

***Microalbuminuria; a cardiovascular or a renal risk factor or both?***

Dick de Zeeuw  
Department of Clinical Pharmacology  
University Medical Center  
Groningen  
The Netherlands

# Common and Novel Risk factors for Cardiovascular and Renal Disease progression

- Age
- Gender
- Body Weight
- Smoking
- Blood pressure
- Cholesterol
- Diabetes

the Framingham Risk Score

*Wilson PWF et al. Circulation 1998; 97: 1837-47*

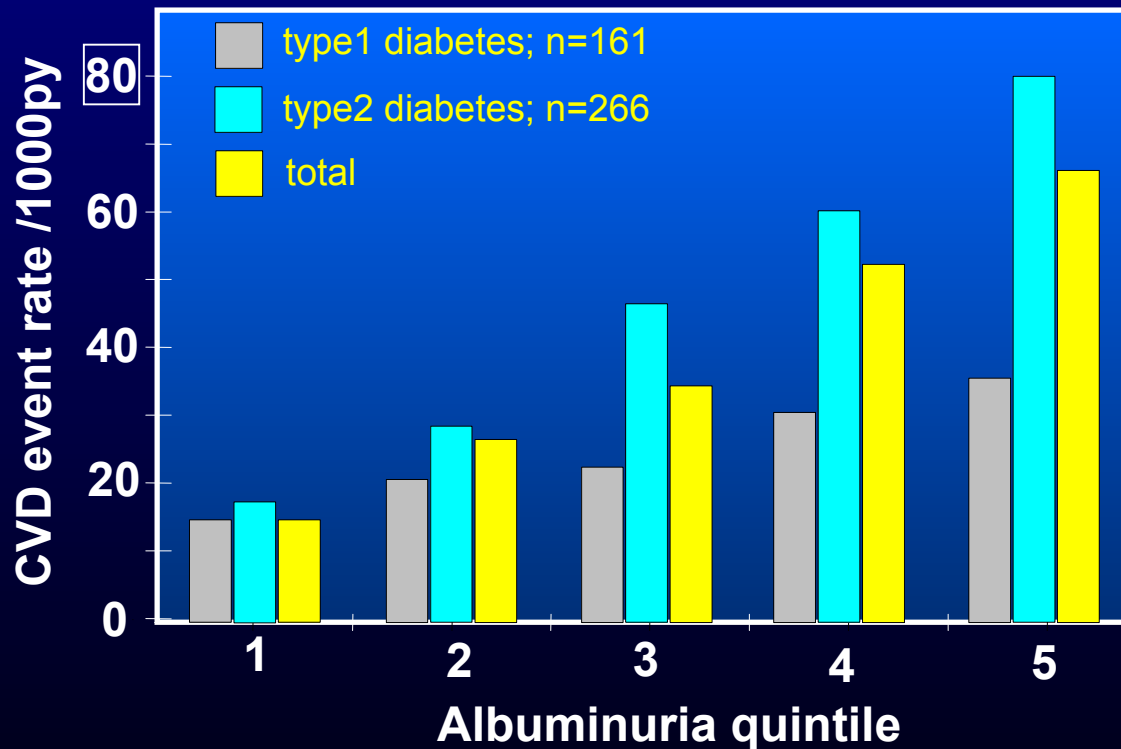
- *CRP, pro-BNP etc*
- Hemoglobin
- **GFR**
- **Albuminuria!**

**Novel Risk markers or FACTORS?**

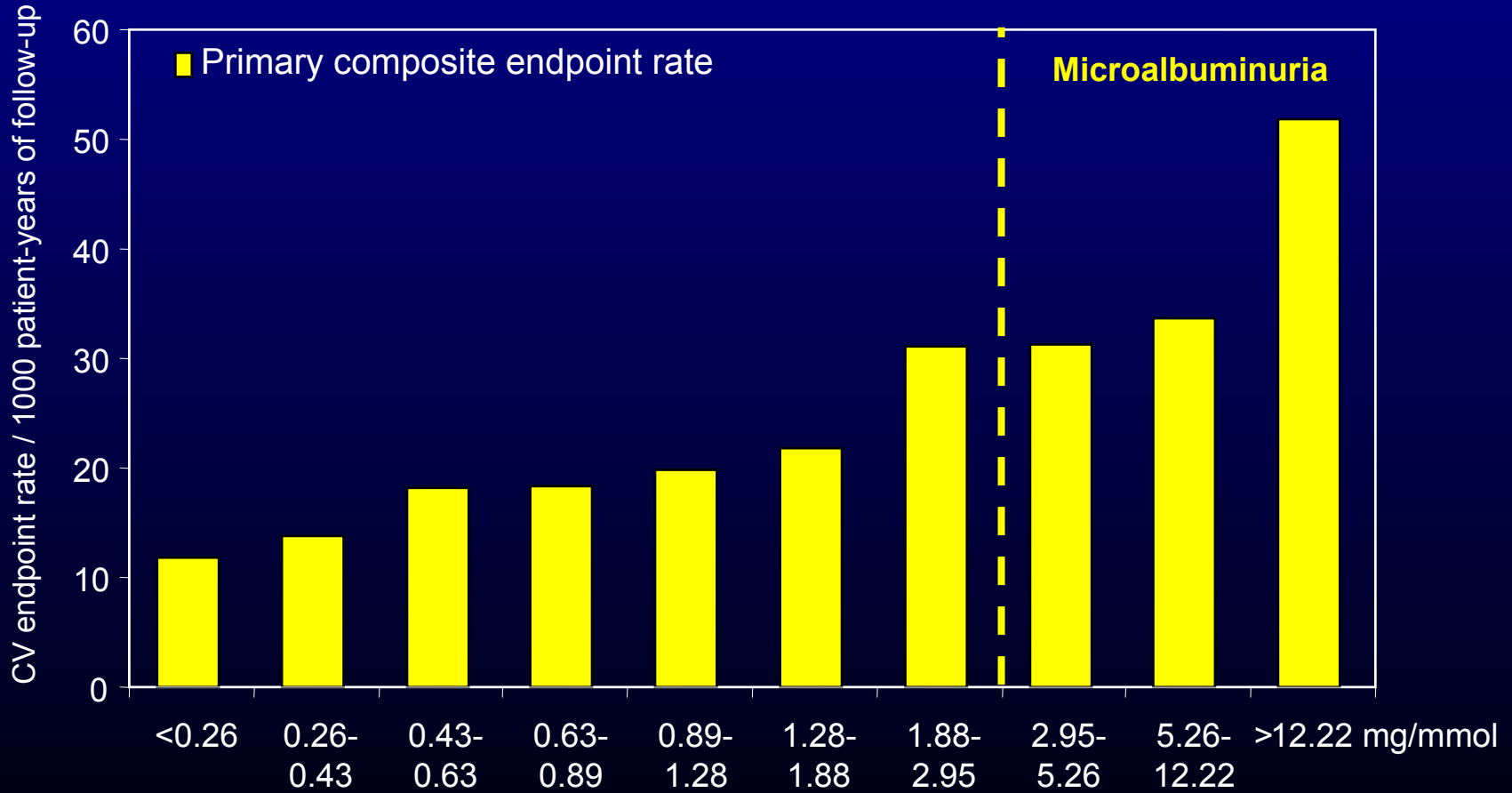
# Albuminuria; a target for renal and cardiovascular protection?

- Albuminuria is related to renal and CV risk:
  - The higher albuminuria, the more risk (for early patients as well as healthy individuals)
  - Independent of other risk markers
  - Preceding other risk markers
- Lowering albuminuria is related to renal and CV risk reduction:
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- Common origin for albuminuria and CV and renal disease?

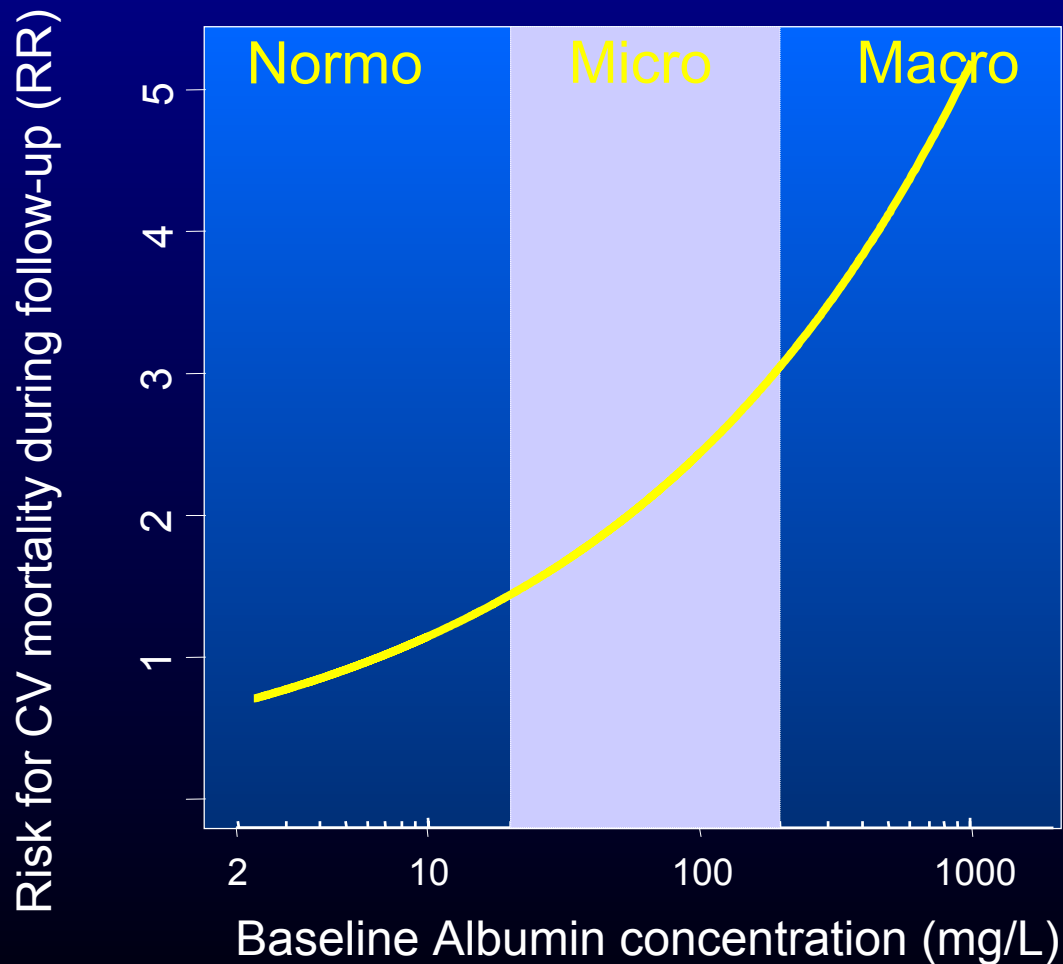
# Addenbrooke's Nephropathy Cohort: Albuminuria predicts CV outcome in diabetes with albuminuria >30mg/d



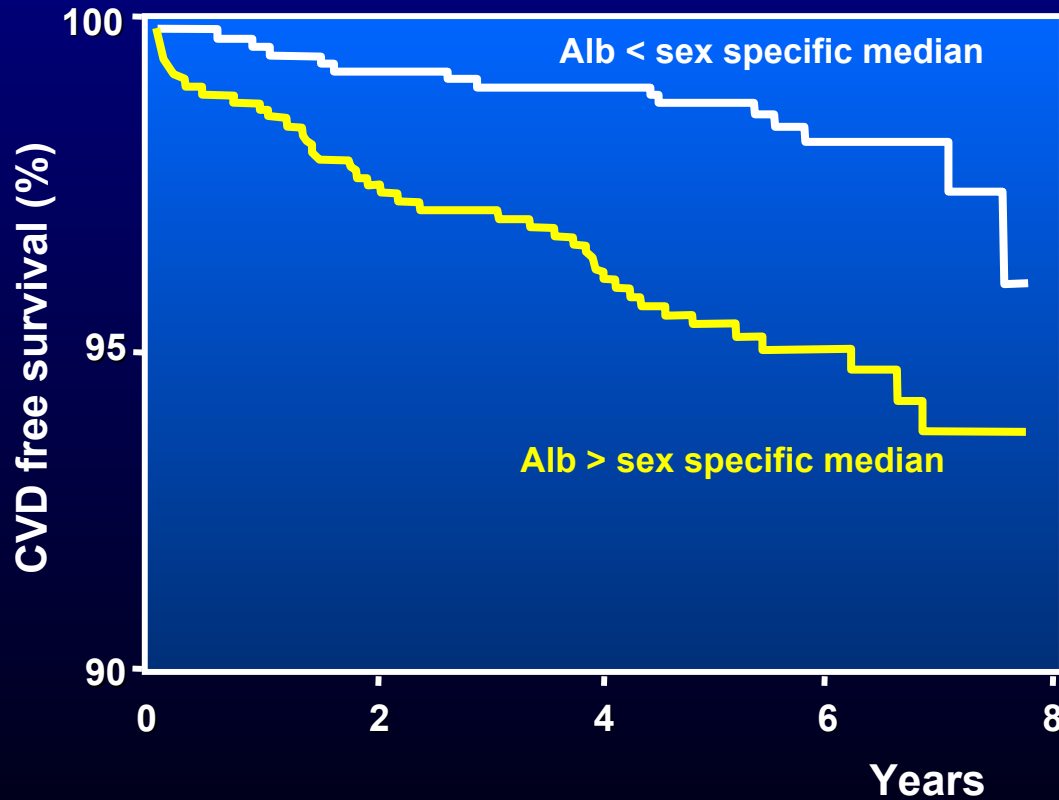
# LIFE; Baseline albuminuria associated with cardiac events *in hypertension with LVH*; (n=8206)



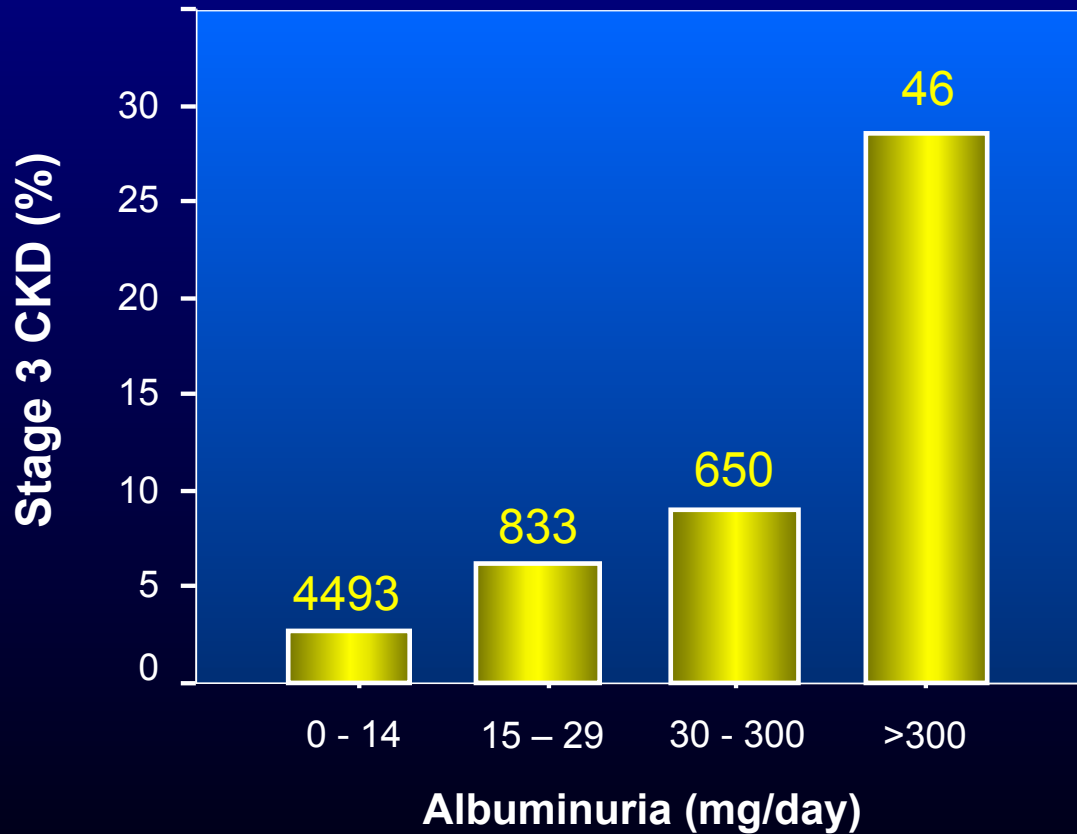
# PREVEND; Albuminuria predicts CV mortality in the general population (4 yr follow-up)



# Framingham; Albuminuria determines survival free CVD the non-diabetic, non-hypertensive subjects (n=1568)



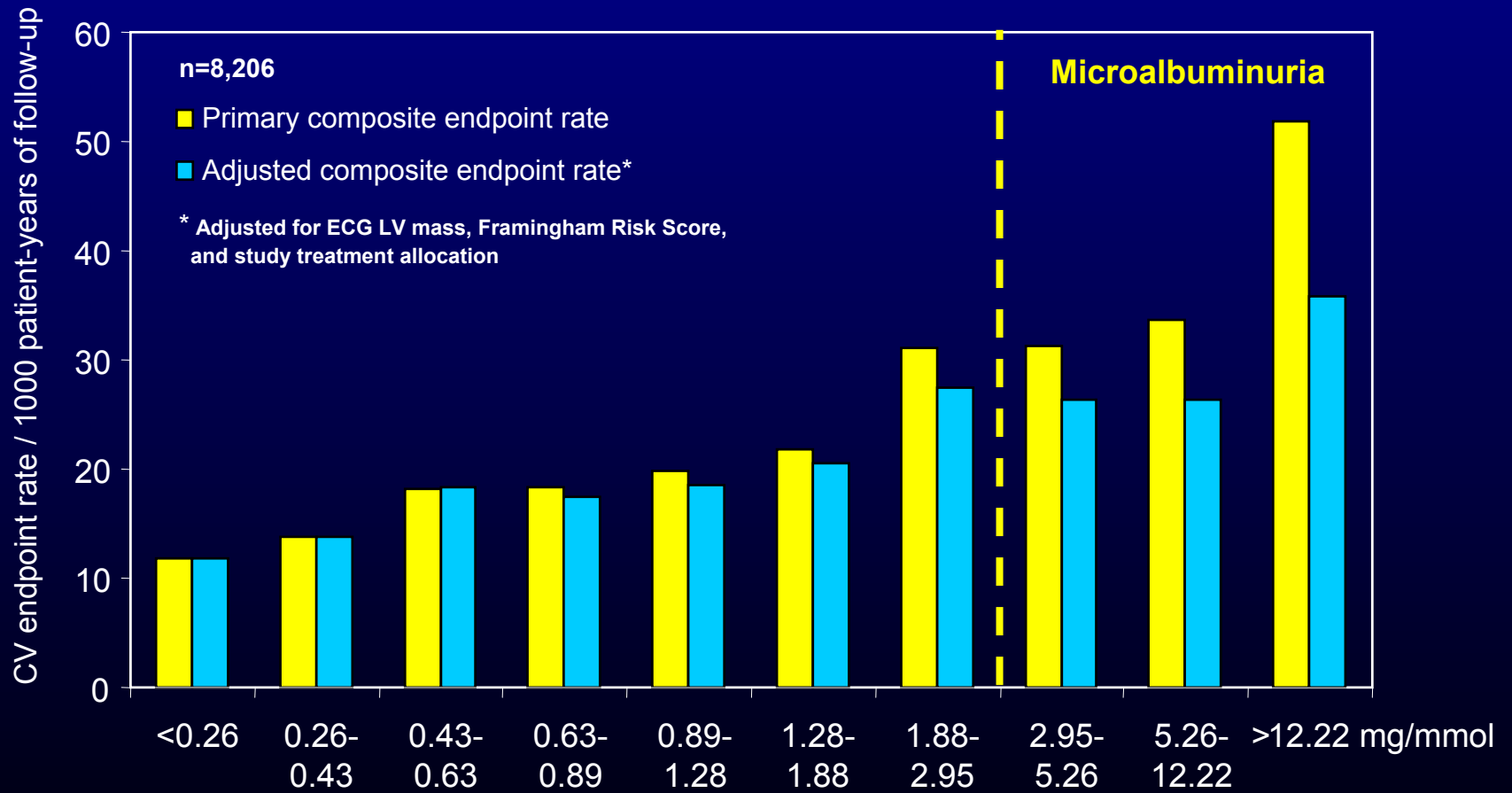
# PREVEND; Albuminuria predicts moderate CKD in the general population (4 jr)



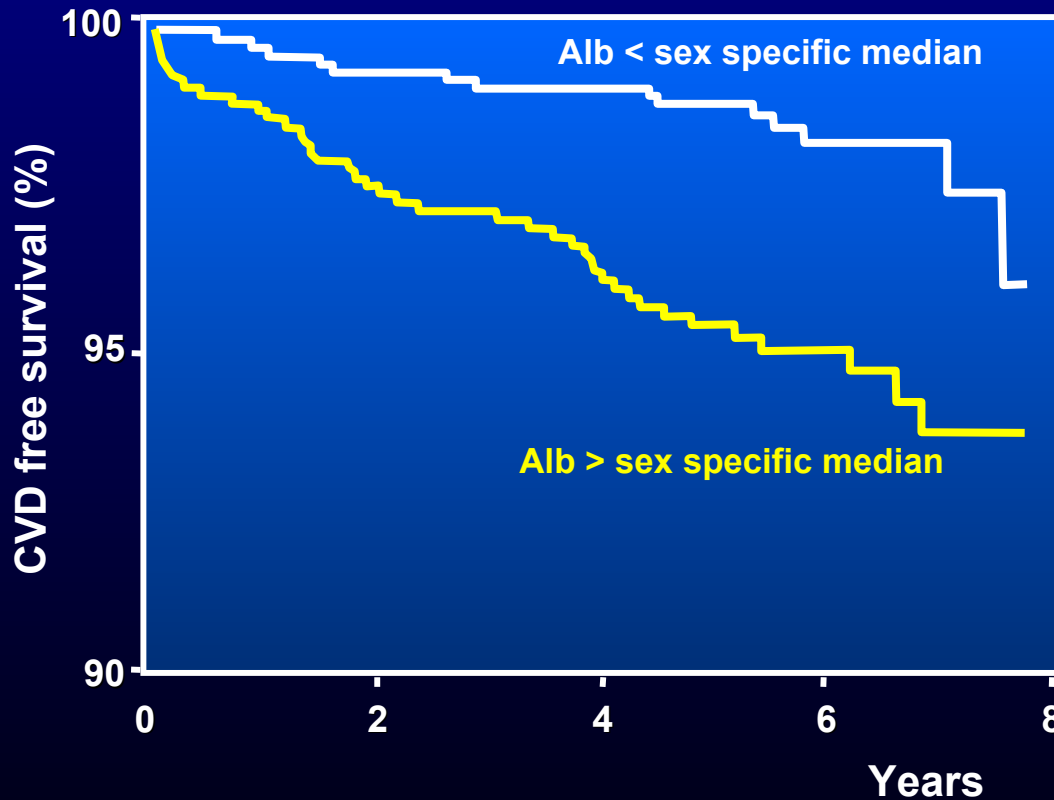
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# LIFE; Baseline albuminuria as determinant of cardiac events in hypertension with LVH



# Framingham; Albuminuria determines survival free CVD the non-diabetic, non-hypertensive subjects (n=1568)

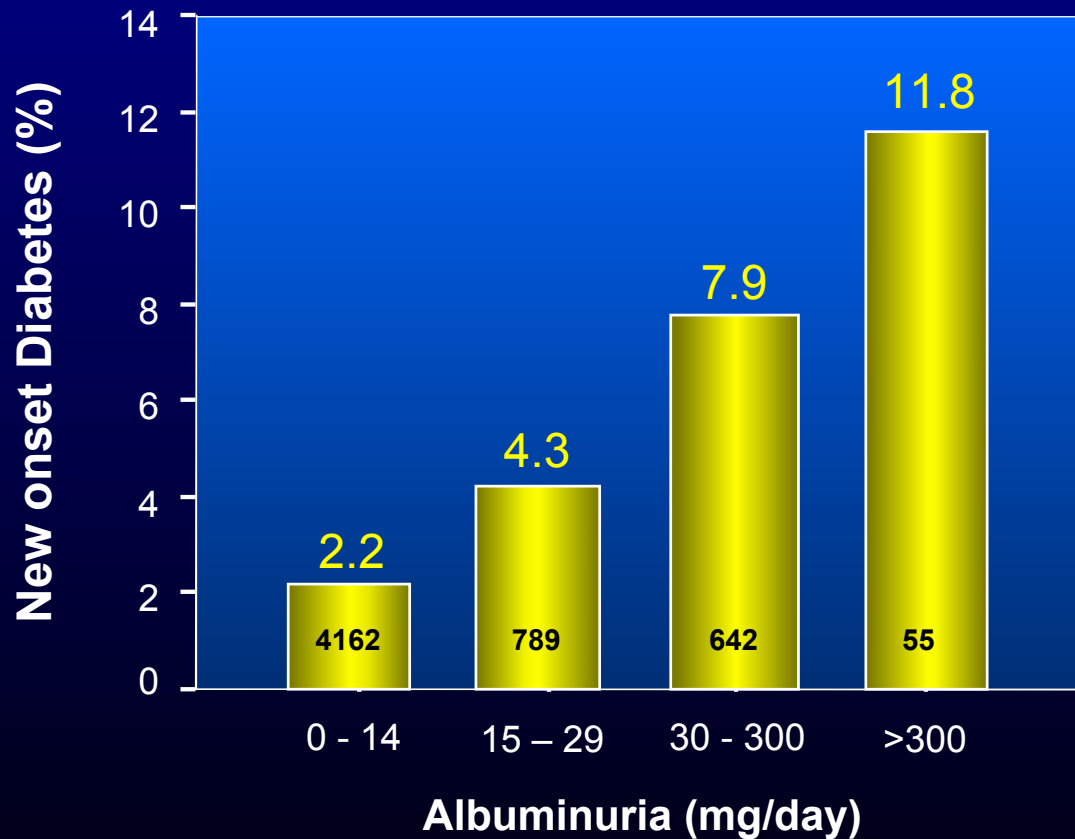


	UACR < median	UACR > median
N	<b>783</b>	<b>785</b>
Age (yr)	<b>54</b>	<b>56</b>
BMI (kg/m <sup>2</sup> )	<b>27.3</b>	<b>26.4</b>
SBP (mmHg)	<b>118</b>	<b>119</b>
Total/HDL chol ratio	<b>4.3</b>	<b>4.1</b>
Screat (mg/dL)	<b>1.1</b>	<b>1.1</b>
IFG (%)	<b>9</b>	<b>8</b>
Smoking (%)	<b>17</b>	<b>17</b>

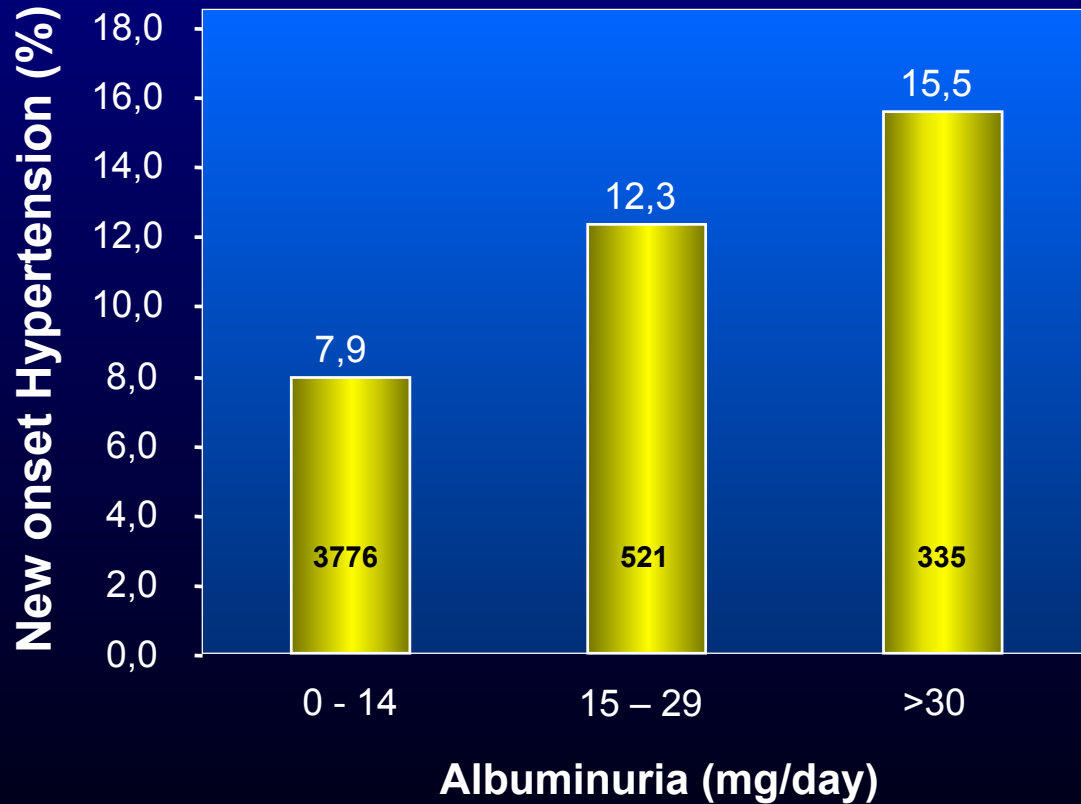
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# PREVEND; Albuminuria predicts new onset diabetes (n= 5654; follow-up 4,2 jr)



# PREVEND; Albuminuria predicts new onset hypertension (n=4635; follow-up 4,2 jr)



# Albuminuria; a target for renal and cardiovascular protection?

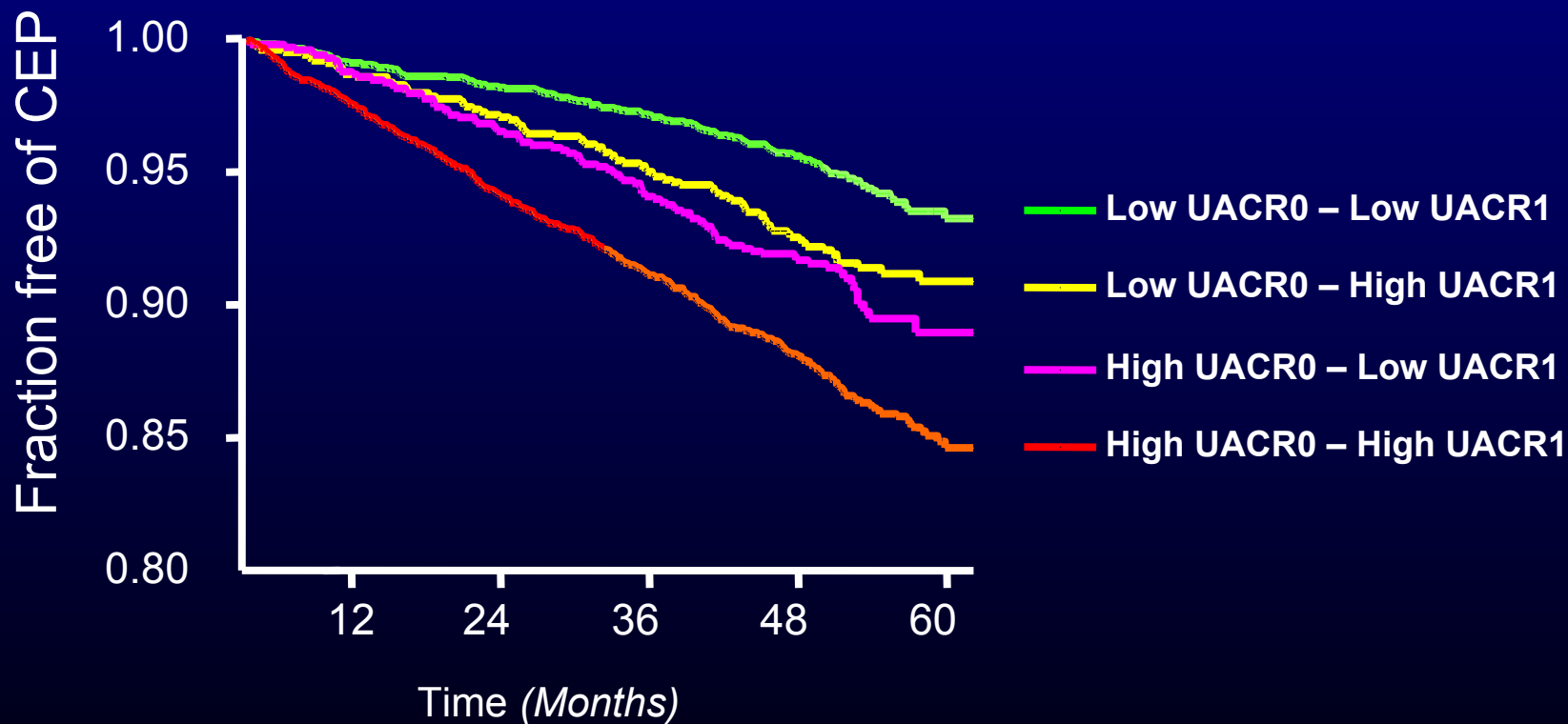
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# Drugs Reducing Albuminuria

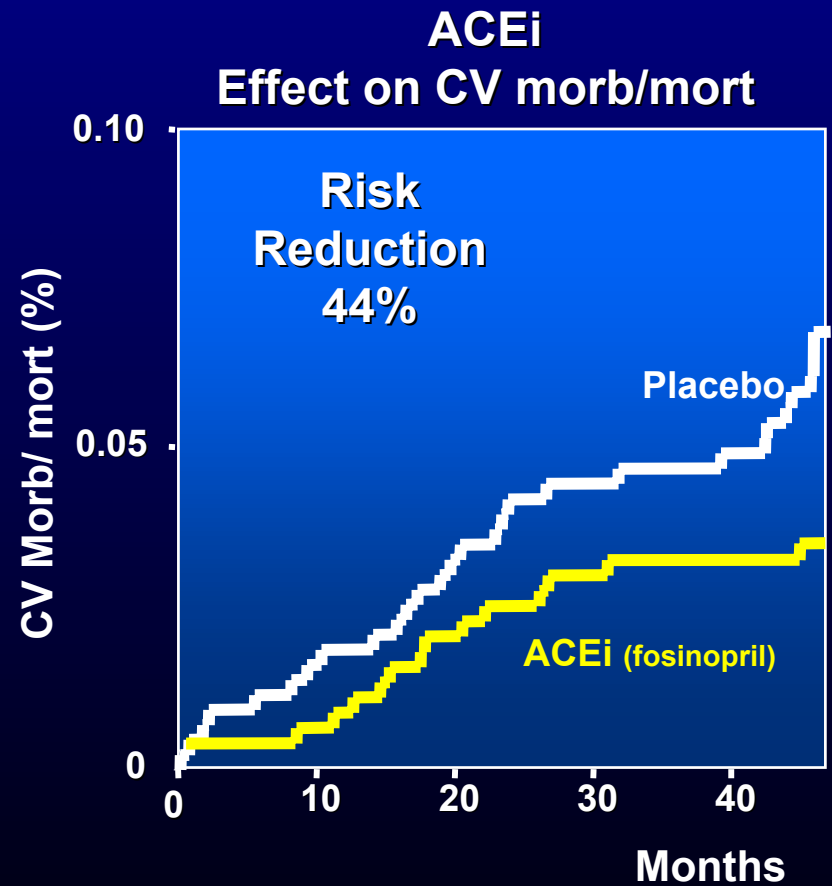
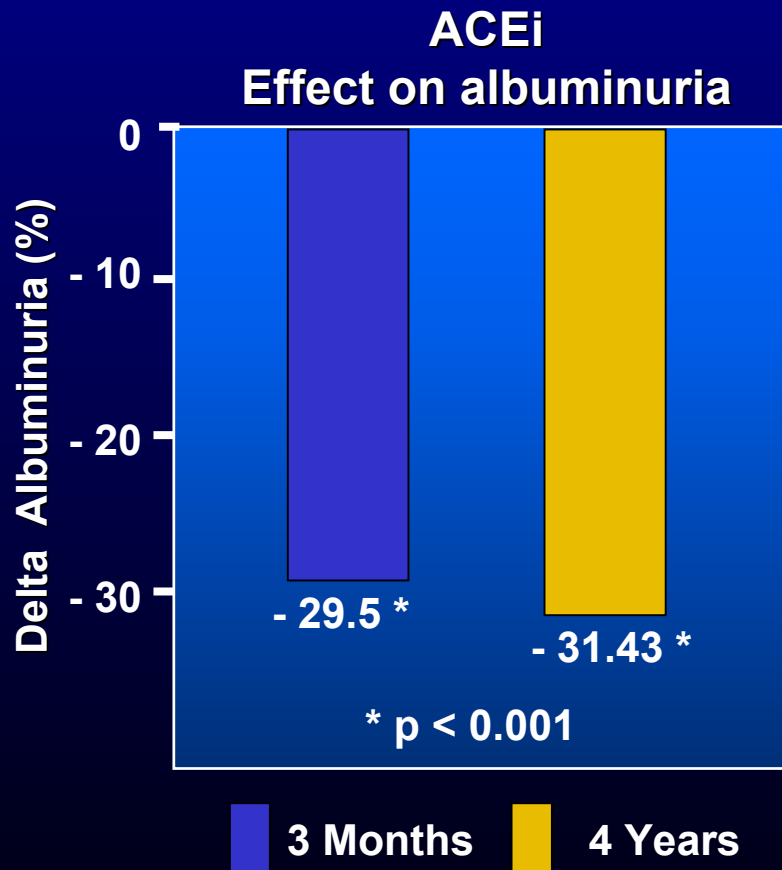
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- RAAS-intervention, ACEi and All-A (end point trials)
- Low Protein Diet (end point trials)
- Non-Steroidal-Antiinflammatory Drugs (no prospective endpoint trials)
- Glucosamino Glycans eg Sulodexide (trial stopped)
- Endothelin Antagonists (trial stopped)
- Statins (trials ongoing)
- Vitamine D analogues (trial ongoing)
- Renin-inhibitors (trial ongoing)

# LIFE; Treatment (ARB, losartan) associated with lowering albuminuria is cardioprotective in hypertension with LVH



# PREVEND-IT; Treatment associated with lowering of albuminuria reduces CV morbidity/mortality in “healthy” microalbuminurics (n=800).

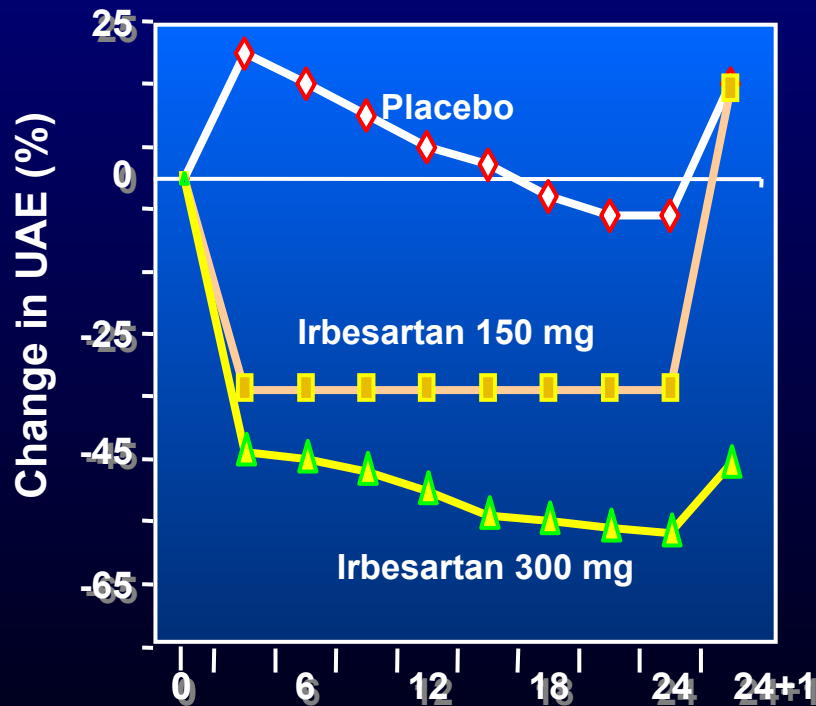


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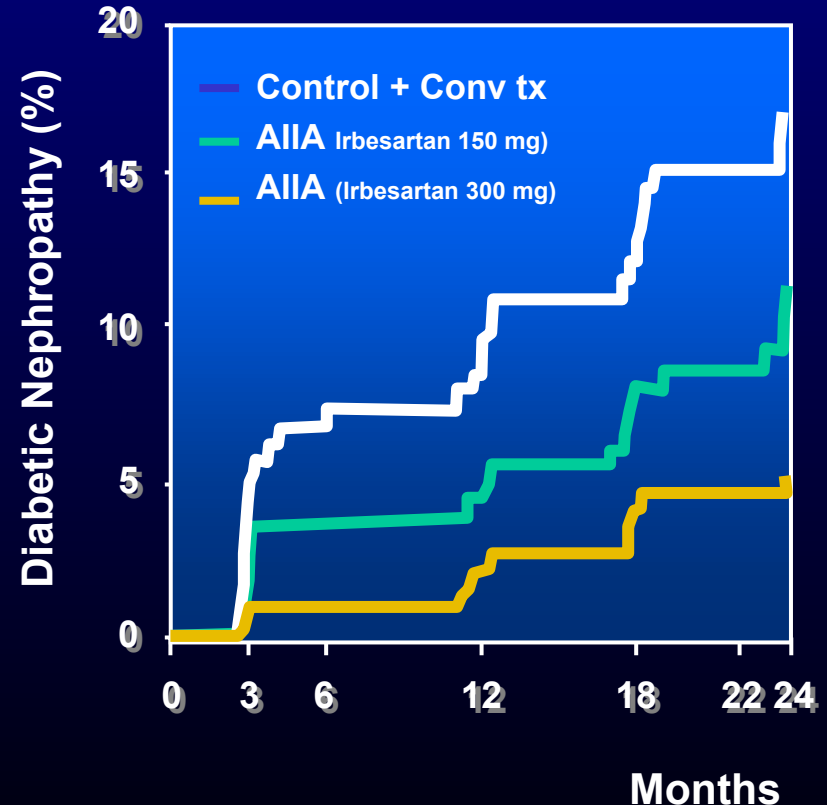
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# IRMA-2; Treatment associated with lowering of albuminuria reduces RENAL morbidity in hypertensive microalbuminuric type 2 diabetes. Prevention of transition to overt proteinuria

### AIIA (irbesartan) Effect on albuminuria

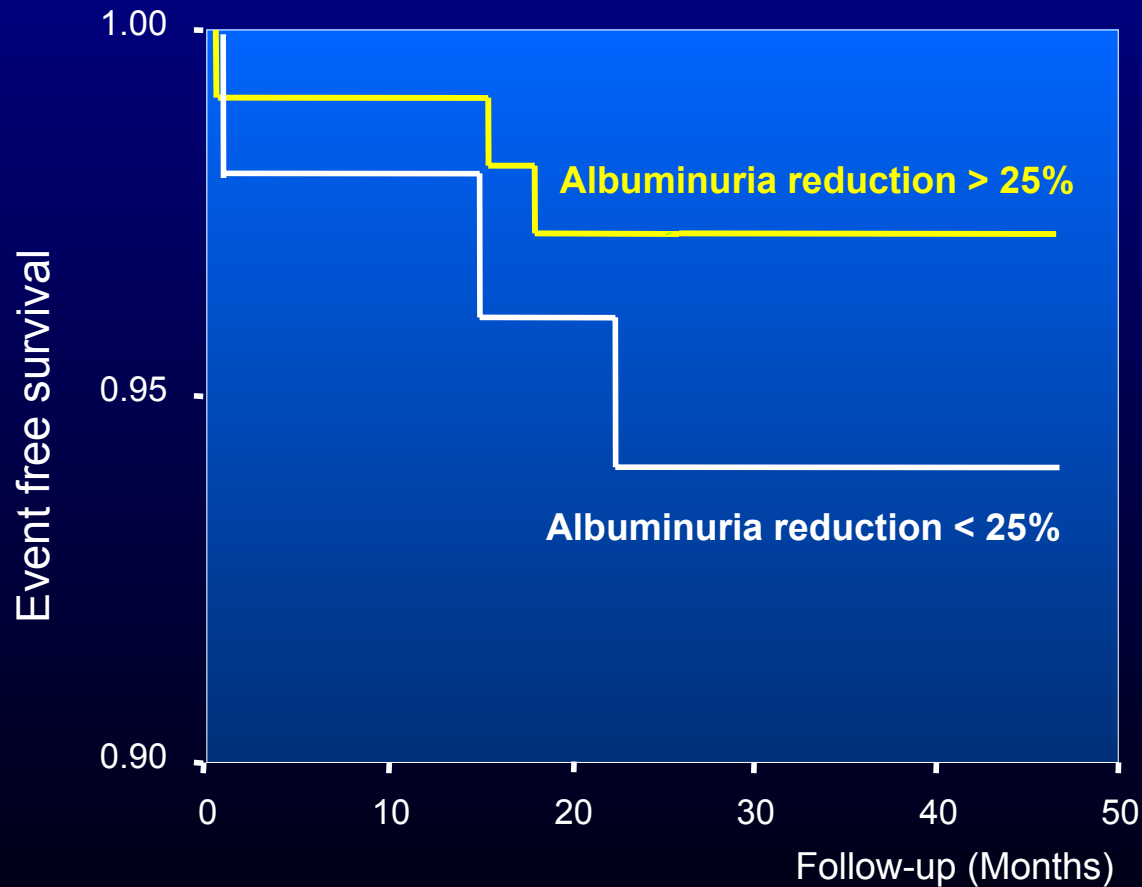


### AIIA (irbesartan) Effect on Renal Morb



Anderson S et al. *Diabetes Care* 2003  
Parving H-H et al. *N Engl J Med* 2001

# PREVEND-IT; Initial ACE-I (fosinopril) induced albuminuria reduction related to CV risk protection (n=800)

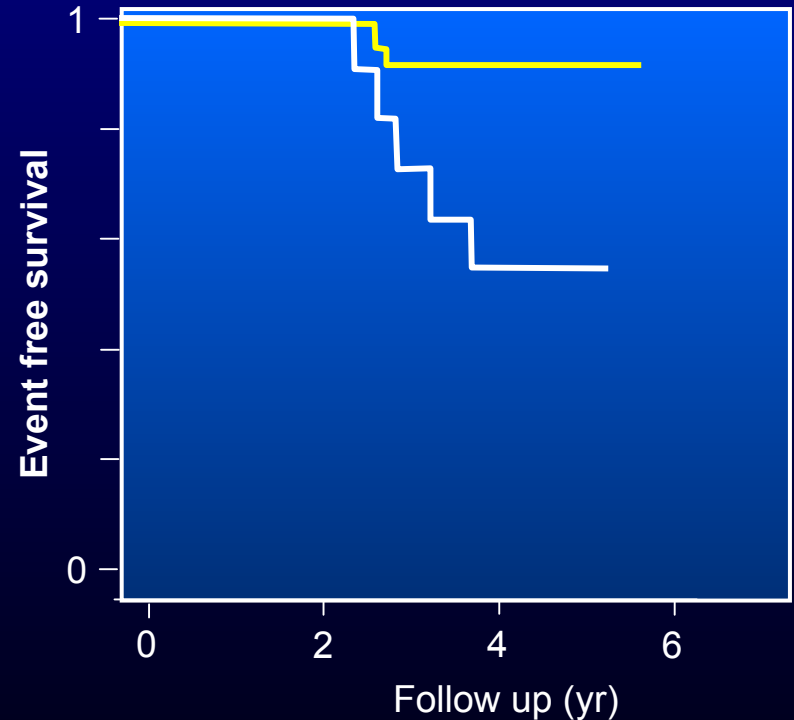
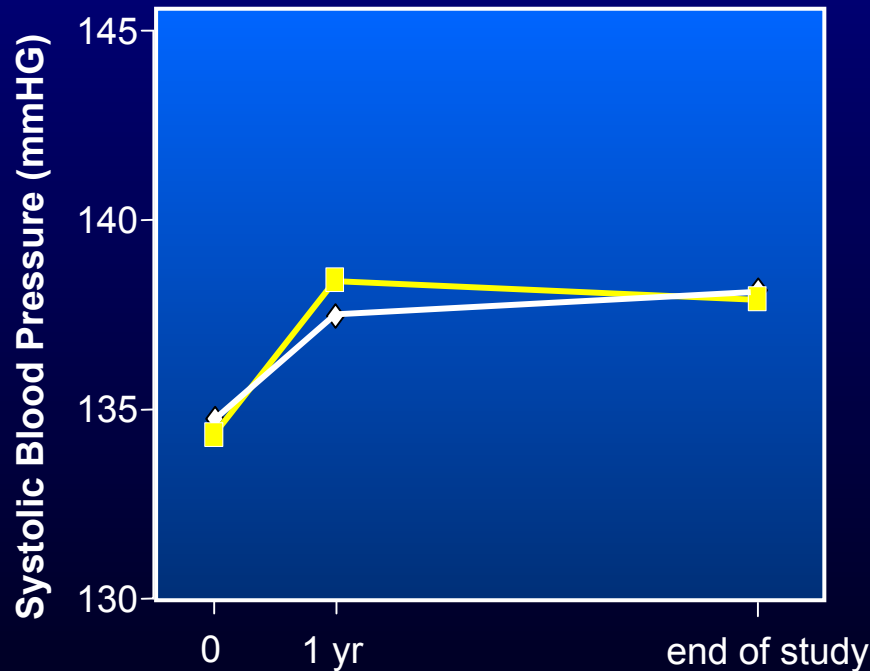


Data adapted from Asselbergs et al; Circulation 2004

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# Initial All-A (losartan) induced reduction in albuminuria predicts long term CV/renal risk in normotensive type diabetes (n=67)



**Albuminuria reduction >30% (70 to 40 mg/d)**

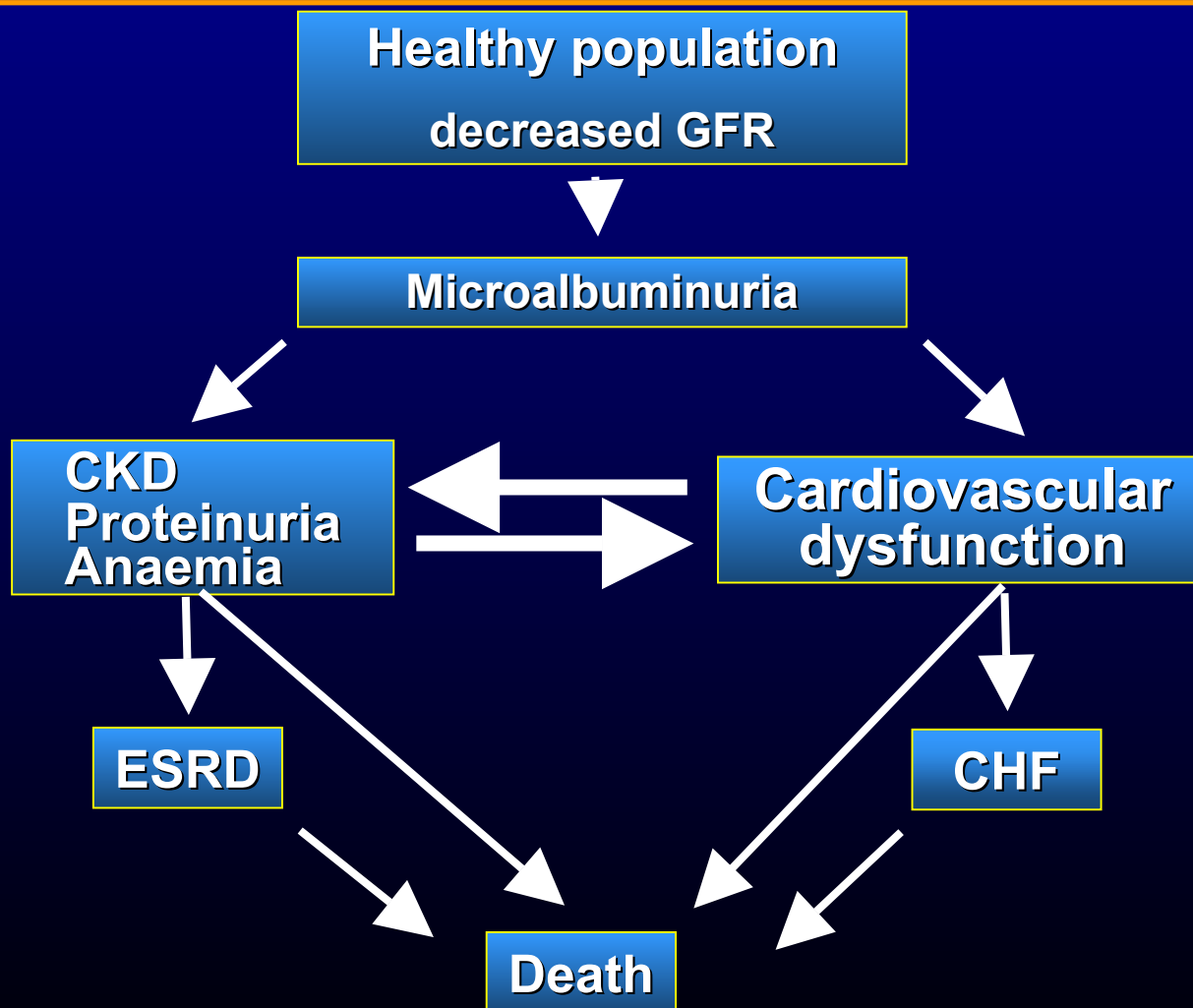
**Albuminuria increase >30% (80 to 220 mg/d)**

*Zandbergen et al; Diabetes Care 2007*

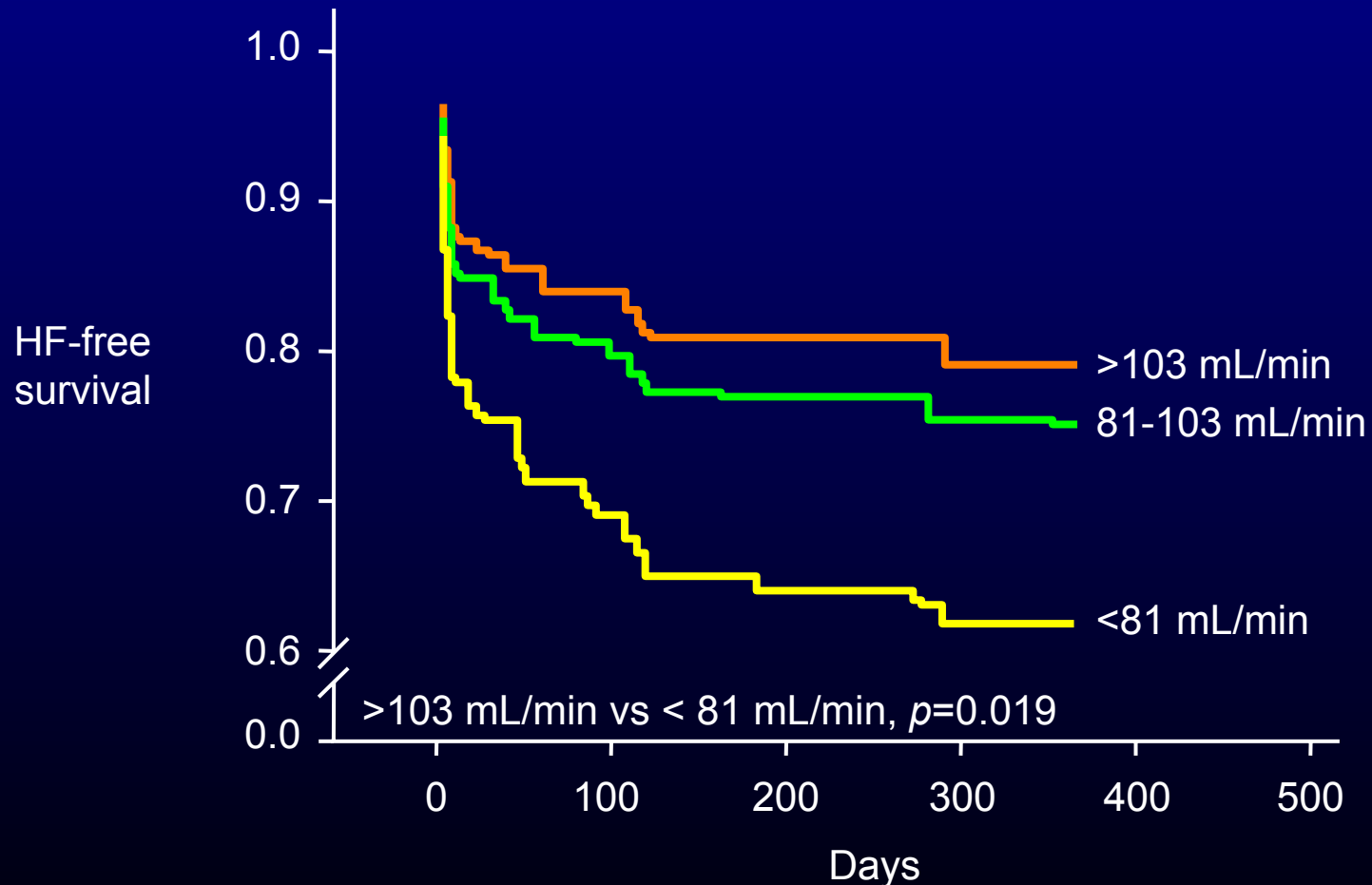
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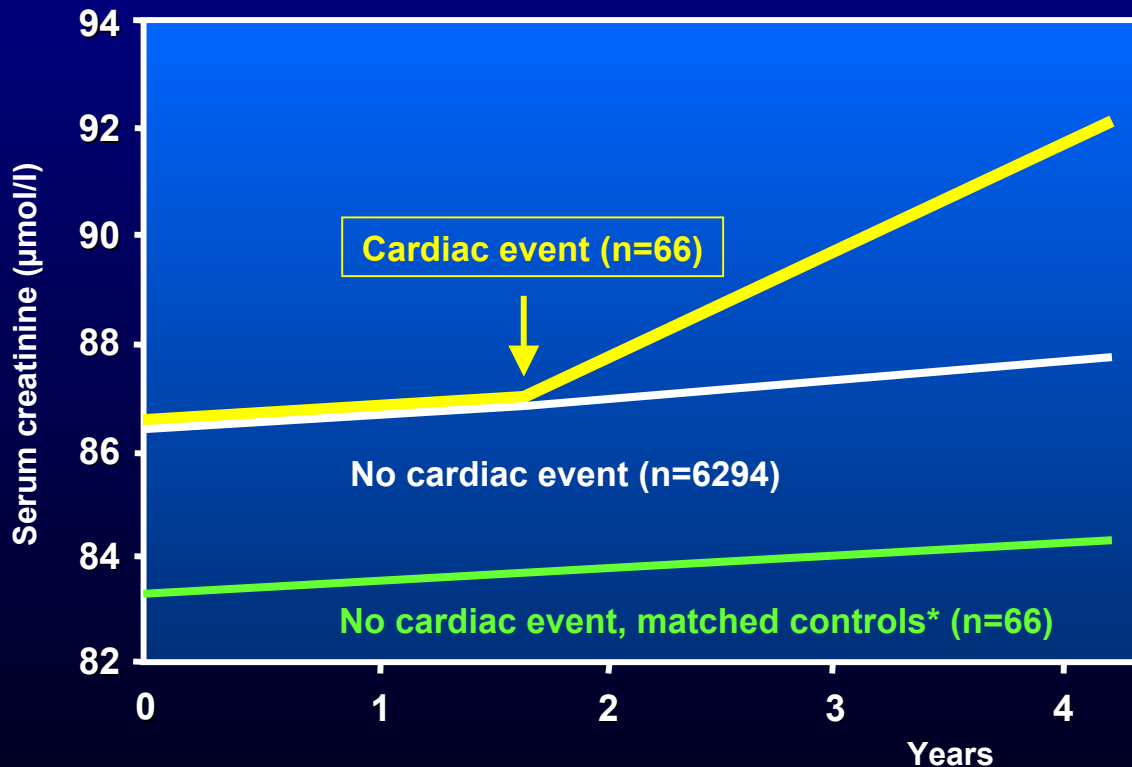
# Possible interaction between Renal dysfunction and Cardiac dysfunction in the general population



# CATS; Renal Function (eGFR) determines CV outcome in first myocardial infarction patients



# PREVEND; Effect of myocardial infarction on renal function in general population

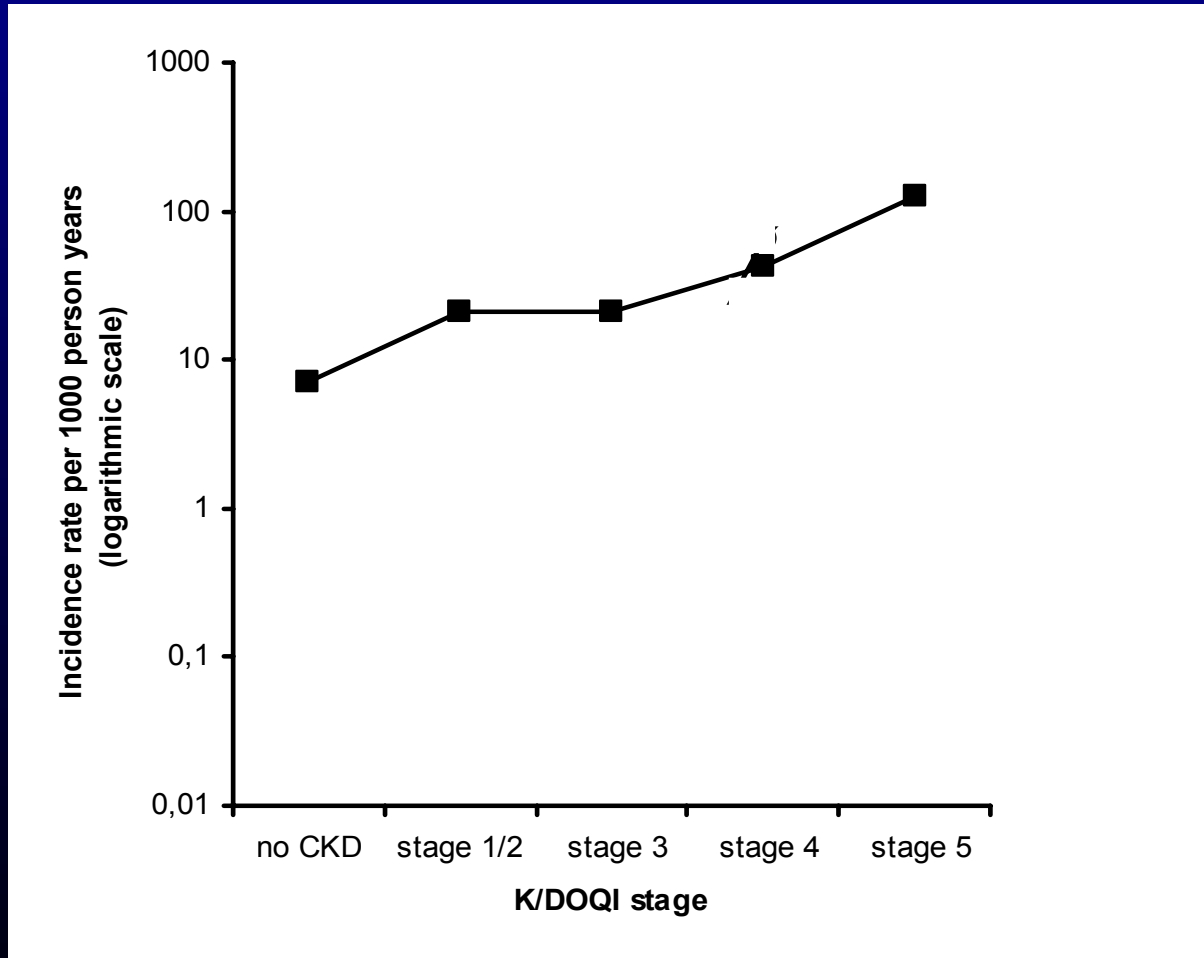


\*\* Matched control cohort of subjects without ischaemic cardiac event, based on age, gender, serum creatinine, urinary albumin excretion, body mass index, mean arterial pressure, serum cholesterol, triglycerides, serum glucose, and smoking.

# KDOQI based Renal dysfunction classes

<b>Stage</b>	<b>GFR (ml/min/1.73 m<sup>2</sup>)</b>	<b>Albuminuria</b>
<b>1</b>	<b>&gt; 90</b>	<b>+</b>
<b>2</b>	<b>60 - 89</b>	<b>+</b>
<b>3</b>	<b>30 - 59</b>	<b>+ or -</b>
<b>4</b>	<b>15 - 29</b>	<b>+ or -</b>
<b>5</b>	<b>&lt; 15 or RRT</b>	<b>+ or -</b>

# PREVEND; Incidence of cardiovascular events for stage of chronic kidney disease

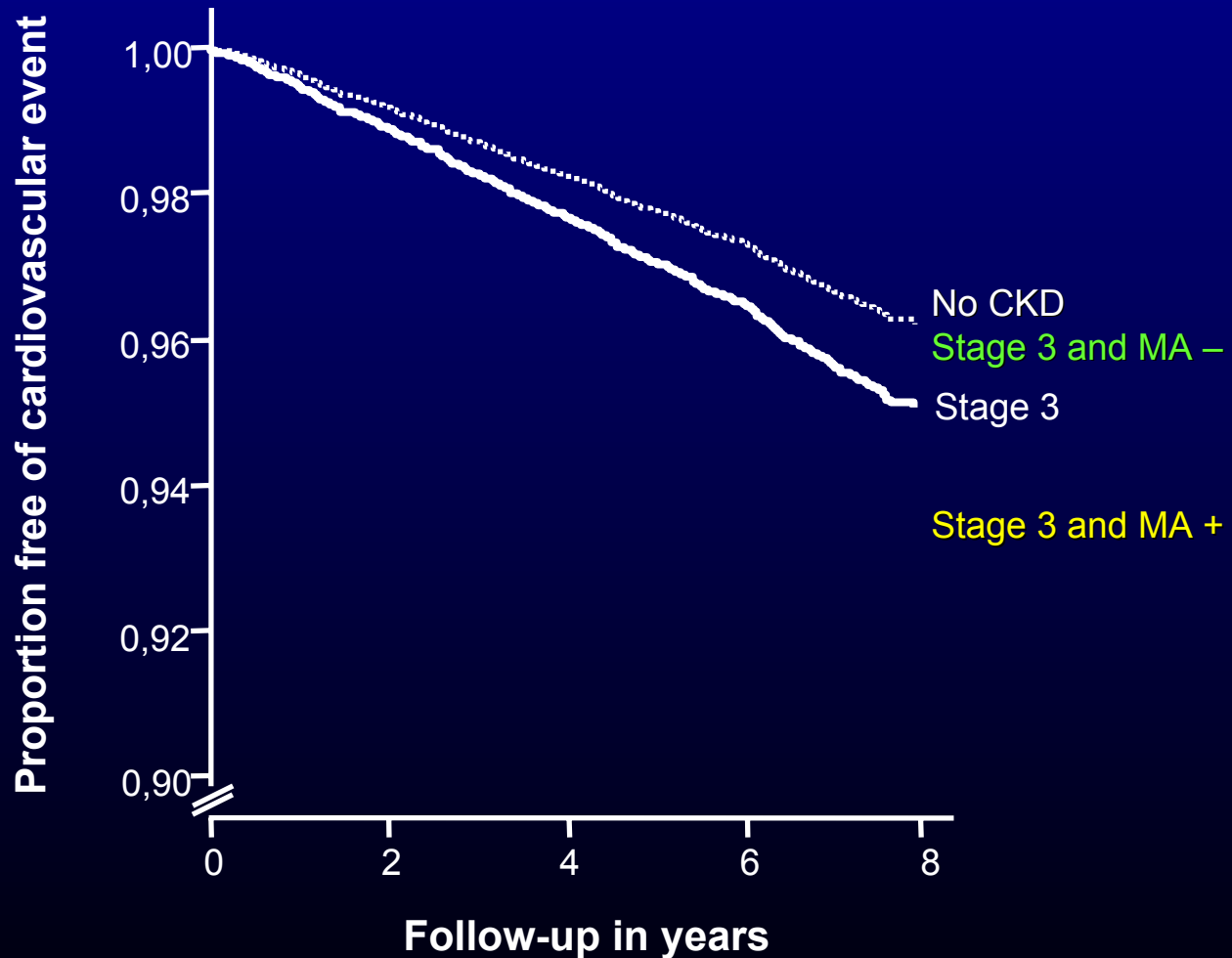


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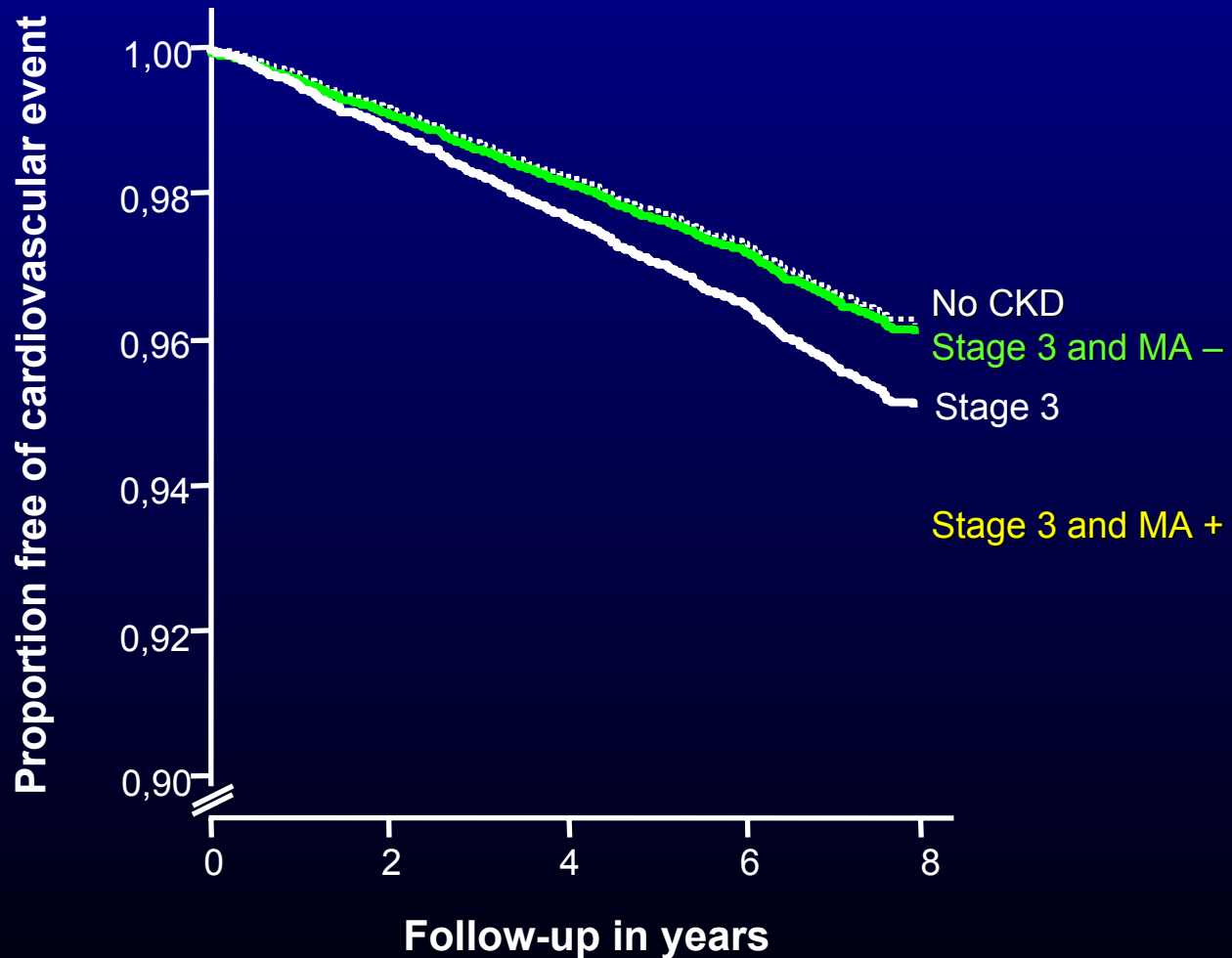
# PREVEND; eGFR or microalbuminuria and CV risk

## Microalbuminuria more important (Age/sex adjusted)



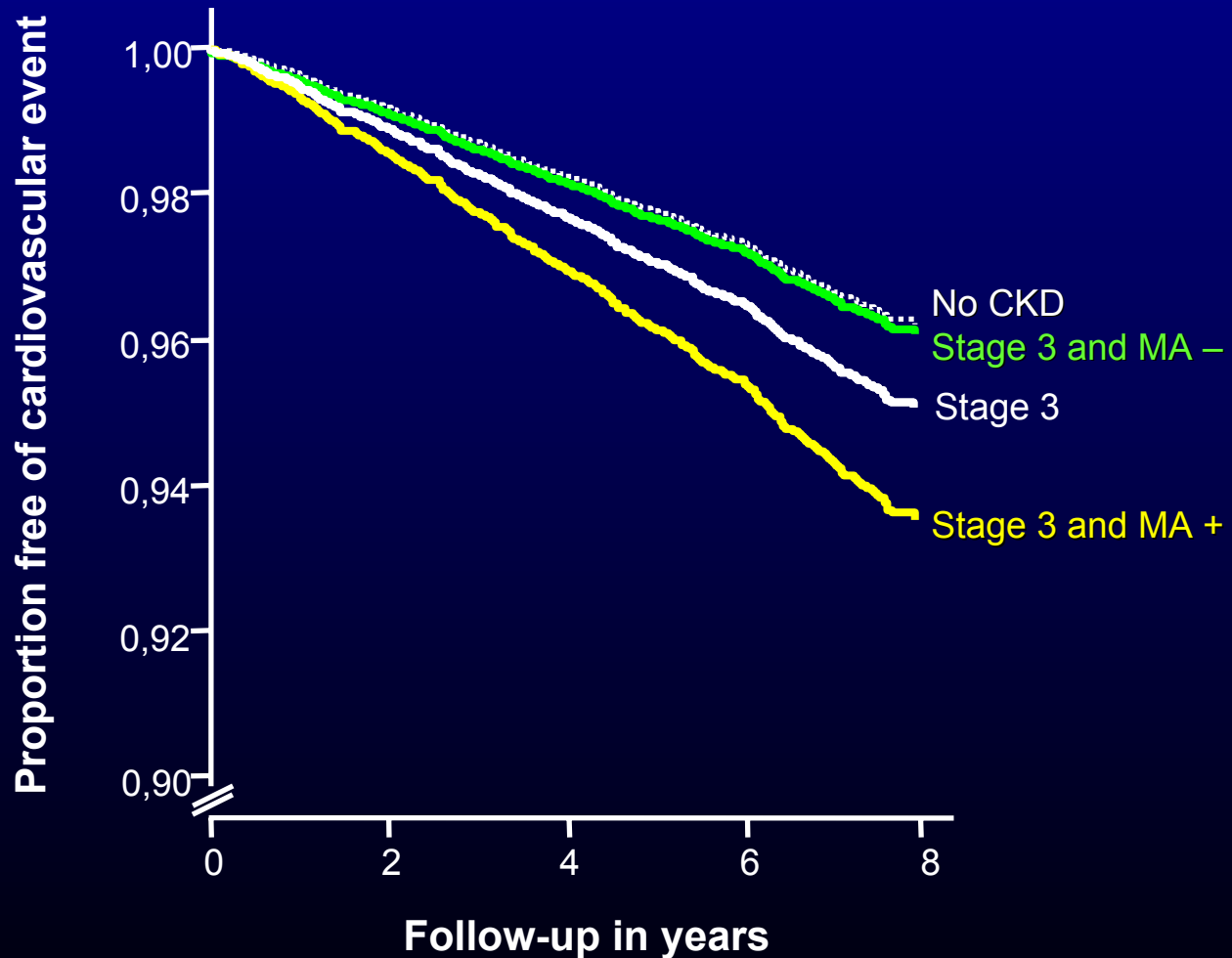
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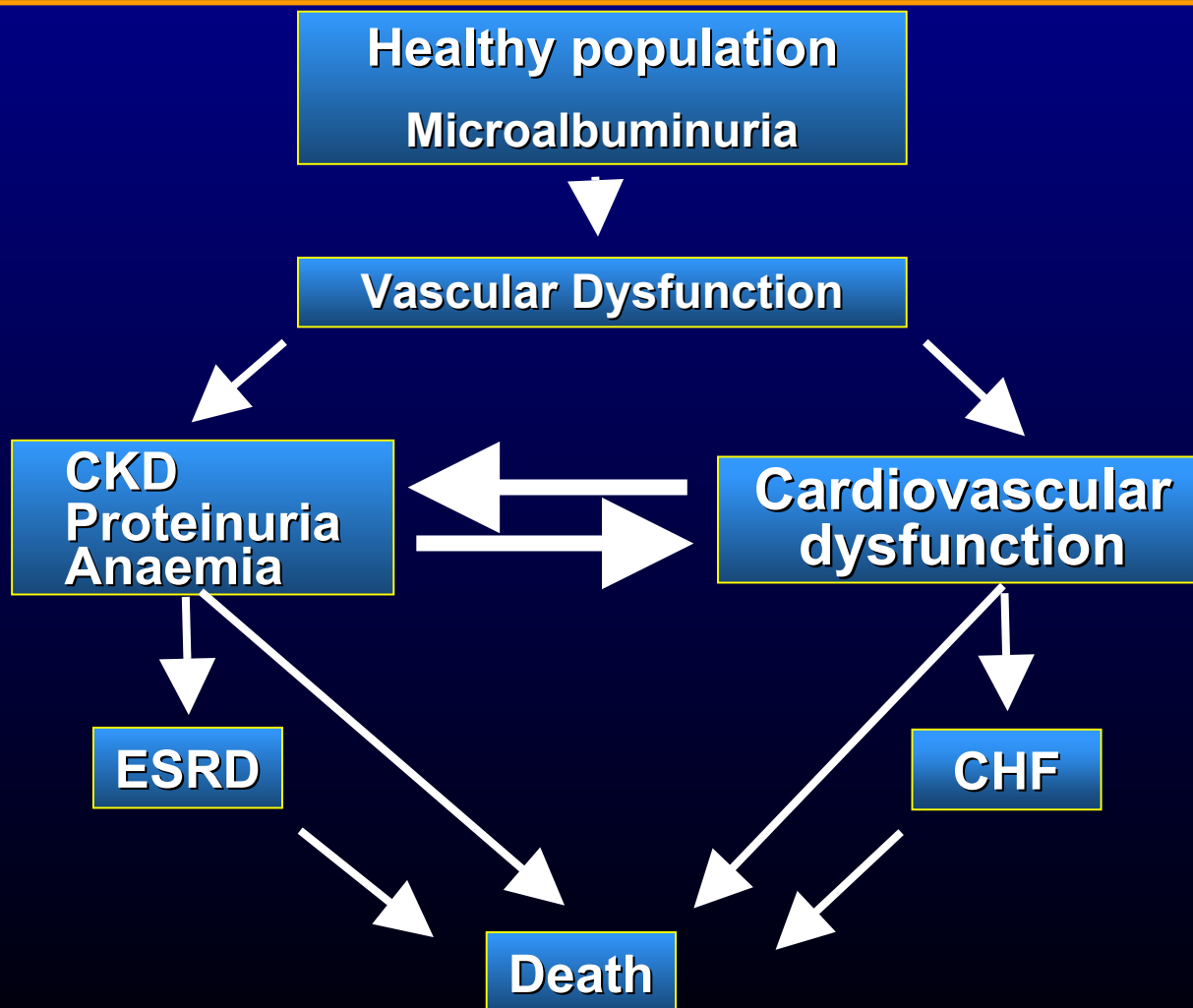


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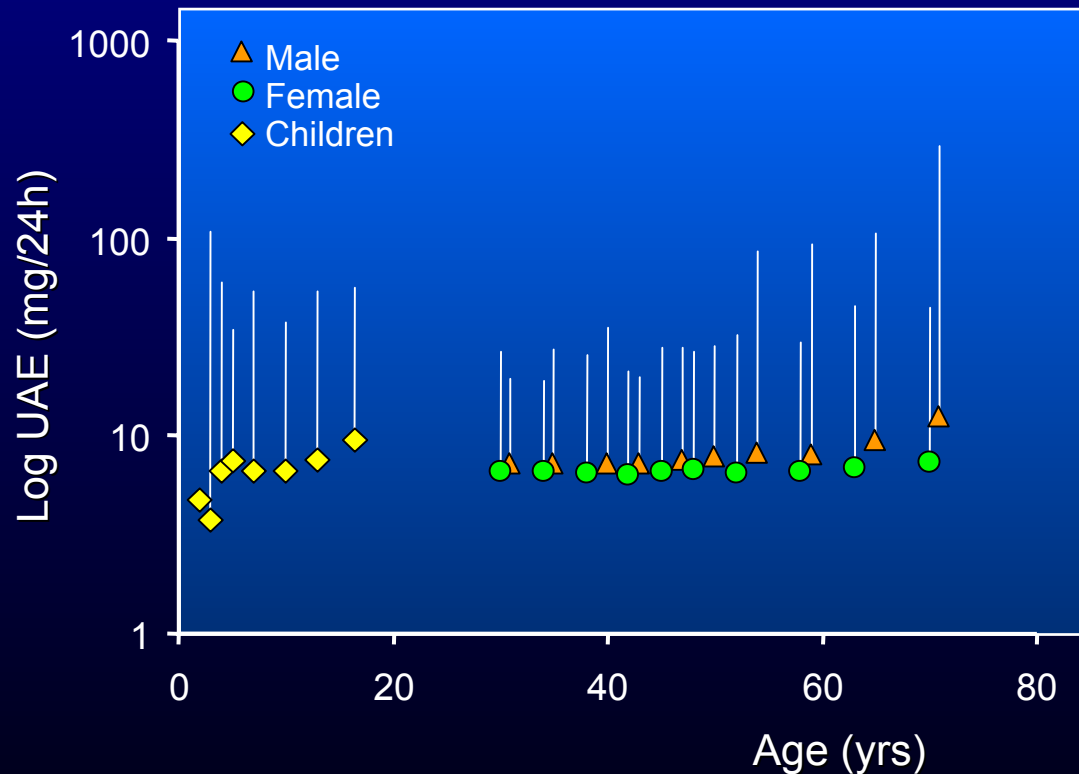
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# Possible interaction between Renal dysfunction and Cardiac dysfunction in the general population



# Urinary albumin excretion and age (cross sectional) in general population children and adults

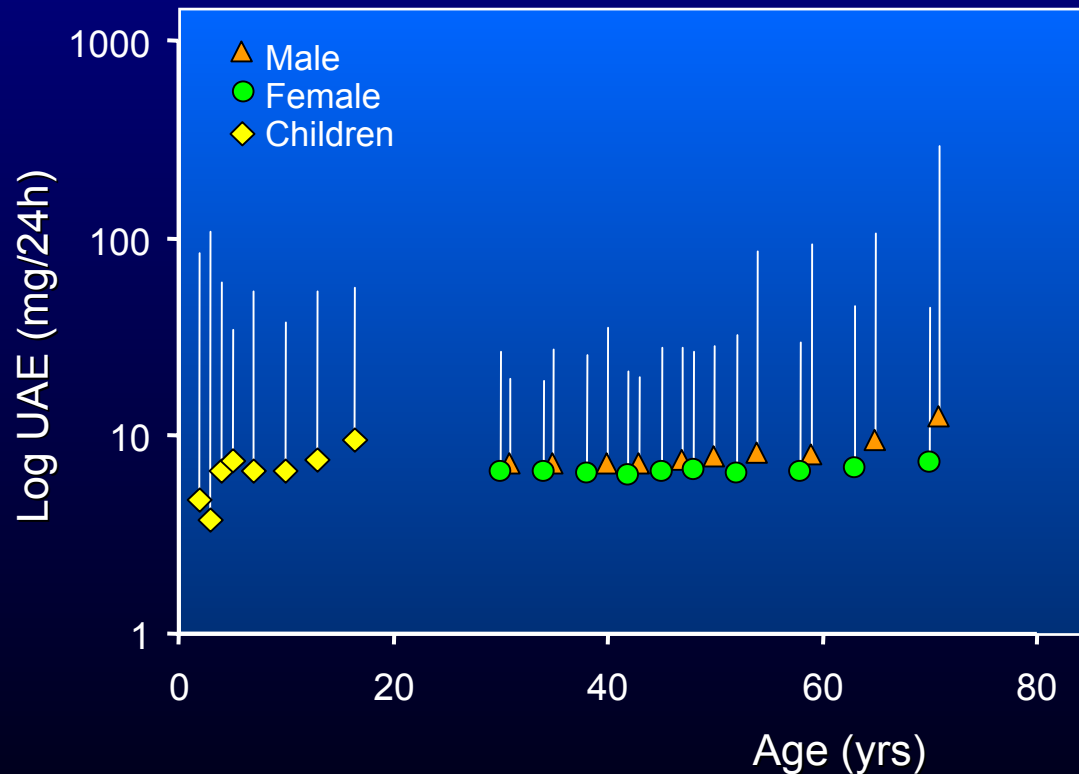


De Zeeuw et al, JASN, 2006

adapted from Verhave et al, JASN 2003

Lehrnbecher et al. *Pediatr Nephrol* 1998 (children);

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# The albumin molecule

cardiovascular protection ?



**The albumin molecule, which ever way you look at it,  
related to cardiovascular protection?**



# Summary

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- Cardiac and renal dysfunction show interactions. Renal dysfunction predicts cardiac dysfunction, and cardiac dysfunction predicts renal dysfunction.
- The mechanism is still unknown, but a common inborn vulnerability of the vasculature could make the kidney and the heart seemingly interact.

# Summary

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# Summary

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- Hypothesis: Increased albumin levels are an early indicator of general vascular dysfunction. This may also affect the kidney resulting in a decreased GFR. Both the vascular dysfunction and the hormonal consequences of renal dysfunction can result in cardiac damage. Cardiac damage may result in further vascular dysfunction with renal implications.

TREATMENT IMPLICATION?

**Treat the kidney to cure the heart.**

**Treat the heart to cure the kidney?**