The ageing kidney/ Chronic kidney failure

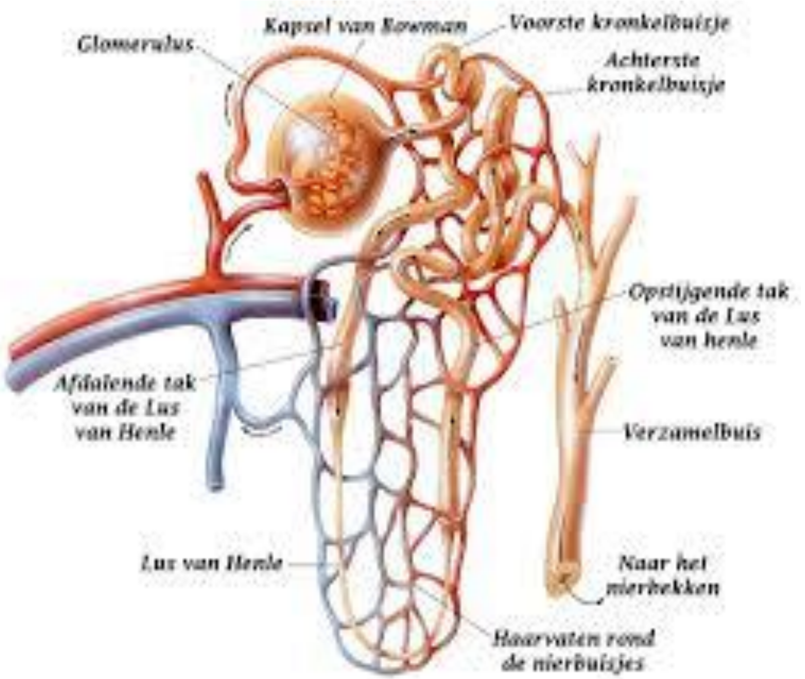
Nele Van Den Noortgate

IUC – 17th May 2018

Content

- Ageing of the kidney
  - Structural and functional changes
  - Mechanisms of age-dependent injury

- Chronic Kidney Disease in the older person
  - Methods to estimate GFR
  - Is a decline in GFR equivalent to CKD?
  - Managing CKD in the older person



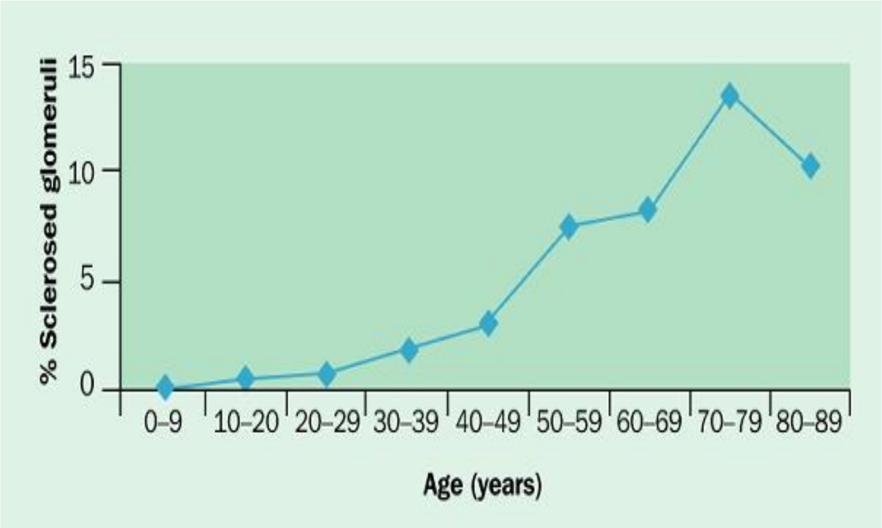
Structural changes in the ageing kidney

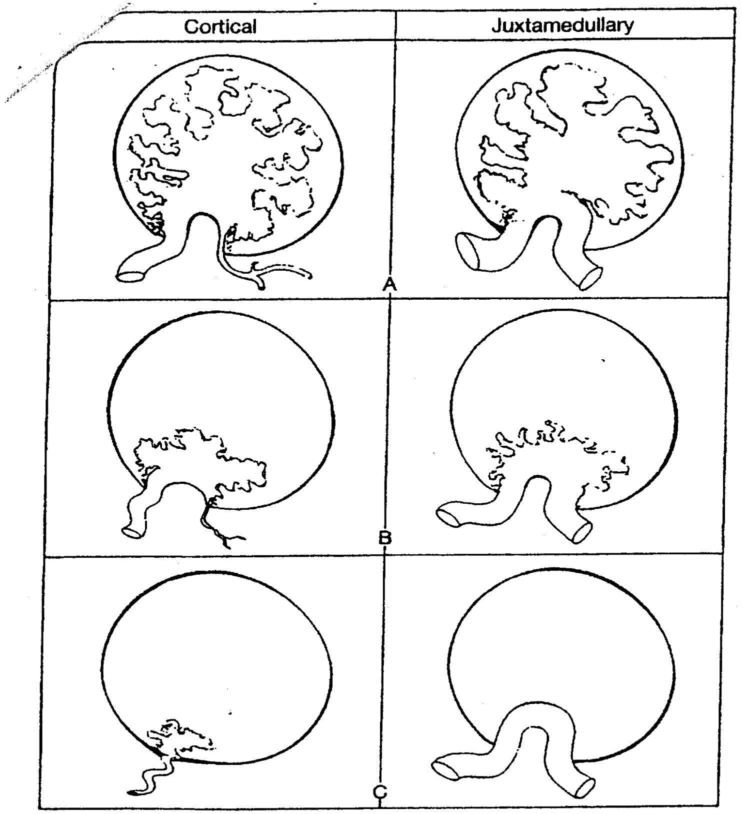
- Macroscopy
  - Decrease weight
  - Decrease size
  - Cortical atrophy
- Microscopy
  - Glomerular
  - Tubular
  - Interstitial
  - Vascular

Progressive loss of renal mass

- Loss of cortical mass due to fall in total number of glomeruli
- Tubular and interstitial changes
- Vascular changes

Age specific incidence of glomerulosclerosis

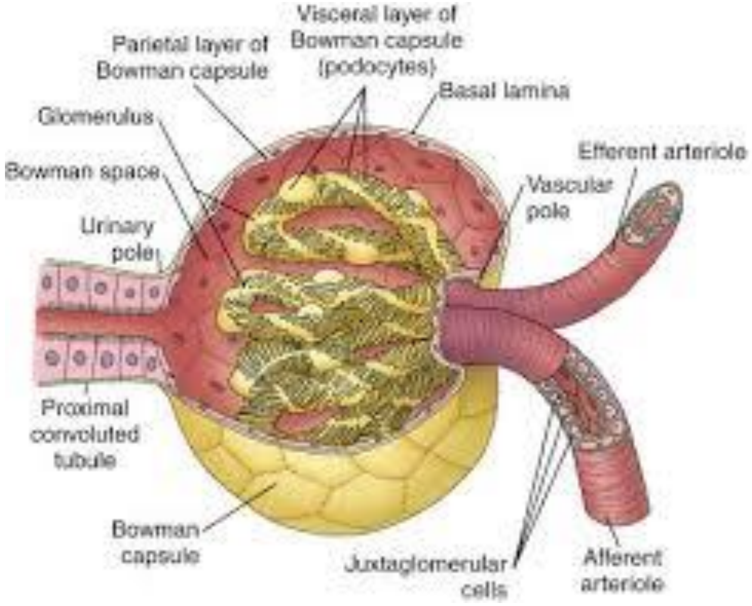


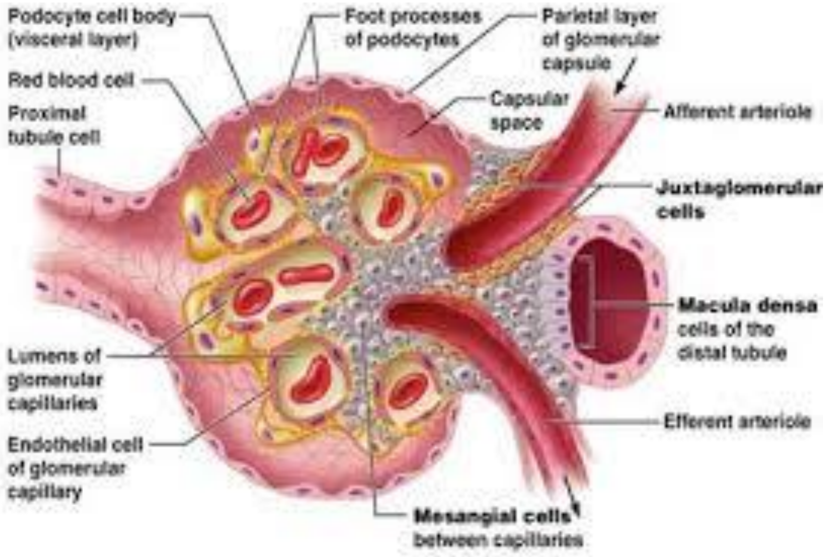


Kaplan et al , Am J Pathol 80:227-234,1975

Glomerular changes

- Thickening of the basement membrane
- Reduplication of Bowman's capsule
- Mesangial matrix expansion
- Fusion of foot processes





Decline in GFR

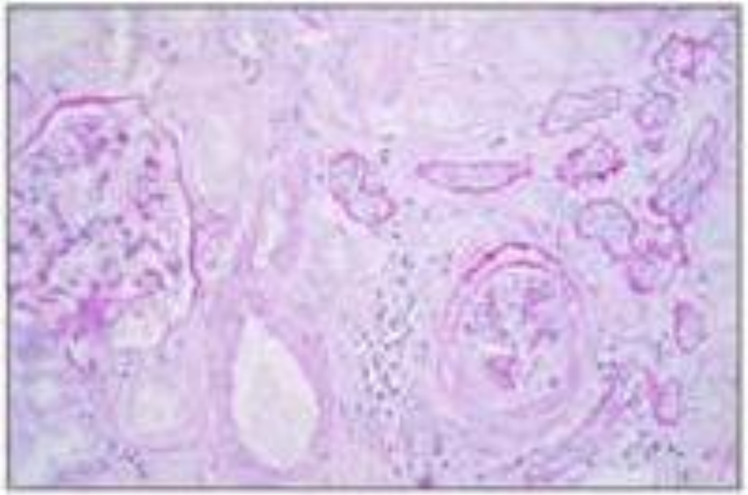
Baltimore Longitudinal study

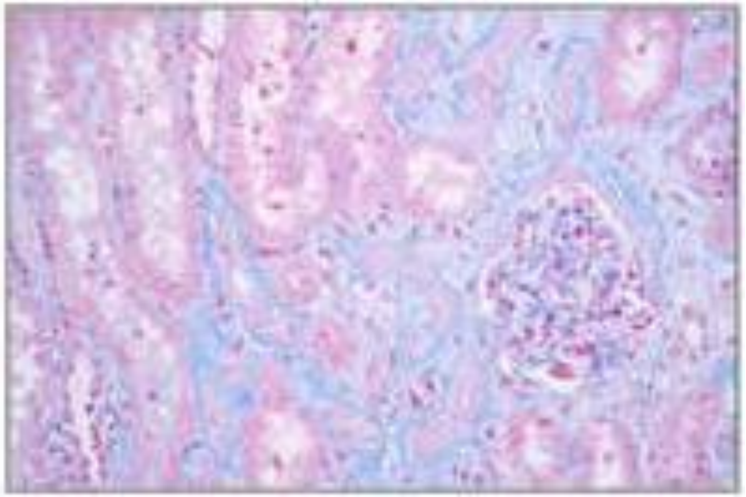
Age (years)	No subjects	creat clearance (ml/min/1.73m²)	creat clearance slope (ml/min/1.73m²/yr)
45-54	95	128.1±1.6	-0.73±0.30
55-64	60	121.8±1.9	-1.64±0.41
65-74	36	110.0±2.6	-1.30±0.57
75-84	17	97.0±3.4	-1.07±0.77

Rowe et al. J Gerontol 1976;31:155-163

Tubular and interstitial changes

- Reduction in proximal tubular volume and number
- Irregular thickening of basal membrane
- Interstitial changes consists of increasing zone of tubular atrophy and fibrosis





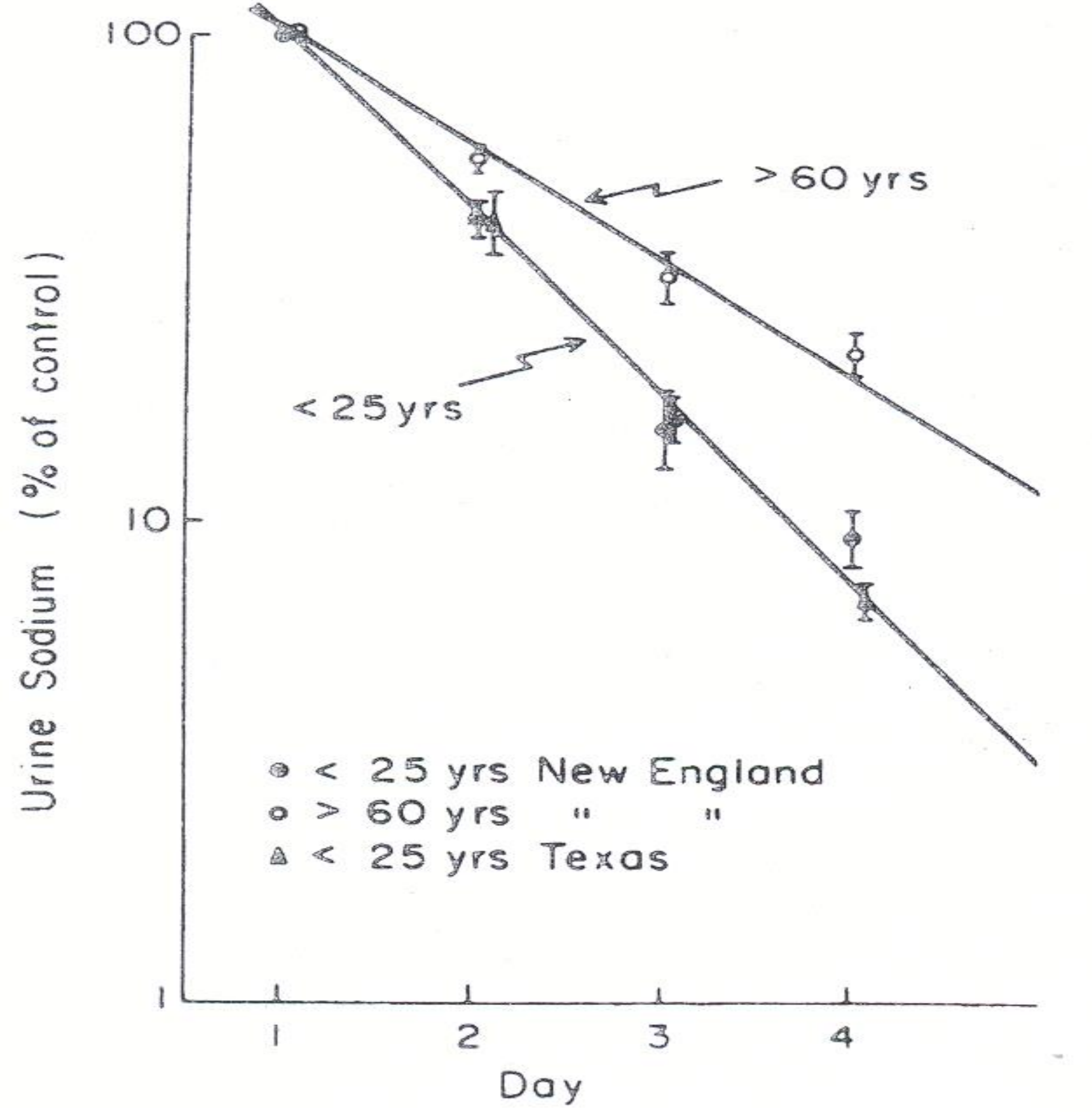
Electrolyte disorders in the old old in an acute geriatric ward (220 pts)

- hypokalaemia (K < 3.5 mmol/l): 26 patients
- hyperkalaemia (K > 5.5 mmol/l): 9 patients
- hyponatraemia (Na < 135 mmol/l): 46 patients
- hypernatraemia (Na > 145 mmol/l): 4 patients
- significant association between hypokalaemia and locomotoric disturbances (p= 0.01); the use of diuretics(p=0.005), laxatives (p=0.006); failure to thrive (p=0.005)

Van Den Noortgate et al. Int Urol Nephrol 2001;32:531-537.

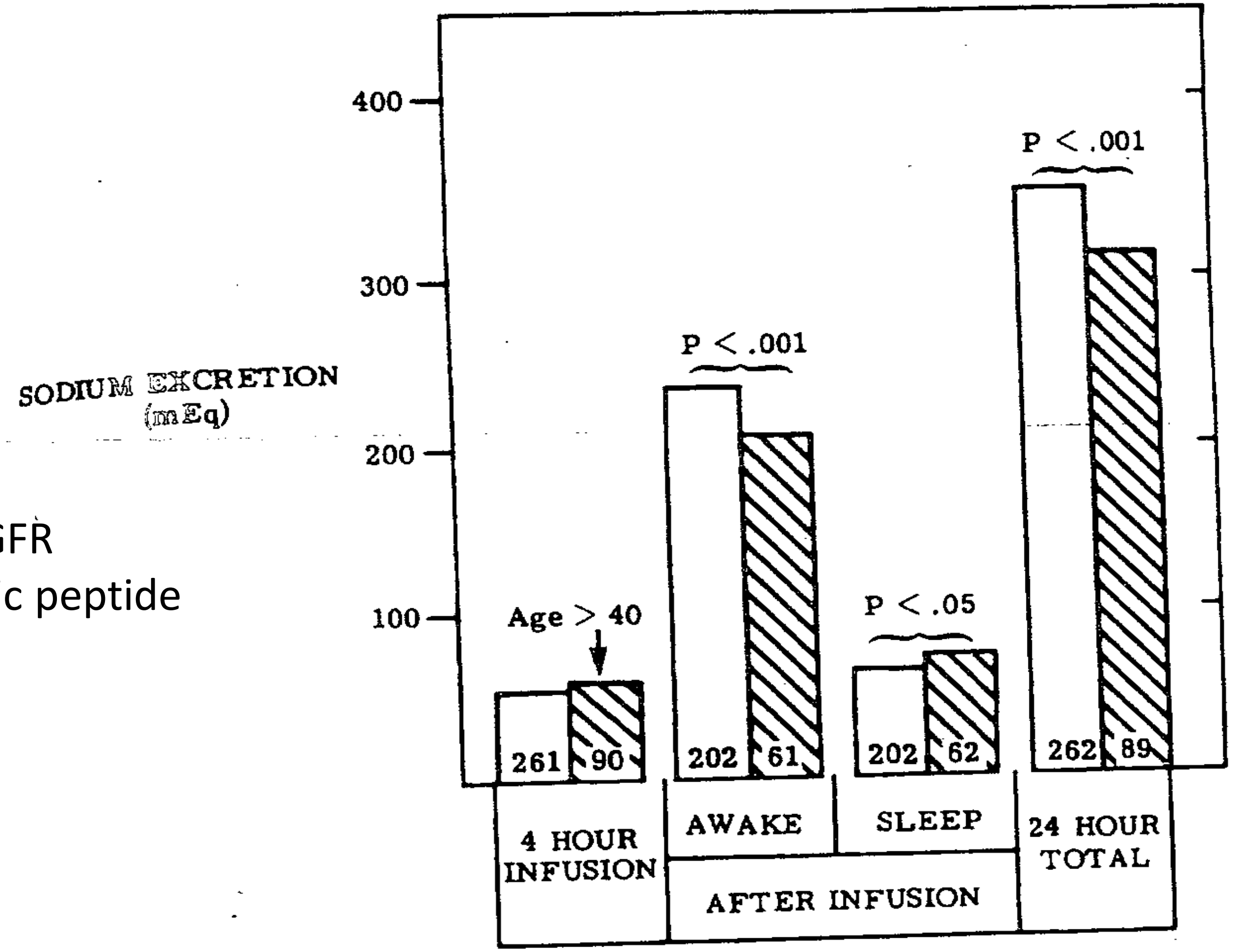
Effect of abrupt salt restriction

Ascending loop of Henle
Blented reponse to renin



Epstein et al. J Lab Clin Med 1976;87:411-17

Effect of salt-loading

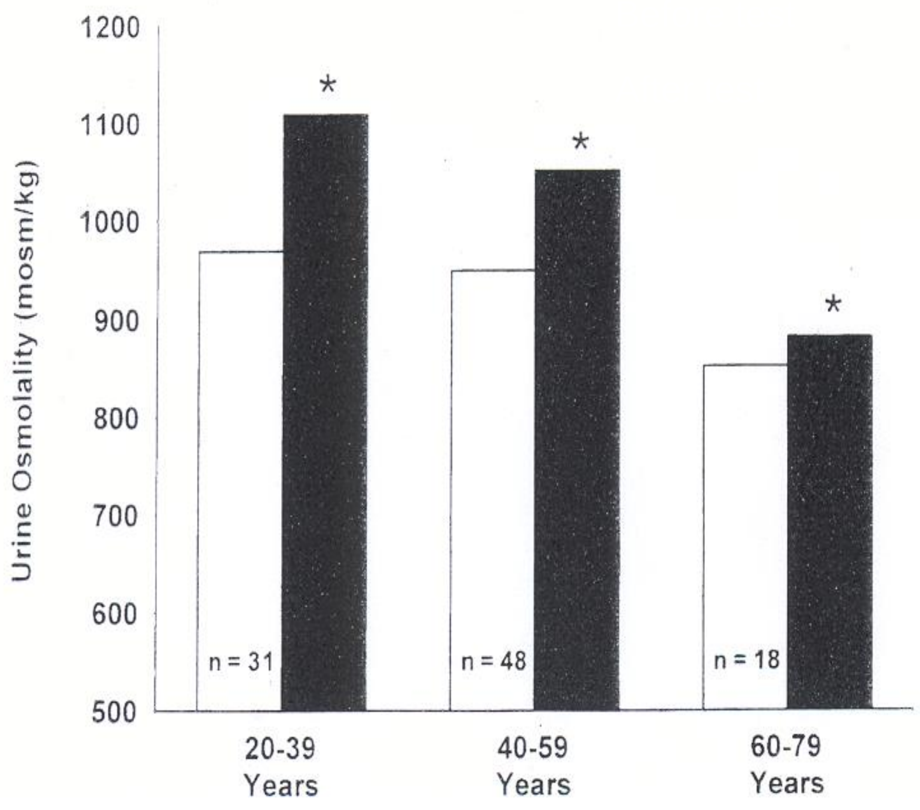


Age related decline in GFR
Blunted atrial nutriuretic peptide

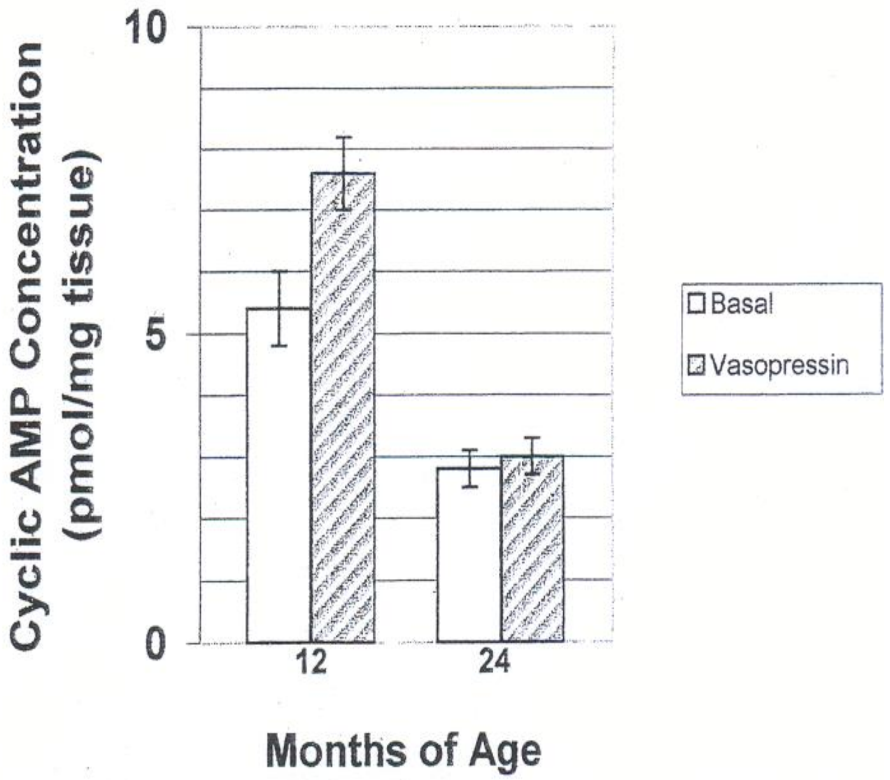
Epstein et al. J Lab Clin Med 1976;87:411-17

The concentrating capacity of the kidney

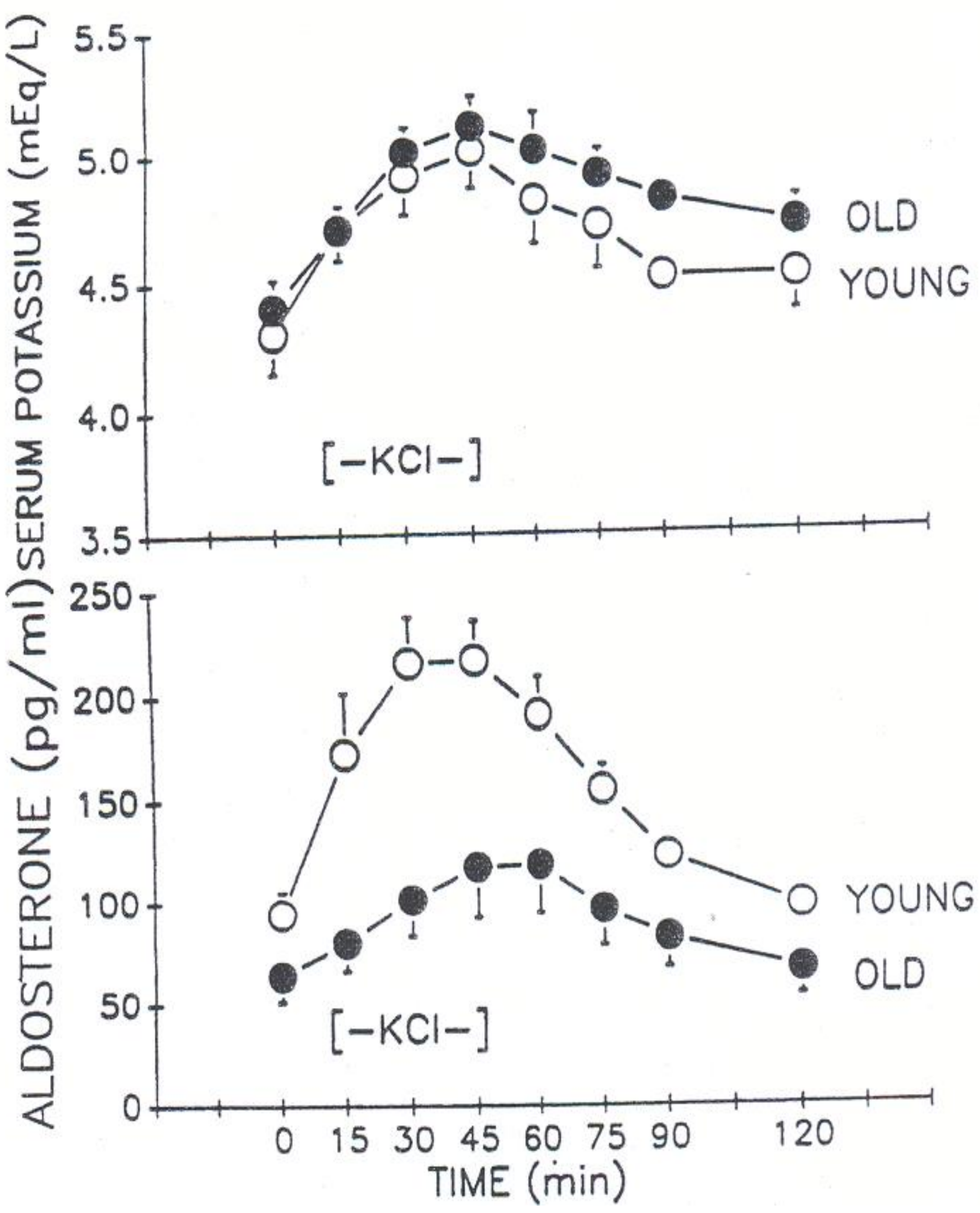
Urine osmolality in response
to 12 hoursof water deprivation



Cyclic AMP concentrations in renal
papillary slices after vasopressin



Rowe et al. Nephron 1976;17:270-78

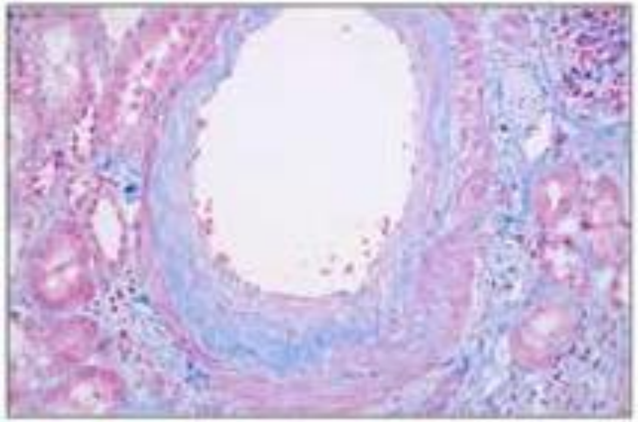
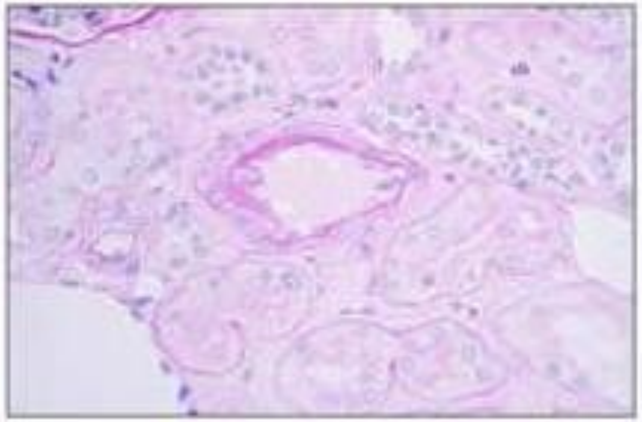


Serum K and aldosterone levels before, during and after infusion with KCl

Mulkerrin et al JASN 6: 1459-1462, 1995

Vascular changes

- Fibrous intima thickening
- Loss of media
- Arteriolar hyalinosis

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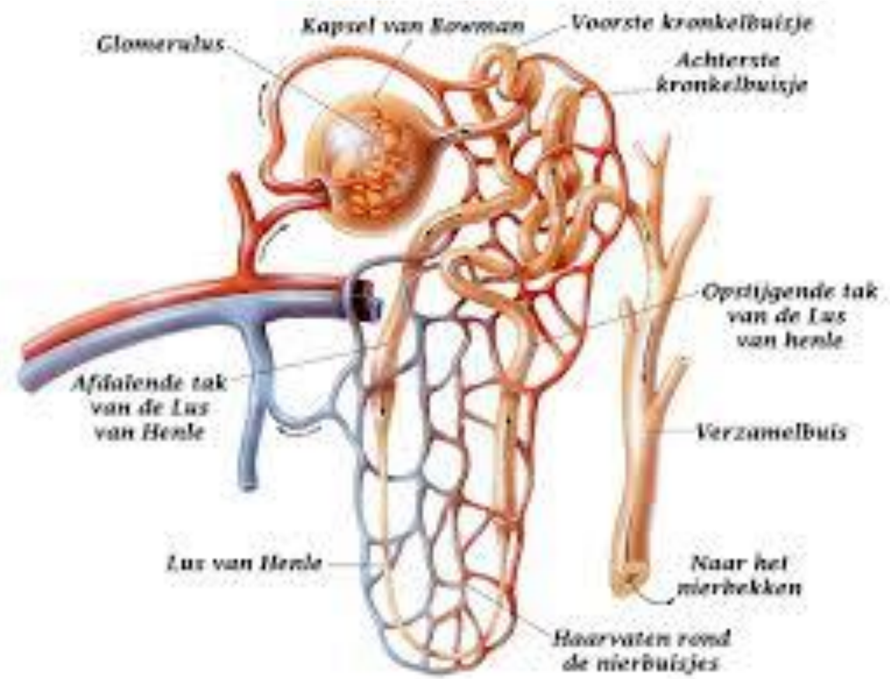


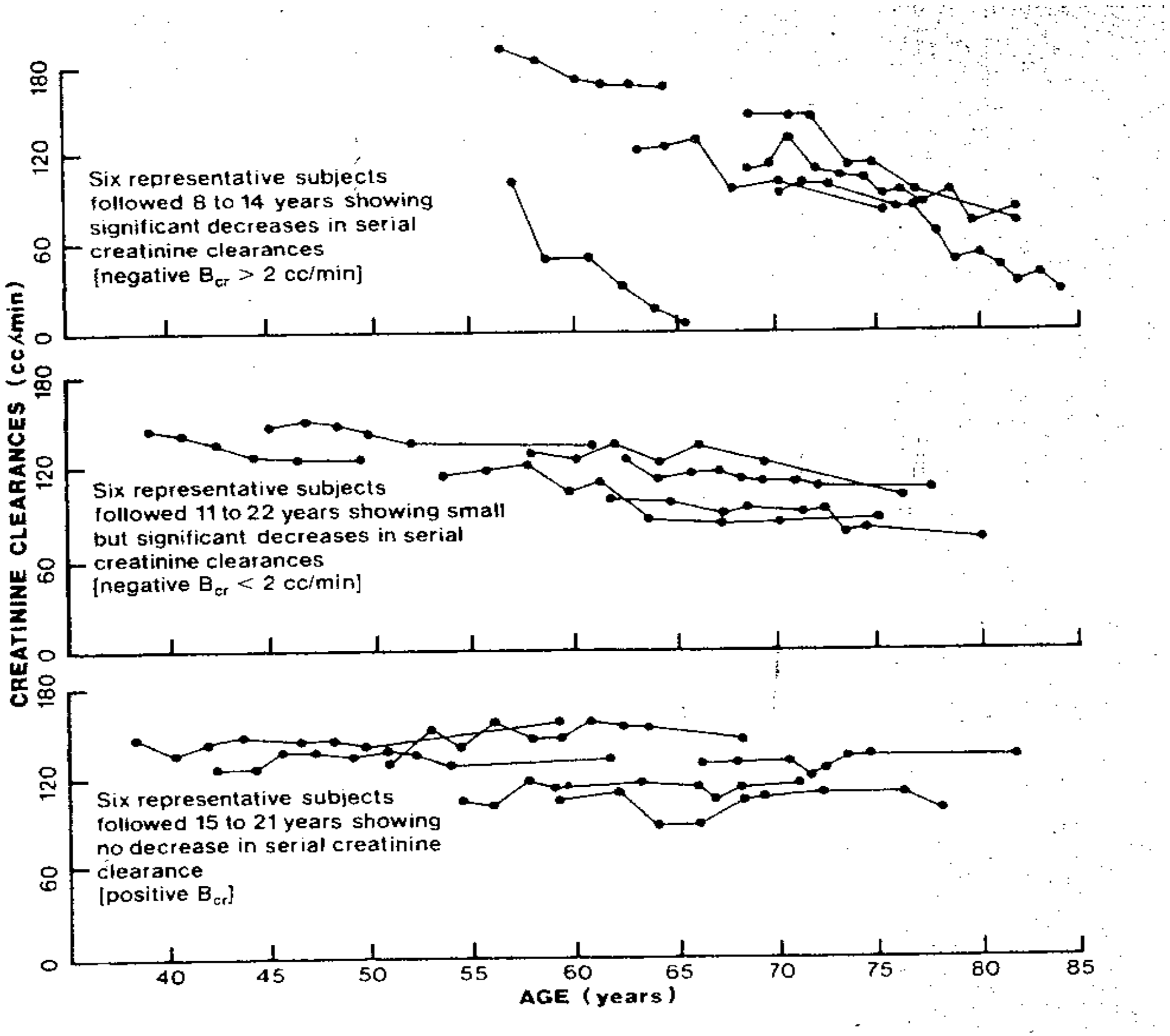
Etiology of ageing (kidney)

Interactions between

- genetically individual susceptibility
- intrinsic stresses
- extrinsic factors

High heterogeneity (in GFR) in the elderly

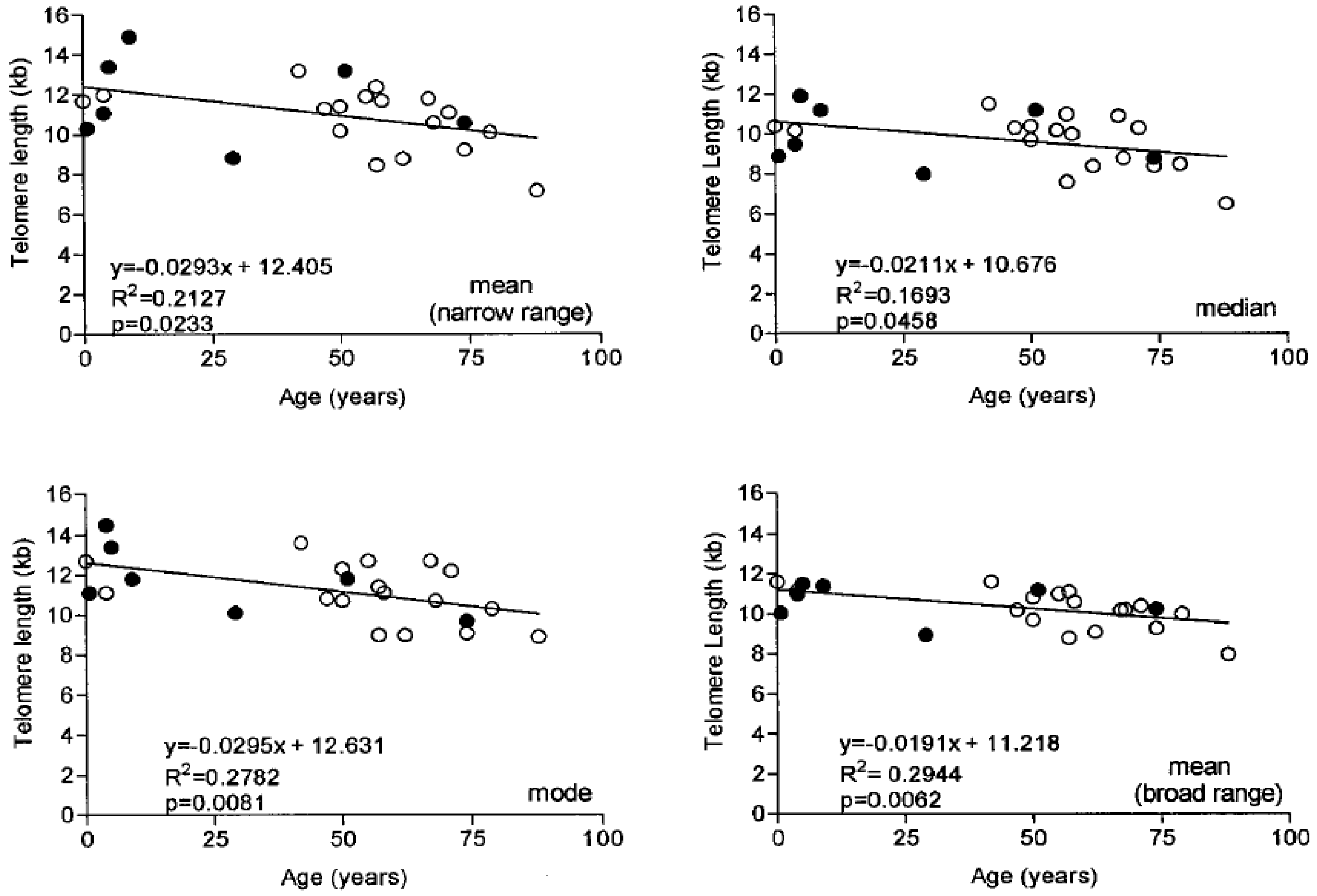
Heterogeneity in GFR in the elderly



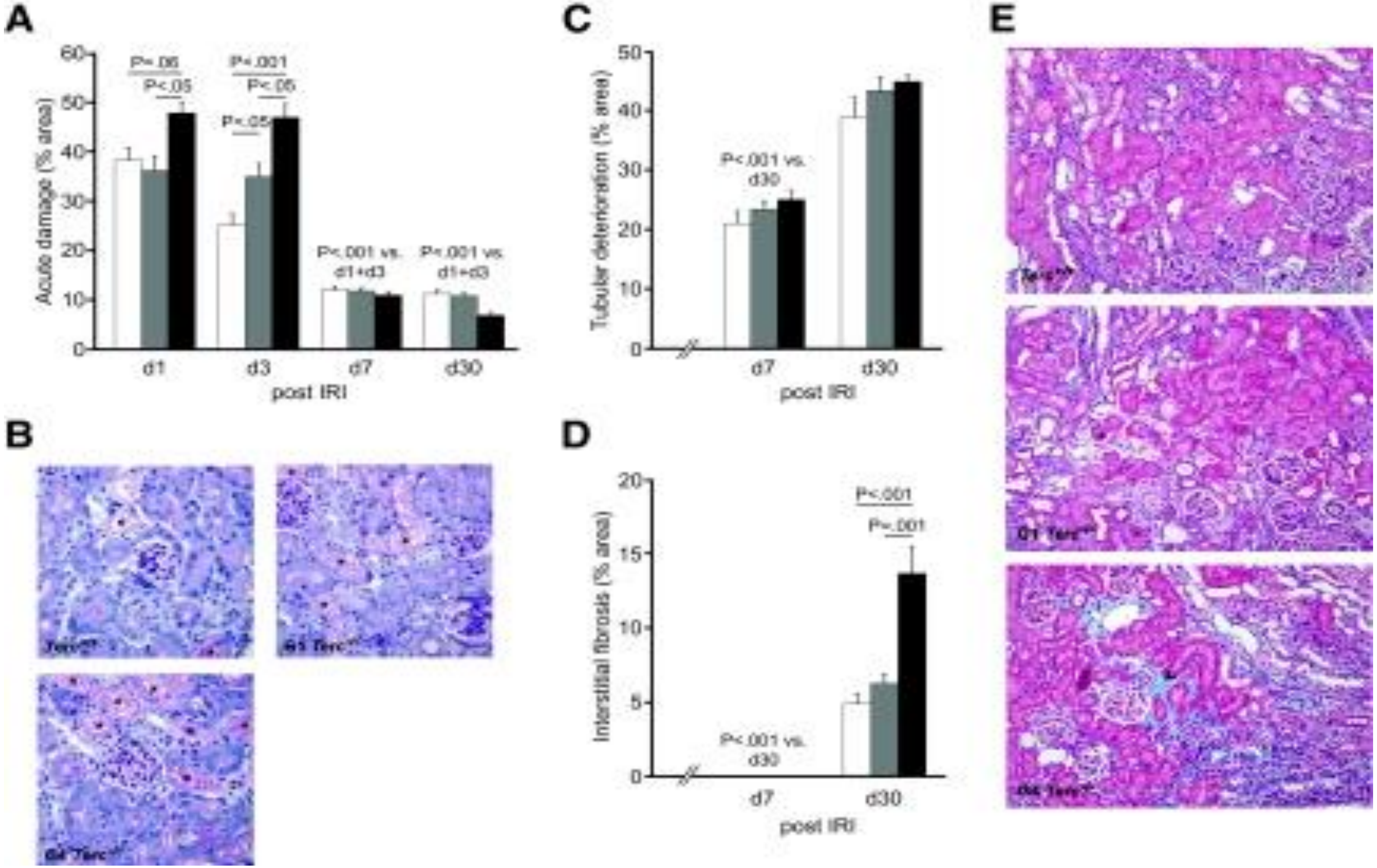
Etiology of the ageing kidney

- Genetic events
  - modulation of lifespan by a large number of genes
  - replicative senescence is determined by shortening of telomeres, cell cycle inhibitory genes, senescence associated beta-galactosidase
    - markers of senescence also present in the ageing kidney

Regression of telomeric length in renal cortex in relation to age



Melk et al JASN, 11: 444-453, 2000



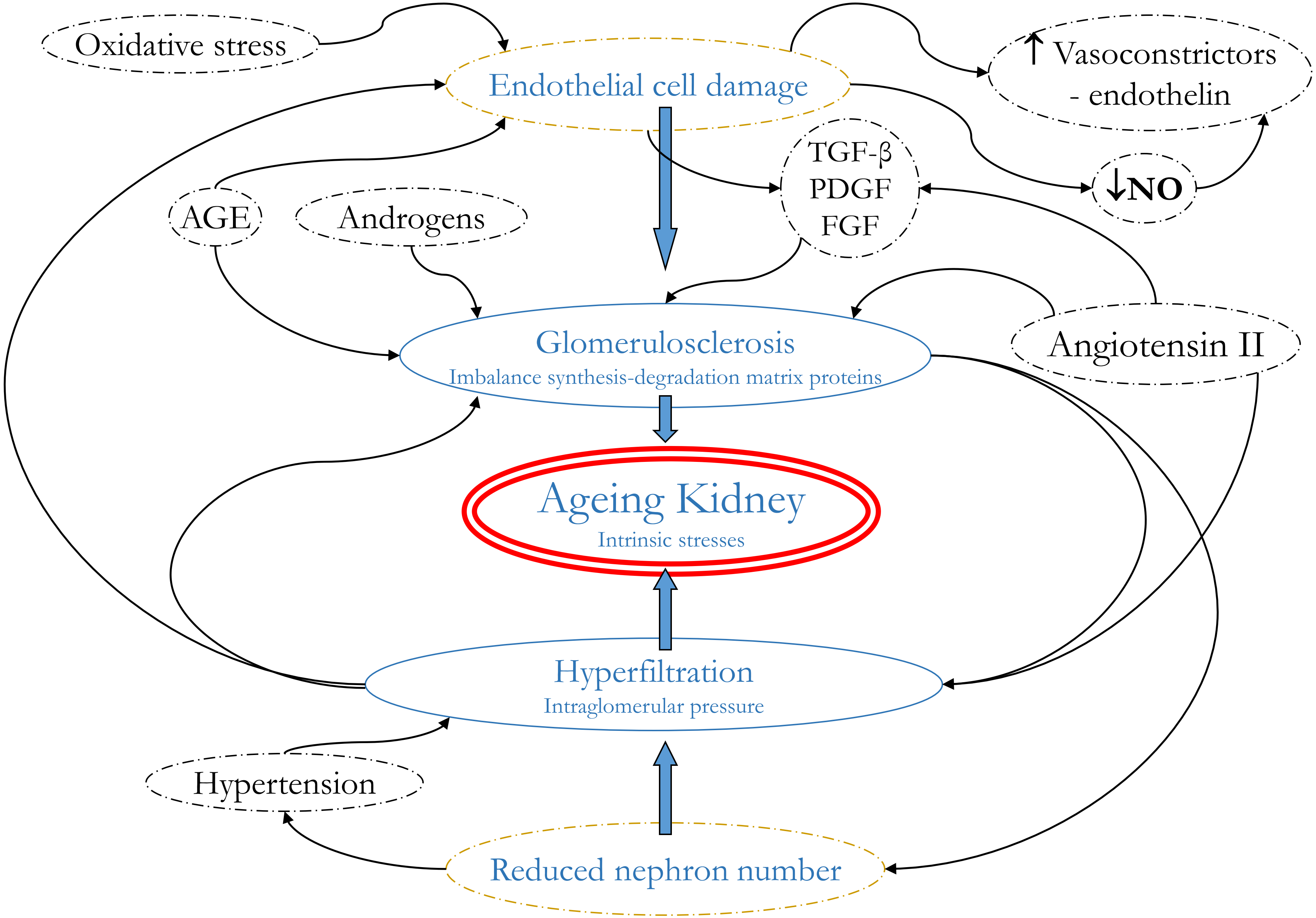
Westhoff et al. JASN 2010;21:327-36

Etiology of the ageing kidney

- Environmental and lifestyle factors
    - Diseases influencing GFR
        - hypertension
        - vascular disease
        - diabetes mellitus
        - heart failure

Frohling et al. Kidney Int 1989;36(suppl 27): 91-95

Etiology of the ageing kidney



Renal vascular resistance in the aged kidney

Increased sympathetic tone
Stimulated norepinephrine levels

Decrease in prostaglandins

↘ ↙

Autoregulatory defence in the aged kidney ⬇

⬆

Increased Intrarenal vascular tone
- Angiotensin II ↑
- Endogenous endothelin ↑
- Nitric Oxide ↓

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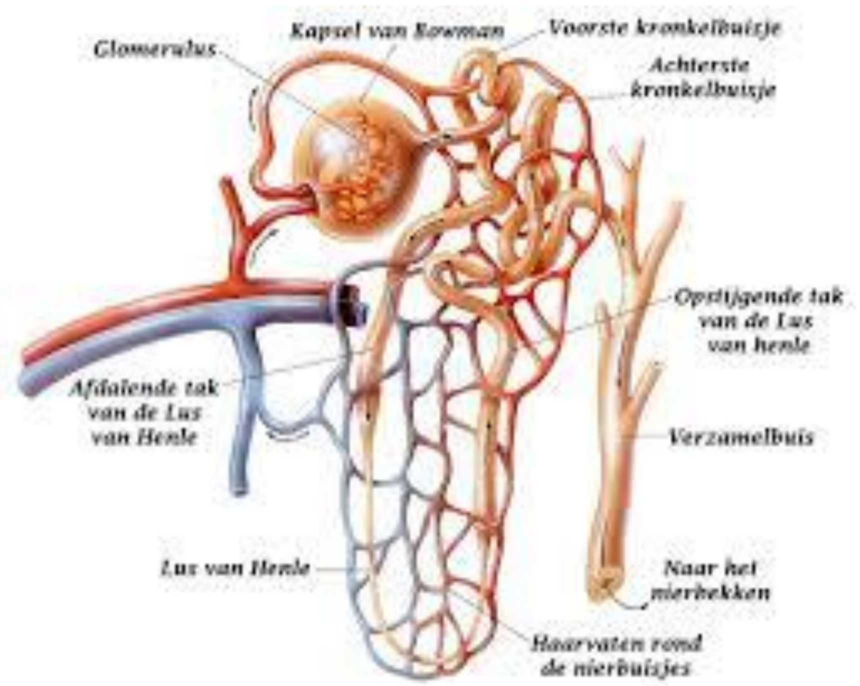
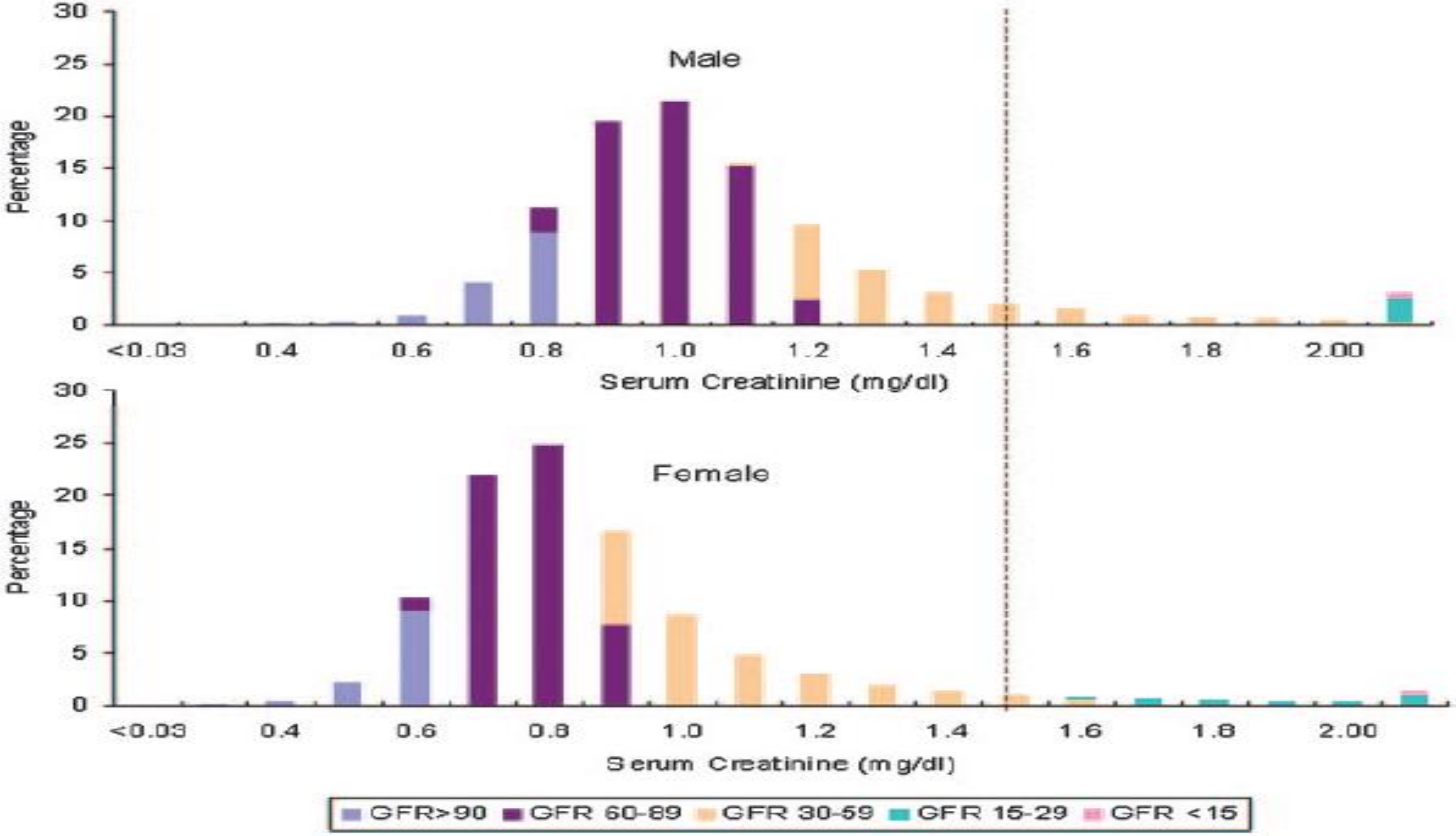




Male
Percentage
30
25
20
15
10
5
0
<0.03
0.4
0.6
0.8
1.0
1.2
1.4
1.6
1.8
2.00
Serum Creatinine (mg/dl)
Female
Percentage
Serum Creatinine (mg/dl)
GFR>90
GFR 60-89
GFR 30-59
GFR 15-29
GFR <15

Methods to measure renal function

- Renal function is estimated by GFR, measured as the renal clearance of a particular substance:

$$GFR = UV/P$$

- Substances used
  - Exogenous (gold standard) - impractical & expensive
    - ^{51}Cr-EDTA; inulin
  - Endogenous
    - Serumcreatinine and cystatin C

Methods to estimate GFR: serum creatinine

- serum creatinine/ reciprocal serum creatinine
  - muscle mass declines with ageing
  - assay for serum creatinine (compensated Jaffé)
- urinary creatinine clearance
  - urine collections
  - tubular secretion of creatinine
- mathematical corrections (age, gender, weight)
  - Cockcroft-Gault formula
  - MDRD-formula
  - CKD-EPI

Methods to measure GFR:
Serum cystatin C

- non-glycosated, low molecular weight protein
- characteristics of an ideal GFR marker
  - endogenously produced at a constant rate
  - freely filtered at the glomerulus, destroyed in the proximal renal tubule, not extrarenally eliminated
  - not dependent on muscle mass, BMI, gender

Newman et al. Kidney Int 1995; 47:312-8.

e-GFR formulas in older persons

Schattingsformules voor renale klaring: mathematisch		
CG	$creatinineklaring = \frac{(140 - leeftijd).Gewicht}{72.Screat}.(0{,}85\ indien\ een\ vrouw)$	
MDRD	$GFR = 186.(Screat)^{-1{,}154}.(leeftijd)^{-0{,}203}$ $.(0{,}742\ indien\ vrouw)$ $.(1{,}210\ indien\ zwarte\ huidskleur)$	
CKD-EPI (blanke ras)	Vrouw + Screat ≤ 0,7mg/dL	$GFR = 144.(Screat/0{,}9)^{-0{,}329}.0{,}993^{leeftijd}$
	Vrouw + Screat > 0,7mg/dL	$GFR = 144.(Screat/0{,}9)^{-1{,}209}.0{,}993^{leeftijd}$
	Man + Screat ≤ 0,9mg/dL	$GFR = 141.(Screat/0{,}9)^{-0{,}411}.0{,}993^{leeftijd}$
	Man + Screat > 0,9mg/dL	$GFR = 141.(Screat/0{,}9)^{-1{,}209}.0{,}993^{leeftijd}$
BIS	$GFR = 3736.\ Screat^{-0{,}87}.leeftijd^{-0{,}95}$	

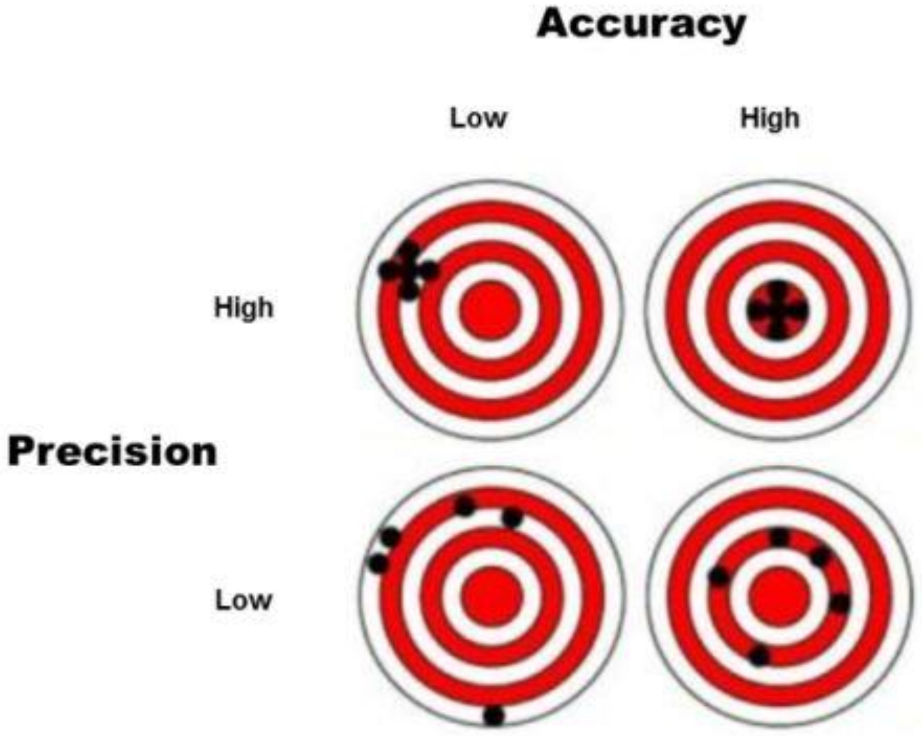
Schattingsformules voor renale klaring: algemeen overzicht				
Formule	**CG**	**MDRD**	**CKD-EPI**	**BIS**
Jaar	1976	1999	2009	2012
(n) patiënten	249	1628	5504	610
populatie	Mannen, ras n.n.o	divers	Alle rassen	Blank
hospitalisatie	gehospitaliseerd	Neen	Ja + neen	Neen
leeftijd	56,8j (18 – 92j)	50,6 ± 12.7j	47 ± 15j	78,5
% 70-plus	23,7%	Exclusie	0,04%	100%
Nierziekte	Nee	Ja	Ja + neen	minimaal
klaring (ml/min)	73 ml/min	39,8 ml/min per 1.73cm²	68 ml/min per 1,73m²	60,3 ml/min per 1,73m²
Gouden standaard	Urinaire creatinineklaring	^{125}I-iothalamaat	^{125}I-iothalamaat	Iohexol plasmaklaring
Creatinine assay	Ongecompenseerd (N-11B autoanalyser)	gecompenseerde Jaffé	Roche enzymatisch	Roche enzymatisch

e-GFR formulas in older persons

- Cross-sectional analysis ; Geriatric ward UH
- 89 patients (25 men, 64 women)
  - Median age 85 years (80 – 89 years)
- renal evaluation on day 7 of admission
  - ^{51}Cr-EDTA clearance
  - blood sample (serum creatinine-compensated jaffé, serum cystatin C, serum albumine, serum urea level)
  - 24h urine collections (measured creatinine clearance)
  - calculated clearance (Cockcroft-Gault - & MDRD abbreviated)
- Second data-analyse for CKD-EPI&BIS in 2015

N Van Den Noortgate et al. JAGS 2002;50:1278-1282

Methdology BIAS: mean/median difference between eGFR - mGFR
PRECISION: standaarddeviation (SD) of interquartielrange (IQR) of bias
ACCURACY: a. % correct classified KDIGO-stadia
b.% eGFR within 30% of the mGFR



Results

total		CG	MDRD	CKD EPI	BIS
bias	mean	-3,0678	15,4112	7,2378	-0,2616
	median	-0,6528	14,1113	8,7611	4,8973
precision	IQR	[-9,78 / 6,73]	[2,50 / 29,74]	[-3,42 / 21,50]	[-11,04 / 11,46]
	SD	16,91	23,94	22,15	20,95
accuracy	P30	68,5%	40,4%	47,2%	66,3%
	stad	56/86 = 65,1%	38/89 = 42,7%	39/89 = 43,8%	45/89 = 50,5%

< 60 ml/min		CG	MDRD	CKD EPI	BIS
bias	mean	1,9796	19,7118	14,0748	7,3599
	median	2,0569	19,0642	12,4710	7,0562
precision	IQR	[-5,52 / 7,88]	[7,47 / 30,84]	[3,2 / 24,92]	[1,92 / 13,71]
	SD	9,89169	18,77556	15,74605	11,45014
accuracy	P30	75,4%	31,3%	34,3%	64,2%
	stad	47/67 = 70,1%	23/67 = 34,3%	24/67 = 35,8%	39/67 = 58,2%
≥ 60 ml/min		CG	MDRD	CKD EPI	BIS
bias	mean	-18,6904	2,3188	-13,5838	-23,4725
	median	-19,6118	-0,2056	-9,3460	-18,9491
precision	IQR	[-32,5 / -7,03]	[-5,7 / 22,17]	[-22,47 / 2,14]	[-32,84 / -11,3]
	SD	23,73	32,47530	25,96735	26,03923
accuracy	P30	57,1%	68,2%	86,4%	72,7%
	stad	9/20 = 45%	15/21 =71,4%	15/21 = 71,4%	6/21 = 28,6%

Methods to evaluate renal function in elderly patients: a systematic literature review

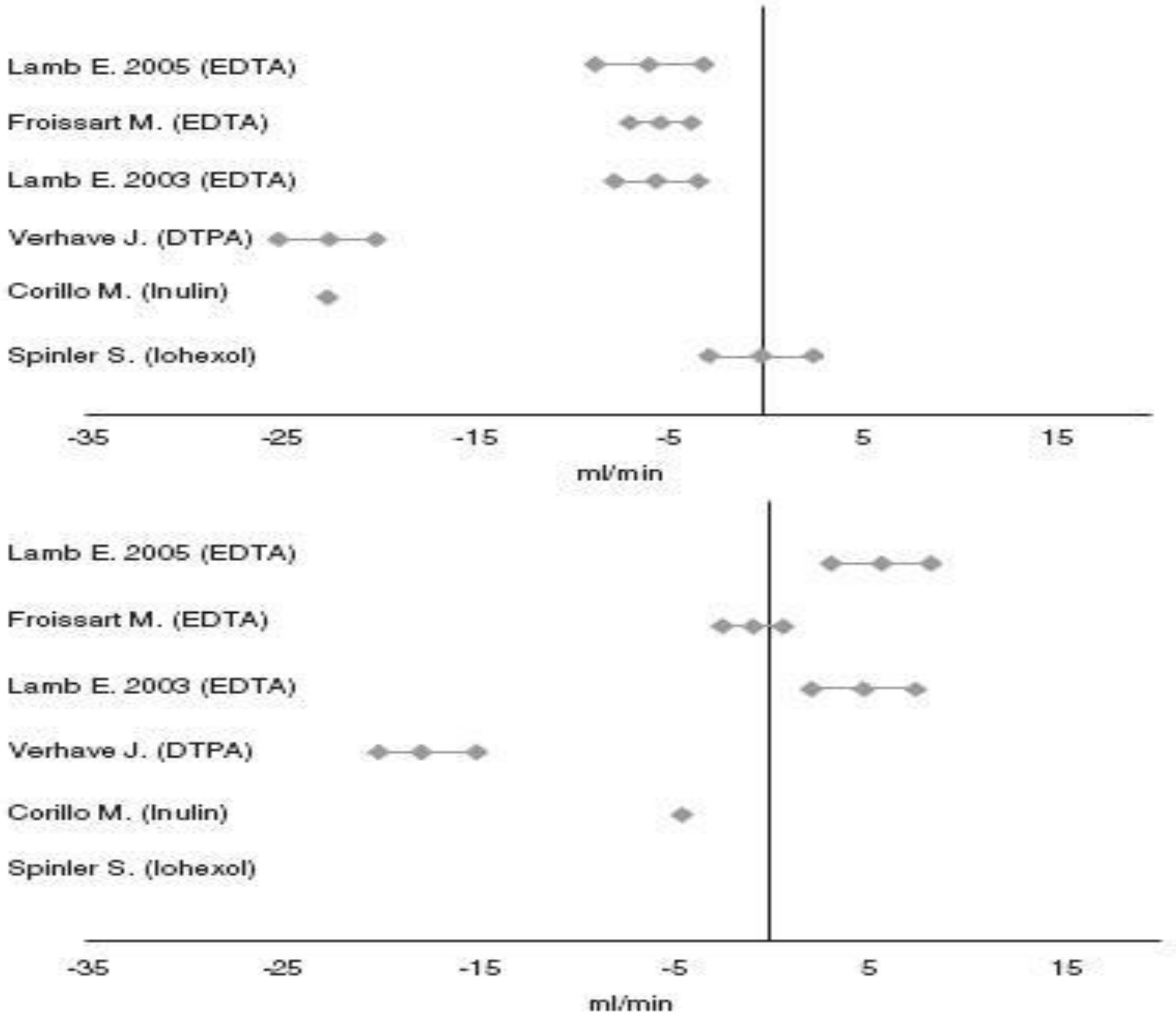


Figure 1. Mean difference between the gold standard and the formula to calculate the GFR (with 95% CIs) for the separate studies. Top: GFR calculated with the CG formula. Bottom: GFR calculated with the MDRD formula.

Van Pottelberghe et al. Age Ageing 2010:39:542-548

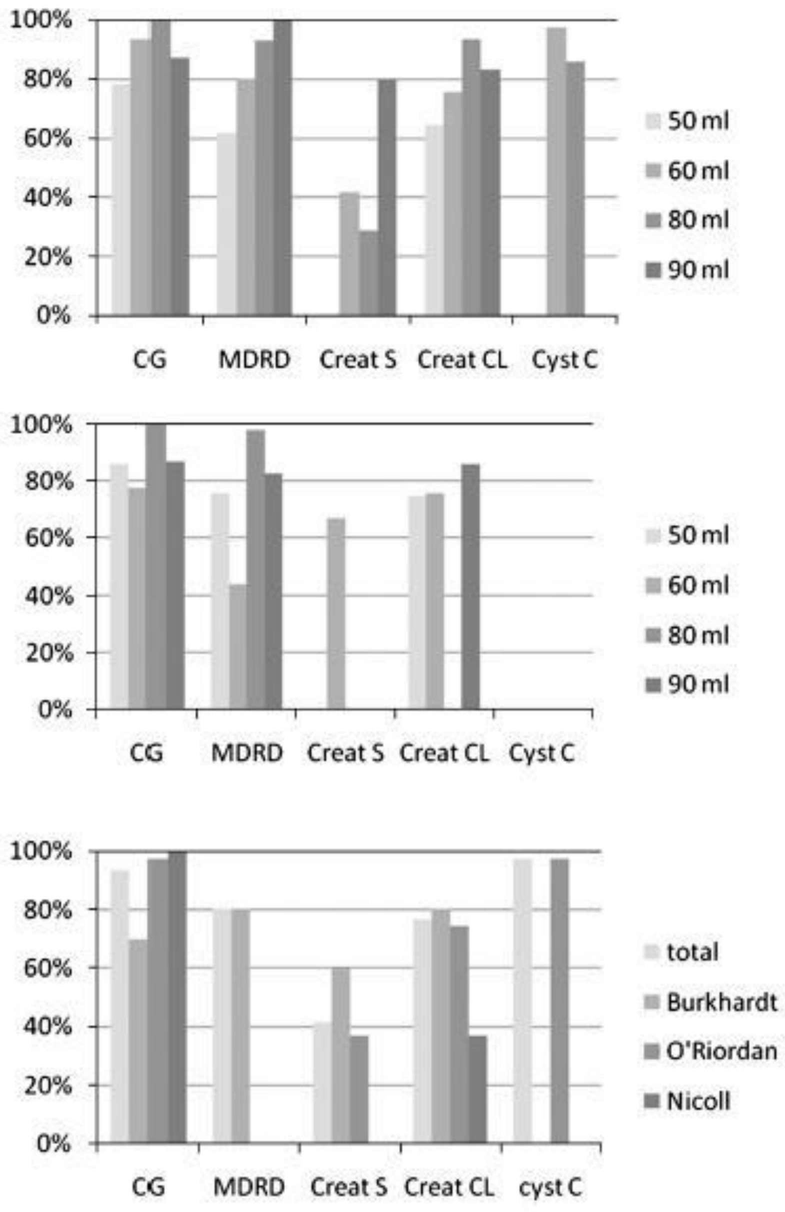


Figure 2. Mean difference between the gold standard and the formula to calculate the GFR (with 95% CIs) for the separate studies. Top: Sensitivity of the CG and MDRD formulas, serum creatinine and cystatin C concentrations and creatinine clearance for the pooled data with cut-off values of 50, 60, 80 and 90 ml/min. Middle: Positive predictive value of the CG and MDRD formulas, serum creatinine and cystatin C concentrations and creatinine clearance for the pooled data with cut-off values of 50, 60, 80 and 90 ml/min. Bottom: Sensitivity of the CG and MDRD formulas, serum creatinine and cystatin C concentrations and creatinine clearance for the cut-off value of 60 ml/min for pooled data and for the separate studies. CG, Cockcroft–Gault formula; MDRD, Modification of Diet in Renal Disease formula; Creat S, serum creatinine; Creat CL, creatinine clearance; cyst C, cystatin C.

Use of e-GFR methods in older persons

- Serum creatinine is an insensitive measure
- CG and BIS are of comparable value in an older hospitalized population with decline in GFR
- MDRD en CKD-epi are more useful to measure early decline in GFR
- Cystatin C is comparable with serum creatinine; it probably performs better in detecting very early decline in GFR

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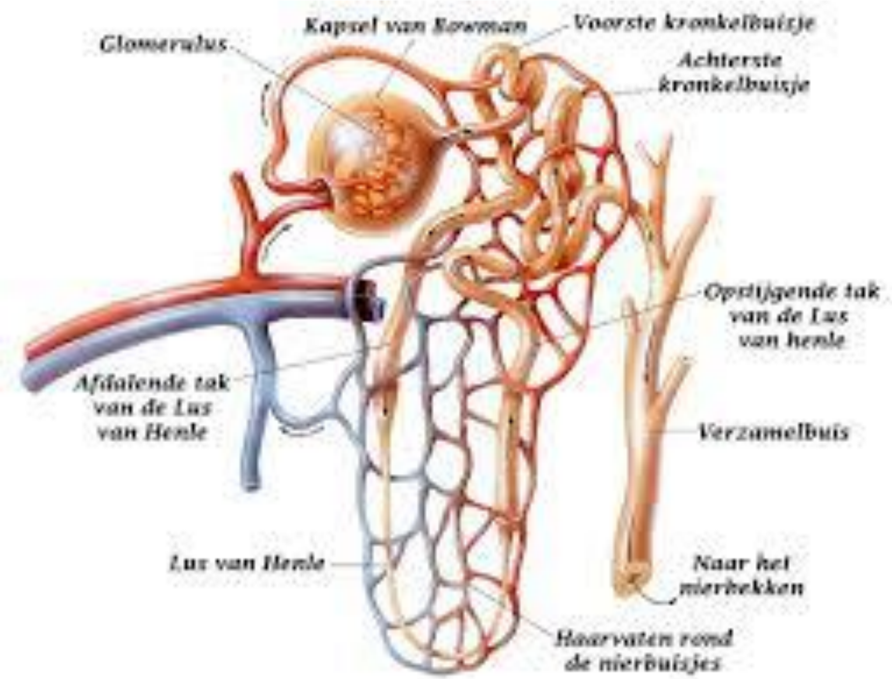


Table 1. Stages of CKD[a]

Stage	Description	GFR (mL/min/1.73 m²)
1	Kidney damage with normal or GFR	≥ 90
2	Kidney damage with mild GFR	89-60
3A	Mild to moderate GFR	59-45
3B	Moderate GFR	45-30
4	Severe GFR	30-15
5	Kidney failure	< 15 or dialysis

CKD, chronic kidney disease; GFR, glomerular filtration rate.

[a]Adapted from the Renal Association. http://www.renal.org/whatwedo/InformationResources/CKDeGUIDE/CKDstages.aspx. Accessed November 16, 2013.

Impairment in eGFR with Ageing

Cross-sectional studies: NHANES III

GFR mL/min/1.73m²	Age Group (years)			
	20 -39	40 - 59	60 - 69	≥ 70
≥ 90	86.0%	55.7%	38.5%	25.5%
60 - 89	13.7%	42.7%	53.8%	48.5%
30 - 59	__*	1.8%	7.1%	24.6%
15 - 29	__*	__*	__*	1.3%

* fewer than 20 cases; data not considered reliable

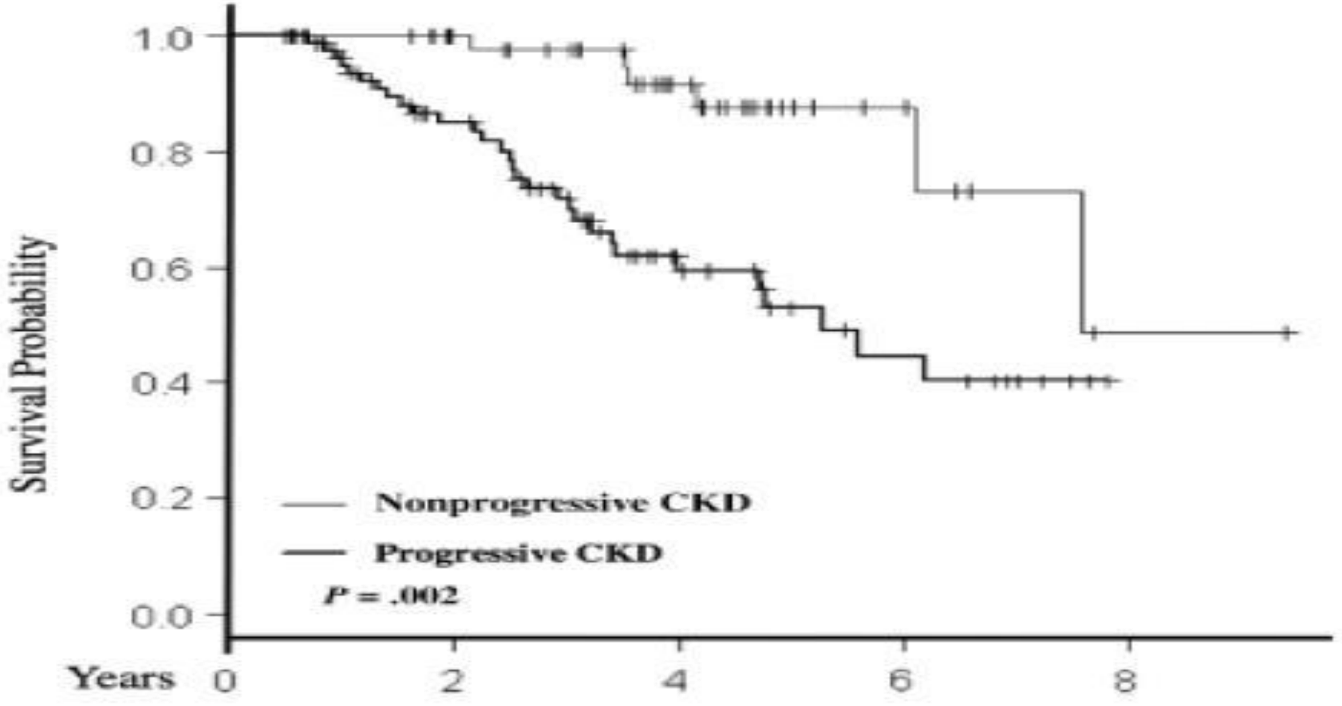
National Kidney Foundation. Am J Kidney Dis 2002; 39 (suppl 1): S58

Prevalence of reduced renal function- acute geriatric ward (UH-Ghent)

GFR (ml/min/1.73m²)	*GFR estimated by MDRD*	*GFR estimated by CC-Gault*
≥ 80	8.7	0
60-79	29.0	3.1
30-59	56.5	70.4
< 30	5.8	26.5

Van Den Noortgate et al. Int Urol Nephrol 2001;32:531-537.

Risk of end-stage renal disease/ mortality in the older population with CKD?



	0	2	4	6	8
Nonprogressors					
N patient(s) at risk	49	42	24	7	1
N cumulated death	0	0	3	4	6
Progressors					
N patient(s) at risk	89	54	23	10	0
N cumulated death	0	11	25	29	30

El-Ghoul , Joly et al. JAGS 2009;57:2217-23

Is decline in eGFR = normal ageing or CKD?

- No good correlation between RR, cardiac function and eGFR in older people
  - = do we measure normal ageing?

- Presence of proteinuria is an important indicator for CV risk and mortality in the older person

Diagnosis of CKD

eGFR < 60 ml/min

&

protein/creatinin ratio > 450 mg/g

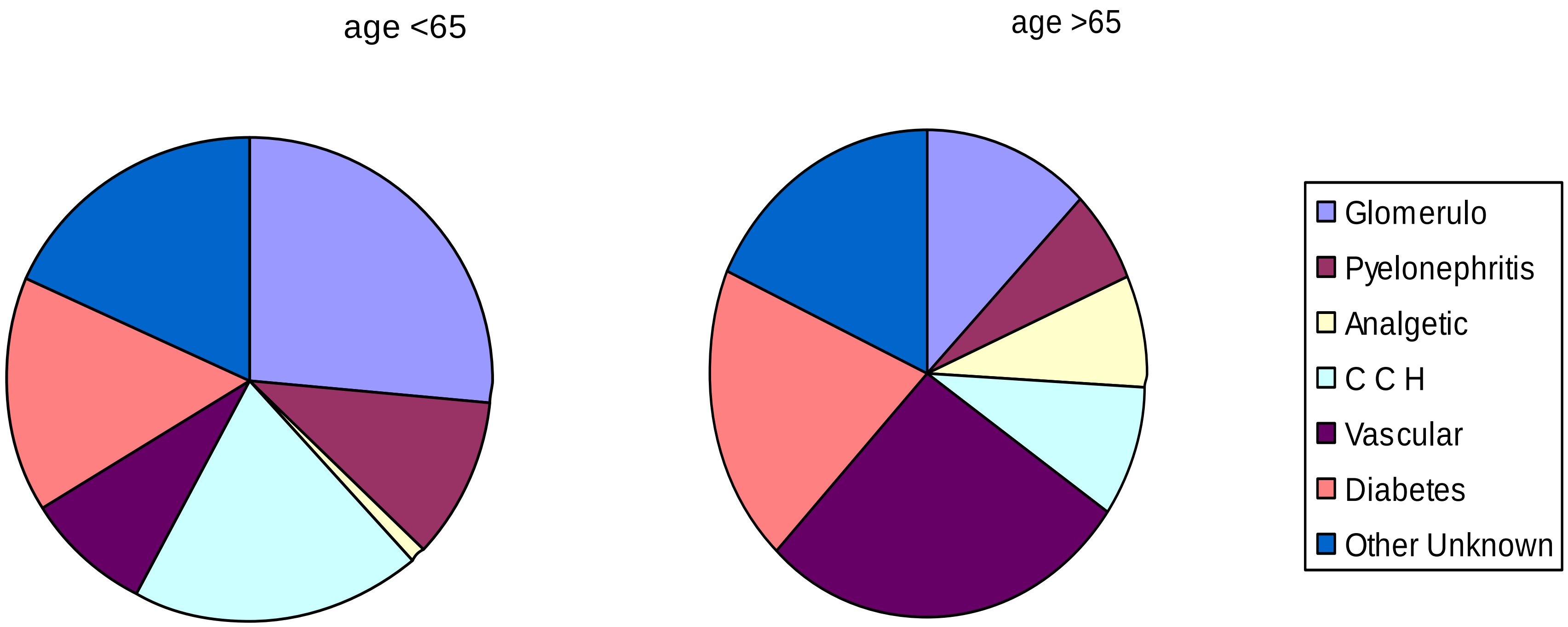
albumin/creatinin ratio (diabetes) > 30 mg/g

= kidney disease with high CV risk; not associated with normal ageing

Diagnosis of CKD

Prognosis of CKD by GFR and albuminuria categories: KDIGO 2012				Persistent albuminuria categories (description and range)		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				< 30 mg/g < 3 mg/mmol	30–300 mg/g 3–30 mg/mmol	> 300 mg/g > 30 mg/mmol
GFR categories (ml/min/1.73 m²) Description and range	G1	Normal or high	≥ 90			
	G2	Mildly decreased	60–89			
	G3a	Mildly to moderately decreased	45–59			
	G3b	Moderately to severely decreased	30–44			
	G4	Severely decreased	15–29			
	G5	Kidney failure	< 15			

Etiology of CKD



Nephrol Dial Transplant (2017) 32: 9–16
doi: 10.1093/ndt/gfw411

NDT Perspectives

Clinical Practice Guideline on management of older patients with chronic kidney disease stage 3b or higher (eGFR<45 mL/min/1.73 m^2): a summary document from the European Renal Best Practice Group

Ken Farrington[1], Adrian Covic[2], Ionut Nistor[2], Filippo Aucella[3], Naomi Clyne[4], Leen De Vos[5], Andrew Findlay[1], Denis Fouque[6], Tomasz Grodzicki[7], Osasuyi Iyasere[8], Kitty J. Jager[9], Hanneke Joosten[10], Juan Florencio Macias[11], Andrew Mooney[12], Evi Nagler[5], Dorothea Nitsch[13], Maarten Taal[14], James Tattersall[12], Marijke Stryckers[5], Dieneke van Asselt[15], Nele Van den Noortgate[16], Sabine van der Veer[17] and Wim van Biesen[5]

Follow up of older people with CKD

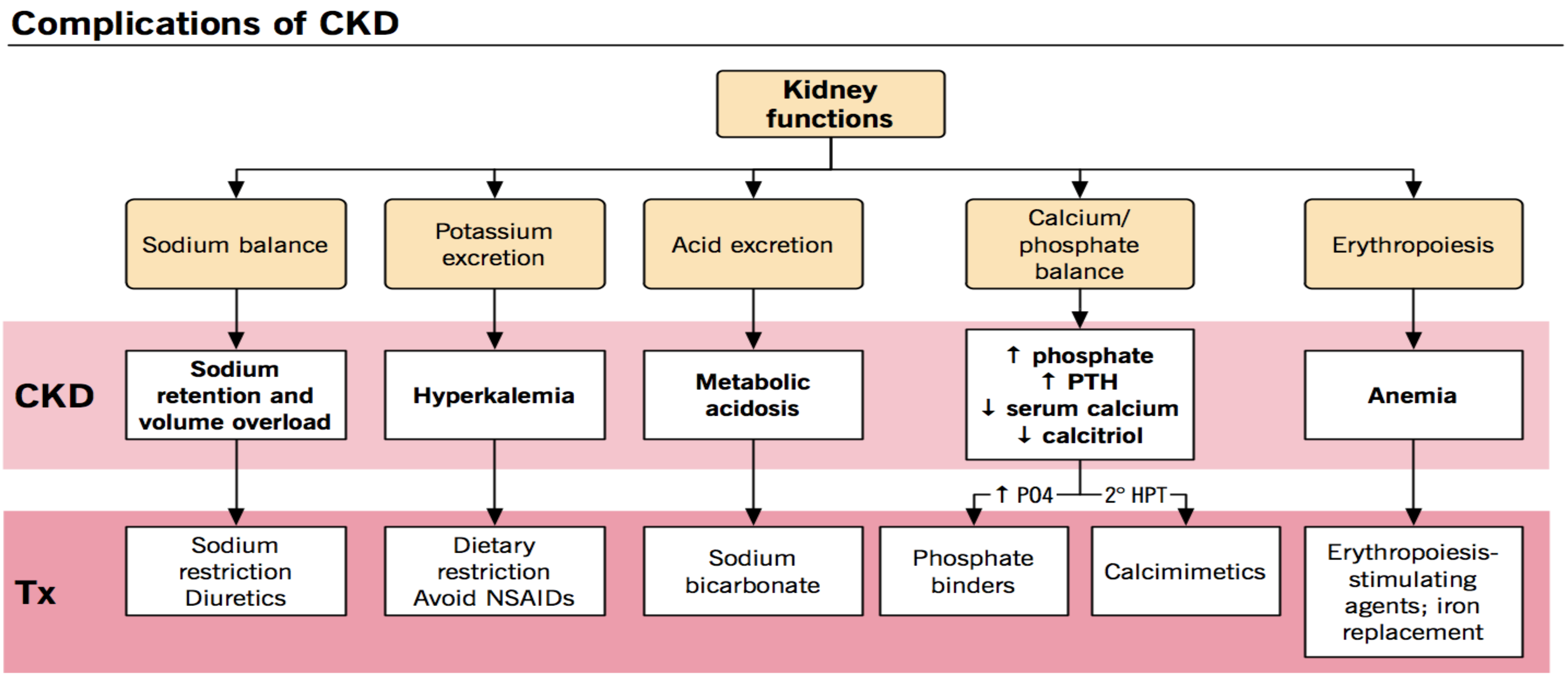
- Treat possible etiologies of CKD
  - Diagnose/treat diabetes mellitus
  - Treat arterial hypertension – SRR>140 mmHg?
  - Ultrasound of kidney

- Detect metabolic abnormalities
  - Hemoglobin/ 25 OH vit D
  - For people with eGFR < 30 ml/min
    - Bicarbonate/Calcium/phosphate/potassium
    - Parathormone

Follow up of older people with CKD

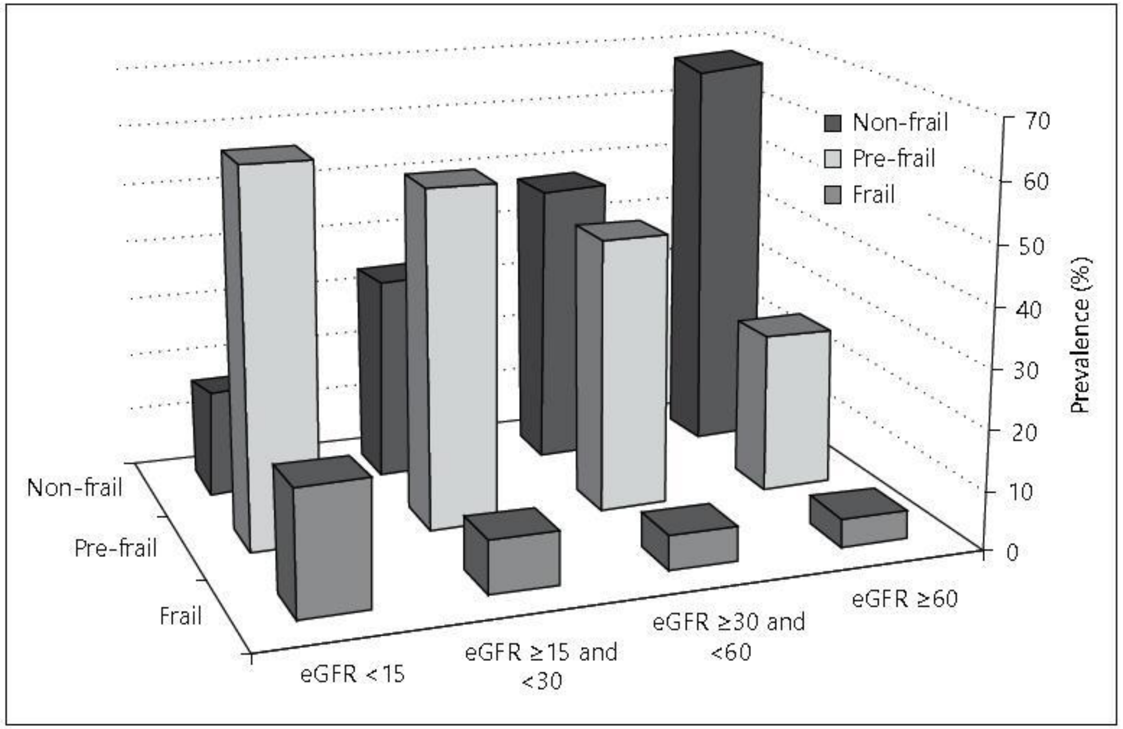
- Prevention of decline in kidney function
  - Start/continue nephroprotective medication
    - ACE-I in people with proteinuria
  - Avoid nephrotoxic medication/contrast
  - Adapt dose of medication with renal clearance (Cockroft-Gault)
  - Start diet low in salt
  - Stop smoking
  - Protein low diet?

Treatment of complications of CKD



Follow up of older people with CKD

- Detect frailty



Reese et al. Am J Nephrol. 2013;38:307-315

Follow up of older people with CKD

Q4A: WHAT IS THE BEST ALTERNATIVE METHOD TO ASSESS FUNCTIONAL DECLINE IN OLDER AND/OR FRAIL PATIENTS WITH ADVANCED CKD?

4a.1 We recommend a simple score be used on a regular basis to assess functional status in older patients with CKD stage 3b–5d with the intention to identify those who would benefit from more in-depth geriatric assessment and rehabilitation (1C)

4a.2 We recommend that most simple scores, including self-report scales and field tests (sit to stand, gait speed or 6-min walk test) have comparable and sufficient discriminating power to identify patients with decreased functional status (1C)

EB interventions in CKD

Q4B: ARE INTERVENTIONS AIMED AT INCREASING FUNCTIONAL STATUS IN OLDER PATIENTS WITH RENAL FAILURE (eGFR <45 ML/MIN/1.73 M^2 OR ON DIALYSIS) OF BENEFIT?

4b.1 We recommend that exercise has a positive impact on the functional status of older patients with CKD stage 3b or higher (1C)
4b.2 We suggest that exercise training be offered in a structured and individualized manner to avoid adverse events (2C)

5b.1 We suggest a trial of structured dietary advice and support with the aim of improving nutritional status (2C)

Indications for referral to nephrologist

- eGFR lower than 30 ml/min
- eGFR between 30 - 45 ml/min and progressive decline in eGFR (> 5 ml/min/2j) or important proteinuria
  - Slower progression of kidney failure in older people:
    - 27% No decline in GFR over 10y
- Sudden decline in eGFR

Domus medica 2013
Rosansky et al. Am J Nephrol 2012;36:1-10

Indications for referral to nephrologist

Figure 2. Referral decision making by estimated glomerular filtration rate (eGFR) and albuminuria

eGFR categories ($mL/min/1.73m^2$) Description and range			Urine ACR categories Description and range		
			A1	A2	A3
			Normal to mildly increased	Moderately increased	Severely increased
			<3mg/mmol	3-30mg/mmol	>30mg/mmol
G1	Normal or high	≥90		Monitor	Refer*
G2	Mildly decreased	60-89		Monitor	Refer*
G3a	Mildly to moderately decreased	45-59	Monitor	Monitor	Refer
G3b	Moderately to severely decreased	30-44	Monitor	Monitor**	Refer
G4	Severely decreased	15-29	Refer*	Refer*	Refer
G5	Kidney failure	<15	Refer	Refer	Refer

Q6: WHAT IS THE BENEFIT OF DIALYSIS IN FRAIL AND OLDER PATIENTS?

6.1 We recommend use of validated tools as explained in Questions 2 and 3 to project likely outcomes and help decide the appropriateness of discussing options for RRT (see Figure 1)
6.2 We recommend that the option for conservative management be discussed during the shared decision-making process on different management options for ESKD (1D)
6.3 We recommend the REIN score can be useful to stratify short term/6 month mortality risk of patients intending to start RRT (1C)

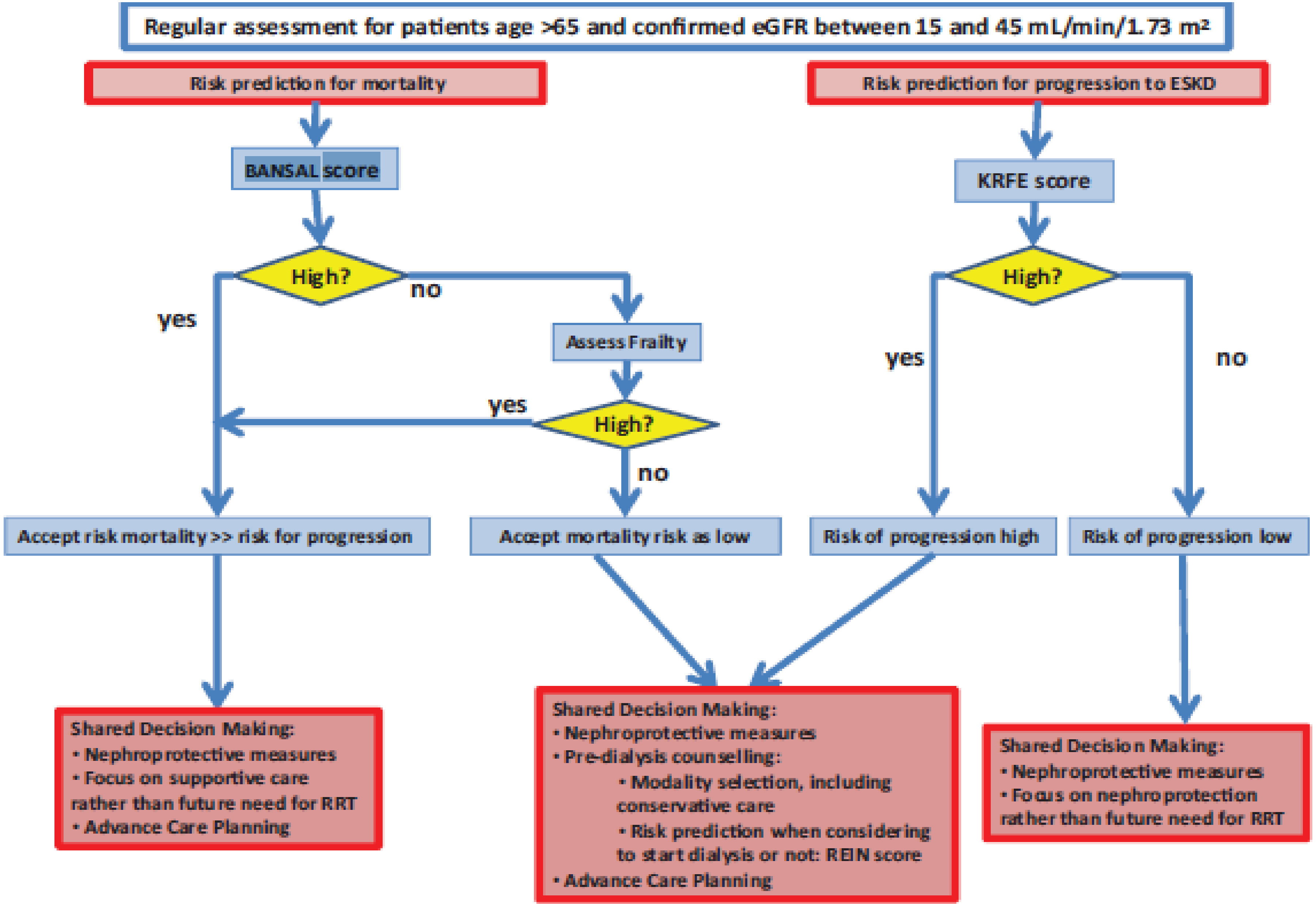


FIGURE 1: Proposed management pathway for older patients with advanced CKD. KRFE score is the 4-variable Kidney Failure Risk Equation (see Question 2). For Bansal and REIN score see Question 3.

BANSAL score

Table 2

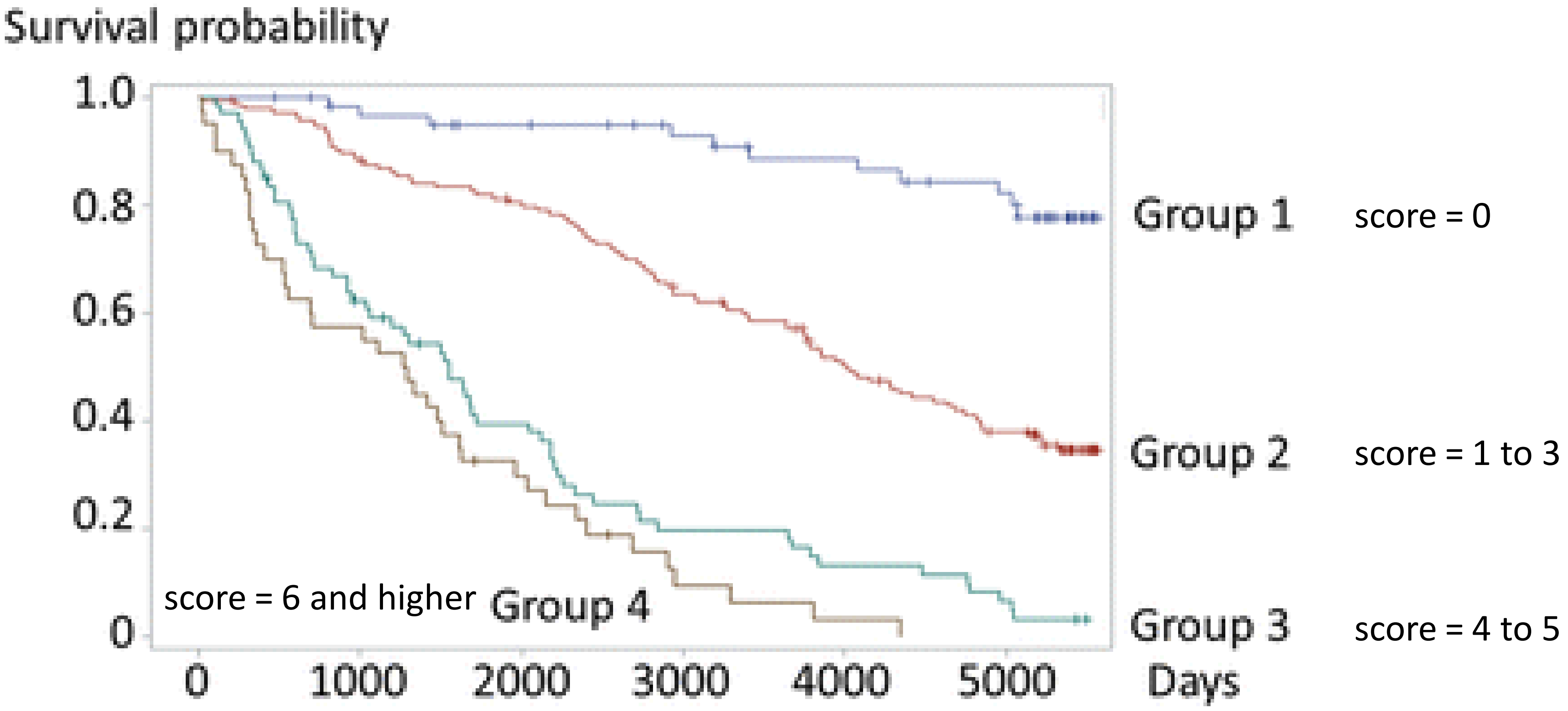
Parameter estimates in the final models and risk score

Variables	Parameter estimate in the final model	Ratio	Score
Older	0.96	2.97	3
DM	0.85	2.63	3
Hypotension	0.41	1.25	1
High CTR	0.38	1.16	1
High BNP level	0.32	1	1
ECG score = 1	0.46	1.43	1
ECG score = 2	1.52	4.69	5

Each parameter estimate in the final models was compared with the smallest parameter estimate (High BNP level). Then, the risk scores were determined.

Older 65 ≤ age, *DM* diabetes mellitus as a cause of end-stage renal disease, *Hypotension* hypotension during hemodialysis, *High CTR* 50 % ≤ cardiothoracic ratio, *High BNP level* 250 pg/mL ≤ plasma brain natriuretic peptide level, *ECG score* the number of abnormal findings in electrocardiogram

BANSAL SCORE



KFRE SCORE

Estimate risk of progression to end-stage renal disease in CKD patients using age, sex, eGFR and proteinuria with KFRE

Sex?
Male
Female
Age?
eGFR?
Urine Albumin Creatinine Ratio? (Note units carefully)
Patient location?
North America
Non-North America

REIN score

Table 2 | Adjusted odds ratios for 3-month mortality in the training set, after imputation, and points assigned to each risk factor

	Mean among 20 imputed data sets		Among 2000 samples (100 resampling)	Multivariate model	Score
Risk factors	*N*	% Death	Number of significant associations (*P*<0.05)	Adjusted odds ratio (95% confidence interval)	Points
Gender					
Male	7549	10.8	1944	1.23 (1.08–1.40)	1
Female	4951	9.7	—		
Age (years)					
(75–80)	5103	10.2	—	1	
(80–85)	4549	13.1	229	1.10 (0.95–1.27)	0
(85–90)	2393	18.1	2000	1.40 (1.19–1.66)	2
⩾ 90			2000	1.79 (1.35–2.38)	3
Diabetes					
No	7437	10.1	—		
Yes	5063	10.8	2		
Congestive heart failure					
No	792	7.8	—	1	
Stage I–II	3185	12.9	2000	1.43 (1.23–1.67)	2
Stage III–IV	1395	19.7	2000	2.15 (1.79–2.59)	4
Peripheral vascular disease					
No or stage I–II	11,520	9.7	—		
Stage III–IV	980	18.2	1536	1.34 (1.09–1.64)	1
Ischemic heart disease					
No	8226	9.7	—		
Without myocardial infaction	2627	11.0	19		
With myocardial infaction	1648	13.1	213		
Cerebral vascular disease					
No	10,833	10.1	—		
Yes	1667	12.7	8		

Couchoud et al. Kidney International (2015) 88, 1178–1186

Dysrhythmia					
No	8296	8.9	—	1	
Yes	4204	13.5	1939	1.25 (1.09–1.43)	1
Chronic respiratory disease					
No	10,624	10.0			
Yes	1876	12.8	2		
Cancer					
No	10,919	9.7	—	1	
Yes	1581	15.4	2000	1.61 (1.36–1.91)	2
Cirrhosis					
No	12,374	10.3	—		
Yes	126	18.3	326		
Severe behavioral disorder					
No	11,997	9.9	—	1	
Yes	503	21.4	1841	1.44 (1.12–1.85)	2
Mobility					
Walks without help	8502	5.8	—	1	
Need assistance for transfer	3159	15.9	2000	2.47 (2.10–2.91)	4
Totally dependent for transfer	839	36.6	2000	6.53 (5.38–7.92)	9
Albuminemia (g/l)					
<25	1175	21.4	2000	5.17 (2.94–2.22)	5
(25–30)	2468	14.4	2000	3.35 (2.01–1.66)	3
(30–35)	3987	10.2	1999	2.16 (1.57–1.30)	2
⩾35	3379	6.4	—	1	
Body mass index (kg/m^2)					
<18.5	430	13.2	57		
(18.5–23)	2616	10.5	5		
(23–35)	1754	9.6	—		
(25–30)	3080	10.1	177		
⩾30	1430	10.7	706		
Area under the curve				0.76 (0.75–0.77)	0.76 (0.75–0.77)

Couchoud et al. Kidney International (2015) 88, 1178–1186

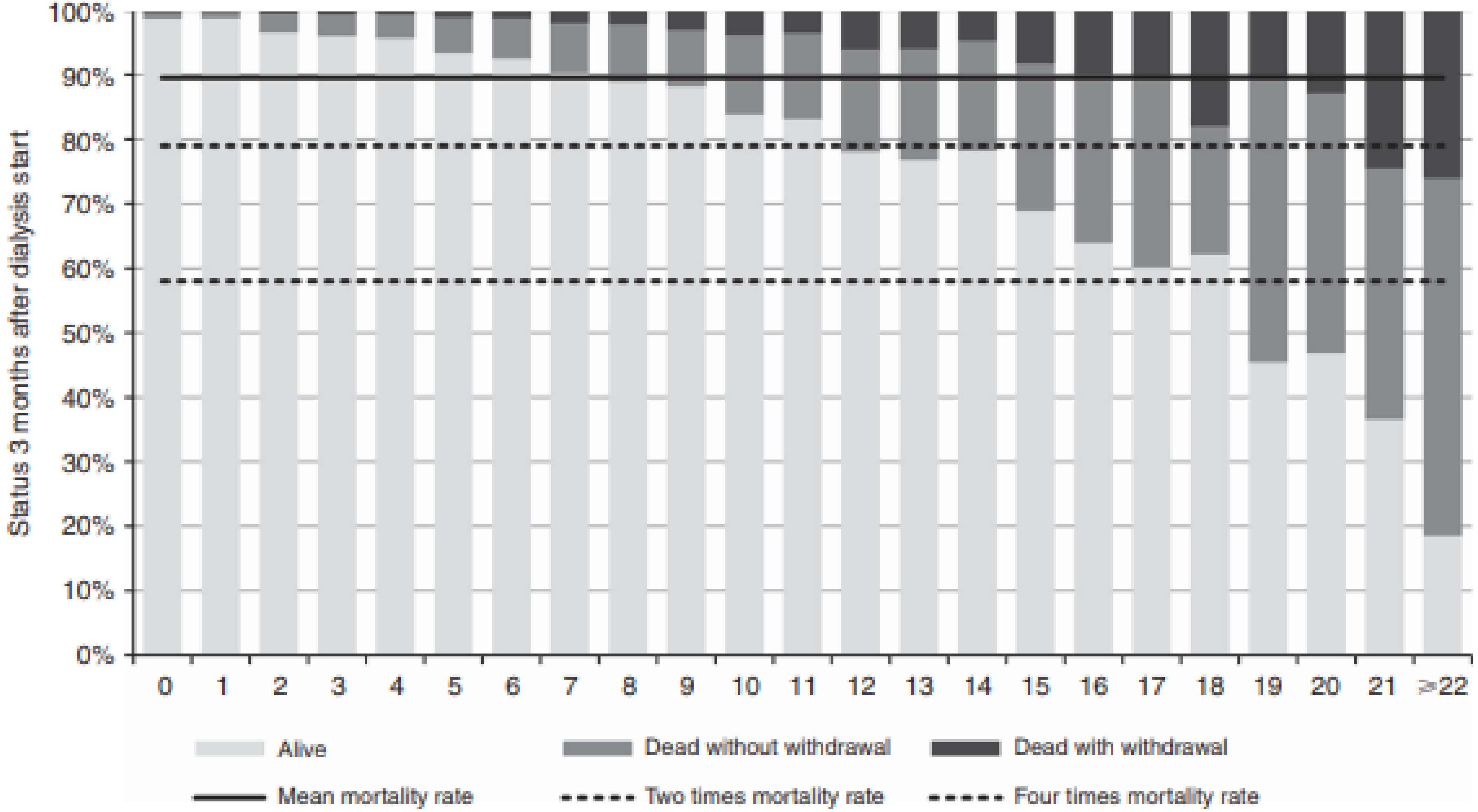


Figure 1 | Distribution of the patients in the validation set, by score, according to vital status and dialysis withdrawal within 3 months.

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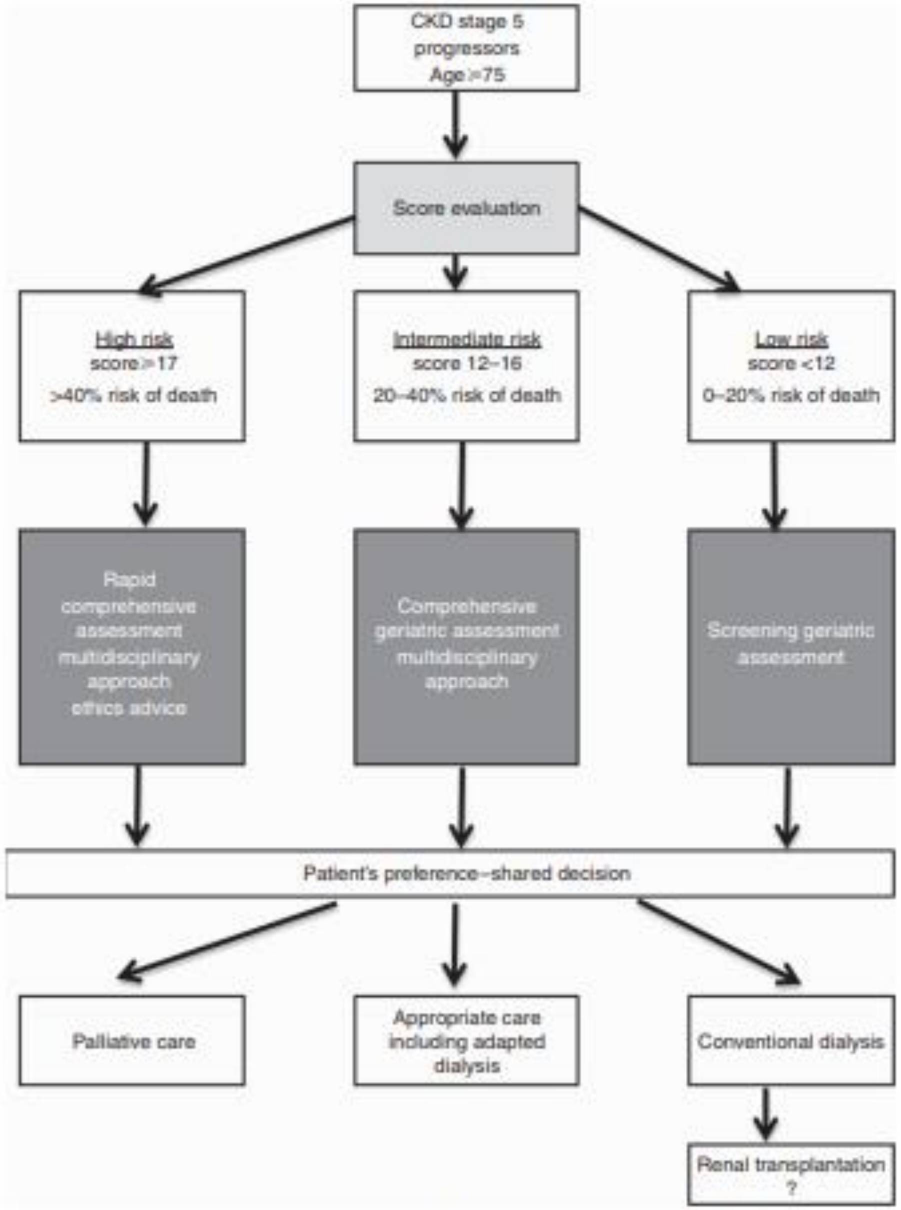

Figure 2 | Proposed risk stratification algorithm to screen for evaluation, evaluate and decide on the appropriate strategy of care for elderly ESRD patients, according to their level of risk of early death. CKD, chronic kidney disease.

Couchoud et al. Kidney International (2015) 88, 1178–1186

Prognostic factors for RRT?

- Bad prognostic factors
  - Fast decline eGFR: 4 à 5 ml/min/year
  - Important proteinuria

- Most studies: 80-plus with CKD stage 4 died before indication to start RRT

Demoulin et al. NDT 2011;26:220-26
O hare et al. JASN 2007;18:2758-65

RRT and mortality in older people

TABLE 2. PROGNOSIS WITH CONSERVATIVE, NONDIALYTIC MANAGEMENT OF END-STAGE RENAL DISEASE

Reference	*Conservative management group*	*Dialysis group*	*Results*
Carson et al., 2009[21]	median age 83.0 13.8% diabetes mean age-adjusted CCI score 7.4 $n=29$	median age 75.0 29.5% diabetes mean age adjusted CCI score 7.2 $n=173$	median survival from first known date of GFR $\leq 10.8^a$: 13.9 months (range 2–44) with CM 37.8 months (range 0–106) with dialysis $p<0.01$
Chanda et al., 2010[17]	mean age 77.5 68.4% over age 75 35.5% diabetes 49.7% high comorbidity $n=155$	mean age 58.5 11.2% over age 75 34.3% diabetes 17.3% high comorbidity $n=689$	median survival from first known date of GFR < 15: 21.2 months with CM[b] 67.1 months with dialysis[b] $p<0.001$
Ellam et al., 2009[19]	median age 80 38% diabetes 32% ischemic heart disease $n=69$	None	median survival from first known date of GFR < 15: 21 months (range 1–100) with CM
Joly et al., 2003[20]	mean age 84.1 51.4% late referral to nephrology 21.6% diabetes 48.6% ischemic heart disease 43.3% socially isolated $n=37$	mean age 83.2 28.9% late referral to nephrology 6.5% diabetes 42.5% ischemic heart disease 14.7% socially isolated $n=107$	median survival from first day of dialysis or decision not to perform dialysis: 8.9 months (95% CI 4–10) with CM 28.9 months (95% CI 24–38) with dialysis $p<0.0001$
Murtagh et al., 2007[18]	median age 83 23.4% diabetes $n=77$	median age 79.6 25.0% diabetes $n=52$	median survival from first known date of GFR < 15: 18.0 months (range 0.1–73.1) with CM 19.6 months (range 2.2–84.2) with dialysis
Smith et al., 2003[15]	$n=34$[c]	$n=10$[c]	median survival from proposed date of dialysis initiation: 6.3 months (range 0–46) with CM 8.3 months (range 2–20) with dialysis
Wong et al., 2007[16]	median age 79 mean GFR 12 28% diabetes 34% ischemic heart disease $n=73$	None	median survival from decision not to perform dialysis: 23.4 months with CM[b]

O'Connor et al. J Pall Med 2012; 15:228-235

No benefit of RRT on mortality

Murtagh et al., 2007[18]	median age 83 23.4% diabetes $n=77$	median age 79.6 25.0% diabetes $n=52$	median survival from first known date of GFR<15: 18.0 months (range 0.1–73.1) with CM 19.6 months (range 2.2–84.2) with dialysis
Smith et al., 2003[15]	$n=34^c$	$n=10^c$	median survival from proposed date of dialysis initiation: 6.3 months (range 0–46) with CM 8.3 months (range 2–20) with dialysis

O'Connor et al. J Pall Med 2012; 15:228-235

Benefit of RRT on mortality

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Chanda et al., 2010[17]	mean age 77.5 68.4% over age 75 35.5% diabetes 49.7% high comorbidity $n = 155$	mean age 58.5 11.2% over age 75 34.3% diabetes 17.3% high comorbidity $n = 689$	median survival from first known date of GFR < 15: 21.2 months with CM[b] 67.1 months with dialysis[b] $p < 0.001$
Ellam et al., 2009[19]	median age 80 38% diabetes 32% ischemic heart disease $n = 69$	None	median survival from first known date of GFR < 15: 21 months (range 1–100) with CM
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Benefit of RRT on mortality

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21.6% diabetes
48.6% ischemic heart disease
43.3% socially isolated
$n = 37$
28.9% late referral to nephrology
6.5% diabetes
42.5% ischemic heart disease
14.7% socially isolated
$n = 107$
or decision not to perform dialysis:
8.9 months (95% CI 4–10) with CM
28.9 months (95% CI 24–38) with dialysis
$p < 0.0001$

Mortality in 80-plus: Risk factor

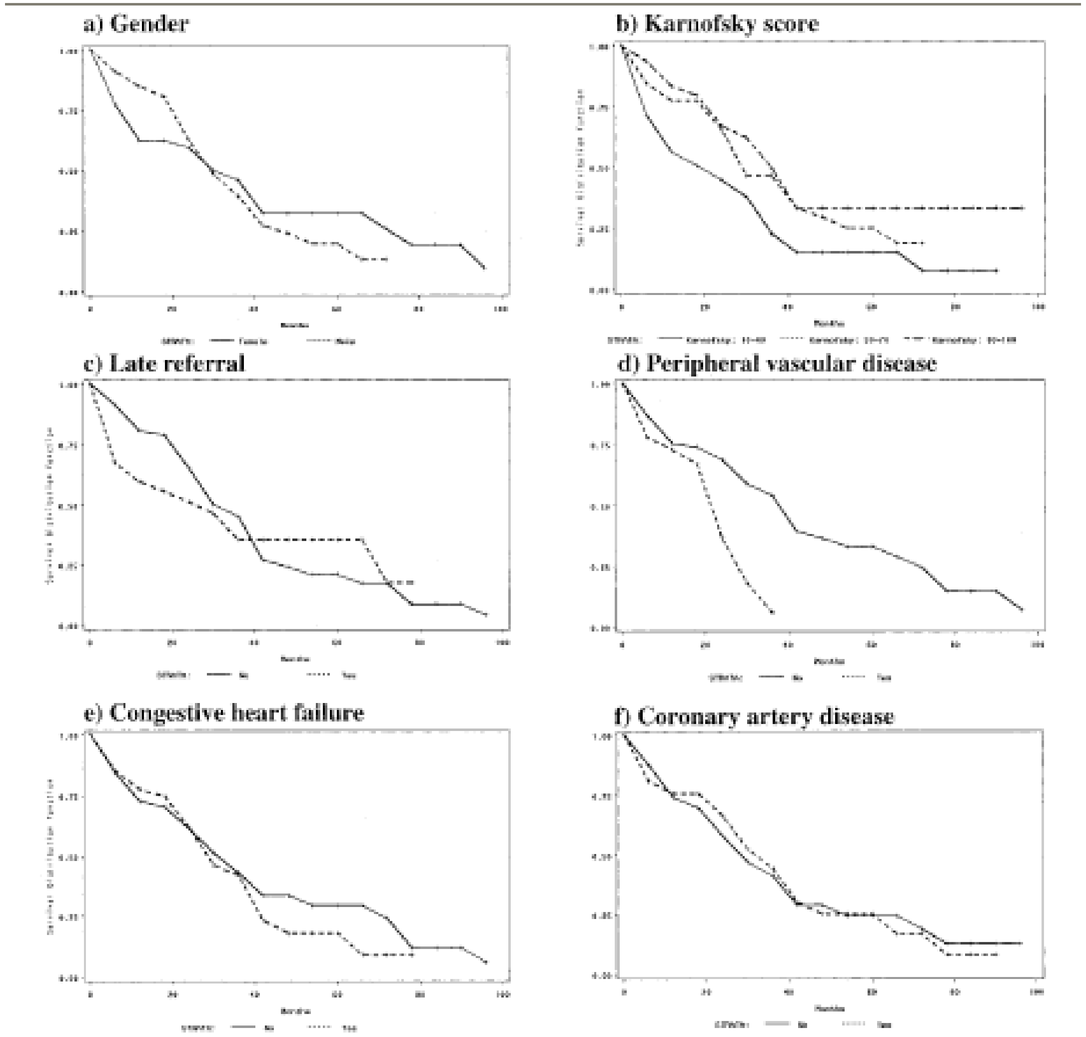


Figure 2. Actuarial survival curves in the group of hemodialyzed patients according to characteristics at inclusion. (a) Effect of gender on survival. (b) Survival in three groups defined by Karnofsky performance scale. (c) Effect of late referral. (e) Effect of peripheral vascular disease. (f) Effect of coronary artery disease. (g) Effect of cardiac failure.

--- KS >= 50
—KS < 50

--- yes
—No

Joly et al. J Am Soc Nephrol 2003;14: 1012-21 therapy or conservative management.

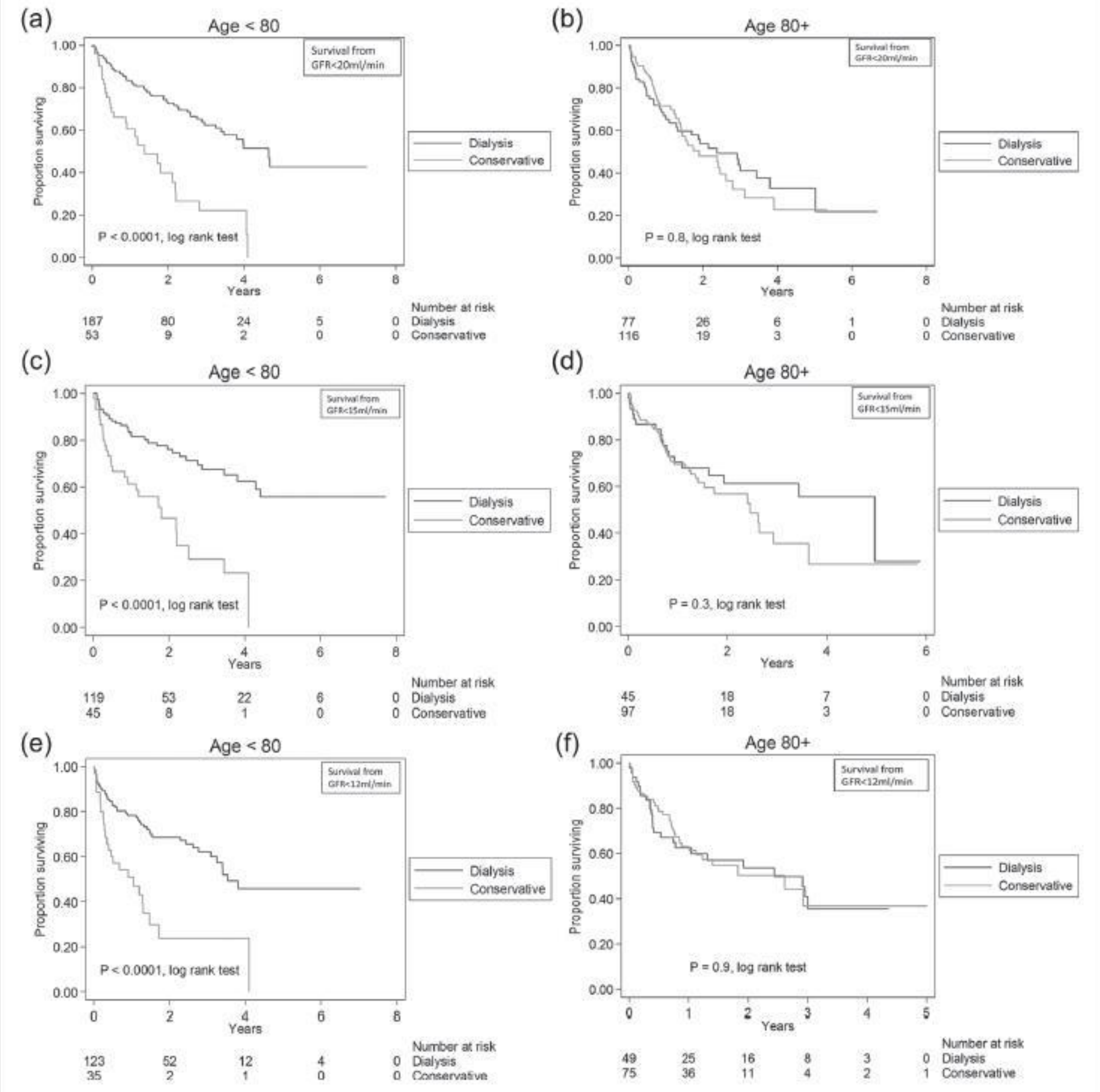
Aims: We aimed to compare survival, hospital admissions and palliative care access of patients aged over 70 years with chronic kidney disease stage 5 according to whether they chose renal replacement therapy or conservative management.

Design: Retrospective observational study.

Setting/participants: Patients aged over 70 years attending pre-dialysis clinic.

Results: In total, 172 patients chose conservative management and 269 chose renal replacement therapy. The renal replacement

Hussain et al. Pall Med 2013;27:829–39



(a)
Age < 80
Survival from GFR<20ml/min
Proportion surviving
Dialysis
Conservative
P < 0.0001, log rank test
Years
Number at risk
187 80 24 5 0 Dialysis
53 9 2 0 0 Conservative
(b)
Age 80+
Survival from GFR<20ml/min
P = 0.8, log rank test
Number at risk
77 26 6 1 0 Dialysis
116 19 3 0 0 Conservative
(c)
Age < 80
Survival from GFR<15ml/min
P < 0.0001, log rank test
Number at risk
119 53 22 6 0 Dialysis
45 8 1 0 0 Conservative
(d)
Age 80+
Survival from GFR<15ml/min
P = 0.3, log rank test
Number at risk
45 18 7 0 Dialysis
97 18 3 0 Conservative
(e)
Age < 80
Survival from GFR<12ml/min
P < 0.0001, log rank test
Number at risk
123 52 12 4 0 Dialysis
35 2 1 0 0 Conservative
(f)
Age 80+
Survival from GFR<12ml/min
P = 0.9, log rank test
Number at risk
49 25 16 8 3 0 Dialysis
75 36 11 4 2 1 Conservative

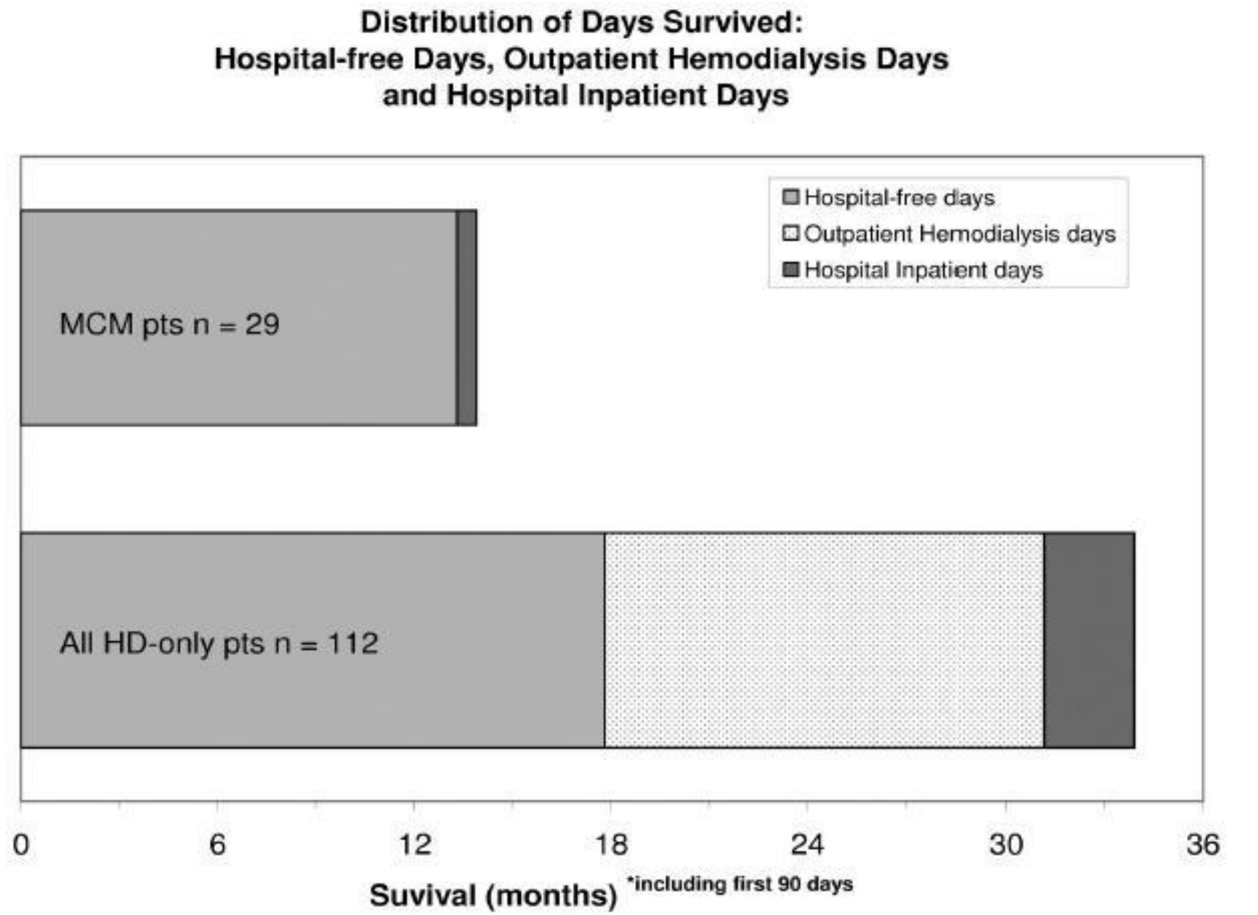


Figure 3. Median survival for MCM cohort and the hemodialysis-only subgroup in the RRT cohort. Data shown are how many days were spent hospital-free, compared with in-patient stays in hospital and outpatient hospital attendances for dialysis.

Carson et al. Clin J Am Soc Nephrol 2009;4:1611-19

Kwaliteit van leven

American Journal of Nephrology

Am J Nephrol 2013;37:231–238
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Trajectory of Quality of Life for Poor Prognosis Stage 5D Chronic Kidney Disease with and without Dialysis

Ying-Ying Seow[a] Yin Bun Cheung[b] Li Min Qu[c] Alethea Chung Pheng Yee[c]

[a]Khoo Teck Phuat Hospital, [b]Duke-NUS Graduate Medical School, and [c]National Cancer Centre, Singapore

Prospectieve studie – 101 patiënten
eGFR 8 – 12 ml/min
≥ 75 jaar oud
Charlson comorbidity index ≥ 8

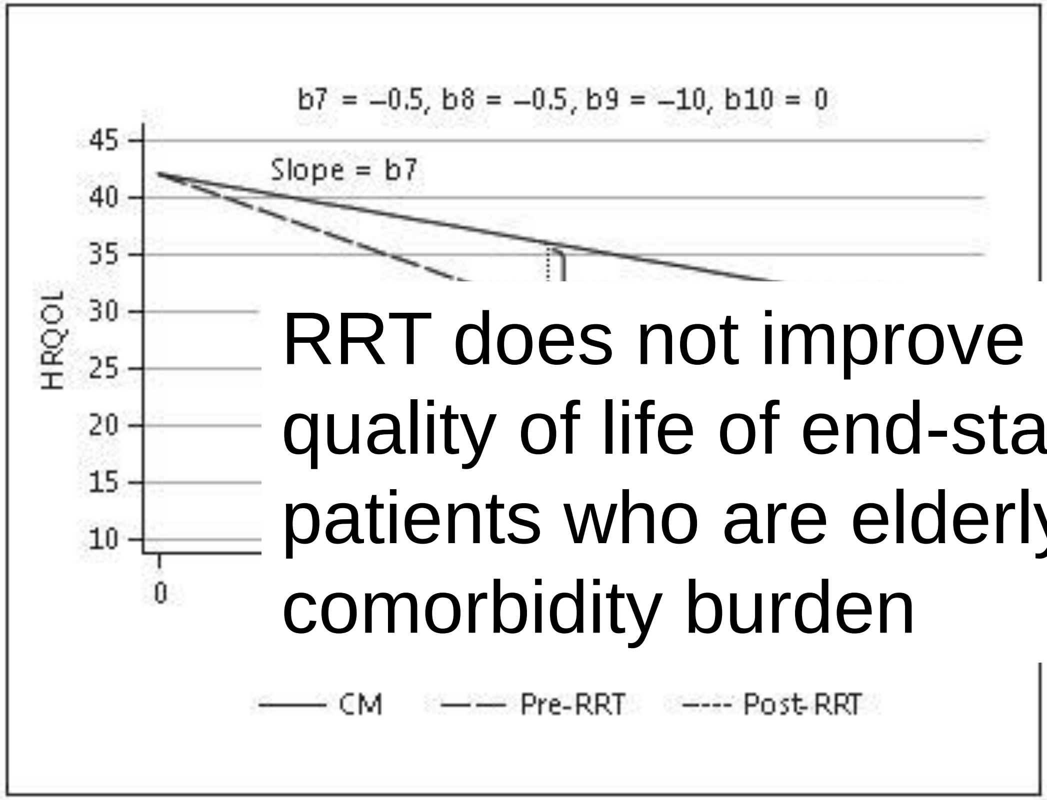

Illustration of regression models. The trajectory of a CM patient whose HRQOL declined by 0.5 points per month (b7 = –0.5) and the trajectory of a patient who

tter patient

= –0.5)

.0 points (b9

rate of decline (b10 = 0) as the CM

RRT does not improve health-related quality of life of end-stage kidney failure patients who are elderly or have a high comorbidity burden

Seow et al. JASN 2013;27:231-238

Renal replacement therapy

- Better outcome in
  - Highly active older people
  - Low comorbidity
  - Younger than 80 years
- Rather conservative in frail older people
  - Comprehensive geriatric evaluation
  - Multidisciplinary evaluation (GP/nephrologist/geriatrician)
  - Evaluation of needs/wishes of patient/family

Take Home Message

- Renal Senescence is characterized by structural and physiological changes leading to reduced reserve capacity
- eGFR equations (CG, MDRD and CKD-EPI) are at this moment the best tools available to estimate renal function, however clinicians should be aware of their pitfalls
- Reduced eGFR should be distinguished from CKD
- CKD should be managed EB with prevention of decline of renal function, physical and nutritional support, regular evaluation through BANS & KRFE & REIN score
- Starting RRT should be a multidisciplinary decision together with patient and family. Conservative treatment can be in individual cases a good alternative.


Thank you for listening