1,2]
- There is an important unmet medical need for a safe and efficacious oral antidiabetic treatment with:
  - No need for dose adjustment in any degree of renal impairment
  - No increased risk of hypoglycemia
  - No associated weight gain, edema or fluid retention

1. National Kidney Foundation. *Am J Kidney Dis* 2007;49(Suppl 2):S62–S73.
2. Zelmanovitz T, *et al*. *Diabetol Metab Syndr* 2009;1:10.

Consider CKD when selecting an anti-diabetes agent

- Clinicians should be aware of the impact of CKD on choice of therapy:
  - Some agents are contraindicated
  - Some agents require dosage adjustment
- Renal function should be assessed before prescribing any new anti-diabetes agent
- Renal function should be routinely monitored for changes that may affect treatment

1. National Kidney Foundation. *Am J Kidney Dis*. 2007;49(suppl 2):S1-S179.

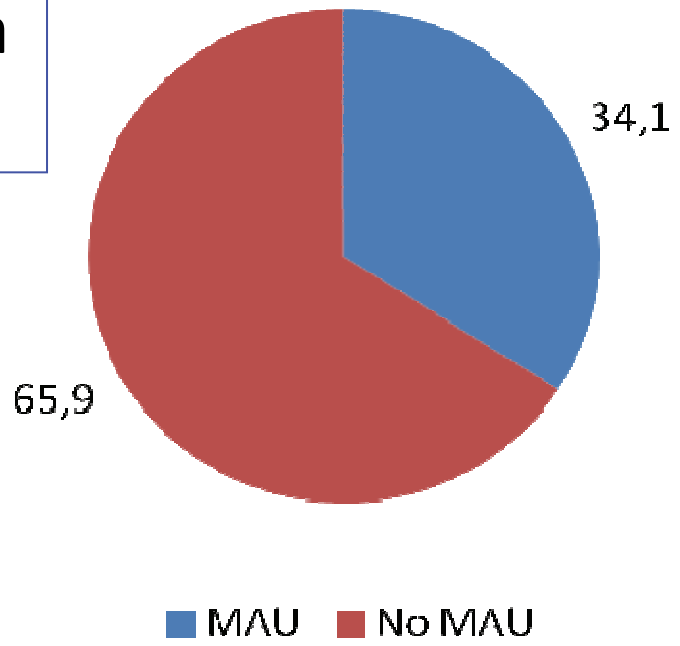
Il dato sulla microalbuminuria era valutabile per 154802 soggetti.

Il dato sul GFR era disponibile per 286749 soggetti.

Il dato sulla microalbuminuria e quello sul GFR erano simultaneamente registrati per 120790 pazienti.

Distribuzione della popolazione in accordo alla presenza di micro/macroalbuminuria (MAU) (%)

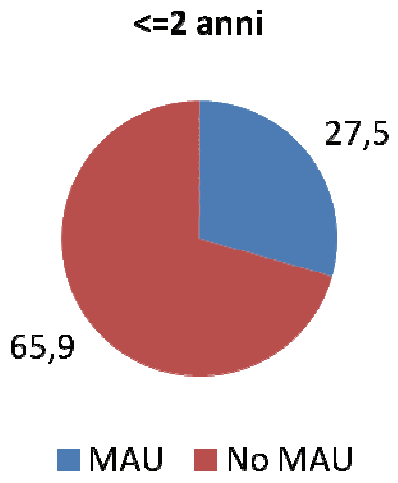
1/3 dei pazienti mostra la presenza di MAU

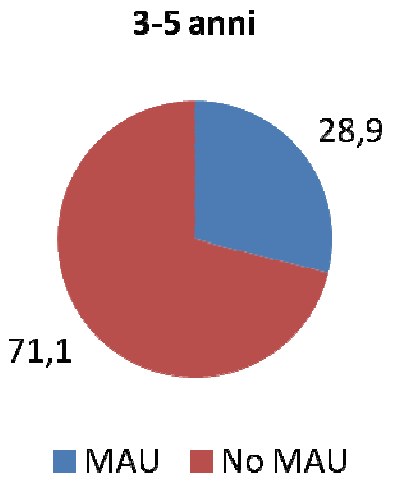


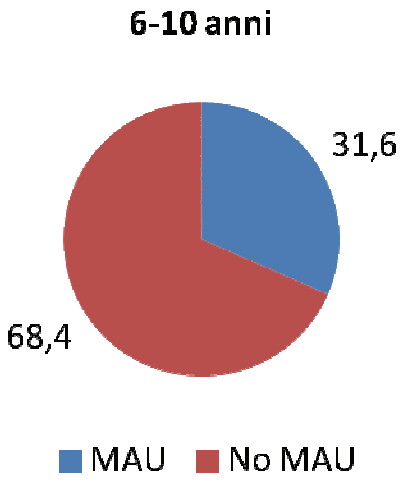
Questo dato di prevalenza, che risulta maggiore rispetto a quelli derivanti da studi epidemiologici, potrebbe riflettere l'attitudine a riportare con maggiore attenzione il dato in cartella in presenza di risultati patologici.

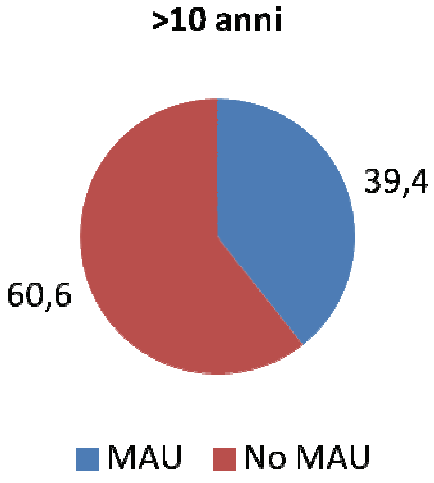
Distribuzione della popolazione divisa per classi di durata del diabete in accordo alla presenza di MAU (%)

Pazienti **con diagnosi recente: > 25% presenta MAU**.



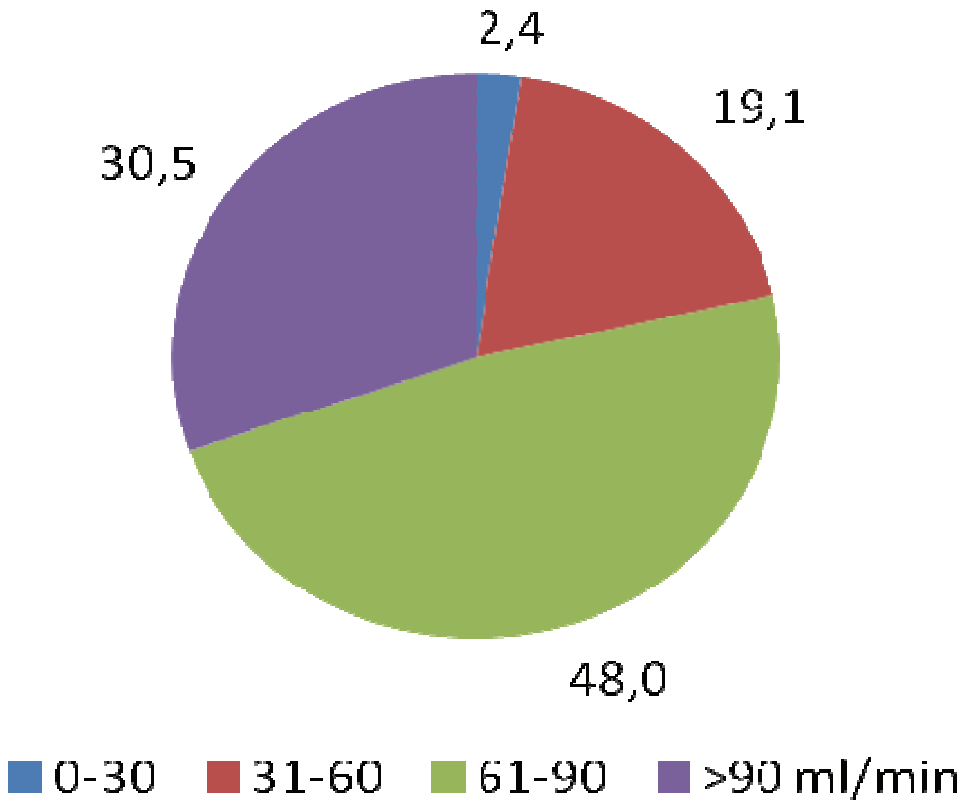






La prevalenza di MAU cresce con la durata del diabete, fino a interessare quasi il **40% dei pazienti con durata superiore ai 10 anni**.

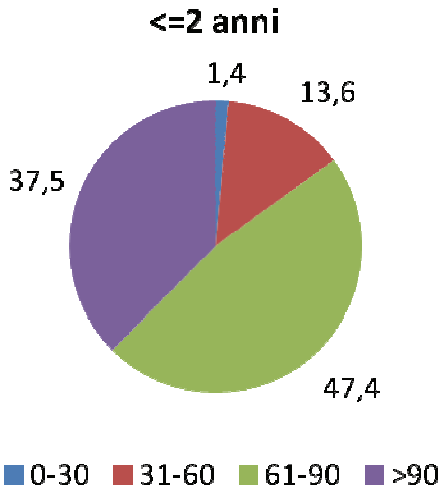
Distribuzione della popolazione per classi di filtrato glomerulare (%)

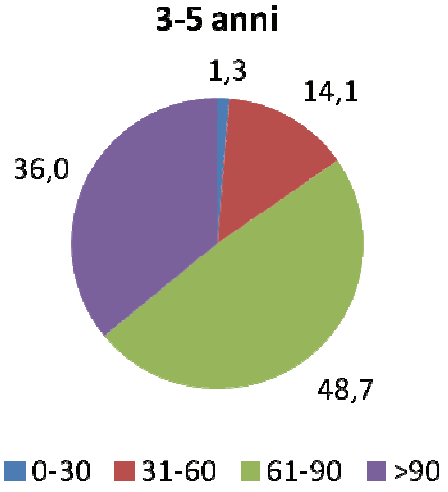


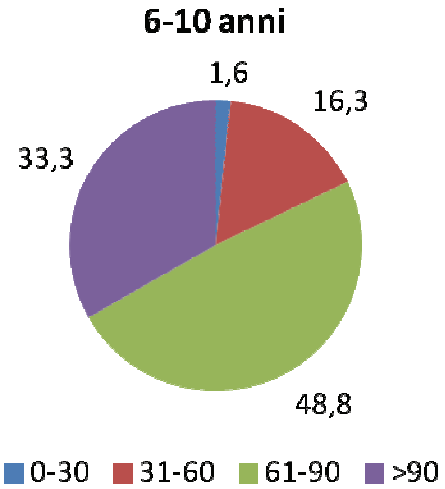
Circa un paziente si cinque presenta una significativa riduzione del filtrato glomerulare.

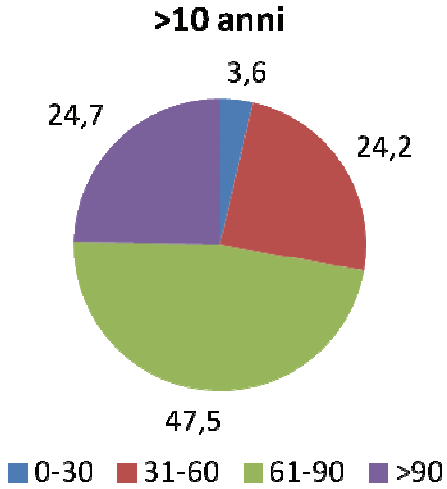
Distribuzione della popolazione divisa per classi di durata del diabete e per classi di filtrato glomerulare (%)

Pazienti con diagnosi recente: riduzione significativa del GFR risulta nel **15% dei casi**.



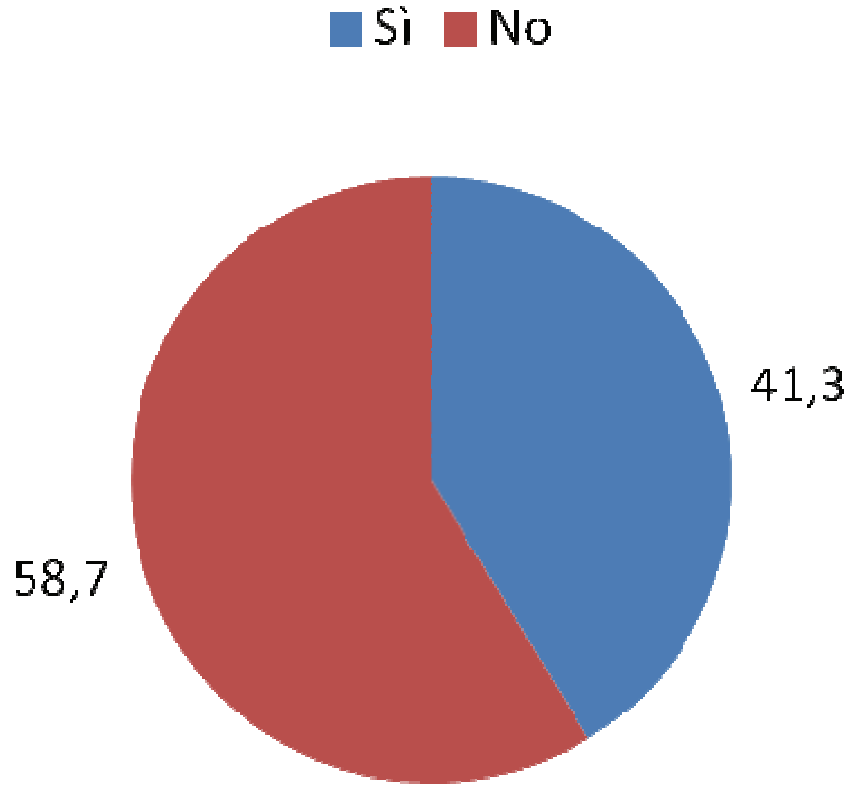






La percentuale aumenta con la durata del diabete, fino a raggiungere il **27.8%** nei soggetti con **durata del diabete >10 anni**.

Soggetti monitorati per MAU (%)



Complessivamente, il monitoraggio della MAU è risultato eseguito nell'anno indice (2009) nel **41.3% dei pazienti**.

Gracias
Thank you
Grazie