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domus medica
vereniging van huisartsen

De falende filter

– nierinsufficiëntie -

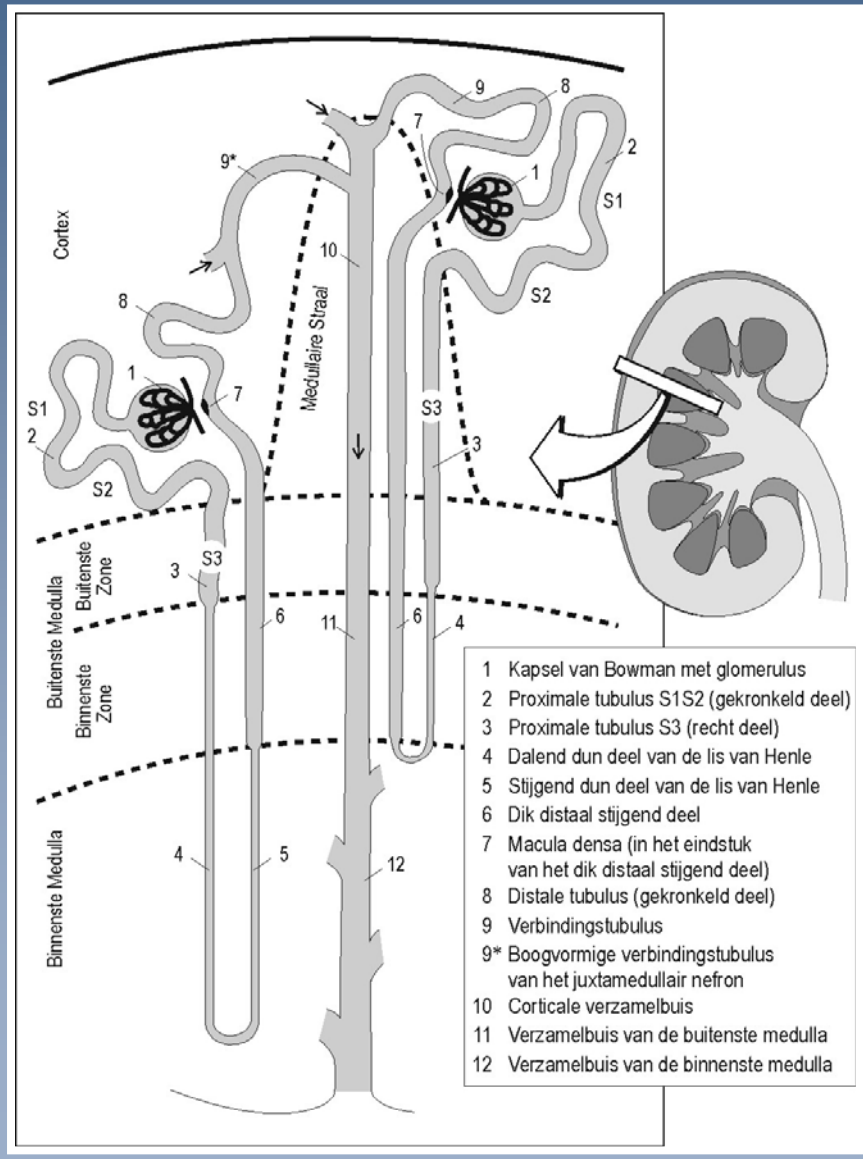
Universiteit Antwerpen
Universitair Ziekenhuis Antwerpen

UZA
kennis / ervaring / zorg

Is de nier louter een filter ?

1. Glomerulus = filter
   - vormt het ultrafiltraat: 180 L/dag
   - produceert renine
2. Tubulus
   - secreteert (H^+, K^+, afvalstoffen, medicatie) en reabsorbeert (H_2O, Na, HCO_3^-)

     $\Rightarrow$ urine: 1 à 1,5 L/dag
   - produceert vitamine D en erythropoïetine



Functies van de nieren

1. Excretie

   afvalstoffen (= eindproducten van metabole processen)

   - vb. ureum

   lichaamsvreemde stoffen

   - vb. medicatie

2. Homeostase

   = de chemische samenstelling van het lichaam constant houden (water, elektrolyten, pH, osmolaliteit)

   $\Rightarrow$ invoer + productie = uitvoer + verbruik

3. Productie van enzymen en hormonen

   - vb. renine, erythropoïetine, vitamine D

De falende filter

1. Hoe evalueren ?

2. Is nierfalen frequent ?

3. Wat is de klinische betekenis ?

De falende filter

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Glomerulaire filtratiesnelheid (GFR)

= som van de filtratie van alle functionele glomeruli of nefronen

= gemeten door middel van de klaring van een stof “x” die vrij gefilterd wordt en noch gereabsorbeerd, noch gesecreteerd wordt door de tubuli

$$GFR \cdot P_x = U_x \cdot V$$

$$GFR = \frac{Ux \cdot V}{Px}$$

Creatinineklaring

Stof “x” = creatinine

maar

→ alleen in steady state

$$GFR = \frac{Ucreat \cdot V}{Pcreat^*}$$

*Pcreat = gemiddelde plasmacreatinine over 24hr

Merkers voor GFR – serum creatinine

Normaalwaarde: 0,6-1,2mg/dl

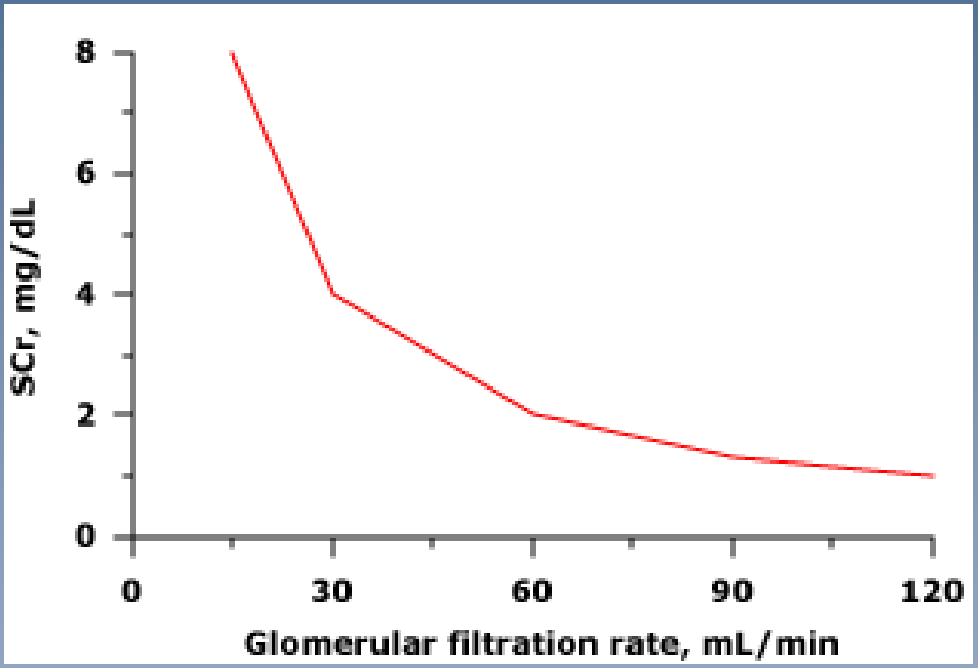
- De waarde is vooral een afspiegeling van de spiermassa afhankelijk van nierfunctie, leeftijd, geslacht, ras
- Verhoogd serum creatinine duidt dus op een verlaagde klaring en een verlaagde glomerulaire filtratie (GFR)
- Let op: overschatting bij ouderen, vrouwen, chronische zieken wegens minder spiermassa
- Let op: medicatie kunnen creatinine beïnvloeden (vb. cotrimoxazol)

Merkers voor nierinsufficiëntie – serum creatinine

Serum creatinine 1 mg/dl
Klaring: 50 ml/min

Serum creatinine 1 mg/dl
Klaring: 130 ml/min

Relatie tussen serumcreatinine en GFR



Idealized steady-state relationship between the serum creatinine concentration (SCr) and the GFR. A fall in GFR decreases creatinine filtration and produces a proportionate rise in the serum creatinine concentration.

Cockroft-Gault formule

$$CCr\ (mL/min) = \frac{(140 - age) \times \text{lean body weight [kg]}}{Cr\ [mg/dL] \times 72} *$$

**(x 0.86 for female)*

Cockroft and Gault

- original population (1976) = 249 healthy men (age 18-92)
- 2 x 24h urine collection
- optimal calibration of serum creatinine for this equation is uncertain (1976)
- for ♀: “arbitrary” x 0,85
- to compare to normal: adjust to BSA !
- practical problem: weight and height

Modification of Diet in Renal Disease (MDRD)

- Original:

  …

- Abbreviated:

  $186{,}3 \times Screat^{-1{,}154} \times age^{-0{,}203} \times 0.742$ (if female)

  $\times\ 1{,}210$ (if black) (ml/min/1.73 m²)

- Re-expressed: for use with creatinine values that are standardized to creatinine reference materials, measured using gold standard techniques:

  $175 \times Screat^{-1{,}154} \times age^{-0{,}203} \times 0.742$ (if female)

  $\times\ 1{,}210$ (if black) (ml/min/1.73 m²)

MDRD

- Original population (1999): n = 1628
  - white
  - non-diabetic kidney disease
  - mean age 51
  - mean GFR 40 ml/min/1.73 m^2
- Method: stepwise regression analysis of clearance of bolus ^{125}I-cothalamate* (S.C.), which is also partially tubular secreted

Recommendations for formal creatinine clearance measurement

- Extremes of age and body size
- Amputees
- Pregnancy
- Severe malnutrition or obesity
- Diseases of skeletal muscle
- Paraplegia or quadriplegia
- Vegetarian diet
- Rapidly changing kidney function
- Prior to dosing drugs with significant toxicity that are excreted by the kidney
- Prior to kidney donation
- Clinical research projects with GFR as a primary outcome

Table 6 from:
Levey AS et al. Definition and classification of chronic kidney disease: a position statement from Kidney Disease: Improving Global Outcomes (KDIGO). Kidney Int 2005; 67(6): 2089-100.

Classification of CKD (regardless of age !)

Stages of chronic kidney disease		
Stage	**Description**	**GFR** (ml/min/1.73 m²)
1	Kidney damage with normal or ↑ GFR	≥ 90
2	Kidney damage with mild ↓ GFR	60-89
3	Moderate ↓ GFR	30-59
4	Severe ↓ GFR	15-29
5	Kidney ↓ failure	< 15 (or dialysis)
Chronic kidney disease is defined as either kidney damage or GFR < 60 ml/min/1.73 m² for 3 months. Kidney damage is defined ad pathologic abnormalities or markers of damage, including abnormalities in blood or urine tests or imaging studies (www.uptodate.com).		

KDOQI stadia

Table 11-1. National Kidney Foundation Disease Outcomes Quality Initiative classification, Prevalence, and Action Plan for Stages of Chronic Kidney Disease.

Stage	Description	GFR, mL/min/1.73m²	Action
–	At increased risk	≥ 60 (with chronic kidney disease risk factors)	Screening: chronic kidney disease risk reduction
1	Kidney damage with normal or increased GFR	≥ 90	Diagnosis and treatment; treatment of comorbid conditions; slowing progression; CVD risk reduction
2	Kidney damage with slightly decreased GFR	60-89	Estimating progression
3*	Moderately decreased GFR	30-59	Evaluating and treating complications
4	Severely decreased GFR	15-29	Preparation for kidney replacement therapy
5	Kidney failure	< 15 (or dialysis)	Kidney replacement (if uremia present)

CVD, cardiovascular disease; GFR, glomerular filtration rate. [National Kidney Foundation-K/DOQI. Clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification: Am J Kidney Dis 2002; 39(Suppl 1): S1-S266.]

Manual of Nephrology (7th Ed.), chapter 11

* 3a: 45-59 3b: 30-44

De lekkende filter

- Proteïnurie
  - Micro-albuminurie:
    - Collectie: tot 300 mg per dag
    - ACR: Op staal tot 30 à 80 mg/g creatinine
  - Proteïnurie:
    - Met stick: sensitiviteit 49-56 % (indien <150-300 mg per dag)
    - Collectie
    - PCR:
      - Excellente correlatie met 24-uursproteinurie
      - Voorkeur voor proteinurie 300-1000 mg per dag
- Hematurie
  - Stick:
    - hoge sensitiviteit
    - Lage specificiteit
  - Fase contrastonderzoek:
    - Bevestiging van glomerulaire hematurie

Wat is de beste diagnostische test om de nierfunctie te meten in de dagelijkse praktijk?

- De evidentie suggereert dat de 4-variabelen MDRD beter presteert dan de Cockrof-Gault formule
- Bij ouderen en mensen met een GFR groter dan 60 ml/min/1.73m² is de MDRD onderhevig aan vertekening en kan de GFR onderschatten
- Proteïne : creatinine ratio (PCR) of albumin: creatinine ratio (ACR) op urinestaal

De falende filter

1. Hoe evalueren ?
2. Is nierfalen frequent ?
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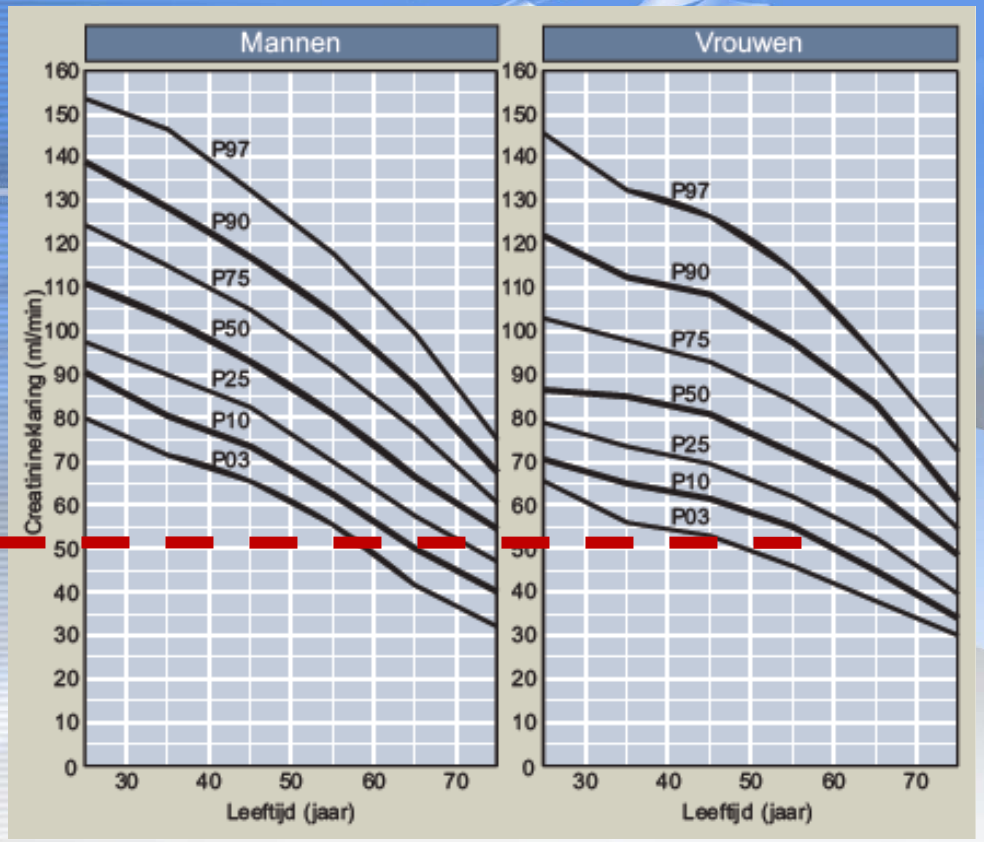
Epidemiologie van chronisch nierlijden

- NHANES (US)
  - 1988-1994 (n=15488): 11% CKD*
  - 1999-2000 (n=4101): 11.7% CKD*

- HUNT (II) (Norway)
  - 1995-1997 (n=65181): 10.2% CKD*

*stages I-IV

Merkers voor nierinsufficiëntie



Elseviers MM, Verpooten GA, De Broe ME, De Backer GG. Interpretator of creatinine clearance. Lancet 1987; 1(8530):457.

Chronic Kidney Disease (CKD)

- HUNT II-studie in Nord-Trøndelag

Prevalence* of CKD in general population by age and GFR (ml/min/1.73m²)			
Age (years)	45-89	30-44	< 30
20-29	0.07	0	0.02
30-39	0.26	0.02	0.01
40-49	0.71	0.09	0.02
50-59	1.81	0.22	0.03
60-69	5.23	0.90	0.28
70-79	11.71	2.68	0.37
80-89	19.82	6.15	1.73
≥ 90	25.00	13.49	3.17

*Given as %. Number needed to screen can be calculated as 1/(prevalence in %/100). E.g.: among people aged 60-69 from general pupulation we need to screen 1/(5.23/100)=19.1 to find one person with GFR 45-59 ml/min/1.73m²

Hallan SI et al. Screening strategies for chronic kidney disease in the general population: follow-up of cross sectional health survey. BMJ 2006 Nov 18;333 (7577): 1047.

Terminaal nierfalen - CKD5

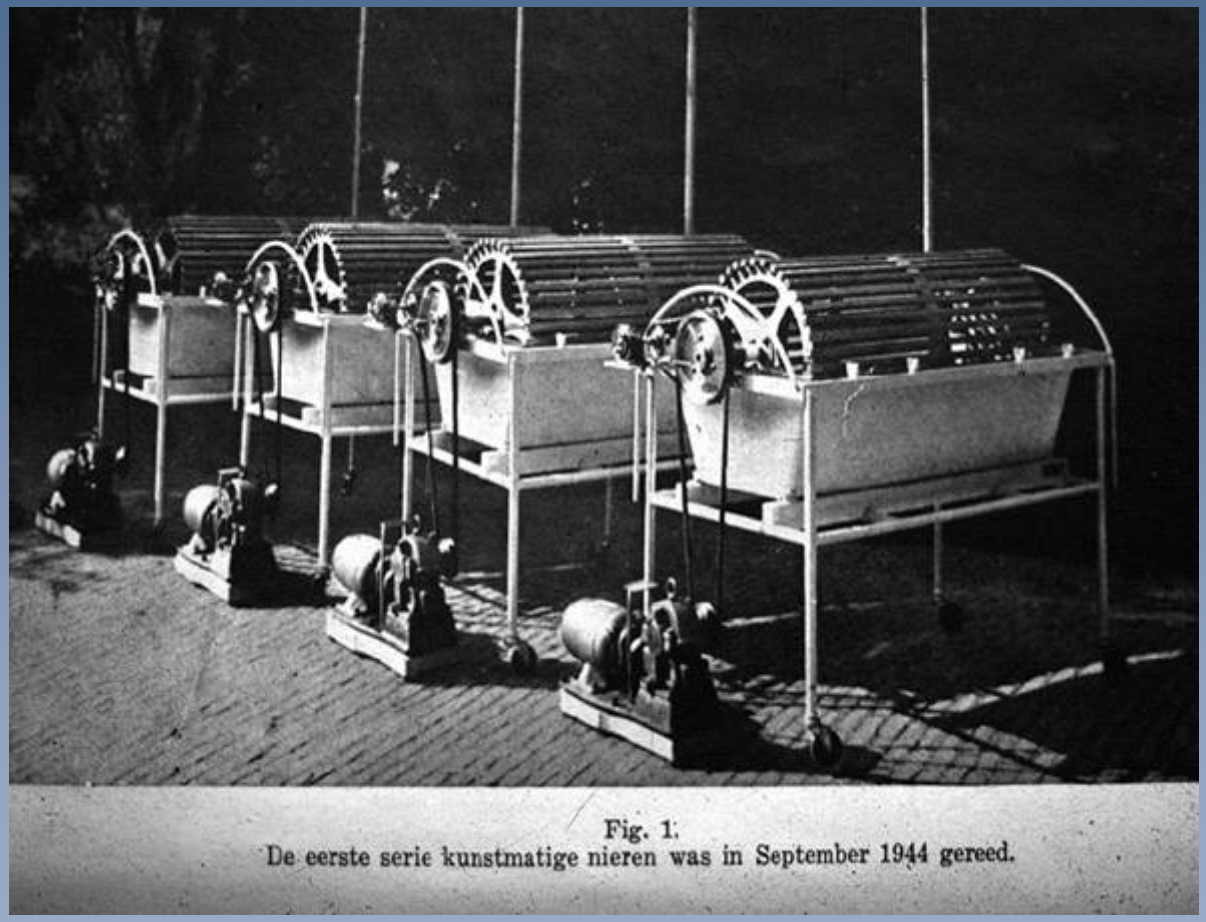
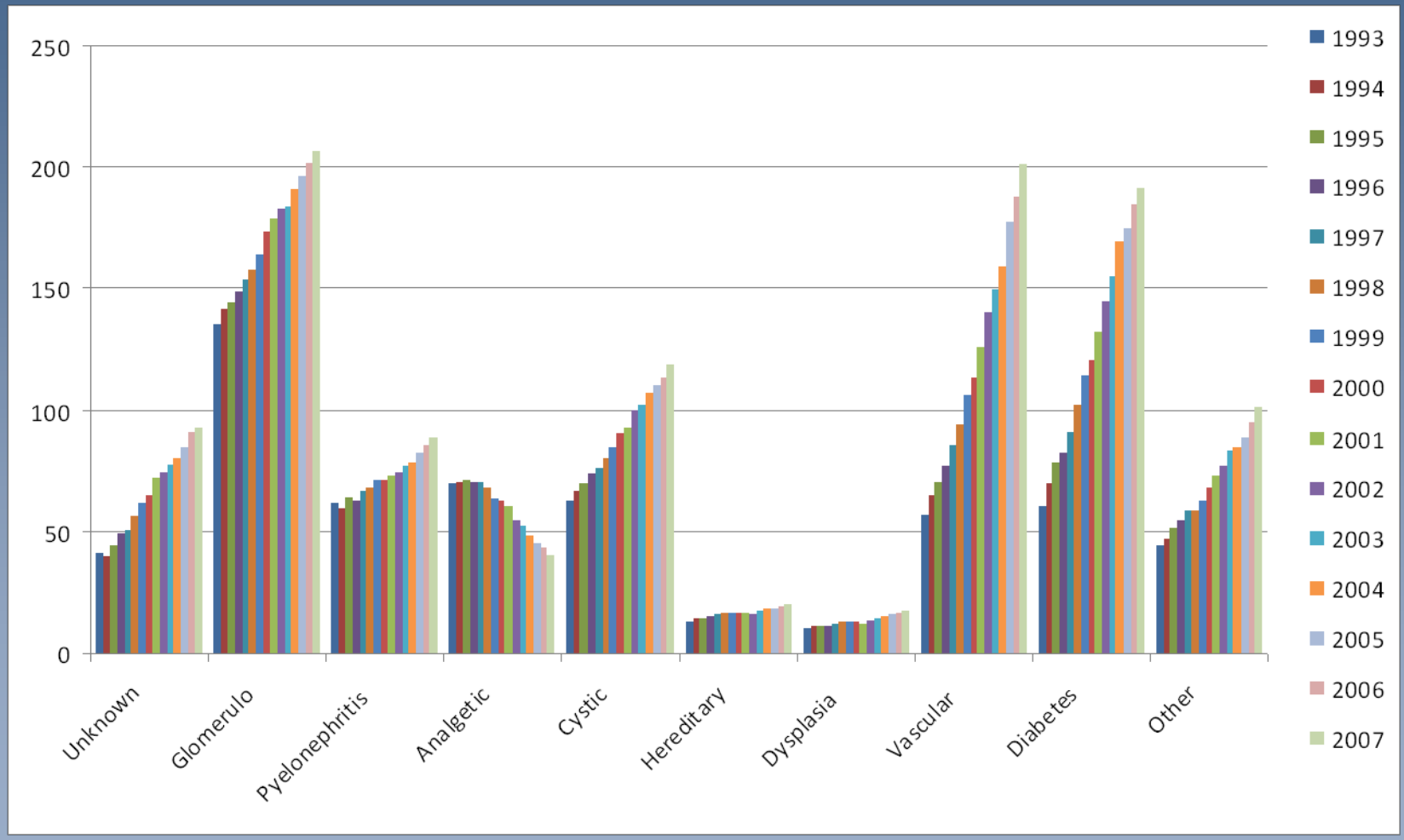


Fig. 1.
De eerste serie kunstmatige nieren was in September 1944 gereed.

Prevalentie van CKD 5 in Vlaanderen pmi



Epidemiologie: conclusies

- De nierfunctie (GFR) neemt af met de leeftijd.
- Ernstig chronisch nierlijden (CKD 4-5) is zeldzaam.

De falende filter

1. Hoe evalueren ?
2. Is nierfalen frequent ?
3. Wat is de klinische betekenis ?

http://www.kidney-international.org

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see commentary on page 245

When laboratories report estimated glomerular filtration rates in addition to serum creatinines, nephrology consults increase

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Serum creatinine alone can be difficult to interpret as a measure of kidney function such that chronic kidney disease might be under-recognized in the general population. In the province of Ontario, Canada, all outpatient laboratories now report estimated glomerular filtration rate (eGFR) in addition to serum creatinine. To determine the impact of this reporting on clinical practice, we linked health administrative data for more than 8 million adults of age 25 years or older over an almost 10-year period and conducted a population-based intervention analysis with seasonal time-series modeling to determine overall trends in the number and type of patients seen by nephrologists. Compared to the period when only serum creatinines were reported, the number of patients seen in consultation by nephrologists increased after eGFR reporting by an average of 24% (an absolute increase of 2.9 consults per 100,000 adults), an increase of about 23 consults per nephrologist per year. The greatest increases were seen in women (39% increase) and those 80 years of age and older (58% increase). Our study found that eGFR reporting was associated with a sudden increase in the number of nephrology consults. However, it remains to be seen whether the routine reporting of eGFR results in improved treatment and outcomes for those with chronic kidney disease.

Kidney International (2009) **76,** 318–323; doi:10.1038/ki.2009.158; published online 13 May 2009

KEYWORDS: chronic kidney disease; eGFR reporting; health administrative data; health resource utilization; nephrology consults; time series analysis

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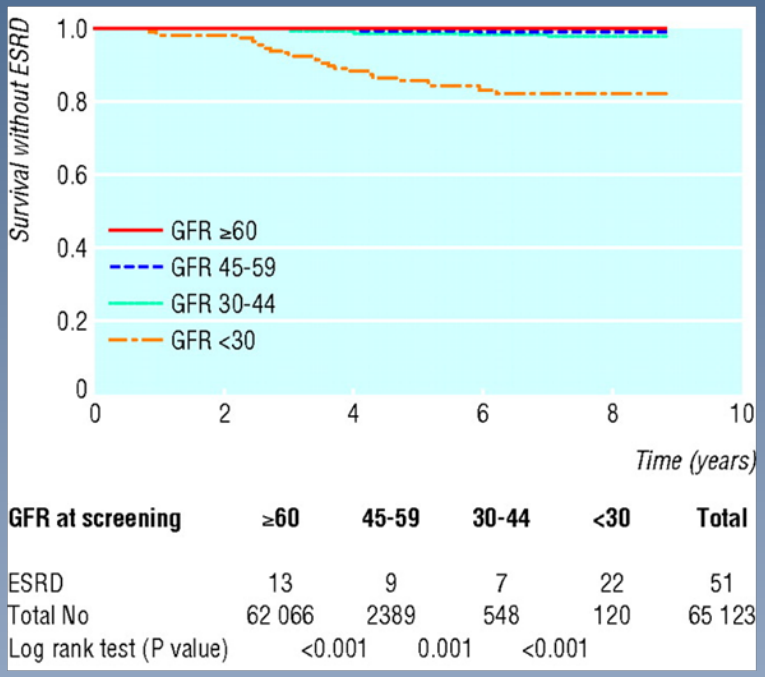
Chronic kidney disease (CKD) has been described as a global health concern.[1,2] A recent estimate suggests that about 8% of adults have CKD stage 3 or 4, when using the US National Kidney Foundation definition of CKD (an estimated glomerular filtration rate (eGFR) of 15–59 ml/min per 1.73 m^2).[3] Some health professionals do not recognize the presence of CKD. This may delay, or result in a complete loss, of an opportunity to counsel and treat patients, improve clinical outcomes, and reduce health-care costs.[4,5] Although timely referral to a nephrologist or a specialized nephrology clinic is associated with improved patient outcomes, a significant proportion of patients requiring assessment by a nephrologist are not referred.[6–8]

In clinical practice, the results of the serum creatinine test are used to estimate kidney function (GFR). However, serum creatinine may remain normal or only mildly elevated in the setting of CKD. Reliance upon serum creatinine alone has been suspected to lead to underdiagnosis of CKD.[9,10] The under-recognition of CKD is particularly prominent among women and the elderly.[11,12]

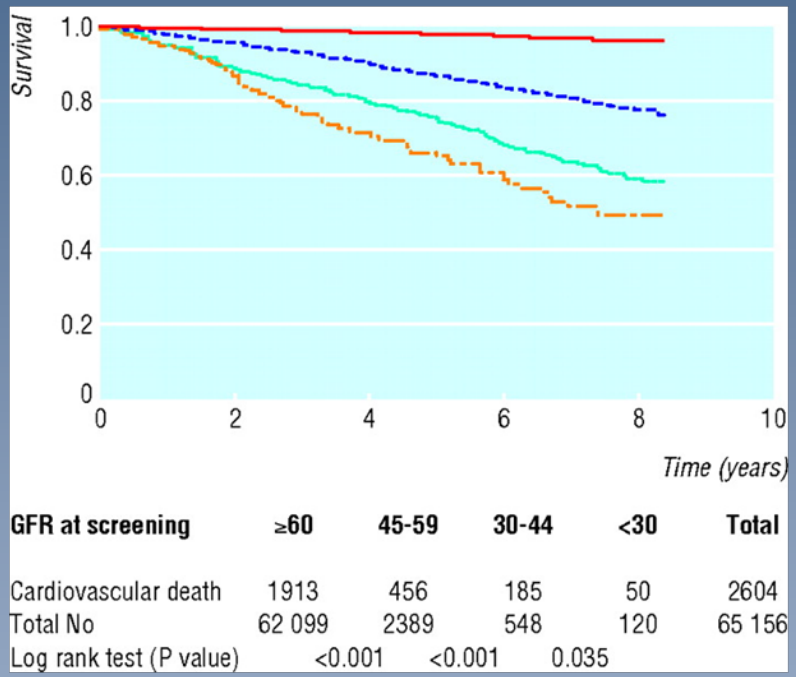
To improve CKD recognition, several international societies now recommend that kidney function be directly estimated with the use of an equation.[13–15] Using the Modification of Diet in Renal Disease equation, a serum creatinine value along with the patient's age, sex, and race are used to calculate a better estimate of GFR than simply using the serum creatinine alone.[16] The addition of such information to a laboratory report is termed 'eGFR reporting.'

Estimated glomerular filtration rate reporting has been implemented in various regions around the world and has been the subject of intense debate.[17–18] A recent survey confirms an increasing trend in the adoption of eGFR reporting among clinical laboratories; as of 2008, it was implemented in 70% of laboratories.[19] Proponents believe

HUNT II-studie in Nord-Trøndelag



GFR at screening	≥60	45-59	30-44	<30	Total
ESRD	13	9	7	22	51
Total No	62 066	2389	548	120	65 123
Log rank test (P value)		<0.001	0.001	<0.001	



GFR at screening	≥60	45-59	30-44	<30	Total
Cardiovascular death	1913	456	185	50	2604
Total No	62 099	2389	548	120	65 156
Log rank test (P value)		<0.001	<0.001	0.035	

Hallan SI et al. Screening strategies for chronic kidney disease in the general population: follow-up of cross sectional health survey. BMJ 2006 Nov 18;333 (7577): 1047.

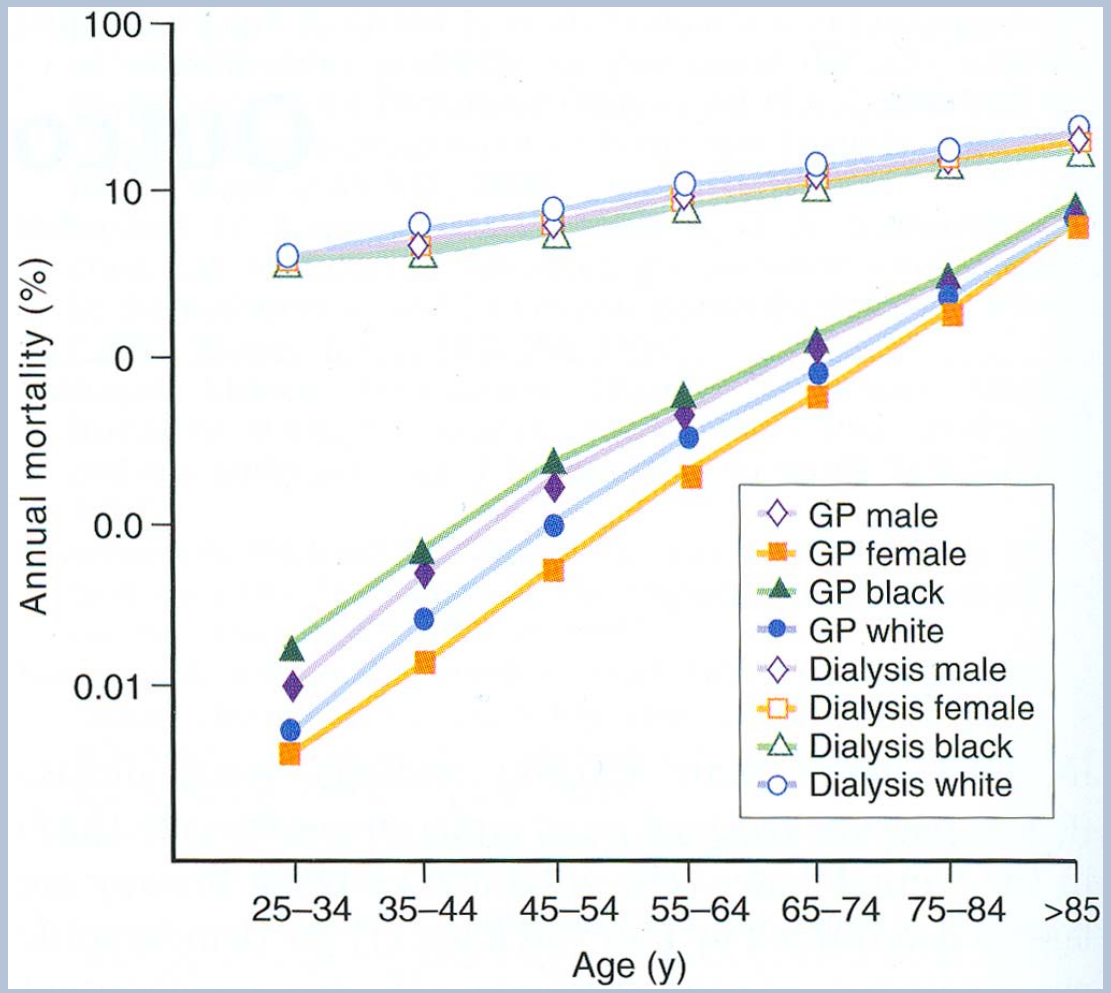
HUNT II-studie in Nord-Trøndelag

- Stadium 1-3 CKD is voorspellend voor mortaliteit en niet voor terminaal nierfalen

- Stadium 4 CKD evolueert naar terminaal nierfalen.

Hallan SI et al. Screening strategies for chronic kidney disease in the general population: follow-up of cross sectional health survey. BMJ 2006; 333 (7577): 1047.

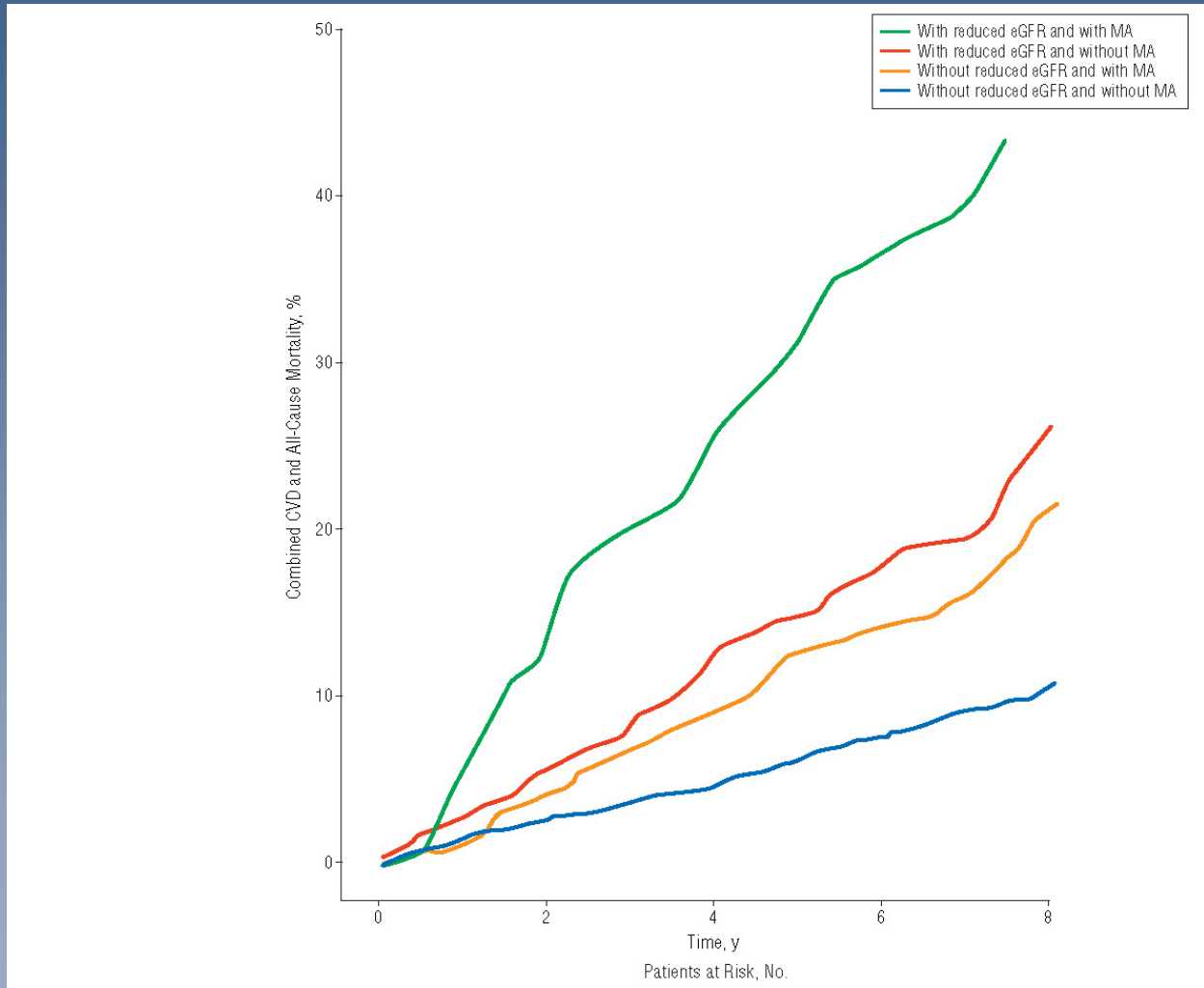
De surplus mortaliteit in CKD is cardiovasculair



Cardiovascular disease mortality in the general population (GP) compared with that in the dialysis population. Data stratified by age, race, and gender (Folley RN et al. Am J Kidney Dis 1998; 32(suppl3): 112-9).

Nierfalen als cardiovasculaire risicofactor

Kaplan-Meier curves of combined cardiovascular events and all-cause mortality based on the cross-classification of reduced reduced estimated glomerular filtrate rate (eGFR) and microalbuminuria (MA).



Patients at Risk, No.

With reduced eGFR and with MA	83	69	59	50
With reduced eGFR and without MA	212	198	181	140
Without reduced eGFR and with MA	279	266	250	237
Without reduced eGFR and without MA	2392	2322	2261	2195

Foster MC et al. Cross-classification of microalbuminuria and reduced glomerular filtration rate. Associations between cardiovascular disease risk factors and clinical outcomes. Arch Intern Med 2007; 167: 1386-92.

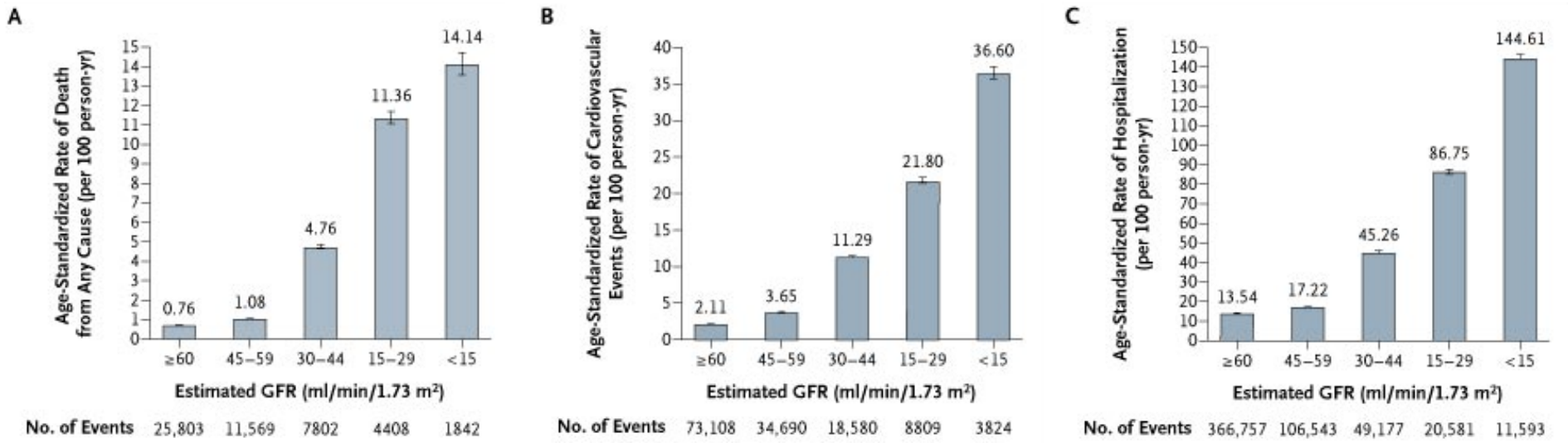


Table 2. Adjusted Hazard Ratio for Death from Any Cause, Cardiovascular Events, and Hospitalization among 1,120,295 Ambulatory Adults, According to the Estimated GFR.*

Estimated GFR	Death from Any Cause	Any Cardiovascular Event	Any Hospitalization
	adjusted hazard ratio (95 percent confidence interval)		
≥60 ml/min/1.73 m²†	1.00	1.00	1.00
45–59 ml/min/1.73 m²	1.2 (1.1–1.2)	1.4 (1.4–1.5)	1.1 (1.1–1.1)
30–44 ml/min/1.73 m²	1.8 (1.7–1.9)	2.0 (1.9–2.1)	1.5 (1.5–1.5)
15–29 ml/min/1.73 m²	3.2 (3.1–3.4)	2.8 (2.6–2.9)	2.1 (2.0–2.2)
<15 ml/min/1.73 m²	5.9 (5.4–6.5)	3.4 (3.1–3.8)	3.1 (3.0–3.3)

* The analyses were adjusted for age, sex, income, education, use or nonuse of dialysis, and the presence or absence of prior coronary heart disease, prior chronic heart failure, prior ischemic stroke or transient ischemic attack, prior peripheral arterial disease, diabetes mellitus, hypertension, dyslipidemia, cancer, a serum albumin level of 3.5 g per deciliter or less, dementia, cirrhosis or chronic liver disease, chronic lung disease, documented proteinuria, and prior hospitalizations.

† This group served as the reference group.

Figure 1. Age-Standardized Rates of Death from Any Cause (Panel A), Cardiovascular Events (Panel B), and Hospitalization (Panel C), According to the Estimated GFR among 1,120,295 Ambulatory Adults.

A cardiovascular event was defined as hospitalization for coronary heart disease, heart failure, ischemic stroke, and peripheral arterial disease. Error bars represent 95% confidence intervals. The rate of events is listed above each bar.

Go AS et al. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization.N Engl J Med 2004; 351: 1296-305.

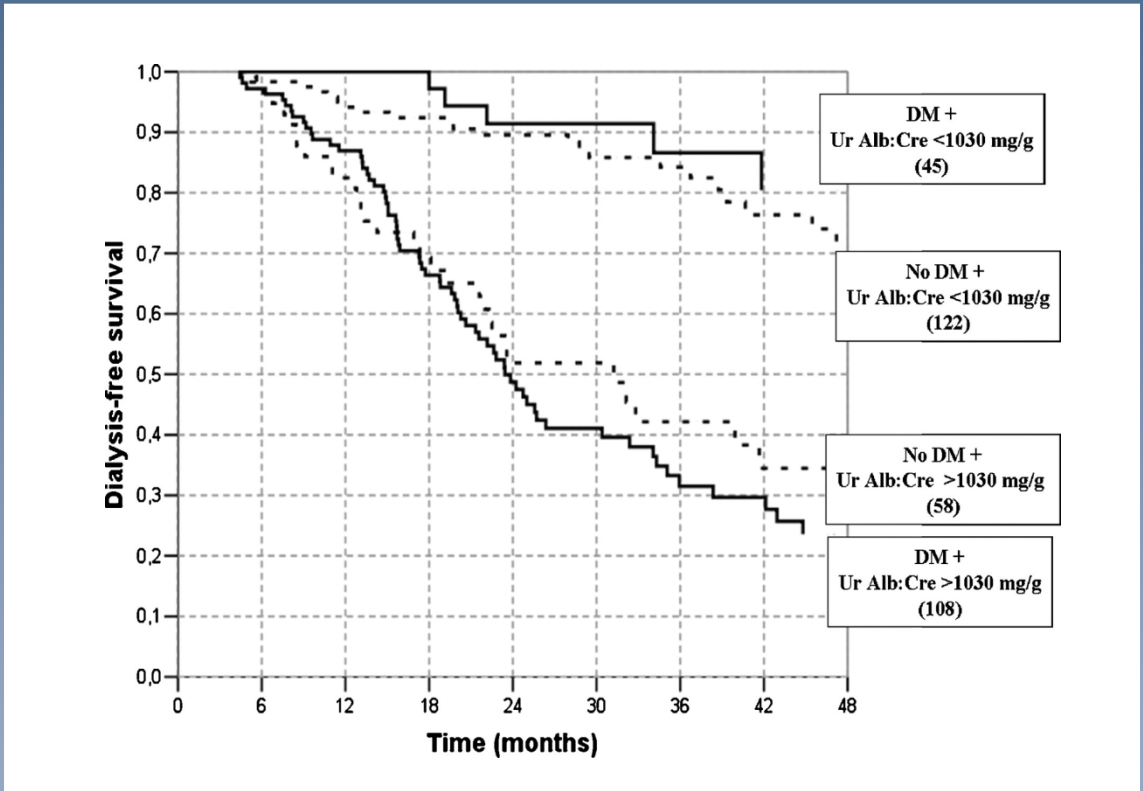
Table 2. Study End points*

End Points	GFR, 60-89; No Proteinuria (n = 14 202)	Stage 2 GFR, 60-89; Proteinuria (n = 1741)	Stage 3 GFR, 30-59 (n = 11 278)	Stage 4 GFR, 15-29 (n = 777)
Disenrolled from plan	14.9	16.2	10.3	6.6
Died (prior to transplant/dialysis)	10.2	19.5	24.3	45.7
Received a transplant	0.01	0.2	0.2	2.3
Initiated dialysis	0.06	0.9	1.1	17.6
None of the above through June 30, 2001	74.8	63.3	64.2	27.8

*Glomerular filtration rates (GFRs) were estimated in milliliters per minute per 1.73 m^2. Other values are given as percentage of patients.

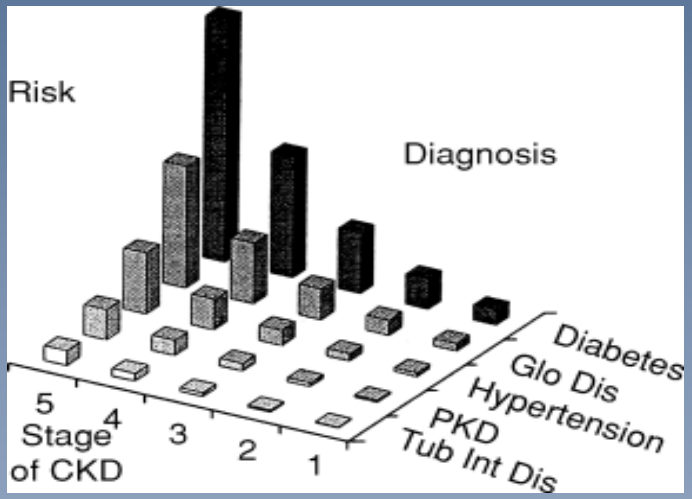
Keith DS et al. Longitudinal follow-up and outcomes among a population with chronic kidney disease in a large managed care organization. Arch Intern Med 2004; 164: 659-63.

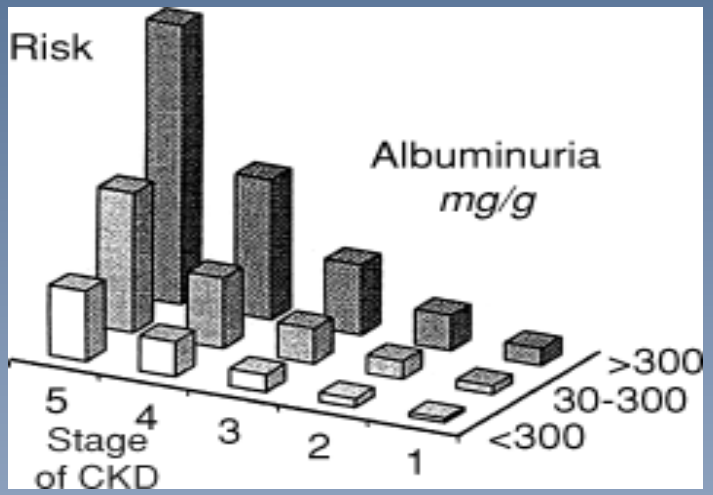
Albuminurie als renale risicofactor



Lorenzo V et al. Nephrol Dial Transplant 2010; 25: 835-41.

Albuminurie als cardiovasculaire risicofactor





Levey AS et al. Definition and classification of chronic kidney disease: a position statement from Kidney Disease: Improving Global Outcomes (KDIGO). Kidney Int 2005; 67(6): 2089-100.

Vertraging van progressie – dieet

- MDRD-studie

Diet†	Study 1 (N = 585)		Study 2 (N = 255)	
	Mean arterial pressure‡			
	usual	low	usual	low
	no. of patients			
Usual protein	145	149	—	—
Low protein	140	151	62	67
Very low protein	—	—	61	65

*Patients in study 1 had a glomerular filtration rate of 25 to 55 ml per minute per 1.73 m^2; patients in study 2 had a rate of 13 to 24 ml per minute per 1.73 m^2.

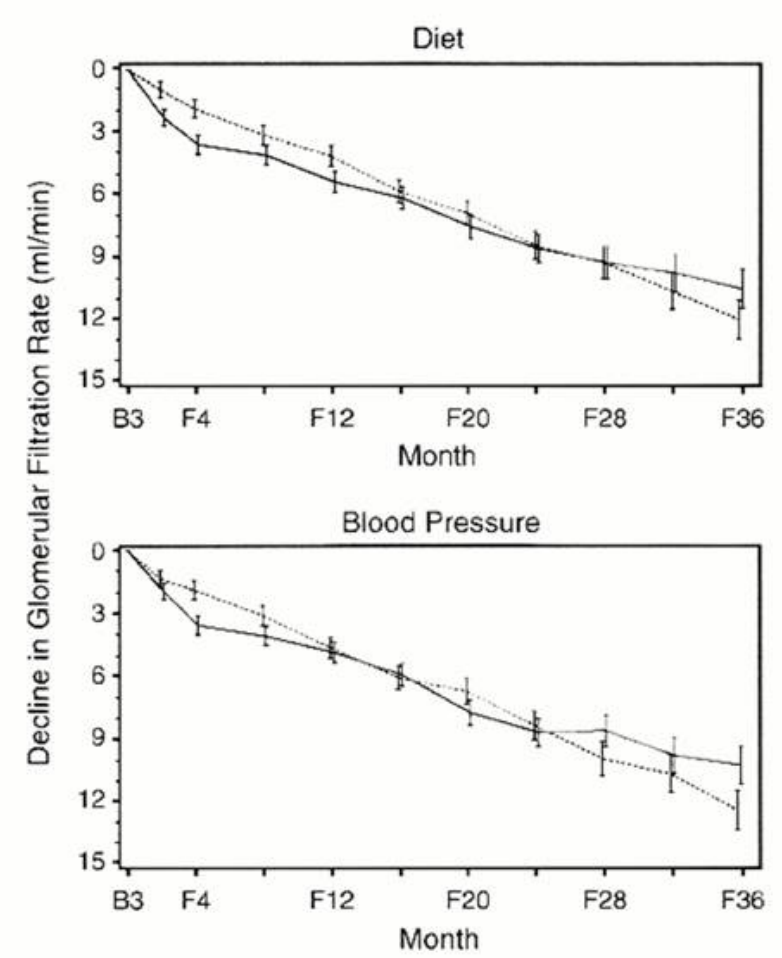
†The usual-protein diet consisted of 1.3 g of protein and 16 to 20 mg of phosphorus per kilogram (standard body weight) per day, the low-protein diet consisted of 0.58 g of protein (≥0.35 g of protein high in essential amino acids) and 5 to 10 mg of phosphorus per kilogram per day, and the very-low-protein diet consisted of 0.28 g of protein and 4 to 9 mg of phosphorus per kilogram per day, supplemented by a keto acid–amino acid mixture (0.28 g per kilogram per day) (Ross Laboratories, Columbus, Ohio).

‡Mean arterial pressure is defined in the Methods section. The usual mean arterial pressure was ≤107 mm Hg for patients 18 to 60 years old at entry (equivalent to 140/90 mm Hg) or ≤113 mm Hg for patients ≥61 years old at entry (equivalent to 160/90 mm Hg); low mean arterial pressure was ≤92 mm Hg for patients 18 to 60 years old at entry (equivalent to 125/75 mm Hg) or ≤98 mm Hg for patients ≥61 years old at entry (equivalent to 145/75 mm Hg).

Klahr S et al. The effects of dietary protein restriction and blood-pressure control on the progression of chronic renal disease. Modification of Diet in Renal Disease Study Group. N Engl J Med. 1994; 330(13) :877-84.

Vertraging van progressie

- MDRD-studie



Klahr S et al. The effects of dietary protein restriction and blood-pressure control on the progression of chronic renal disease. Modification of Diet in Renal Disease Study Group. N Engl J Med. 1994; 330(13) :877-84.

Therapeutische beschouwingen: Vertraging van progressie

- T2DM-IDNT-studie

TABLE 2. OUTCOMES ACCORDING TO STUDY GROUP.*

VARIABLE	IRBESARTAN GROUP (N=579)	AMLODIPINE GROUP (N=567)	PLACEBO GROUP (N=569)	ALL PATIENTS (N=1715)
Primary composite outcome — no. (%)	189 (32.6)	233 (41.1)	222 (39.0)	644 (37.6)
Doubling of serum creatinine concentration	98 (16.9)	144 (25.4)	135 (23.7)	377 (22.0)
End-stage renal disease	82 (14.2)	104 (18.3)	101 (17.8)	287 (16.7)
Death from any cause	87 (15.0)	83 (14.6)	93 (16.3)	263 (15.3)
Secondary composite outcome — no. (%)	138 (23.8)	128 (22.6)	144 (25.3)	410 (23.9)
Never received study medication — no. (%)†	2 (0.3)	8 (1.4)	6 (1.1)	16 (0.9)
Lost to follow-up — no. (%)‡	5 (0.9)	2 (0.4)	4 (0.7)	11 (0.6)
Completed study without primary outcome — no. (%)	385 (66.5)	332 (58.6)	343 (60.3)	1060 (61.8)
Mean duration of follow-up — days§	952	924	921	932

*The numbers of patients with the composite end points are lower than the sums of those with the various components because some patients reached more than one component.

†Patients who never received study medication were included in all analyses according to the intention-to-treat principle.

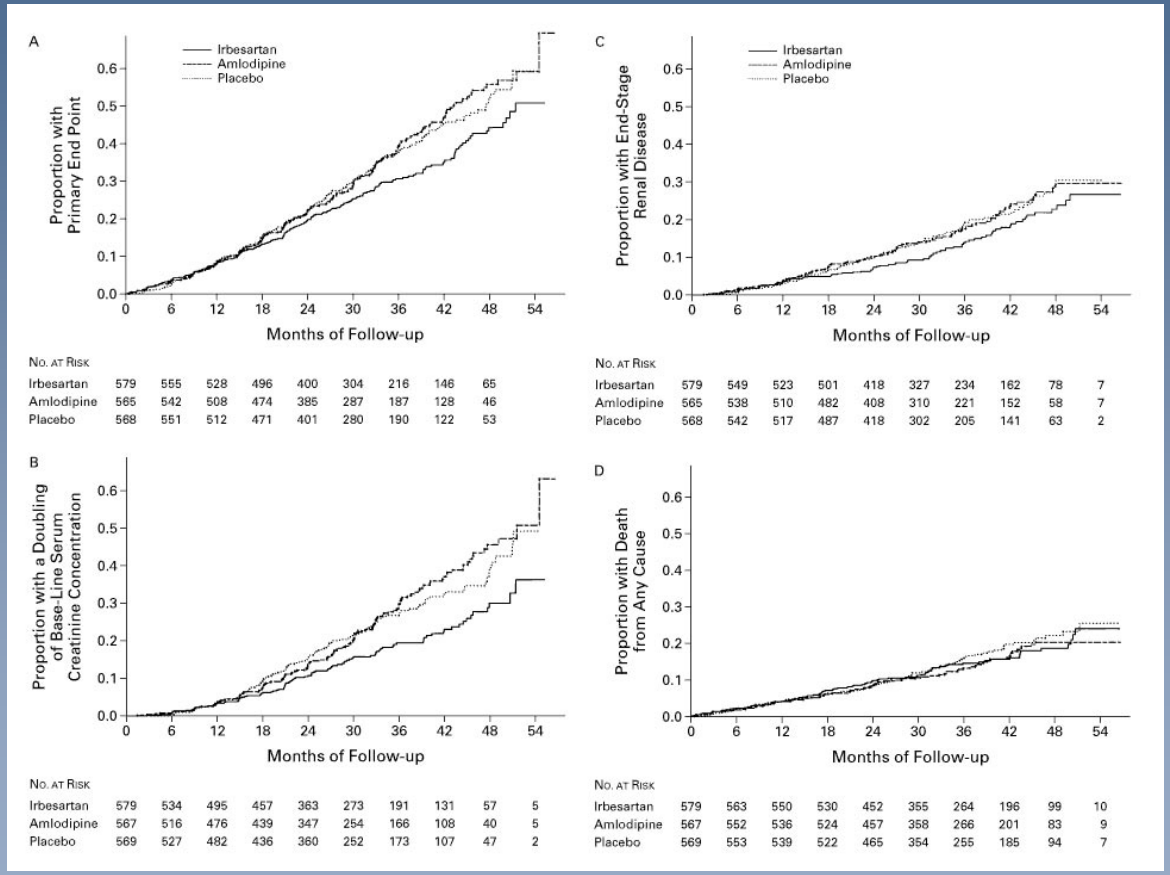
‡Data are for patients lost to follow-up before reaching the primary outcome or the last scheduled study visit.

§The duration of follow-up was calculated from the time of randomization to the occurrence of the first primary outcome or the date of the last scheduled visit when data were censored.

Lewis EJ et al. Renoprotective effect of the angiotensin-recepto antagonist irbesartan in patients with nephropathy due to type 2 diabetes. N Engl J Med 2001; 345(12): 851-60.

Vertraging van progressie

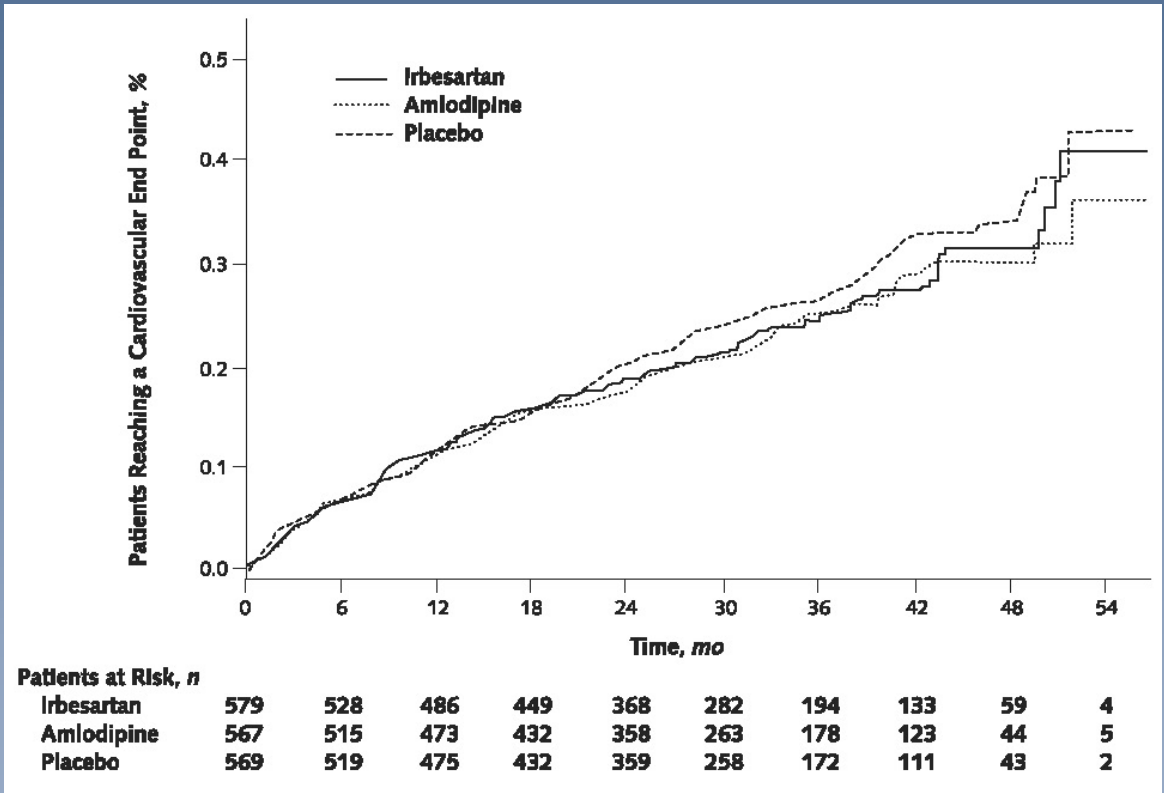
- T2DM-IDNT-studie



Lewis EJ et al. Renoprotective effect of the angiotensin-receptor antagonist irbesartan in patients with nephropathy due to type 2 diabetes. N Engl J Med 2001; 345(12): 851-60.

Vertraging van progressie

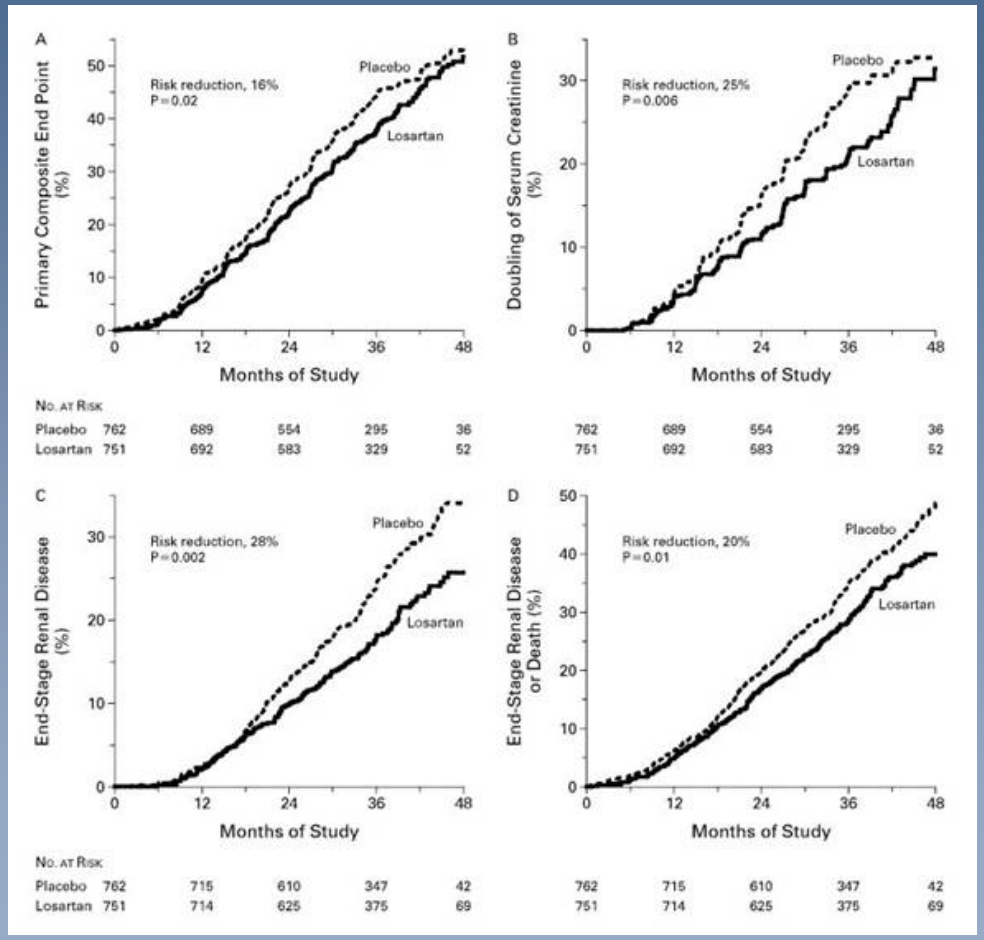
- T2DM-IDNT-studie



Berl T et al. Cardiovascular outcomes in the Irbesartan Diabetic Nephropathy Trial of patients with type 2 diabetes and overt nephropathy. Ann Intern Med 2003; 138(7): 542-9.

Vertraging van progressie

- T2DM-RENAAL-studie



Brenner BM et al. Effects of losartan on renal and cardiovascular outcomes in patients with type 2 diabetes and nephropathy. N Engl J Med 2001; 345(12): 861-9.

Vertraging van progressie

- T2DM-HOPE-studie

Outcome	Ramipril (n=1808)	Placebo (n=1769)	Relative risk reduction (95% CI)	p
Primary outcome				
Combined	277 (15·3%)	351 (19·8%)	25% (12 to 36)	0·0004
Myocardial infarction	185 (10·2%)	229 (12·9%)	22% (6 to 36)	0·01
Stroke	76 (4·2%)	108 (6·1%)	33% (10 to 50)	0·0074
Cardiovascular death	112 (6·2%)	172 (9·7%)	37% (21 to 51)	0·0001
Secondary outcomes				
Total mortality	196 (10·8%)	248 (14·0%)	24% (8 to 37)	0·004
Unstable angina*	213 (11·8%)	207 (11·7%)	0 (−21 to 17)	0·99
Heart failure*	81 (4·5%)	79 (4·5%)	1% (−34 to 28)	0·93
Revascularisation	254 (14·0%)	291 (16·4%)	17% (2 to 30)	0·031
Overt nephropathy†	117 (6·5%)	149 (8·4%)	24% (3 to 40)	0·027
Other outcomes				
Any heart failure	198 (11·0%)	236 (13·3%)	20% (4 to 34)	0·019
Transient ischaemic attacks	80 (4·4%)	104 (5·9%)	26% (1 to 45)	0·04
Worsening angina	363 (20·1%)	397 (22·4%)	13% (0 to 24)	0·057
Laser therapy‡	170 (9·4%)	186 (10·5%)	22% (−9 to 28)	0·24
Dialysis	10 (0·5%)	8 (0·5%)	−20% (−205 to 53)	0·70
Overt nephropathy,† laser therapy, or dialysis	273 (15·1%)	312 (17·6%)	16% (1 to 29)	0·036

*Requiring admission. †Based on positive 24 h urine collection or albumin/creatinine ratio ≥36 mg/mmol if no 24 h urine available. ‡Laser therapy for retinopathy.

Table 3: **Clinical outcomes for ramipril and placebo groups**

No authors listed. Effects of ramipril on cardiovascular and microvascular outcomes in people with diabetes mellitus: results of the HOPE study and MICRO-HOPE substudy. Heart Outcomes Prevention Evaluation Study Investigators. Lancet 2000; 355(9200): 253-9 [Erratum in: Lancet 2000; 356(9232): 860]

Vertraging van progressie

- T2DM-microHOPE-studie

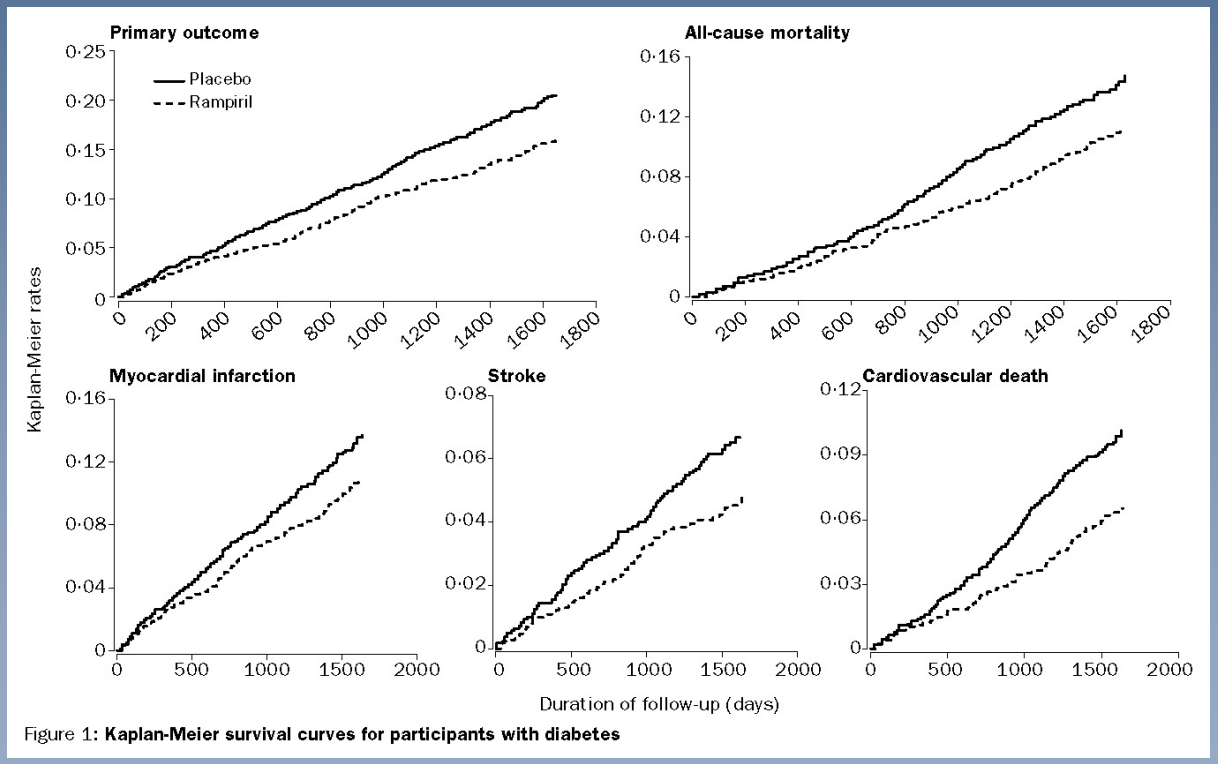


Figure 1: **Kaplan-Meier survival curves for participants with diabetes**

No authors listed. Effects of ramipril on cardiovascular and microvascular outcomes in people with diabetes mellitus: results of the HOPE study and MICRO-HOPE substudy. Heart Outcomes Prevention Evaluation Study Investigators. Lancet 2000; 355(9200): 253-9 [Erratum in: Lancet 2000; 356(9232): 860]

The link between risk factors, early risk markers and late end organ damage for the kidney and various other organ systems

risk factors
(hypertension, diabetes, hypercholesterolaemia)

↓

markers of early end organ dammage
(albuminuria, intima-media thickness, left ventricular hypertrophy, coronary calcium score)

↓

late end organ damage

heart	**peripheral**	**cerebral**	**kidney**
angina	int. claudicatio	TIA	GFR 30-60
myoc. infarct	arterial ulcer	CVA	GFR 15-30
heart failure	gangrene	dementia	GFR <15

de Jong PE et al. Nephrol Dial Transplant 2010; 25: 656-8.

Conclusie – nieuw paradigma

- Stadium 1-3 van chronisch nierlijden en albuminurie zijn in afwezigheid van een primaire nierziekte merkers van verhoogd cardiovasculair risico.

- Stadium 4 van chronisch nierlijden is meestal de uiting van een progressieve nierziekte die leidt tot terminaal nierfalen.

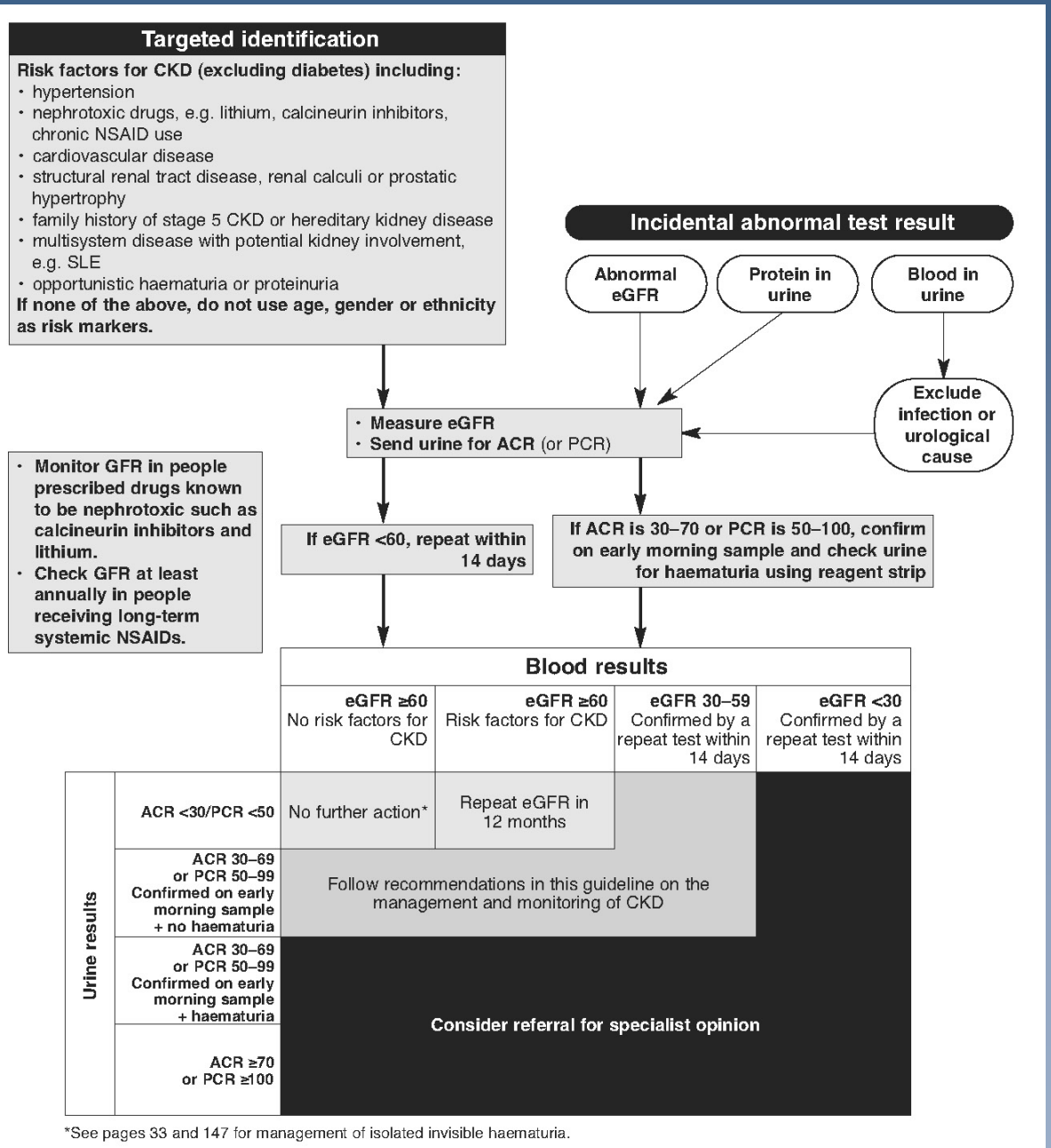
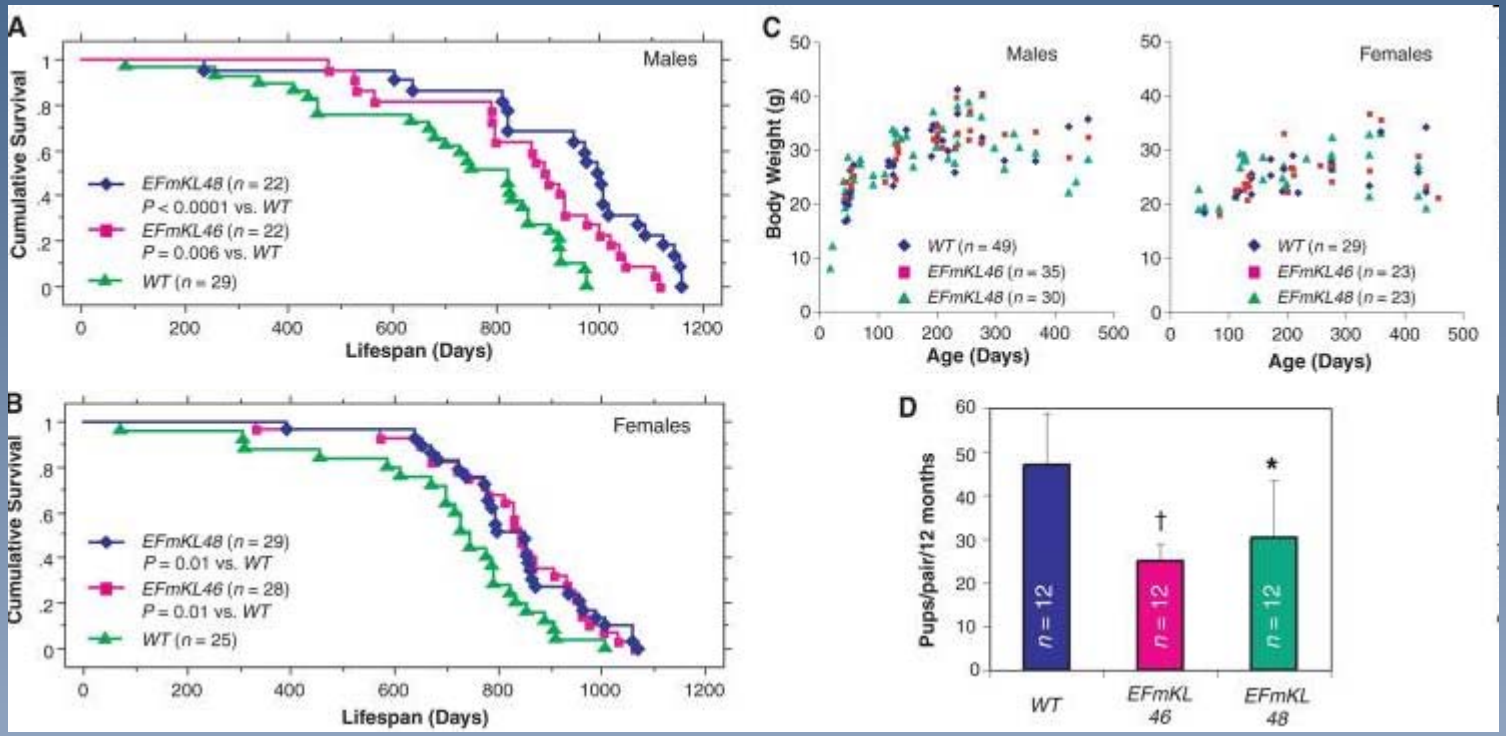


Figure 3.2 Identification, diagnosis and referral of patients with CKD but without diabetes. eGFR is expressed as ml/min/1.73m^2. Albumin:creatinine ratio (ACR) and protein:creatinine ratio (PCR) are expressed as mg/mmol.

National Collaborating Centre for Chronic Conditions. Chronic kidney disease: national clinical guideline for early identification and management in adults in primary and secondary care. London: Royal College of Physicians, September 2008.

Klotho



Kurosu H et al. Suppression of Aging in Mice by the Hormone Klotho. Science 2005; 309: 1829-33.