Sessione VI: MALATTIA RENALE CRONICA E DIABETE

La nuova epidemiologia della malattia renale cronica

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Disclosure

Dichiaro di aver ricevuto negli ultimi due anni compensi o finanziamenti dalle seguenti Aziende Farmaceutiche e/o Diagnostiche per relazioni/moderazioni/partecipazioni a board retribuite:

- Astra-Zeneca;
- Bayer;
- Boehringer Ingelheim;
- Eli Lilly;
- Mundipharma;
- Novo Nordisk.

Dichiaro altresì il mio impegno ad astenersi, nell'ambito dell'evento, dal nominare, in qualsivoglia modo o forma, aziende farmaceutiche e/o denominazione commerciale e di non fare pubblicità di qualsiasi tipo relativamente a specifici prodotti di interesse sanitario (farmaci, strumenti, dispositivi medico-chirurgici, ecc.).

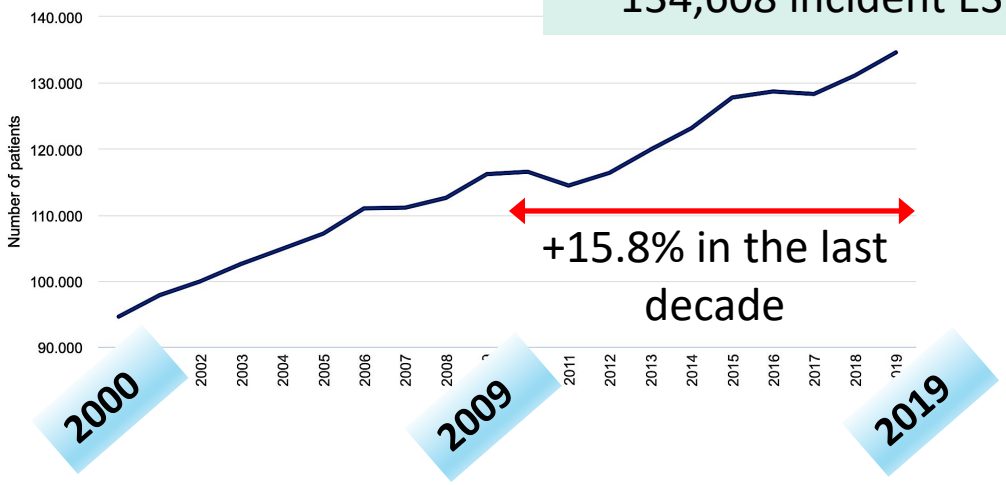
In fede

Giuseppe Pugliese

Diabetes as a cause of end-stage renal disease (ESRD)

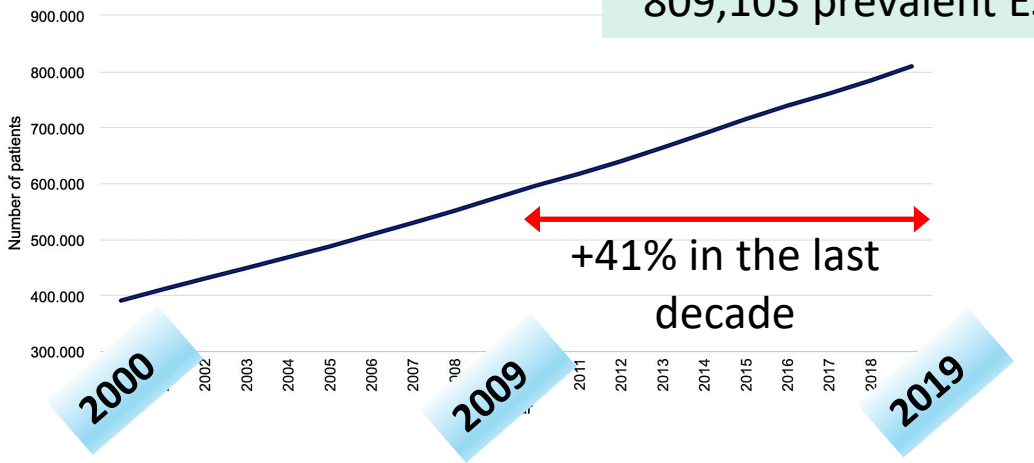
Incidence count

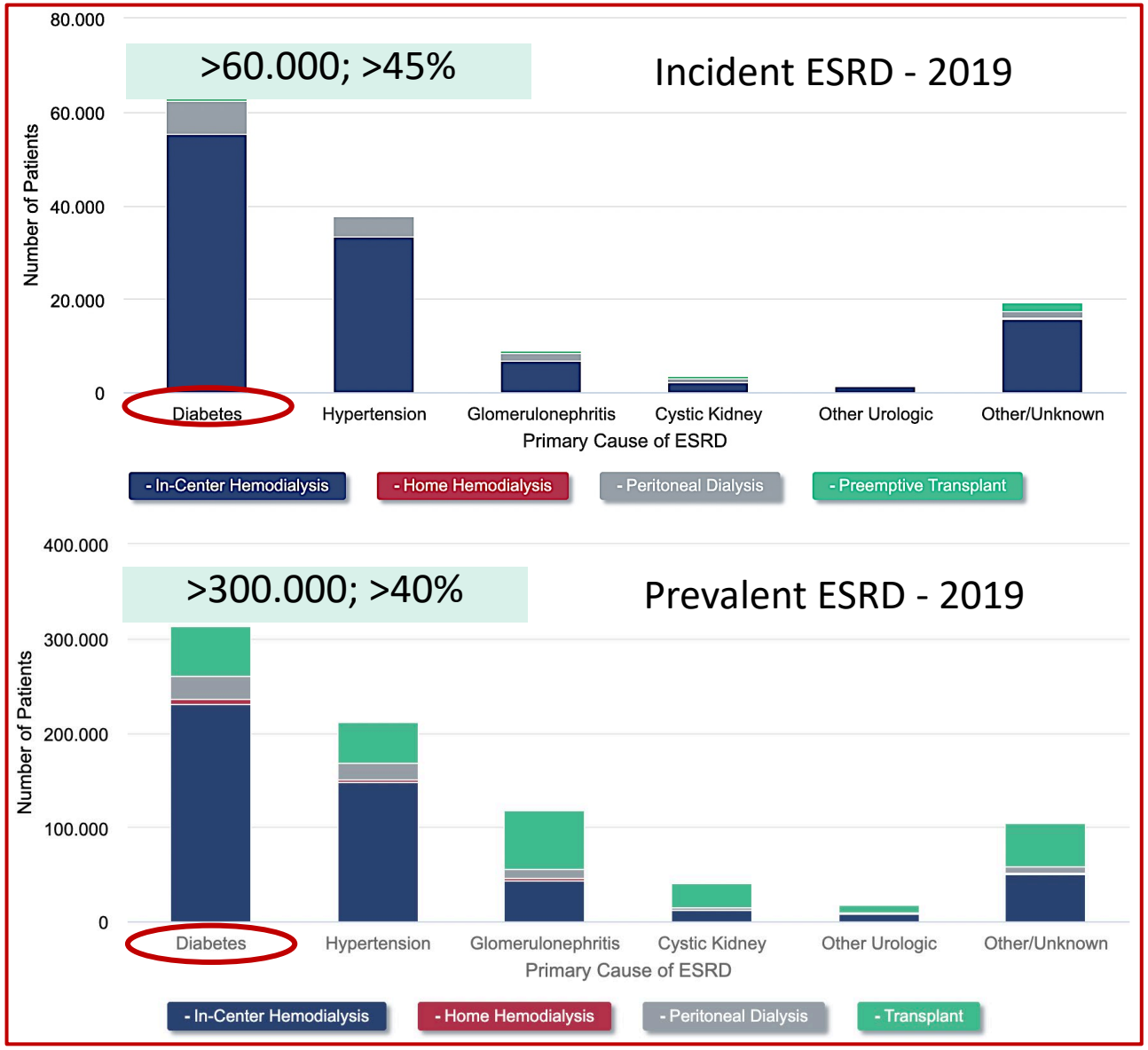
134,608 incident ESRD



Prevalence count

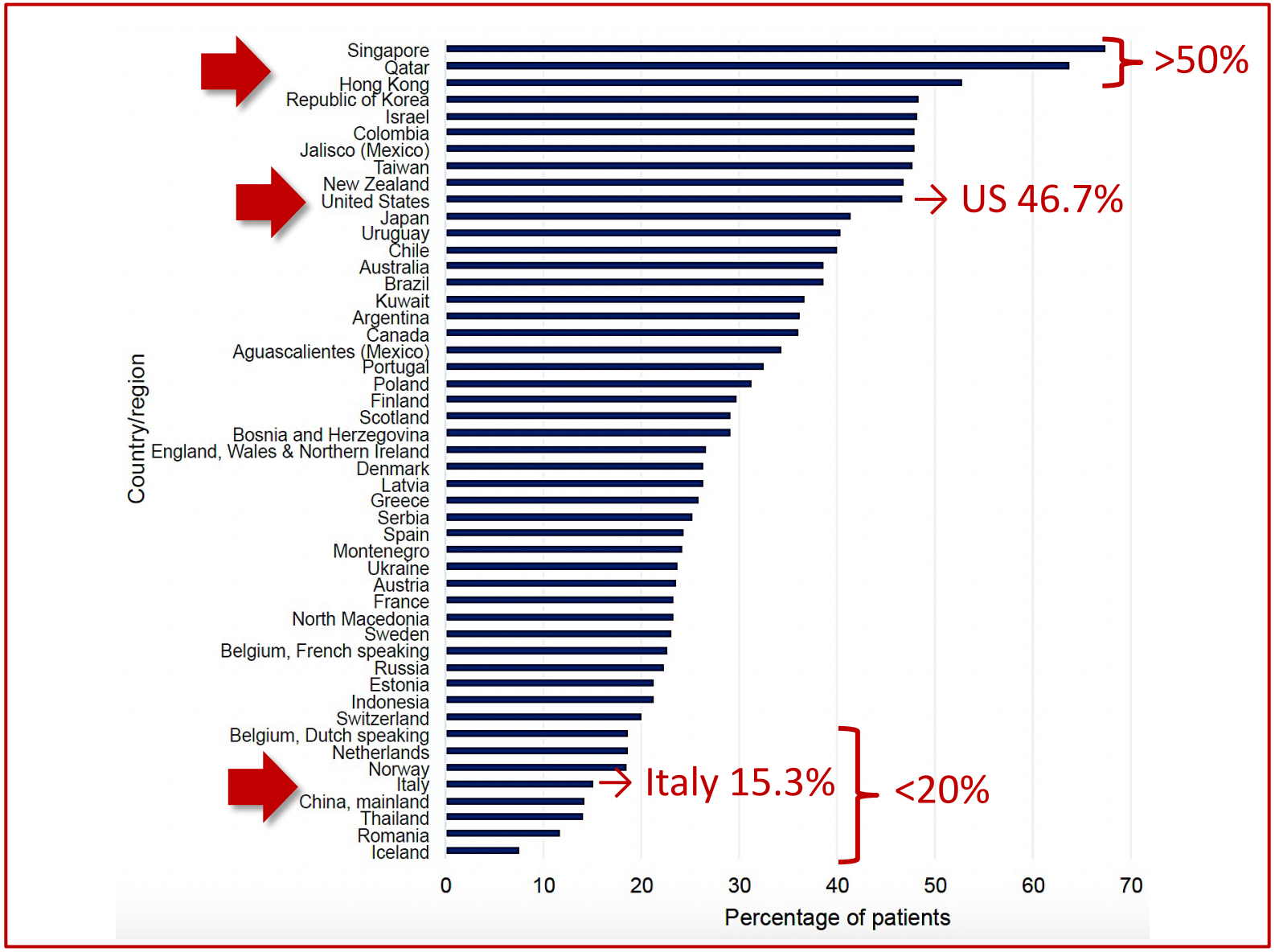
809,103 prevalent ESRD





2021 US Renal Data System. *Am J Kidney Dis.* 2022;79:S178–S575

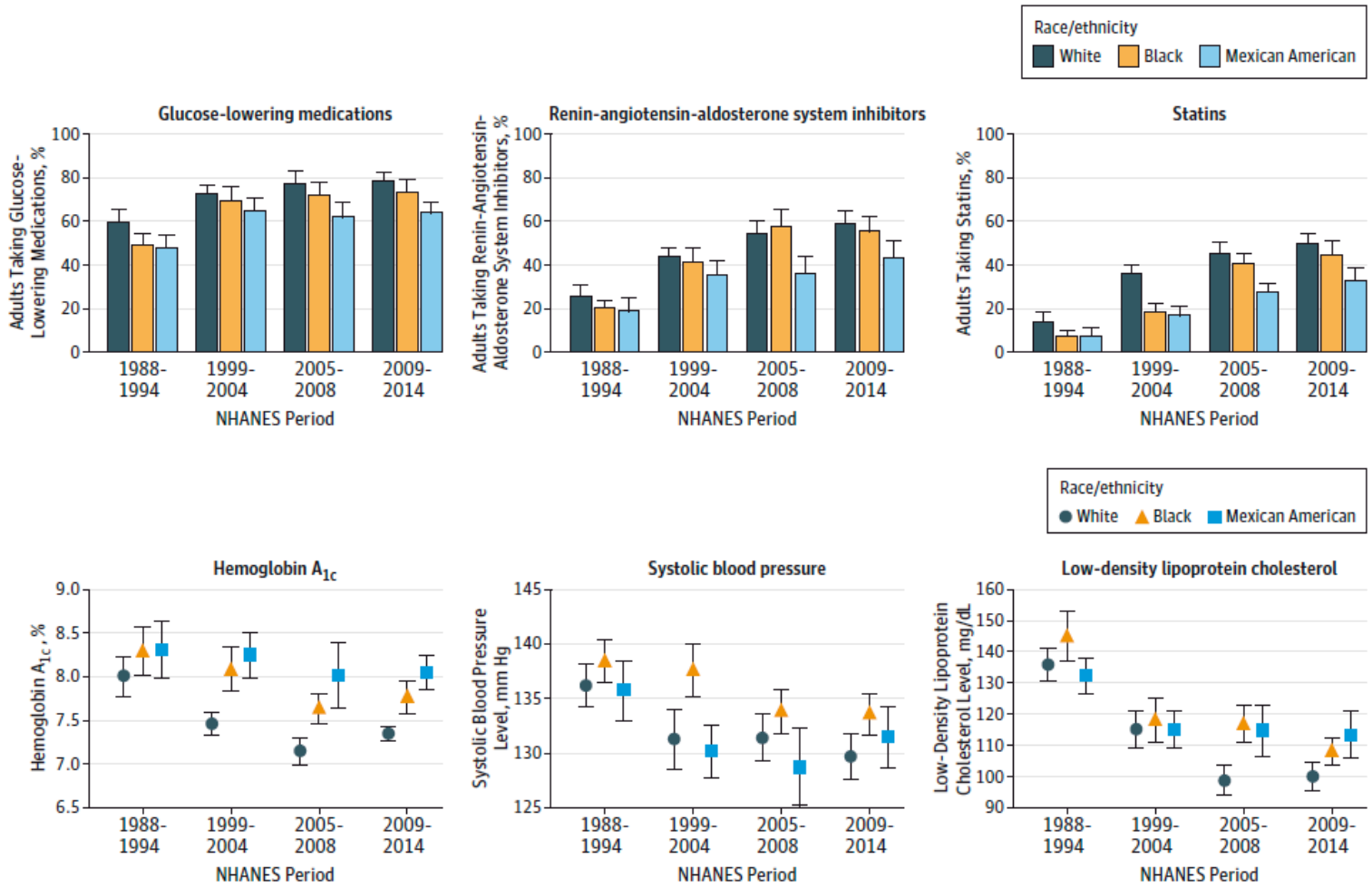
Diabetes as a cause of end-stage renal disease (ESRD)



2021 US Renal Data System. *Am J Kidney Dis.* 2022;79:S178–S575

Temporal trends in diabetes management

The National Health and Nutrition Examination Survey (NHANES), 1988–2014

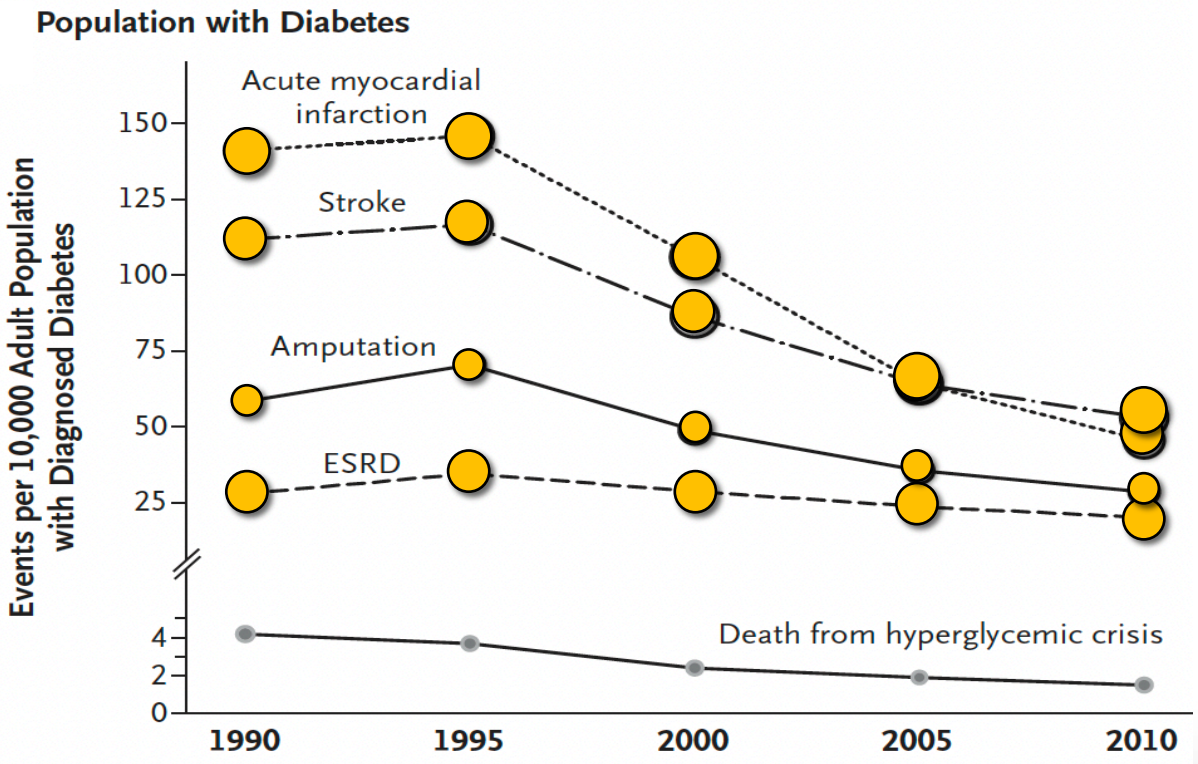


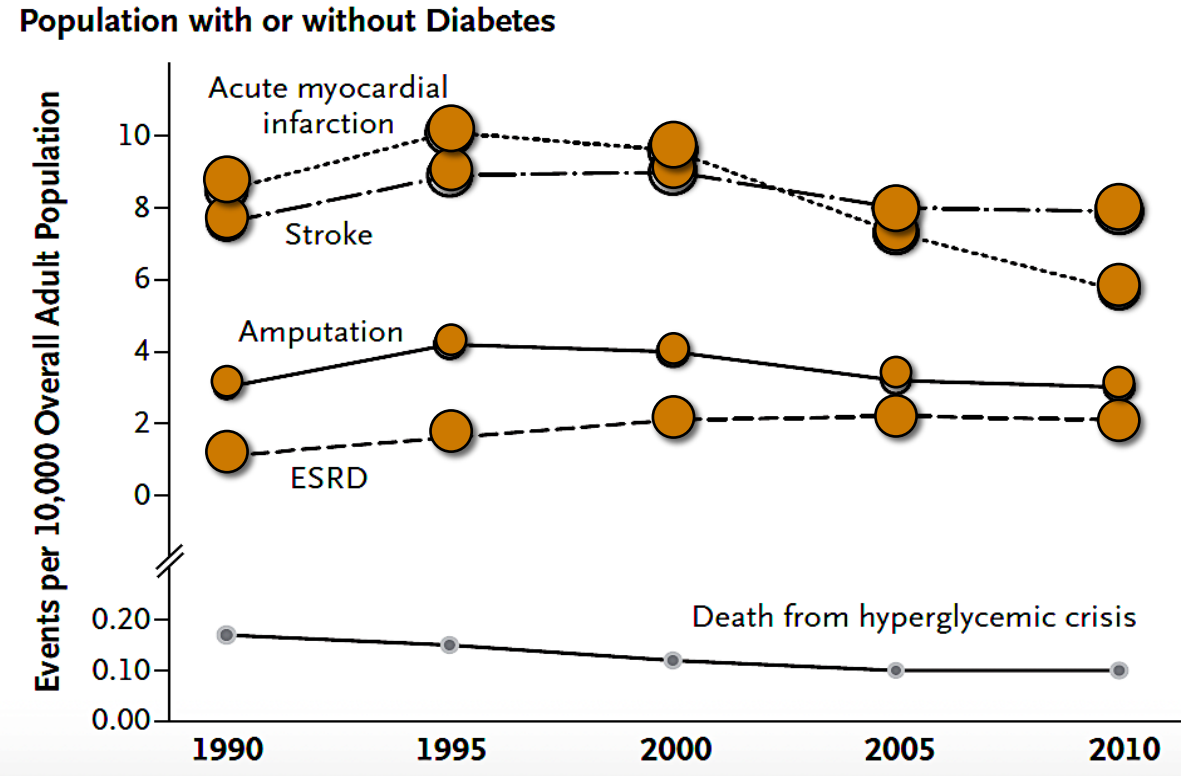
Medication use and clinical targets among US adults with diagnosed diabetes

Afkarian M et al. *JAMA*. 2016;316:602–610

Temporal trends in major diabetic complications

The National Health Interview Survey, National Hospital Discharge Survey, U.S. Renal Data System, and U.S. National Vital Statistics System



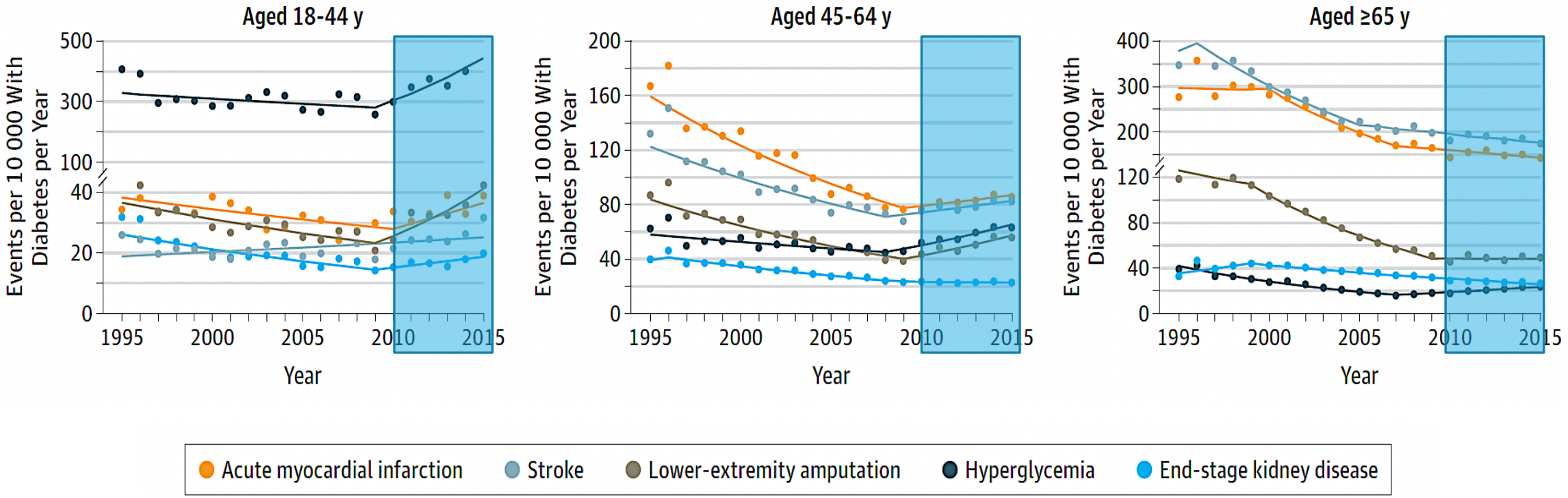


Population	AMI	Stroke	Amputation	ESRD	Death from hyperglycemic crisis
with diabetes	-68%	-53%	-51%	-28%	-64%
with or without diabetes	-32%	+3.4%	-0.5%	+91%	-42%

Gregg EW et al. *N Engl J Med*. 2014;370:1514–1523

Temporal trends in major diabetic complications

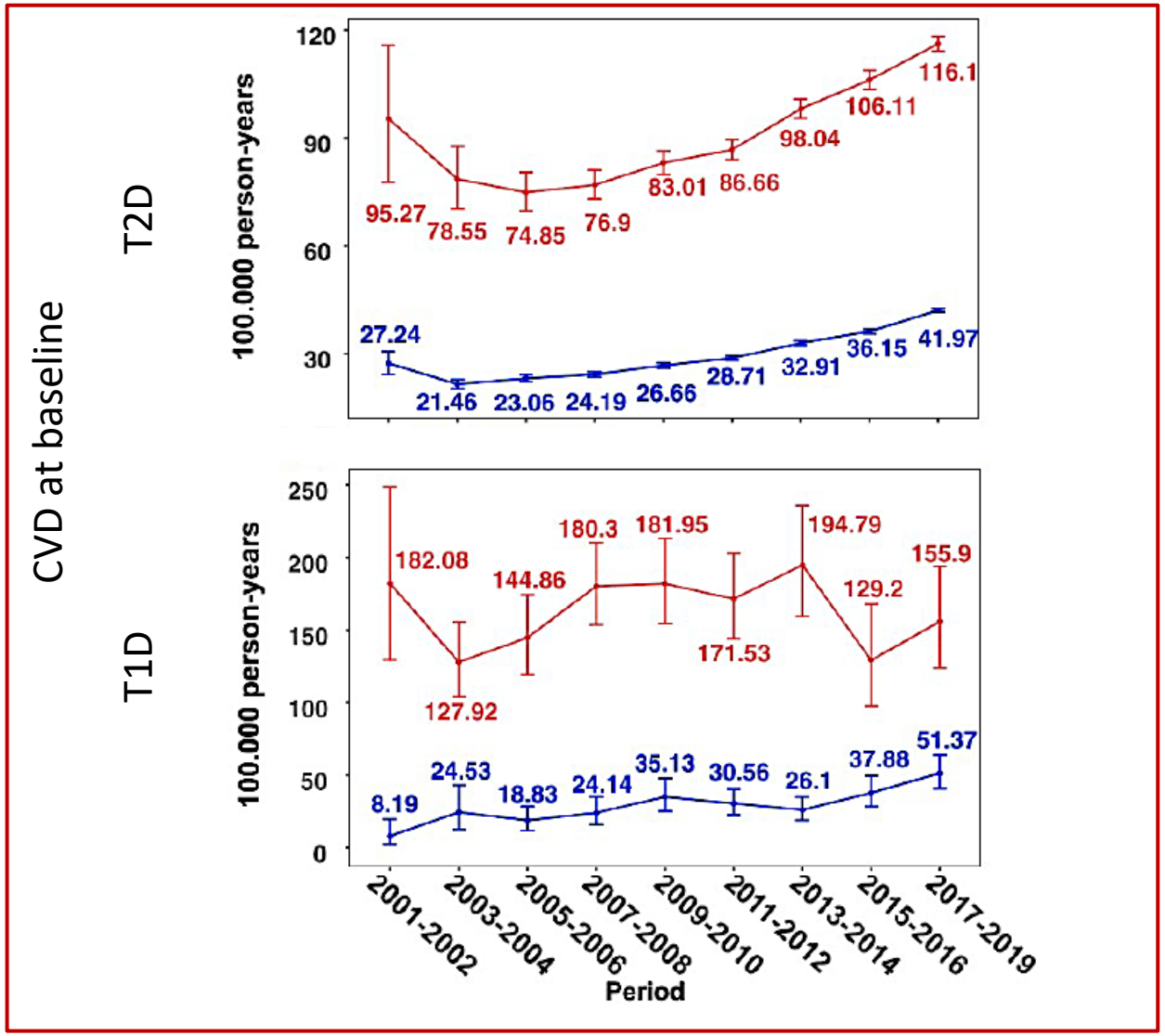
The US Centers for Disease Control and Prevention

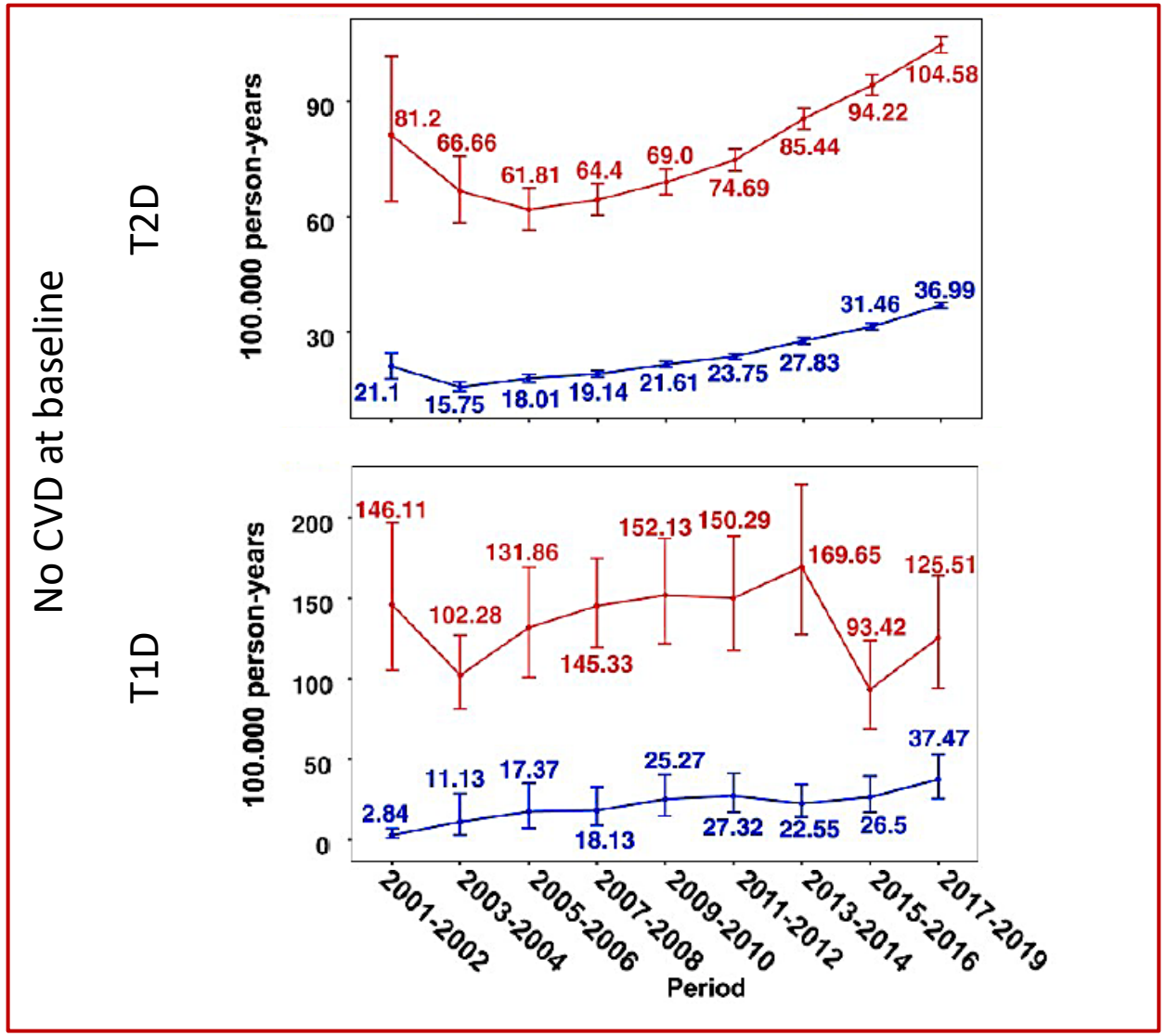


Gregg EW et al. *JAMA*. 2019;321:1867–1868

Temporal trends in end-stage renal disease (ESRD) in people with and without diabetes

The Swedish National Diabetes Register

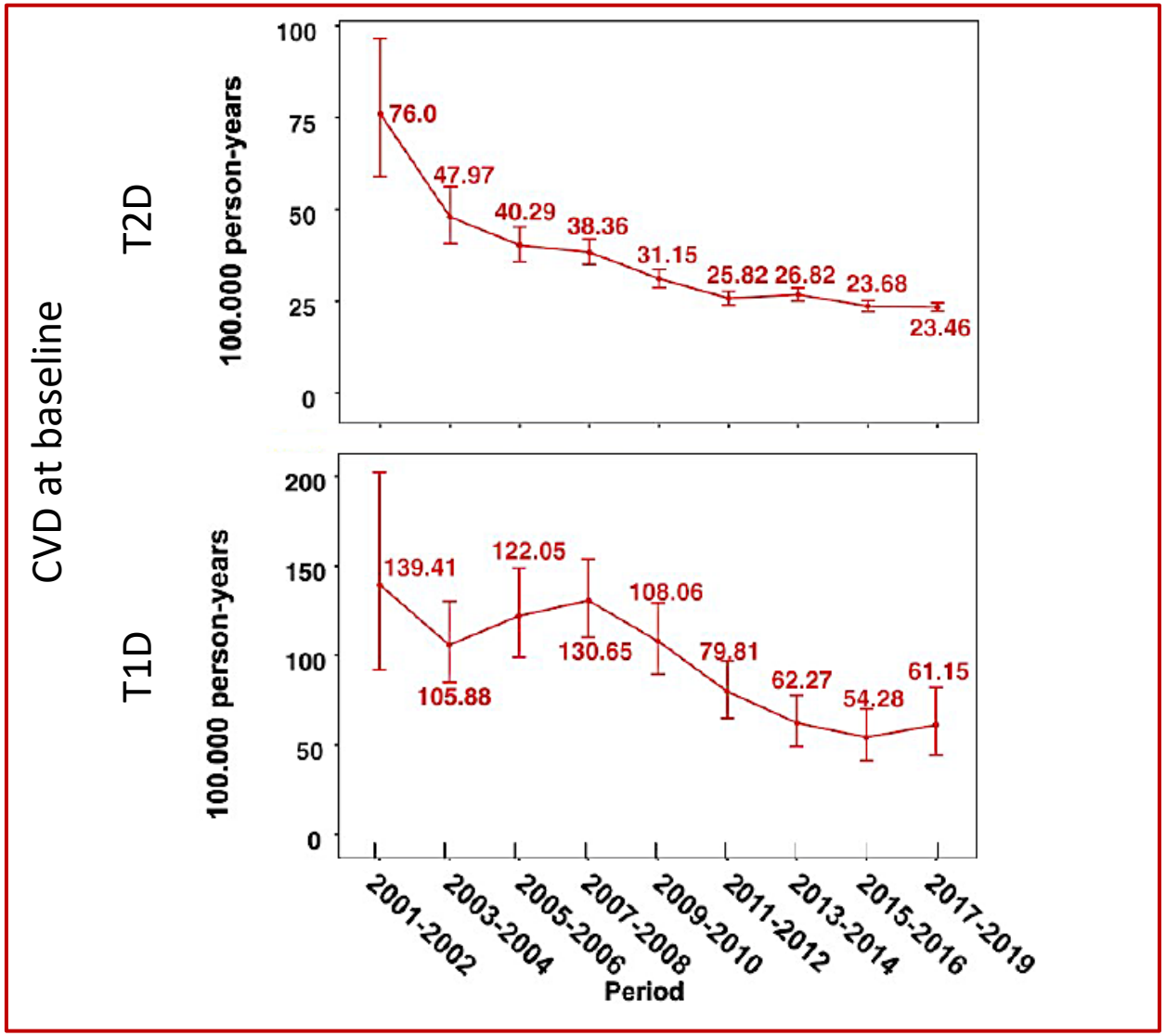


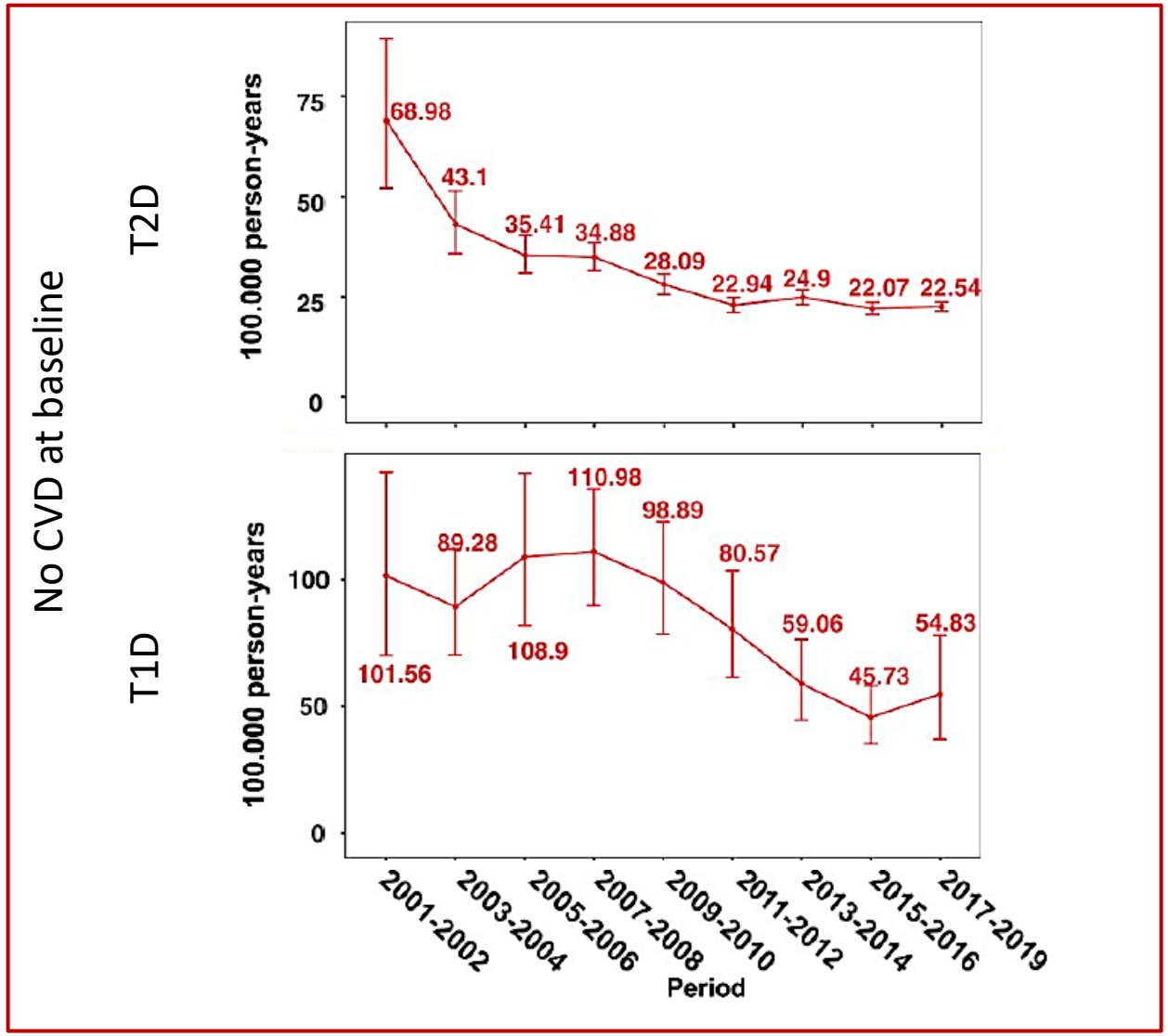


Halminen WA et al. *J Diabetes Care.* 2022;45:2326–2335

Temporal trends in chronic kidney disease (CKD) in people with diabetes

The Swedish National Diabetes Register

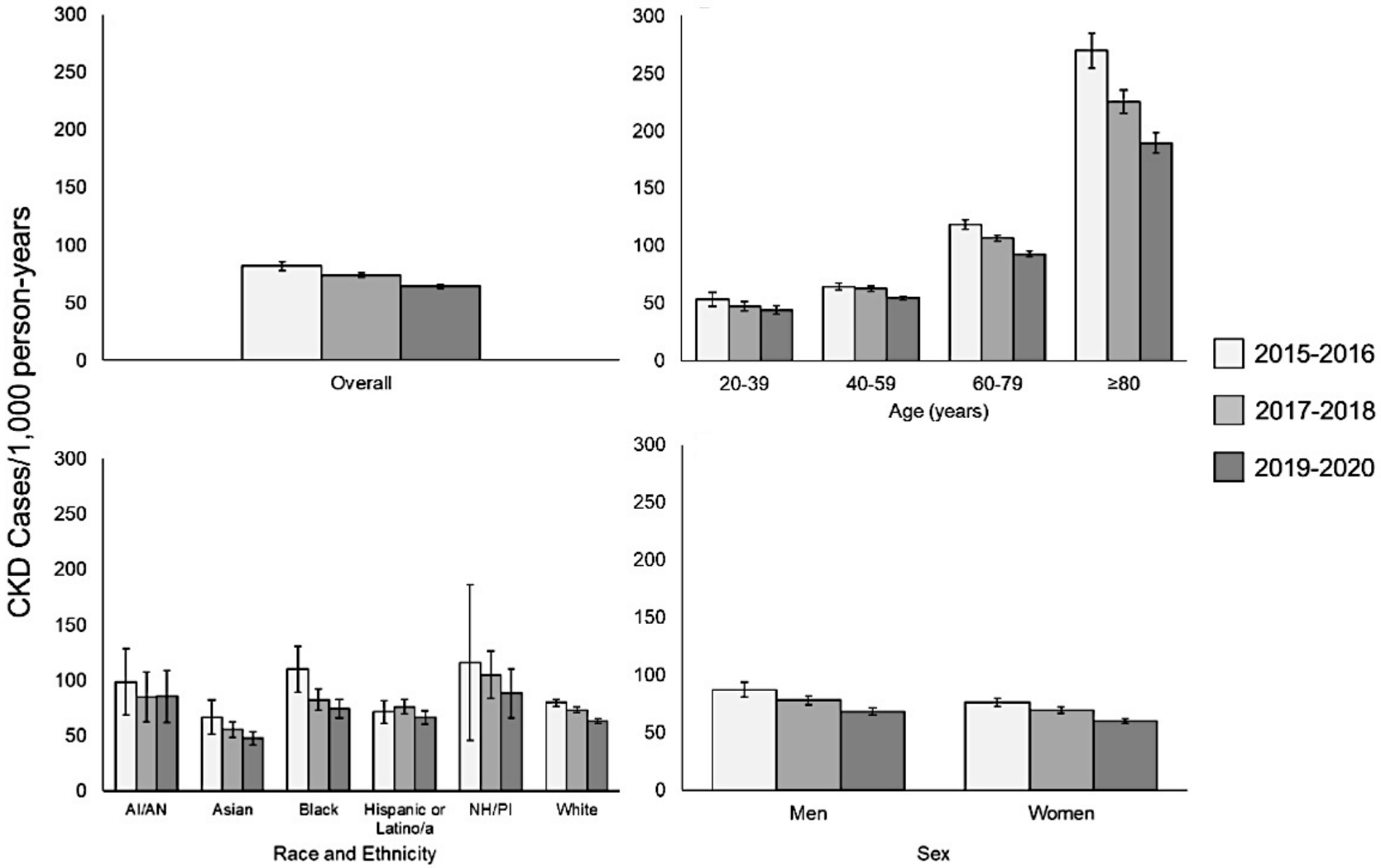




Halminen WA et al. *J Diabetes Care.* 2022;45:2326–2335

Temporal trends in chronic kidney disease (CKD) in people with diabetes

The Center for Kidney Disease Research, Education, and Hope (CURECKD) registry

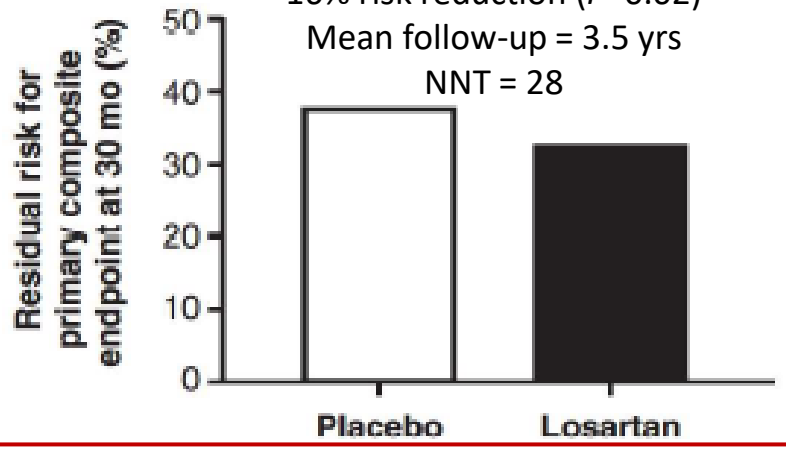


Tuttle KR et al. *New Engl J Med.* 2022;387:1430–1431

Residual renal risk after therapy with renoprotective drugs

The Reduction of Endpoints in NIDDM with the Angiotensin II Antagonist Losartan (RENAAL) trial

16% risk reduction (*P*=0.02)
Mean follow-up = 3.5 yrs
NNT = 28

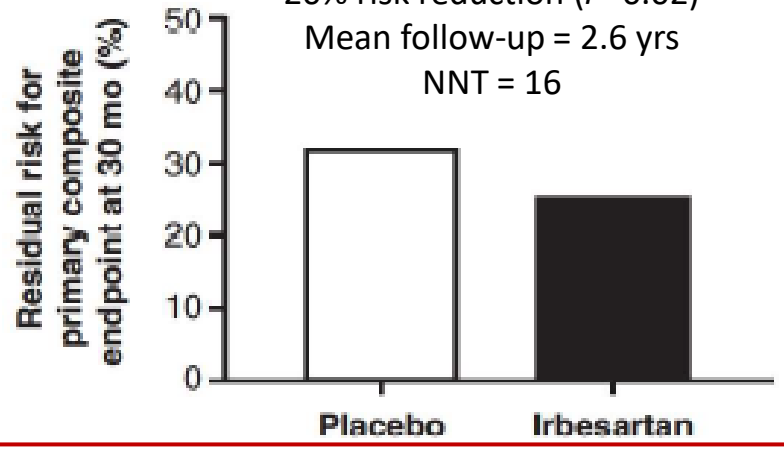


ARBs

Doubling Screat, ESKD or death

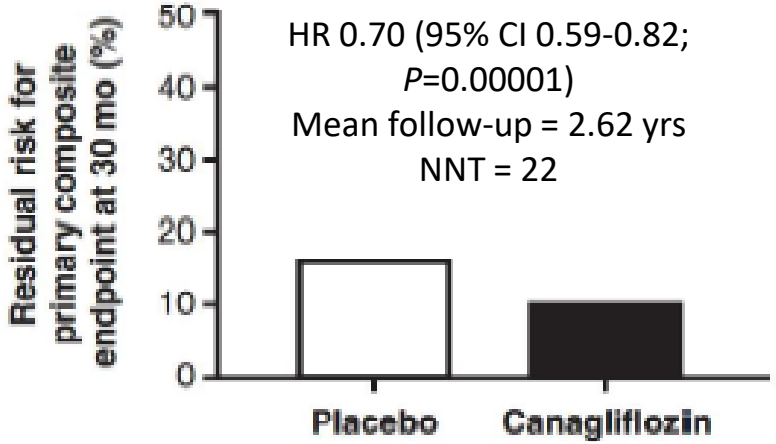
The Irbesartan Diabetic Nephropathy Trial (IDNT)

20% risk reduction (*P*=0.02)
Mean follow-up = 2.6 yrs
NNT = 16



The Canagliflozin and Renal Events in Diabetes with Established Nephropathy Clinical Evaluation (CREDENCE) trial

HR 0.70 (95% CI 0.59-0.82; *P*=0.00001)
Mean follow-up = 2.62 yrs
NNT = 22

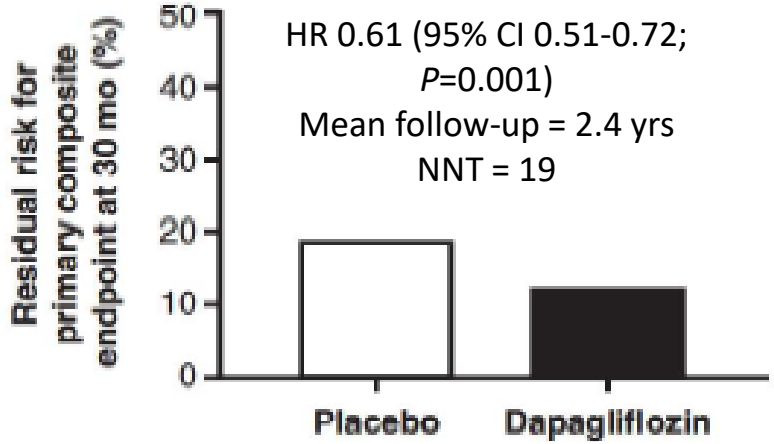


SGLT-2 inhib

Doubling Screat, ESKD or CV/renal death

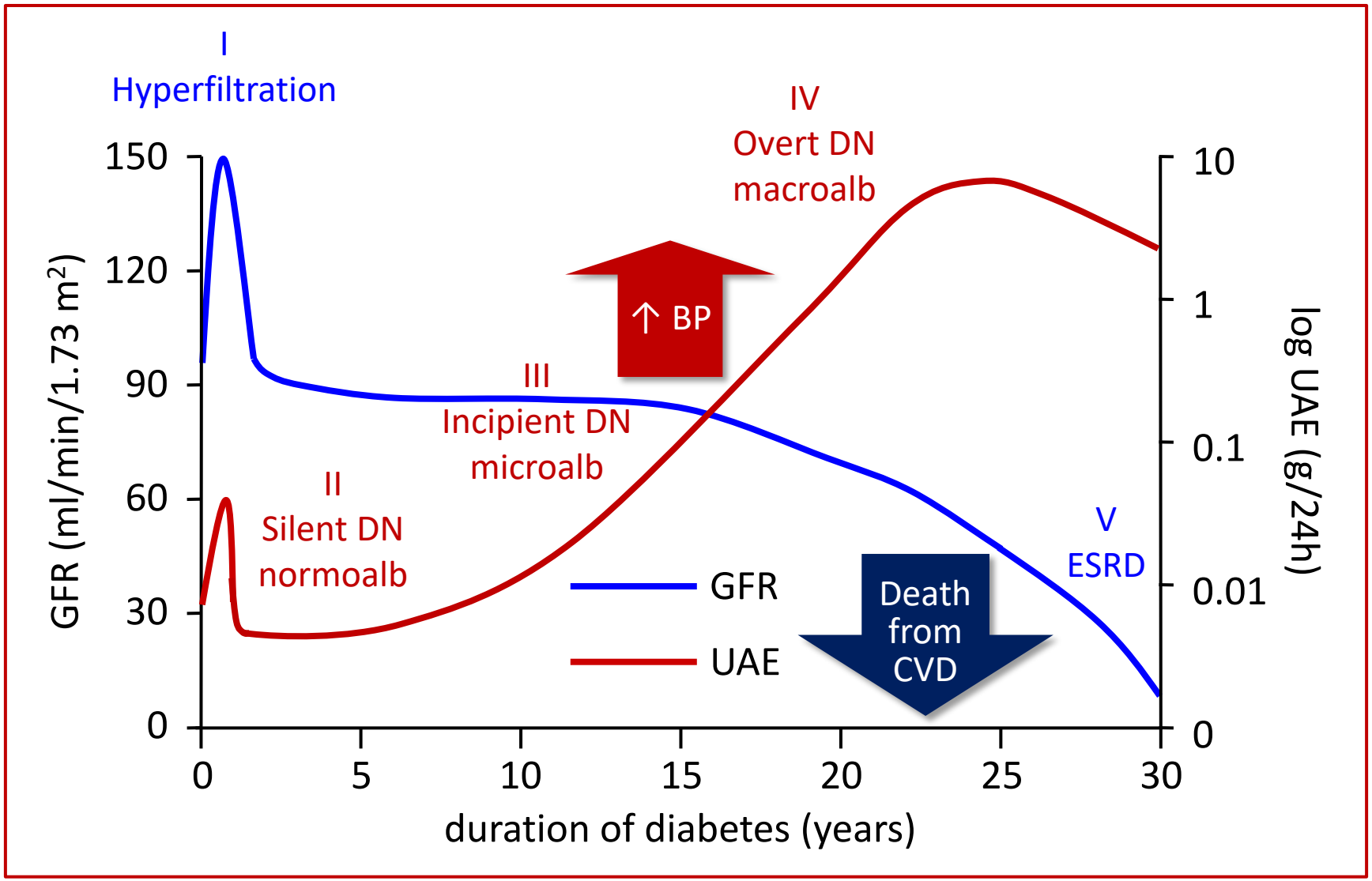
The Dapagliflozin and Prevention of Adverse Outcomes in Chronic Kidney Disease (DAPA-CKD) trial

HR 0.61 (95% CI 0.51-0.72; *P*=0.001)
Mean follow-up = 2.4 yrs
NNT = 19



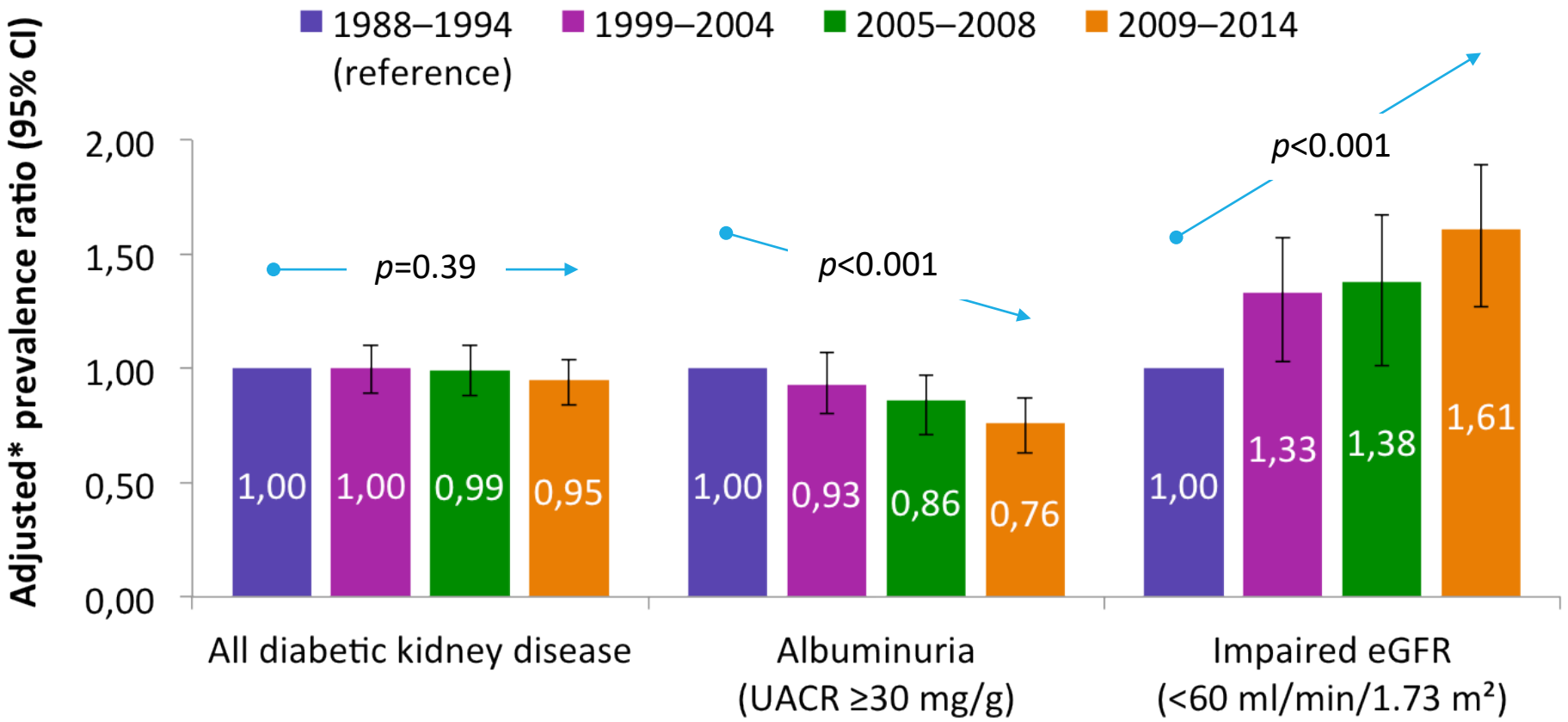
Chaudhuri A et al. *Diabetes Obes Metab.* 2022;24:365–376

The natural history of diabetic kidney disease (DKD)



Temporal trends in albuminuria and eGFR in people with diabetes

The National Health and Nutrition Examination Survey (NHANES) 1988–2014



*Adjusted for age, sex, and race/ethnicity. p-values are for trend

Afkarian M et al. *JAMA*. 2016;316:602–610

Temporal trends in albuminuria and eGFR in people with diabetes

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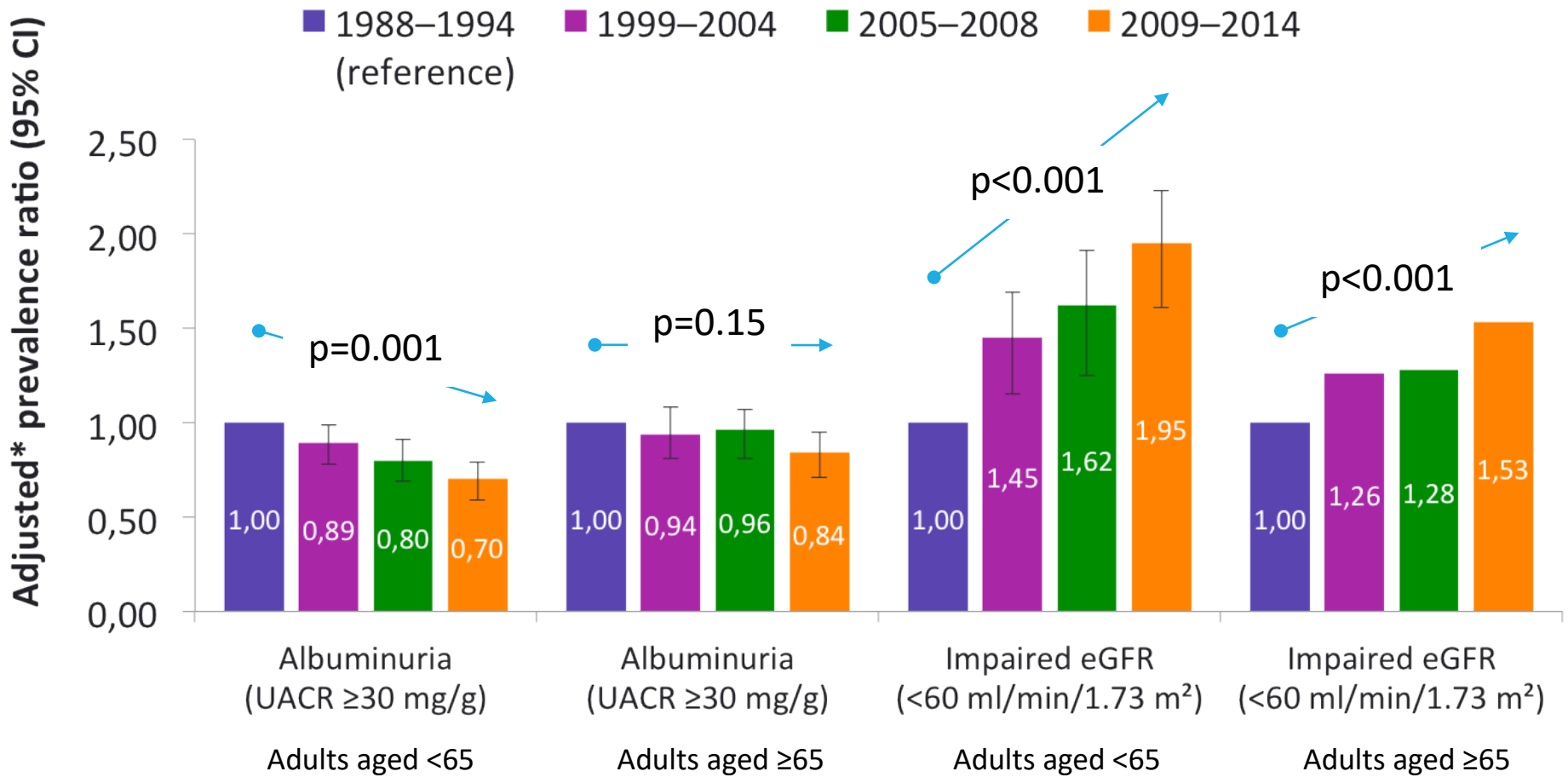


*Adjusted for age, sex, and race/ethnicity. p-values are for trend

Afkarian M et al. *JAMA*. 2016;316:602–610

Remission/regression of albuminuria in people with diabetes

The Joslin Study of the Natural History of Microalbuminuria

386 T1D patients with persistent microalbuminuria

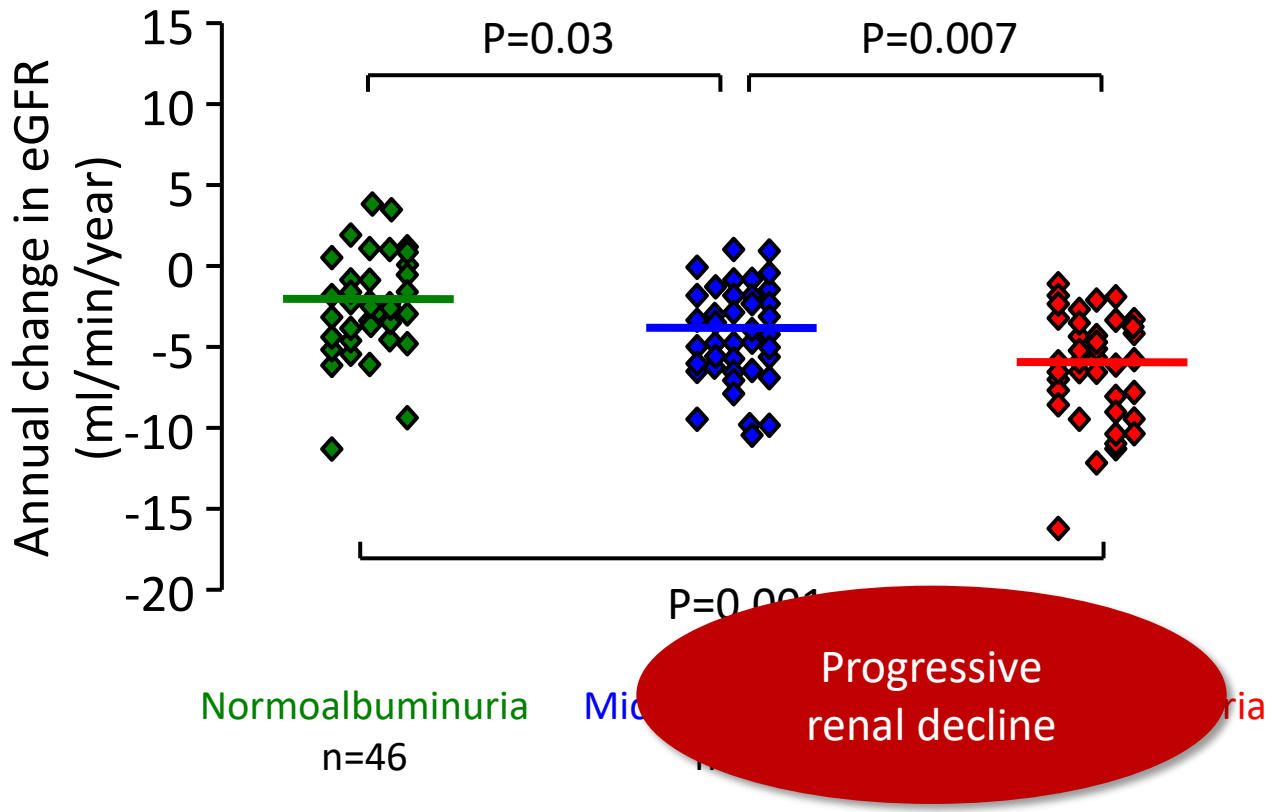
Status, n (%)	Initial evaluation period	1st evaluation period	2nd evaluation period	3rd evaluation period
Proteinuria	-	24 (7)	37 (13)	33 (15)
Microalbuminuria	386 (100)	191 (54)	141 (49)	99 (45)
Normoalbuminuria	-	136 (39)	110 (38)	88 (40)
Tot		51 (100)	288 (100)	220 (100)

Nonalbuminuric renal impairment

Afte ter length of potential follow-up in the incidence cohort, the completeness of follw-up was 91%, 83%, and 77% in the 1st, 2nd, and 3˚ period, respectively.

The Steno-2 Study

151 T2D patients with persistent microalbuminuria

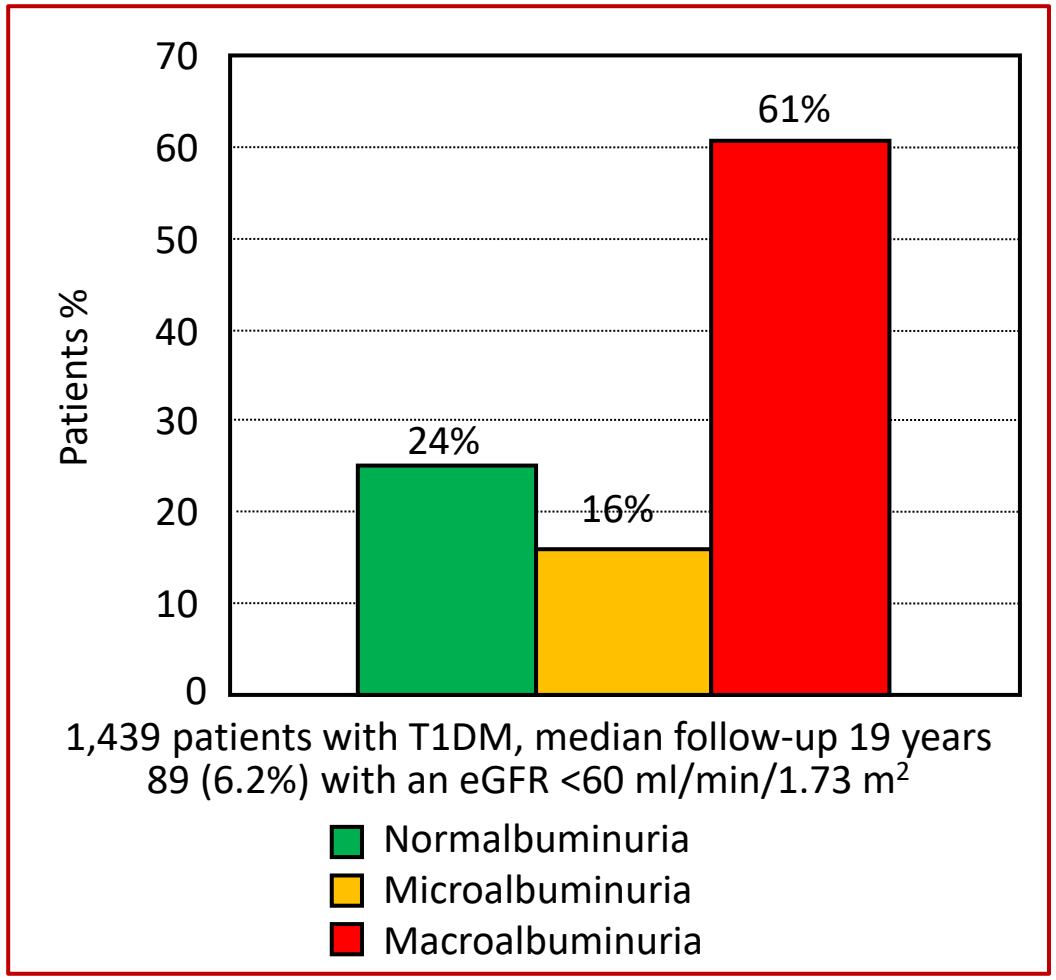


Perkins BA et al. *N Engl J Med.* 2003;48:2285–2293

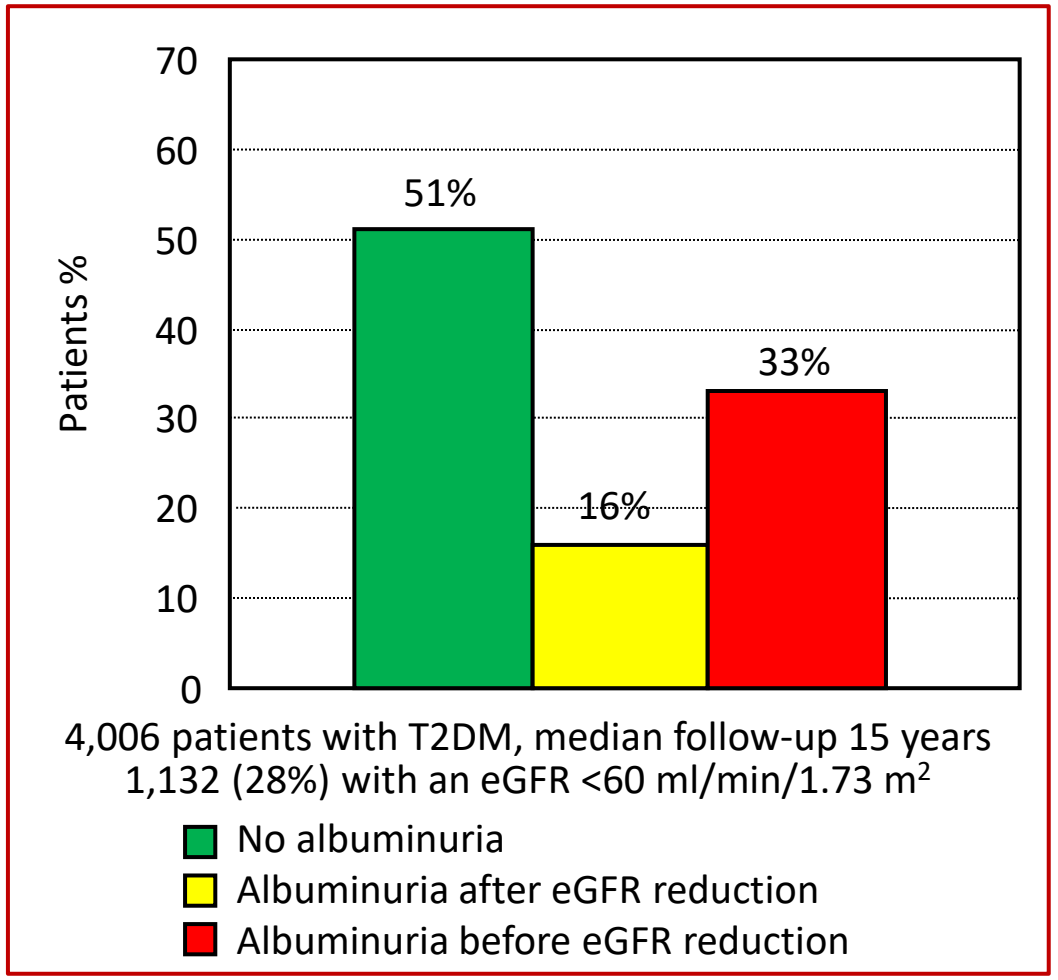
Gaede P et al. *Nephrol Dial Transplant.* 2004;19:2784–2788

Nonalbuminuric renal impairment in people with diabetes

The Diabetes Control and Complications Trial (DCCT) / Epidemiology of Diabetes Interventions and Complications (EDIC)



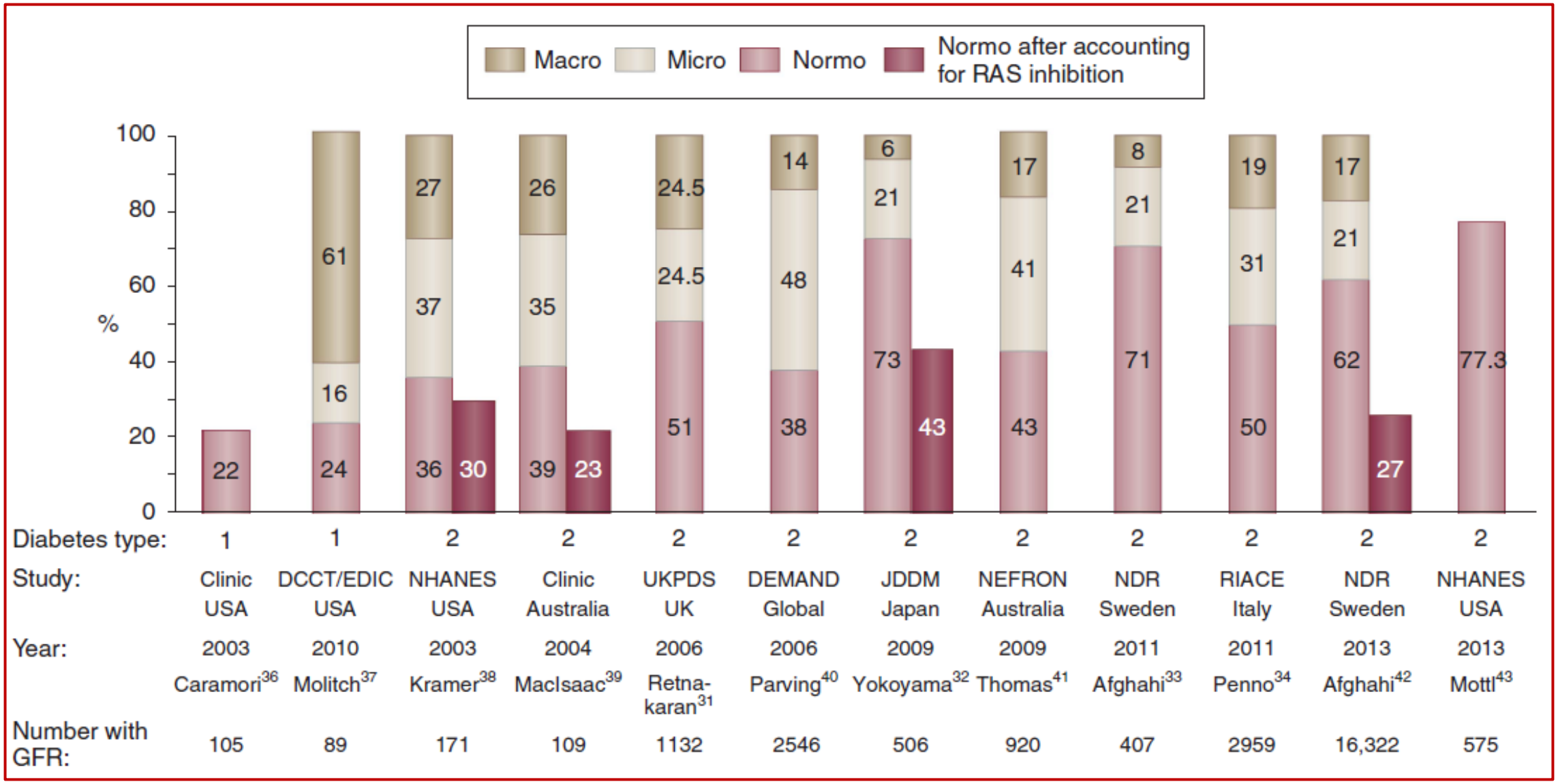
The United Kingdom Prospective Diabetes Study (UKPDS)



Molitch ME et al. *Diabetes Care.* 2010;33:1536–1543

Retnakaran R et al. *Diabetes.* 2006;55:1832–1839

Nonalbuminuric renal impairment in people with diabetes



Diabetes type:	1	1	2	2	2	2	2	2	2	2	2	2
Study:	Clinic USA	DCCT/EDIC USA	NHANES USA	Clinic Australia	UKPDS UK	DEMAND Global	JDDM Japan	NEFRON Australia	NDR Sweden	RIACE Italy	NDR Sweden	NHANES USA
Year:	2003	2010	2003	2004	2006	2006	2009	2009	2011	2011	2013	2013
	Caramori[36]	Molitch[37]	Kramer[38]	MacIsaac[39]	Retna-karan[31]	Parving[40]	Yokoyama[32]	Thomas[41]	Afghahi[33]	Penno[34]	Afghahi[42]	Mottl[43]
Number with GFR:	105	89	171	109	1132	2546	506	920	407	2959	16,322	575

MacIsaac RJ et al. *Kidney Int.* 2014;86:50–57

Progressive renal decline in people with diabetes

The Joslin Kidney Studies

eGFR decline ml/min/year	Normoalbuminuria % (n)	Microalbuminuria % (n)	Macroalbuminuria % (n)	Total % (n)
T1D				
<2.9	91	78	49	81
3-4.9	6	11	16	8
5-9.9	2	7	19	7
≥10	1	4	16	4
Total	100 (932)	100 (525)	100 (275)	100 (1,732)
T2D				
<2.9	80	67	32	72
3-4.9	13	18	17	15
5-9.9	6	12	30	10
≥10	1	3	21	3
Total	100 (681)	100 (418)	100 (82)	100 (1,181)

Krolewski AS et al. *Kidney Int.* 2017;91:1300–1311

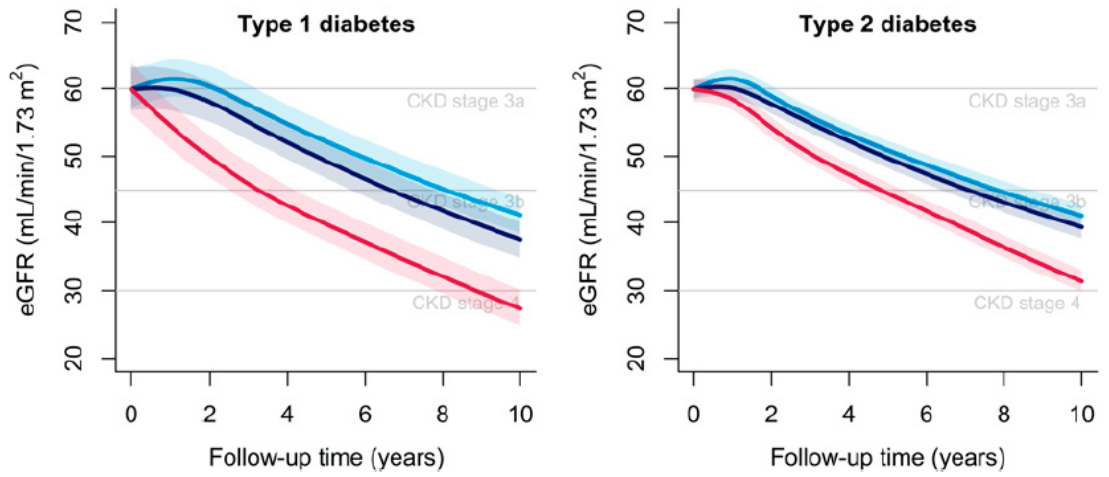
eGFR decline according to baseline albuminuria

The Steno Diabetes Center database

Type 1 diabetes

eGFR loss (mL/min/1.73 m^2)

Normo	1.9
Micro	2.3
Macro	3.3



Type 2 diabetes

eGFR loss (mL/min/1.73 m^2)

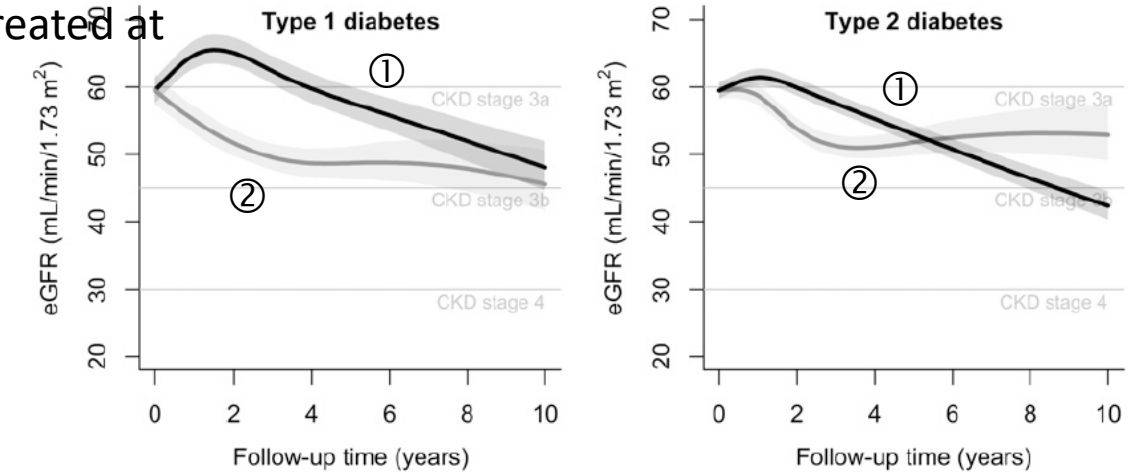
Normo	1.9
Micro	2.1
Macro	3.0

treated at

Type 1 diabetes

Trajectory 1: 86%

Trajectory 2: 14%



Type 2 diabetes

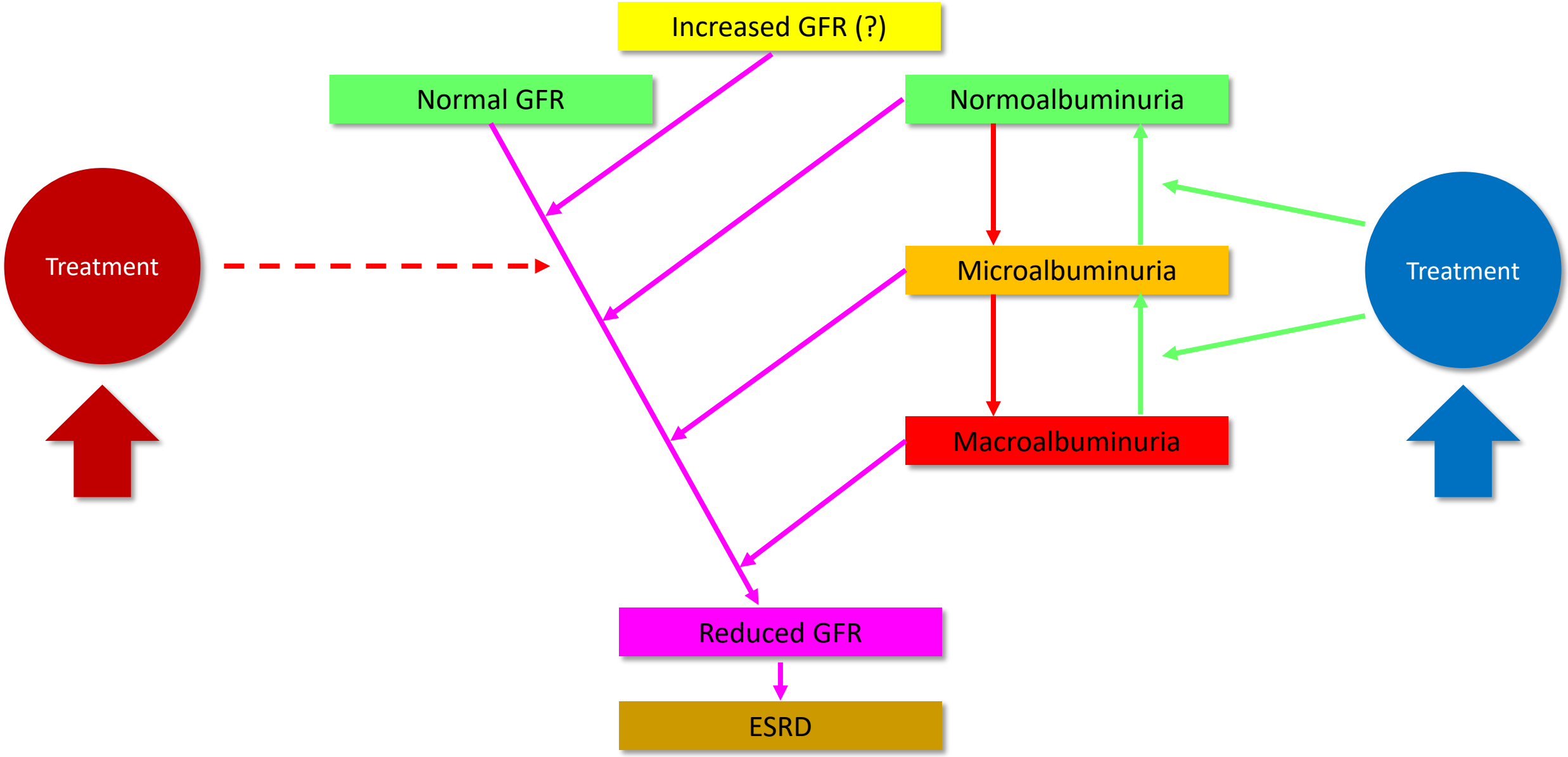
Trajectory 1: 90%

Trajectory 2: 10%

3,343 adults with type 1 diabetes (n=935) or type 2 diabetes (n=1,984) from 01.01.2001 to 31.05.2017 with at least one eGFR <60 mL/min/1.73 m^2

Vistisen D et al. *Diabetes Care.* 2019;42:1886–1894

Albuminuric and nonalbuminuric pathways to end-stage renal disease (ESRD)



Pugliese G et al. *Nutr Metab Cardiovasc Dis* 2019;29:1127–1150

Classification of chronic kidney disease (CKD)

Kidney Disease: Improving Global Outcomes (KDIGO)

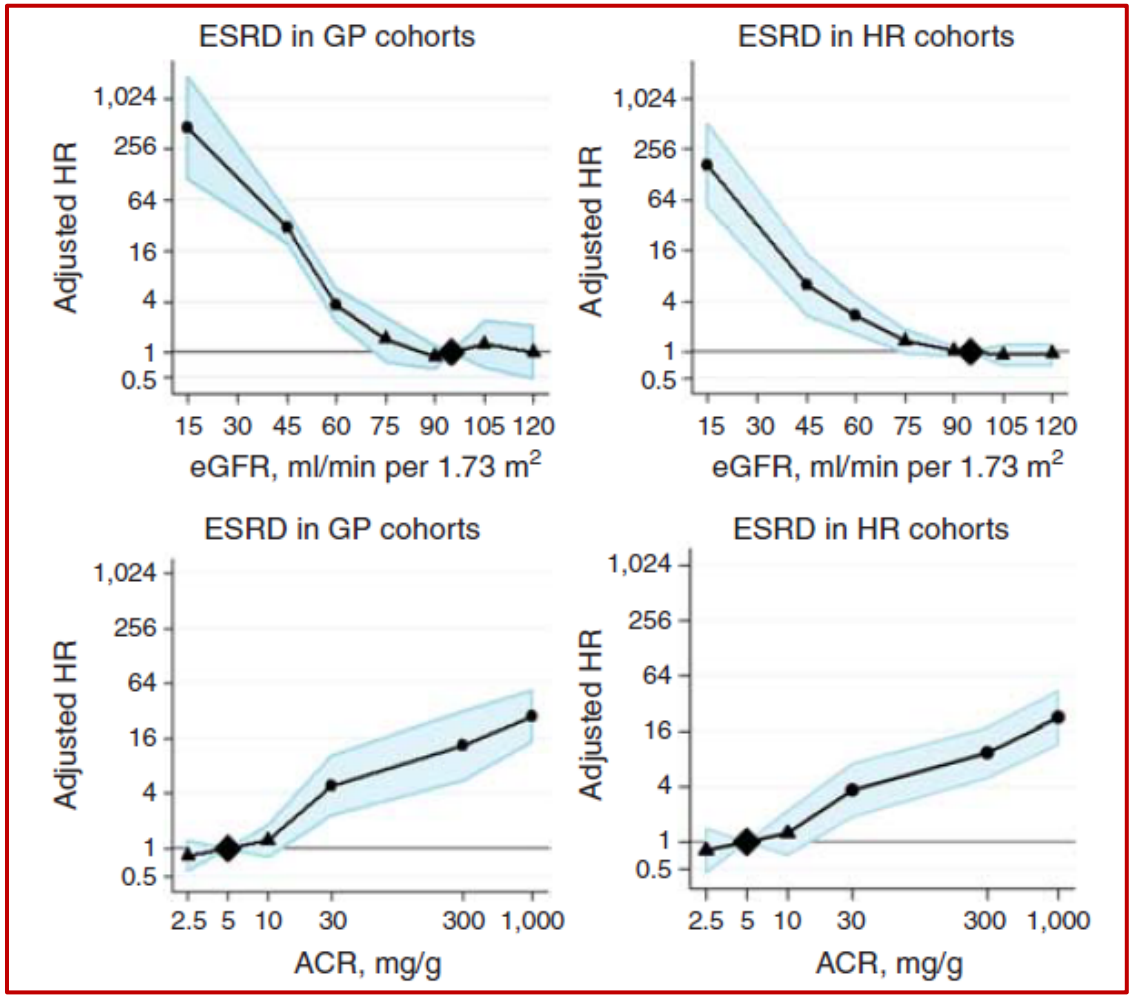
- Low-risk category
- Moderate-risk category
- High-risk category
- Very high-risk category

Estinated GFR (eGFR, ml/min/1.73 m²)				Albuminuria (ACR, mg/g creatinine)				
				A1		A2	A3	
				Normo		Micro	Macro	
				Optimal	High-normal	High	Very high	Nephrotic
				<15	15-29	30-299	300-1,999	>2,000
	G1	High	≥105					
		Optimal	90-104					
	G2	Mildly decreased	75-89					
			60-74					
	G3a	Mildly-to-moderately decreased	45-59					
	G3b	Moderately-to-severely decreased	30-44					
	G4	Severely decreased	15-29					
	G5	Kidney failure	<15					

Levey AS et al. *Kidney Int Suppl.* 2013;3:1–2150

Albuminuria, reduced eGFR and progression to end-stage renal disease (ESRD)

Collaborative meta-analysis of 9 general population (GP) and 8 high-risk (HR) cohorts



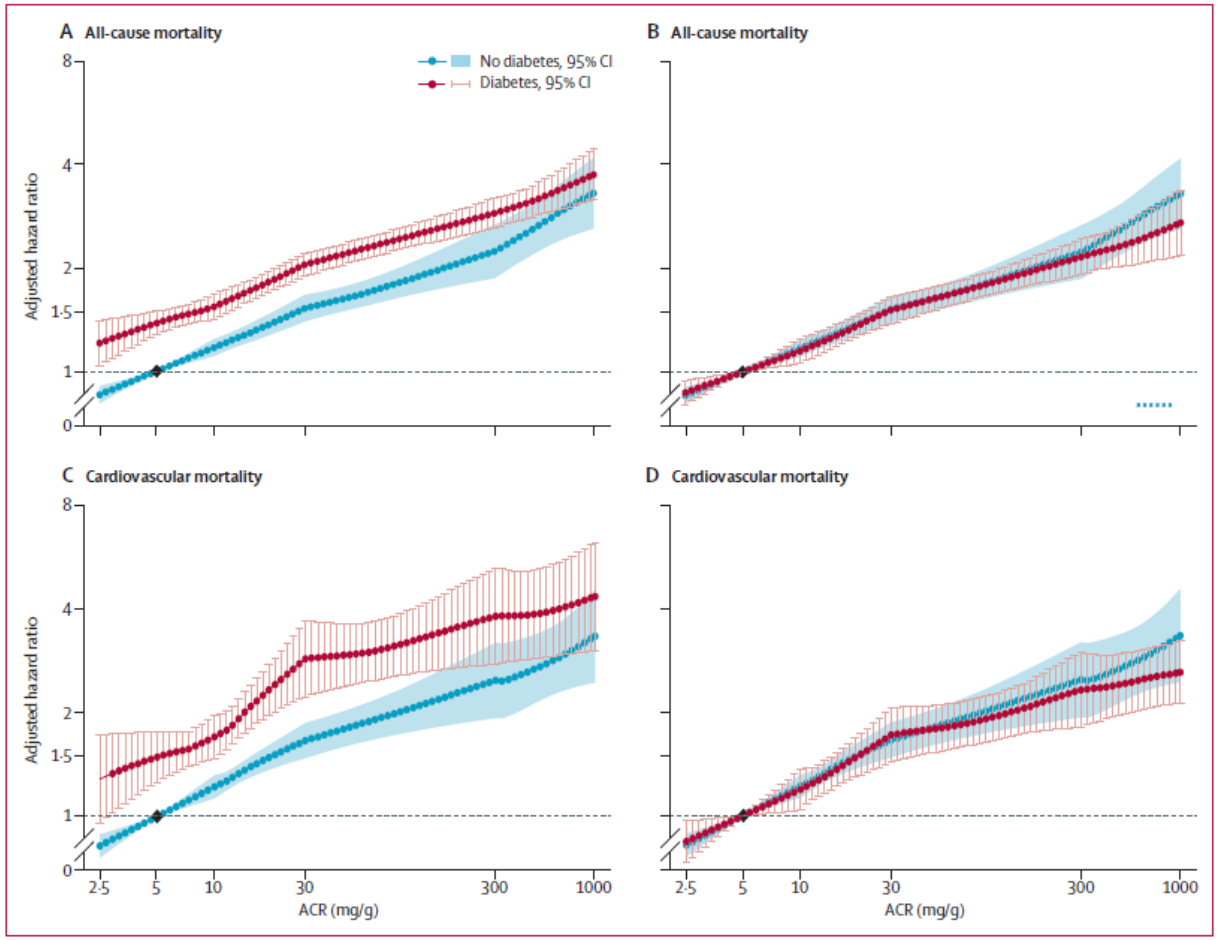
Risk for progression to ESRD according to eGFR and ACR

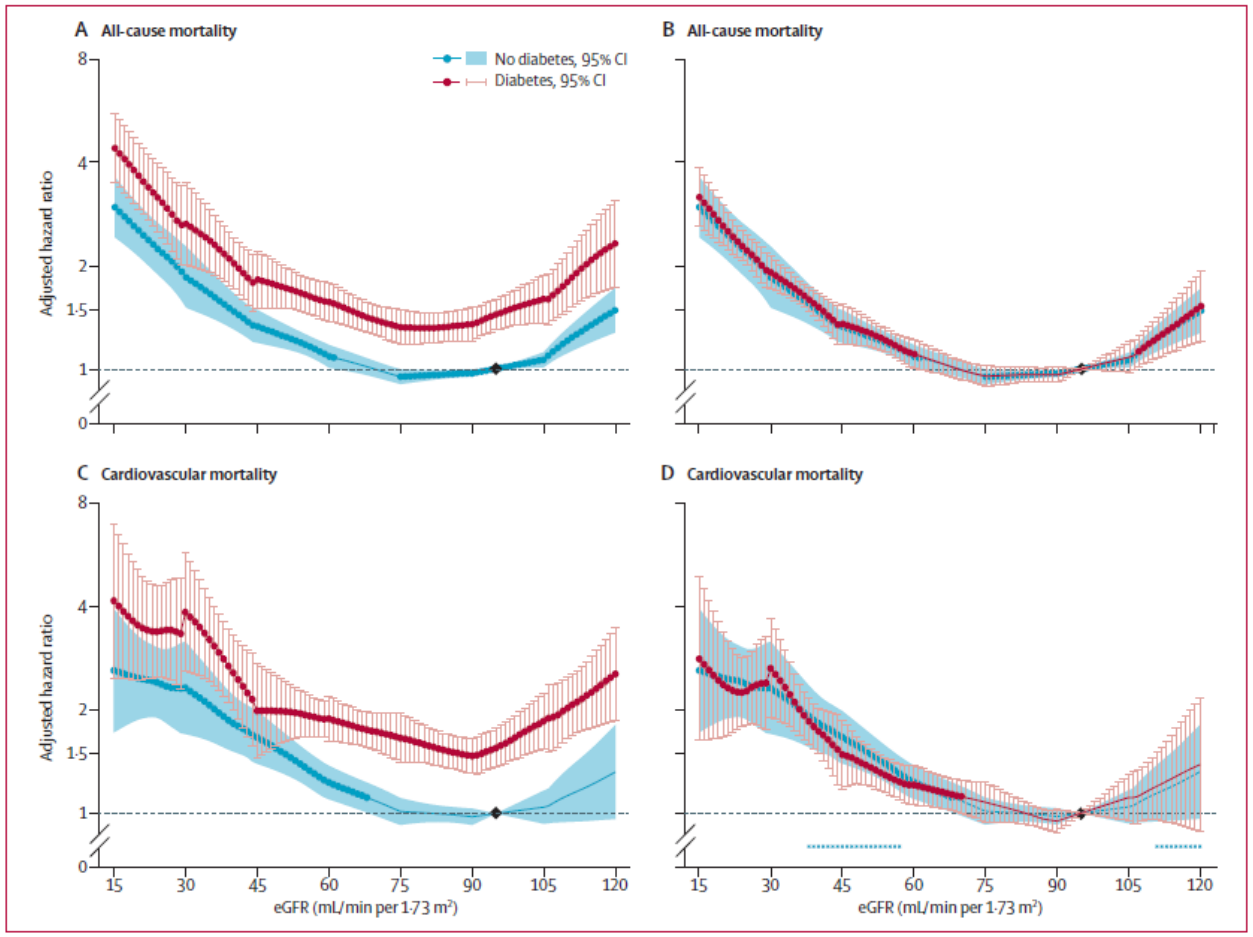
(n=845,125 general population and 173,892 high-risk; 2,179 ESRD)

Gansevoort RT et al. *Kidney Int.* 2011;80:93–104

Albuminuria, reduced eGFR and all-cause and cardiovascular mortality

Meta-analysis of from 30 general population and high CVD risk cohorts and 13 CKD cohorts



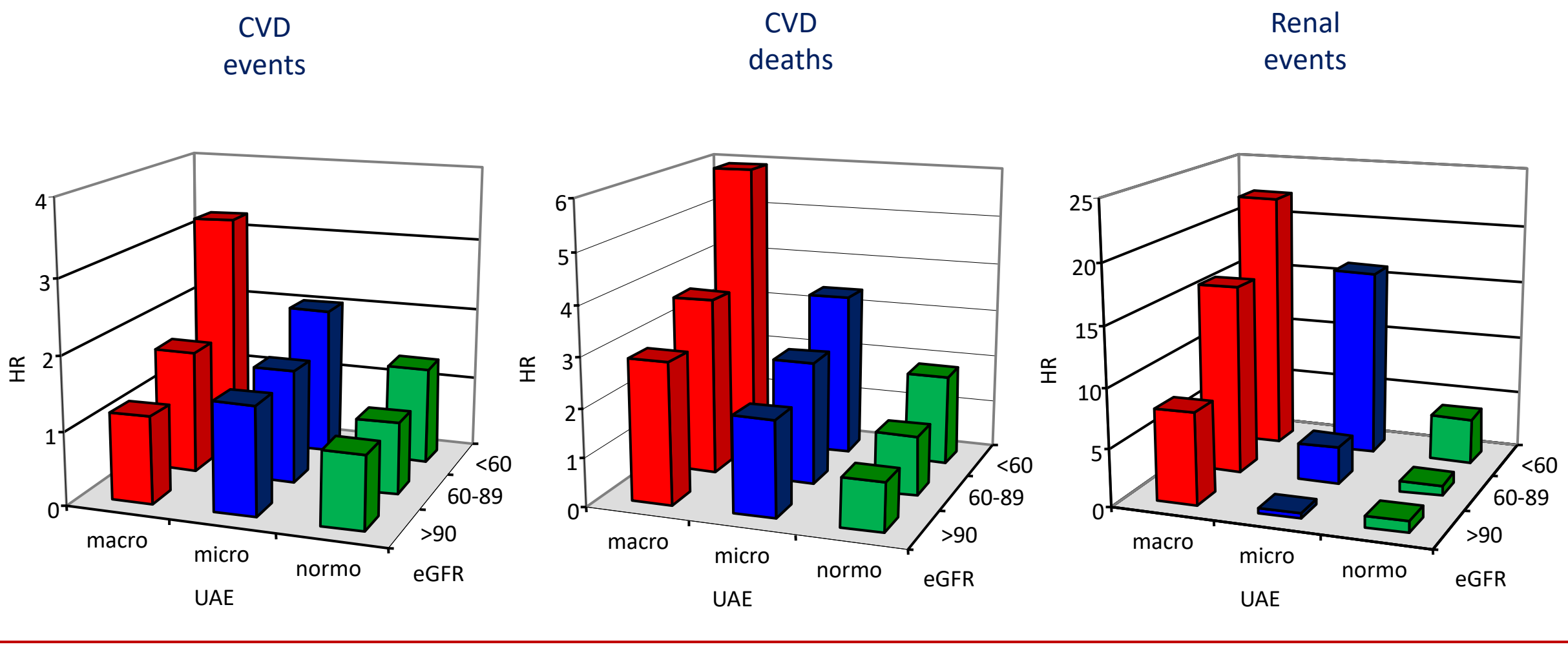


Risk for all-cause and CVD mortality according to eGFR and ACR in individuals with and without diabetes

(n=1,024,977, 128,505 with diabetes; 75,306 deaths)

Albuminuria, eGFR and cardiovascular and renal outcomes

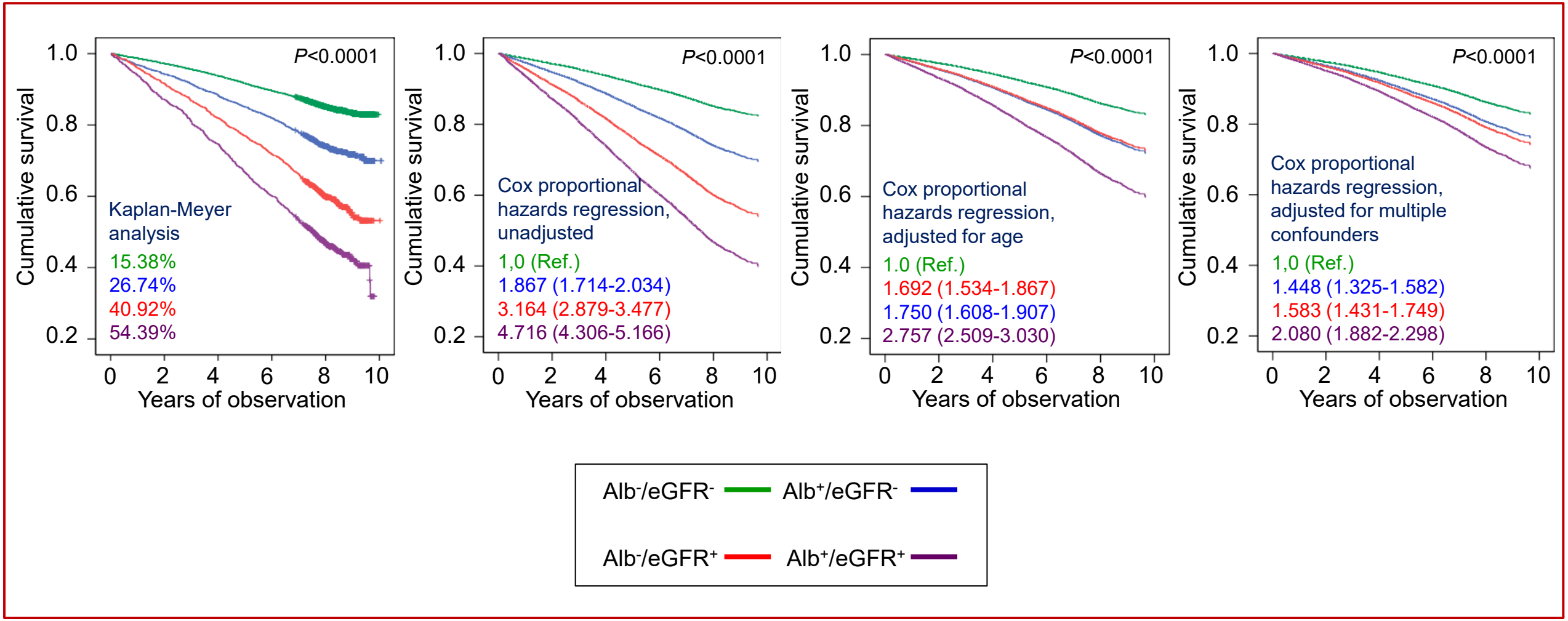
The Action in Diabetes and Vascular disease: preterAx and diamicroN-MR Controlled Evaluation (ADVANCE) Study



Ninomiya T et al. *J Am Soc Nephrol.* 2009;20:1813–1821

Association with all-cause mortality by diabetic kidney disease (DKD) phenotype

The Renal Insufficiency And Cardiovascular Events (RIACE) Italian Multicenter Study



Survival analysis according to DKD phenotype in patients with type 2 diabetes (n=15,656)

Penno G et al. *Diabetologia.* 2018;61:2277–2289

Association with all-cause mortality by KDIGO categories

The Renal Insufficiency And Cardiovascular Events (RIACE) Italian Multicenter Study

KDOGO risk categories			Albuminuria category (mg/g)			
			A1a	A1b	A2	A3
			<10	10-29	30-299	≥300
eGFR category (ml/min/1.73 m²)	G1	>90	1 (Ref.)	0.936 (0.780-1.124)	1.313 (1.079-1.599)	2.192 (1.546-3.108)
	G2a	75-89	0.798 (0.667-0.956)	1.050 (0.885-1.246)	1.310 (1.089-1.575)	2.477 (1.816-3.379)
	G2b	60-74	1.104 (0.833-1.120)	1.057 (0.878-1.273)	1.388 (1.148-1.678)	1.706 (1.232-2.362)
	G3a	45-59	1.316 (1.071-1.-617)	1.389 (1.138-1.694)	1.482 (1.218-1.804)	2.263 (1.708-3.000)
	G3b	30-44	1.847 (1.400-2.438)	2.248 (1.791-2.821)	2.089 (1.686-2.590)	2.784 (2.136-3.629)
	G4-5	<30	1.613 (0.876-2.968)	2.245 (1.494-3.374)	2.785 (2.094-3.703)	4.662 (3.590-6.054)

Cox proportional hazards regression, adjusted for multiple confounders, according to KDIGO categories in patients with type 2 diabetes (n=15,656)

Penno G et al. *Diabetologia.* 2018;61:2277–2289

Associations with cardiorenal outcomes by diabetic kidney disease (DKD) phenotype

The Action to Control Cardiovascular Risk in Diabetes (ACCORD) Study

Settings & Participants	Analysis	Results		
Action to Control Cardiovascular Risk in Diabetes ACCORD	**Exposures**			
Multicenter randomized , controlled trial	No diabetic kidney disease (DKD)			
N = 10,185	Decreased eGFR only			
Follow-up: 8.8 years	Albuminuria only			
	Decreased eGFR + albuminuria			
	• No DKD as reference group	Mortality	CVD	CKD Progression
		HR (95% CI)		
	Decreased eGFR only	**1.42** (1.14-1.78)	**1.44** (1.13-1.84)	**0.76** (0.34-1.70)
	Albuminuria only	**1.82** (1.59-2.08)	**1.88** (1.63-2.16)	**1.72** (1.27-2-34)
	Decreased eGFR + albuminuria	**2.38** (1.92-2.90)	**2.37** (1.89-2.97)	**4.52** (2.91-7.01)

Buyadaa O et al. *Diabetes Care. 2020;*43:122–129

Associations with cardiorenal outcomes by diabetic kidney disease (DKD) phenotype

The Hong Kong Diabetes Biobank

Settings & Participants	Analysis	Results
HONG KONG DIABETES BIOBANK 香港糖尿病生物庫	**Exposures**	
Multicenter, prospective, cohort study	No diabetic kidney disease (DKD)	
N = 19,025	Decreased eGFR only	
Follow-up: 3.1 years	Albuminuria only	
	Decreased eGFR + albuminuria	
	• No DKD as reference group	

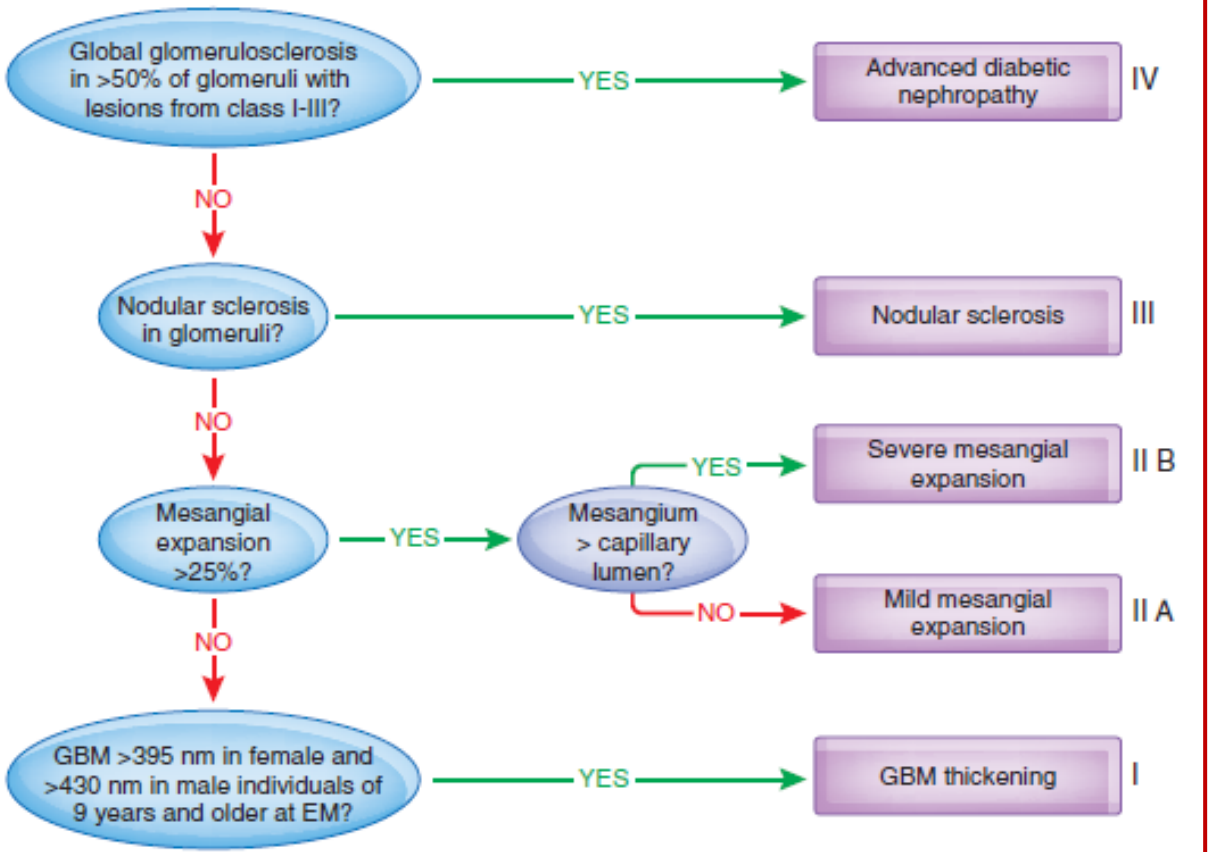
	Mortality	CVD	HHF	CKD Progression
	HR (95% CI)			
Decreased eGFR only	1.59 (1.04-2.44)	1.14 (0.88-1.48)	3.08 (1.82-5.21)	2.37 (1.63-3.43)
Albuminuria only	2.00 (1.52-2.63)	1.19 (1.02-1.40)	3.14 (2.09-4.73)	3.77 (3.05-4.66)
Decreased eGFR + albuminuria	3.26 (2.43-4.38)	1.47 (1.23-1.76)	5.50 (3.63-8.34)	14.01 (11.31-17.36)

Jin Q et al. *Am J Kidney Dis.* 2022;80:196–206.e1

Anatomic features of diabetic nephropathy

Renal Pathology Society Classification

Glomerular lesions

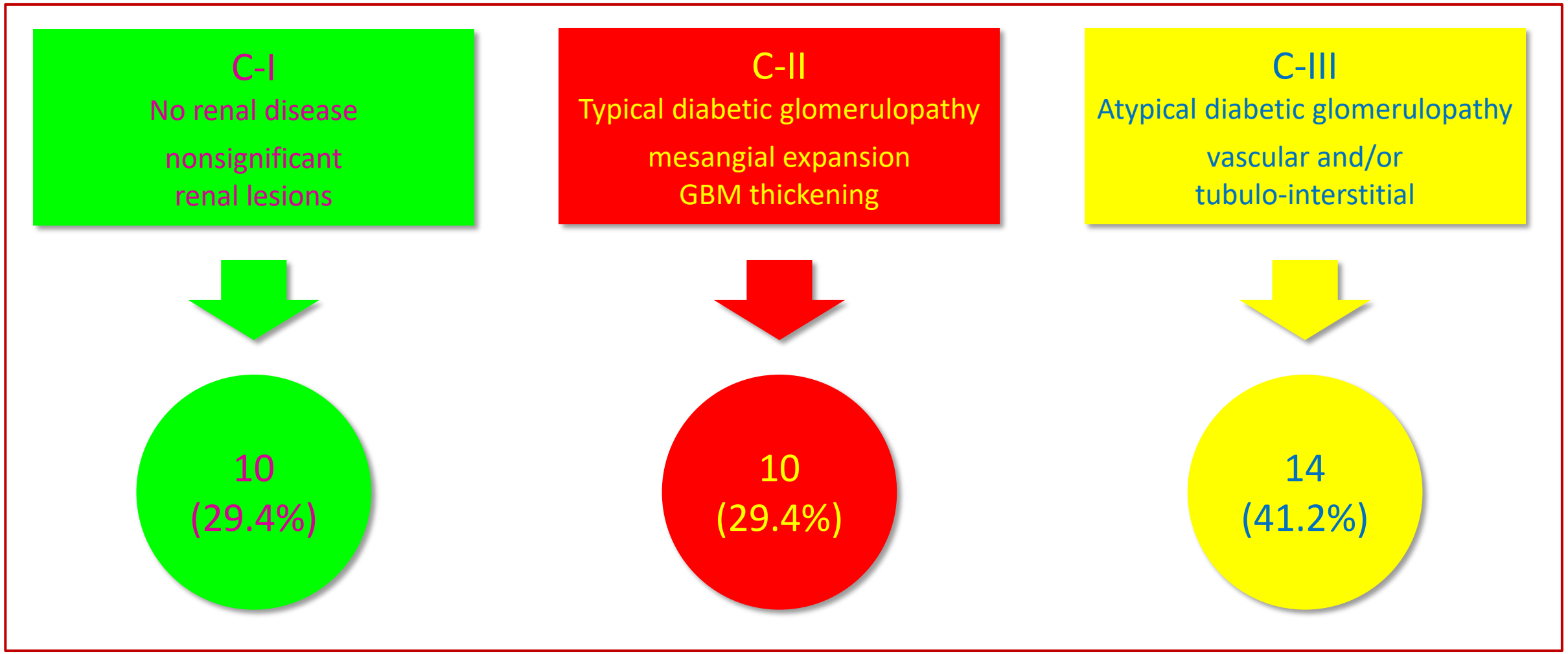


Tubulo-interstitial and vascular lesions

Lesion	Criteria	Score
Interstitial lesions		
IFTA	No IFTA	0
	<25%	1
	25% to 50%	2
	>50%	3
interstitial inflammation	Absent	0
	Infiltration only in relation to IFTA	1
	Infiltration in areas without IFTA	2
Vascular lesions		
arteriolar hyalinosis	Absent	0
	At least one area of arteriolar hyalinosis	1
	More than one area of arteriolar hyalinosis	2
presence of large vessels	–	Yes/no
arteriosclerosis (score worst artery)	No intimal thickening	0
	Intimal thickening less than thickness of media	1
	Intimal thickening greater than thickness of media	2

Tervaert TW et al. *J Am Soc Nephrol.* 2010;21:556–563

Renal pathology in patients with type 2 diabetes

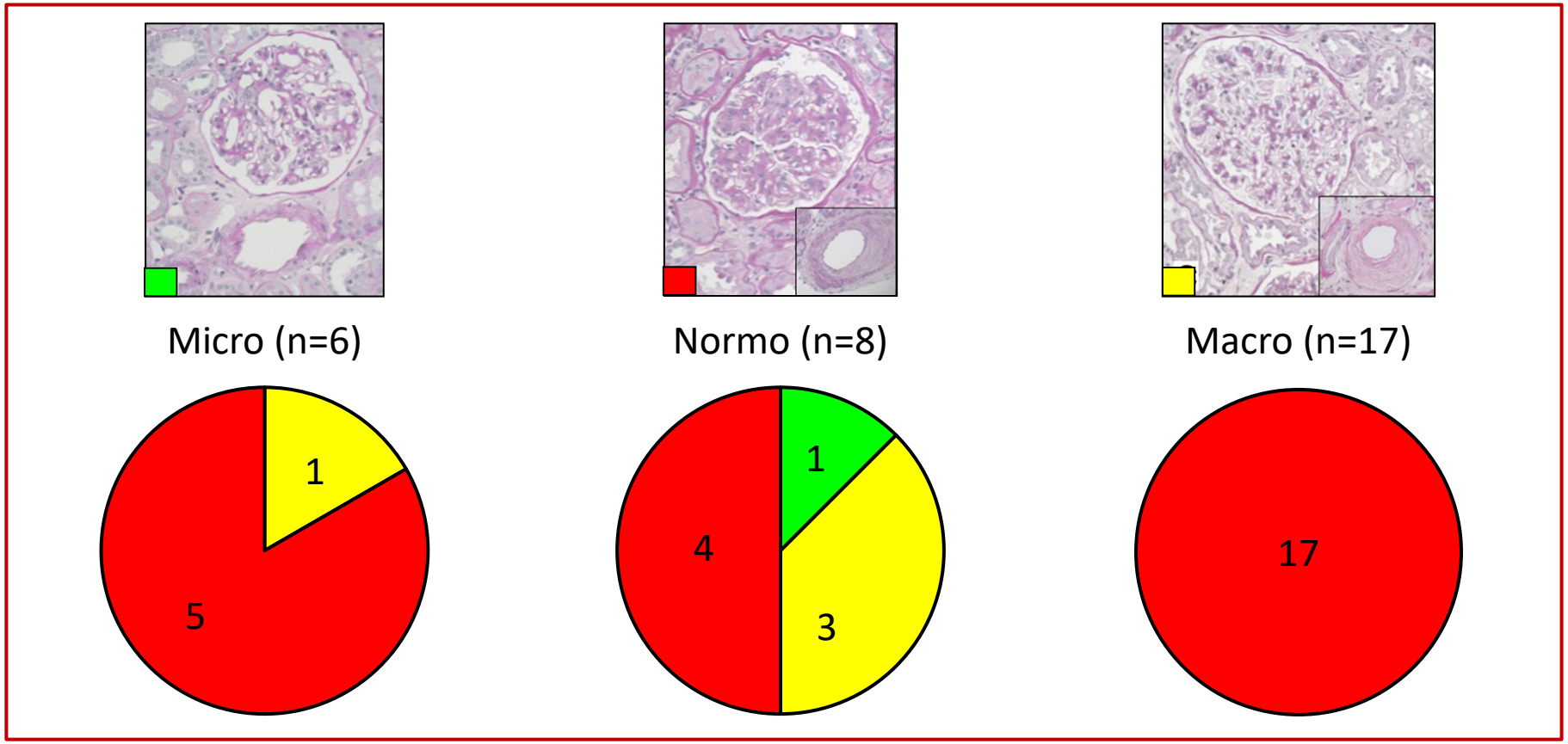


34 patients with type 2 diabetes, normal GFR and microalbuminuria

Fioretto P et al, *Diabetologia.* 1996; 39:1569–1576

Renal pathology in patients with type 2 diabetes

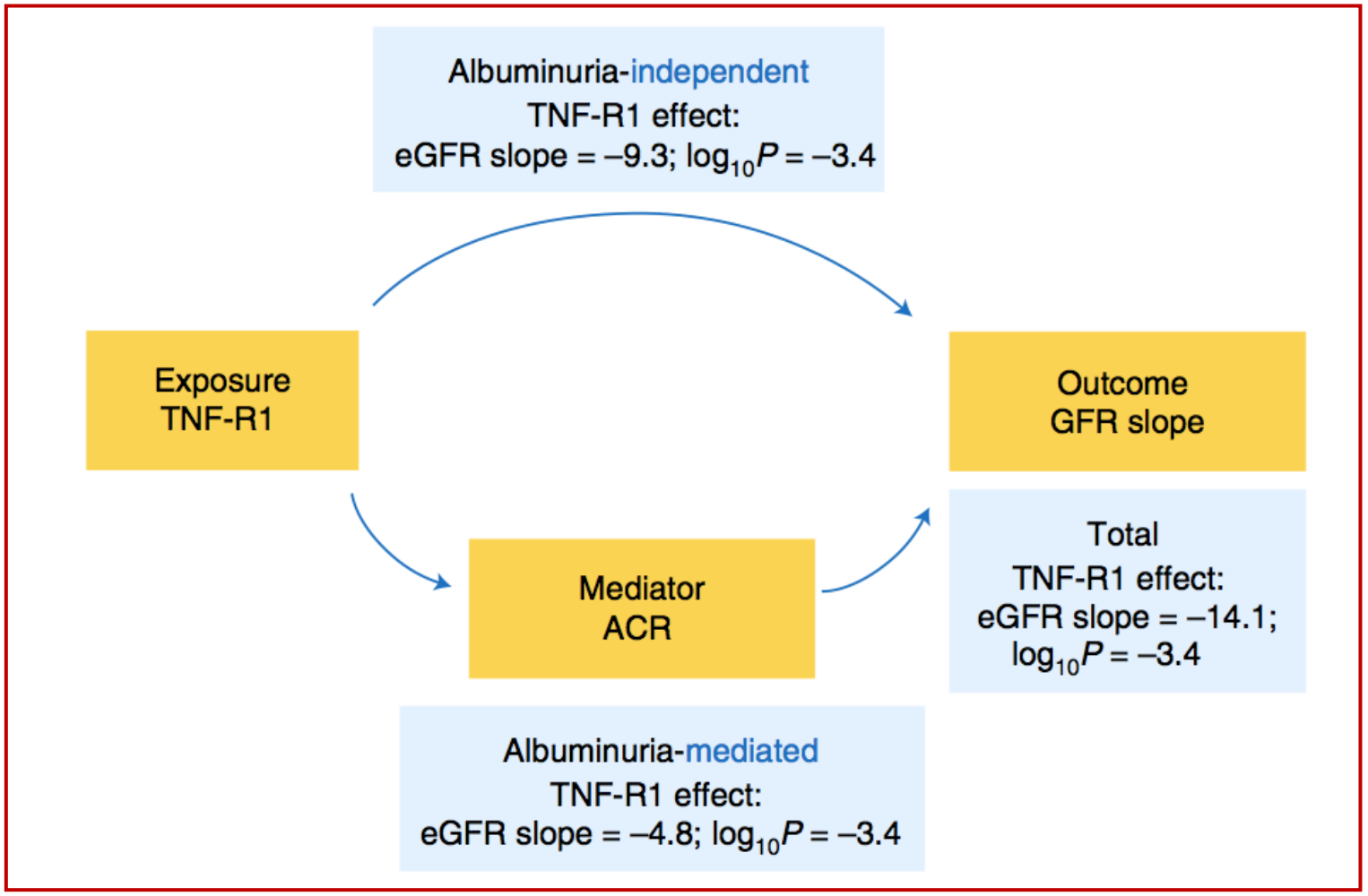
The Austin Health Diabetes Clinics database



31 patients with type 2 diabetes, eGFR <60 ml/min/1.73 m^2 BSA and normo to macroalbuminuria

Ekinci EI et al. *Diabetes Care.* 2013;36:3620–3626

The Joslin Kidney Studies and the Pima Indians Study



Discovery cohort of 219 and validation cohort of 144 patients with type 1 and 2 diabetes

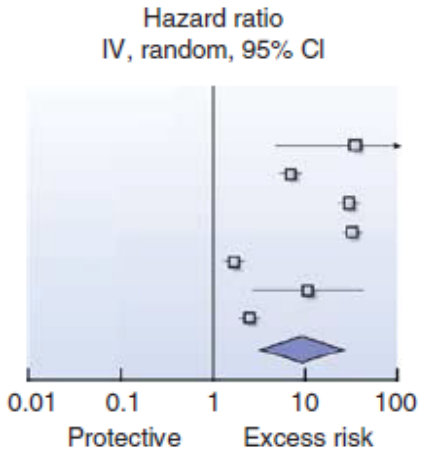
Acute kidney injury (AKI) and risk of adversae renal outcomes

Meta-analysis of 13 cohort studies

CKD

Study or subgroup	Weight (%)	Hazard ratio IV, random, 95% CI
Weiss *et al.* (13)	10.0	32.79 (4.30–249.77)
Amdur *et al.* (22)	15.5	6.64 (5.05–8.74)
Lo *et al.* (11)	15.5	28.08 (21.01–37.53)
James *et al.* (16)	15.6	29.99 (24.32–36.99)
James *et al.* (15,23)	15.5	1.60 (1.20–2.14)
Ando *et al.* (19)	12.4	9.91 (2.48–39.63)
Ishani *et al.* (21)	15.6	2.33 (1.83–2.96)
Total (95% CI)	100.0	8.82 (3.05–25.48)

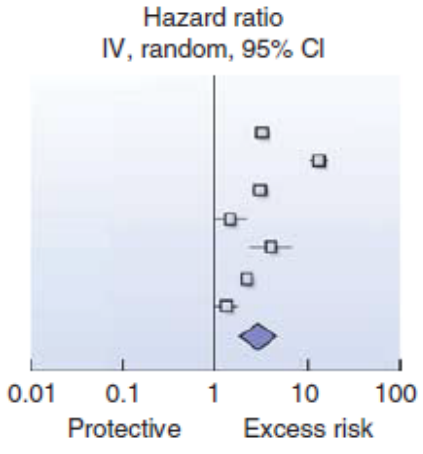
Heterogeneity: $\tau^2 = 1.87$; $\chi^2 = 446.89$, d.f. = 6 ($P < 0.00001$); $I^2 = 99\%$. Test for overall effect: $Z = 4.02$ ($P < 0.0001$)



ESRD

Study or subgroup	Weight (%)	Hazard ratio IV, random, 95% CI
Newsome *et al.* (14)	15.0	3.26 (2.87–3.70)
Ishani *et al.* (20)	14.8	12.99 (10.57–15.96)
Wald *et al.* (17)	14.9	3.22 (2.70–3.85)
Hsu *et al.* (10)	13.5	1.47 (0.95–2.28)
James *et al.* (15,23)	12.5	4.15 (2.32–7.41)
Lafrance *et al.* (18)	15.0	2.33 (2.08–2.61)
Choi *et al.* (12)	14.4	1.37 (1.02–1.84)
Total (95% CI)	100.0	3.10 (1.91–5.03)

Heterogeneity: $\tau^2 = 0.40$; $\chi^2 = 252.85$, d.f. = 6 ($P < 0.00001$); $I^2 = 98\%$. Test for overall effect: $Z = 4.58$ ($P < 0.00001$)



Coca SG et al. *Kidney Int.* 2012;81:442–448

Renal protection with RAS blockers

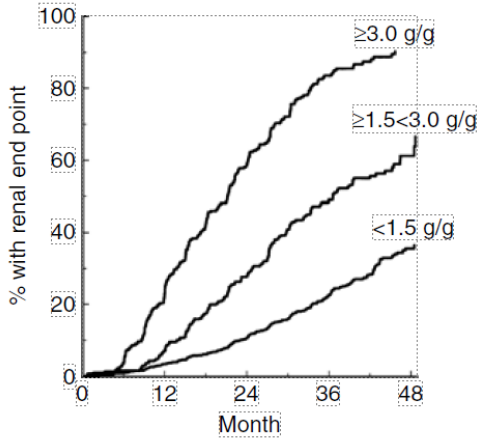
The Reduction of Endpoints in NIDDM with the Angiotensin II Antagonist Losartan (RENAAL) trial

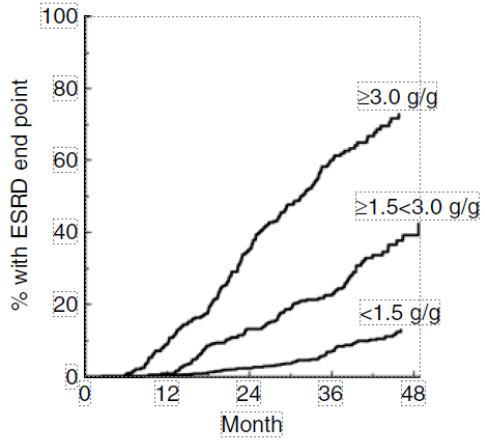
Renal end point

	Unadjusted HR	Unadjusted *P* values	Adjusted HR	Adjusted *P* values
Alb: ≥1.5<3.0 vs. <1.5 g/g	2.47	<.0001	2.22	<.0001
Alb: ≥3.0 vs. <1.5 g/g	6.52	<.0001	5.18	<.0001
Alb: ≥3.0 vs. ≥1.5<3.0 g/g	2.64	<.0001	2.33	<.0001

ESRD

	Unadjusted HR	Unadjusted *P* values	Adjusted HR	Adjusted *P* values
Alb: ≥1.5<3.0 vs. <1.5 g/g	4.01	<.0001	3.23	<.0001
Alb: ≥3.0 vs. <1.5 g/g	11.49	<.0001	8.10	<.0001
Alb: ≥3.0 vs. ≥1.5<3.0 g/g	2.86	<.0001	2.51	<.0001



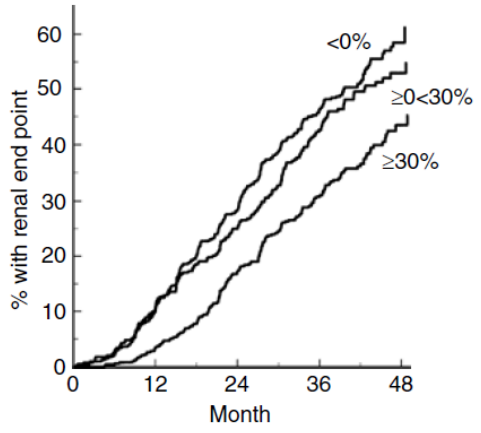


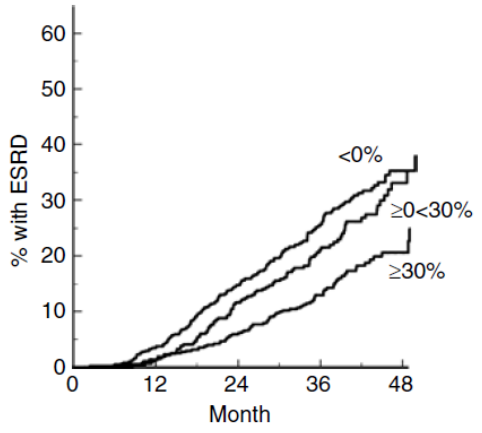
Renal end point

	Unadjusted HR	Unadjusted *P* values	Adjusted HR	Adjusted *P* values
Δ Alb: ≥0<30 vs. <0%	0.88	0.1570	0.76	0.0028
Δ Alb: ≥30 vs. <0%	0.60	<.0001	0.46	<.0001
Δ Alb: ≥30 vs. ≥0<30%	0.68	0.0003	0.61	<.0001

ESRD

	Unadjusted HR	Unadjusted *P* values	Adjusted HR	Adjusted *P* values
Δ Alb: ≥0<30 vs. <0%	0.82	0.1242	0.62	<.0003
Δ Alb: ≥30 vs. <0%	0.51	<.0001	0.37	<.0001
Δ Alb: ≥30 vs. ≥0<30%	0.62	0.0019	0.60	0.0010

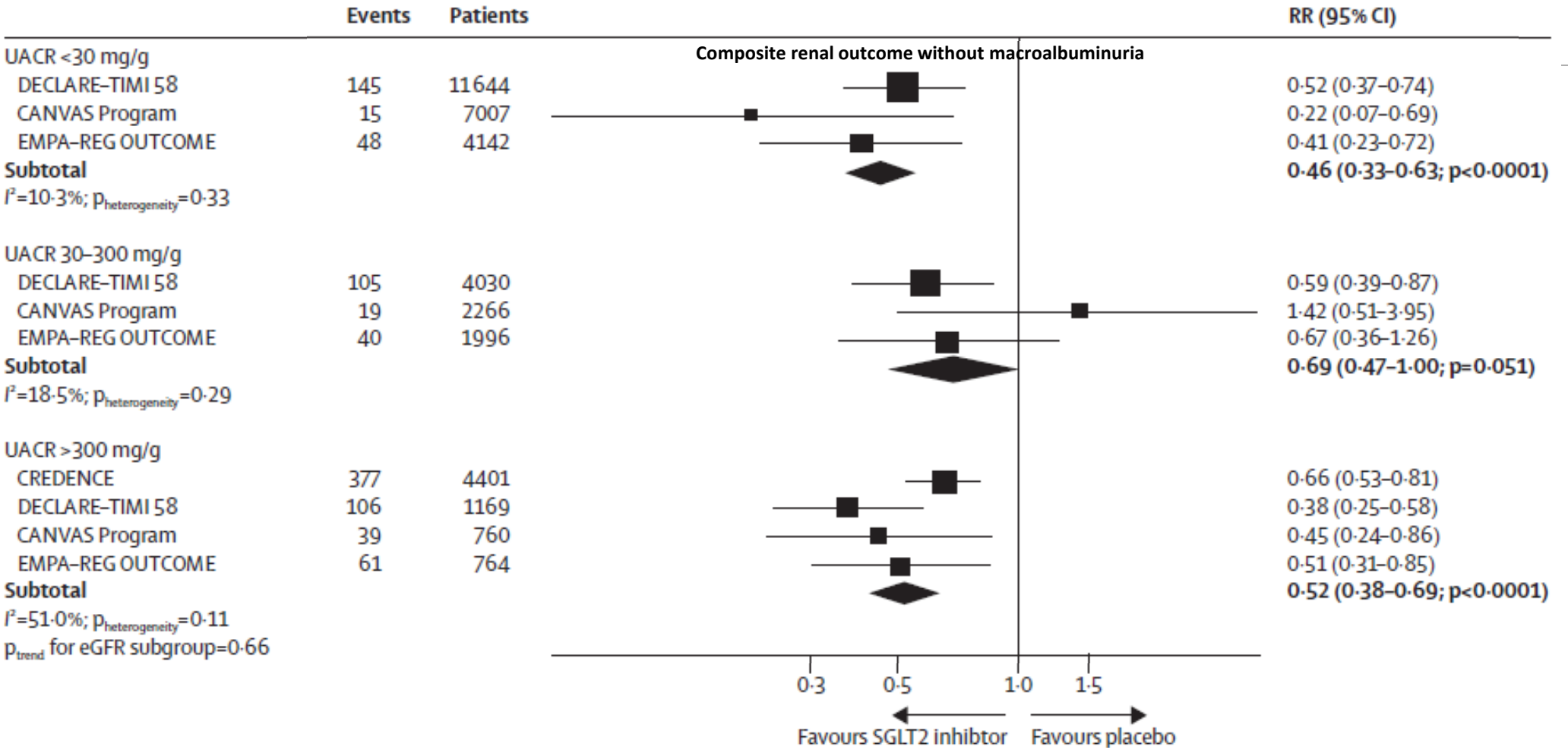




De Zeeuw D et al. *Kidney Int.* 2004;65:2309–2320

Renal protection with SGLT-2 inhibitors by albuminuria

Systematic review and meta-analysis of 4 randomized trials with SGLT-2 inhibitors

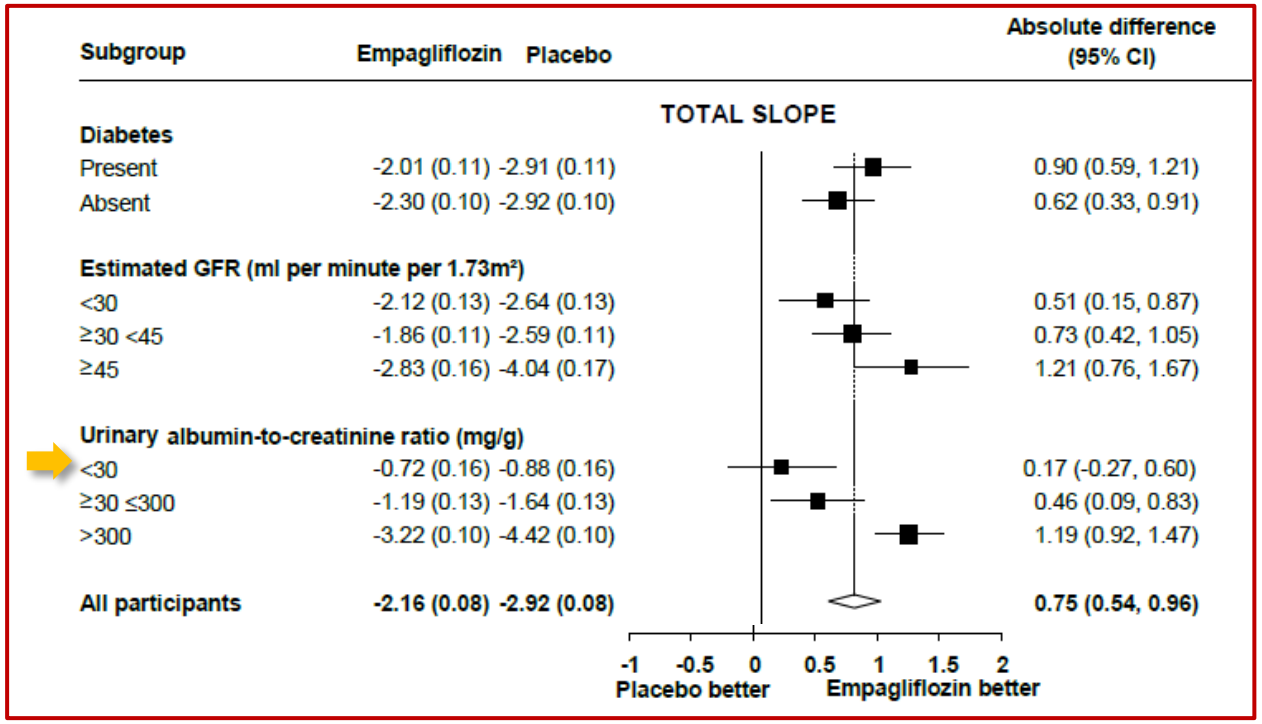


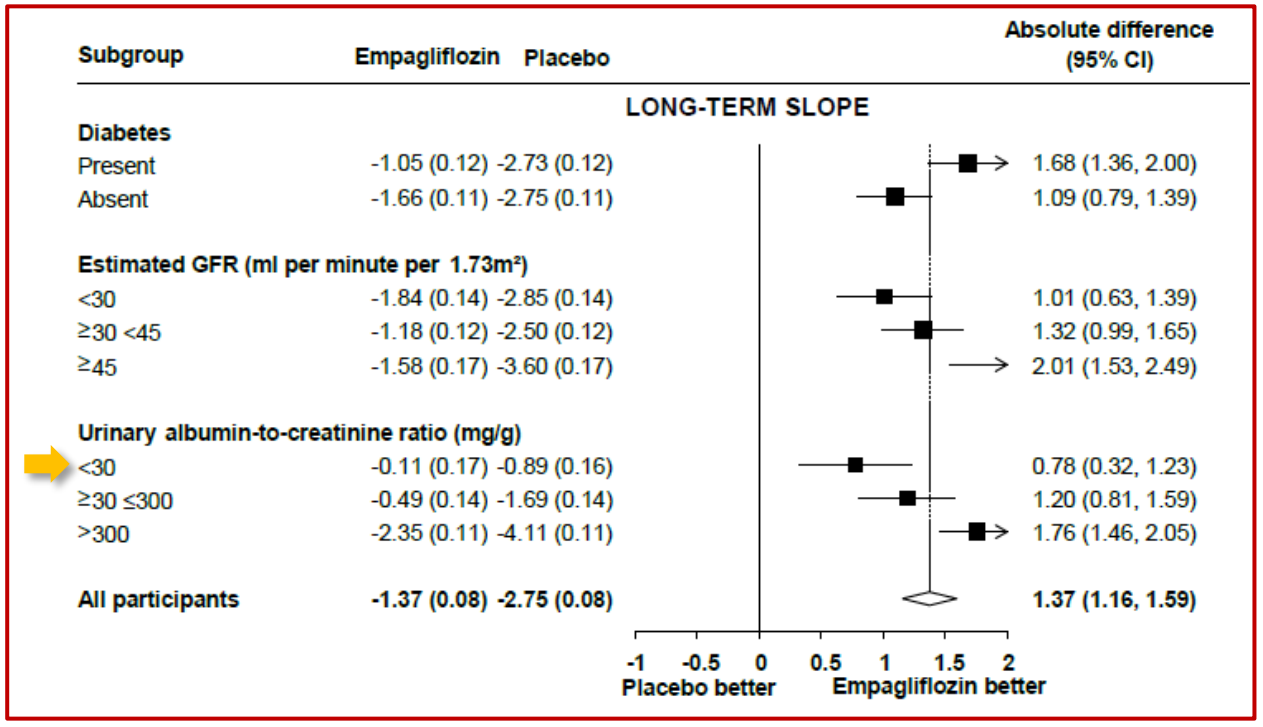
Neuen BL et al. *Lancet Diabetes Endocrinol.* 2019;7:845–854

Treatment with SGLT-2 inhibitors by eGFR and albuminuria categories

The Study of Heart and Kidney Protection with Empagliflozin (EMPA-KIDNEY)

Secondary outcome: Mean annual rate of eGFR change (ml/min/1.73 m^2/year)





6,609 patients with diabetic and nondiabetic CKD, randomized to placebo or empagliflozin (10 mg/day) for a median follow-up of 2.0 years

The EMPA-KIDNEY Collaborative Group. *N Engl J Med.* 2023;388:117–127

Albuminuric versus nonalbuminuric phenotypes

Characteristics	DKD phenotype	
	Albuminuric	Nonalbuminuric
Prevalence	Decreasing	Increasing
Sex	Male	Female
Smoking	Yes	No
Association with HbA_{1c}	Yes	No
Association with hypertension	Strong	Weak
Association with retinopathy	Strong	Weak
Histology	Mainly typical	Often atypical
CVD risk	High	High
ESRD risk	Higher	Lower
Biomarker(s)	Albuminuria	TNFR1 & 2, KIM-1, β_2-micro
RAS blockade	Effective	Not effective?
SGLT2 inhibition	Effective	Effective

Nondiabetic renal diseases in patients with type 2 diabetes

	Class 1 Diabetic glomerulosclerosis		Class 2 Vascular/ischemic disease		Class 3 Glomerulonephritis	
	CUP	CRPs	CUP	CRPs	CUP	CRPs
No. of patients	99	57	30	30	61	111
Sex ratio (M/F)	1.8	2.16	2	2.94	1.77	2.08
Age (y)	61.96 ± 10.24	60.10 ± 10.07	62.42 ± 9.86	57.41 ± 11.94	63.81 ± 9.27	61.49 ± 11.33
Duration of diabetes (y)	11.3 ± 7.73	11.3 ± 8.82	10.6 ± 7.52	7.28 ± 7.88	8.82 ± 10.27	7.01 ± 7.18
Serum creatinine (mg/dL)	2.23 ± 1.73	2.19 ± 1.77	2.8 ± 2.1	2.6 ± 1.8	2.73 ± 2.24	2.66 ± 2.5
Proteinuria (g/d)	4.7 ± 4.7	5.08 ± 3.8	2.4 ± 1.77	3.03 ± 1.9	5.7 ± 6.26	4.8 ± 3.7
Arterial blood pressure (mm Hg)	157/88 ± 17.4/9.7	150/85 ± 15.8/8.8	143/84 ± 16.1/8.7	147/84 ± 19.2/9.3	161/90 ± 14.7/9.1	147/83 ± 19.7/9.8

156 (40.2%)

60 (15.5%)

172 (44.3%)

393 patients with type 2 diabetes with restricted (CRPs) or unrestricted (CUP] renal biopsy

Mazzucco C et al. *Am J Kidney Dis.* 2002;39:713–720

Indications for renal biopsy in patients with diabetes

Joint position statement of the Italian Society of Nephrology and the Italian Diabetes Society

Diagnostic definition in all patients with clinical suspicion of NDRD for the presence of one or more of the following features:

- Diabetic disease duration <5 years (in type 1 diabetes);
- Absence of diabetic retinopathy (particularly in type 1 diabetes);
- Rapid onset and progression of albuminuria or sudden onset of nephrotic syndrome;
- Rapid decline of renal function (GFR) with or without albuminuria;
- Presence of hematuria (dysmorphic erythrocytes);
- Active urine sediment;
- Clinical suspicion of other nephropathies (e.g., vasculitis, amyloidosis);
- Positivity for *markers* of other systemic diseases (e.g., ANCA, ANA, dsDNA, low complement factors, cryoglobulinemia).

Prognostic evaluation in selected patients with clinical suspicion of DN.

Di Paolo S et al. *Nutr Metab Cardiovasc Dis.* 2020;30:2123–2132

Conclusions

- There is a decreasing trend in the incidence of diabetic kidney disease, but a recent resurgence in the incidence of end-stage renal disease in younger patients.
- Prevalence of albuminuria is decreasing and prevalence of reduced eGFR is increasing, with the emergence of the phenotypes of nonalbuminuric renal impairment and progressive renal decline indicating the existence of a nonalbuminuric or albuminuria-independent pathway to end-stage renal disease.
- The albuminuric ad nonalbuminuric phenotypes have different diagnostic and prognostic implications and seem to underly different pathogenetic and anatomic features.
- Nondiabetic renal diseases are not uncommon in people with type 2 diabetes and renal biopsy is indicated in case of clinical suspicion.