St Vincent's Hospital Melbourne

THE UNIVERSITY OF MELBOURNE

Albuminuria versus GFR as markers of diabetic CKD progression

KDIGO Controversies Conference:
"Diabetic Kidney Disease"
New Delhi, March 2012

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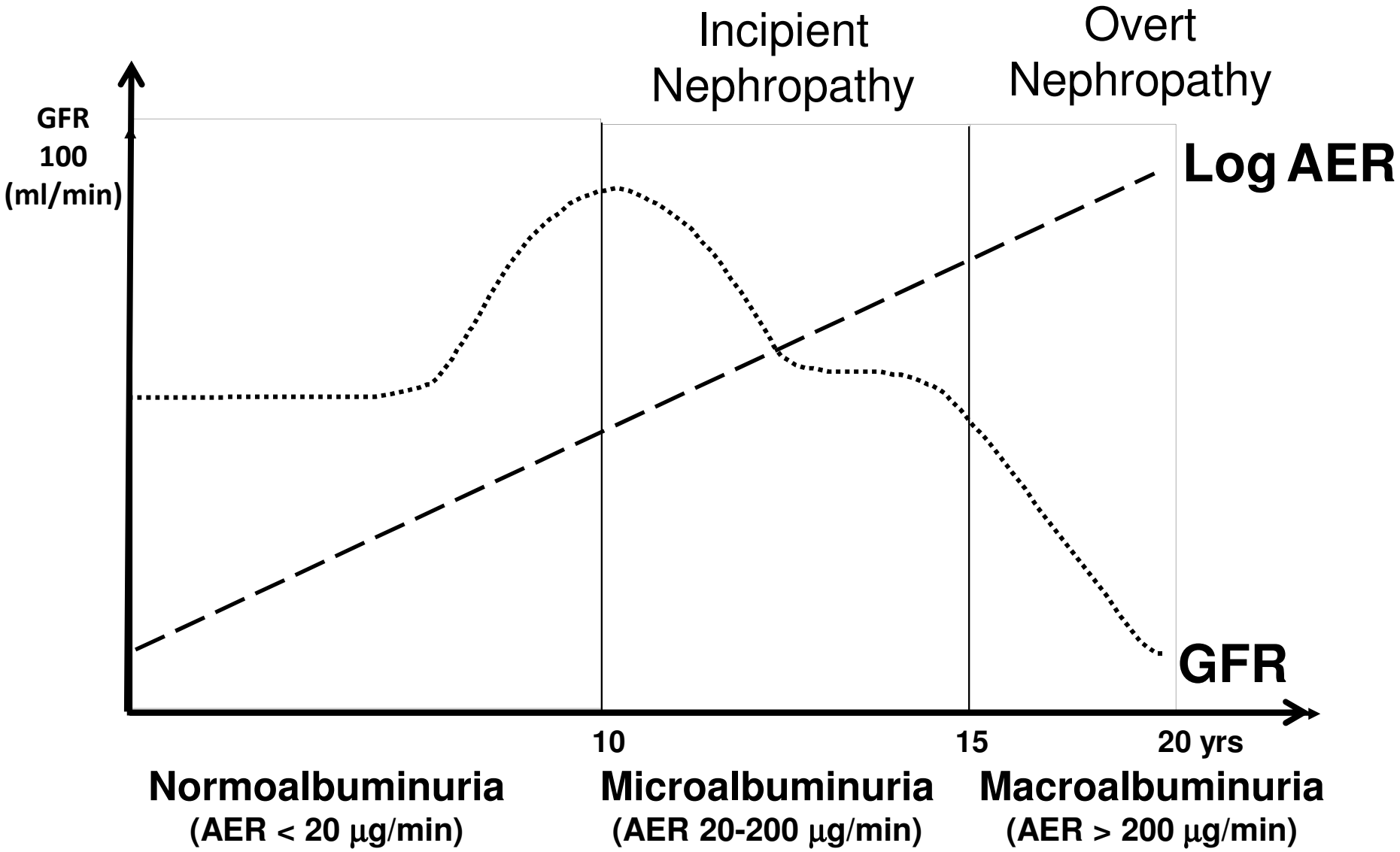
Evolution of Diabetic CKD



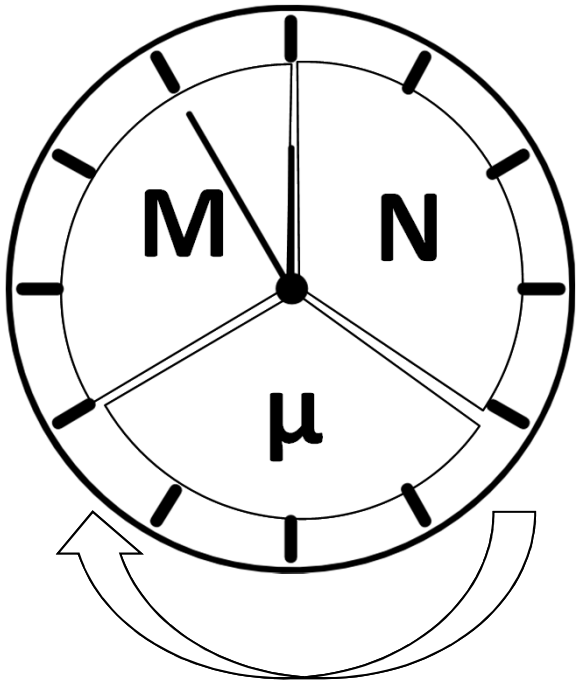
Stages of CKD

Stage	eGFR (ml/min/1.73 m^2)	Description	Predominant AER status
1	> 90	Kidney damage with normal/high GFR	**Normo- Micro-**
2	60-89	Kidney damage with mild reduction in GFR	**Micro-**
3	30-59	Kidney damage with moderate reduction in GFR	**Micro/Macro-**
4	15-29	Kidney damage with severe reduction in GFR	**Macro-**
5	< 15	Kidney failure	

Albuminuria versus GFR as markers of diabetic CKD progression

1. Albuminuria as a predictor of diabetic CKD
2. GFR as a predictor of diabetic CKD
3. Albuminuria & GFR uncoupling/coupling
4. Summary

Albuminuria as a marker of diabetic CKD progression

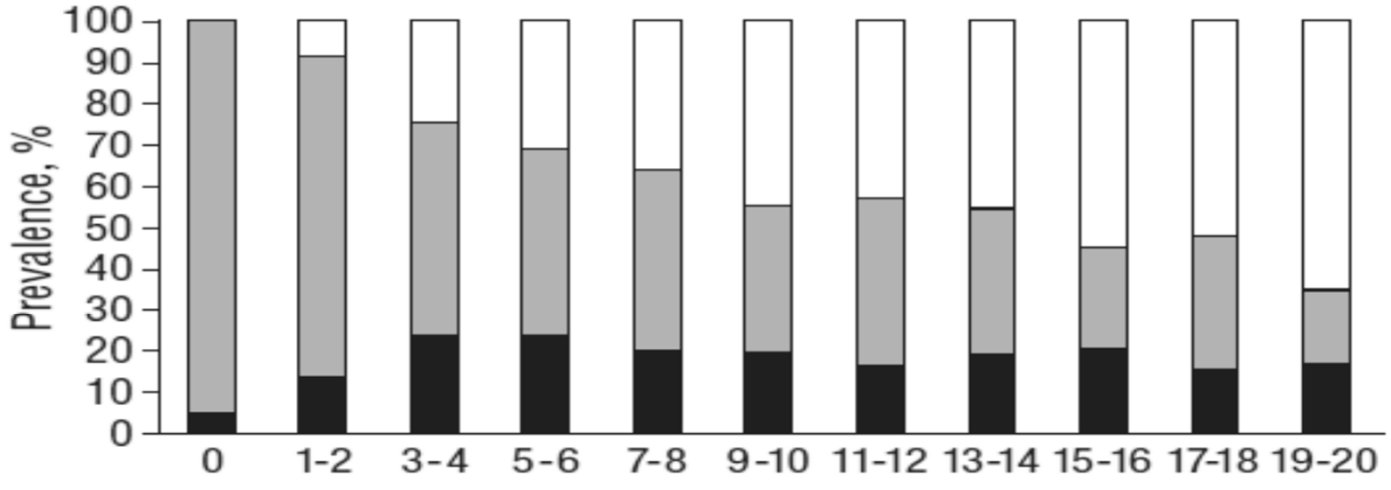


- High **Variability**
- Low **Specificity**
- Spontaneous **Regression**
- **Δ AER ≠ Δ GFR**

Long-term Renal Outcomes of Patients With Type 1 Diabetes Mellitus and Microalbuminuria

An Analysis of the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Cohort

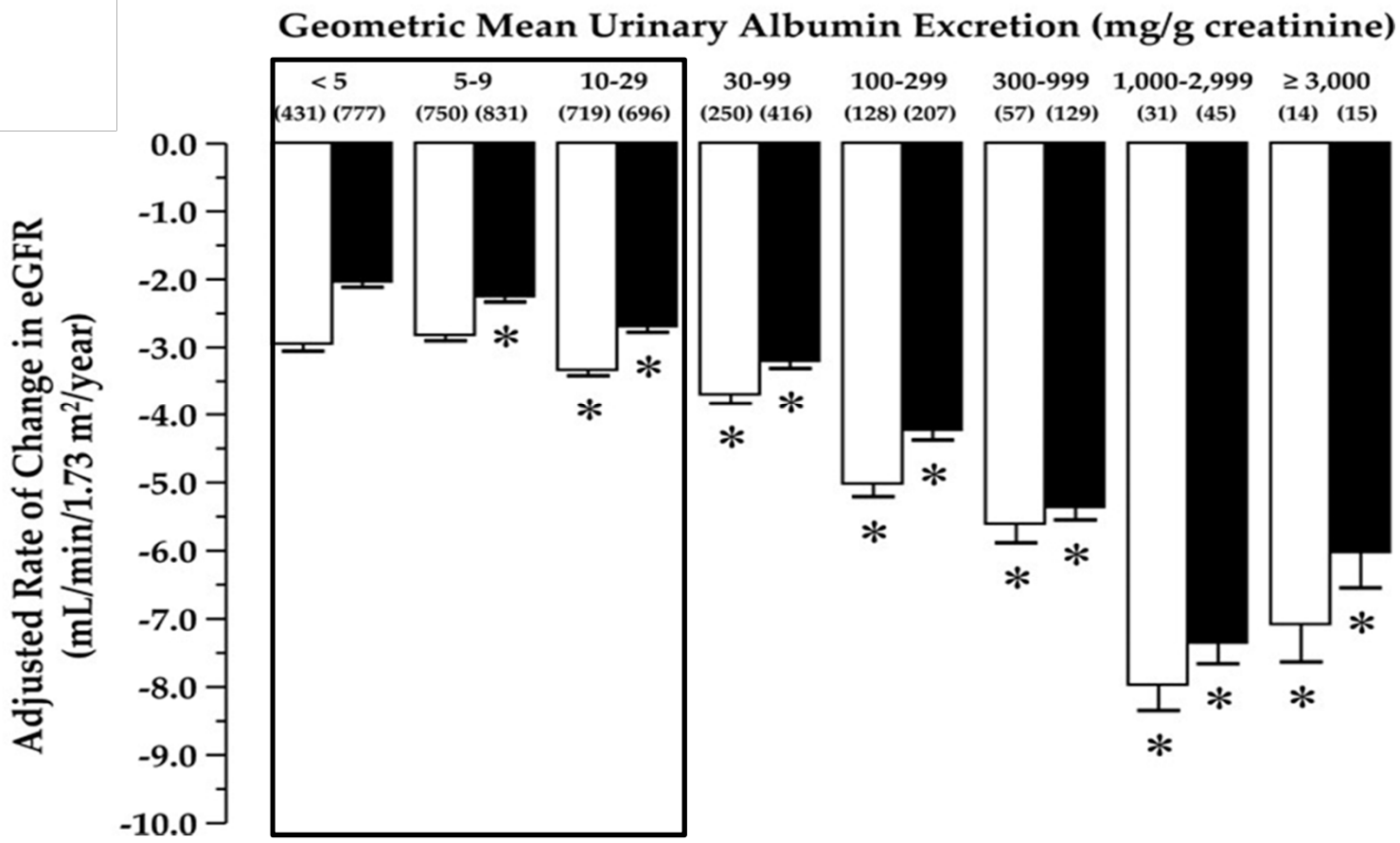
Arch Intern Med. 2011;171(5):412-420



No. of participants	325	315	281	255	230	208	166	135	117	85	54
Prevalence of RAAS Inhibitor Use, %											
Normoalbuminuria	...	0	22	27	34	34	39	39	50	55	51
Microalbuminuria	7	24	30	44	51	69	59	71	86	71	80
Macroalbuminuria	6	31	55	72	67	78	93	92	92	85	89

Higher levels of urinary albumin excretion within the normal range predict faster decline in glomerular filtration rate in diabetic patients

Babazono T et al. Diabetes Care 2009;32:1518-1520



Albuminuria versus GFR as markers of diabetic CKD progression

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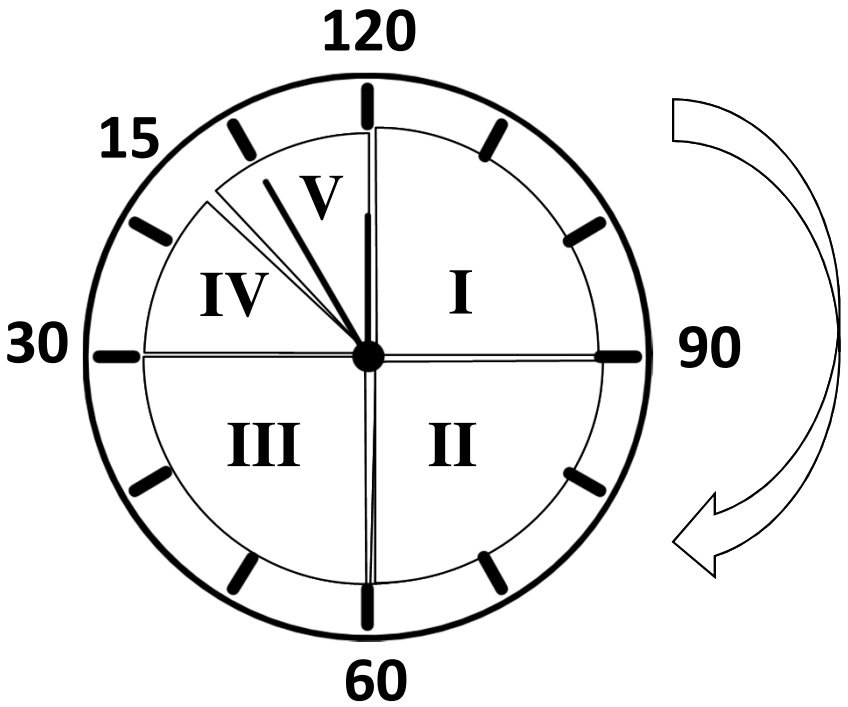
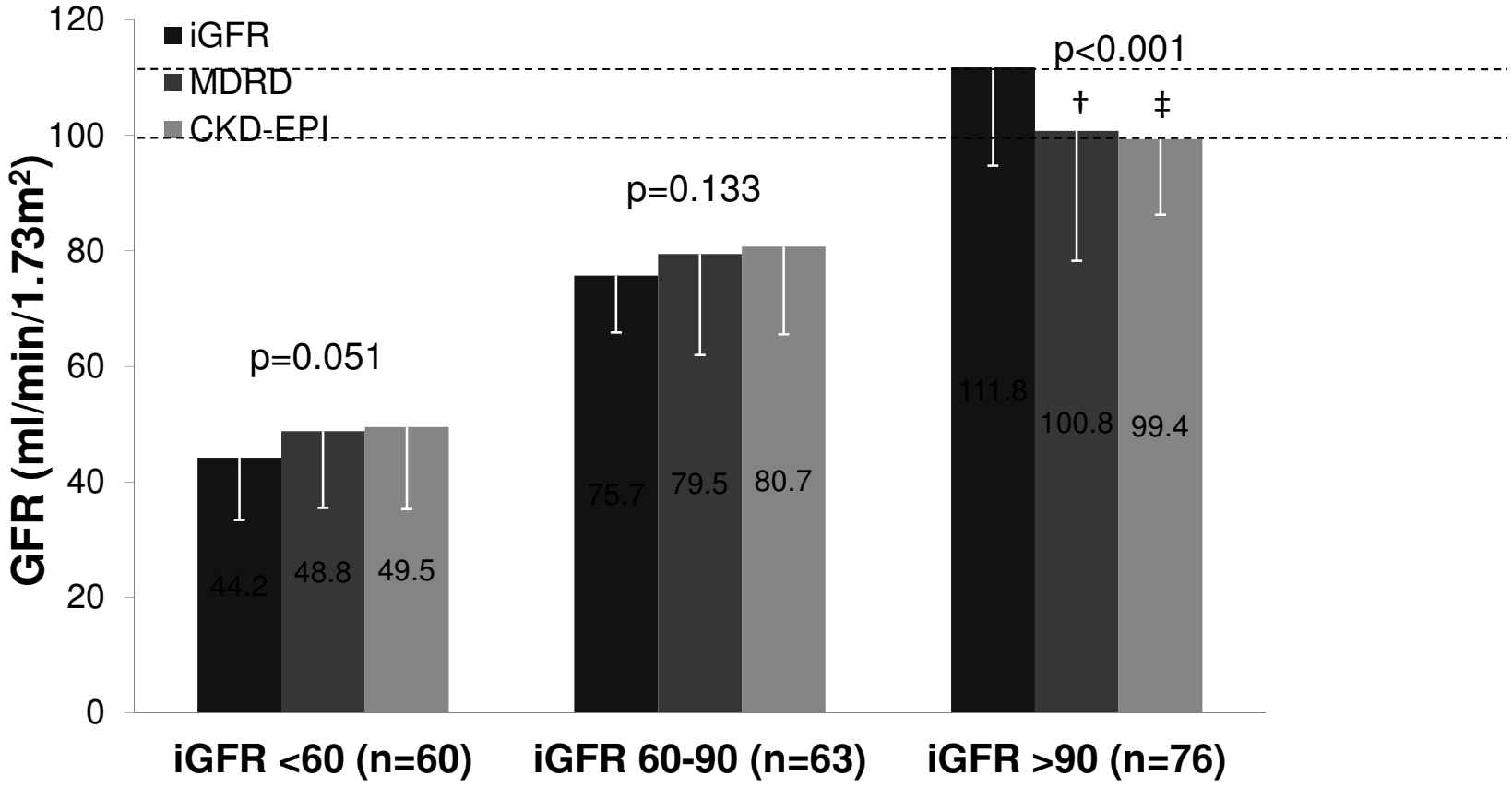
GFR as index of diabetic CKD progression



- Low **Variability**
- High **Specificity**
- Infrequent **Regression**
- **GFR = best index of kidney function**

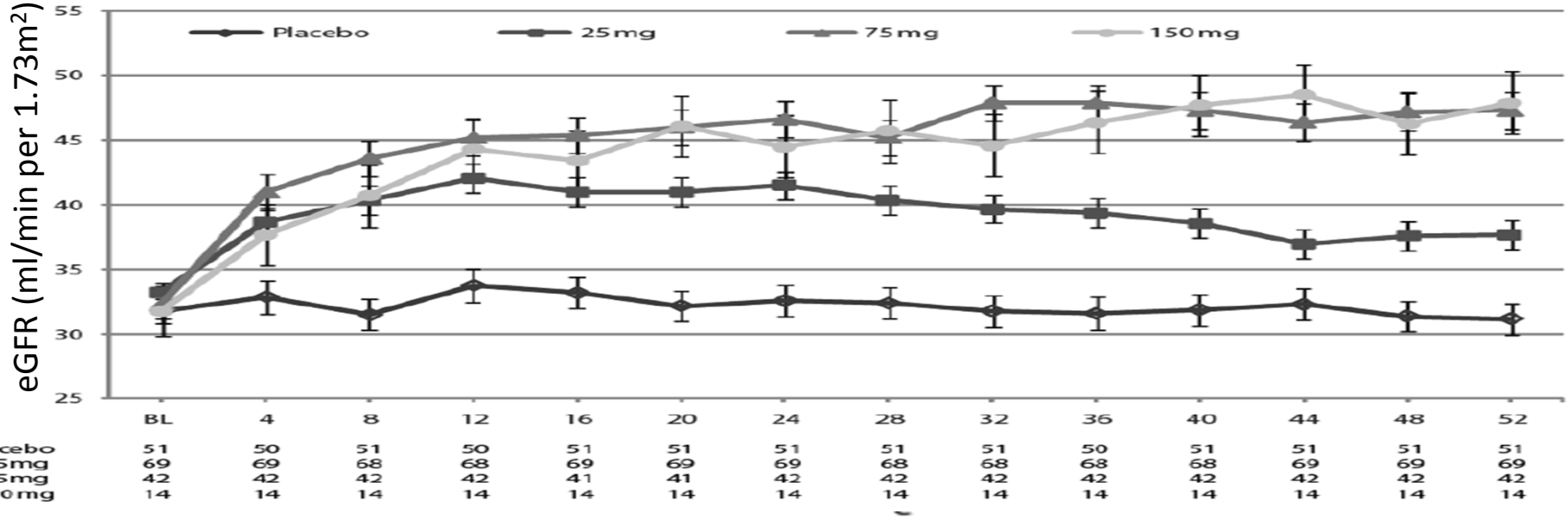
CKD-EPI formula underestimates measured GFR > 90 ml/min/1.73m^2 to the same extent as the MDRD formula in type 2 diabetes

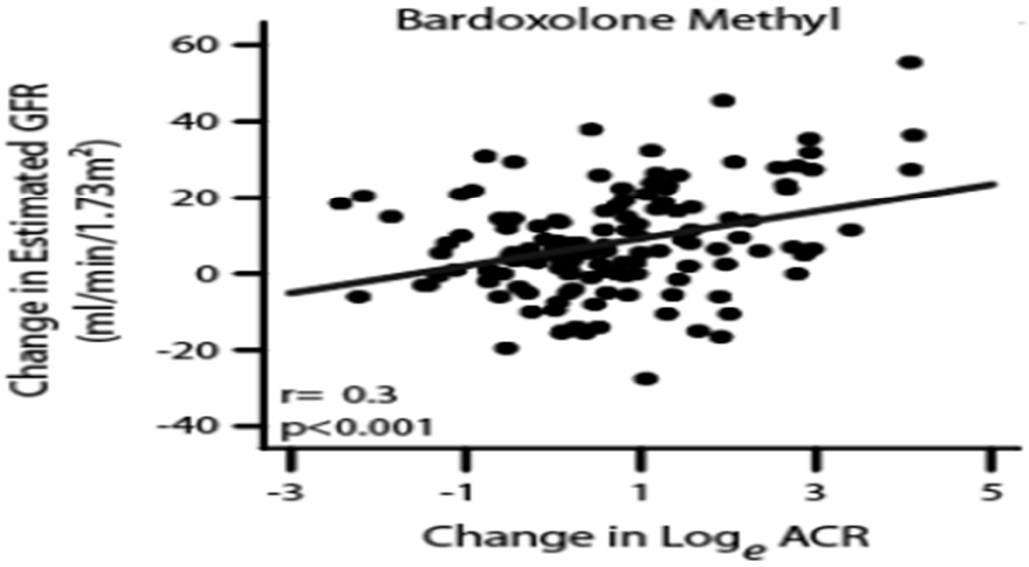
RJ MacIsaac (unpublished)



Possible regression of eGFR with bardoxolone

Pergola PE NEJM 2011, 28, 327-36





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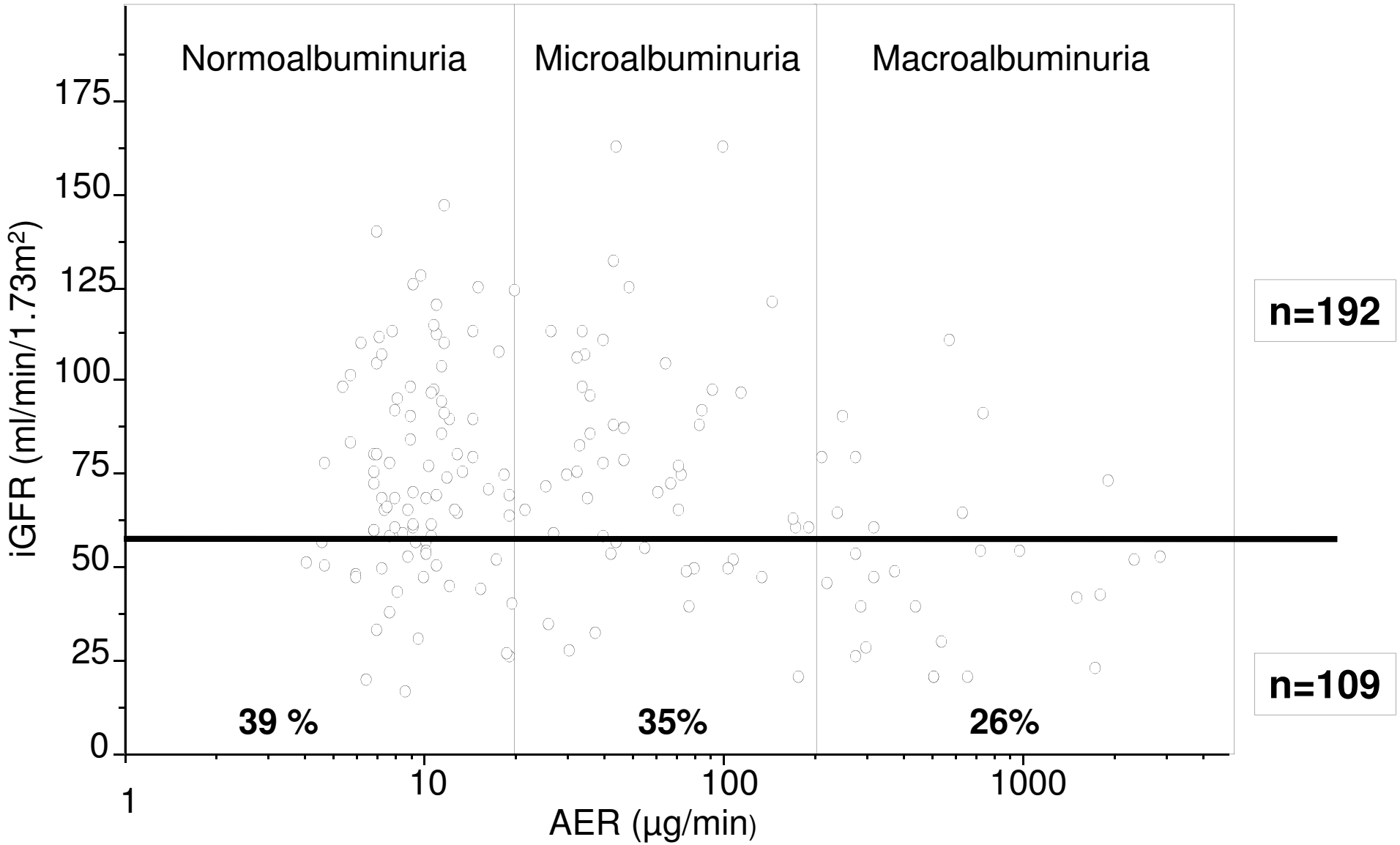
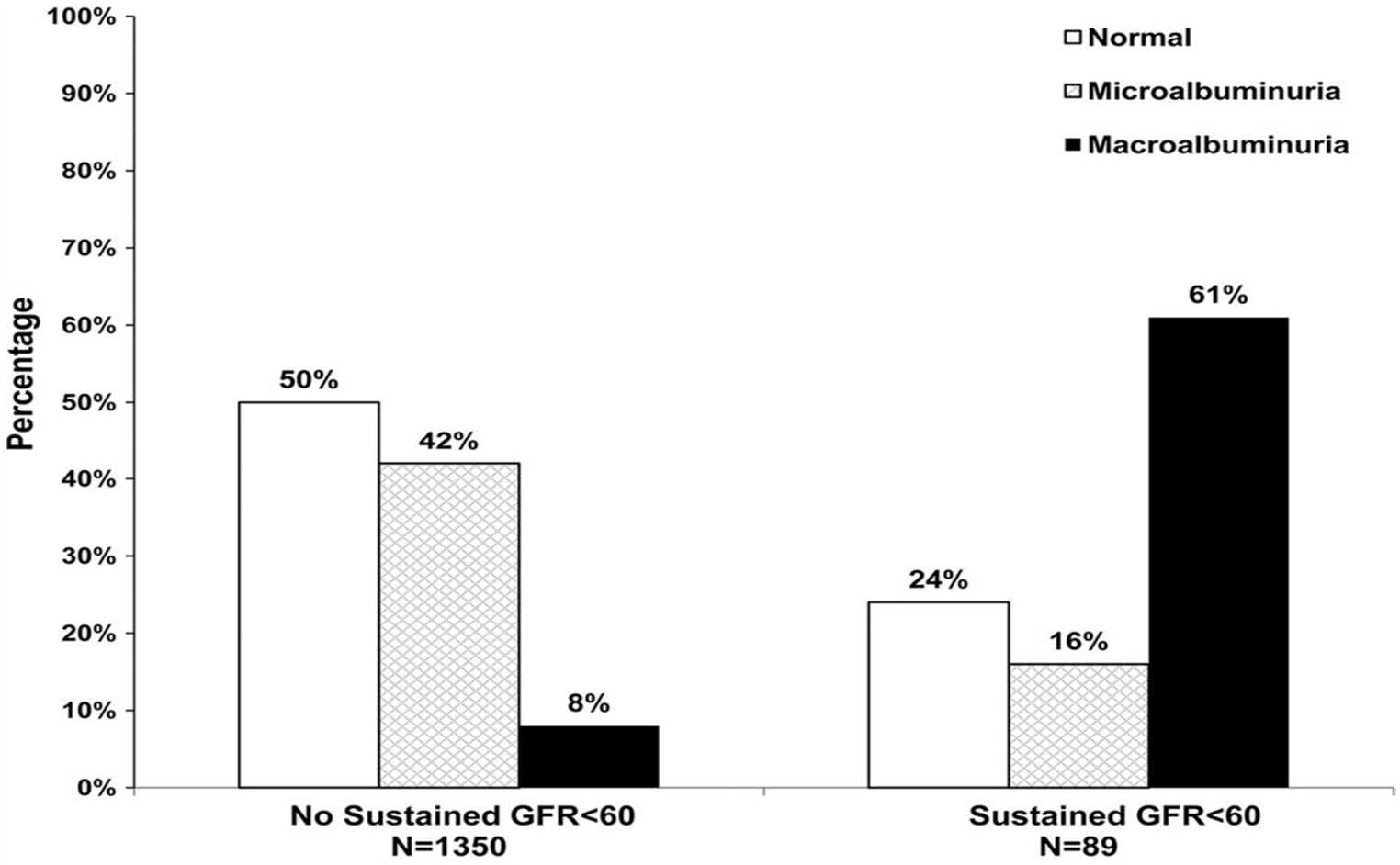
AER vs isotopic GFR in Type 2 Diabetes

RJ MacIsaac et al Diabetes Care 2004



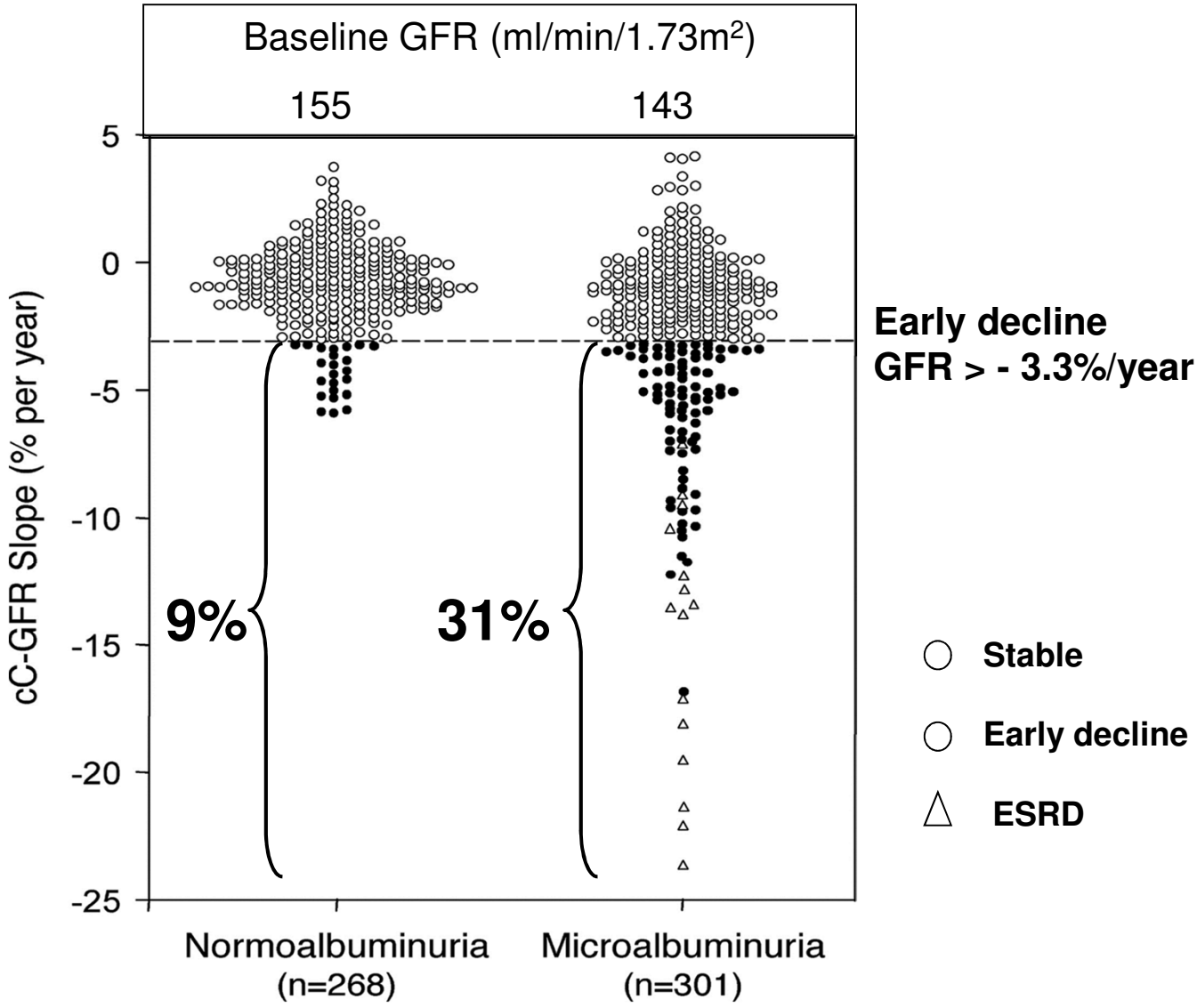
AER vs eGFR in Type 1 Diabetes

ME Molitch et al Diabetes Care, 33, 1536-1543 2010



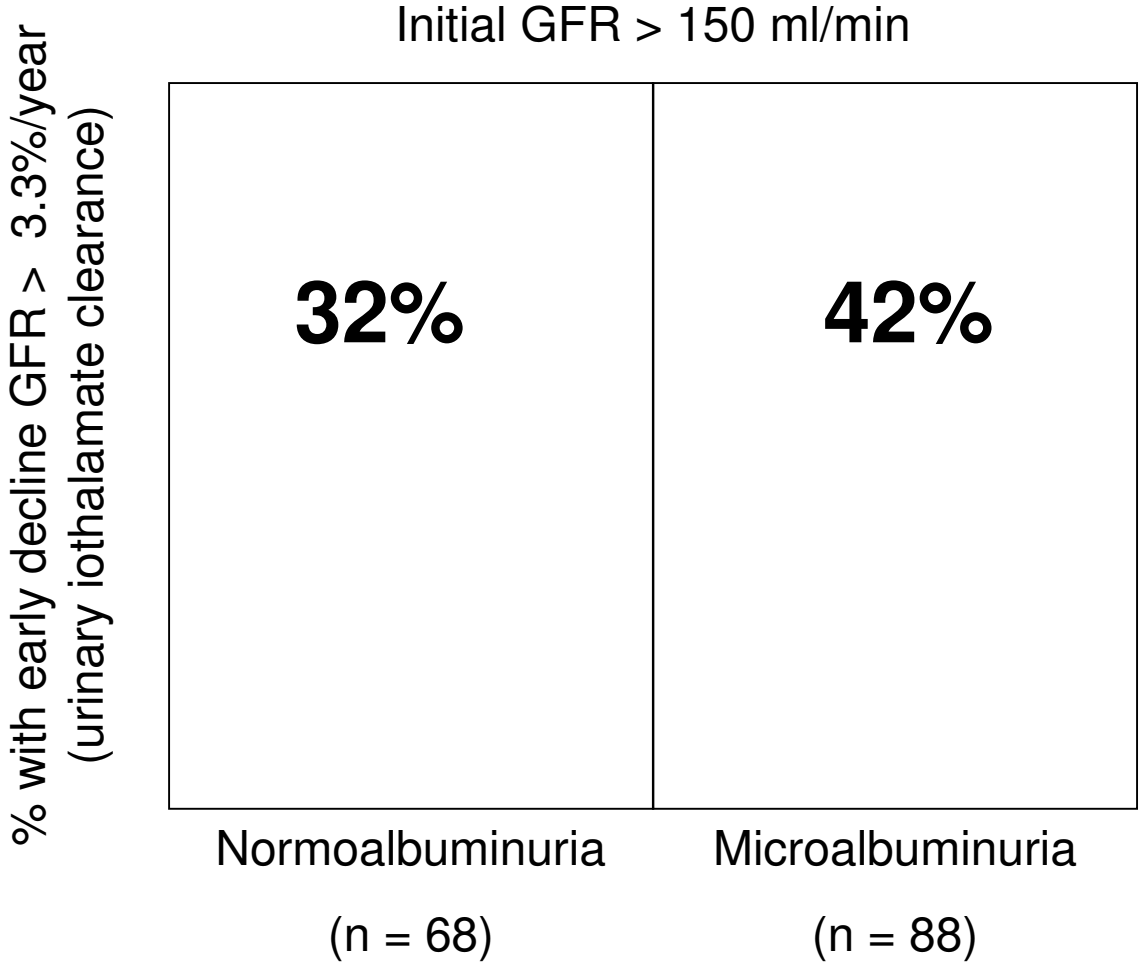
Microalbuminuria and the risk for early progressive renal function decline in type 1 diabetes

Perkins BA et al. JASN 2007, 18, 1353-1361



Early Renal Function Decline in Type 2 Diabetes

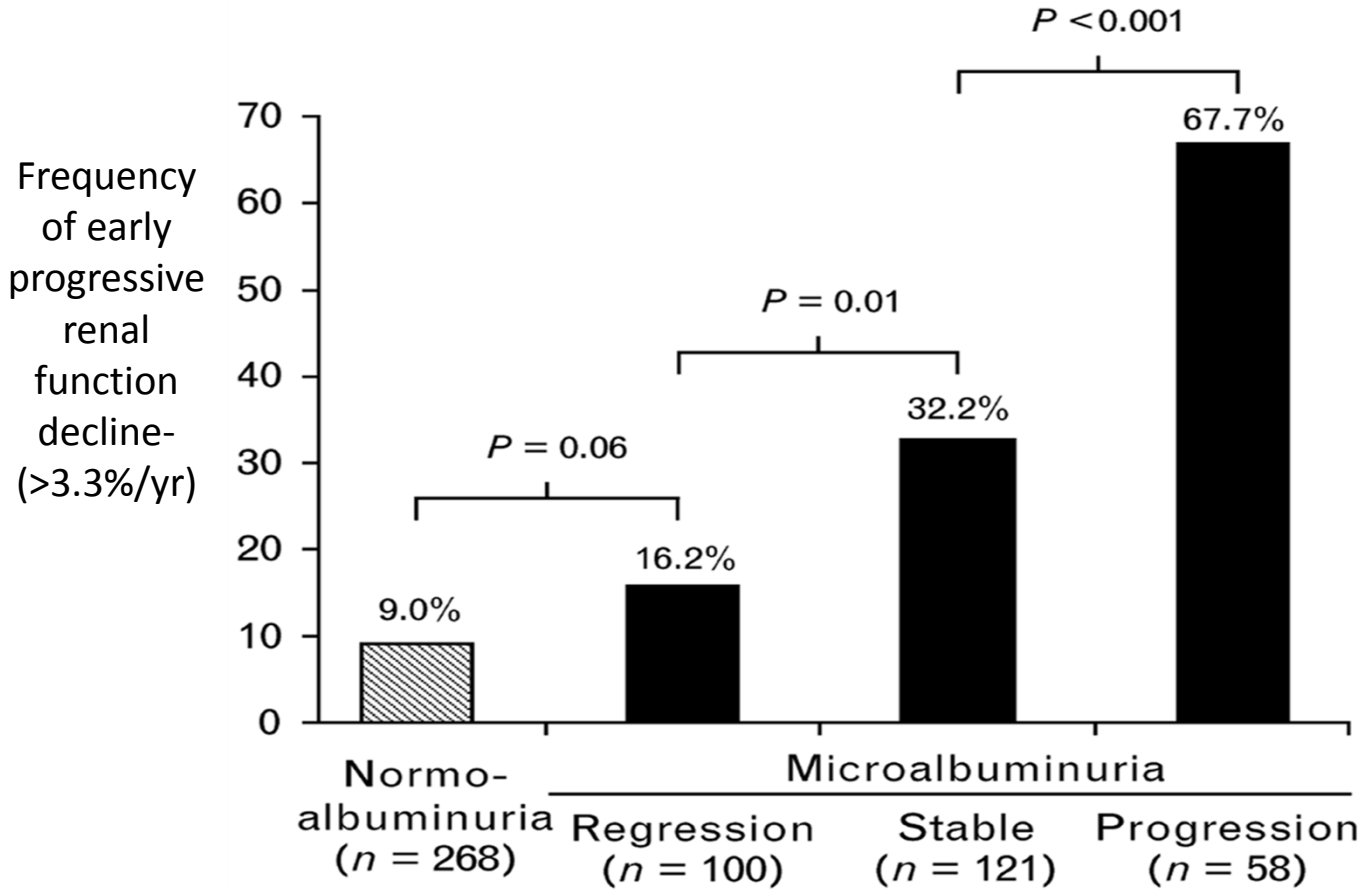
Pavkov ME et al CJASN 2011



Microalbuminuria and the risk for early progressive renal function decline in type 1 diabetes

Perkins BA et al. JASN 2007, 18, 1353-1361

Frequency of early progressive renal function decline in patients with T1DM and normoalbuminuria or microalbuminuria divided according to the 4-year course of microalbuminuria



Early Renal Function Decline in Type 2 Diabetes

Pavkov ME et al CJASN 2011

Decline in early renal function and subsequent development of ESRD is strongly dependent on progression to macroalbuminuria in type 2 diabetes

Table 3. Cumulative incidence of diabetic ESRD at 10 years of follow-up

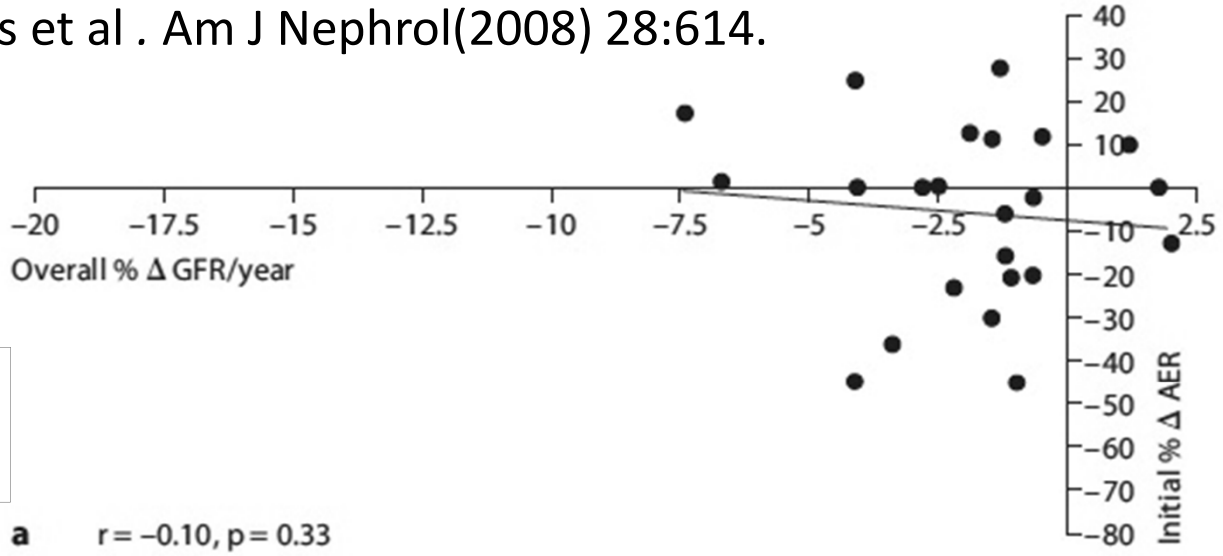
	Normoalbuminuria (ACR <30 mg/g)	Microalbuminuria (ACR 30 to <300mg/g)	Macroalbuminuria (ACR ≥300 mg/g)
RFD−, %	8.4 (2 events)	6.1 (2 event)	39.5 (6 events)
RFD+, %	0	11.9 (2 events)	74.8 (31 events)

Forty-three of 49 cases of ESRD occurred during this period. The cumulative incidence is presented according to albuminuria levels at the end of the initial period. The initial period was used to determine the presence or absence of renal function decline. In the follow-up period these participants were followed for ESRD according to the previously defined GFR slope. RFD−, no renal function decline; RFD+, renal function decline; ACR, urinary albumin/creatinine ratio.

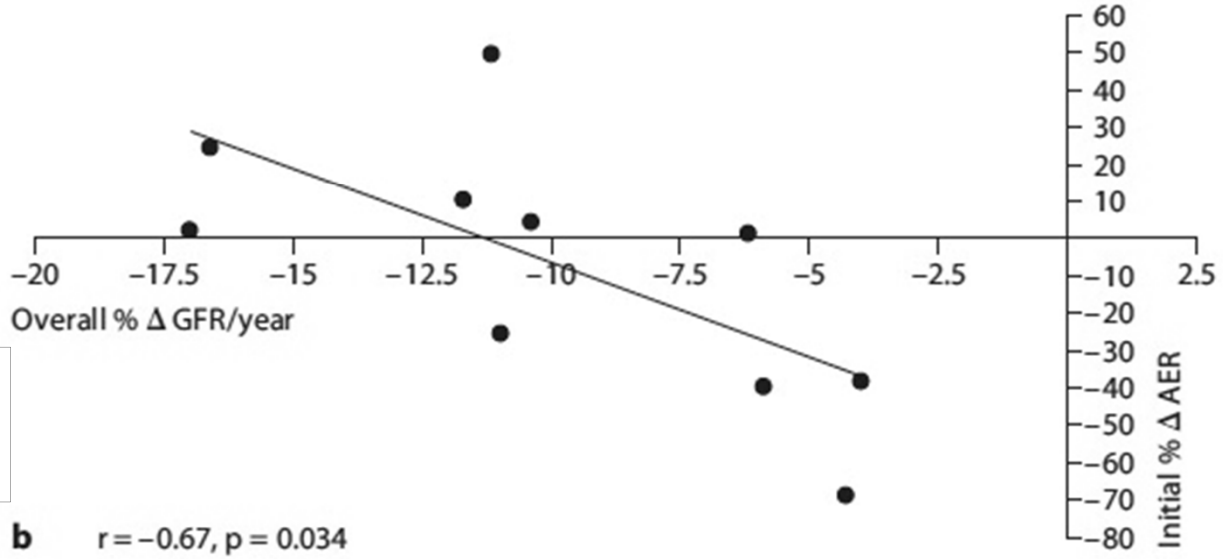
Relationship between initial change in AER and overall change in GFR per year in type 1 diabetes: Intention to treat analysis

Jerums et al . Am J Nephrol(2008) 28:614.

23 study groups (9 studies)
Early DN
n=1181



10 study groups (5 studies)
Late DN
n=510



Intensified multifactorial intervention in patients with T2 DM and microalbuminuria: STENO 2 Study

P Gaede et al. Lancet (1999) 353:617-622, P Gaede et al. N Engl J Med (2003) 348:383-393

Analysis according to intention to treat (n=160)			
		Standard n = 80	Intensive n = 80
Median AER (mg/24h)	Baseline 3.8 yr 7.8 yr	69 79 99	78 66* 58* ($p < 0.01$)
Mean iGFR (ml/min/1.73m^2)	Baseline 3.8 yr 7.8 yr	118 105 86	116 105 86

Intensified multifactorial intervention in patients with T2 DM and microalbuminuria: STENO 2 Study

P Gaede et al. Nephrol Dial Transplant (2004) 19:2784-8

Post Hoc Analysis: according to AER during follow-up (n = 151)			
Baseline AER	Micro	Micro	Micro
Follow-up AER	↓ Normo	↓ Micro	↓ Macro
	n = 46	58	47
GFR Decline (ml/min/year)	2.3 ± 0.4	3.7 ± 0.4	5.4 ± 0.5 (Anova, $p < 0.001$)

Conclusion Remission to normoalbuminuria is associated with decreased GFR decline during 7.8 yr follow-up

Albuminuria and GFR as markers of diabetic CKD progression

1. Albuminuria as predictor of diabetic CKD
2. Estimating or measuring GFR in diabetic CKD
3. Albuminuria & GFR uncoupling/coupling
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Conclusions

- Both albuminuria and GFR should be assessed **as markers of diabetic CKD progression**
- Changes in albuminuria are **variable** whereas changes in GFR are usually **progressive**
- A decline in GFR is usually accompanied by a rise in albuminuria but some patients follow a **non-albuminuric** pathway to renal impairment (GFR < 60 ml/min/1.73m^2)
- Progression to **ESRD is usually strongly dependent** on progression to macroalbuminuria
- Albuminuria and GFR have **complementary** roles in staging and stratifying the risk of progressive diabetic CKD

The definition, classification, and prognosis of chronic kidney disease: a KDIGO Controversies Conference report

Levey A et al Kidney International (2011) **80,** 17–28

Composite ranking for relative risks by GFR and albuminuria (KDIGO 2009)

GFR stages, description and range (ml/min per 1.73 m^2)				Albuminuria stages, description and range (mg/g)				
				A1		A2	A3	
				Optimal and high-normal		High	Very high and nephrotic	
				<10	10–29	30–299	300–1999	⩾2000
	G1	High and optimal	>105					
			90–104					
	G2	Mild	75–89					
			60–74					
	G3a	Mild-moderate	45–59					
	G3b	Moderate-severe	30–44					
	G4	Severe	15–29					
	G5	Kidney failure	<15					

Acknowledgements

G Jerums
S. Panagiotopoulos
E. Premaratne
E. Ekinci
K. Cheong
S. Verma
S. Finch