CKD diagnosis in the aging population

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Category	Disclosure Information
Employer	Nothing to disclose.
Ownership Interest	Nothing to disclose.
Consultancy	IDS; Nephrolytix; Alentis Therapeutics; ARK Bioscience;
Research Funding	Nothing to disclose.
Honoraria	IDS; Fresenius Kabi; Fresenius Medical Care; Nephrolytix; Alentis Therapeutics; ARK Bioscience; AstraZeneca;
Patents or Royalties	Nothing to disclose.
Advisory or Leadership Role	Nothing to disclose.
Speakers Bureau	Nothing to disclose.
Other Interests or Relationships	Nothing to disclose.

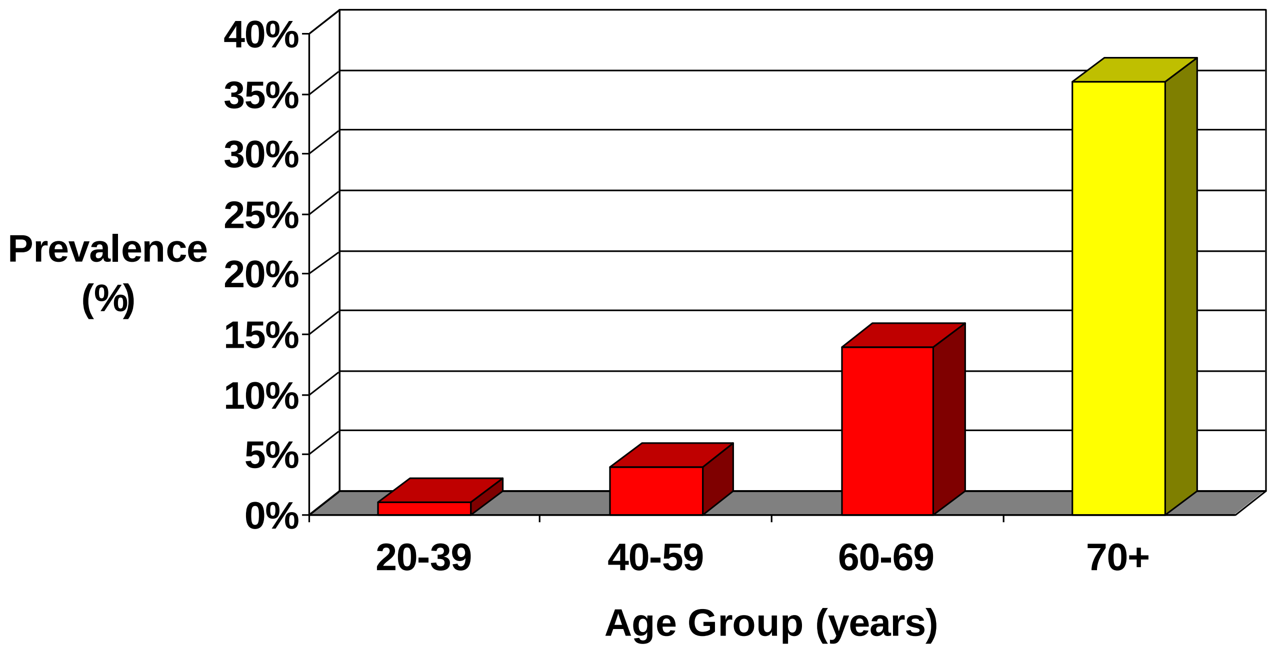
CKD prevalence is around ≈10%

11,1% (♂: 10,4% ♀: 11,8%) **in Mills KT, Kidney Int, 2015, p950**
Stage 3-5 : 5,3%
13,4% (♂: 12,8% ♀: 14,6%) **in Hill NR, PlosOne, 2016, e0158765**
Stage 3-5: 8,1%
10,4% (♂: 11,3% ♀: 9,5%) **in Mazhar F, Kidney Int, 2022, epub**
Stage 3-5: 5,4%

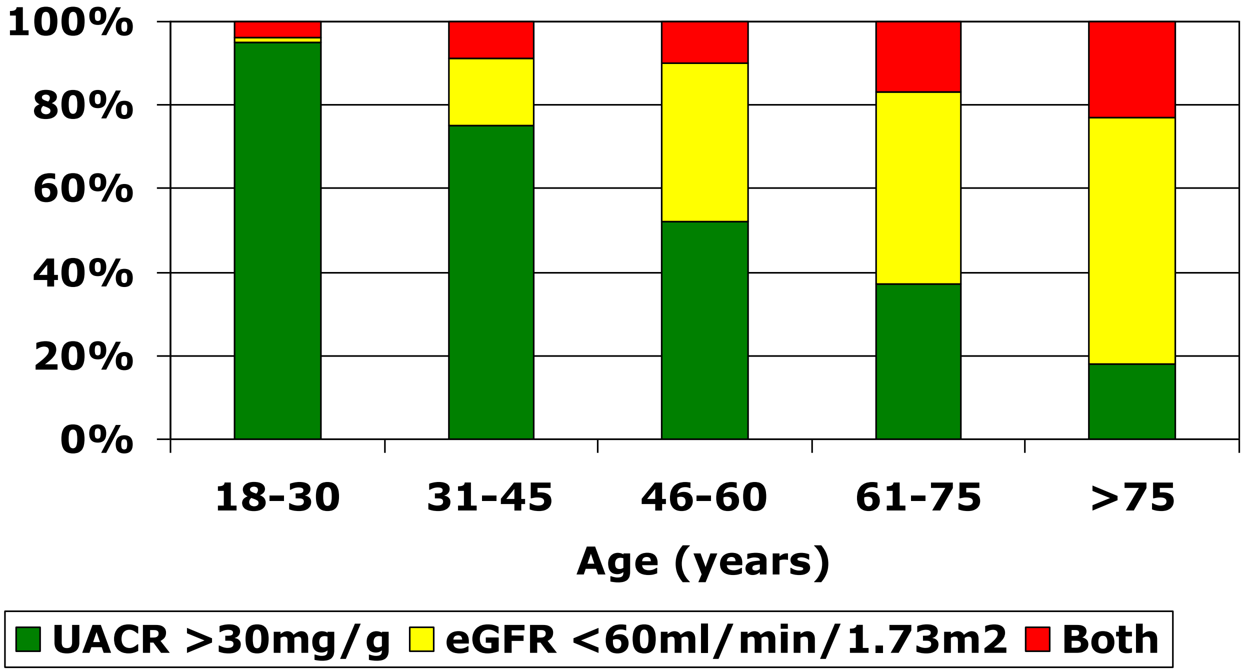
Stage 3-5= based on eGFR alone (<60 mL/min/173m^2)

Prevalence of stage 3 according to age in NHANES study

(and all other studies)

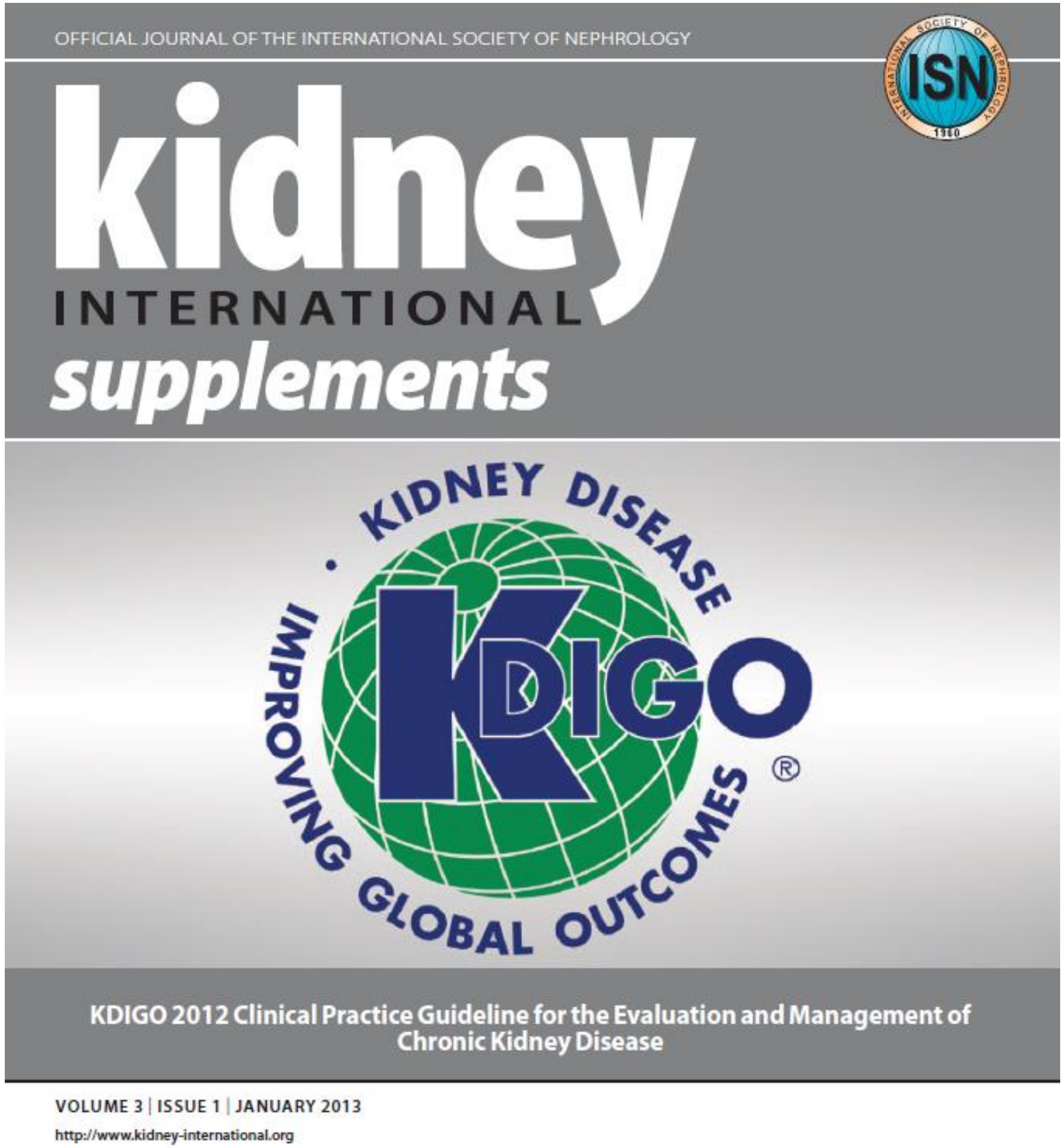


Characteristics of CKD populations



Courtesy by RJ Glassock, Adapted from James MT, et al Lancet 375:1296, 2010

International guidelines in Nephrology



GFR categories in CKD

GFR category	GFR (ml/min/1.73 m^2)	Terms
G1	≥90	Normal or high
G2	60-89	Mildly decreased*
G3a	45-59	Mildly to moderately decreased
G3b	30-44	Moderately to severely decreased
G4	15-29	Severely decreased
G5	<15	Kidney failure

Abbreviations: CKD, chronic kidney disease; GFR, glomerular filtration rate.
*Relative to young adult level
In the absence of evidence of kidney damage, neither GFR category G1 nor G2 fulfill the criteria for CKD.

In the absence of evidence of kidney damage, neither GFR category G1 nor G2 fulfill the criteria for CKD.

60 mL/min/1.73 m^2

Justification of this unique cut-off

- Simplicity
- Half of measured GFR in young adults but arbitrary (and maybe not correct)
- Because GFR < 60 mL/min/1.73 m^2 is associated with a higher mortality risk

How to define a disease?

- as a statistical departure from normality
- as a condition that is associated causally with an increased risk of a disease -defined event or death

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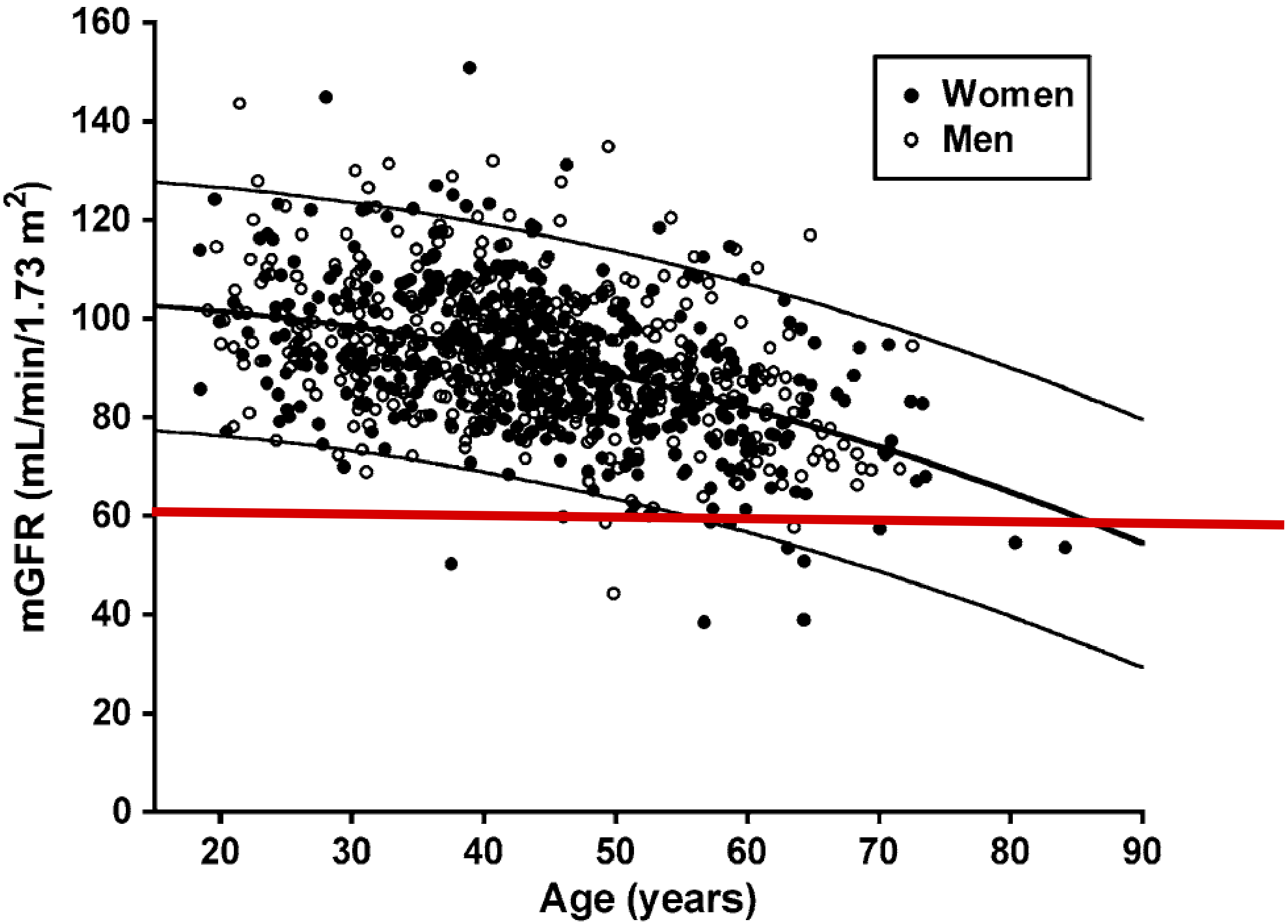

GFR measured by ^{51}Cr-EDTA in 904 potential living kidney donors

Blake GM et al, Int Urol Nephrol, 2013, p1445

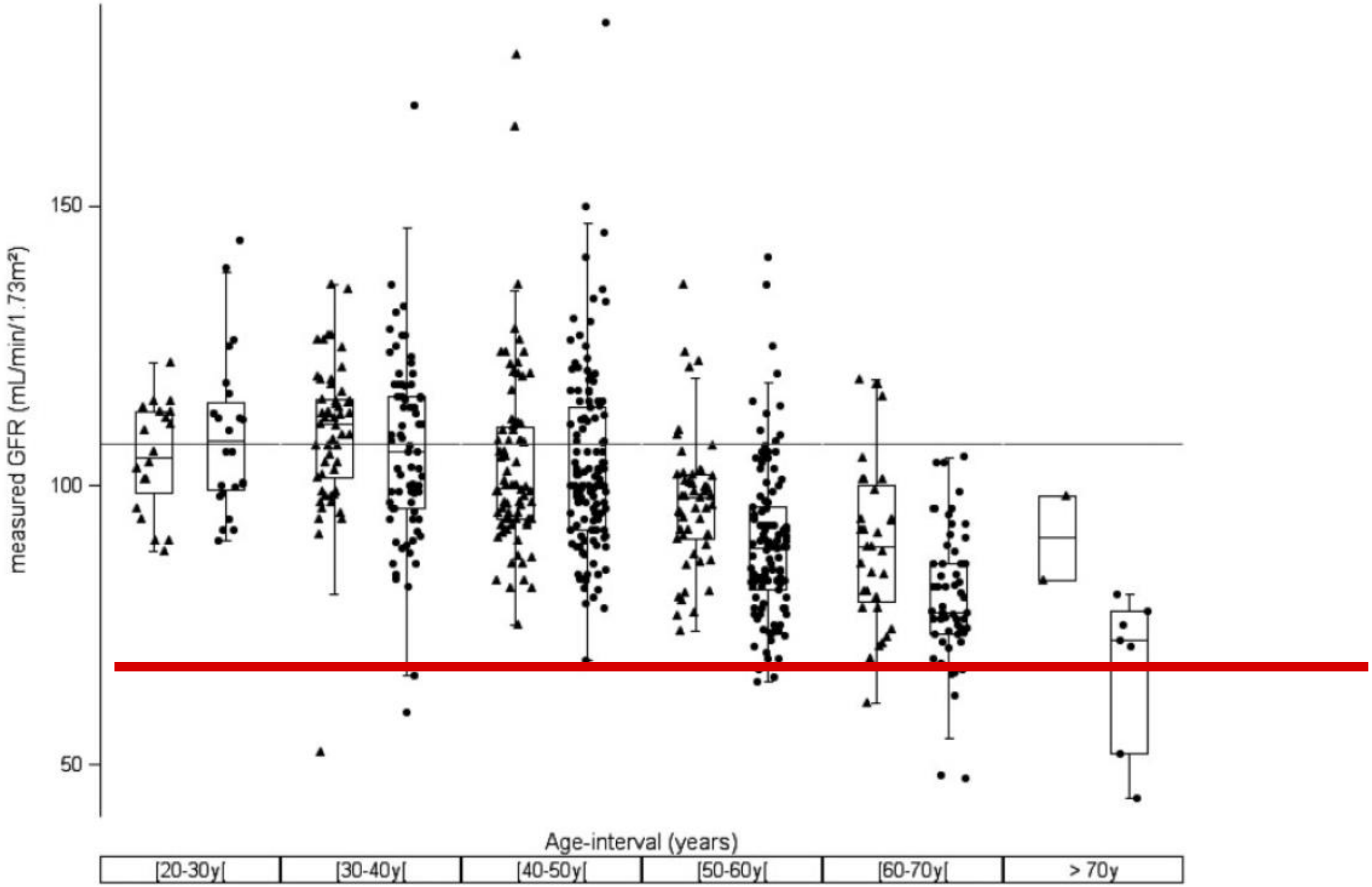

Fig. 1. Box plot for mGFR versus age decades for female (filled circles) and male (filled triangles) potential kidney donors ($n = 633$). A horizontal reference line is drawn at GFR = 107.3 mL/min/1.73 m^2.

GFR in 633 living kidney donors (Belgium, France)

Pottel H, Clin Kidney J, 2017, p545

Performance of creatinine- or cystatin C–based equations to estimate glomerular filtration rate in sub-Saharan African populations

Check for updates

see commentary on page 1017

Justine B. Bukabau[1,7], Eric Yayo[2,7], Appolinaire Gnionsahé[3], Dagui Monnet[2], Hans Pottel[4], Etienne Cavalier[5], Aliocha Nkodila[1], Jean Robert R. Makulo[1], Vieux M. Mokoli[1], François B. Lepira[1], Nazaire M. Nseka[1], Jean-Marie Krzesinski[6], Ernest K. Sumaili[1,7] and Pierre Delanaye[6,7]

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Kidney International (2019) **95,** 1181–1189; https://doi.org/10.1016/j.kint.2018.11.045

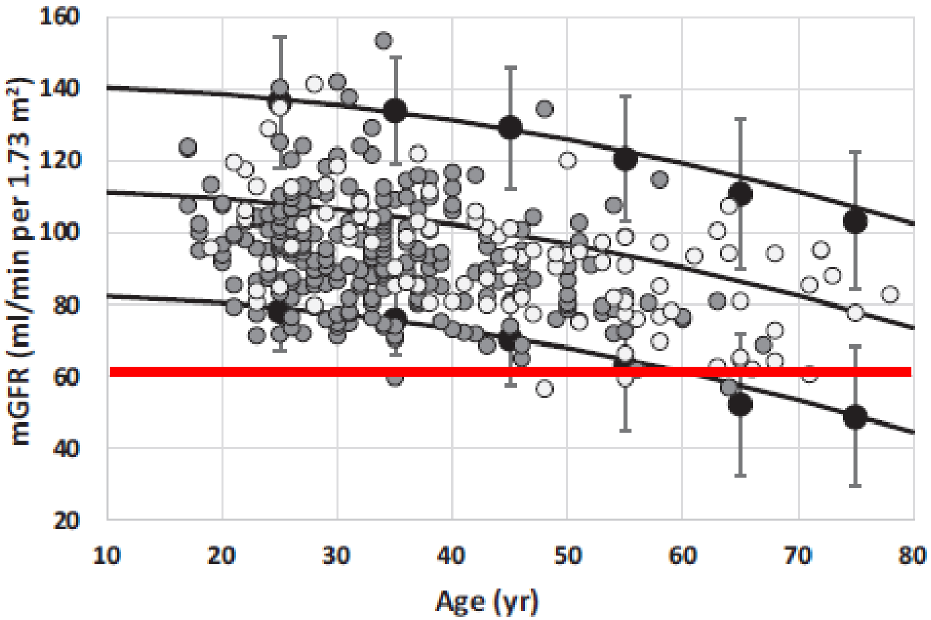

Figure 2 | Comparison of measured glomerular filtration rate (mGFR) values in healthy Whites, Congolese, and Ivorian subjects. Solid gray circles represent mGFR results and solid black lines represent 2.5th percentile (Pct), 50th Pct, and 97.5th Pct for mGFR in the Ivorian population (n = 237).[18] Solid black circles with error bars represent upper and lower reference limits obtained from the meta-analysis including 633 White potential living kidney donors.[26] Added white circles represent Congolese healthy subjects (n = 95).

RDC n=95

Côte d'Ivoire n=237

Iohexol

- Measured GFR is declining with aging
- …but few data over 65 years

DE GRUYTER Clin Chem Lab Med 2022; 60(3): 401–407

Pierre Delanaye*, François Gaillard, Jessica van der Weijden, Geir Mjøen, Ingela Ferhman-Ekholm, Laurence Dubourg, Natalie Ebert, Elke Schaeffner, Torbjörn Åkerfeldt, Karolien Goffin, Lionel Couzi, Cyril Garrouste, Lionel Rostaing, Marie Courbebaisse, Christophe Legendre, Maryvonne Hourmant, Nassim Kamar, Etienne Cavalier, Laurent Weekers, Antoine Bouquegneau, Martin H. de Borst, Christophe Mariat, Hans Pottel and Marco van Londen

Age-adapted percentiles of measured glomerular filtration in healthy individuals: extrapolation to living kidney donors over 65 years

Table 1: Comparison of the development, internal and validation cohorts.

Variable	Development cohort (n=1,983)	Internal validation cohort (n=147)	External validation cohort (n=329)	p-Value
Age, years	47.3 (±10.5)	68.8 (±2.9)[a]	71.4 (±6.4)[a,b]	<0.001
Gender, n (%) of women	1,212 (60.9)	91 (63.2)	187 (56.8)	0.47
Weight, kg	71.1 (±13.7)	70 (±13.8)	74.1 (±12.7)[a,b]	<0.001
Height, cm	168.1 (±8.9)	165.7 (±9.3)[a]	170 (±9.2)[a,b]	<0.001
BMI, kg/m^2	25.1 (±4)	25.3 (±3.7)	25.6 (±3.4)	0.12
BSA, m^2	1.80 (±0.20)	1.77 (±0.20)	1.85 (±0.19)[a,b]	<0.001
mGFR, mL/min/1.73 m^2	99.9 (±16.4)	86.4 (±14)[a]	82.7 (±15.5)[a,b]	<0.001
GFR tracer				<0.001
^{51}Cr-EDTA, n (%)	1,119 (56.3)	87 (60.4)	9 (2.7)	
Inulin, n (%)	294 (14.8)	47 (32.6)	3 (0.9)	
Iohexol, n (%)	576 (29.0)	10 (6.9)	133 (40.4)	
^{99m}Tc-DTPA, n (%)	0 (0.0)	0 (0.0)	34 (10.3)	
^{125}I-Iothalamate, n (%)	0 (0.0)	0 (0.0)	150 (45.6)	

[a]Significantly different from the development cohort. [b]Significantly different from the internal validation cohort. BMI, body mass index; BSA, body surface area; GFR, glomerular filtration rate; mGFR, measured GFR; Cr-EDTA, chrome-ethylenediaminetetra-acetic acid; Tc-DTPA, technetium diethylenetriaminepenta-acetic acid.

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Uppsala 12 LKD

Lyon 17 HP, 2LKD

Stockholm 51 HP

Norway 79 LKD

Berlin 18 HP

Groningen 150 LKD

Age, years	P5	P10	P50	P90	P95
18	82	88	106	125	130
20	82	88	106	125	130
25	82	88	106	125	130
30	82	88	106	125	130
35	82	88	106	125	130
40	82	88	106	125	130
40	82	88	106	125	130
42	81	86	104	123	128
45	78	83	102	120	126
50	74	79	97	116	121
55	69	74	93	112	117
60	65	70	89	107	112
65	60	66	84	103	108
70	**56**	**61**	**80**	**98**	**104**
75	**52**	**57**	**75**	**94**	**99**
80	**47**	**52**	**71**	**90**	**95**
85	**43**	**48**	**67**	**85**	**90**
90	**38**	**44**	**62**	**81**	**86**
95	**34**	**39**	**58**	**76**	**82**

All values in mL/min/1.73 m^2. P, percentile; mGFR, measured GFR.

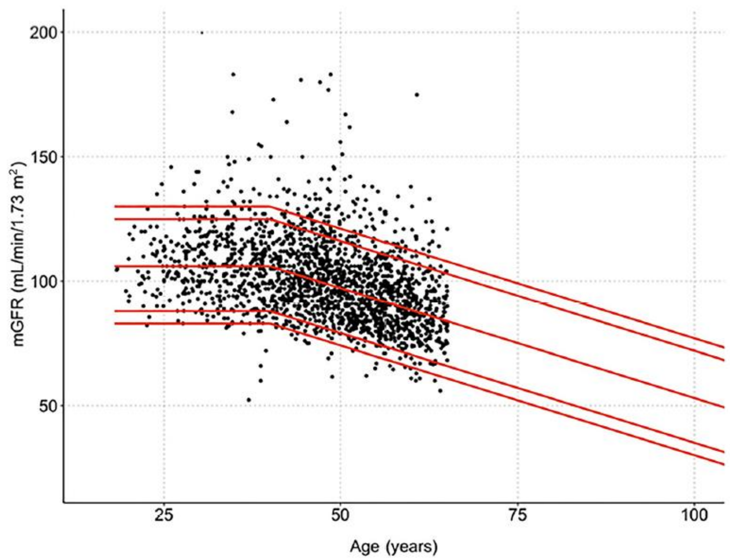

Figure 1: mGFR according to age in the development cohort (n=1,983).
Red lines are percentiles 5, 10, 50, 90 and 95, calculated from kidney donors younger than 65 years and extrapolated for ages >65 years.

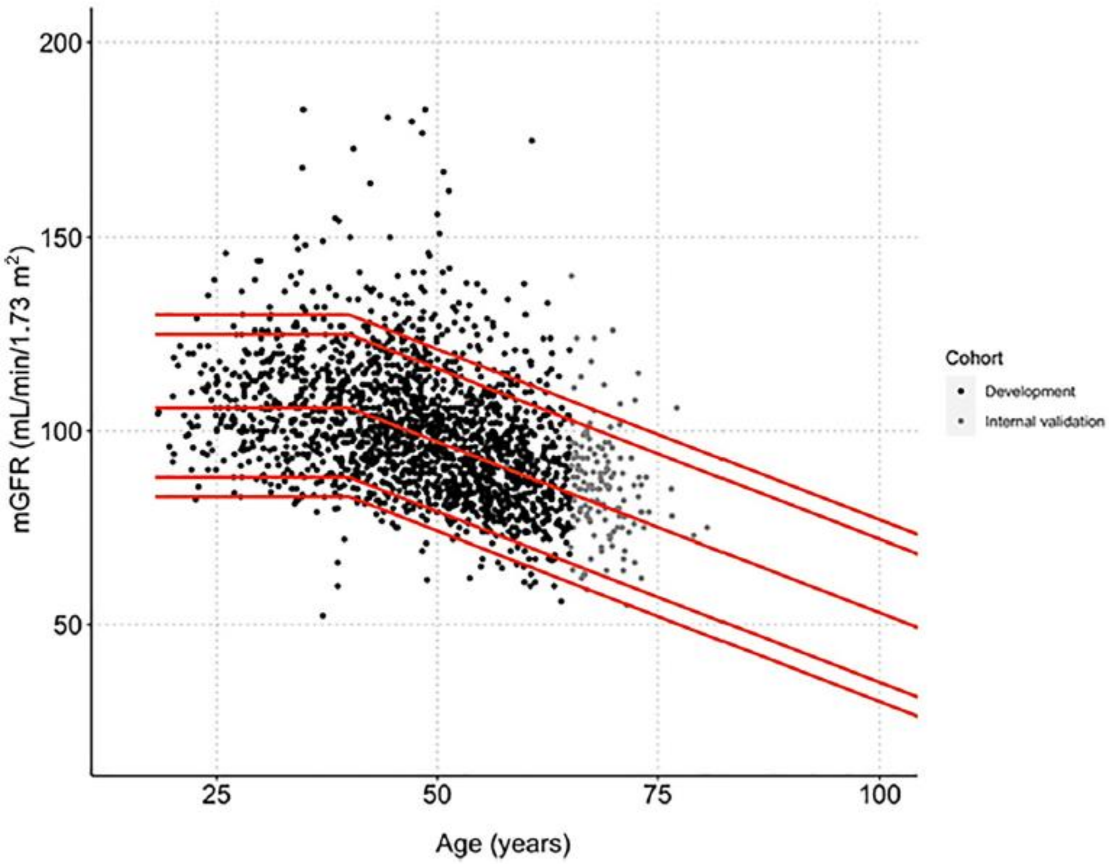

Figure 2: mGFR according to age in the development (dark dots) and internal validation cohort (n=147) (gray dots). Red lines are percentiles 5, 10, 50, 90 and 95, calculated from kidney donors younger than 65 years and extrapolated for ages >65 years.

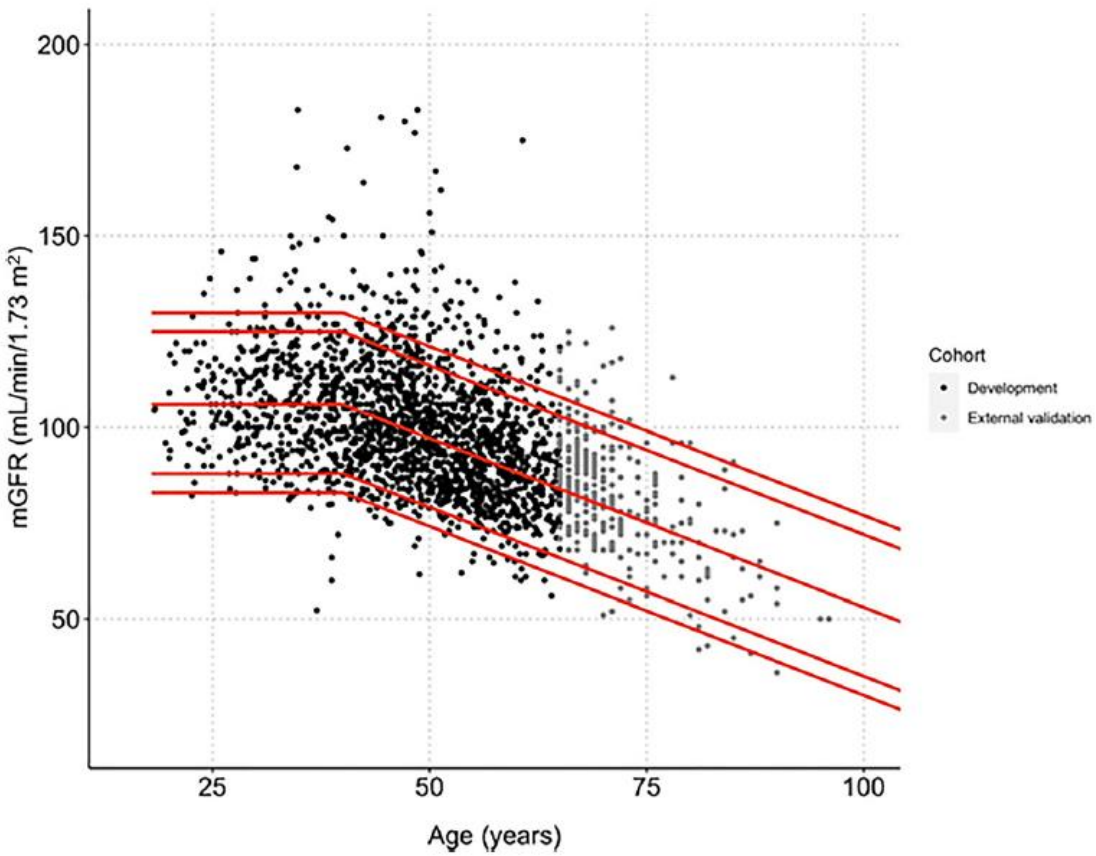

Figure 3: mGFR according to age in the development (dark dots) and external validation cohort (n=329) (gray dots). Red lines are percentiles 5, 10, 50, 90 and 95, calculated from kidney donors younger than 65 years and extrapolated for ages >65 years.

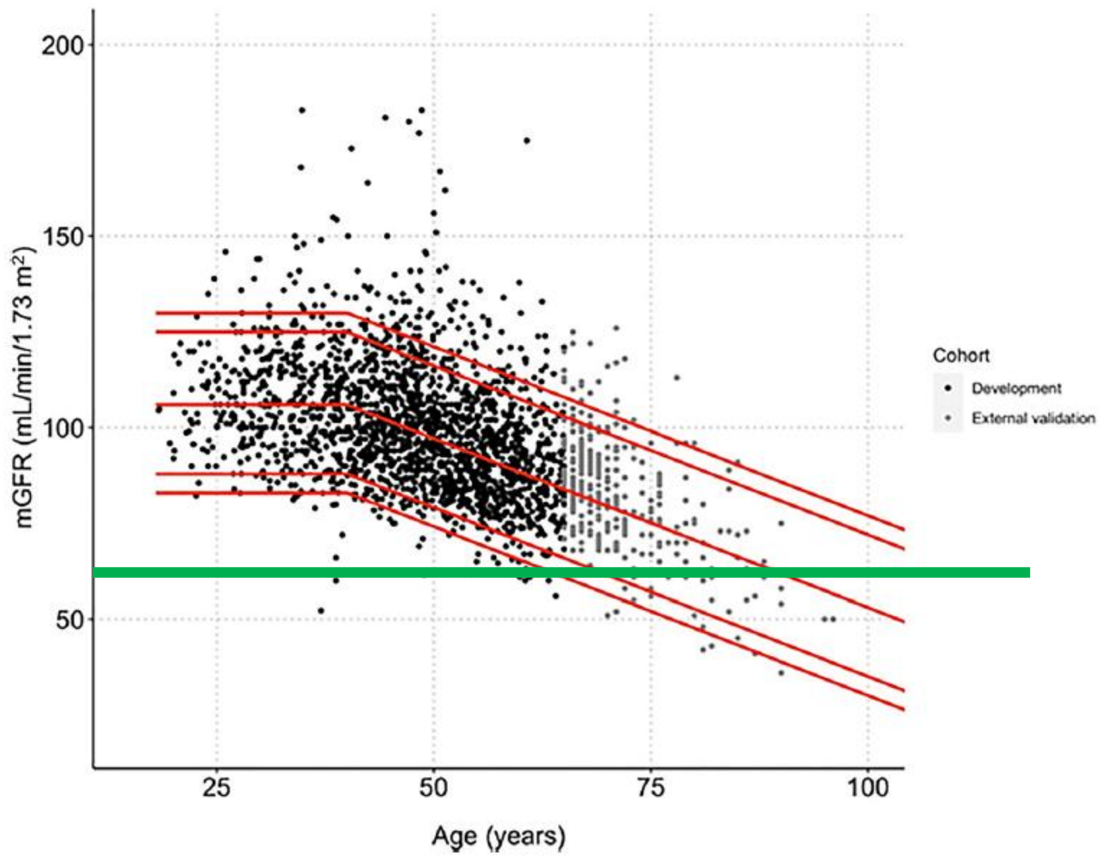

Figure 3: mGFR according to age in the development (dark dots) and external validation cohort (n=329) (gray dots). Red lines are percentiles 5, 10, 50, 90 and 95, calculated from kidney donors younger than 65 years and extrapolated for ages >65 years.

Age, years	P5	P10	P50	P90	P95
18	82	88	106	125	130
20	82	88	106	125	130
25	82	88	106	125	130
30	82	88	106	125	130
35	82	88	106	125	130
40	82	88	106	125	130
40	82	88	106	125	130
42	81	86	104	123	128
45	78	83	102	120	126
50	74	79	97	116	121
55	69	74	93	112	117
60	65	70	89	107	112
65	60	66	84	103	108
70	**56**	**61**	**80**	**98**	**104**
75	**52**	**57**	**75**	**94**	**99**
80	**47**	**52**	**71**	**90**	**95**
85	**43**	**48**	**67**	**85**	**90**
90	**38**	**44**	**62**	**81**	**86**
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All values in mL/min/1.73 m^2. P, percentile; mGFR, measured GFR.

CLINICAL EPIDEMIOLOGY www.jasn.org

GFR in Healthy Aging: an Individual Participant Data Meta-Analysis of Iohexol Clearance in European Population-Based Cohorts

Bjørn O. Eriksen,[1,2] Runolfur Palsson,[3,4] Natalie Ebert,[5] Toralf Melsom,[1,2] Markus van der Giet,[6] Vilmundur Gudnason,[4,7] Olafur S. Indridasson,[3] Lesley A. Inker,[8] Trond G. Jenssen,[1,9] Andrew S. Levey,[8] Marit D. Solbu,[1,2] Hocine Tighiouart,[10,11] and Elke Schaeffner[5]

Due to the number of contributing authors, the affiliations are listed at the end of this article.

J Am Soc Nephrol. 2020 Jul;31(7):1602-1615.

mGFR Between 50 and 97 years old

Tromso, Berlin, Reykjavik

HEALTHY: n=935 (22%)

Table 1. Characteristics of the population-based cohorts

Characteristic	RENIS-T6[a]	RENIS-FU[a]	BIS	AGES-Kidney
Number of participants, *n* (%)	1622 (100.0)	1324 (100.0)	547 (100.0)	716 (100.0)
Age, yr (SD)	58.1 (3.8)	63.6 (4.0)	78.4 (6.2)	80.3 (4.1)
Male sex, *n* (%)	797 (49.1)	657 (49.6)	311 (56.9)	317 (44.3)
Body weight, kg (SD)	79.7 (14.4)	79.4 (14.3)	77.3 (14.0)	77.1 (14.1)
Height, cm (SD)	170.6 (8.7)	170.6 (8.7)	166.2 (8.5)	167.7 (9.4)
Body mass index, kg/m^2 (SD)	27.3 (4.0)	27.2 (4.1)	27.9 (4.3)	27.4 (4.3)
Body surface area, m^2 (SD)	1.9 (0.2)	1.9 (0.2)	1.9 (0.2)	1.9 (0.2)
Cardiovascular disease, *n* (%)				
Myocardial infarction	1 (0.1)	18 (1.4)	83 (15.2)	89 (12.4)
Myocardial revascularization	5 (0.3)	26 (2.0)	93 (17.0)	113 (15.8)
Angina pectoris	2 (0.1)	12 (0.9)	56 (10.2)	60 (8.4)
Stroke	3 (0.2)	24 (1.8)	42 (7.7)	53 (7.4)
Diabetes, *n* (%)	19 (1.2)	42 (3.2)	136 (24.9)	81 (11.3)
Cancer, *n* (%)	76 (4.7)	120 (9.1)	123 (22.5)	134 (18.7)
Hypertension, *n* (%)[b]	692 (42.7)	693 (52.3)	503 (92.0)	623 (87.0)
Systolic BP, mm Hg (SD)	129.7 (17.6)	130.7 (17.0)	144.9 (21.5)	142.3 (20.3)
Diastolic BP, mm Hg (SD)	83.4 (9.8)	81.9 (9.3)	82.3 (13.0)	69.6 (10.7)
Antihypertensive medication, *n* (%)	298 (18.4)	420 (31.7)	425 (77.7)	524 (73.2)
Digoxin or digitoxin, *n* (%)	1 (0.1)	6 (0.5)	18 (3.3)	24 (3.4)
Lipid-lowering medication, *n* (%)	106 (6.5)	232 (17.5)	202 (36.9)	287 (40.1)
Antidiabetic medication, *n* (%)	0 (0.0)	11 (0.8)	99 (18.1)	44 (6.1)
Smoking, *n* (%)				
Never	503 (31.0)	432 (32.6)	263 (48.1)	295 (41.2)
Current	344 (21.2)	177 (13.4)	32 (5.9)	42 (5.9)
Previous	775 (47.8)	715 (54.0)	252 (46.1)	379 (52.9)

Table 2. GFR (ml/min per 1.73 m^2) according to health status of participants in the population-based cohorts

Study	Number of Participants		Median		2.5th Percentile		97.5th Percentile	
	Unhealthy	Healthy[a]	Unhealthy	Healthy[a]	Unhealthy	Healthy[a]	Unhealthy	Healthy[a]
RENIS-T6[b]	1109	513	94.2	93.1	65.6	63.0	123.1	118.9
RENIS-FU[b]	964	360	89.2	90.1	57.5	66.5	117.5	115.3
BIS	529	18	60.4	69.8[c]	29.7	44.2	88.7	96.2
AGES-Kidney	672	44	62.5	72.4[c]	26.2	42.4	90.5	98.4
Total	3274	935	82.6	90.8	34.0	59.7	117.8	118.0

[a]Healthy was defined as no cardiovascular disease, cancer, diabetes, hypertension, smoking, lipid-lowering medication, or digoxin, as well as body mass index <30 kg/m^2 and urinary ACR <30 mg/g.
[b]RENIS-T6 and RENIS-FU are the baseline and follow-up examinations of the same cohort.
[c]*P*<0.05 for difference between unhealthy and healthy category in the BIS and AGES-Kidney cohorts.

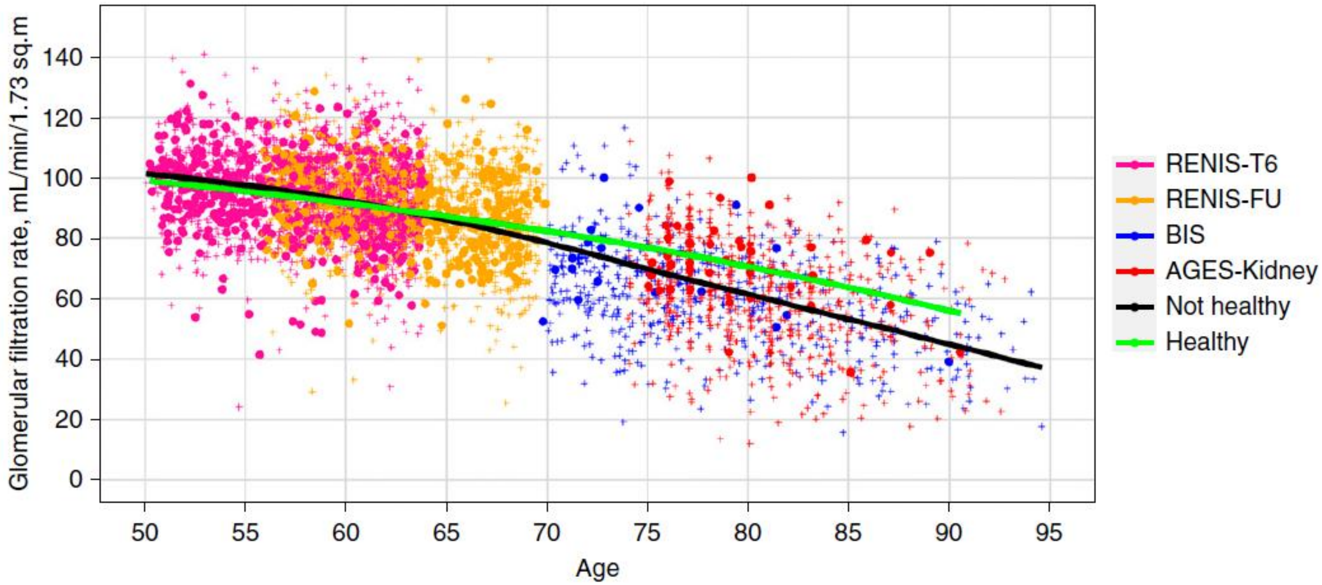
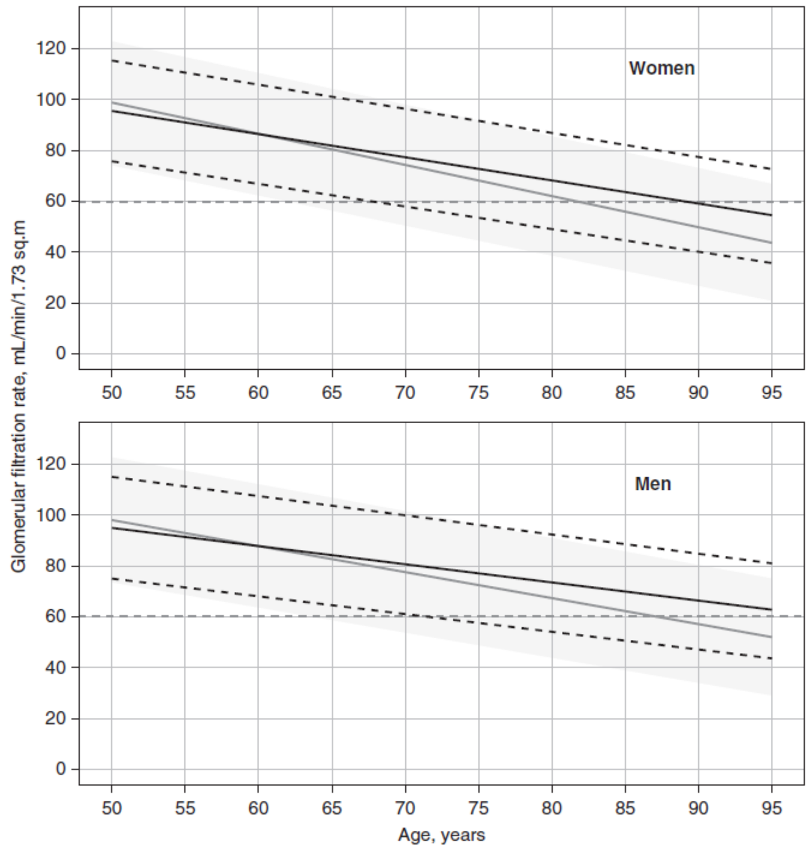


Figure 2. Unadjusted GFR according to cohort and health status. Body surface area–indexed GFR measured as plasma iohexol clearance and plotted against age in the RENIS, BIS, and AGES-Kidney cohorts (n=4209). The marker colors indicate cohort membership. Filled circles indicate measurements in persons who were healthy and crosses in persons who were unhealthy. Measurements for both the baseline (RENIS-T6) and the follow-up examinations (RENIS-FU) of the same persons in the RENIS cohort are shown. The red and green curves represent unadjusted locally estimated scatterplot smoothing fits to measurements in people who were unhealthy and healthy, respectively.



-0,92 mL/min/1.73m²/y

-0,72 mL/min/1.73m²/y

Figure 3. GFR according to sex and health status. Predicted median (bold black line) and 2.5th and 97.5th percentiles (dashed black lines) as a function of age for healthy women (upper panel) and men (lower panel). The predicted median (gray line) and 95% inter-percentile intervals (dark gray band) are shown for persons classified as unhealthy for comparison. The gray dashed line indicates the 60 ml/min per 1.73 m^2 level.

CLINICAL EPIDEMIOLOGY www.jasn.org

Sex Differences in Age-Related Loss of Kidney Function

Toralf Melsom,[1,2] Jon Viljar Norvik,[1,2] Inger Therese Enoksen,[2] Vidar Stefansson,[2] Ulla Dorte Mathisen,[1] Ole Martin Fuskevåg,[3] Trond G. Jenssen,[2,4] Marit D. Solbu,[1,2] and Bjørn O. Eriksen[1,2]

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[4] Department of Transplant Medicine, Oslo University Hospital and University of Oslo, Oslo, Norway

- Measured GFR is declining with aging
- …but few data over 65 years
- Most data are cross-sectional

A prospective controlled study of metabolic and physiologic effects of kidney donation suggests that donors retain stable kidney function over the first nine years

Check for updates

see commentary on page 57

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Kidney International (2020) **98,** 168–175;

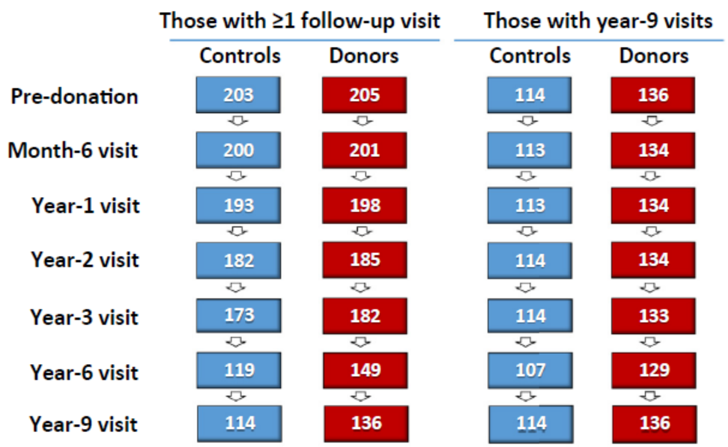


Figure 1 | Number of study visits. Shown are the numbers of visits for those completing a pre-donation baseline visit plus at least 1 post-donation visits (columns 2 and 3), and visits for those completing a pre-donation visit and a follow-up visit at 9 years (columns 4 and 5).

8 US centers

GFR measured by iohexol plasma clearance

Before donation and after 6 months, 1, 2, 3, 6 et 9 years

CONTROL GROUP

Table 1 | Demographics of study participants compared to all US donors[a]

Baseline pre-donation characteristic	Baseline in those with any follow-up visits		Baseline in those with year-9 study visits		
	Controls (203)	Donors (205)	Controls (114)	Donors (136)	US donors (31,114)[b]
Biologically related to recipient	21.2	51.5[c]	15.8	47.7[c]	58.3
Male sex	35.0	32.2	33.3	36.0	39.8
White	95.1	94.6	93.9	94.1	69.7
Age (yr)					
18–34	30.5	27.8	31.6	27.2	30.9
35–49	36.0	40.5	33.3	39.0	43.8
50–64	31.0	29.3	30.7	32.4	23.9
≥65	2.5	2.4	4.4	1.5	1.5
Body mass index[d] (kg/m^2)					
<25	42.1	36.6	45.1	36.6[e]	37.3
25–29	35.2	41.1	36.3	41.0	40.6
30–34	15.4	18.3	11.5	20.2	18.3
35–49	7.4	4.0	7.1	2.2	3.5
≥50	0.0	0.0	0.0	0.0	0.3

[a]Values are percentages.
[b]All living donors in the US donating 2006–2010.
[c]$P < 0.001$ for study donors vs. study controls by χ^2.
[d]Body mass index was not available for 0.5% (1) controls and 1.5% (2) donors with any follow-up visits, 0.9% (1) controls and 1.5% (2) donors with year-9 follow-up visits, and 27.8% (8,650) of US donors.
[e]$P = 0.057$ for study donors vs. study controls by χ^2.

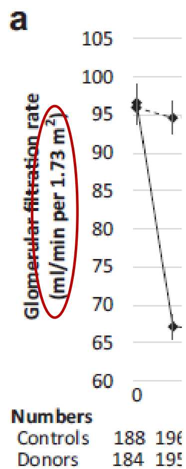


Figure 3 | Clinical correlates of kidney donation. (**a**) Shown are glomerular filtration rate means and 95% confidence intervals, $P < 0.0001$ donors versus controls in the follow-up period. (**b**) Shown are urine albumin-to-creatinine ratio medians and quartiles. (Continued)

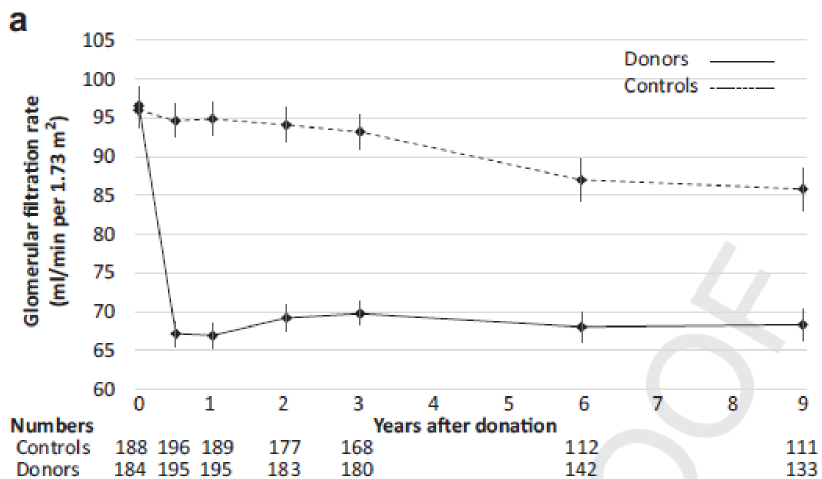


Figure 3 | Clinical correlates of kidney donation. (**a**) Shown are glomerular filtration rate means and 95% confidence intervals, $P < 0.0001$ donors versus controls in the follow-up period. (**b**) Shown are urine albumin-to-creatinine ratio medians and quartiles. (Continued)

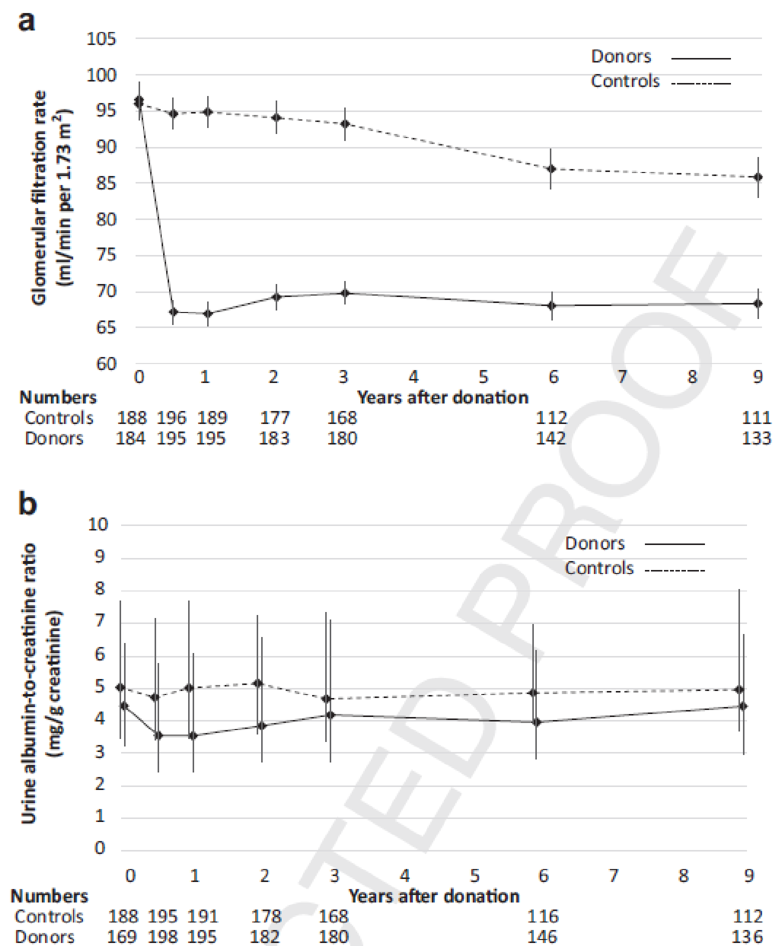


Figure 3 | Clinical correlates of kidney donation. (**a**) Shown are glomerular filtration rate means and 95% confidence intervals, $P < 0.0001$ donors versus controls in the follow-up period. (**b**) Shown are urine albumin-to-creatinine ratio medians and quartiles. (Continued)

Table 2 | Linear slopes of glomerular filtration rate[a]

Interval	Controls, mean (95% CI)	Donors, mean (95% CI)	*P* value
6 mo–9 yr	−1.26 (−1.52 to −1.00); $n = 113$	0.02 (−0.16 to 0.20); $n = 133$	<0.0001
6 mo–3 yr	−0.46 (−1.05 to 0.14); $n = 169$	0.94 (0.49 to 1.39); $n = 179$	0.0003
3–9 yr	−1.48 (−1.93 to −1.02); $n = 113$	−0.29 (−0.56 to −0.01); $n = 133$	<0.0001

CI, confidence interval.

[a]Glomerular filtration rate was measured by iohexol clearances with slopes determined by least-squares linear regression. Participants not completing year-9 visits were included. *P* values were generated by *t* tests (controls vs. donors). Units are ml/min per 1.73 m^2 per year.

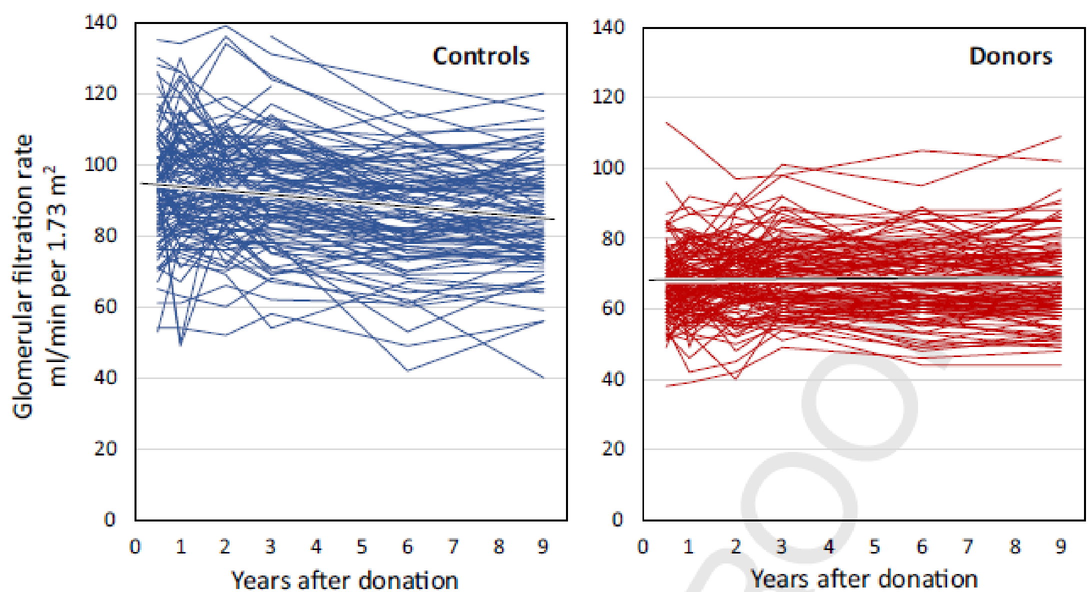


Figure 2 | Glomerular filtration rate in controls and donors after donation. Only participants that completed year-9 follow-up visits are included. Blue lines are composite trend lines. For actual values, see Supplementary Table S3.

- Measured GFR is declining with aging
- …but few data over 65 years
- Most data are cross-sectional
- Still, there are reasons to think that some healthy subjects over 65 years have measured GFR below 60 mL/min/1.73m^2

=> What about estimating GFR?

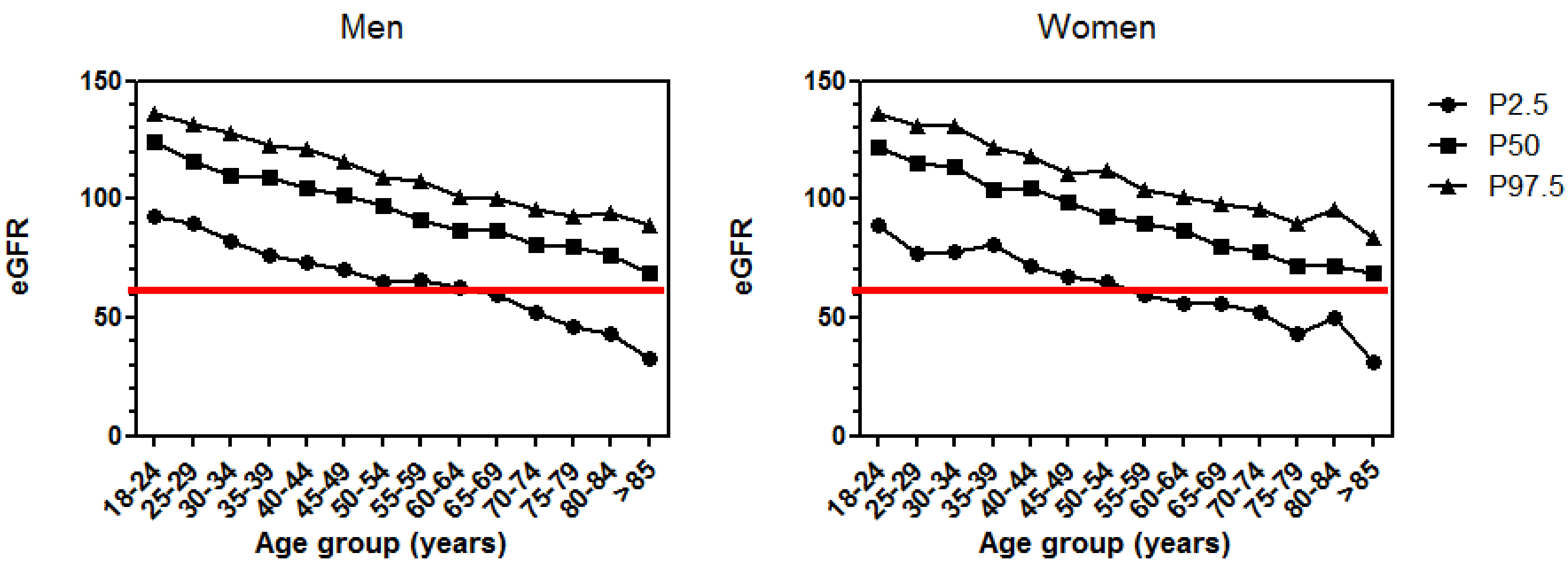
- Healthy population in the Netherlands
- CKD-EPI equation to estimate GFR
- No diabetes, no hypertension, no specific therapy
- 1663 men 2073 women

Nephrol Dial Transplant (2011) 26: 3176–3181
doi: 10.1093/ndt/gfr003
Advance Access publication 16 February 2011

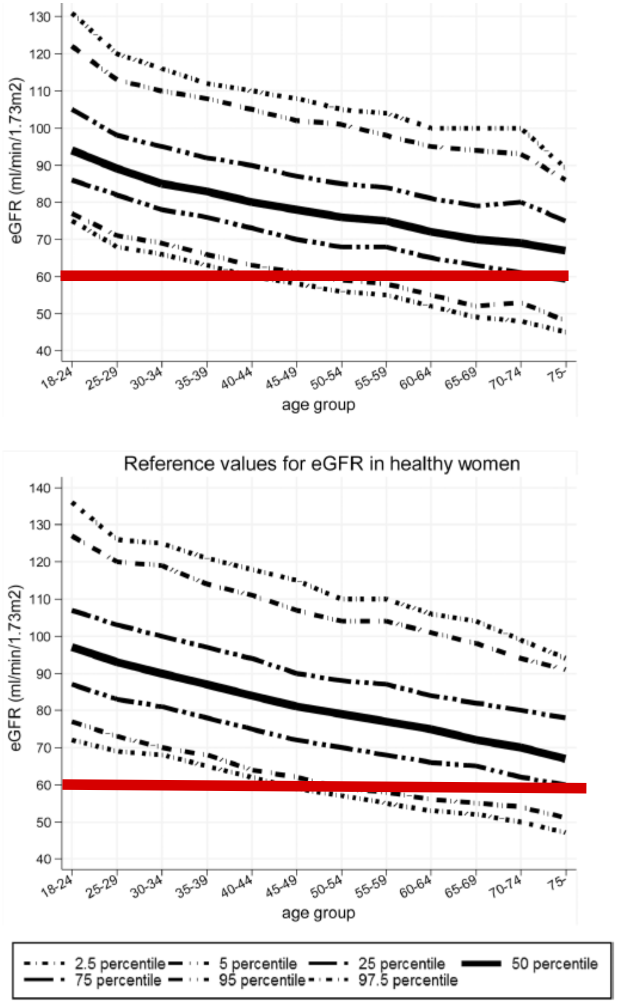
Introduction of the CKD-EPI equation to estimate glomerular filtration rate in a Caucasian population

Jan A.J.G. van den Brand[1], Gerben A.J. van Boekel[1], Hans L. Willems[2], Lambertus A.L.M. Kiemeney[3], Martin den Heijer[3,4] and Jack F.M. Wetzels[1]

[1]Department of Nephrology, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands, [2]Department of Laboratory Medicine, Radboud University Medical Centre, Nijmegen, The Netherlands, [3]Department of Epidemiology, Biostatistics and Health Technology Assessment, Radboud University Medical Centre, Nijmegen, The Netherlands and [4]Department of Endocrinology, Radboud University Medical Centre, Nijmegen, The Netherlands



Men
Women
150
100
50
0
eGFR
18-24
25-29
30-34
35-39
40-44
45-49
50-54
55-59
60-64
65-69
70-74
75-79
80-84
>85
Age group (years)
P2.5
P50
P97.5



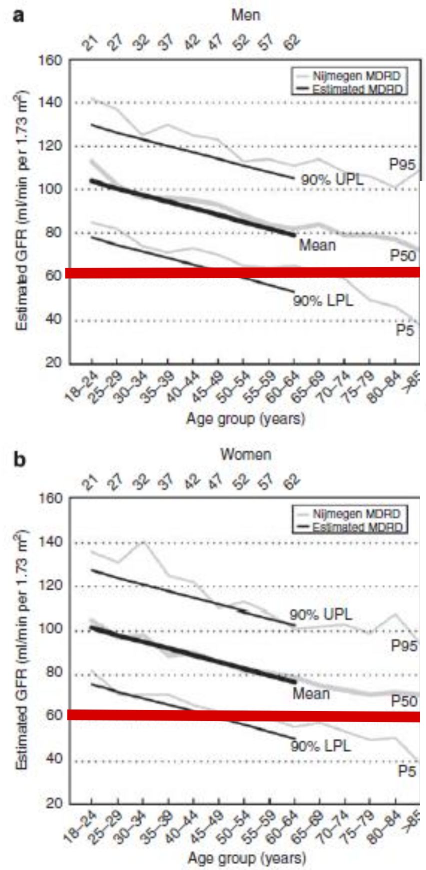
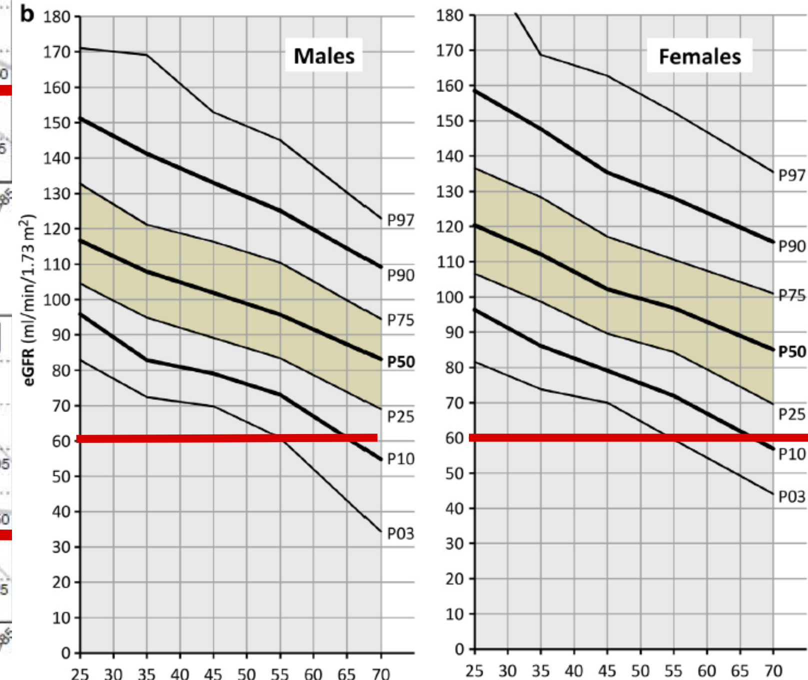


Figure 5 | Comparison of estimated GFR in two different cohorts. Mean, 5th, and 95th percentiles for expected eGFR by the re-expressed MDRD equation in living kidney donors (black lines) and eGFR by the re-expressed MDRD equation in subjects participating in the Nijmegen study[28] (gray lines) among different age groups for (**a**) men and (**b**) women.



The same in Japan…

The same in USA…

The same in Morocco…

Baba M, PlosOne, 2015

Poggio ED, Kidney Int, 2009

Benghanem Gharbi M, Kidney Int, 2016

- Concordant data worldwide
- eGFR is declining with aging
- A significant part of healthy subjects over 65 years have $eGFR<60 mL/min/1.73m^2$

How to define a disease?

- as a statistical departure from normality and it must be age-calibrated because of the physiology of human senescence.

- as a condition that is associated causally with an increased risk of a disease -defined event or death

Associations of kidney disease measures with mortality and end-stage renal disease in individuals with and without diabetes: a meta-analysis

Caroline S Fox, Kunihiro Matsushita, Mark Woodward, Henk J G Bilo, John Chalmers, Hiddo J Lambers Heerspink, Brian J Lee, Robert M Perkins, Peter Rossing, Toshimi Sairenchi, Marcello Tonelli, Joseph A Vassalotti, Kazumasa Yamagishi, Josef Coresh, Paul E de Jong, Chi-Pang Wen, Robert G Nelson, for the Chronic Kidney Disease Prognosis Consortium

Associations of kidney disease measures with mortality and end-stage renal disease in individuals with and without hypertension: a meta-analysis

Bakhtawar K Mahmoodi, Kunihiro Matsushita, Mark Woodward, Peter J Blankestijn, Massimo Cirillo, Takayoshi Ohkubo, Peter Rossing, Mark J Sarnak, Bénédicte Stengel, Kazumasa Yamagishi, Kentaro Yamashita, Luxia Zhang, Josef Coresh, Paul E de Jong, Brad C Astor, for the Chronic Kidney Disease Prognosis Consortium

ONLINE FIRST

Age and Association of Kidney Measures With Mortality and End-stage Renal Disease

BMJ 2013;346:f324 doi: 10.1136/bmj.f324 (Published 29 January 2013) Page 1 of 14

RESEARCH

Associations of estimated glomerular filtration rate and albuminuria with mortality and renal failure by sex: a meta-analysis

Measures of chronic kidney disease and risk of incident peripheral artery disease: a collaborative meta-analysis of individual participant data

*Kunihiro Matsushita, Shoshana H Ballew, Josef Coresh, Hisatomi Arima, Johan Ärnlöv, Massimo Cirillo, Natalie Ebert, Jade S Hiramoto, Heejin Kimm, Michael G Shlipak, Frank L J Visseren, Ron T Gansevoort, Csaba P Kovesdy, Varda Shalev, Mark Woodward, Florian Kronenberg, for the Chronic Kidney Disease Prognosis Consortium**

Estimated glomerular filtration rate and albuminuria for prediction of cardiovascular outcomes: a collaborative meta-analysis of individual participant data

Kunihiro Matsushita, Josef Coresh, Yingying Sang, John Chalmers, Caroline Fox, Eliseo Guallar, Tazeen Jafar, Simerjot K Jassal, Gijs W D Landman, Paul Muntner, Paul Roderick, Toshimi Sairenchi, Ben Schöttker, Anoop Shankar, Michael Shlipak, Marcello Tonelli, Jonathan Townend, Arjan van Zuilen, Kazumasa Yamagishi, Kentaro Yamashita, Ron Gansevoort, Mark Sarnak, David G Warnock, Mark Woodward, Johan Ärnlöv,

http://www.kidney-international.org

clinical investigation

Relative risks of chronic kidney disease for mortality and end-stage renal disease across races are similar

Chi Pang Wen[1,2], Kunihiro Matsushita[3], Josef Coresh[3], Kunitoshi Iseki[4], Muhammad Islam[5], Ronit Katz[6], William McClellan[7], Carmen A. Peralta[8], HaiYan Wang[9], Dick de Zeeuw[10], Brad C. Astor[11,12], Ron T. Gansevoort[13], Andrew S. Levey[14], Adeera Levin[15] and for the Chronic Kidney Disease Prognosis Consortium

Lower estimated glomerular filtration rate and higher albuminuria are associated with all-cause and cardiovascular mortality. A collaborative meta-analysis of high-risk population cohorts

Marije van der Velde[1], Kunihiro Matsushita[2], Josef Coresh[2], Brad C. Astor[2], Mark Woodward[3], Andrew S. Levey[4], Paul E. de Jong[1], Ron T. Gansevoort[1] and the Chronic Kidney Disease Prognosis Consortium

Lower estimated GFR and higher albuminuria are associated with adverse kidney outcomes. A collaborative meta-analysis of general and high-risk population cohorts

Ron T. Gansevoort[1], Kunihiro Matsushita[2], Marije van der Velde[1], Brad C. Astor[2], Mark Woodward[3], Andrew S. Levey[4], Paul E. de Jong[1], Josef Coresh[2] and the Chronic Kidney Disease Prognosis Consortium

Lower estimated glomerular filtration rate and higher albuminuria are associated with mortality and end-stage renal disease. A collaborative meta-analysis of kidney disease population cohorts

Brad C. Astor[1], Kunihiro Matsushita[1], Ron T. Gansevoort[2], Marije van der Velde[2], Mark Woodward[3], Andrew S. Levey[4], Paul E. de Jong[2], Josef Coresh[1] and the Chronic Kidney Disease Prognosis Consortium

Association of estimated glomerular filtration rate and albuminuria with all-cause and cardiovascular mortality in general population cohorts: a collaborative meta-analysis

Chronic Kidney Disease Prognosis Consortium*

Lancet 2010; 375: 2073–81

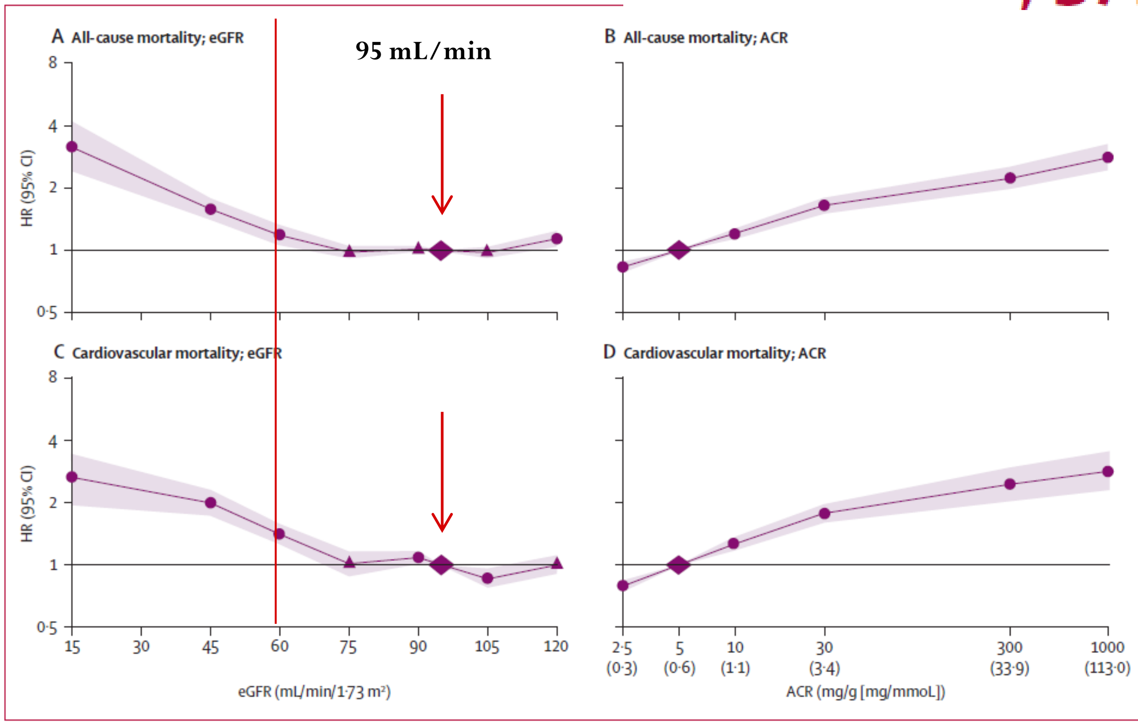


Figure 2: Hazard ratios and 95% CIs for all-cause and cardiovascular mortality according to spline estimated glomerular filtration rate (eGFR) and albumin-to-creatinine ratio (ACR)
Hazard ratios and 95% CIs (shaded areas) according to eGFR (A, C) and ACR (B, D) adjusted for each other, age, sex, ethnic origin, history of cardiovascular disease, systolic blood pressure, diabetes, smoking, and total cholesterol. The reference (diamond) was eGFR 95 mL/min/1·73 m² and ACR 5 mg/g (0·6 mg/mmol), respectively. Circles represent statistically significant and triangles represent not significant. ACR plotted in mg/g. To convert ACR in mg/g to mg/mmol multiply by 0·113. Approximate conversions to mg/mmol are shown in parentheses.

- 105,872 subjects from 14 studies with ACR
- 1,128,310 subjects from 7 studies with dipstick

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/ 1.73m²) 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			

Figure 9 | Prognosis of CKD by GFR and albuminuria category. Green, low risk (if no other markers of kidney disease, no CKD); Yellow, moderately increased risk; Orange, high risk; Red, very high risk. CKD, chronic kidney disease; GFR, glomerular filtration rate; KDIGO, Kidney Disease: Improving Global Outcomes. Modified with permission from Macmillan Publishers Ltd: *Kidney International*. Levey AS, de Jong PE, Coresh J, et al.[30] The definition, classification, and prognosis of chronic kidney disease: a KDIGO controversies conference report. Kidney Int 2011; 80: 17-28; accessed http://www.nature.com/ki/journal/v80/n1/full/ki2010483a.html

There is a discrepancy between

descriptive data that demonstrate a decline in « normal GFR values » with aging
=> argument for an age-calibrated threshold

predictive data that confirm the choice of the fixed threshold for CKD definition

=> argument for a fixed threshold (60 mL/min)

- A single absolute threshold of eGFR overestimates CK**D** in the healthy elderly

But…

- What about the prognostic argument?
- Do we have an alternative?
- Is it relevant from an epidemiological point of view?

So...

- A single absolute threshold of eGFR overestimates CK**D** in the healthy elderly

But…

- What about the prognostic argument?
- Do we have an alternative?
- Is it relevant from an epidemiological point of view?

Back to the « prognostic » argument

ORIGINAL CONTRIBUTION

ONLINE FIRST

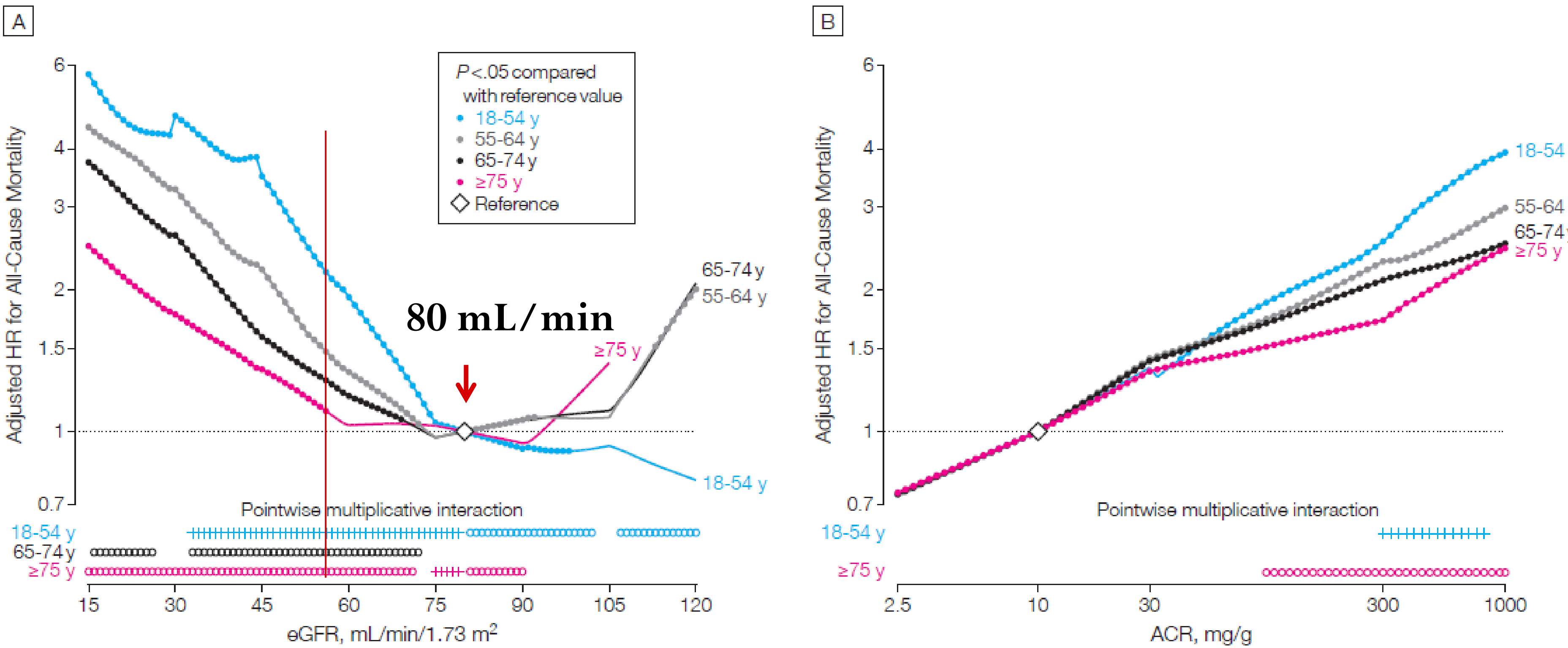
Age and Association of Kidney Measures With Mortality and End-stage Renal Disease

Stein I. Hallan, MD, PhD
Kunihiro Matsushita, MD, PhD
Yingying Sang, MS
Bakhtawar K. Mahmoodi, MD, PhD
Corri Black, MBChB, MSc, FFPH
Areef Ishani, MD, MS
Nanne Kleefstra, MD, PhD
David Naimark, MD, MSc, FRCP(C)
Paul Roderick, MD, FRCP
Marcello Tonelli, MD, SM
Jack F. M. Wetzels, MD, PhD
Brad C. Astor, PhD, MPH
Ron T. Gansevoort, MD, PhD
Adeera Levin, MD
Chi-Pang Wen, MD, MPH, DrPH
Josef Coresh, MD, PhD
for the Chronic Kidney Disease Prognosis Consortium

JAMA. 2012;308(22):2349-2360

N=2,051,044
33 general or high risk cohorts
13 CKD cohorts
Mean follow-up: 5.3 years

Figure 1. Adjusted Hazard Ratios (HRs) for All-Cause Mortality and Mean Mortality Rates According to eGFR and ACR Within Each Age Category



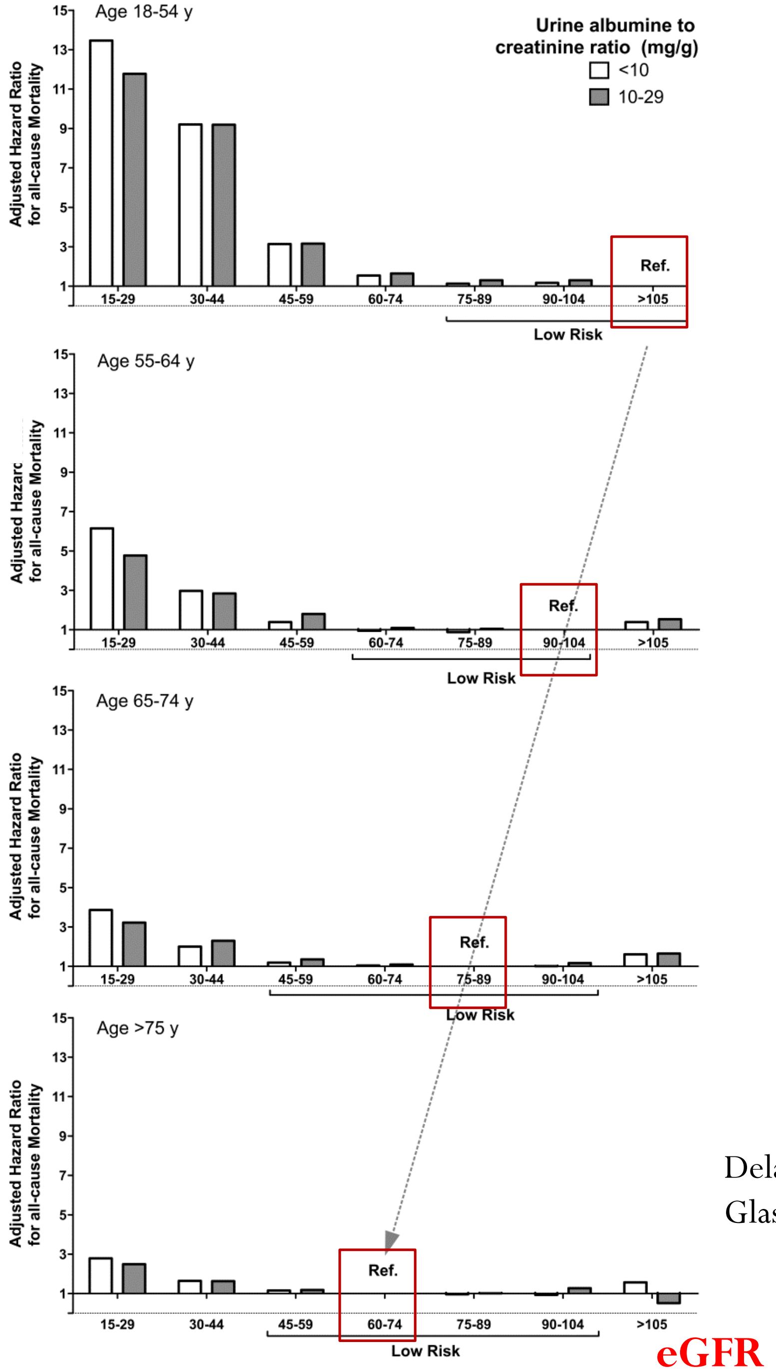
- The same GFR reference group is considered for all age
- Reference group can however be changed
- In each age category, we propose to choose as the reference group, the eGFR group was the lowest mortality

Age 18-54 y =>

Age 55-64 y =>

Age 65-74 y =>

Age >75 y =>



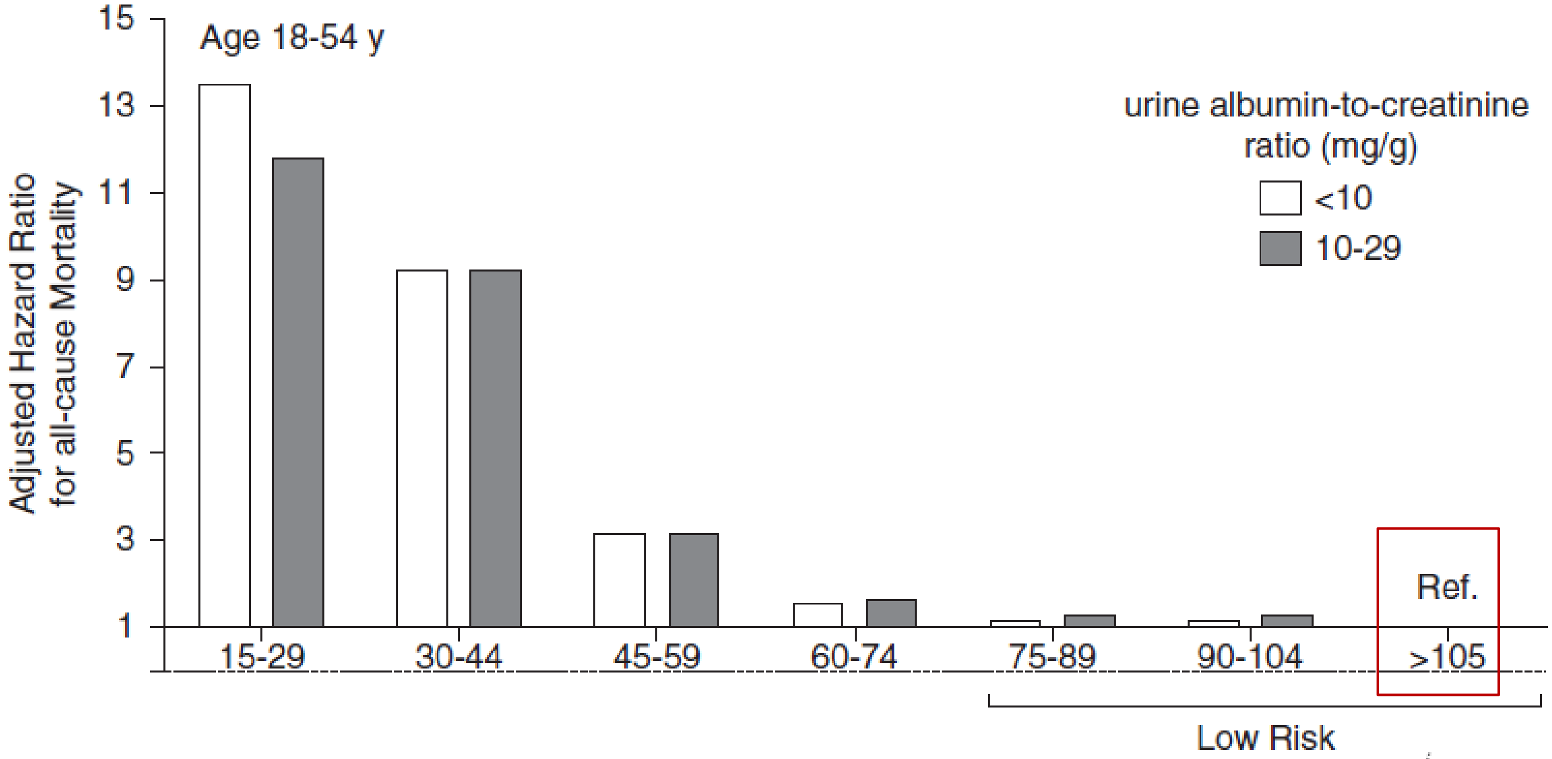
Data from:

JAMA. 2012;308(22):2349-2360

Delanaye P, Clin Biochem Rev, 2016, p17

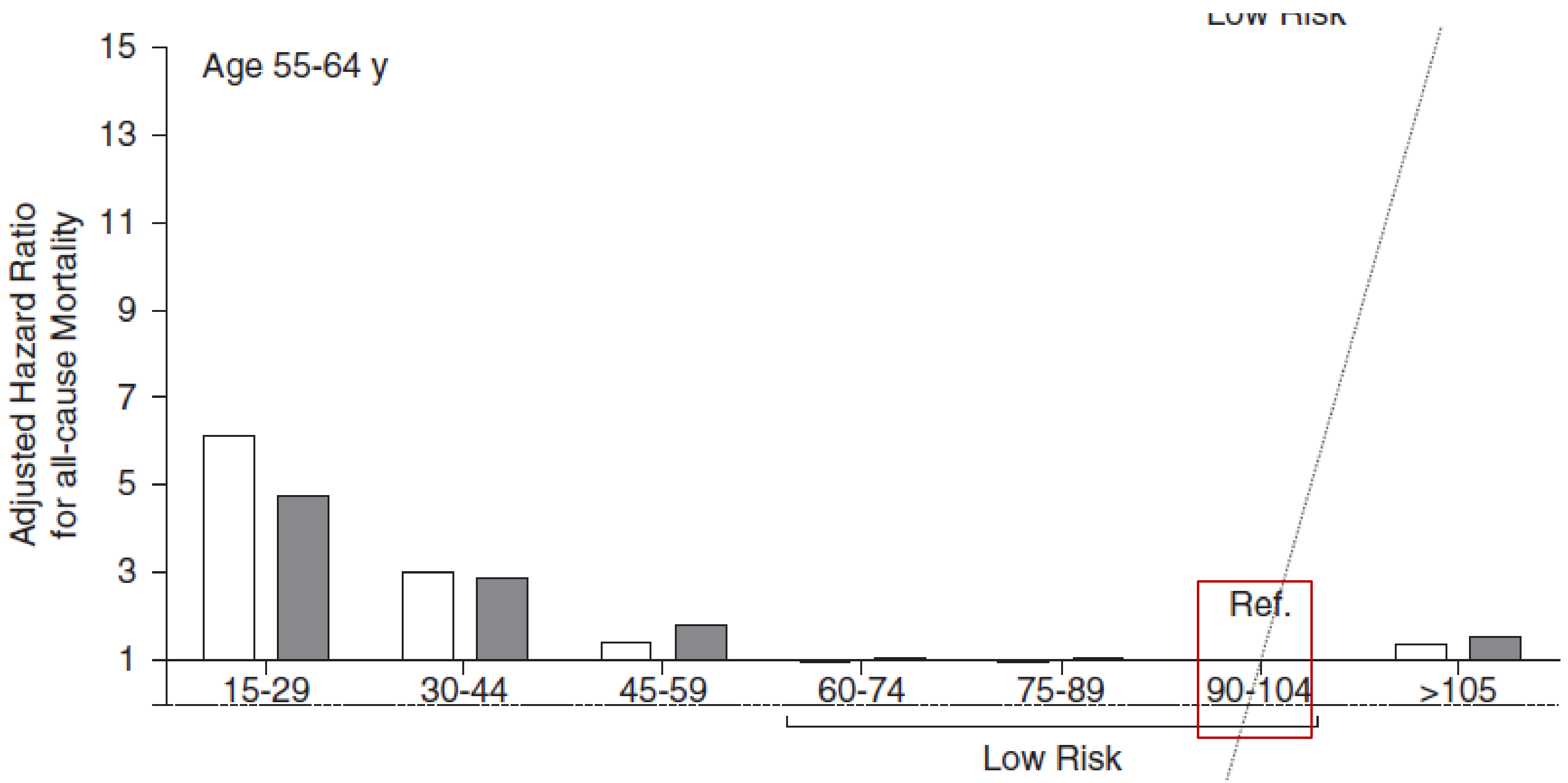
Glassock RJ, J Bras Nefrol, 2017, p59

Age 18-54 y



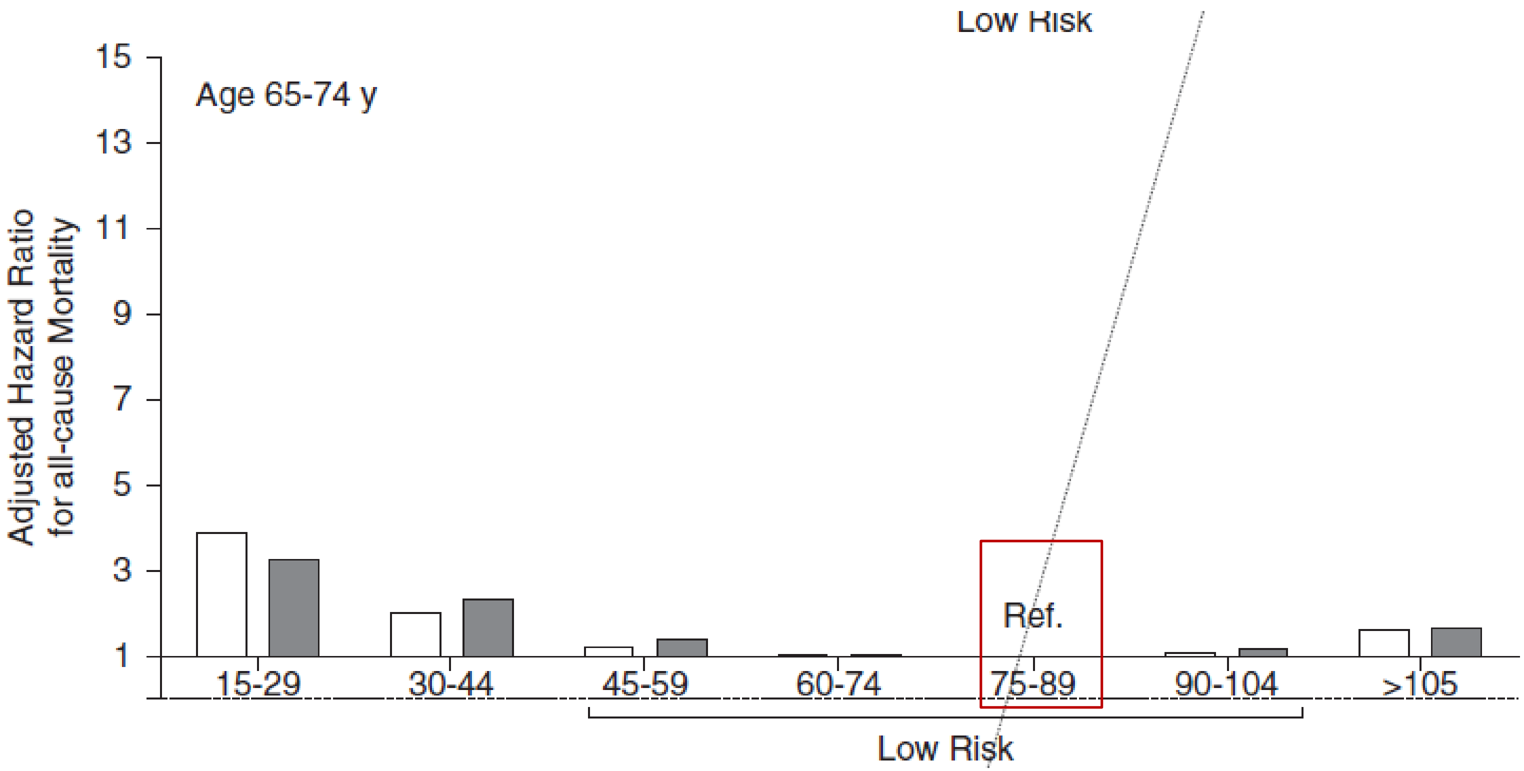
Age 18-54 y
Adjusted Hazard Ratio for all-cause Mortality
15
13
11
9
7
5
3
1
urine albumin-to-creatinine ratio (mg/g)
<10
10-29
Ref.
15-29
30-44
45-59
60-74
75-89
90-104
>105
Low Risk

Age 55-64 y



Low Risk
Age 55-64 y
Adjusted Hazard Ratio for all-cause Mortality
15
13
11
9
7
5
3
1
Ref.
15-29
30-44
45-59
60-74
75-89
90-104
>105
Low Risk

Age 64-75 y



Low Risk
Age 65-74 y
Adjusted Hazard Ratio for all-cause Mortality
15
13
11
9
7
5
3
1
Ref.
15-29
30-44
45-59
60-74
75-89
90-104
>105
Low Risk

PLOS | MEDICINE

RESEARCH ARTICLE

Chronic Kidney Disease in Primary Care: Outcomes after Five Years in a Prospective Cohort Study

Adam Shardlow[1,2]*, Natasha J. McIntyre[1], Richard J. Fluck[1], Christopher W. McIntyre[3], Maarten W. Taal[1,2]

1 Renal Unit, Royal Derby Hospital, Derby, United Kingdom, **2** Centre for Kidney Research and Innovation, Division of Medical Sciences and Graduate Entry Medicine, School of Medicine, The University of Nottingham, Royal Derby Hospital, Derby, United Kingdom, **3** Division of Nephrology, Schulich School of Medicine and Dentistry, University of Western Ontario, London, Ontario, Canada

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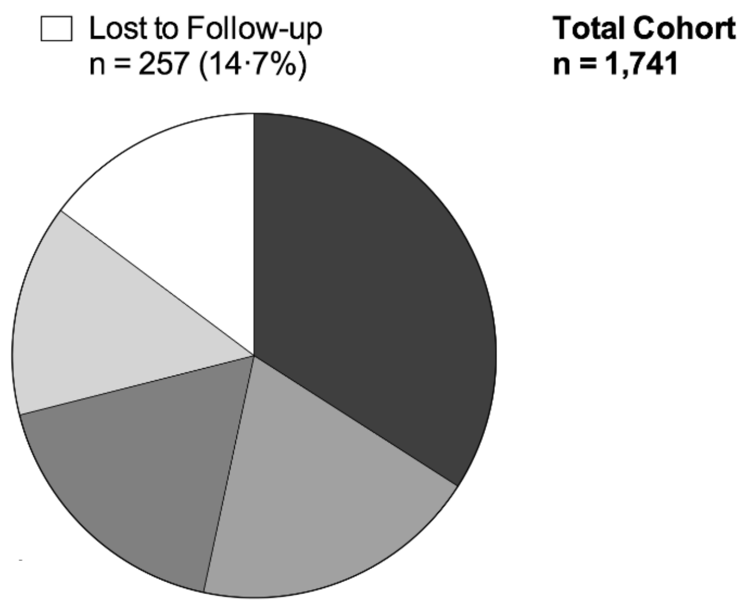
2016 PLOS Medicine | DOI:10.1371/

- Renal Risk in Derby study: a longitudinal cohort study
- Follow-up (5 years) of patients with confirmed stage 3 CKD (primary care)
- N=1741
- Regression: eGFR>60 mL/min/1.73m^2 AND no albuminuria
- Progression: 25% decline in GFR, coupled with a worsening of GFR category, or an increase in albuminuria category.

Variable (*n*)	Total (1,741)
Female Sex (%)	1,052 (60.4)
Age (years)	72.9 ± 9.0
eGFR–CKD-EPI (ml/min/1.73 m^2)	53.5 ± 11.8
eGFR–MDRD (ml/min/1.73 m^2)	52.5 ± 10.4
uACR (mg/mmol)	0.3 (0.0–1.5)

Diabetes (%)	294 (16.9)
CVD (%)	387 (22.2)
Current or Previous Smoker (%)	947 (54.4)
ACE/ARB use (%)	1,123 (64.5)
Weight (kg)	78.2 ± 15.5
BMI (kg/m^2)	29.0 ± 5.1
Waist:Hip Ratio	0.91 ± 0.09
SBP (mmHg)	134.0 ± 18.3
DBP (mmHg)	72.8 ± 11.0



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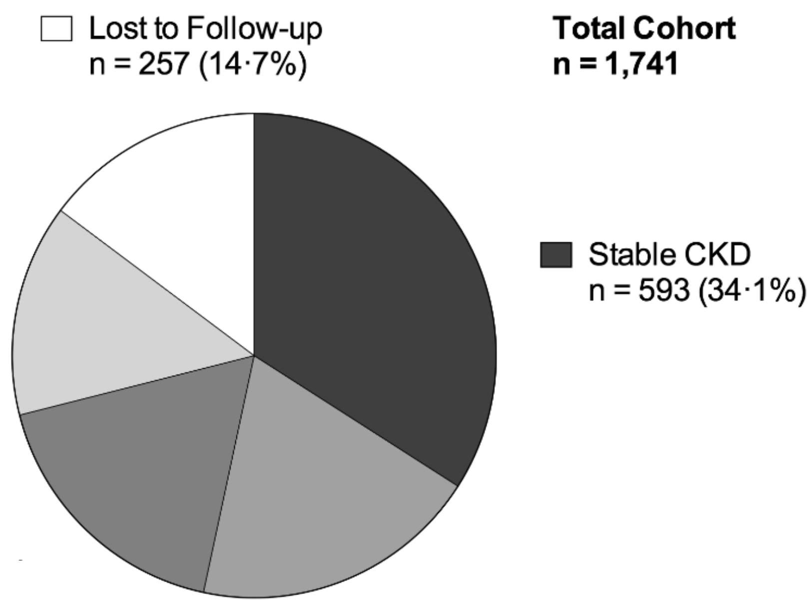

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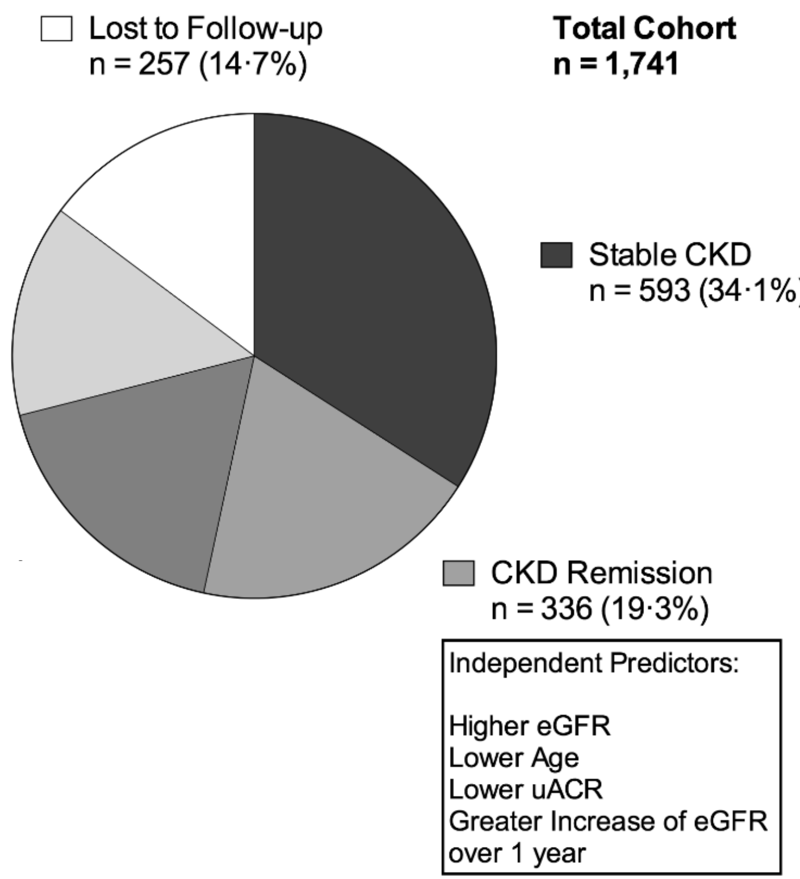

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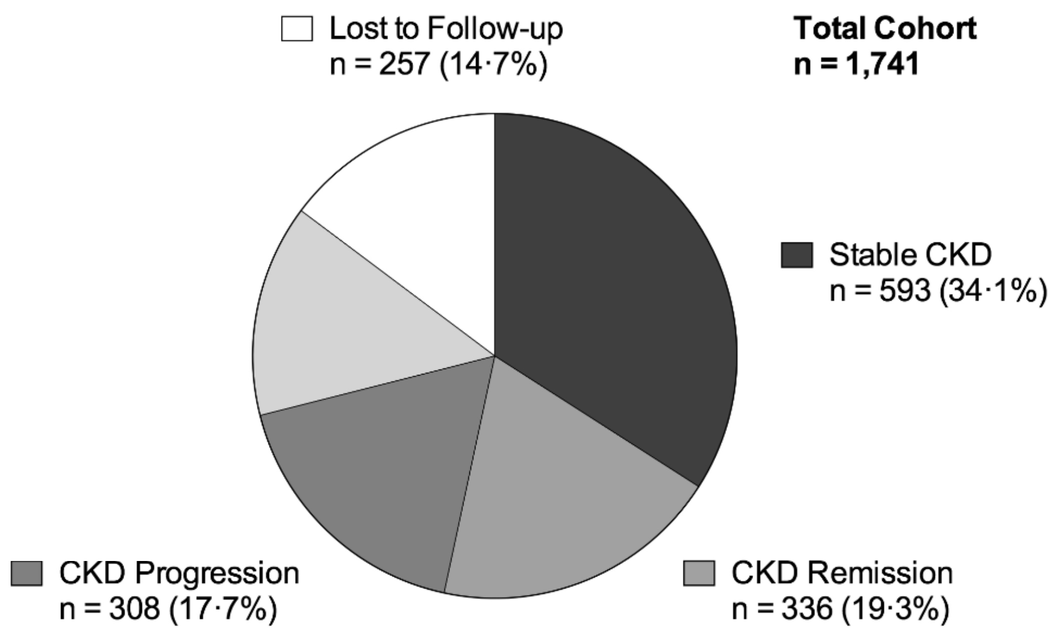

Independent Predictors:

Lower eGFR
Higher uACR
Male Gender
Lower Haemoglobin
Lower Bicarbonate
Diabetes
Greater loss of eGFR over 1 year

Independent Predictors:

Higher eGFR
Lower Age
Lower uACR
Greater Increase of eGFR over 1 year

ESRD: n=4 (0,2%)

Variable (*n*)	Total (1,741)
Female Sex (%)	1,052 (60.4)
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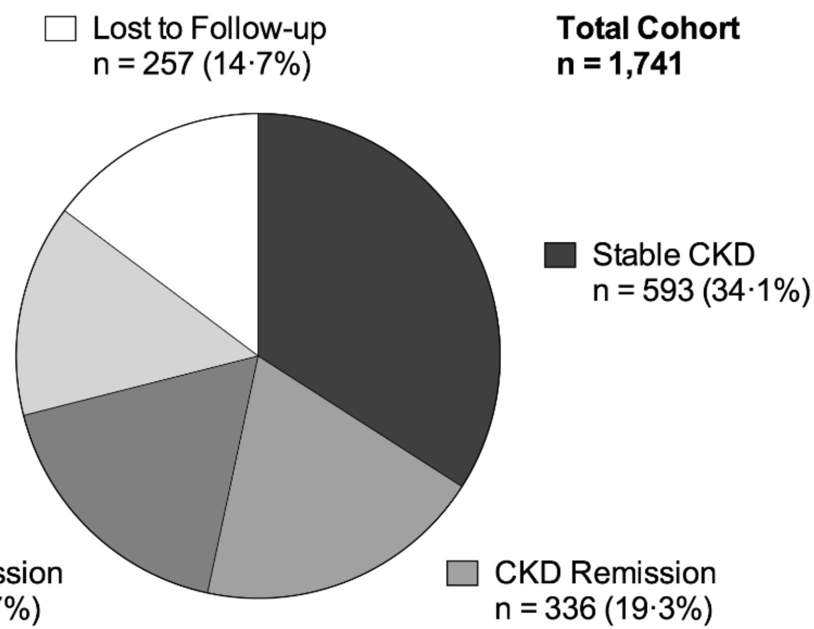

Independent Predictors (Died Before Year 5):

Lower eGFR
Greater Age
Male Gender
Higher uACR
Previous CVD
Lower Haemoglobin
Lower Albumin
Higher Bicarbonate

Independent Predictors (CKD Progression):

Lower eGFR
Higher uACR
Male Gender
Lower Haemoglobin
Lower Bicarbonate
Diabetes
Greater loss of eGFR over 1 year

Independent Predictors (CKD Remission):

Higher eGFR
Lower Age
Lower uACR
Greater Increase of eGFR over 1 year

ESRD: n=4 (0,2%)

«overall age- and sex-standardized mortality rates were similar to general population rates, mortality was higher among participants with stage 3b or stage 4 CKD at baseline.”

Wyatt CM, Kidney Int, 2017, p4

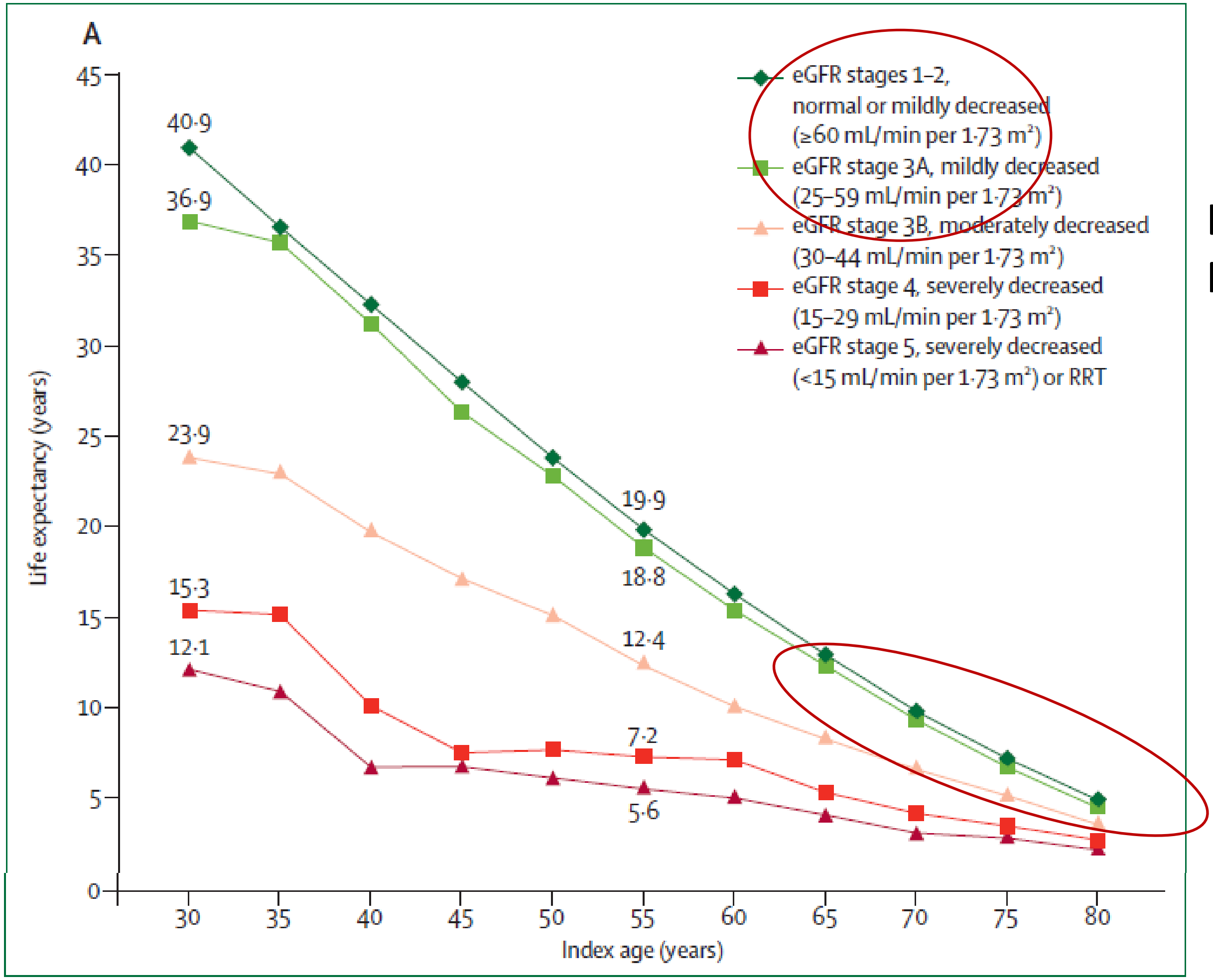

Figure 2: **Life expectancy, according to chronic kidney disease stages (Canadian data)**
(A) eGFR stages and (B) albuminuria stages. Data are adjusted per eGFR and albuminuria stage for sex to the WHO world average in 2000–05. eGFR=estimated glomerular filtration rate. RRT=renal replacement therapy. Based on data in references 24 and 25 (appendix pp 1–2).

Life expectancy for stage 3A
N=949,119

Gansevoort R et al, Lancet, 2013, p339

So…

- A single absolute threshold of eGFR overestimates CK**D** in the healthy elderly

But…

- **What about the prognostic argument?**

It can be challenged…

Stage 3A (without any other kidney damage) is not CKD in the elderly

- Do we have an alternative?
- Is it relevant from an epidemiological point of view?

There is a discrepancy between

descriptive data that demonstrate a decline in « normal GFR values » with aging
=> argument for an age-calibrated threshold

predictive data that confirm the choice of the fixed threshold for CKD definition
=> argument for a fixed threshold (60 mL/min)

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descriptive data that demonstrate a decline in « normal GFR values » with aging
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predictive data that confirm the choice of the fixed threshold for CKD definition
=> ~~argument for a fixed threshold (60 mL/min)~~
=> argument for an age-calibrated threshold

There is a no discrepancy anymore

descriptive data that demonstrate a decline in « normal GFR values » with aging
=> argument for an age-calibrated threshold

predictive data that confirm the choice of the fixed threshold for CKD definition
=> ~~argument for a fixed threshold (60 mL/min)~~
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So...

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- Is it relevant from an epidemiological point of view?

REVIEW www.jasn.org

CKD: A Call for an Age-Adapted Definition

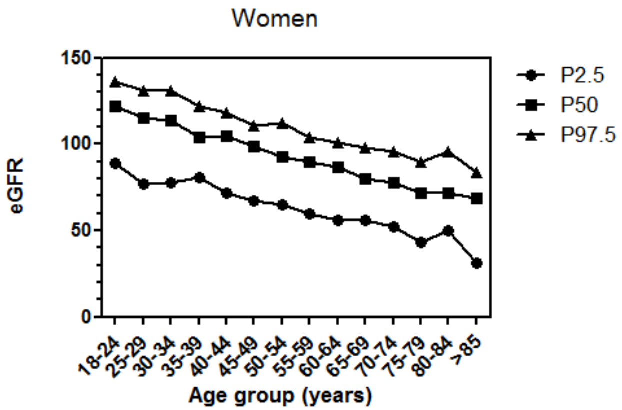
Pierre Delanaye,[1] Kitty J. Jager,[2] Arend Bökenkamp,[3] Anders Christensson,[4] Laurence Dubourg,[5] Bjørn Odvar Eriksen,[6,7] François Gaillard,[8] Giovanni Gambaro,[9] Markus van der Giet,[10] Richard J. Glassock,[11] Olafur S. Indridason,[12] Marco van Londen,[13] Christophe Mariat,[14] Toralf Melsom,[6,7] Olivier Moranne,[15] Gunnar Nordin,[16] Runolfur Palsson,[12,17] Hans Pottel,[18] Andrew D. Rule,[19] Elke Schaeffner,[20] Maarten W. Taal,[21] Christine White,[22] Anders Grubb,[23] and Jan A. J. G. van den Brand[24]

Due to the number of contributing authors, the affiliations are listed at the end of this article.

J Am Soc Nephrol. 2019 Oct;30(10):1785-1805.

Alternative 1

- Percentiles (like pediatrics)



Age, years	P5	P10	P50	P90	P95
18	82	88	106	125	130
20	82	88	106	125	130
25	82	88	106	125	130
30	82	88	106	125	130
35	82	88	106	125	130
40	82	88	106	125	130
40	82	88	106	125	130
42	81	86	104	123	128
45	78	83	102	120	126
50	74	79	97	116	121
55	69	74	93	112	117
60	65	70	89	107	112
65	60	66	84	103	108
70	**56**	**61**	**80**	**98**	**104**
75	**52**	**57**	**75**	**94**	**99**
80	**47**	**52**	**71**	**90**	**95**
85	**43**	**48**	**67**	**85**	**90**
90	**38**	**44**	**62**	**81**	**86**
95	**34**	**39**	**58**	**76**	**82**

All values in mL/min/1.73 m^2. P, percentile; mGFR, measured GFR.

- Too complex…(so we assume that adult nephrologists are more stupid than pediatricians)
- …maybe not with good files and help from labs…

Alternative 2

- Stage 3A (without any kidney damage) is not CKD anymore if age > 65 years
- Stage 3B and 45 mL/min become the pathological level if age > 65 years

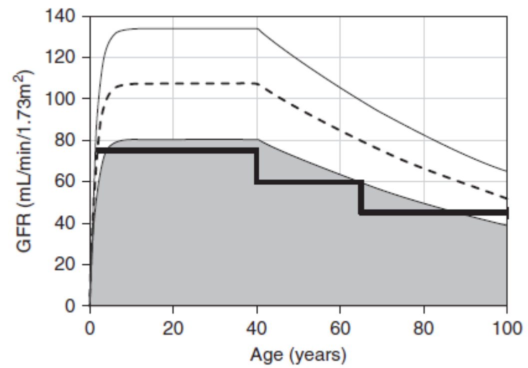


Figure 3. Age-specific thresholds in relation to age-specific GFR percentiles. GFR cut-off values and percentiles according to age (here percentiles of eGFR are calculated using the FAS equation). The bold line represents an age-adapted threshold for CKD: 75 ml/min per 1.73 m^2 for age below 40 years, 60 ml/min per 1.73 m^2 for age between 40 and 65 years, and 45 ml/min per 1.73 m^2 for age above 65 years. The dashed line represents the median (50th percentile) and the thin solid lines represent the 97.5th and 2.5th percentiles. The shaded zone is considered as below the normal reference intervals for GFR (<2.5th percentile).

Glassock RJ, Delanaye P, El-Nahas M, JAMA, 2012, p 559

So...

- A single absolute threshold of eGFR overestimates CK**D** in the healthy elderly

But…

- What about the prognostic argument?
- Do we have an alternative?
- Is it relevant from an epidemiological point of view?

The prevalence of chronic kidney disease in Iceland according to KDIGO criteria and age-adapted estimated glomerular filtration rate thresholds

Check for updates

see commentary on page 1090

Arnar J. Jonsson[1,2], Sigrun H. Lund[1], Bjørn O. Eriksen[3], Runolfur Palsson[1,2,4] and Olafur S. Indridason[2,4]

[1]Faculty of Medicine, School of Health Sciences, University of Iceland, Reykjavik, Iceland; [2]Internal Medicine Services, Landspitali–The National University Hospital of Iceland, Reykjavik, Iceland; [3]Metabolic and Renal Research Group, UiT The Arctic University of Norway, Tromsø, Norway; and [4]Division of Nephrology, Landspitali–The National University Hospital of Iceland, Reykjavik, Iceland

Kidney Int. 2020 Nov;98(5):1286-1295.

2,120,147 creatinine measurements in 218,437 of Icelandic people aged over 18 y (mean 5/subject)

53.1% of women

0,2% during hospitalization

The prevalence of chronic kidney disease in Iceland according to KDIGO criteria and age-adapted estimated glomerular filtration rate thresholds

see commentary on page 1090

Check for updates

Arnar J. Jonsson[1,2], Sigrun H. Lund[1], Bjørn O. Eriksen[3], Runolfur Palsson[1,2,4] and Olafur S. Indridason[2,4]

[1]Faculty of Medicine, School of Health Sciences, University of Iceland, Reykjavik, Iceland; [2]Internal Medicine Services, Landspitali–The National University Hospital of Iceland, Reykjavik, Iceland; [3]Metabolic and Renal Research Group, UiT The Arctic University of Norway, Tromsø, Norway; and [4]Division of Nephrology, Landspitali–The National University Hospital of Iceland, Reykjavik, Iceland

Table 4 | Mean annual prevalence of chronic kidney disease defined by the KDIGO criteria or age-adapted eGFR thresholds

	KDIGO criteria			Age-adapted eGFR thresholds		
Criteria for CKD	eGFR	eGFR and proteinuria	eGFR, proteinuria, and kidney disease diagnosis	eGFR	eGFR and proteinuria	eGFR, proteinuria, and kidney disease diagnosis
All						
Single-value criterion[a]	6.41 (6.36–6.49)	11.60 (11.54–11.65)	12.14 (12.08–12.20)	3.98 (3.94–4.01)	9.66 (9.61–9.71)	10.34 (10.29–10.40)
KDIGO criteria	4.72 (4.68–4.76)	5.35 (5.31–5.38)	5.94 (5.90–5.98)	2.20 (2.18–2.22)	2.93 (2.90–2.96)	3.64 (3.61–3.67)

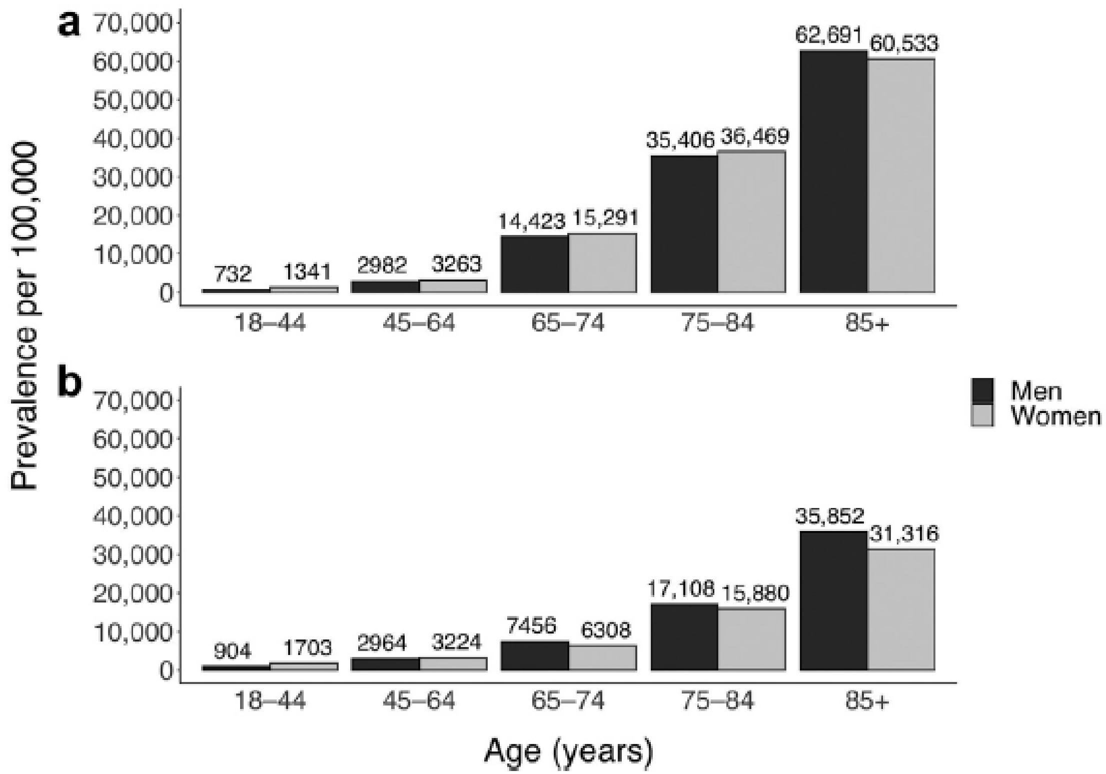


Figure 2| Mean annual prevalence of chronic kidney disease stages 1–5 by age group and sex, using (a) the Kidney Disease: Improving Global Outcomes (KDIGO) definition and (b) age-adapted estimated glomerular filtration rate (eGFR) thresholds.

ARTICLE IN PRESS

www.kidney-international.org

clinical investigation

Chronic kidney disease, hypertension, diabetes, and obesity in the adult population of Morocco: how to avoid "over"- and "under"-diagnosis of CKD

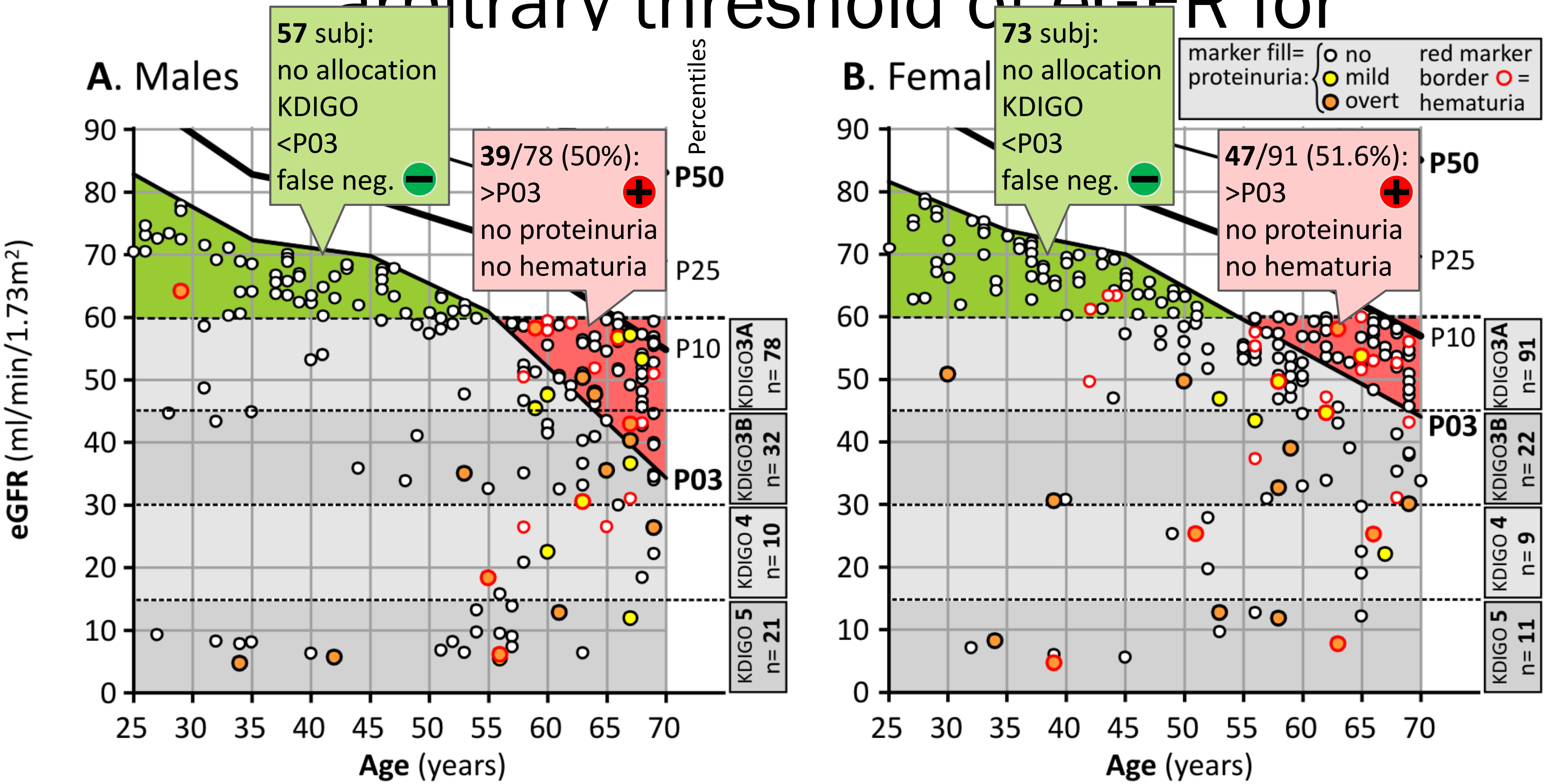
Mohammed Benghanem Gharbi[1,6], Monique Elseviers[2,6], Mohamed Zamd[1], Abdelali Belghiti Alaoui[3], Naïma Benahadi[3], El Hassane Trabelssi[3], Rabia Bayahia[4], Benyounès Ramdani[1] and Marc E. De Broe[5,6]

[1]Faculty of Medicine and Pharmacy, University Hassan II, Casablanca, Morocco; [2]Department of Biostatistics, Center for Research and Innovation in Care, University of Antwerp, Antwerp, Belgium; [3]Ministry of Health, Rabat, Morocco; [4]Faculty of Medicine and Pharmacy, University Mohammed V, Rabat, Morocco; and [5]University of Antwerp, Antwerp, Belgium

Kidney Int. 2016 Jun;89(6):1363-71.

- Two Moroccan towns
- 26-70y, n=10,524
- Creatinine and dipstick
- Chronicity confirmed at 3 months

False negatives and false positives by using the arbitrary threshold of eGFR for



Kidney Int. 2016 Jun;89(6):1363-71.

Some pathological data…

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Single-Nephron Glomerular Filtration Rate in Healthy Adults

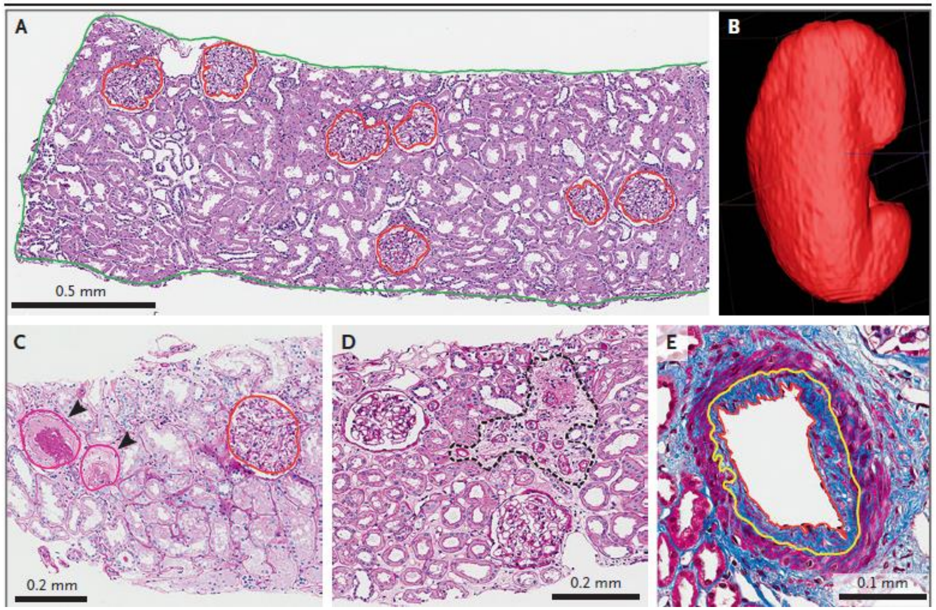
Aleksandar Denic, M.D., Ph.D., Jerry Mathew, M.D.,
Lilach O. Lerman, M.D., Ph.D., John C. Lieske, M.D., Joseph J. Larson, B.S.,
Mariam P. Alexander, M.D., Emilio Poggio, M.D., Richard J. Glassock, M.D.,
and Andrew D. Rule, M.D.

N Engl J Med 2017;376:2349-57.

Living kidney donors, Mayo Clinic, from 2000 to 2011
+65 y from 2012 to 2015
CT scan (with contrast)
GFR measured by iothalamate
Renal biospy during donation

Table 1. Characteristics of the Living Kidney Donors at Donation.*

Characteristic	Donors (N=1388)
Age — yr	44.2±11.9
Female sex — no. (%)	809 (58.3)
Height — cm	171.0±9.5
Race — no. (%)†	
White or unknown	1301 (93.7)
Black	30 (2.2)
American Indian or Alaska Native	10 (0.7)
Asian	20 (1.4)
Other	27 (2.0)
Risk factors	
Family history of end-stage renal disease — no. (%)	728 (52.5)
Mild hypertension — no. (%)	167 (12.0)
Body-mass index‡	27.9±4.9
Uric acid — mg/dl§	5.2±1.4
Kidney function	
Measured total GFR — ml/min	115±24
24-hr urinary albumin excretion — mg¶ N=1221	5.2±8.7



Density if non-sclerosis glomerulus
Cortex volume measured by 3D CT-SCan
Volume cortex x glomerulus density = nbr of nephrons
« Single nephron GFR »= GFR/nbr of nephrons
Glomerulus is sclerosed if more than +10 %
Interstitial fibrosis if more than+5%
Arteriosclerosis if intima is % of the lumen

Table 2. Age-Group Differences in the Number of Nephrons per Kidney, the Single-Nephron GFR, and Total GFR among 1388 Living Kidney Donors.

Age Group	No. of Donors	No. of Nephrons	Single-Nephron GFR	Total GFR
			nl/min	*ml/min*
18–29 yr	190	970,000±430,000	79±42	127±25
30–39 yr	339	930,000±350,000	77±36	124±24
40–49 yr	417	850,000±360,000	81±42	114±23
50–59 yr	300	810,000±360,000	80±40	106±20
60–64 yr	73	750,000±310,000	79±36	101±18
65–69 yr	56	720,000±260,000	76±33	95±17
70–75 yr	13	480,000±170,000	110±44	96±25

This attrition of nephrons is accompanied by an increase in global glomerulosclerosis, but not segmental glomerulosclerosis, and the increase in interstitial fibrosis/tubular atrophy (IF/TA) is minimal compared with CKD

Table 3. Demographic and Clinical Characteristics as Predictors of the Number of Nephrons per Kidney, Single-Nephron GFR, and Total GFR.*

Characteristic	No. of Nephrons		Single-Nephron GFR		Total GFR	
	Estimate	P Value	Estimate	P Value	Estimate	P Value
			nl/min		*ml/min*	
Age, per 10 yr	−60,000	<0.001	1	0.28	−7.1	<0.001
Female sex	−60,000	0.03	6	0.08	−3.8	0.01
Body-mass index, per SD	0	0.85	6	<0.001	9.6	<0.001
Height, per SD†	30,000	0.03	4	0.006	9.2	<0.001
Uric acid, per SD	−40,000	0.002	1	0.42	−3.7	<0.001
Family history of end-stage renal disease	−70,000	<0.001	8	<0.001	0.8	0.43
Mild hypertension	−20,000	0.59	3	0.39	1.5	0.36

- Number of nephrons and GFR are decreasing with age
- snGFR remains stable with age
- Probably a reflect of a decrease of metabolic needs with aging

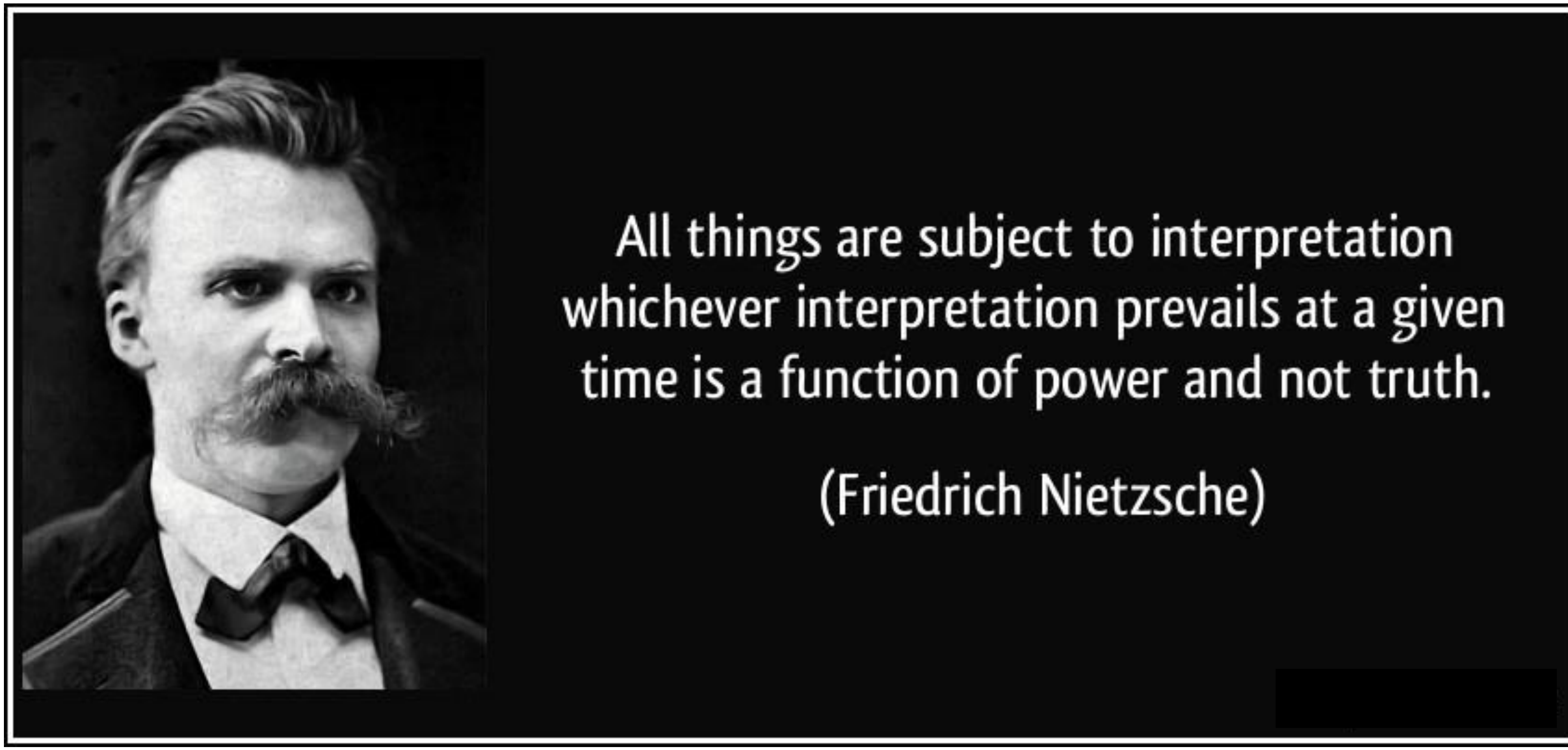
Perspective

The Kidney in Normal Aging
A Comparison with Chronic Kidney Disease

Aleksandar Denic,[1] Richard J. Glassock,[2] and Andrew D. Rule[1]

CJASN 17: 137–139, 2022.

Is it nihilism?



Research

Original Investigation

Interpreting Treatment Effects From Clinical Trials in the Context of Real-World Risk Information
End-Stage Renal Disease Prevention in Older Adults

Ann M. O'Hare, MA, MD; John R. Hotchkiss, MD; Manjula Kurella Tamura, MD, MPH; Eric B. Larson, MD, MPH; Brenda R. Hemmelgarn, MD, PhD; Adam Batten, BA; Thy P. Do, PhD; Kenneth E. Covinsky, MD, MPH

JAMA Intern Med. 2014;174(3):391-397.

VA

97% male

Age>70 y

Mean age: 77.8 ± 4.6 y

eGFR: 48 ± 11.7 ml/min/1.73 m^2

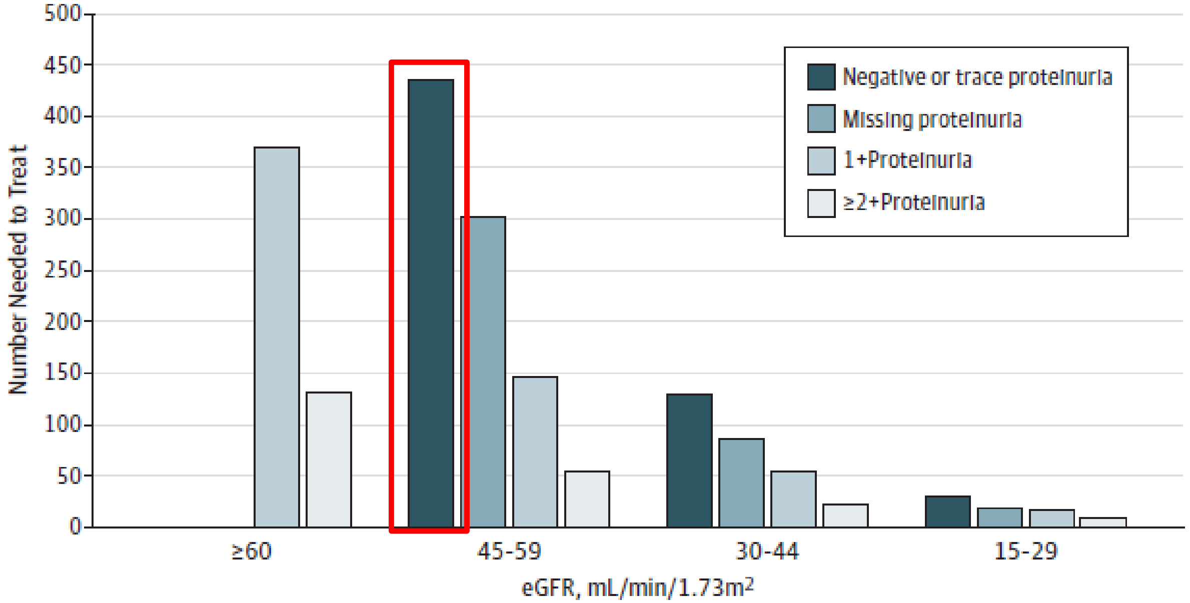
n=371.470

Protective effect of ACE inhibitors to prevent ESRD

Table 1. Entry Criteria and Outcomes of Major Trials Reporting a Protective Effect of ACE Inhibitors or ARBs on Progression to ESRD

				Entry Criteria				Mortality, %		ESRD, %		ESRD Outcomes[a]		
Source	No. of Patients	Intervention	Mean FU, y	Age, y	DM	Renal Function	Dipstick Proteinuria Measurement	Control Group	INT Group	Control Group	INT Group	RRR, %	ARR, %	NNT
Brenner et al,[18] 2001	1513	Losartan potassium vs placebo	3.4	31-70	Yes	Scr level, 1.3-3.0 mg/dL	ACR >300 mg/g	20.3	21.0	25.5	19.6	23.0	5.9	17
Lewis et al,[19] 1993	409	Captopril vs placebo	3.0	18-49	Yes	Scr level, ≤2.5 mg/dL	Urine protein level, ≥500 mg/g	6.9	3.9	15.4	9.7	37.0	5.7	18
Ruggenenti et al,[20] 1999	352	Ramipril vs placebo	2.6	18-70	Type 1 DM excluded	CrCl, 20-70 mL/min	Stratum 1: urine protein level ≥1 and <3 g/d	0	1.0	20.7	9.1	56.0	11.6	9
Agodoa et al,[21] 2001	1094	Ramipril vs amlodipine besylate	3.0	18-70	No	GFR, 20-65 mL/min/1.73 m^2	Urinary ratio of protein to creatinine levels, ≤2.5 mg/mg	6.0	4.1	14.8	10.8	27.0	4.0	25

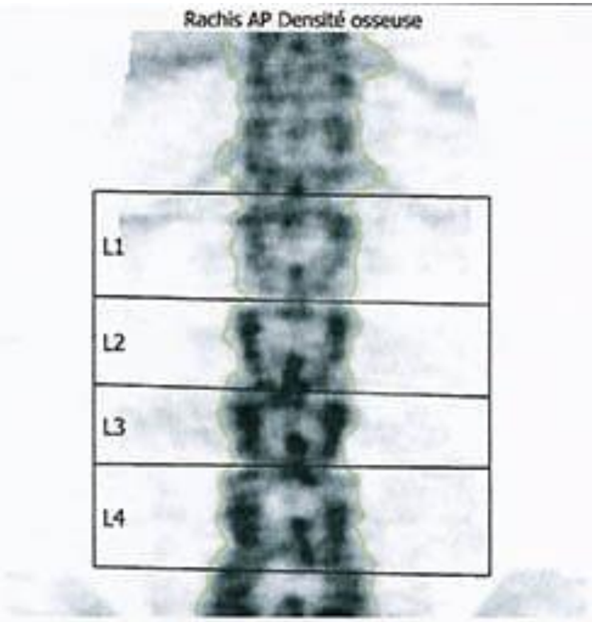
Figure. Number Needed to Treat (NNT) to Prevent 1 Case of End-Stage Renal Disease (ESRD) Over 10 Years

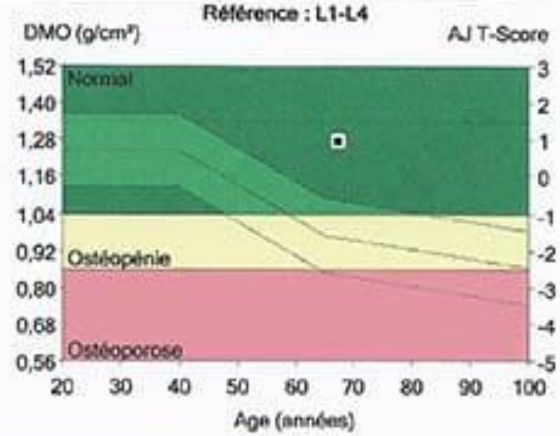


The NNT is calculated assuming a 30% reduction in relative risk over 10 years.

+ number needed to harm?

An osteoporosis-like approach

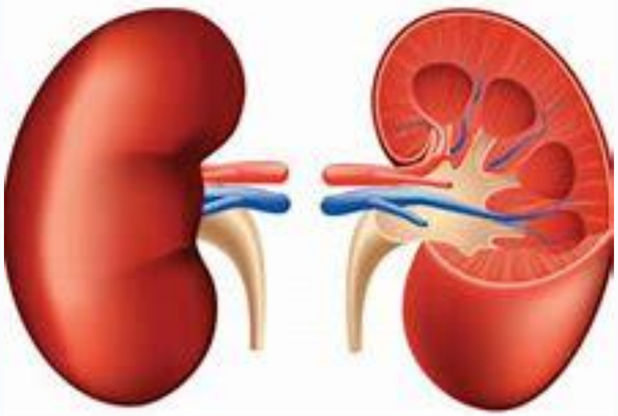


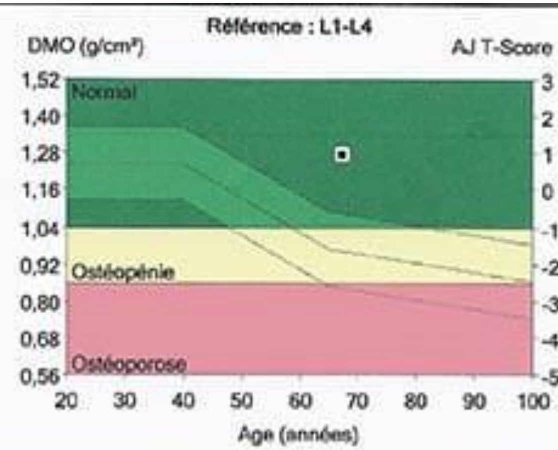


Région	DMO[1] (g/cm²)	Adulte-Jeune[2] T-Score	Age-Egal[3] Z-Score
L1	1,071	-0,3	1,3
L2	1,311	1,1	2,7
L3	1,473	2,4	4,1
L4	1,304	1,0	2,7
L1-L2	1,182	0,3	2,0
L1-L3	1,266	1,0	2,6
L1-L4	1,277	1,0	2,6
L2-L3	1,386	1,7	3,4
L2-L4	1,352	1,4	3,1

FRAX

An osteoporosis-like approach





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FRAX

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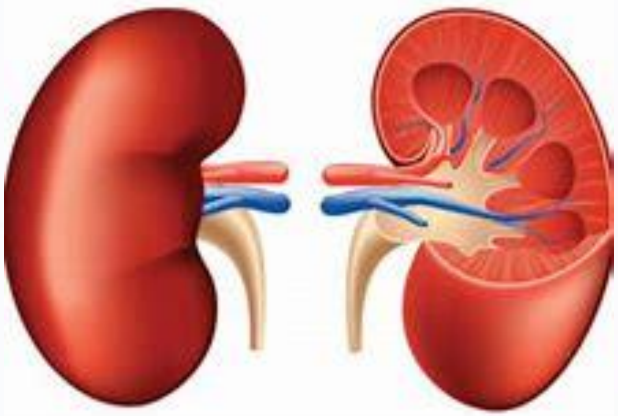

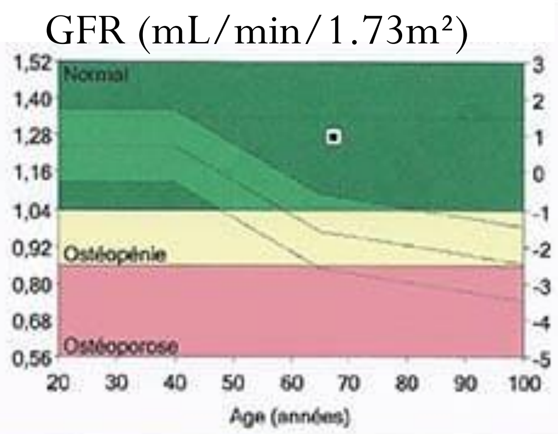

Région	1 G F R	2 Adulte-Jeune T-Score	3 Age-Egal Z-Score
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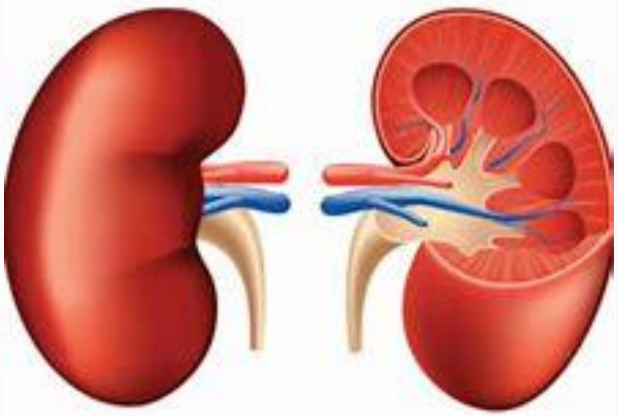
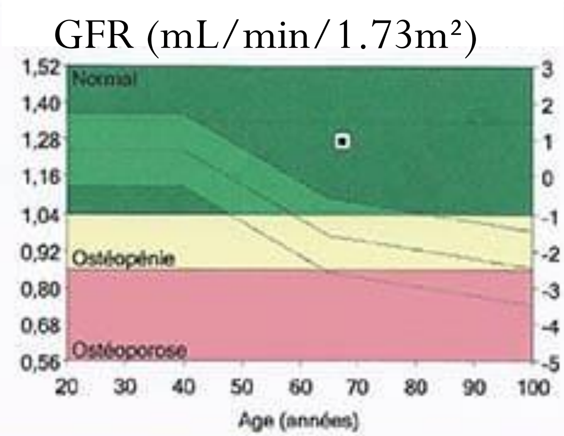
An osteoporosis-like approach





Région	GFR [1]	Adulte-Jeune T-Score [2]	Age-Egal Z-Score [3]
L1		-0,3	1,3
L2		1,1	2,7
L3		2,4	4,1
L4		1,0	2,7
L1-L2		0,3	2,0
L1-L3		1,0	2,6
L1-L4		1,0	2,6
L2-L3		1,7	3,4
L2-L4		1,4	3,1

KFRE (kidney failure risk equation: age, sex, GFR, ACR)

100 mg/g
URINE ALBUMIN

M
SEX

70
AGE

40 mL/min/1.73 m2
GFR

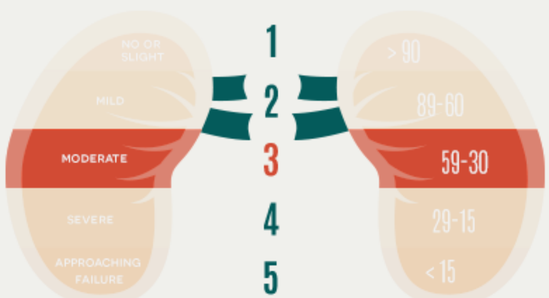
ASSESSMENT

STAGE 3

MODERATE DECREASE IN FUNCTION

CKD STAGES

GLOMERULAR FILTRATION RATE



Patient risk of progression to kidney failure requiring dialysis or transplant:

AT 2 YEARS

0.96 %

AT 5 YEARS

3.68 %

Risk thresholds used in health systems include:

- 3-5 % over 5 years for referral to a kidney doctor
- 10 % over 2 years for team based care (Kidney Doctor, Nurse, Dietician, Pharmacist)
- 20-40 % over 2 years for planning a transplant or fistula

PRECISION MEDICINE?

Old people have one advantage; they know they have been young…

…whereas no young people are sure to become old one day…


3 - 6 OCTOBRE 2023
8ÈME CONGRÈS DE LA SOCIÉTÉ FRANCOPHONE DE NÉPHROLOGIE, DIALYSE ET TRANSPLANTATION
PALAIS DES CONGRÈS
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Thank you!