Lower GFR and ageing: distinguish physiological and disease-related

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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%

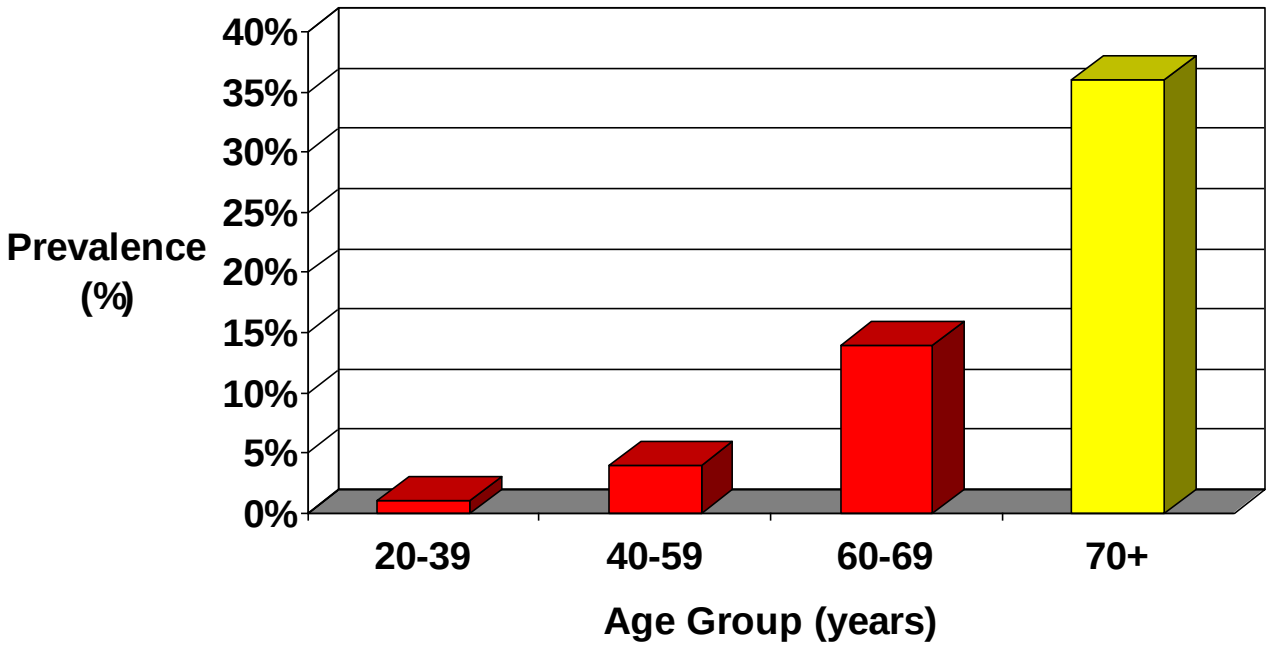
10,4% (♂: 11,3% ♀: 9,5%) **in Mazhar F, Kidney Int, 2023, p416**

Stage 3-5: 5,4%

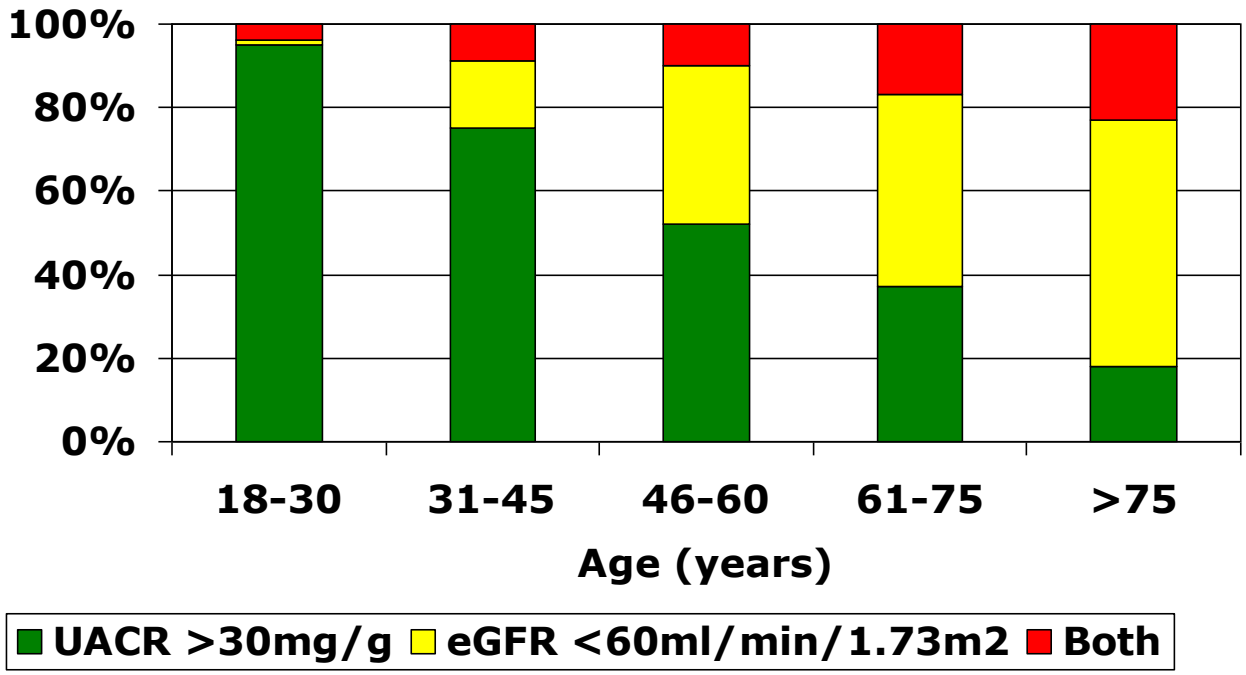
Stage 3-5= based on eGFR alone (<60 mL/min/173m²)

Prevalence of stage 3 according to age in NHANES study

(and all other studies)

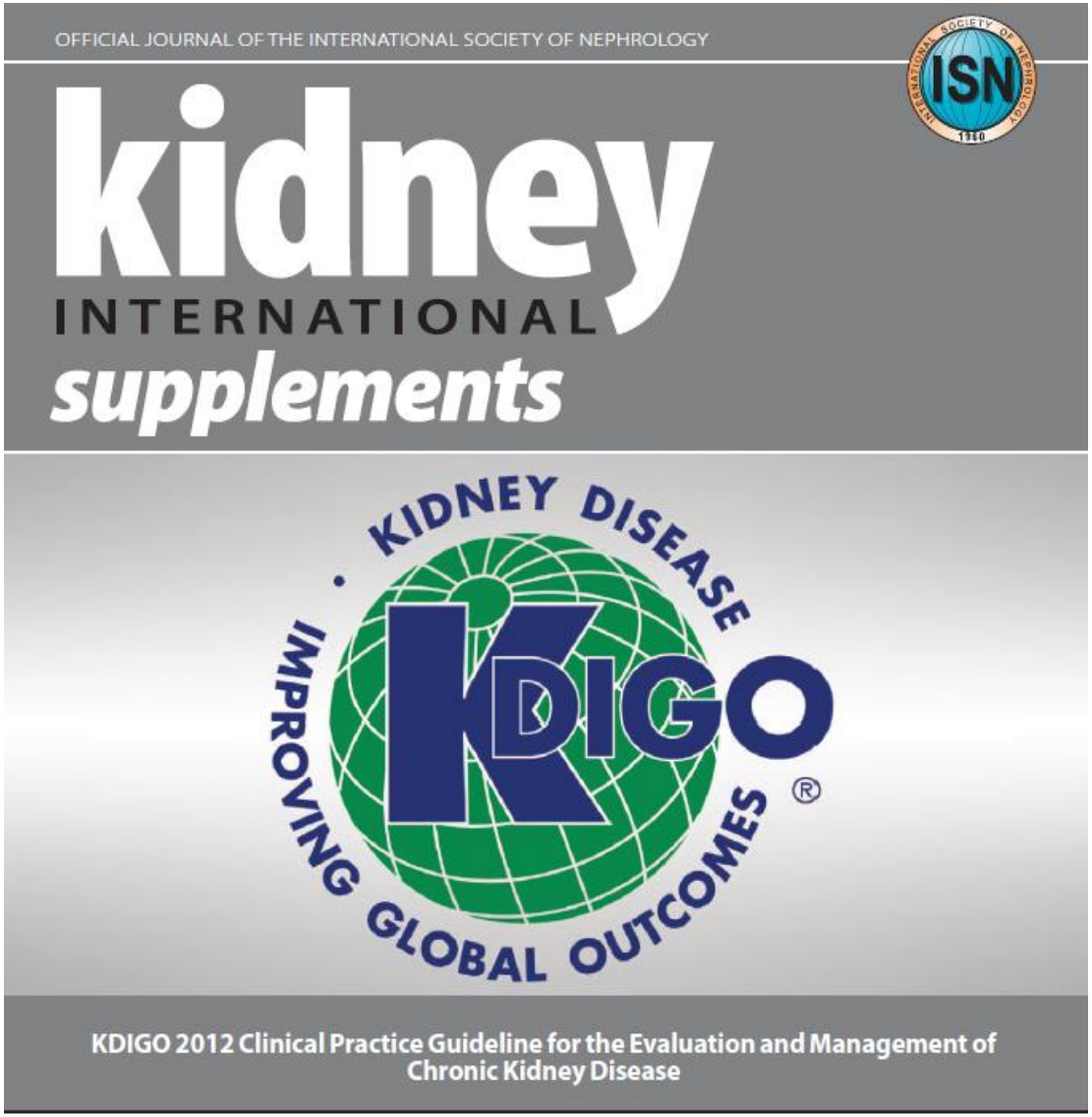


Characteristics of CKD populations



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.

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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 m² 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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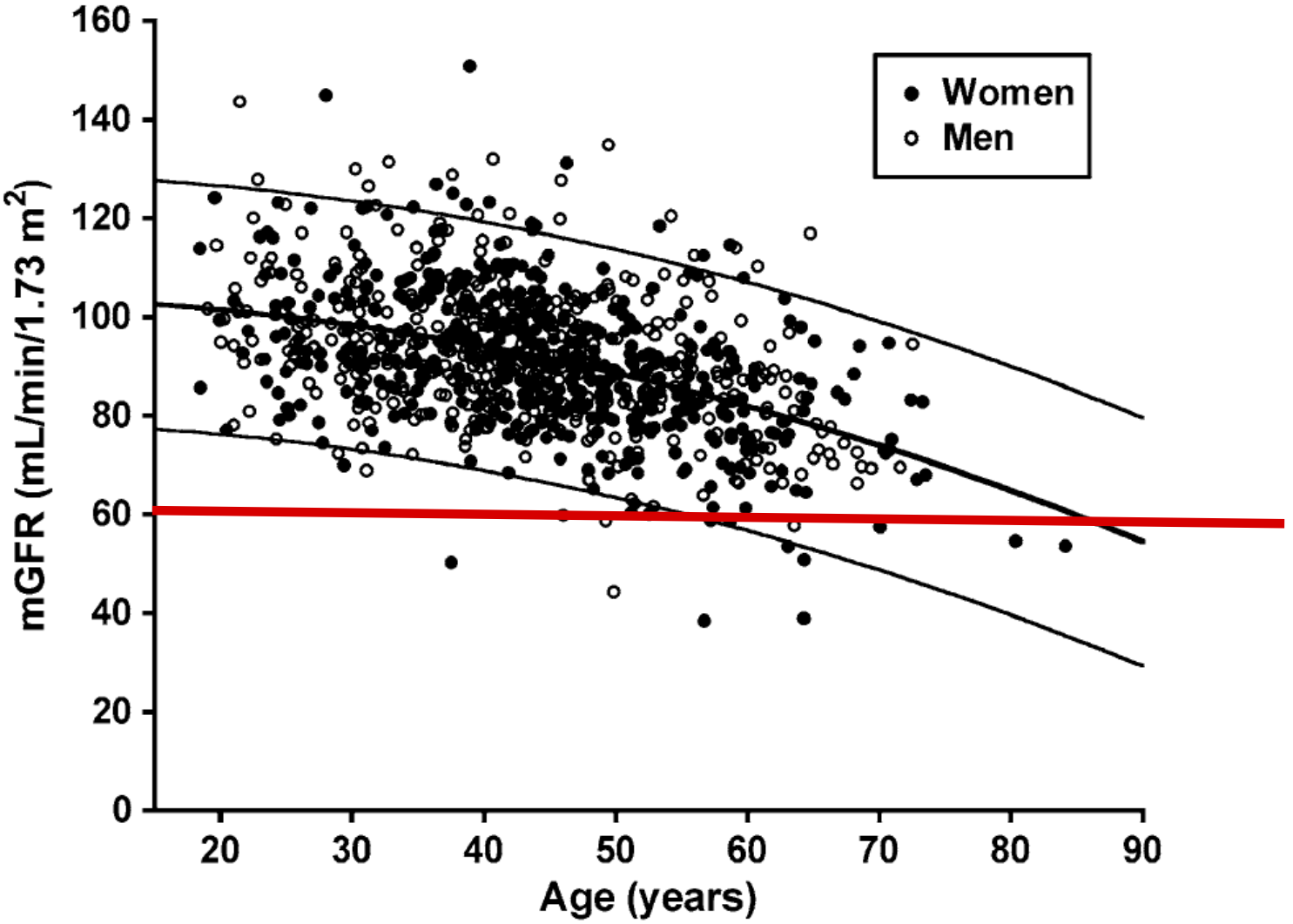

GFR measured by ^{51}Cr-EDTA in 904 potential living kidney donors

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

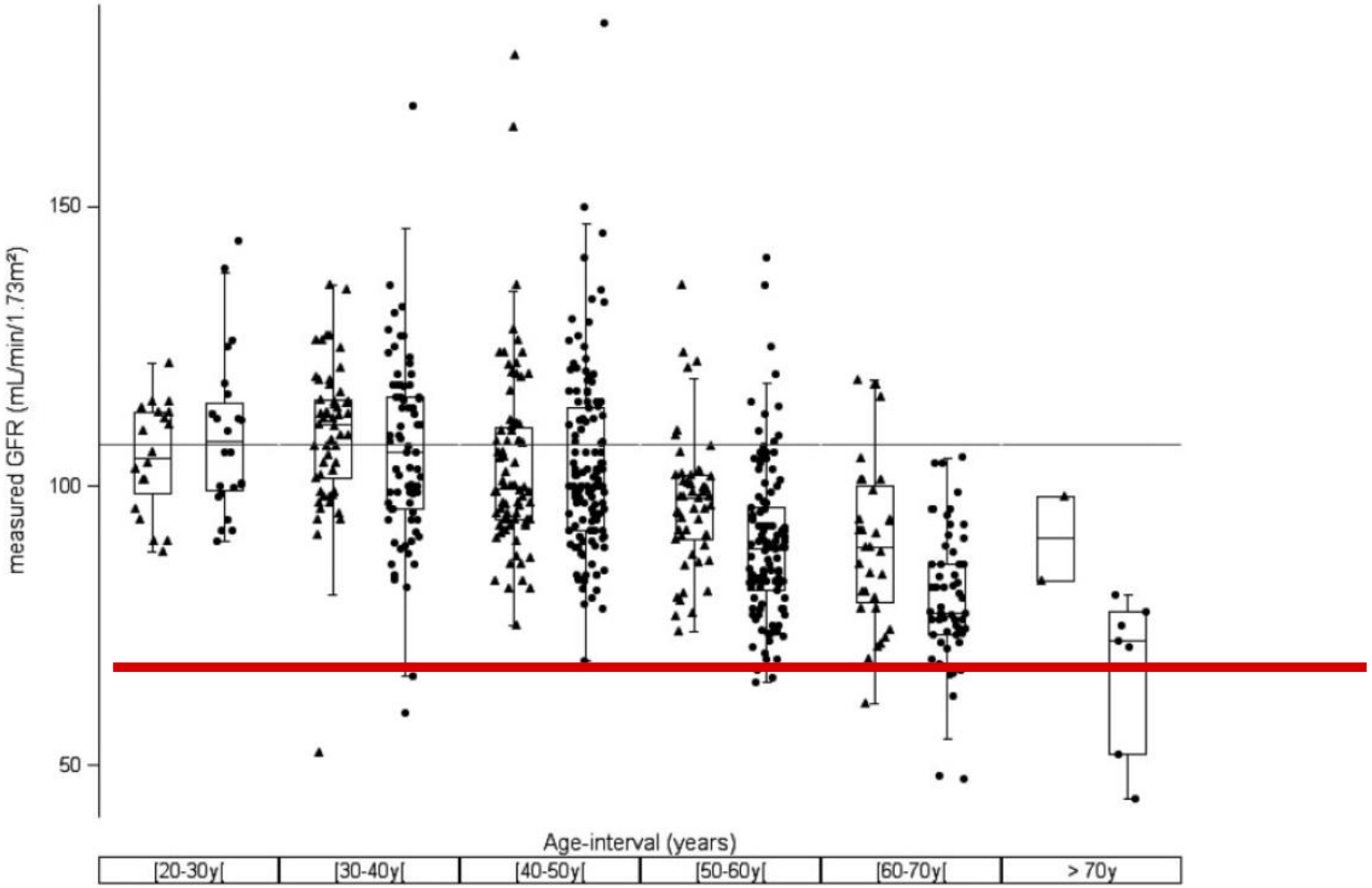

Fig. 1. Box plot for mGFR versus age decades for female (filled circles) and male (filled triangles) potential kidney donors ($n = 633$). A horizontal reference line is drawn at GFR = 107.3 mL/min/1.73 m^2.

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

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]

[1]Renal Unit, Department of Internal Medicine, Kinshasa University Hospital, University of Kinshasa, Kinshasa, Democratic Republic of Congo; [2]Département de Biochimie, UFR Sciences Pharmaceutiques et Biologiques, Université Felix Houphouet Boigny, Abidjan, Ivory Coast; [3]Département de Néphrologie, UFR Sciences Médicales, Université Felix Houphouet Boigny, Abidjan, Ivory Coast; [4]Department of Public Health and Primary Care, KU Leuven Campus Kulak Kortrijk, Kortrijk, Belgium; [5]Division of Clinical Chemistry, CHU Sart Tilman (ULg CHU), University of Liège, Liège, Belgium; and [6]Division of Nephrology-Dialysis-Transplantation, CHU Sart Tilman (ULg CHU), University of Liège, Liège, Belgium

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

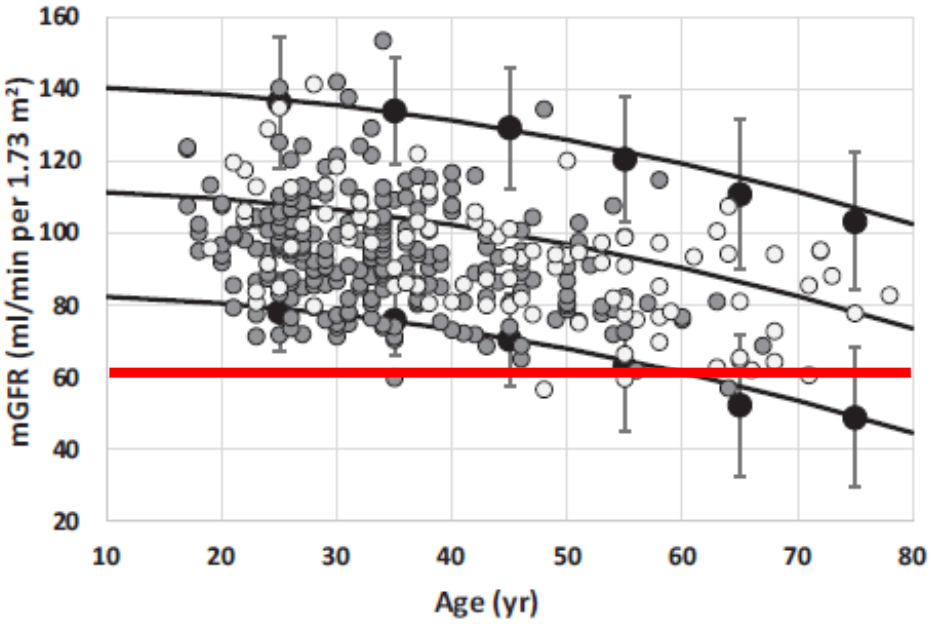

Figure 2 | Comparison of measured glomerular filtration rate (mGFR) values in healthy Whites, Congolese, and Ivorian subjects. Solid gray circles represent mGFR results and solid black lines represent 2.5th percentile (Pct), 50th Pct, and 97.5th Pct for mGFR in the Ivorian population (n = 237).[18] Solid 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

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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.

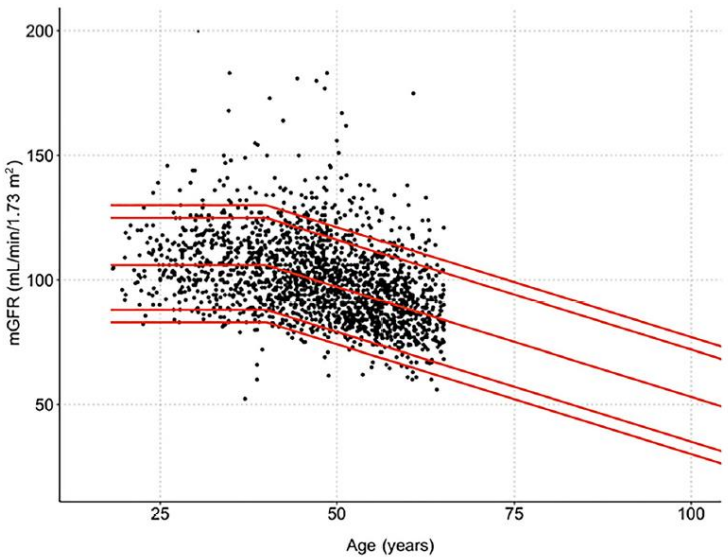


Figure 1: mGFR according to age in the development cohort (n=1,983).
Red lines are percentiles 5, 10, 50, 90 and 95, calculated from kidney donors younger than 65 years and extrapolated for ages >65 years.

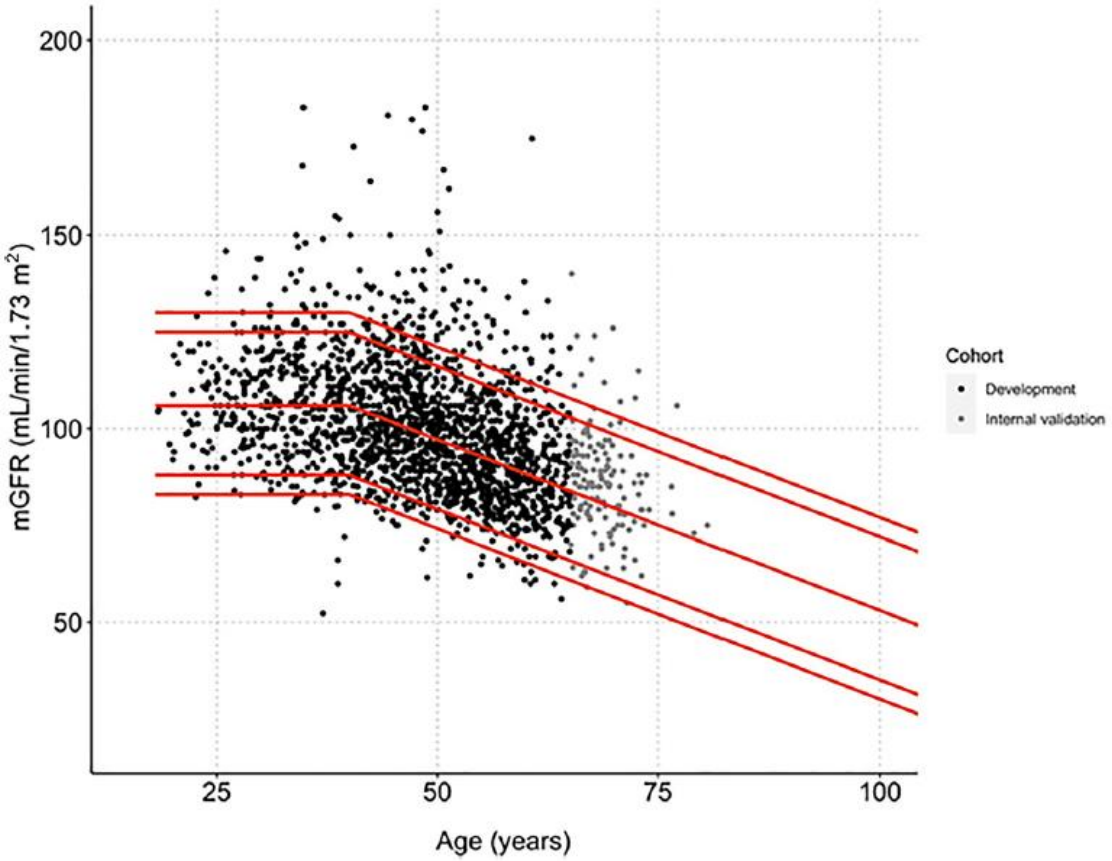


Figure 2: mGFR according to age in the development (dark dots) and internal validation cohort (n=147) (gray dots). Red lines are percentiles 5, 10, 50, 90 and 95, calculated from kidney donors younger than 65 years and extrapolated for ages >65 years.

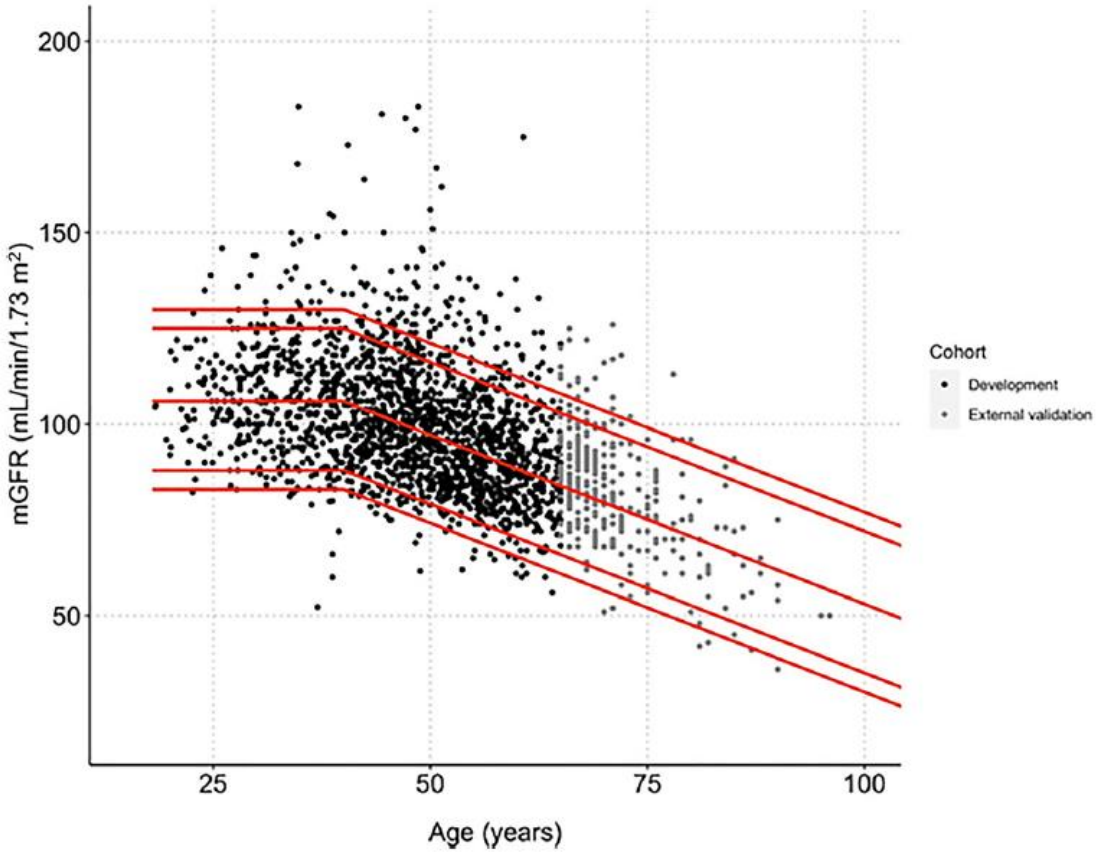
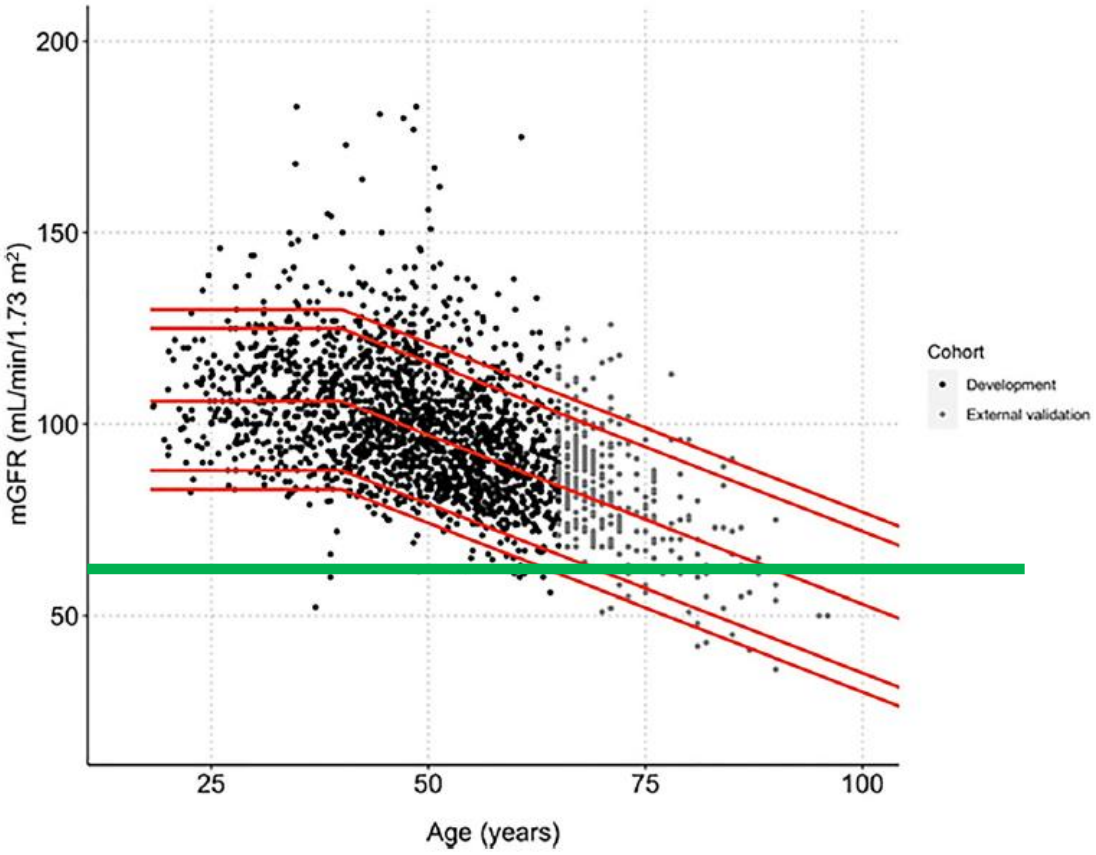


Figure 3: mGFR according to age in the development (dark dots) and external validation cohort (n=329) (gray dots). Red lines are percentiles 5, 10, 50, 90 and 95, calculated from kidney donors younger than 65 years and extrapolated for ages >65 years.



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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.

- Measured GFR is declining with aging
- There are reasons to think that some healthy subjects over 65 years have measured GFR below 60 mL/min/1.73m²

=> What about estimating GFR?

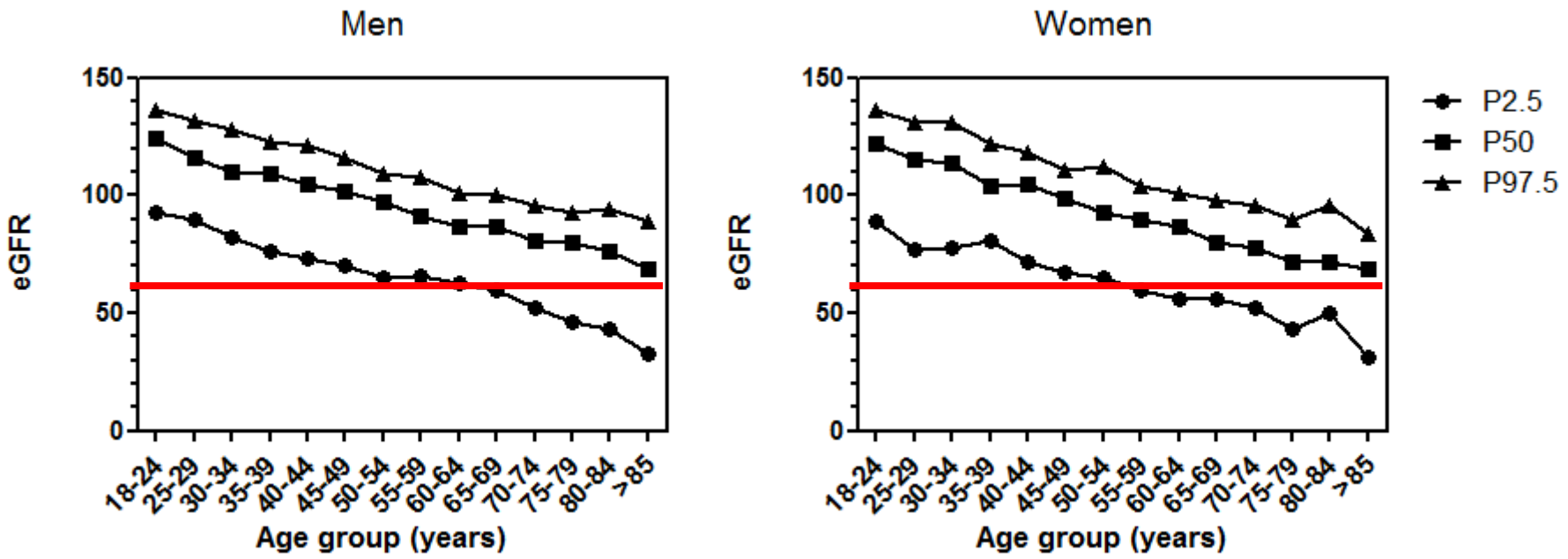
- Healthy population in the Netherlands
- CKD-EPI equation to estimate GFR
- No diabetes, no hypertension, no specific therapy
- 1663 men 2073 women

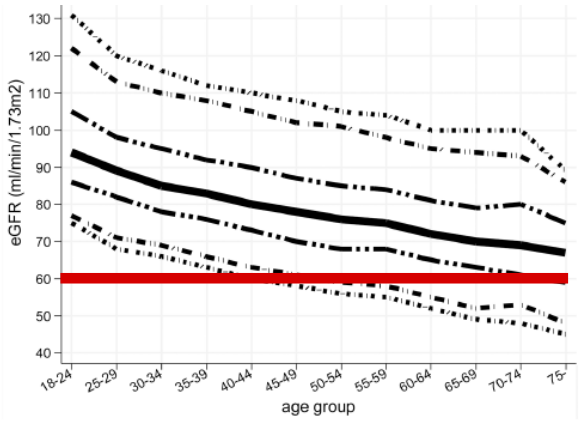
Nephrol Dial Transplant (2011) 26: 3176–3181
doi: 10.1093/ndt/gfr003
Advance Access publication 16 February 2011

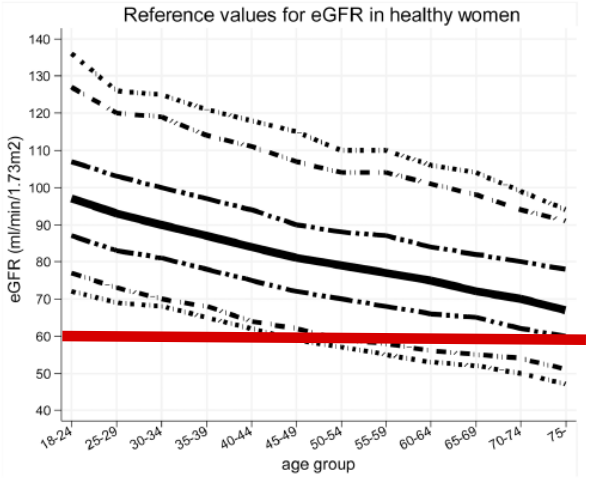
Introduction of the CKD-EPI equation to estimate glomerular filtration rate in a Caucasian population

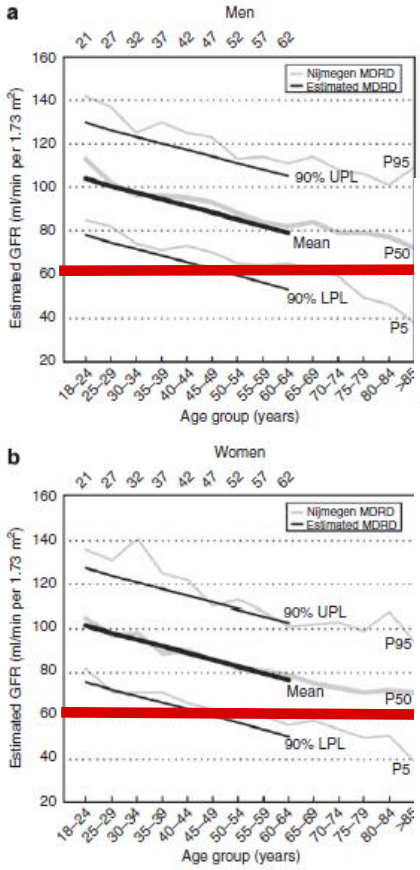
Jan A.J.G. van den Brand[1], Gerben A.J. van Boekel[1], Hans L. Willems[2], Lambertus A.L.M. Kiemeney[3], Martin den Heijer[3,4] and Jack F.M. Wetzels[1]

[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
eGFR
150
100
50
0
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







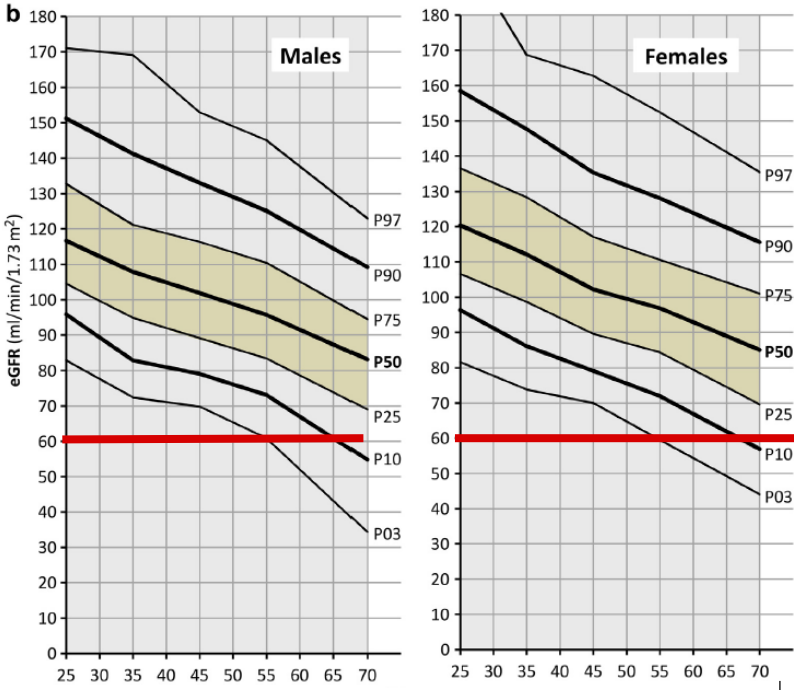


Figure 5 | Comparison of estimated GFR in two different cohorts. Mean, 5th, and 95th percentiles for expected eGFR by the re-expressed MDRD equation in living kidney donors (black lines) and eGFR by the re-expressed MDRD equation in subjects participating in the Nijmegen study[28] (gray lines) among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

The same in Japan…

Baba M, PlosOne, 2015

The same in USA…

Poggio ED, Kidney Int, 2009

The same in Morocco…

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<60mL/min/1.73m²

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)

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

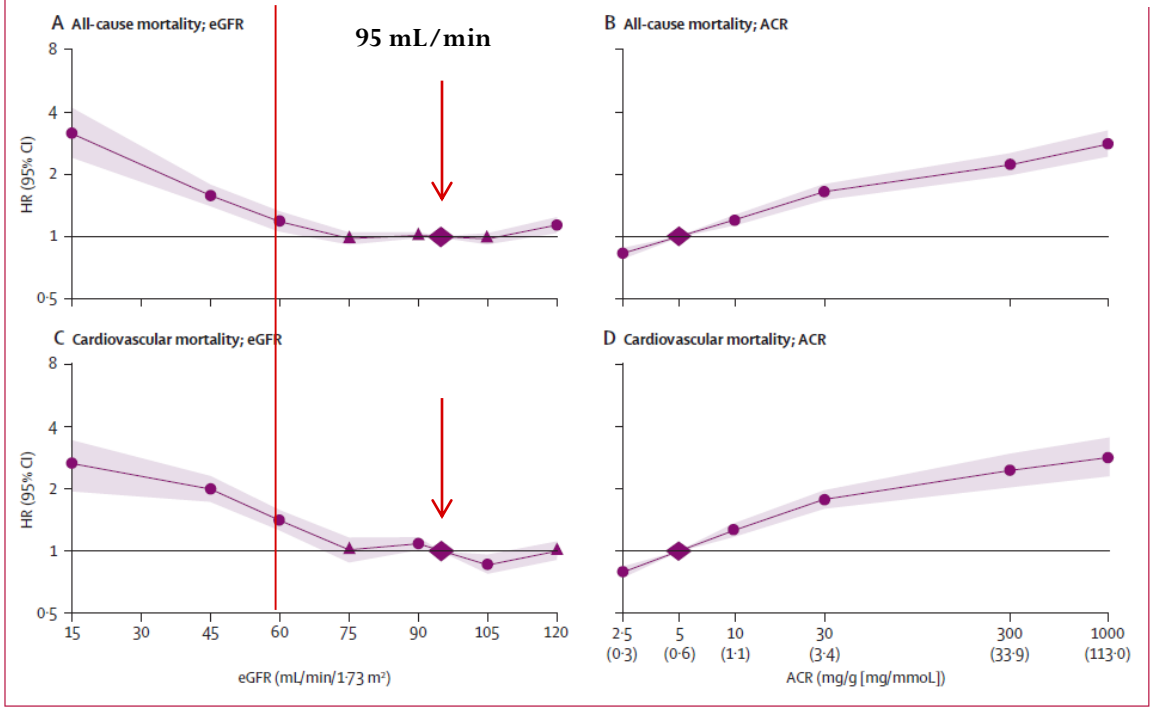


Figure 2: **Hazard ratios and 95% CIs for all-cause and cardiovascular mortality according to spline estimated glomerular filtration rate (eGFR) and albumin-to-creatinine ratio (ACR)**

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

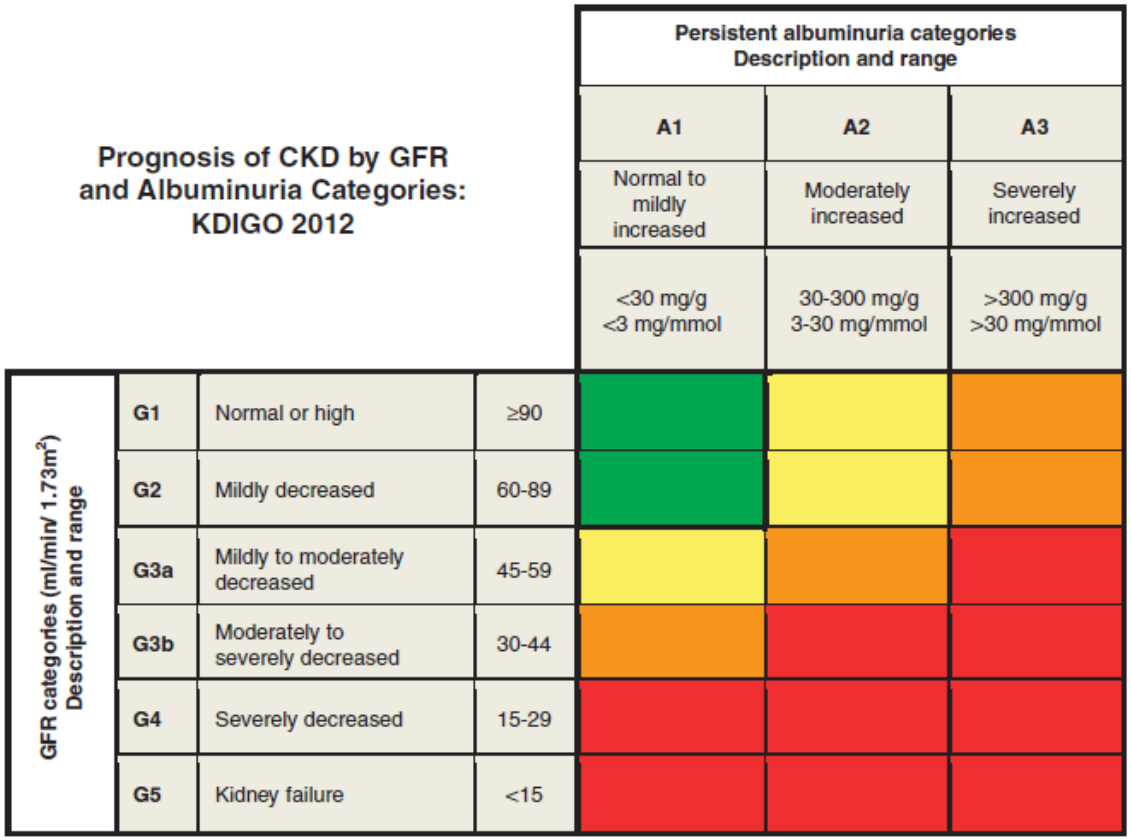


Figure 9 | Prognosis of CKD by GFR and albuminuria category. Green, low risk (if no other markers of kidney disease, no CKD); Yellow, moderately increased risk; Orange, high risk; Red, very high risk. CKD, chronic kidney disease; GFR, glomerular filtration rate; KDIGO, Kidney Disease: Improving Global 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 CKD 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 CKD in the healthy elderly

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- Is it relevant from an epidemiological point of view?

Back to the « prognostic » argument

ORIGINAL CONTRIBUTION

ONLINE FIRST

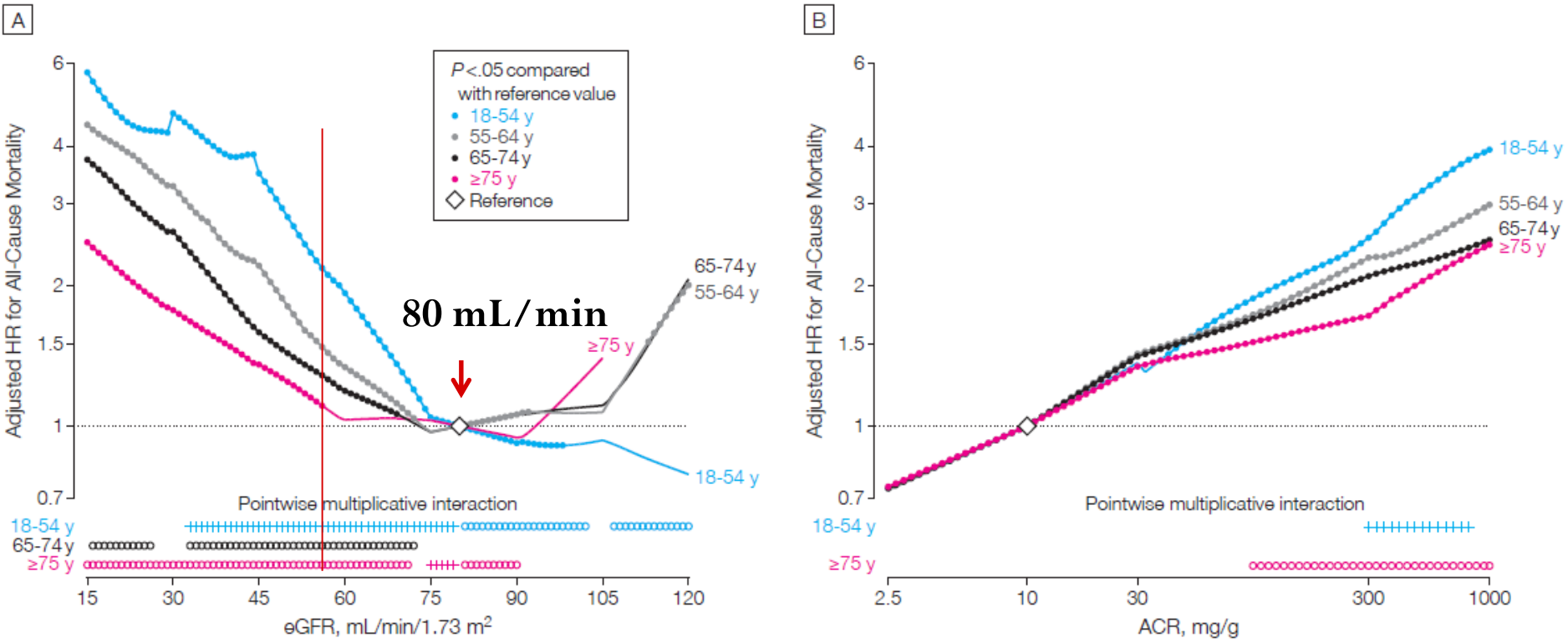
Age and Association of Kidney Measures With Mortality and End-stage Renal Disease

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



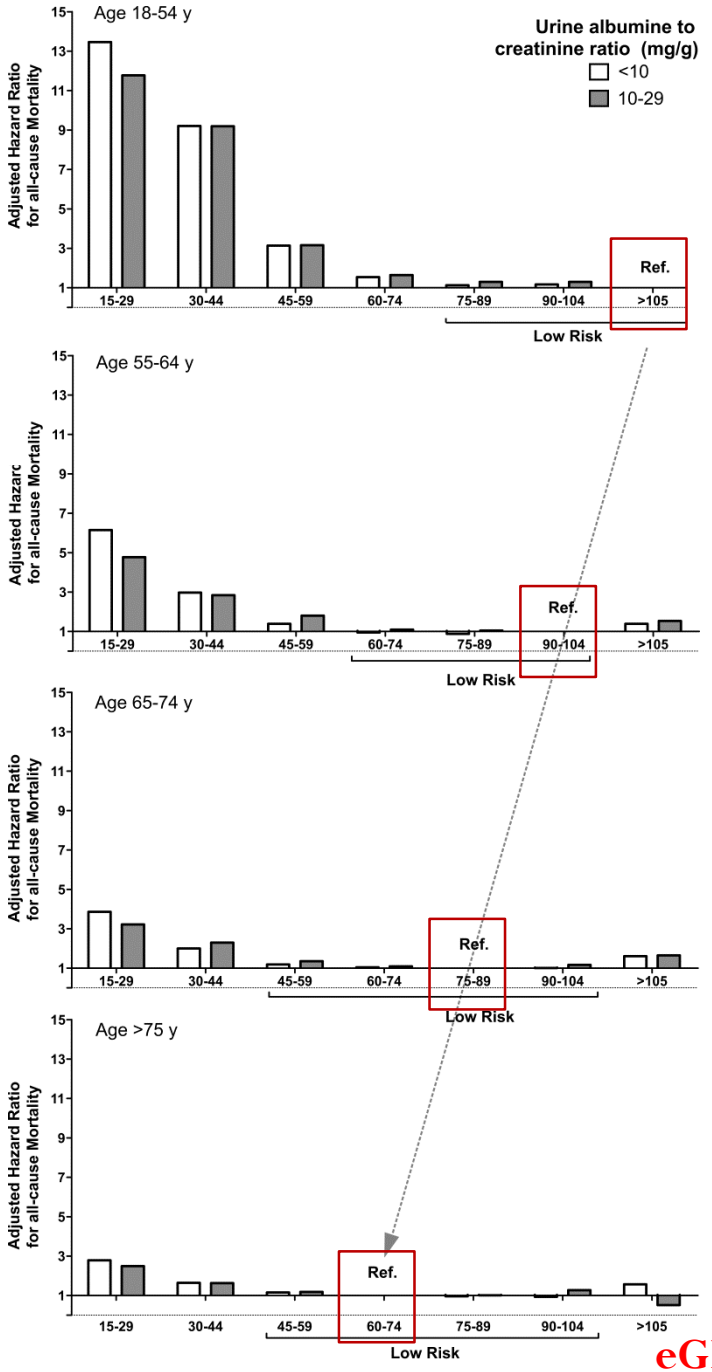
- The same GFR reference group is considered for all age
- Reference group can however be changed
- In each age category, we propose to choose as the reference group, the eGFR group was the lowest mortality

Age 18-54 y =>

Age 55-64 y =>

Age 65-74 y =>

Age >75 y =>



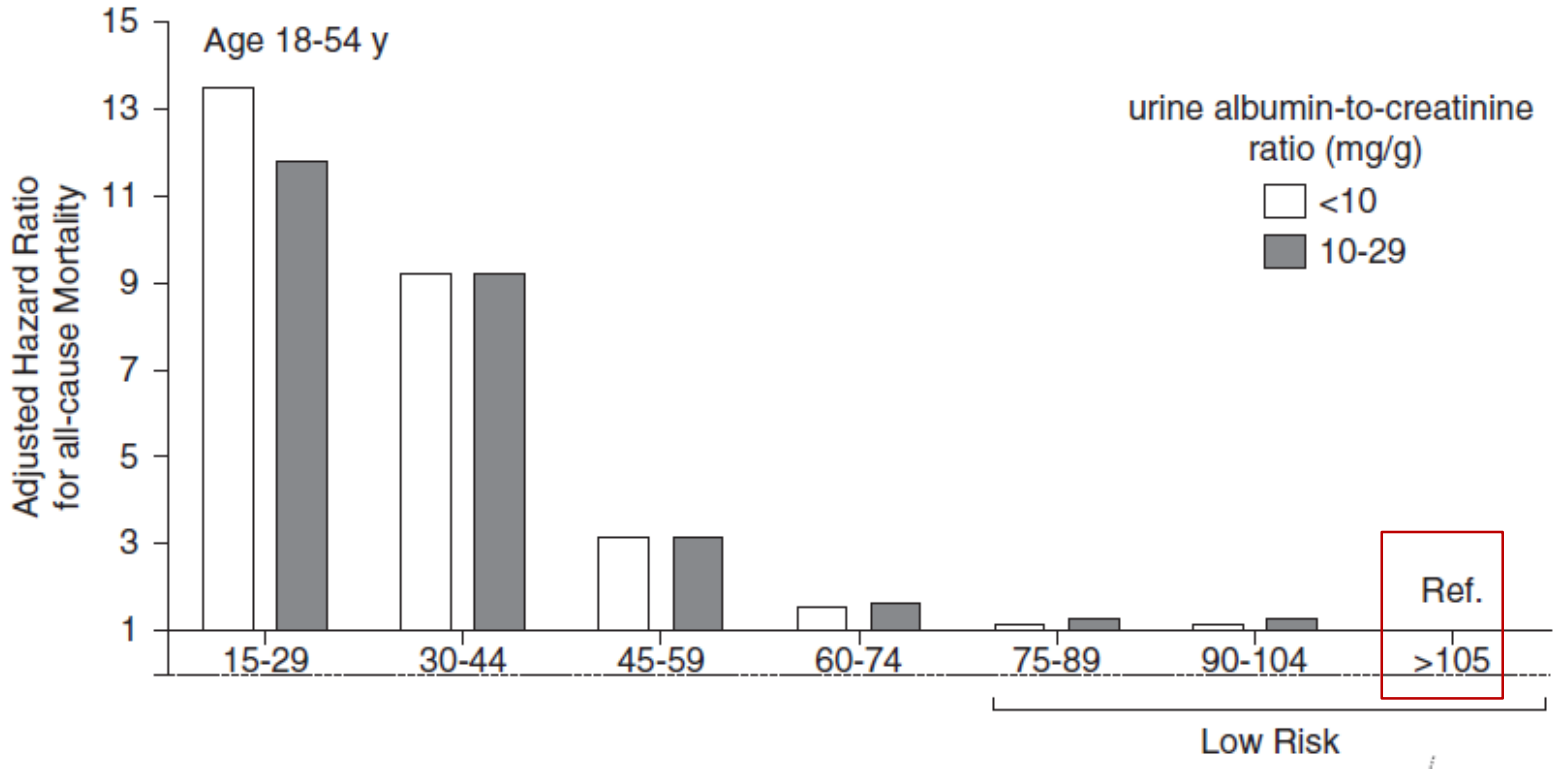
Data from:

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

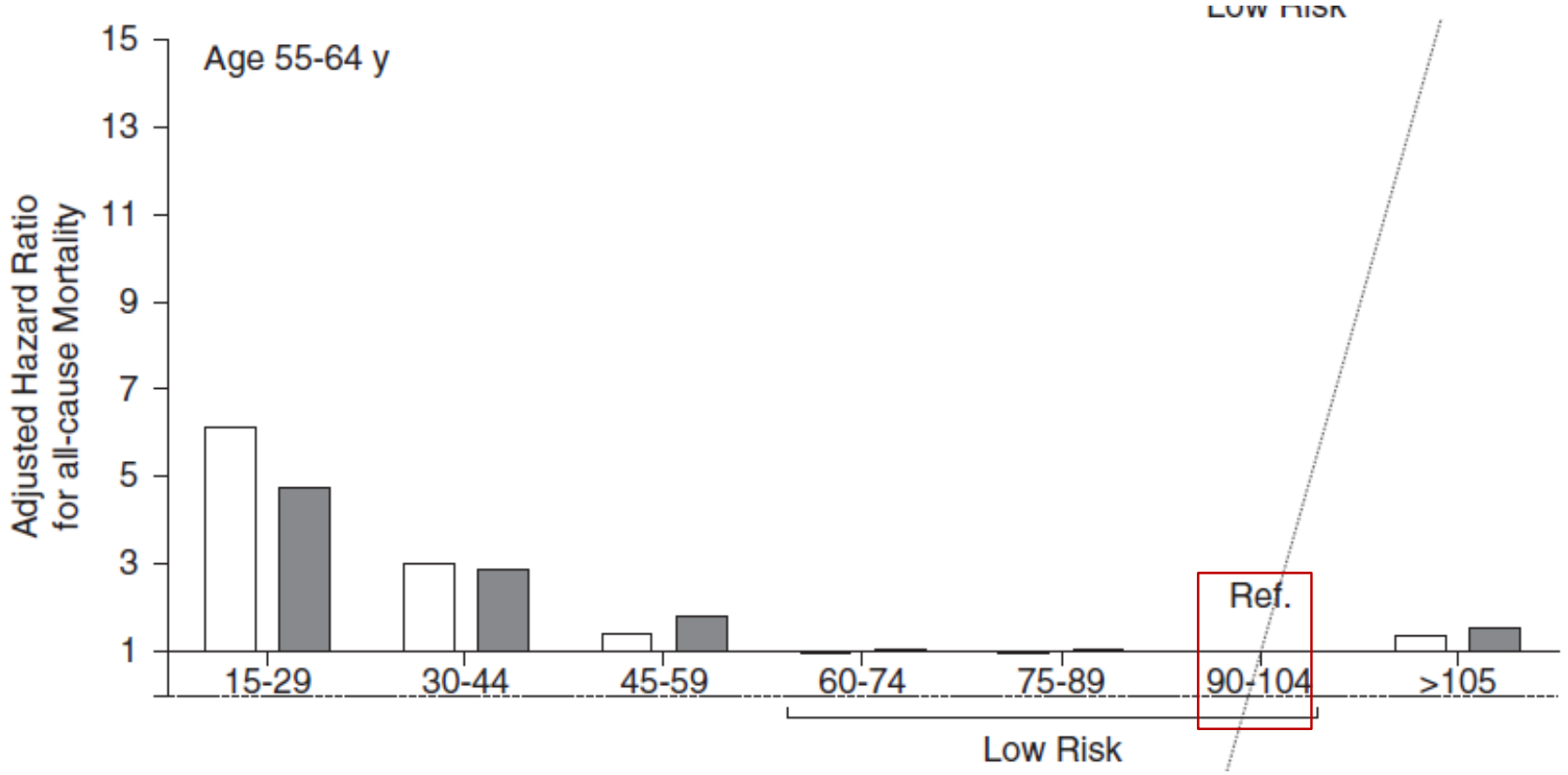
Delanaye P, Clin Biochem Rev, 2016, p17
Glassock RJ, J Bras Nefrol, 2017, p59

eGFR

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
15-29
30-44
45-59
60-74
75-89
90-104
>105
Ref.
Low Risk

Age 55-64 y


Age 55-64 y
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15
13
11
9
7
5
3
1
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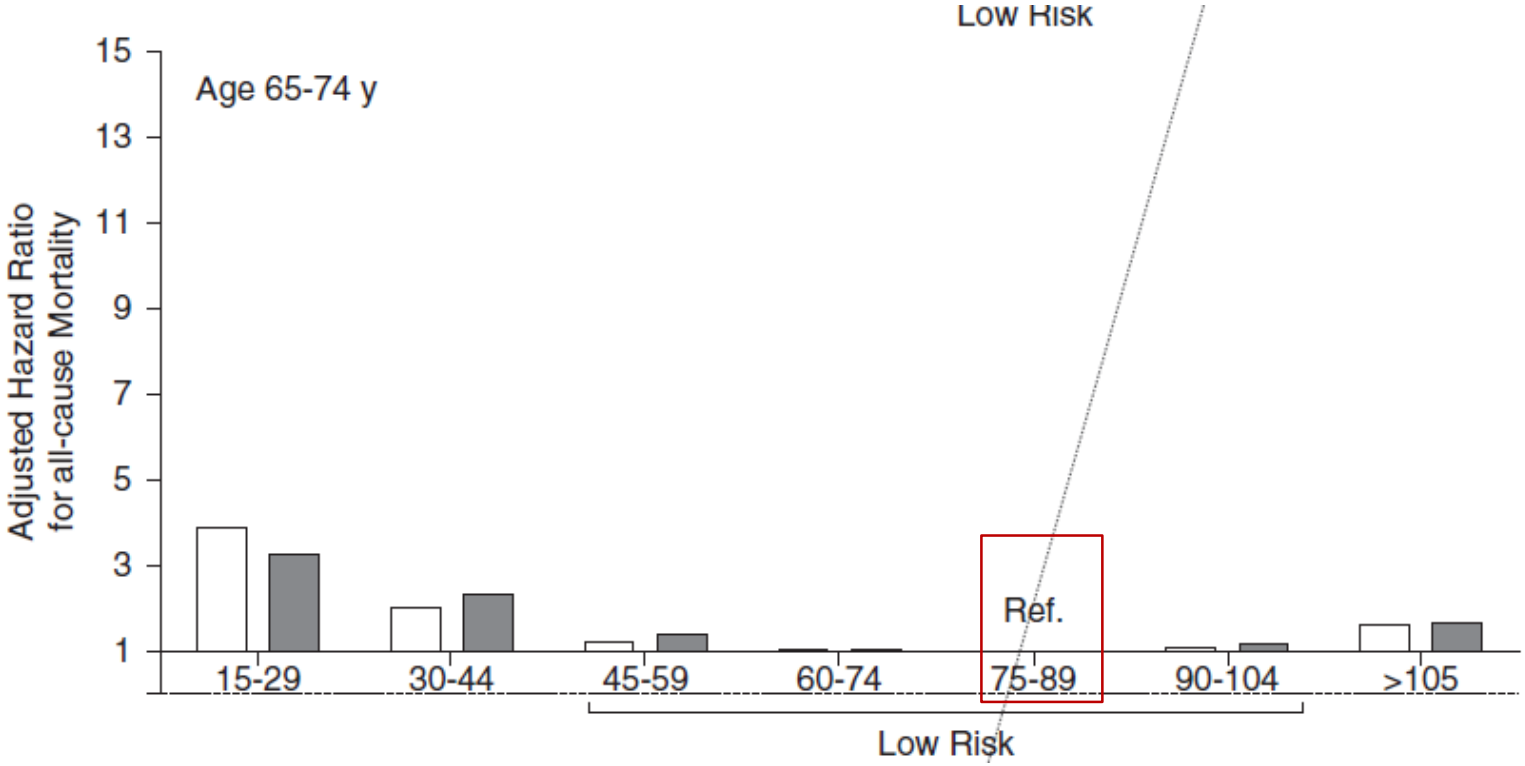
45-59
60-74
75-89
90-104
>105
Ref.
Low Risk

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

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?

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

REVIEW www.jasn.org

CKD: A Call for an Age-Adapted Definition

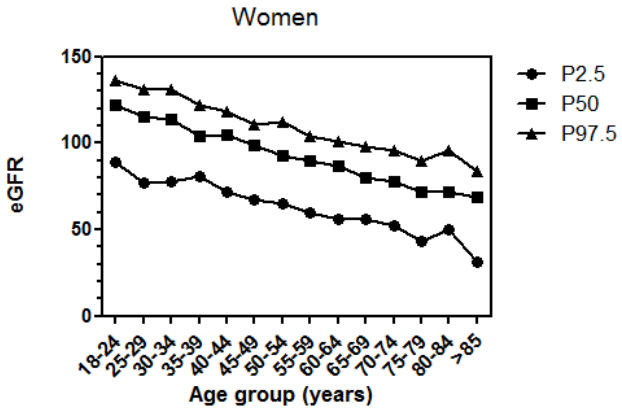
Pierre Delanaye,[1] Kitty J. Jager,[2] Arend Bökenkamp,[3] Anders Christensson,[4] Laurence Dubourg,[5] Bjørn Odvar Eriksen,[6,7] François Gaillard,[8] Giovanni Gambaro,[9] Markus van der Giet,[10] Richard J. Glassock,[11] Olafur S. Indridason,[12] Marco van Londen,[13] Christophe Mariat,[14] Toralf 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

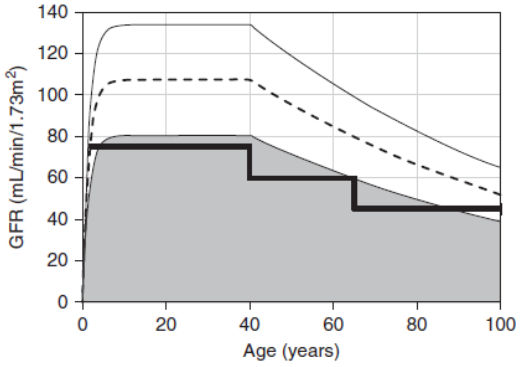


Figure 3. Age-specific thresholds in relation to age-specific GFR percentiles. GFR cut-off values and percentiles according to age (here percentiles of eGFR are calculated using the FAS equation). The bold line represents an age-adapted threshold for CKD: 75 ml/min per 1.73 m^2 for age below 40 years, 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...

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But…

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clinical investigation www.kidney-international.org

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

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

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)

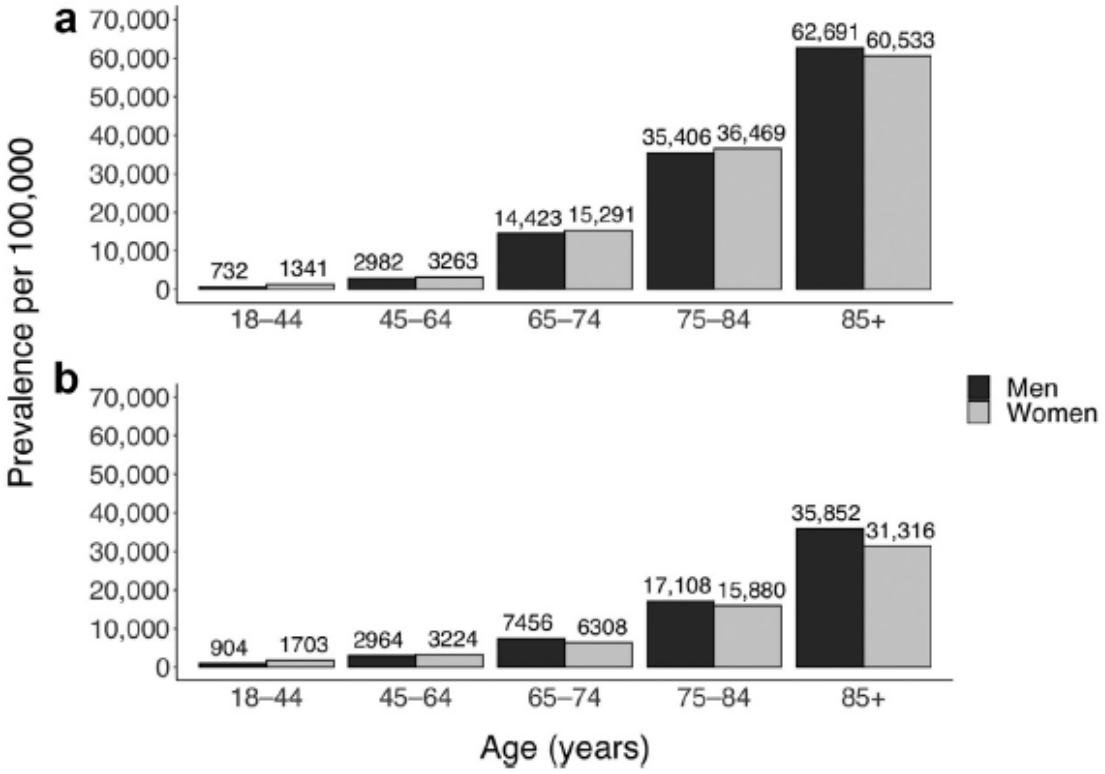


Figure 2| Mean annual prevalence of chronic kidney disease stages 1–5 by age group and sex, using (a) the Kidney Disease: Improving Global Outcomes (KDIGO) definition and (b) age-adapted estimated glomerular filtration rate (eGFR) thresholds.

Some pathological data…

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Single-Nephron Glomerular Filtration Rate in Healthy Adults

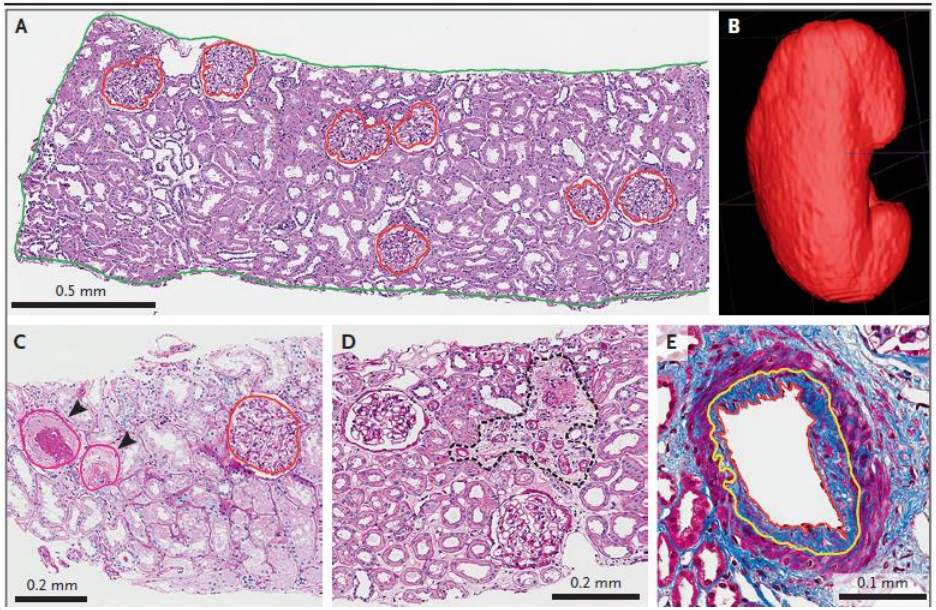
Aleksandar Denic, M.D., Ph.D., Jerry Mathew, M.D.,
Lilach O. Lerman, M.D., Ph.D., John C. Lieske, M.D., Joseph J. Larson, B.S.,
Mariam P. Alexander, M.D., Emilio Poggio, M.D., Richard J. Glassock, M.D.,
and Andrew D. Rule, M.D.

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

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.

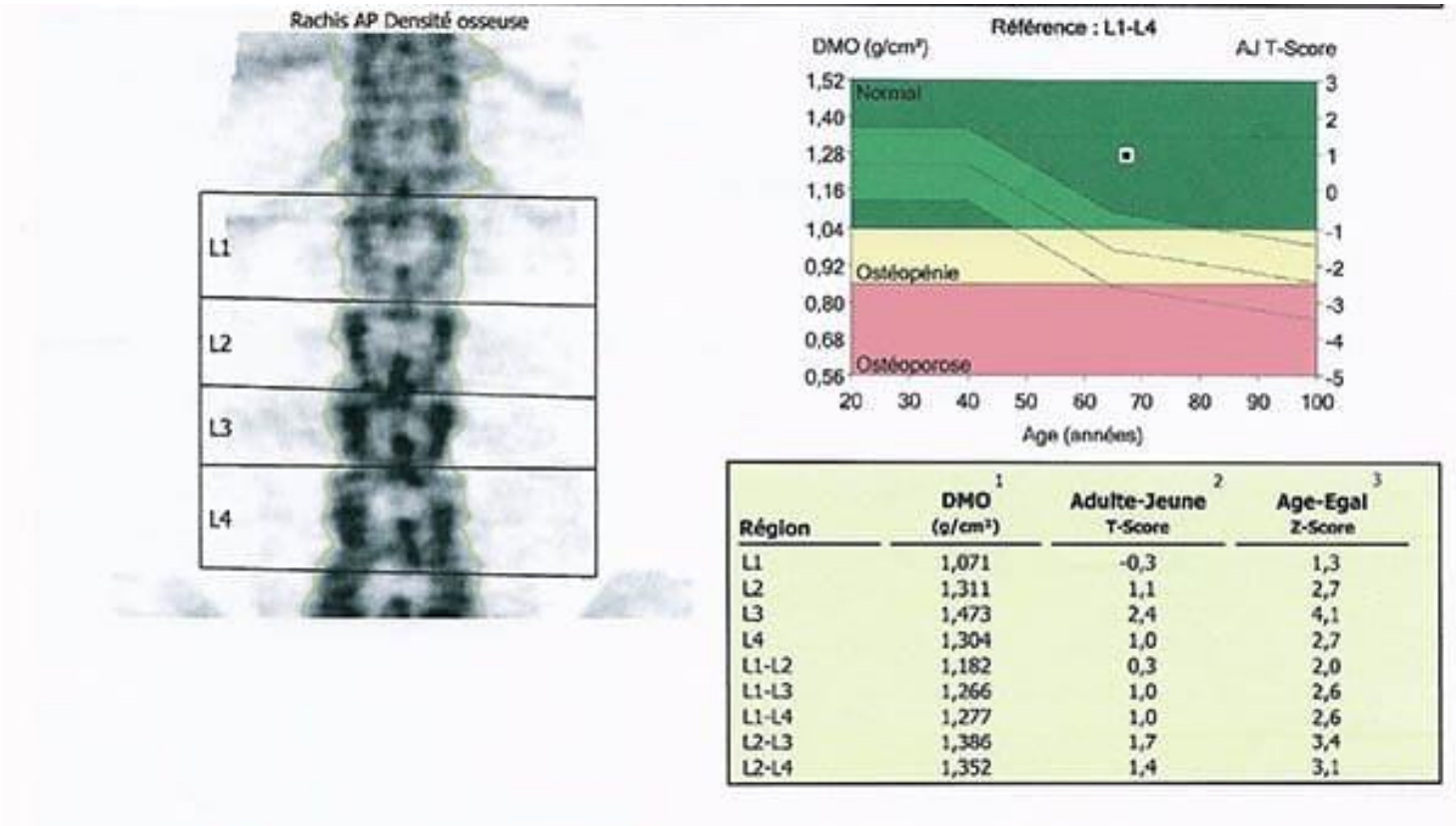
JASN® Journal of the American Society of Nephrology

Authors: Asghar, MS; Denic, A; Mullan, AF; Moustafa, A; Barisoni, L; Alexander, MP; Stegall, MD; Augustine, J; Leibovich, BC; Thompson, H; Rule, AD

Title: Age-Based versus Young-Adult Thresholds for Nephrosclerosis on Kidney Biopsy and Prognostic Implications for Chronic Kidney Disease

Manuscript Type: Original Article - Clinical Epidemiology

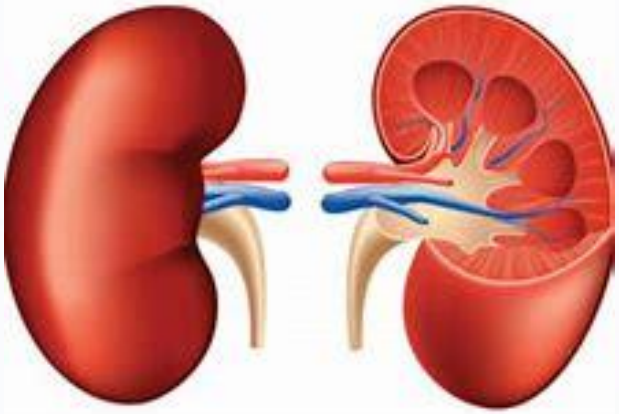
An osteoporosis-like approach

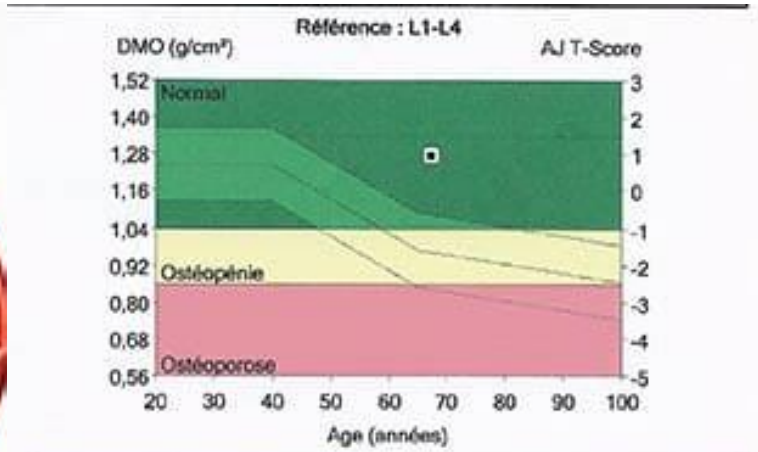


Région	DMO [1] (g/cm²)	Adulte-Jeune [2] T-Score	Age-Egal [3] Z-Score
L1	1,071	-0,3	1,3
L2	1,311	1,1	2,7
L3	1,473	2,4	4,1
L4	1,304	1,0	2,7
L1-L2	1,182	0,3	2,0
L1-L3	1,266	1,0	2,6
L1-L4	1,277	1,0	2,6
L2-L3	1,386	1,7	3,4
L2-L4	1,352	1,4	3,1

FRAX

An osteoporosis-like approach





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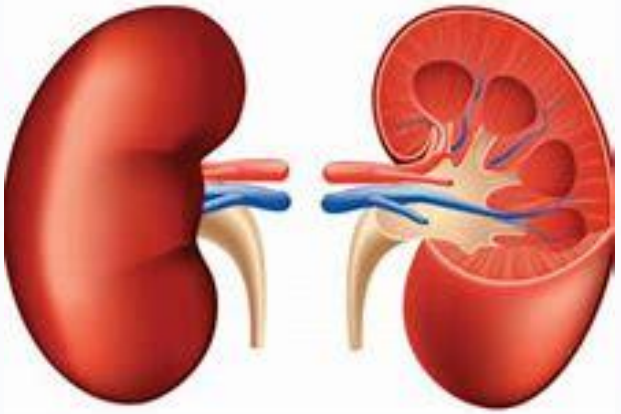

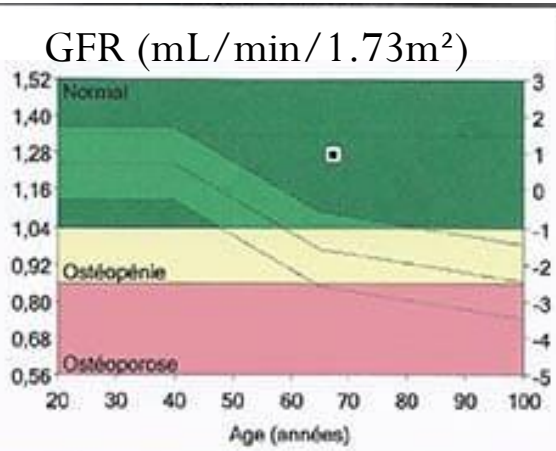

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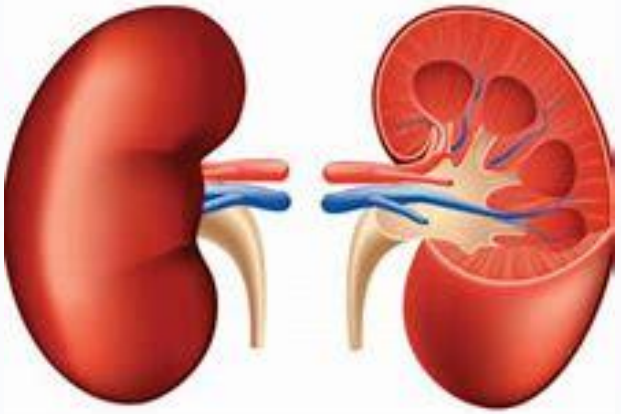
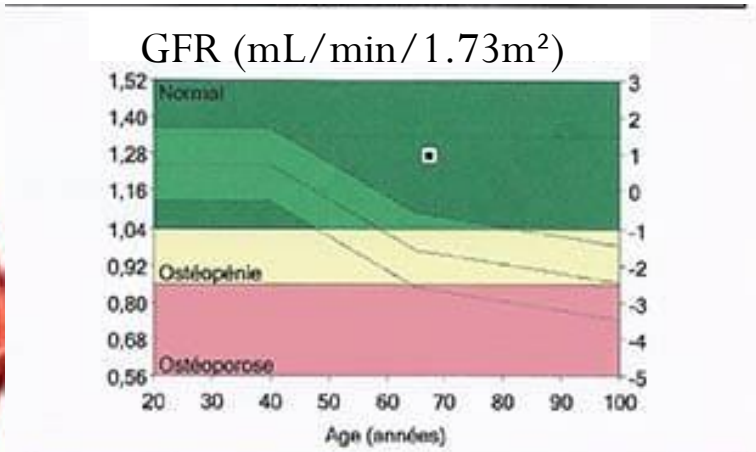
L1-L4		1,0	2,6
L2-L3		1,7	3,4
L2-L4		1,4	3,1

G F R

FRAX

An osteoporosis-like approach





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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

G F R

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

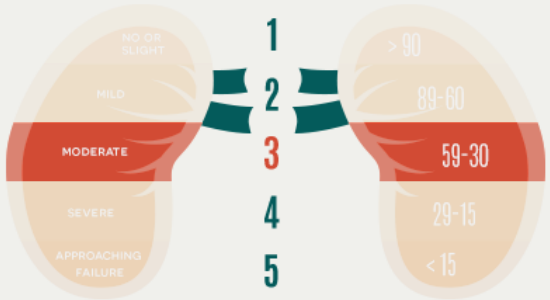
ASSESSMENT

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	AT 5 YEARS
0.96 %	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 LIÈGE
DATES À RETENIR
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Thank you!