



EPIDEMIOLOGY OF DKD

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Disclosures of interest

Honoraria

Astra Zeneca, Boehringer Ingelheim, Eli Lilly, Genzyme, MSD Finland, Novartis, Novo Nordisk

Grants

Eli Lilly, Roche

Advisory boards

Abbott, AbbVie, Boehringer Ingelheim, Cebix, Eli Lilly, Medscape, Novartis

Board member

Medix Laboratories

Stock/shareholder

No



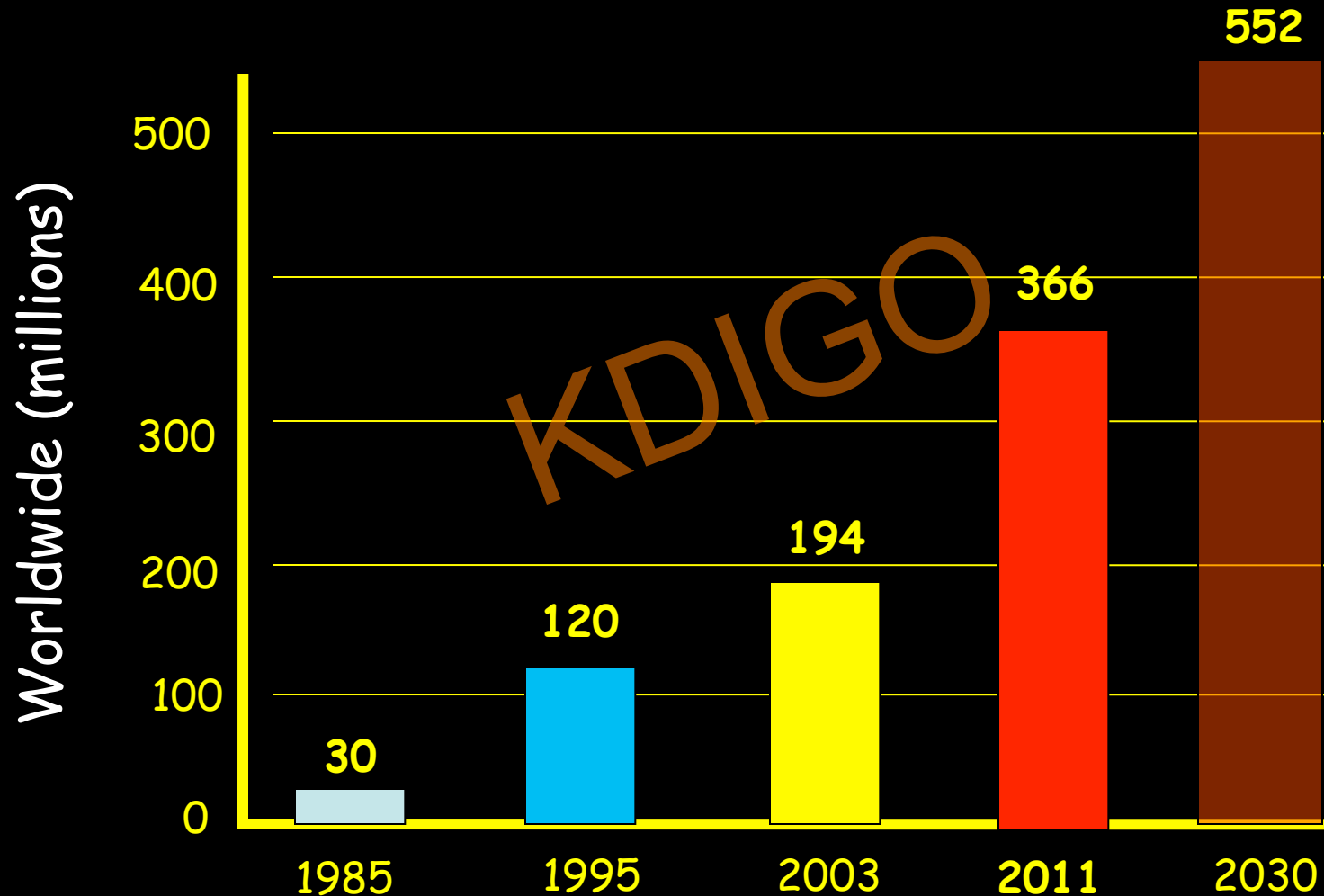
Outline of the presentation

- The diabetes epidemic
- Consequences of DKD
- Screening tools (albuminuria)
- Tools to screen for renal function (eGFR)
- Prevalence of DKD
- Take home messages



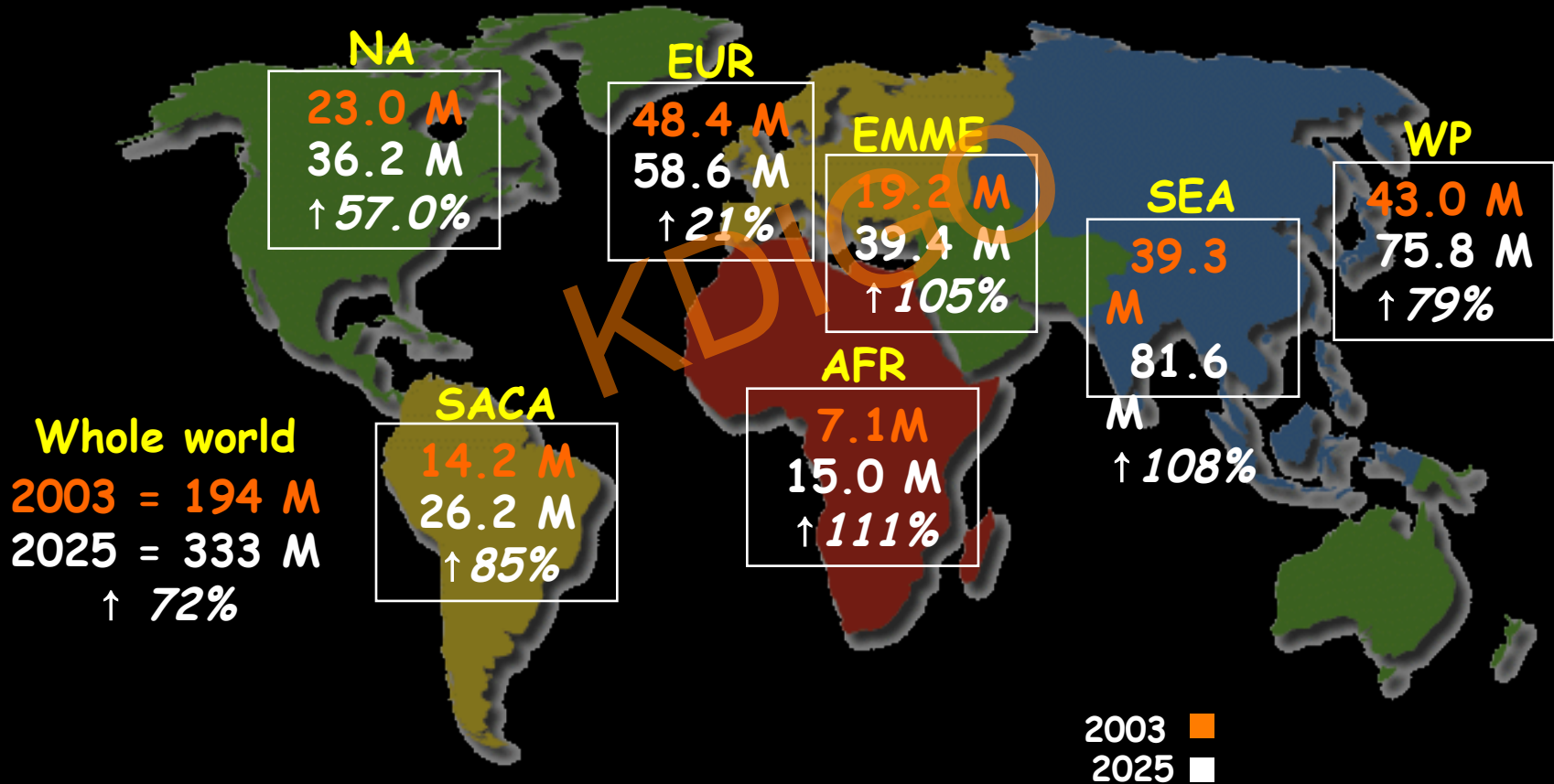
The diabetes epidemic

The diabetes epidemic

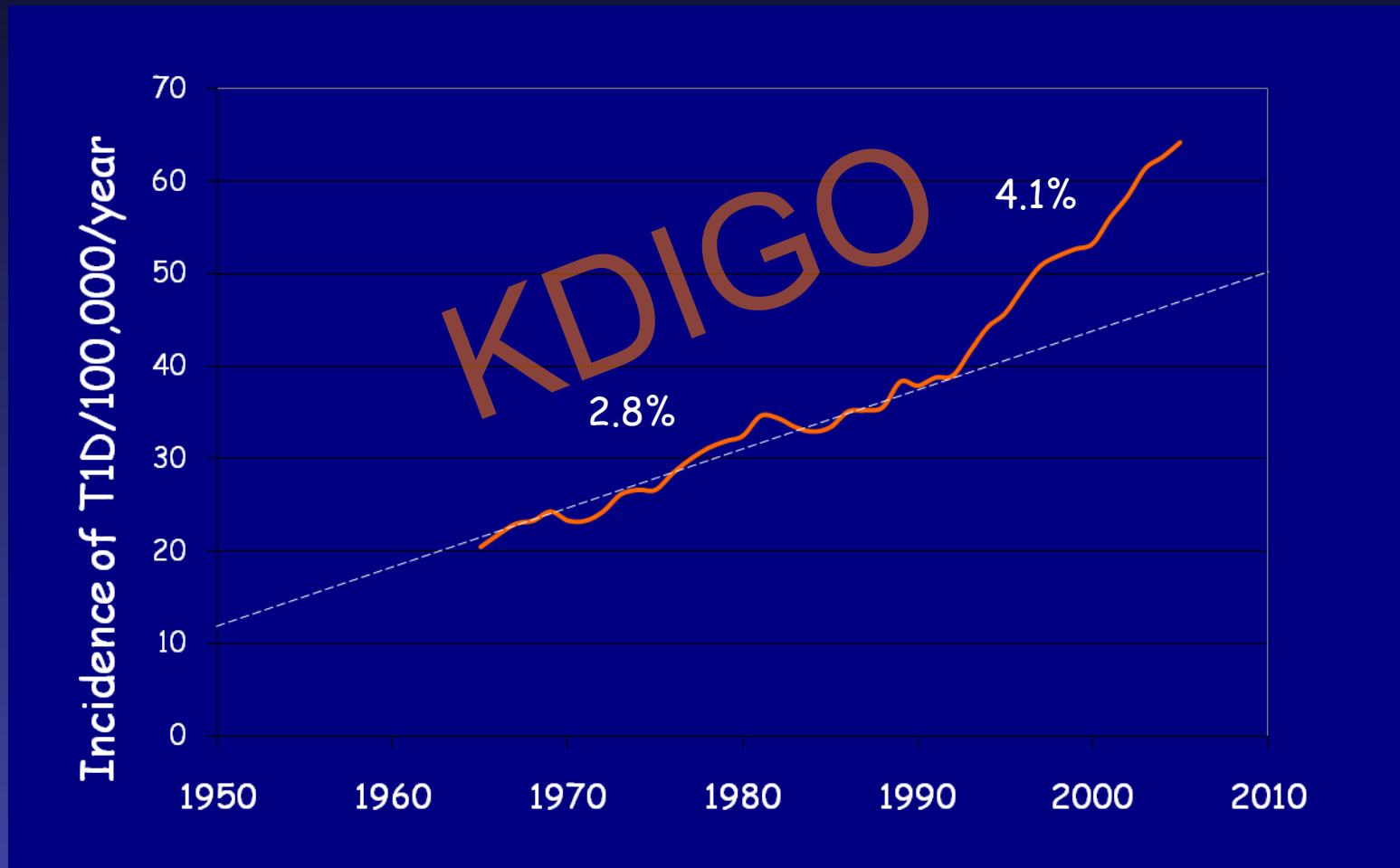


IDF World Atlas of Diabetes 5th Edition 2011 (www.idf.org/diabetesatlas/)

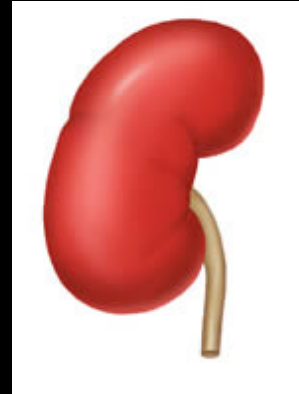
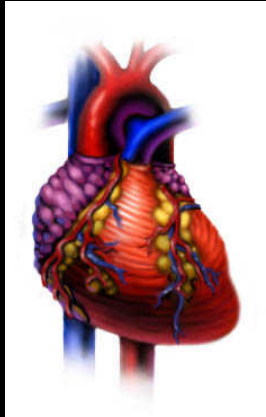
Diabetes is a global epidemic



Type 1 diabetes incidence continues to increase, faster than ever before

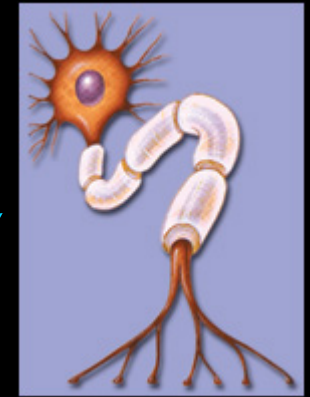


MI, Cardiac failure



Nephropathy

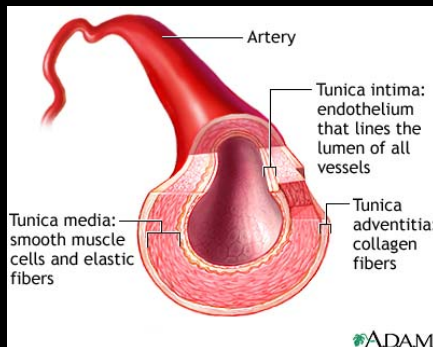
Neuropathy



Diabetic complications

KDIGO

Retinopathy

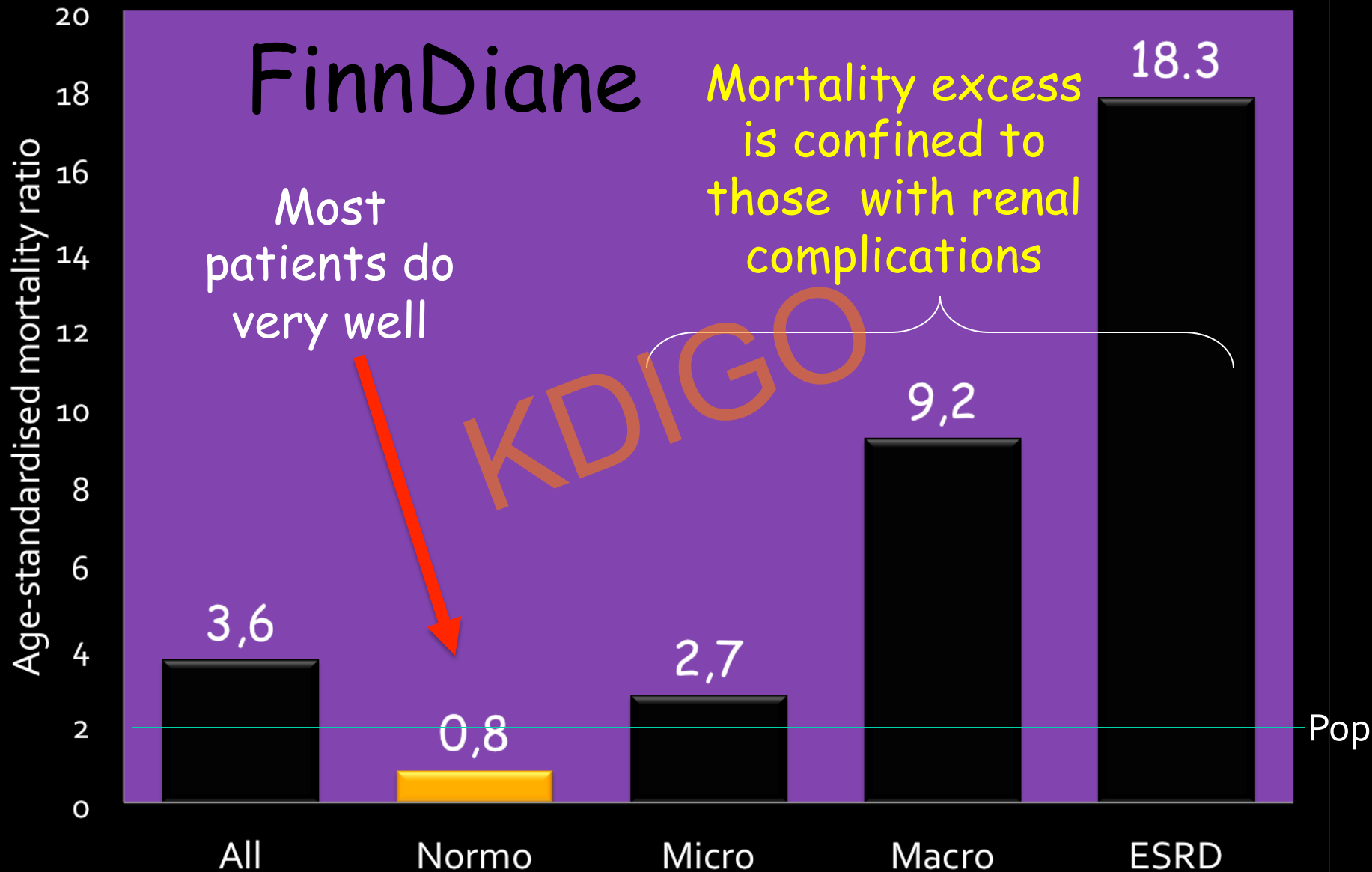


Stroke, PVD



Consequences of diabetic nephropathy and/or DKD

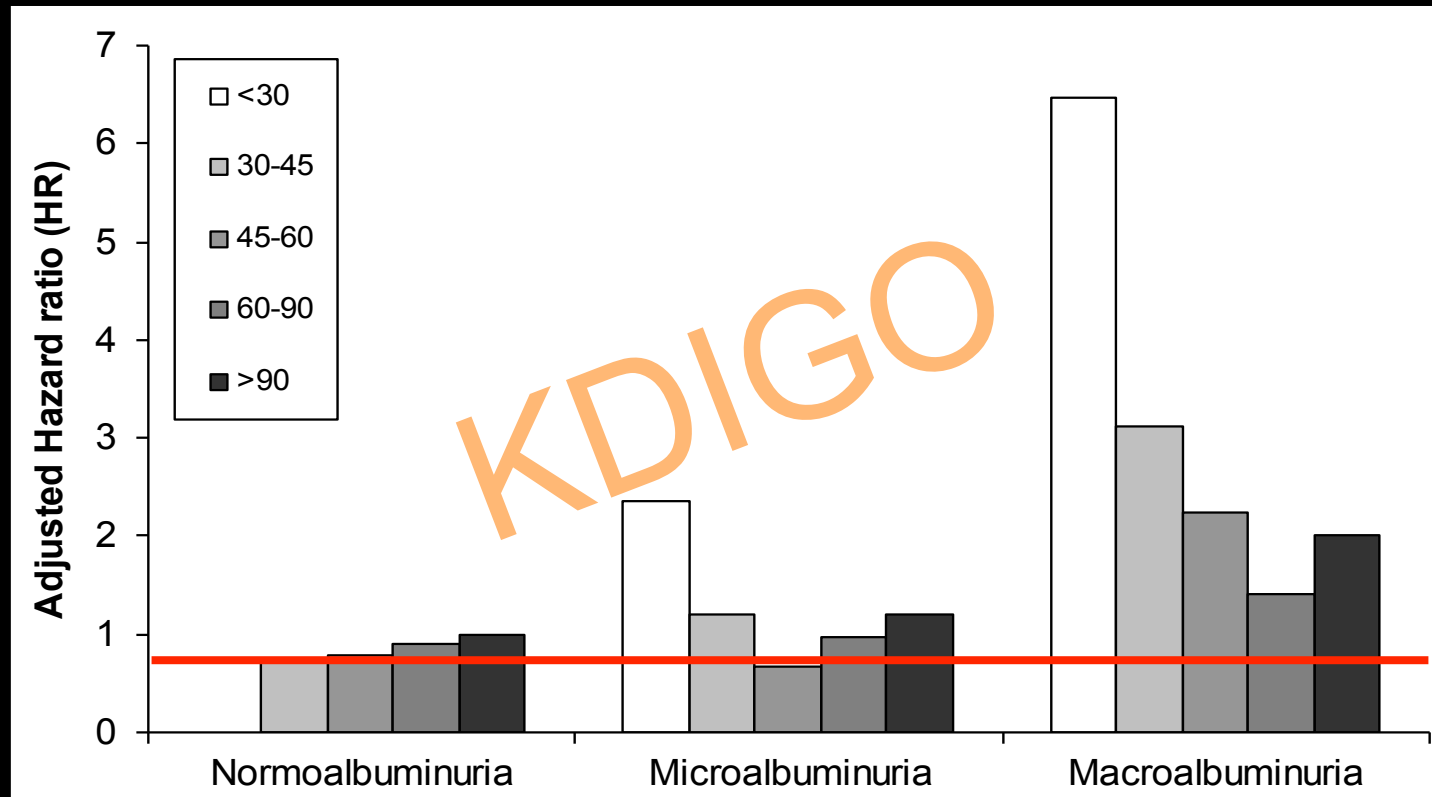
Mortality in adults with type 1 diabetes



ESRD = end-stage renal disease

Groop et al. Diabetes. 2009;58(7):1651-8.

DKD is the major predictor of mortality in type 2 diabetes

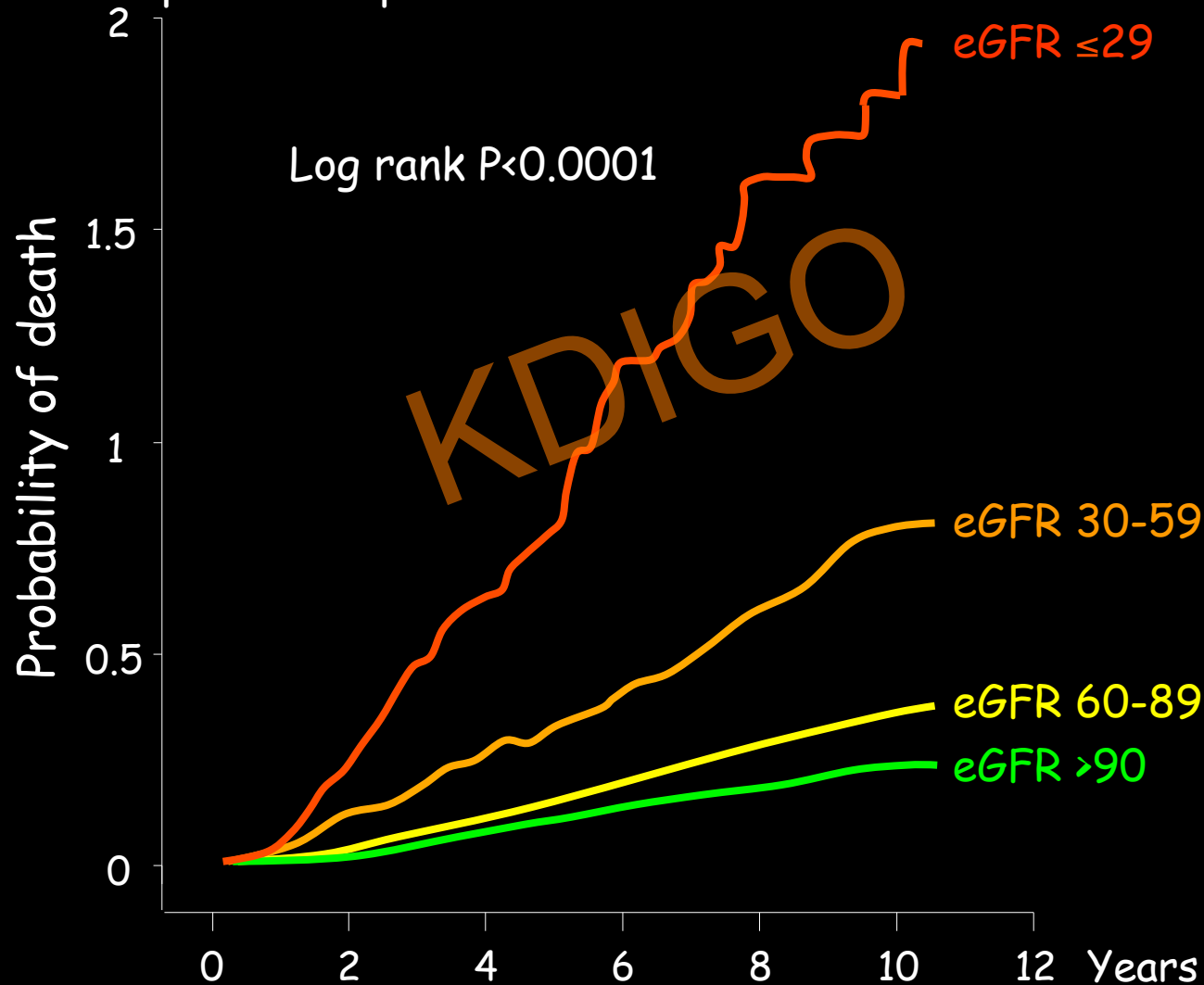


Population-based study of 1,565 individuals with known type 2 diabetes who were resident in the town of Casale Monferrato in north-west Italy in 1988. There were 670 deaths during 10,780 person years of follow-up

Bruno G et al. *Diabetologia* 2007;50(5):941-8.

All-cause mortality in patients with type 2 diabetes stratified by baseline eGFR

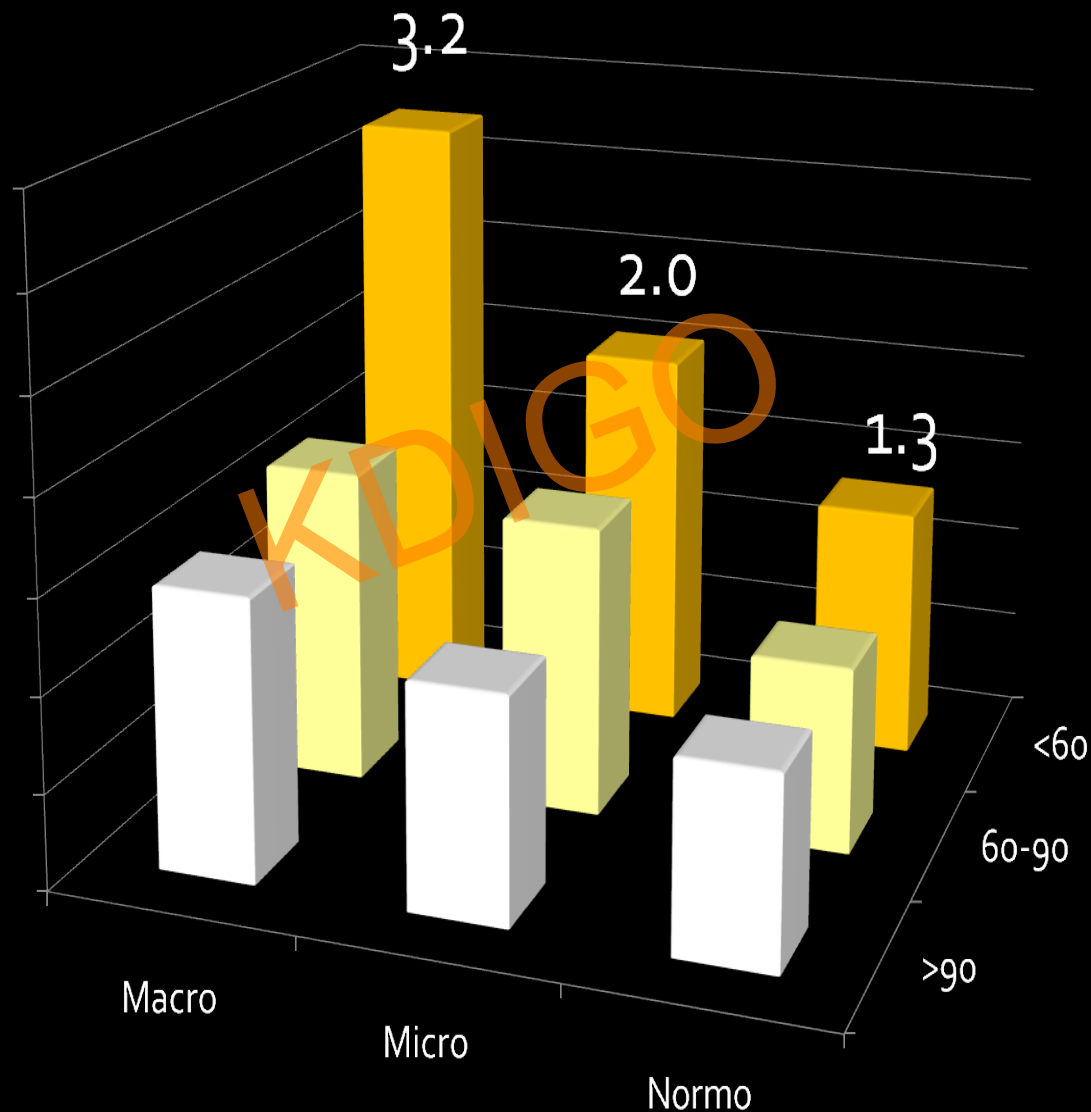
10-year follow-up of 3288 patients in the South Tees Diabetes Mortality Study



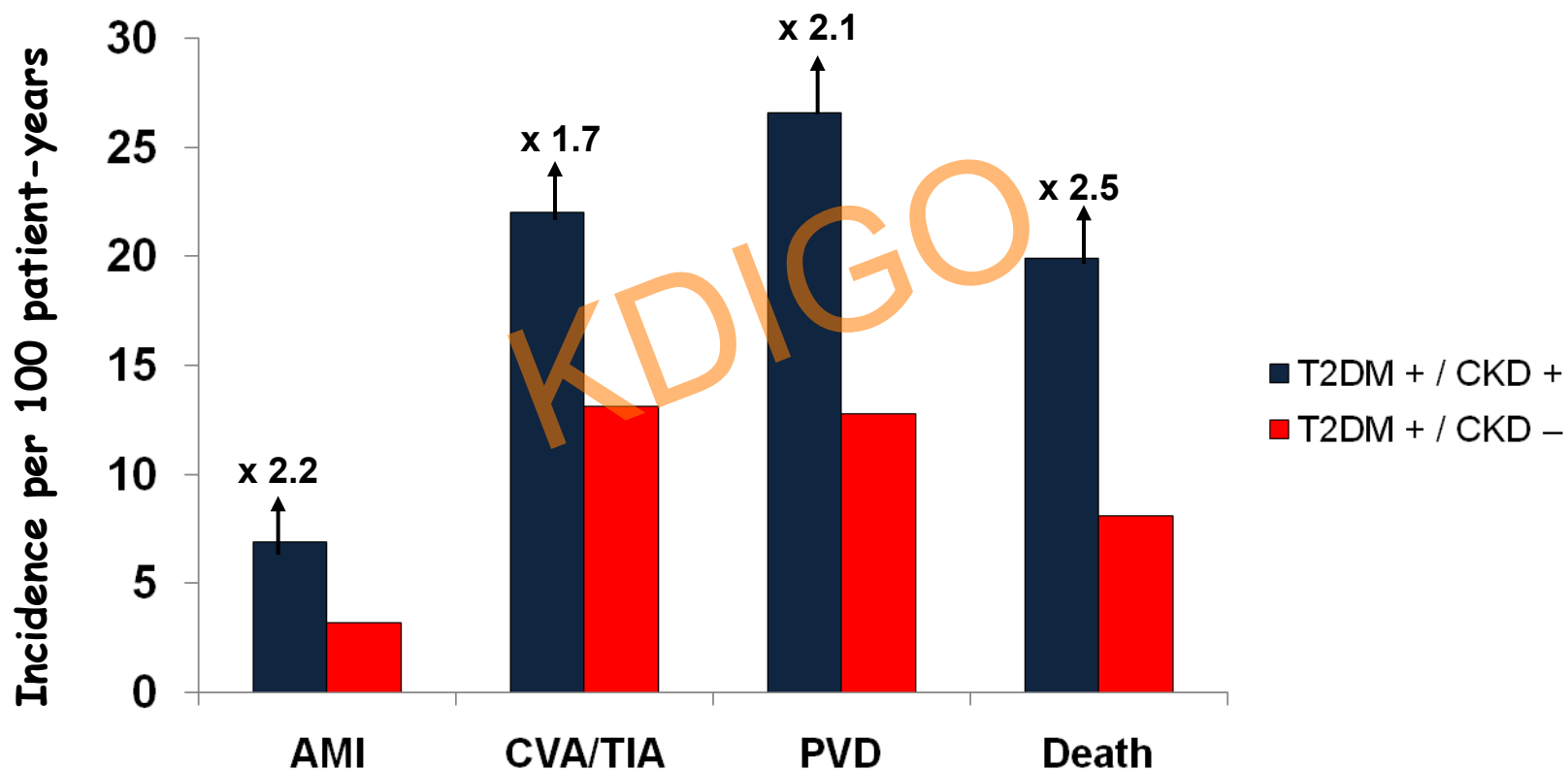
eGFR = estimated glomerular filtration rate

Nag S et al. *Diabet Med* 2007;24(1):10-7.

ADVANCE: Cardiovascular events



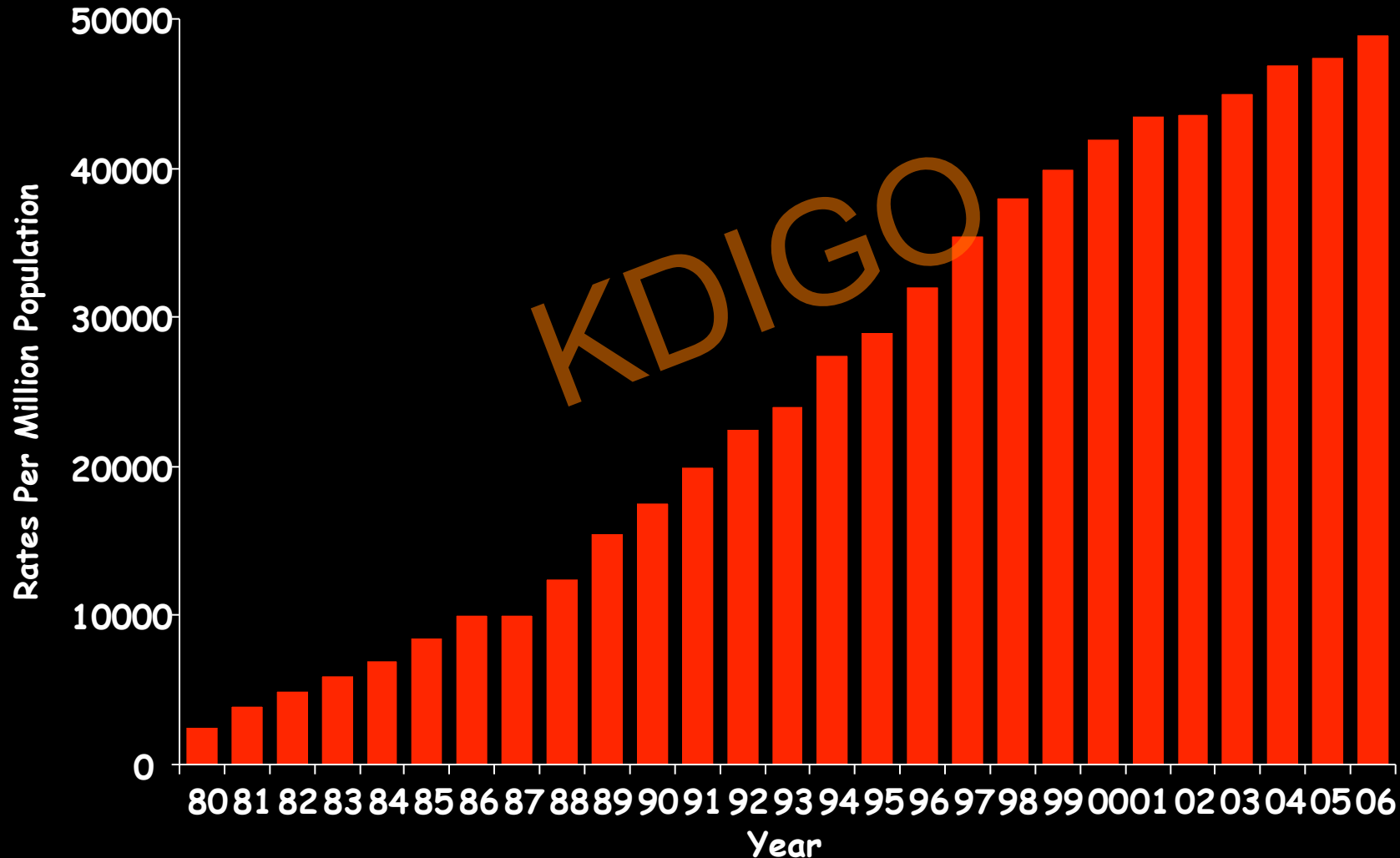
Cardiovascular risk is greatest when both diabetes and CKD are present



Among patients with diabetes and CKD, the rate of cardiovascular events is more than twice that among patients with diabetes only

Changes in the numbers of ESRD cases due to diabetes in the US over 25 years

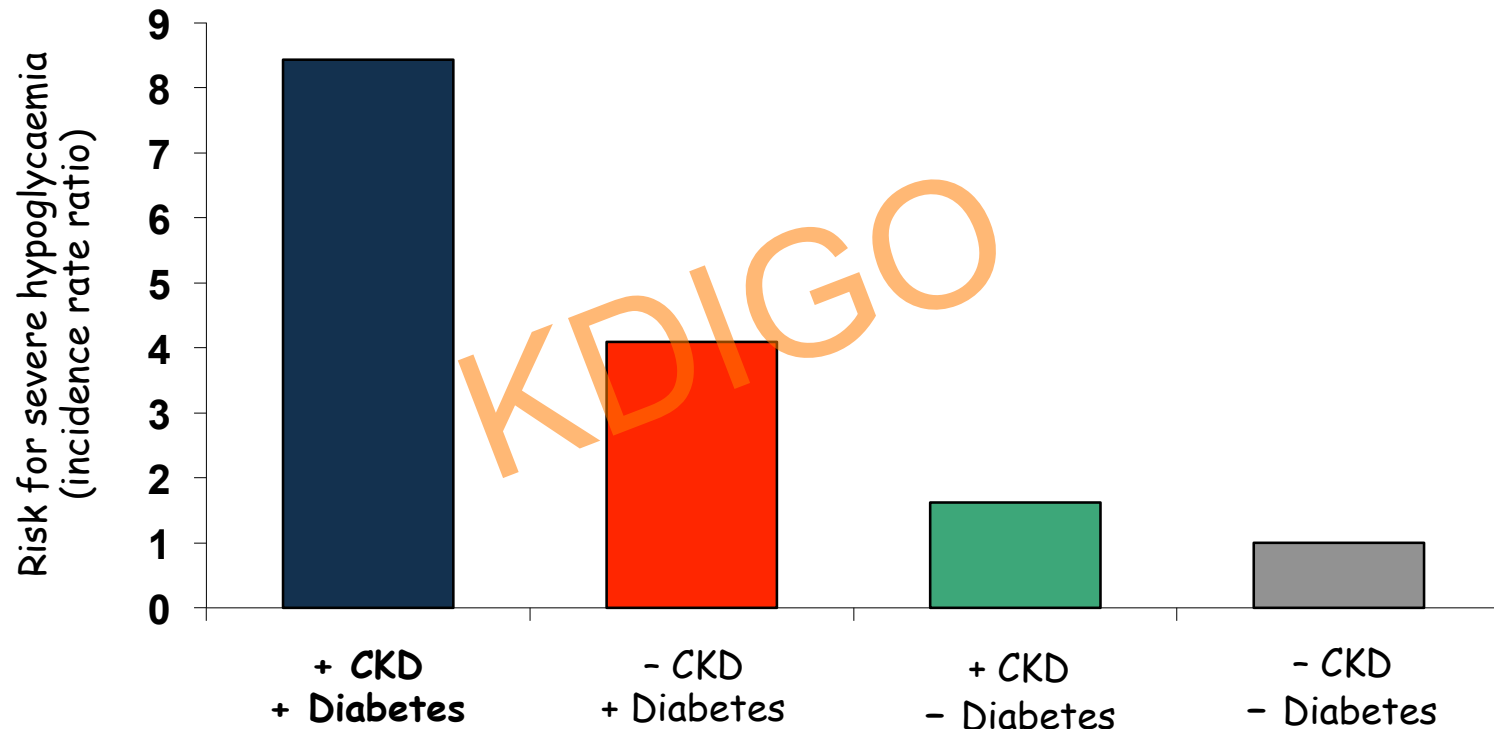
Number of people initiating treatment for ESRD 1980-2006



U.S. Renal Data System, USRDS 2008 Annual Data Report

Declining renal function also increases risk of severe hypoglycaemia

Increased risk most dramatic in patients with renal dysfunction and type 2 diabetes



Around 74% of sulphonylurea-induced severe hypoglycaemic events (loss of consciousness) occurs in patients with reduced renal function

Screening tools (albuminuria)

Screening for microalbuminuria



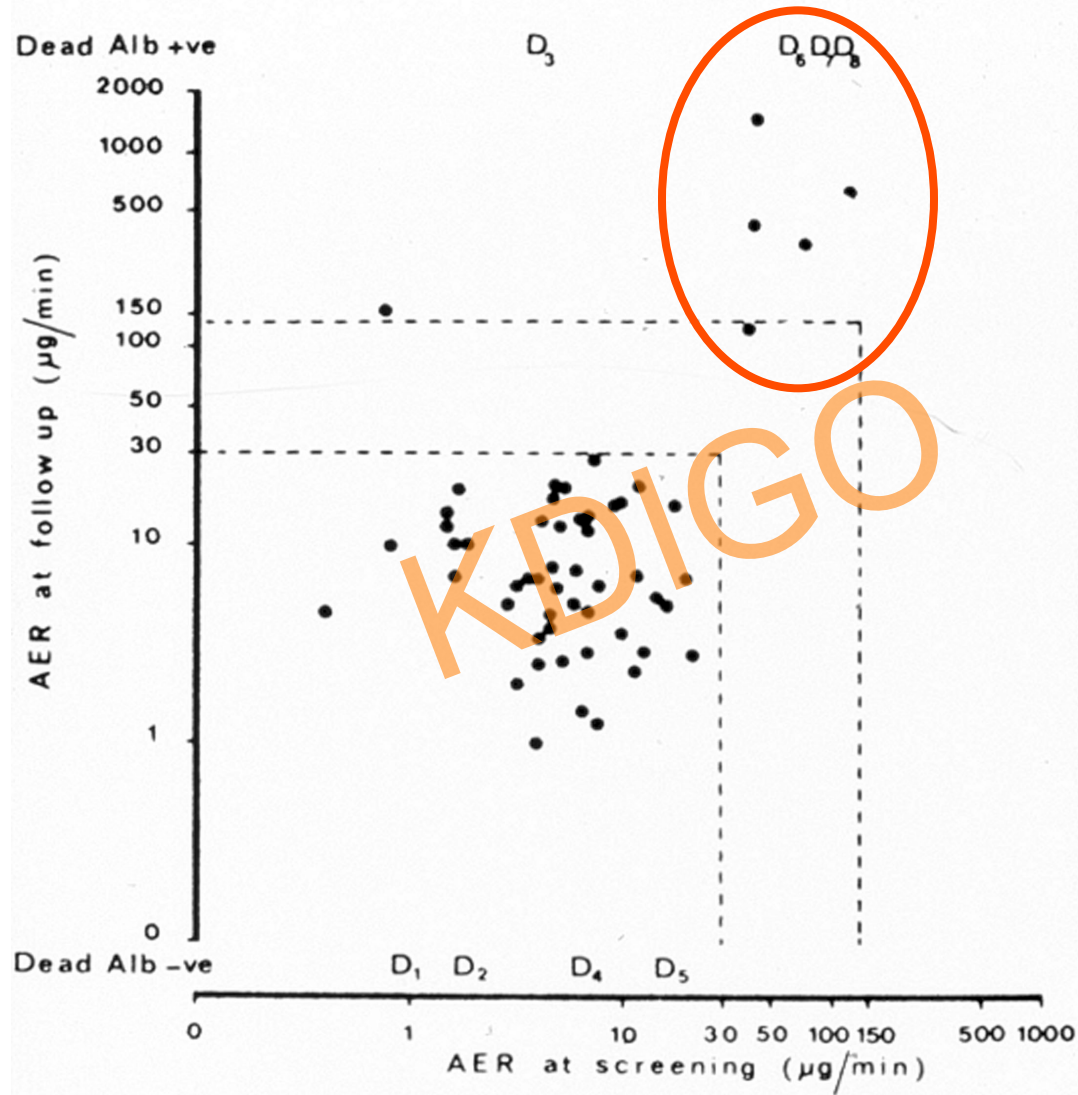
Courtesy of Hans-Henrik Parving

Definitions of albuminuria

Normoalbuminuria: a timed overnight urinary albumin excretion rate (AER) $<20 \mu\text{g}/\text{min}$ or $<30 \text{ mg}/24 \text{ h}$ or an albumin-creatinine ratio (ACR) of $<2.5 \text{ mg}/\text{mmol}$ for men and <3.5 for women in a first morning urine sample

Microalbuminuria: AER $20\text{-}200 \mu\text{g}/\text{min}$ or $30\text{-}300 \text{ mg}/24 \text{ h}$ or an ACR of $2.5\text{-}25 \text{ mg}/\text{mmol}$ for men and $3.5\text{-}35$ for women in a first morning urine sample

Macroalbuminuria: AER $>200 \mu\text{g}/\text{min}$ or $>300 \text{ mg}/24 \text{ h}$ or an ACR of $>25 \text{ mg}/\text{mmol}$ for men and >35 for women in a first morning urine sample

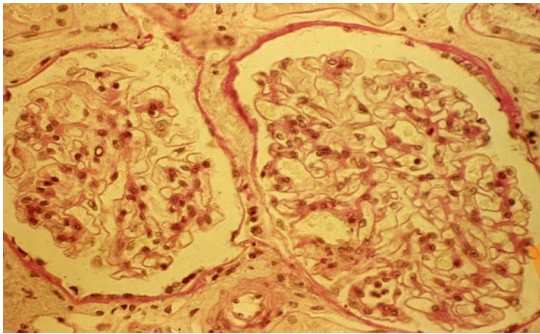


Type 1 diabetes

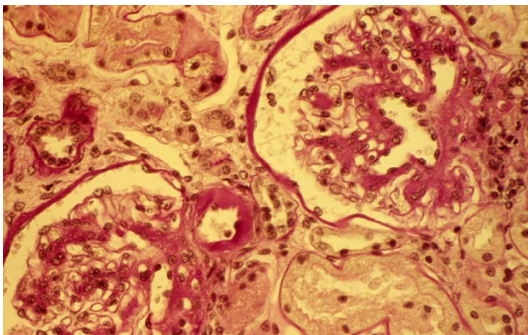
Viberti et al Lancet 1982

Microalbuminuria type 2 diabetes

NEAR NORMAL HISTOLOGY
(C1) - 30 %

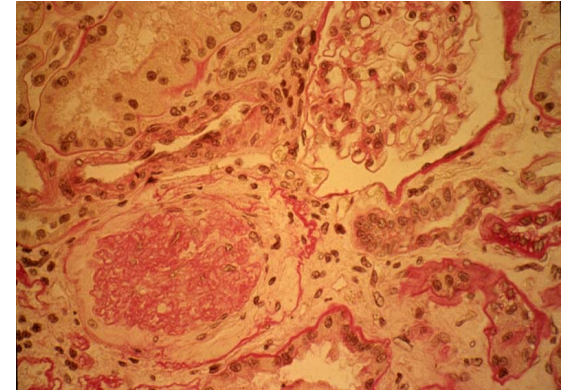


TYPICAL DIABETIC
NEPHROPATHY (C2) - 30 %

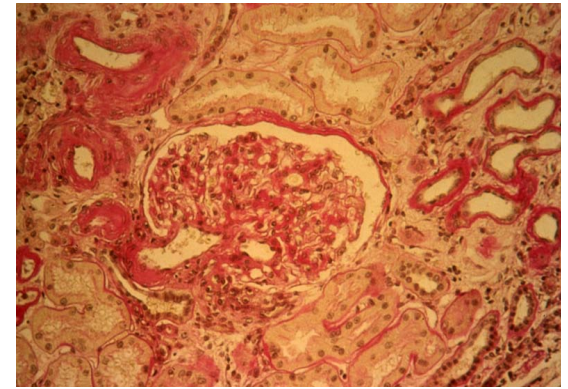


NON-SPECIFIC FINDINGS (C3) - 40 %

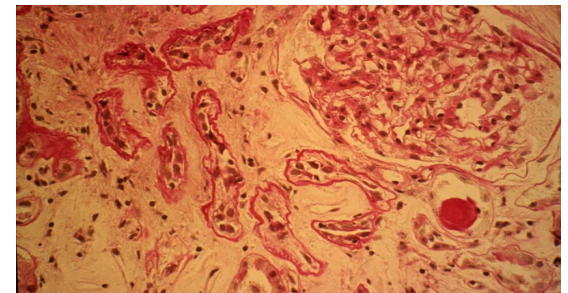
(a) Both normal
and totally
destroyed
glomeruli



(b) Severe
arterioliohyalinosis

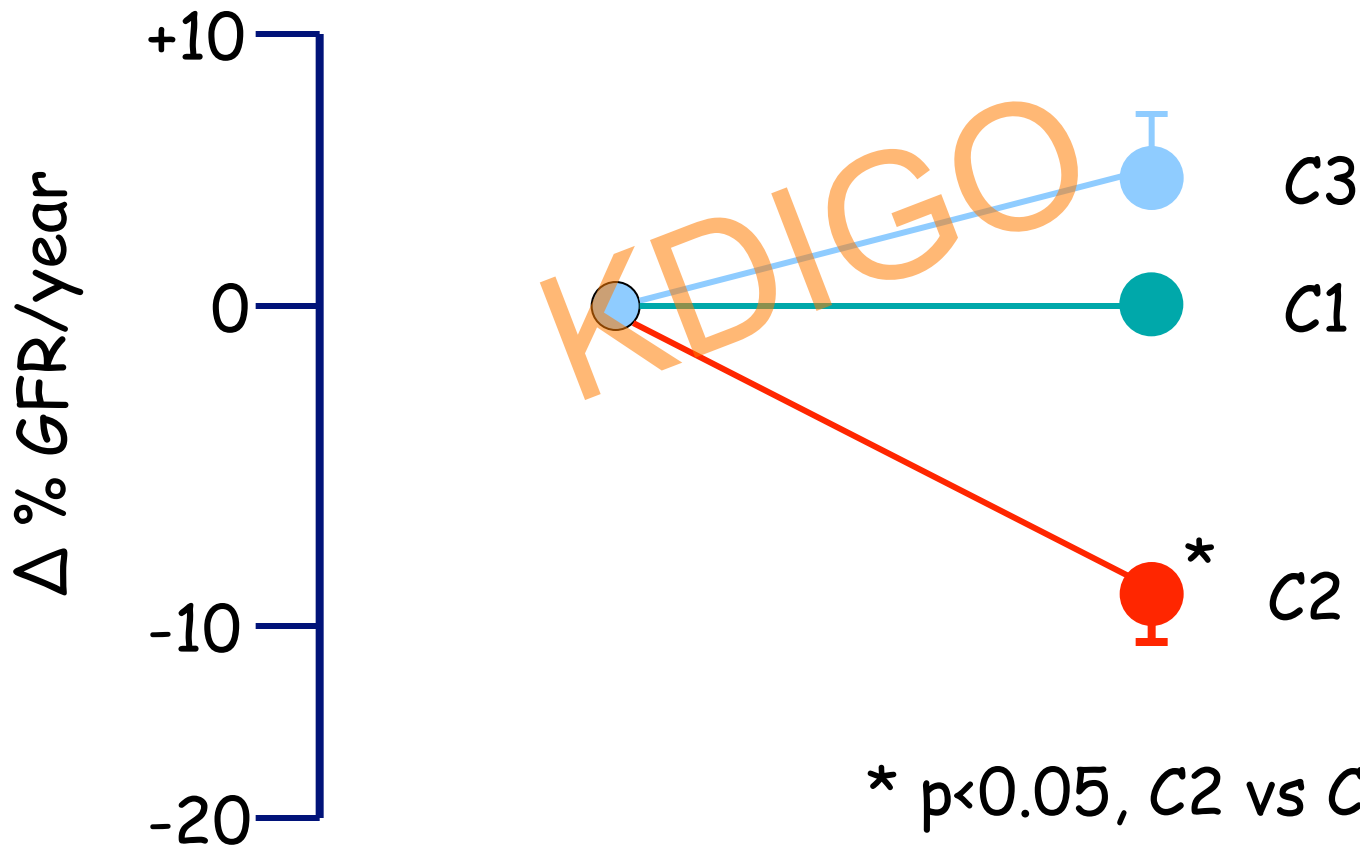


(c) Tubulointerstitial
fibrosis



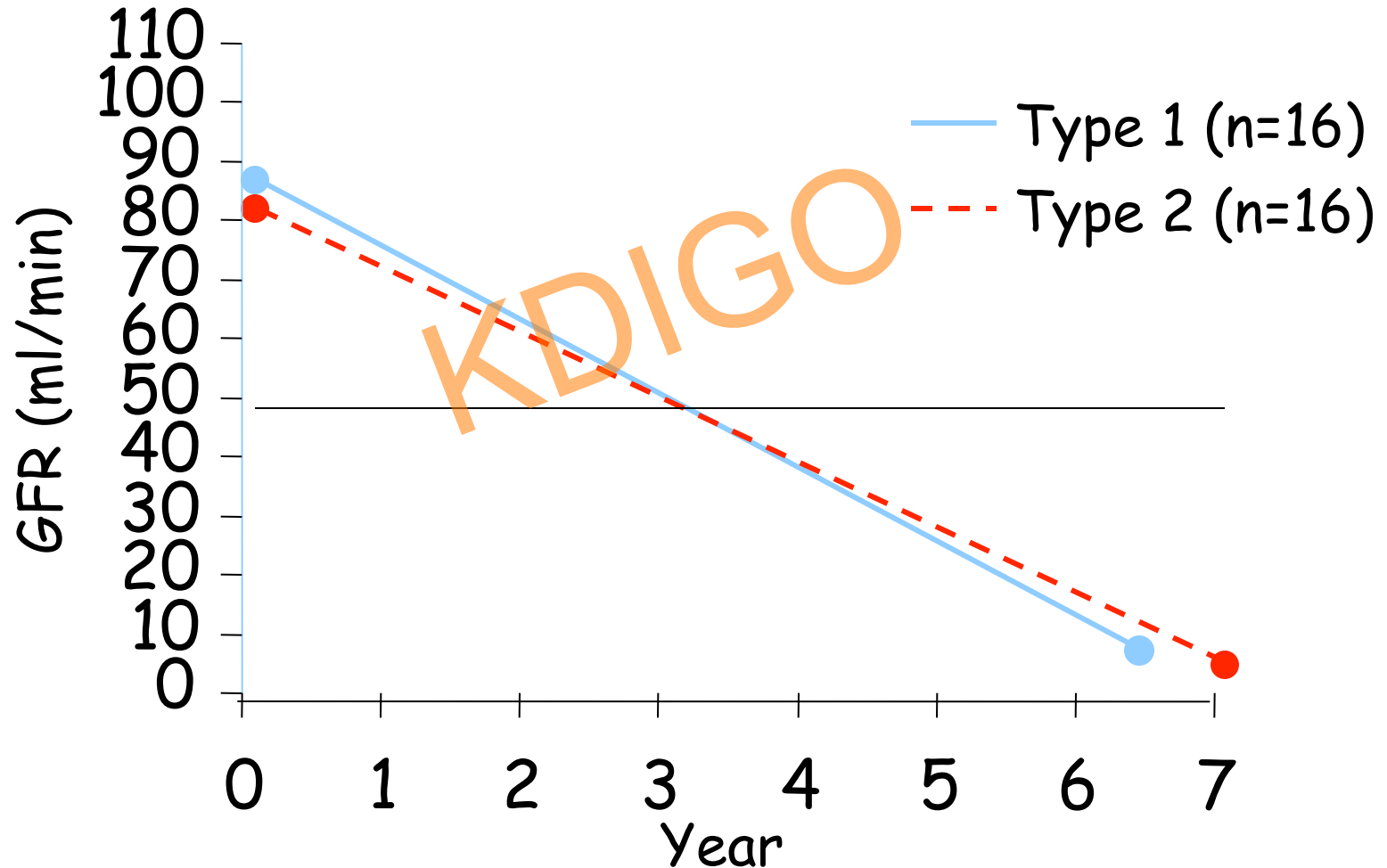
Change in GFR (%) in patients with type 2 diabetes and microalbuminuria

(n=33, 4 year follow-up)



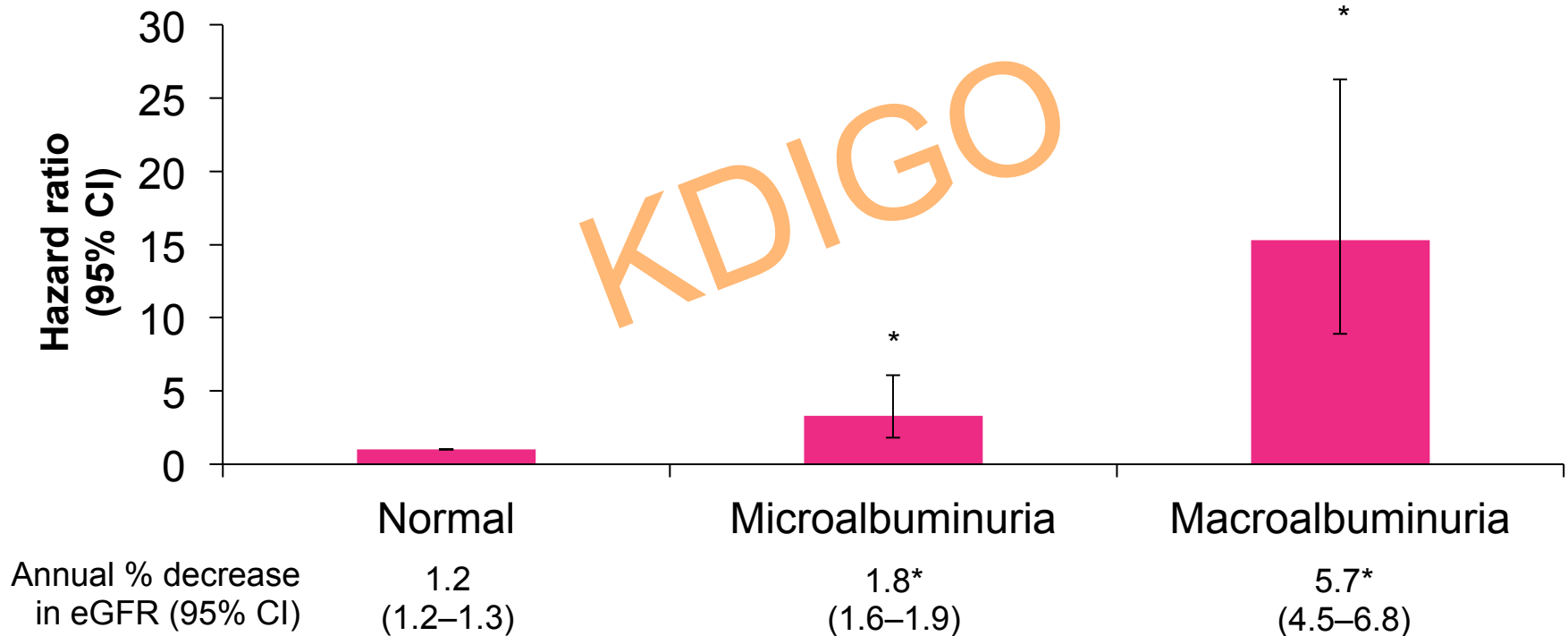
Progression of diabetic nephropathy

Proteinuria ≥ 500 mg/24 h and average S-Crea $88 \mu\text{mol/l}$ at baseline



Albuminuria: a risk factor for DKD

Risk of developing sustained eGFR < 60 mL/min/1.73 m²



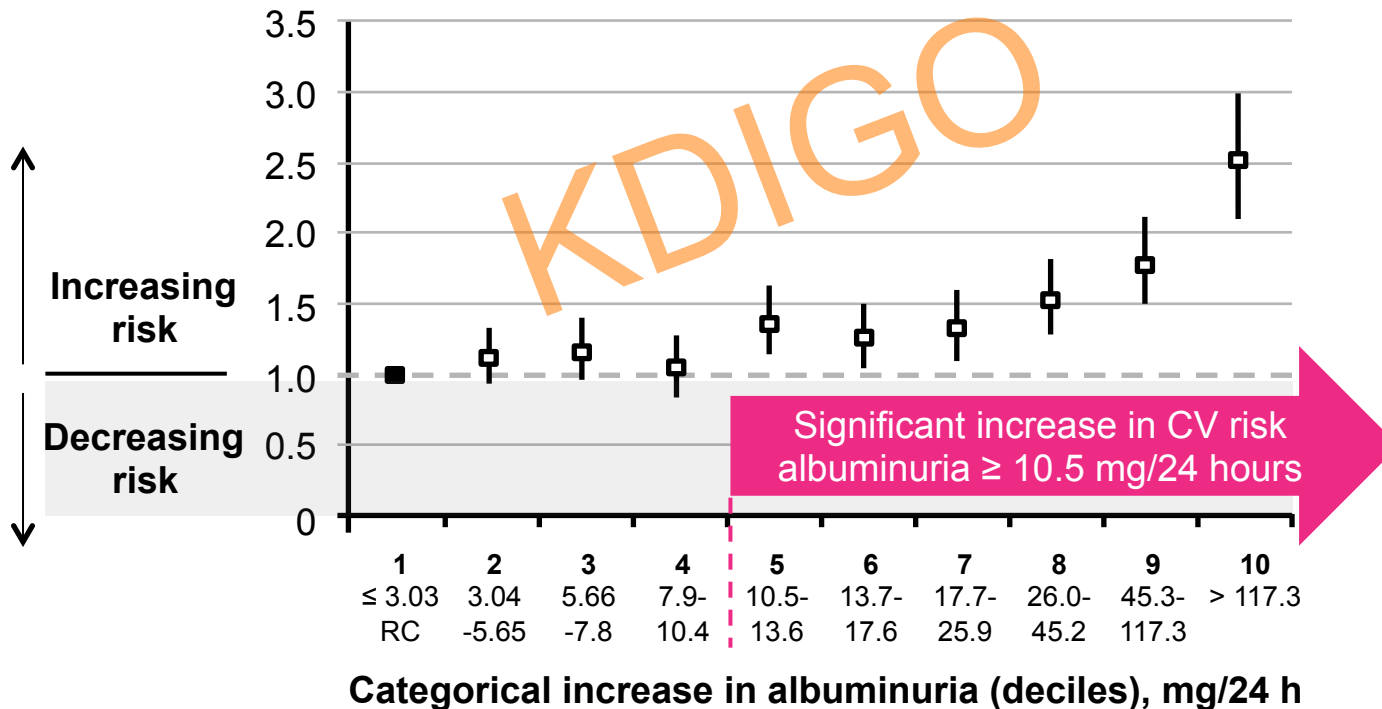
* p < 0.001 versus normal.

Moltich ME, et al. Diabetes Care. 2010;33:1536-1543.

Albuminuria: a risk factor for CVD

The risk of CV outcomes according to degree of albuminuria in patients with T2DM: The Renal Insufficiency and Cardiovascular Events Study, N = 15,773

Odds ratio (95% CI) for major acute CVD events



*Coronary events (including myocardial infarction and/or coronary revascularization); cerebrovascular events (including stroke and/or carotid revascularization; and peripheral events including ulcer/gangrene/amputation and/or lower limb revascularization). Solini et al. *Diabetes Care*. 2012;35:143–149.

Tools to estimate renal
function (eGFR)

Estimation of renal function

The *Cockcroft-Gault formula* provides an estimate of the creatinine clearance (eCCr)

Cockcroft DW, Gault MH. *Nephron* 1976;16(1):31-41.

The *MDRD-4 formula* provides an estimate of the glomerular filtration rate (eGFR)

Levey AS et al. *Ann Intern Med* 1999;130(6):461-70.

Levey AS et al. *Ann Intern Med* 2006;145(4):247-54.

The *CKD-EPI equation* provides an estimate of the glomerular filtration rate (eGFR)

Levey AS et al. *Ann Intern Med* 2009;150(9):604-12.

Stages of renal function

Stage 1 - eGFR >90 ml/min + persistent albuminuria

Stage 2 - eGFR 60-89 ml/min + persistent albuminuria

Stage 3a - eGFR 45-59 ml/min

Stage 3b - eGFR 30-44

Stage IV - eGFR 15-29 ml/min

Stage V - eGFR <15 ml/min

Prevalence of DKD

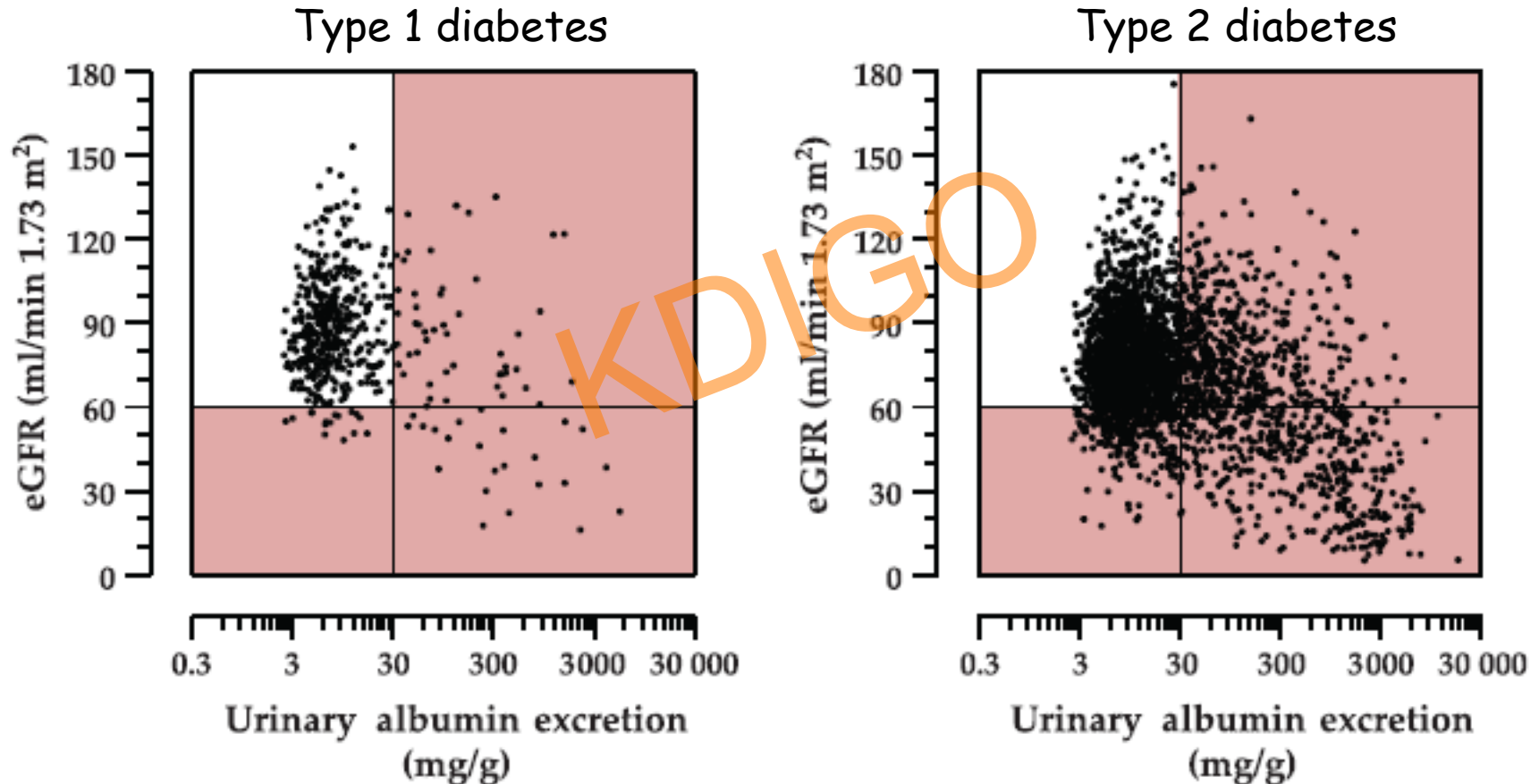
Prevalence depends on the definition?

Impossible to make causal inference

“so it is clinically defined in patients with diabetes and an eGFR <60 ml/min/1.73m² and/or an elevated urinary ACR (≥ 30 mg/g)

= essentially CKD in diabetes or DKD

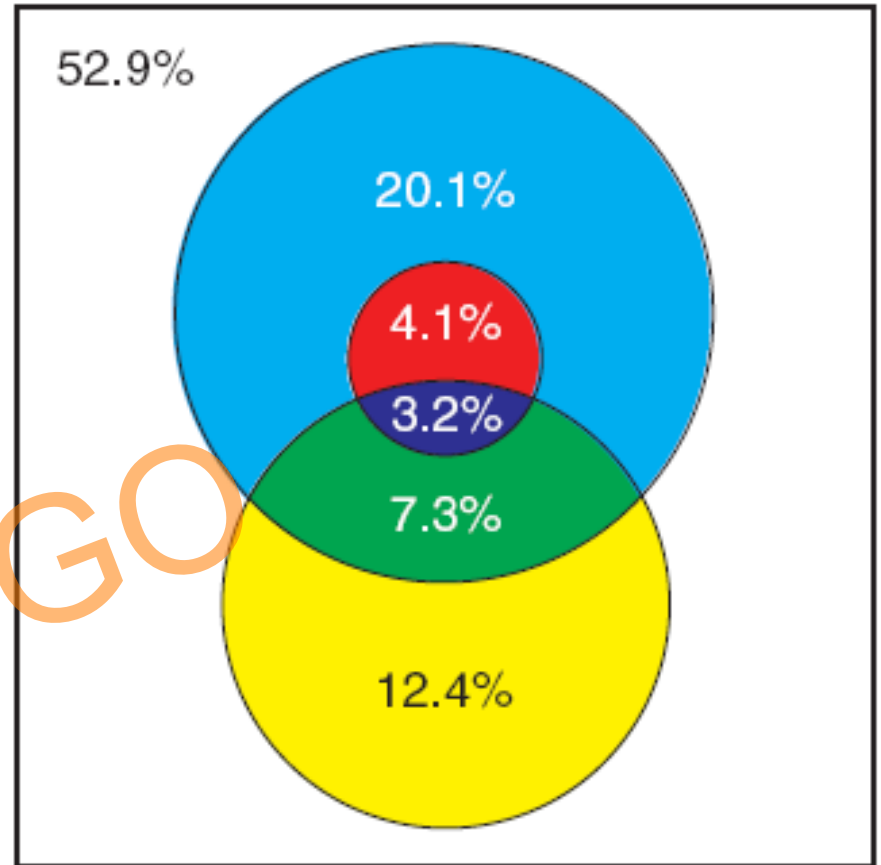
Scatter plots for eGFR against ACR in type 1 and type 2 diabetes



Shaded area denotes CKD defined as ACR ≥ 30 mg/g and/or eGFR < 60 ml/min/1.73 m²

The distribution of albuminuria and an eGFR <60 ml/min/1.73 m² in patients with T2D in Australia

Nefron Study
N=3.893 patients with
Type 2 diabetes
52% males

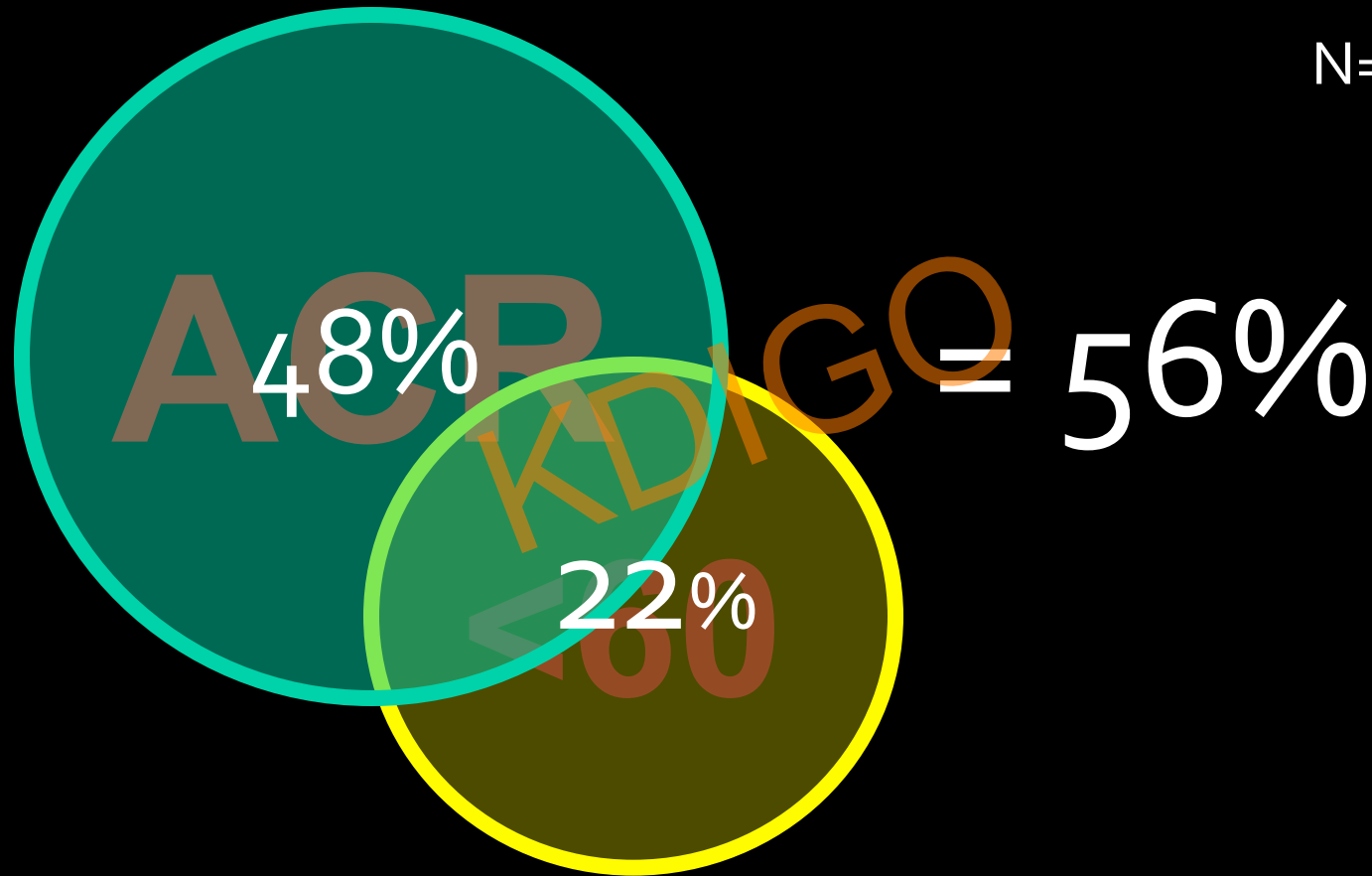


- Microalbuminuria
- Macroalbuminuria
- eGFR < 60 mL/min/1.73 m²

* The unshaded area denotes patients without chronic kidney disease (52.9%).

Global perspective

N=24.151



Developing Education on Microalbuminuria for Awareness of renal and cardiovascular risk in Diabetes (DEMAND)

Epidemiology of CKD in diabetes

Varies considerably across countries and settings

- > African Americans
- > Middle Eastern
- > Hispanic
- > Asian
- > Polynesian
- > Indigenous peoples

INCREASED RISK

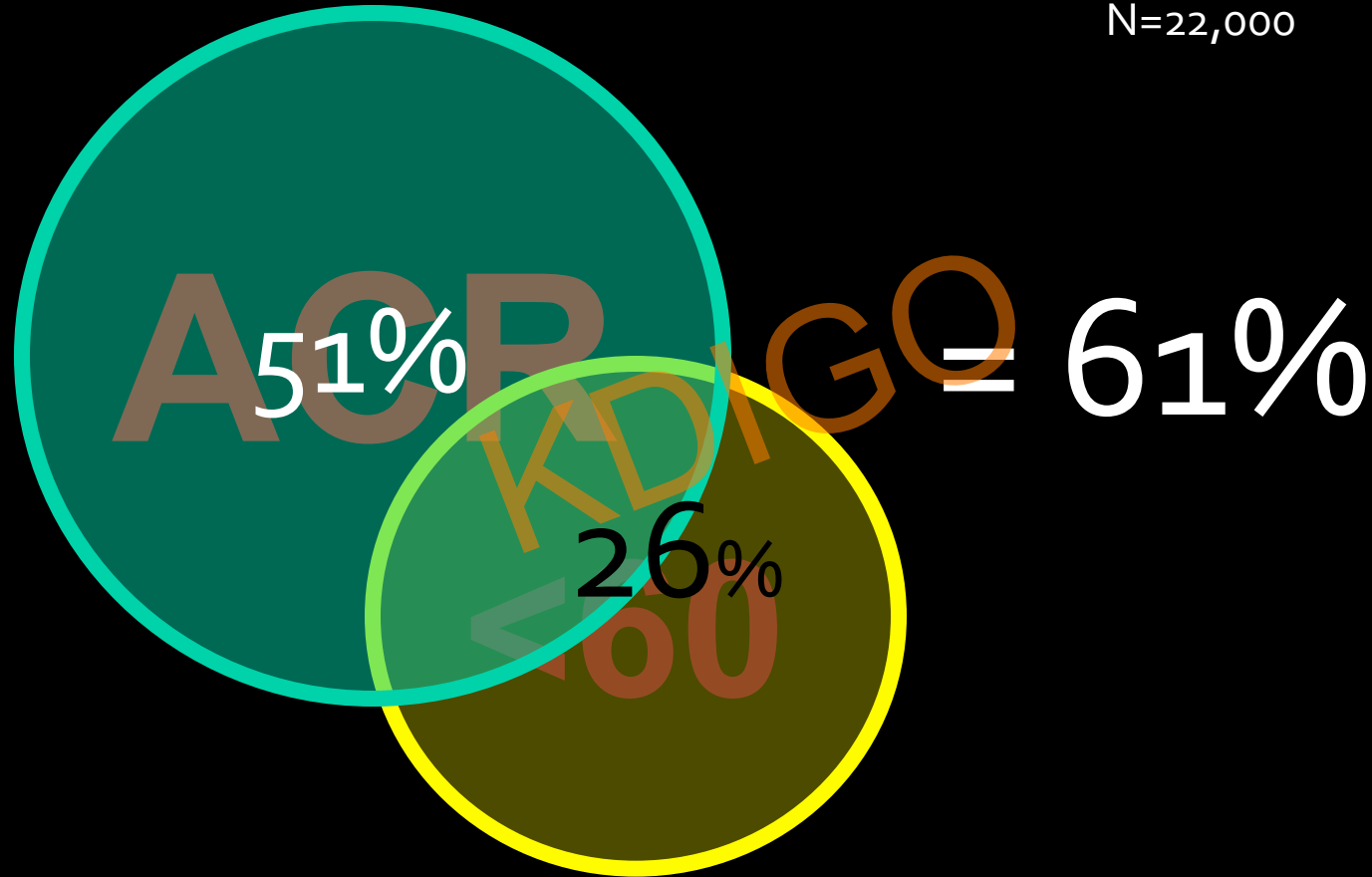
KDIGO

economic, social or educational disadvantage, access to and uptake of care, lower achievement of treatment goals, lower screening rates, suboptimal early treatment of complications, diet and lifestyle factors, smoking, obesity, genetic factors and probably also developmental programming.



Latin American perspective

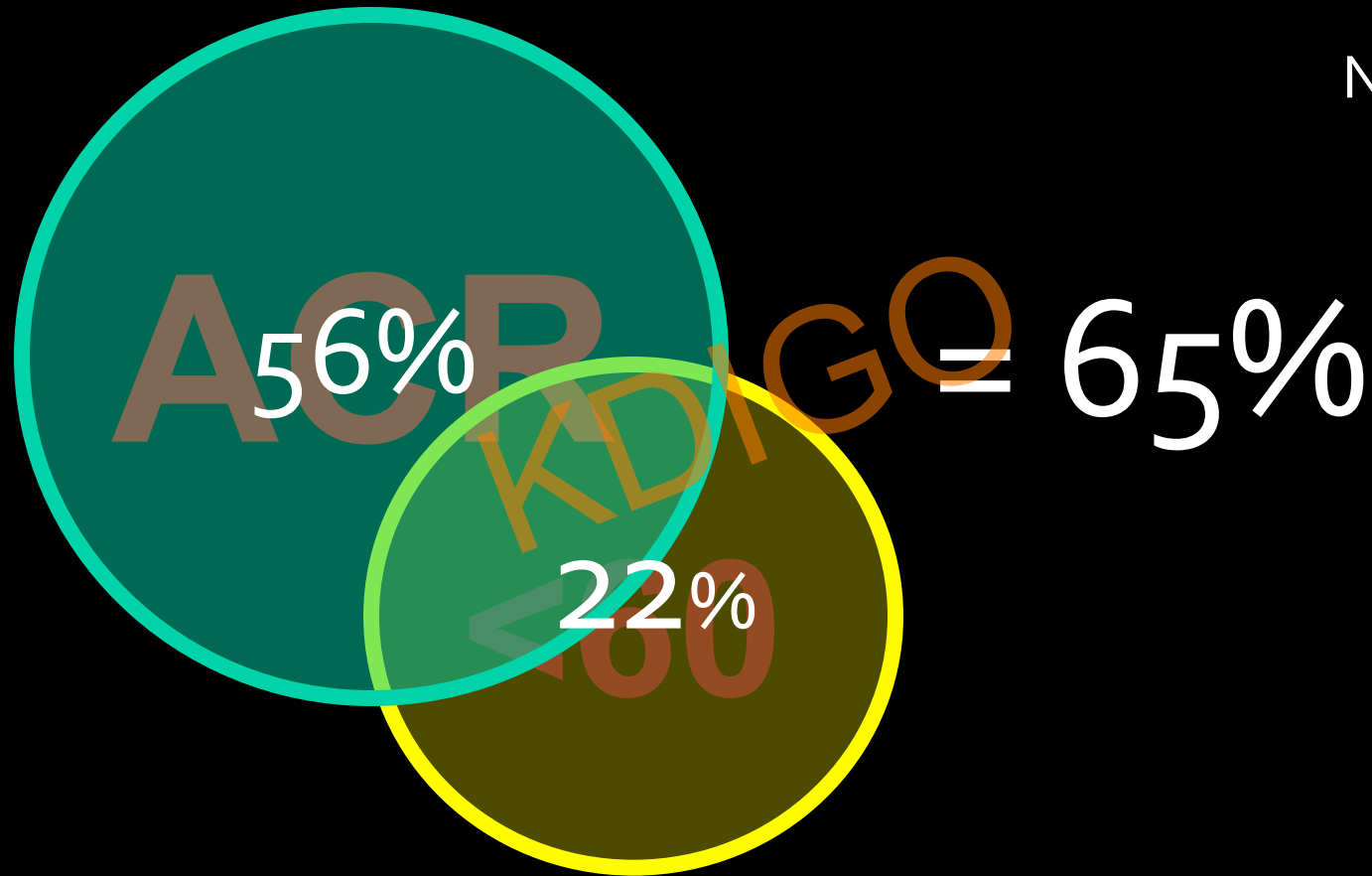
N=22,000



Developing Education on Microalbuminuria for Awareness of renal and cardiovascular risk in Diabetes (DEMAND)

Asian perspective

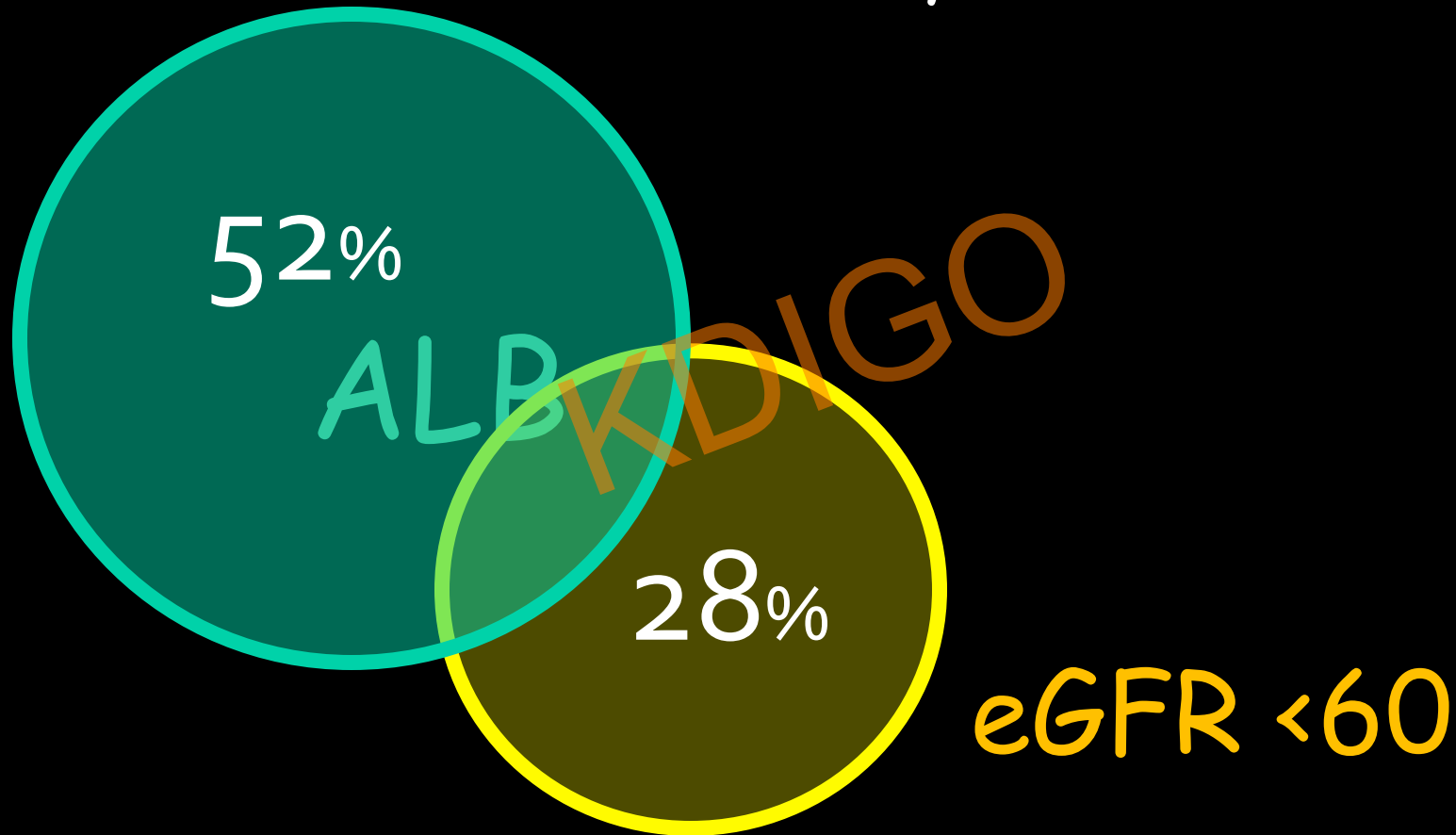
N=9.111



Developing Education on Microalbuminuria for Awareness of renal and cardiovascular risk in Diabetes (DEMAND)

Epidemiology of CKD in the UKPDS

After 15 years of follow-up



Only 14% developed both

Epidemiology of CKD in diabetes

HOW MANY OF THESE ACTUALLY
HAVE DIABETIC KIDNEY DISEASE?

How many have age-related decline, hypertensive or dyslipidemic nephropathy, obesity-related, glomerular atherosclerosis?

DOES IT MATTER?



Epidemiology of CKD in diabetes

Do you need retinopathy to have DKD?

Do you need albuminuria to have DKD?

Do you need histology to have DKD?

Take home messages

- Diabetes is increasing with epidemic proportions all over the world
- DKD is a common complication
- The consequences of DKD are grim
- We have to take action which is the scope of this controversy meeting



KDIGO

Thank you for your attention

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