Too much Nephrology?
The CKD "epidemic" is overstated!

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55th ERA-EDTA CONGRESS
Copenhagen Denmark May 24th - 27th 2018

- I have no conflict of interest to declare

CKD prevalence is around ≈10%

11,1% (♂: 10,4% ♀: 11,8%) **in Mills KT, Kidney Int, 2015, p950**

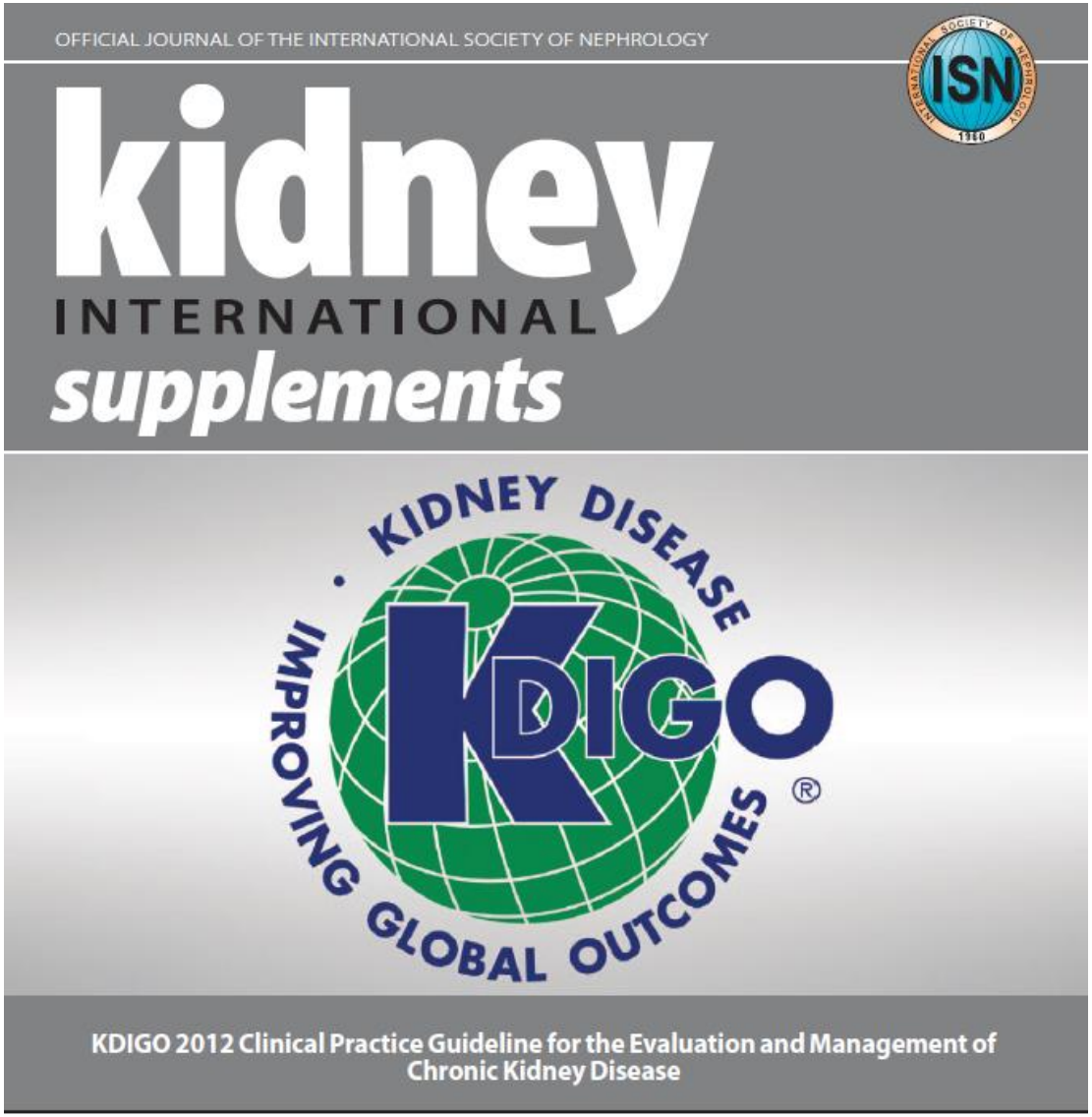
Stage 3-5 : 5,3%

13,4% (♂: 12,8% ♀: 14,6%) **in Hill NR, PlosOne, 2016, e0158765**

Stage 3-5: 8,1%

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

International guidelines in Nephrology



GFR categories in CKD **Chronic Kidney Disease**

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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1.4.1: Evaluation of chronicity

1.4.1.1: In people with GFR <60 ml/min/1.73 m^2 (GFR categories G3a-G5) or markers of kidney damage, review past history and previous measurements to determine duration of kidney disease. (*Not Graded*)

- If duration is >3 months, CKD is confirmed. Follow recommendations for CKD.
- If duration is not >3 months or unclear, CKD is not confirmed. Patients may have CKD or acute kidney diseases (including AKI) or both and tests should be repeated accordingly.

60 mL/min/1.73 m²

Two topics

- Age and CKD definition
- Chronicity

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 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

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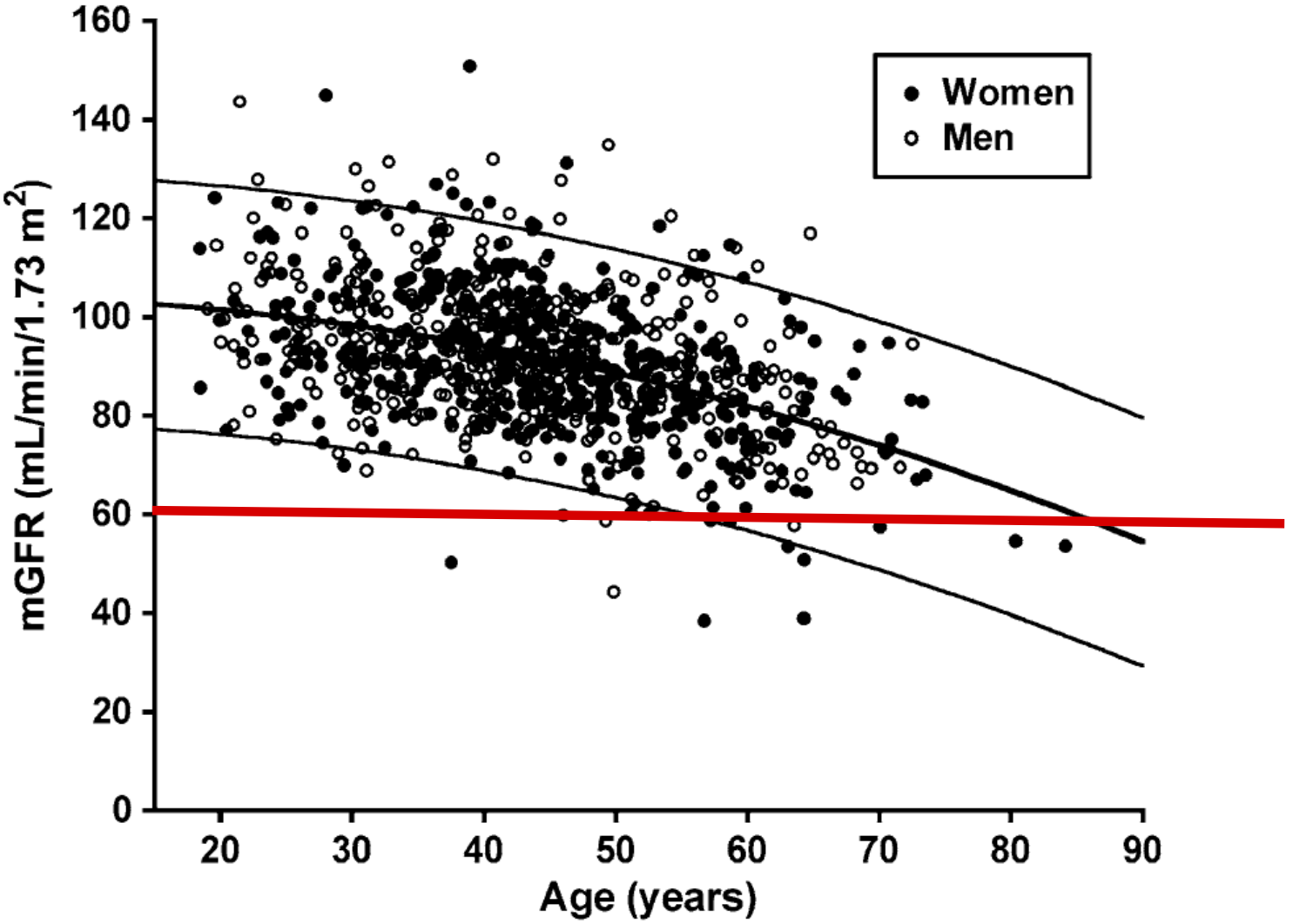


GFR measured by ^{51}Cr-EDTA in 904 potential living kidney donors

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

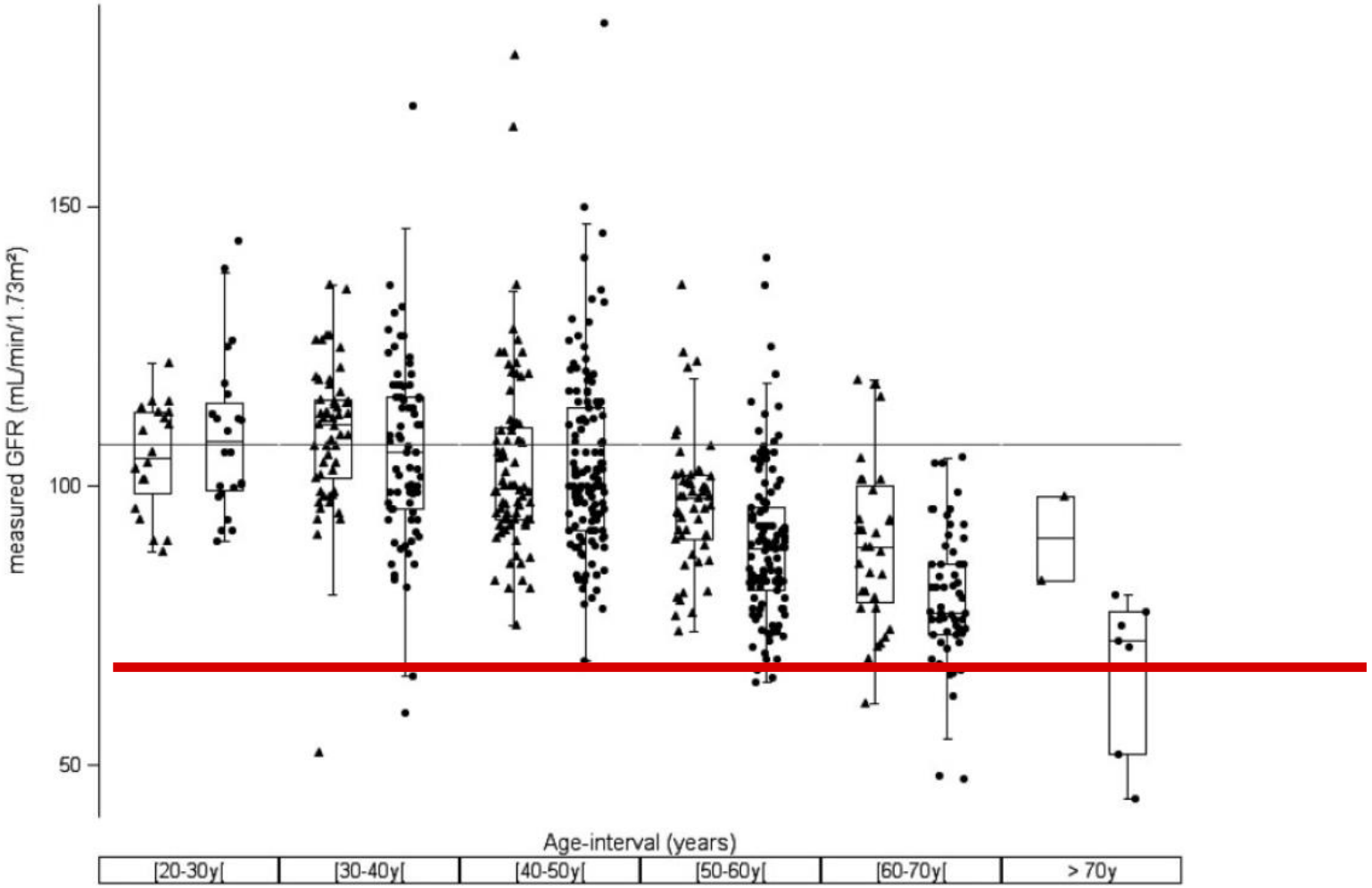


Fig. 1. Box plot for mGFR versus age decades for female (filled circles) and male (filled triangles) potential kidney donors ($n = 633$). A horizontal reference line is drawn at GFR = 107.3 mL/min/1.73 m^2.

GFR in 633 living kidney donors (Belgium, France)

Pottel H, Clin Kidney J, 2017, p545

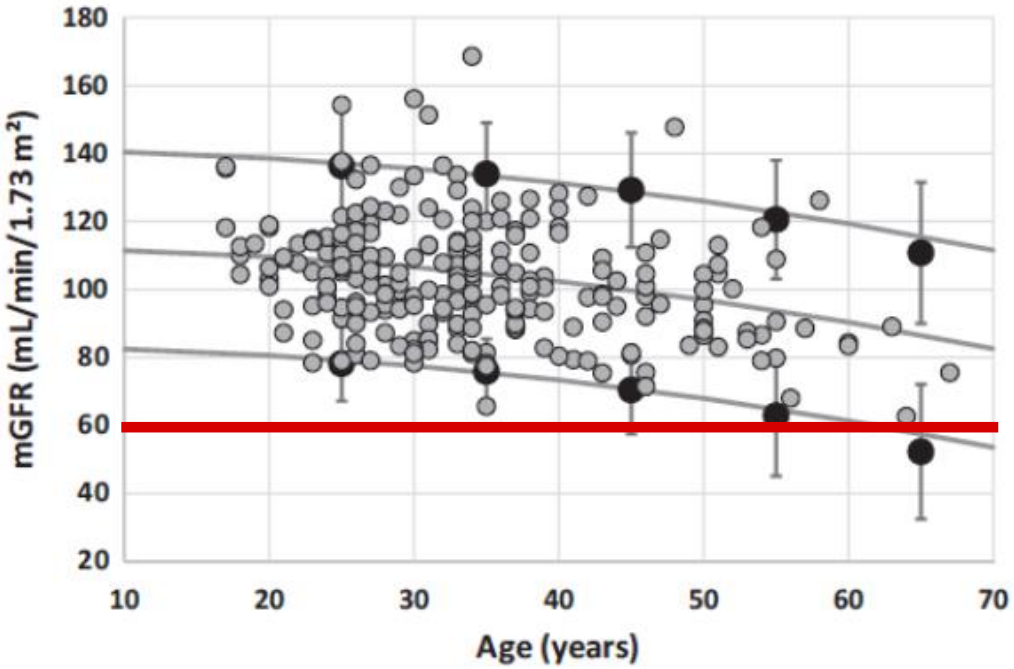


FIGURE 2: mGFR percentiles according to age. The solid grey circles are mGFR results and solid grey lines are 2.5th, 50th and 97.5th percentiles for mGFR in the current African population. The solid black circles with error bars are upper and lower reference limits obtained from the meta-analysis study including 633 Caucasian potential living kidney donors.

GFR by iohexol plasma clearance in 237 healthy blood donors (Ivory Coast)

Yayo E, Nephrol Dial Transplant, 2018, in press

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

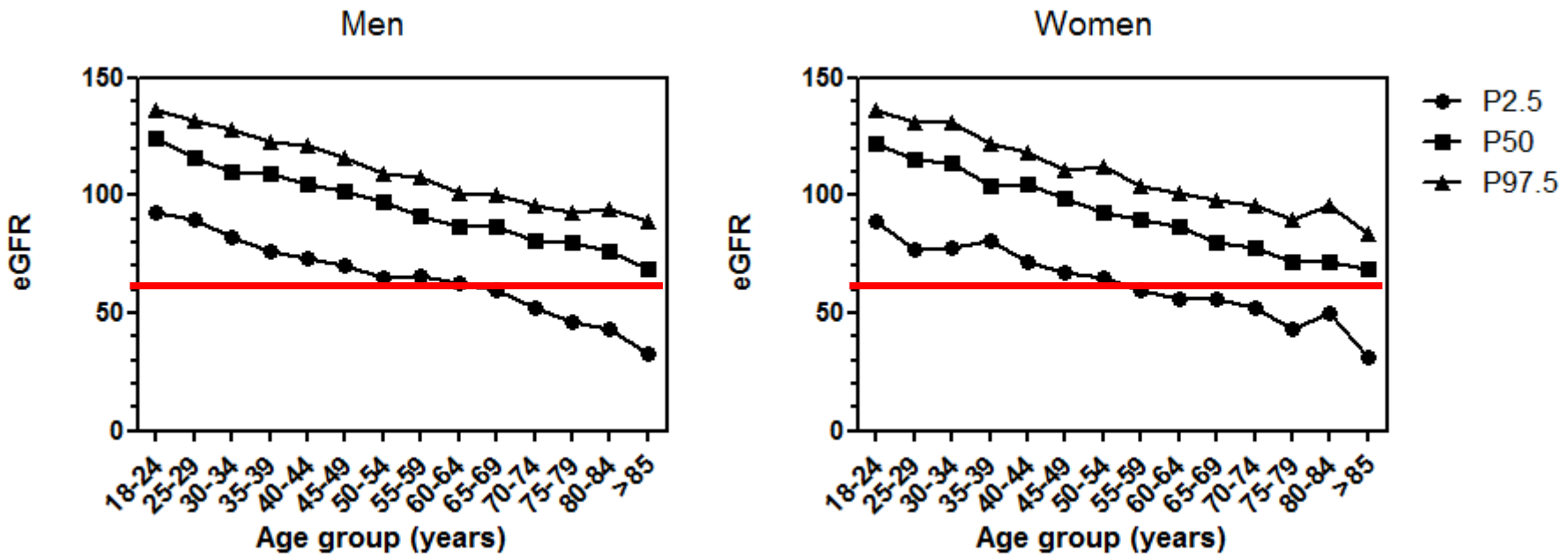
- Healthy population in the Netherlands
- CKD-EPI equation to estimate GFR
- No diabetes, no hypertension, no specific therapy
- 1663 men 2073 women

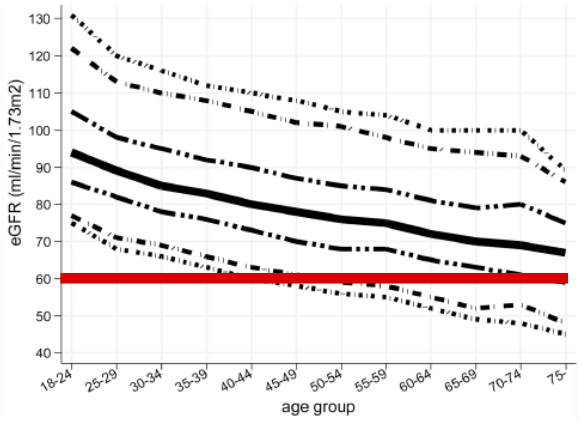
Nephrol Dial Transplant (2011) 26: 3176–3181
doi: 10.1093/ndt/gfr003
Advance Access publication 16 February 2011

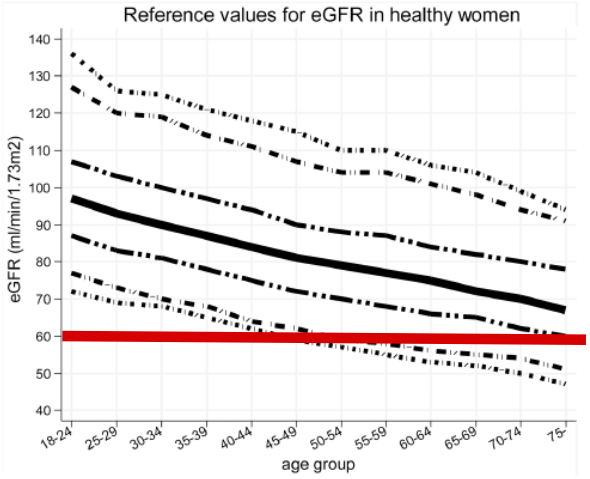
Introduction of the CKD-EPI equation to estimate glomerular filtration rate in a Caucasian population

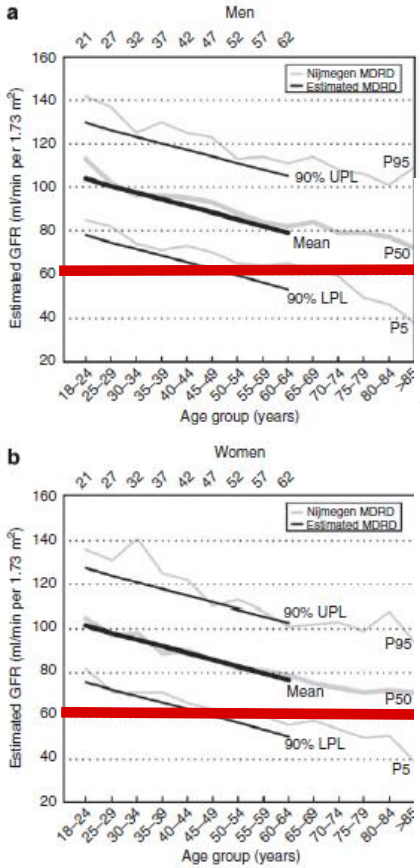
Jan A.J.G. van den Brand[1], Gerben A.J. van Boekel[1], Hans L. Willems[2], Lambertus A.L.M. Kiemeney[3], Martin den Heijer[3,4] and Jack F.M. Wetzels[1]

[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







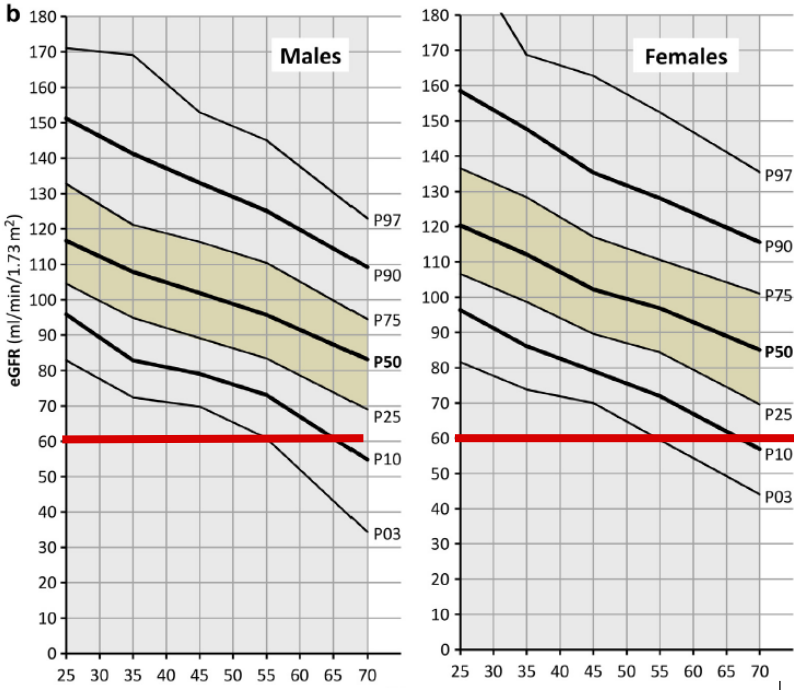


Figure 5 | Comparison of estimated GFR in two different cohorts. Mean, 5th, and 95th percentiles for expected eGFR by the re-expressed MDRD equation in living kidney donors (black lines) and eGFR by the re-expressed MDRD equation in subjects participating in the Nijmegen study[28] (gray lines) among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

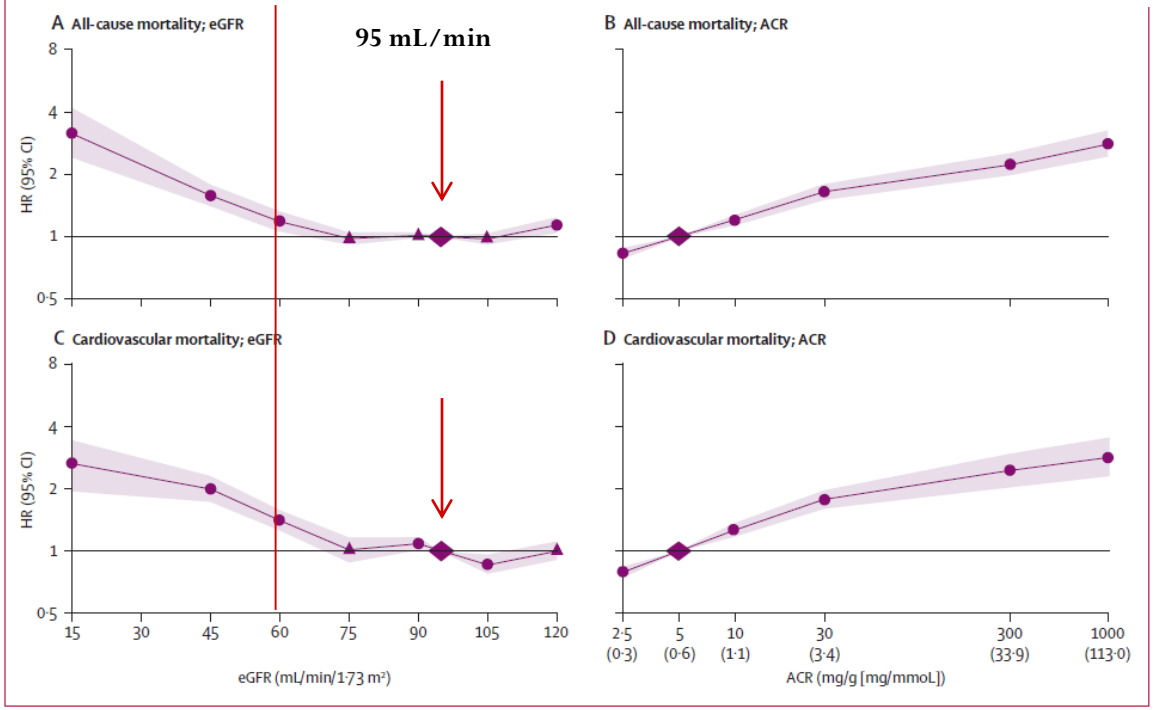


Figure 2: **Hazard ratios and 95% CIs for all-cause and cardiovascular mortality according to spline estimated glomerular filtration rate (eGFR) and albumin-to-creatinine ratio (ACR)**

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

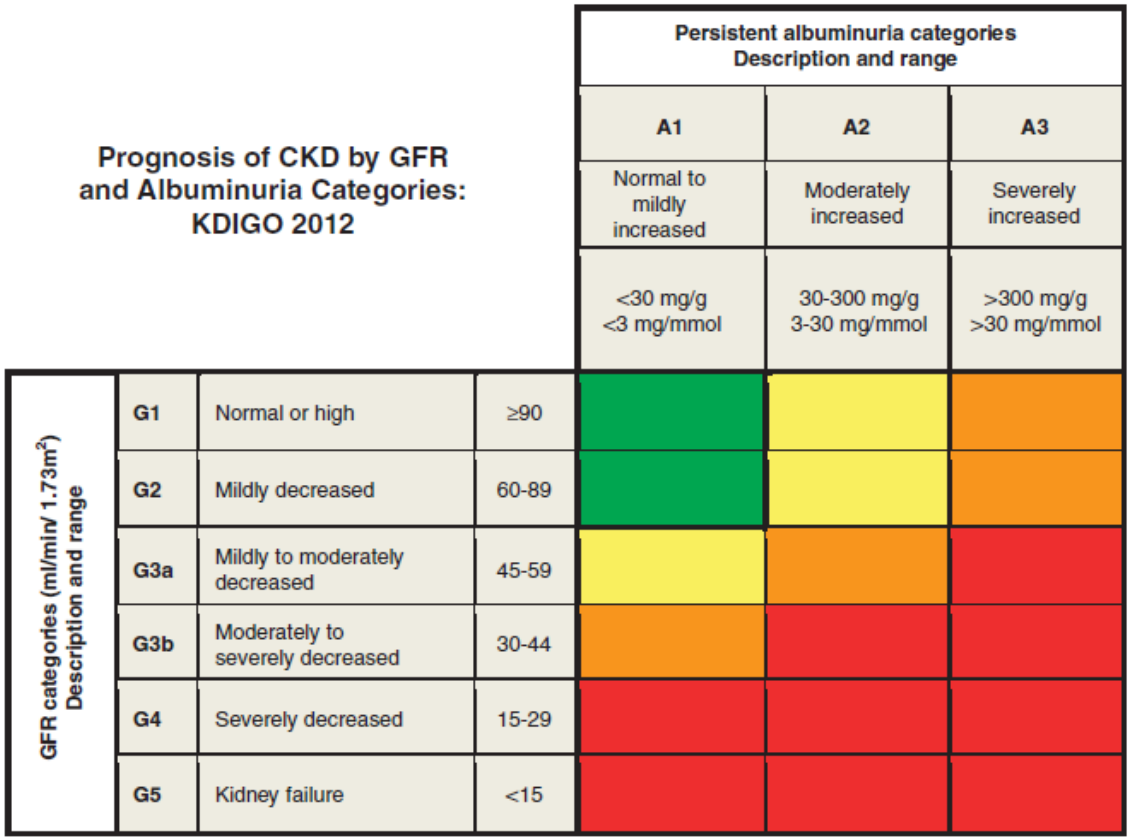


Figure 9 | Prognosis of CKD by GFR and albuminuria category. Green, low risk (if no other markers of kidney disease, no CKD); Yellow, moderately increased risk; Orange, high risk; Red, very high risk. CKD, chronic kidney disease; GFR, glomerular filtration rate; KDIGO, Kidney Disease: Improving Global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

But…

- What about the prognostic argument?
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Back to the « prognostic » argument

ORIGINAL CONTRIBUTION

ONLINE FIRST

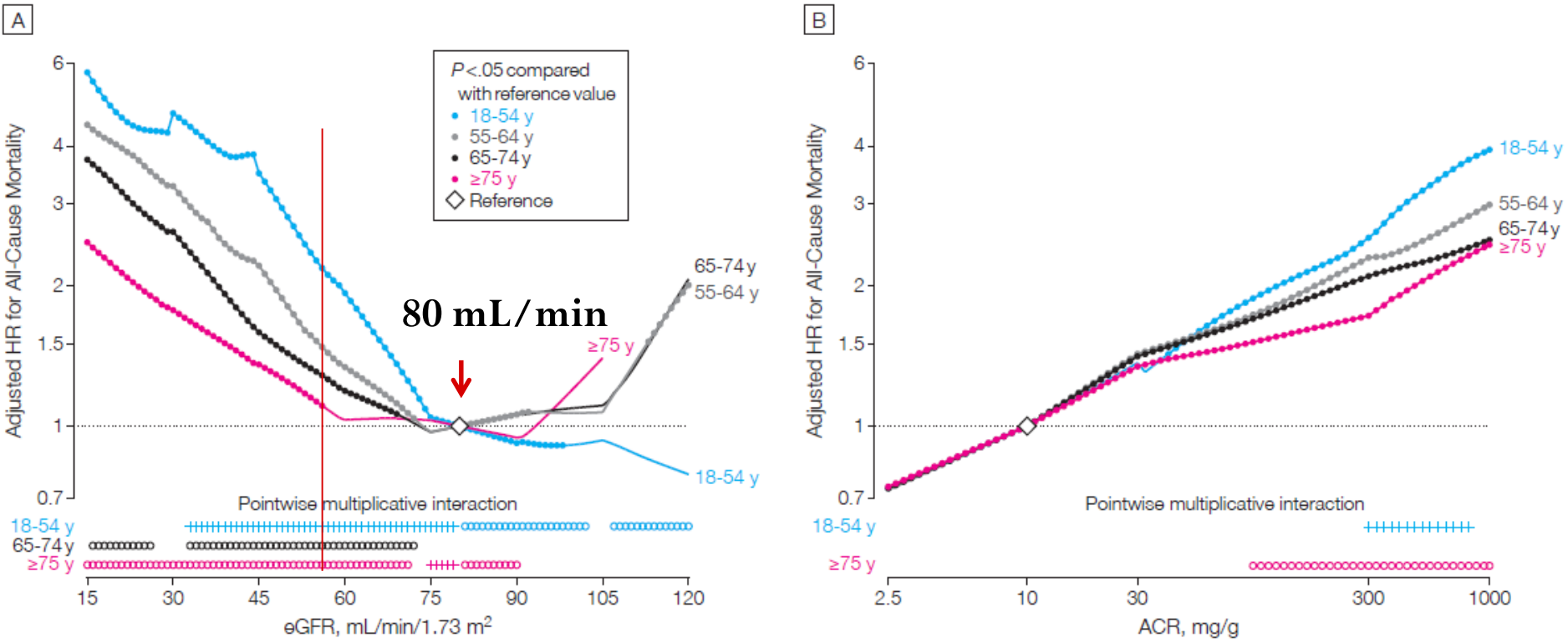
Age and Association of Kidney Measures With Mortality and End-stage Renal Disease

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



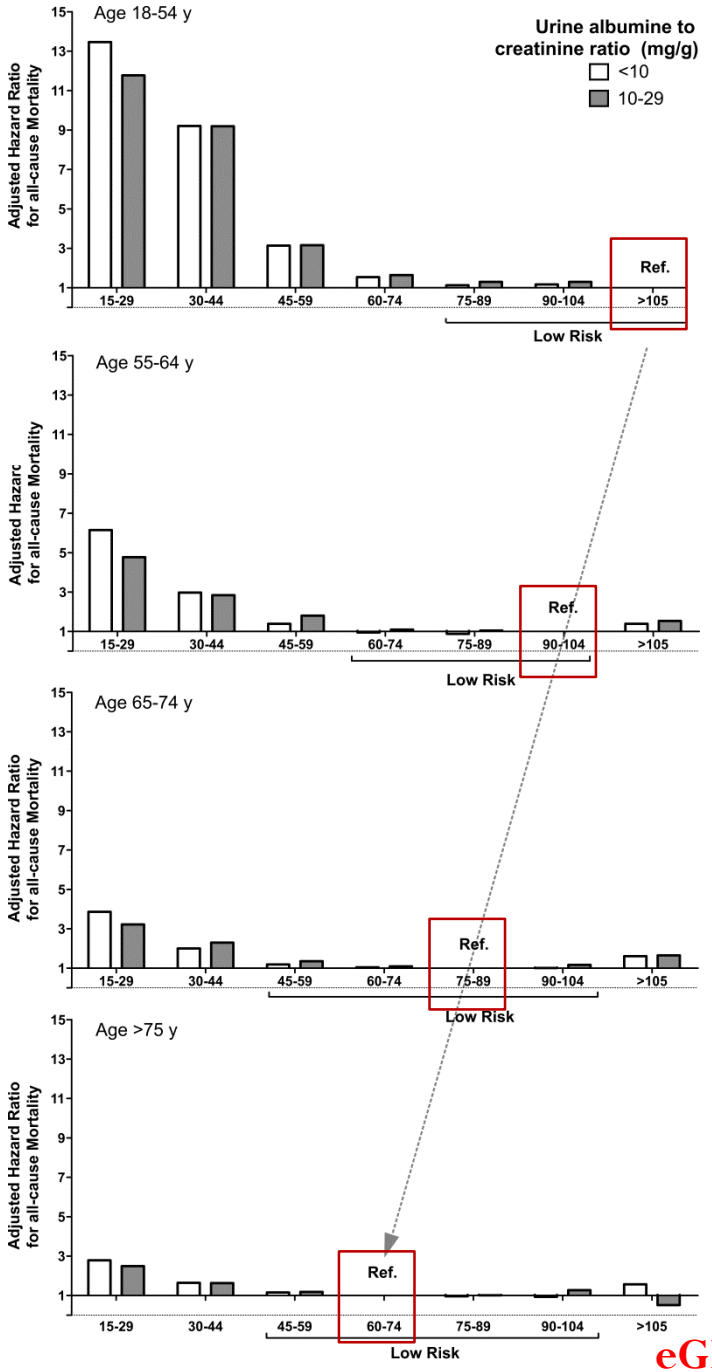
- The same GFR reference group is considered for all age
- Reference can however change
- In each age category, we propose to choose as the reference group, the eGFR group was the lowest mortality

Age 18-54 y =>

Age 55-64 y =>

Age 65-74 y =>

Age >75 y =>



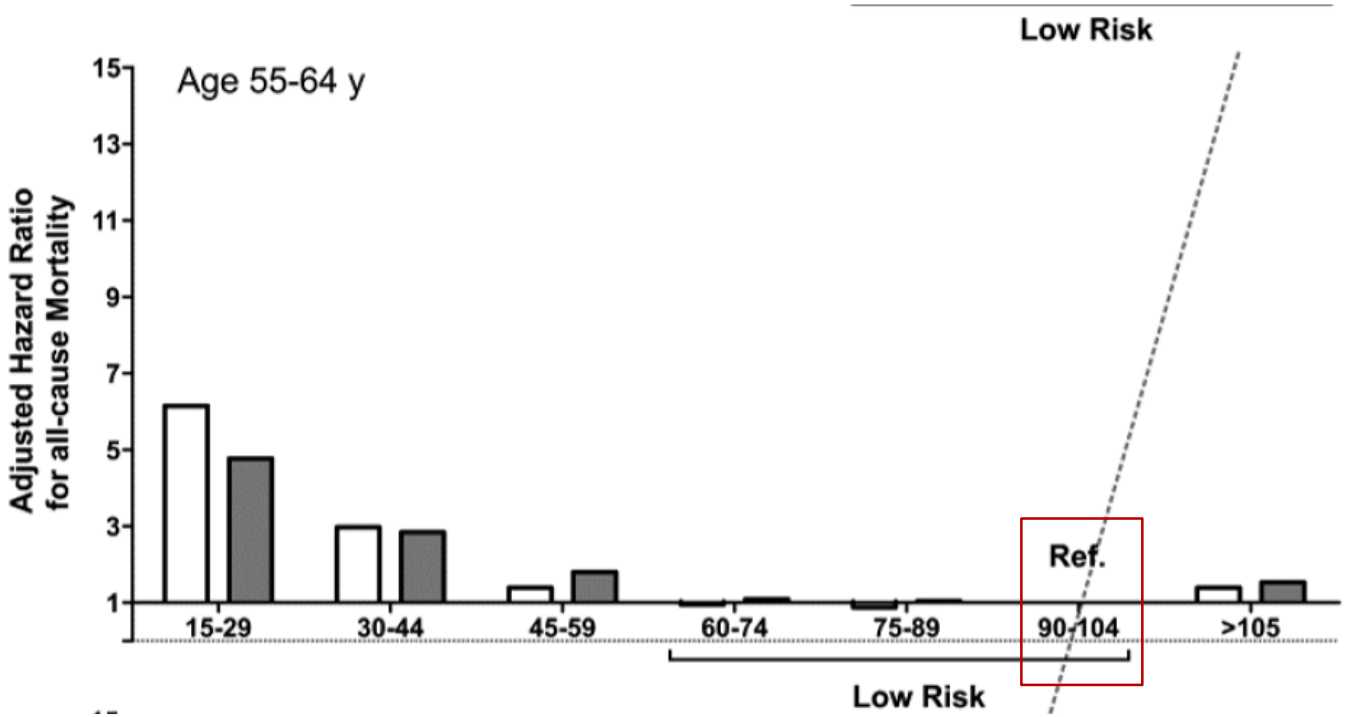
Data from:

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

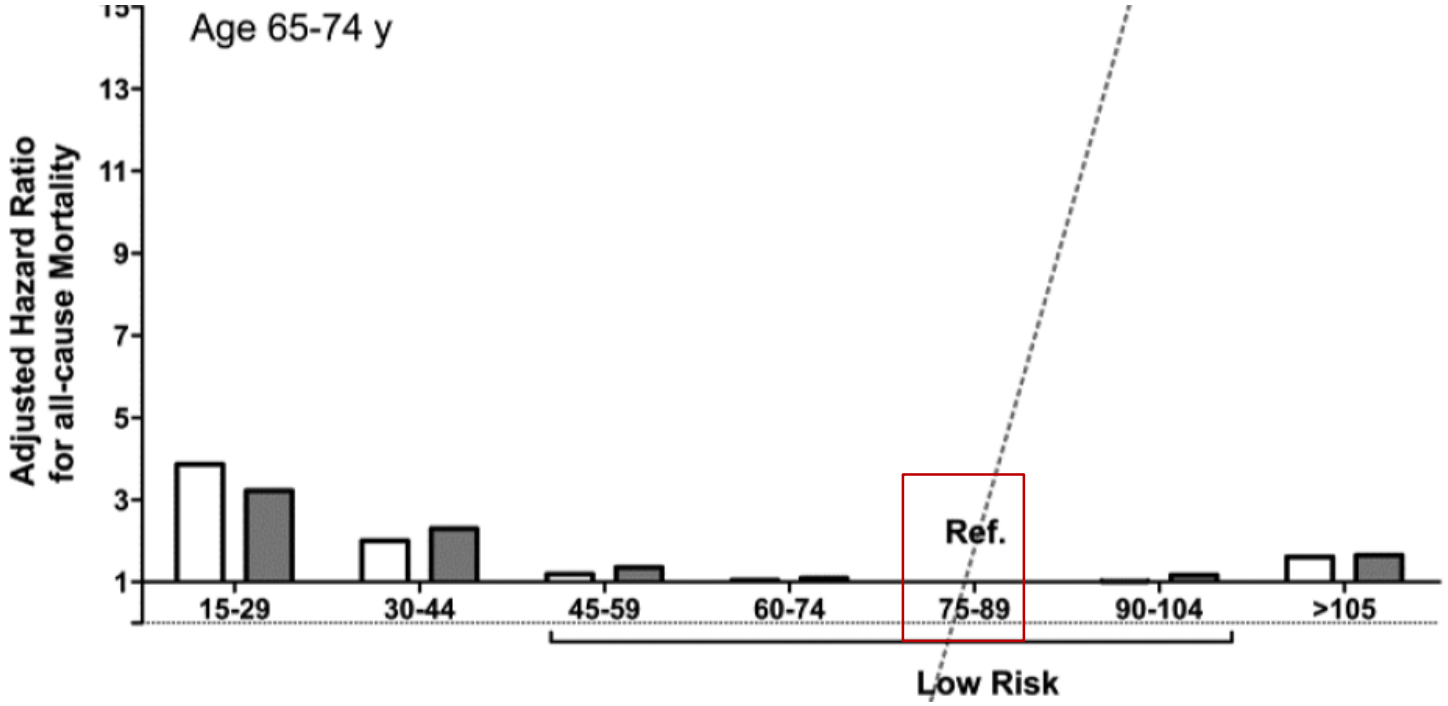
Delanaye P, Clin Biochem Rev, 2016, p17
Glassock RJ, J Bras Nefrol, 2017, p59

eGFR

Age 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


Age 65-74 y
Adjusted Hazard Ratio for all-cause Mortality
13
11
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3
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Low Risk

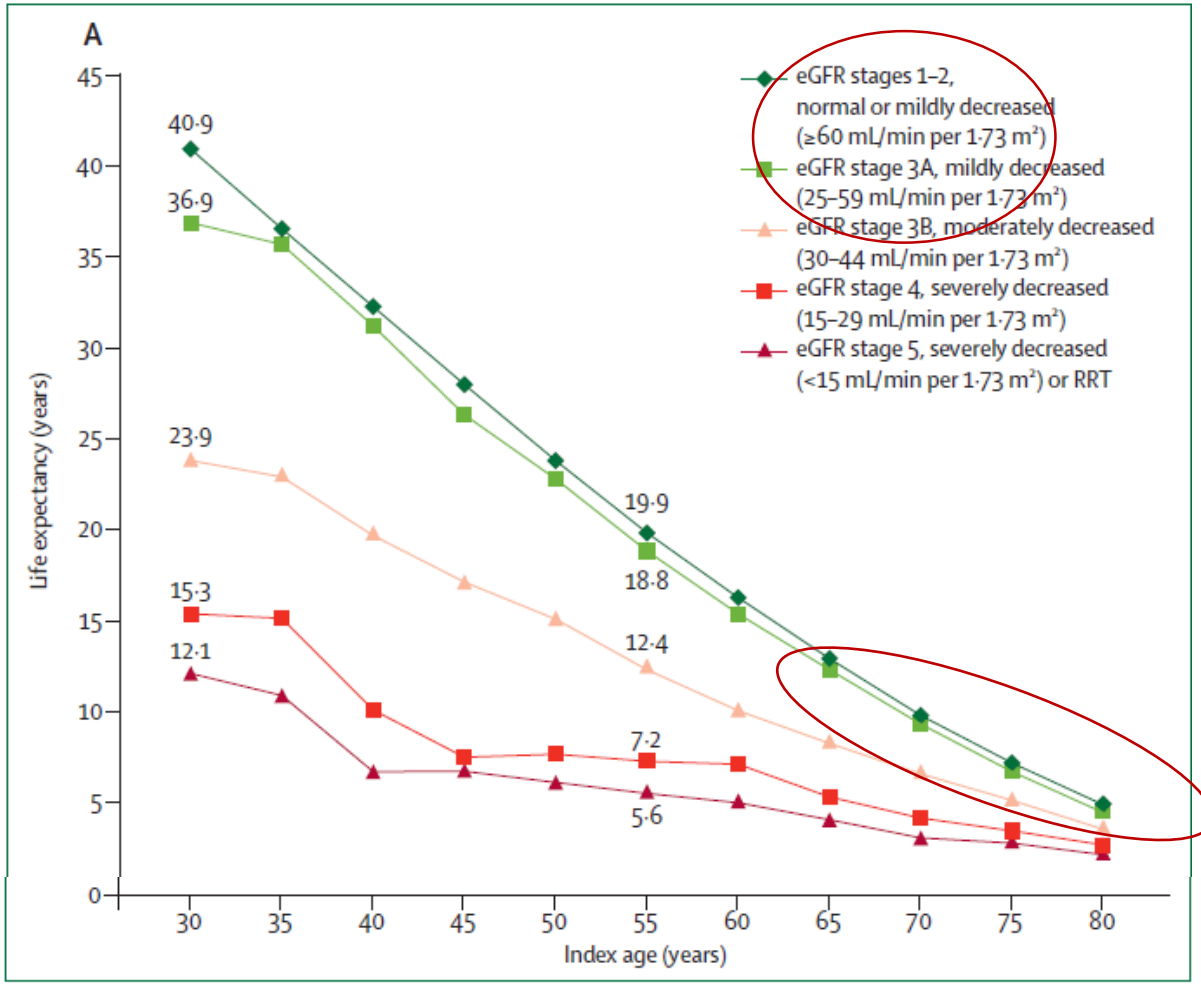


Figure 2: **Life expectancy, according to chronic kidney disease stages (Canadian data)**
(A) eGFR stages and (B) albuminuria stages. Data are adjusted per eGFR and albuminuria stage for sex to the WHO world average in 2000–05. eGFR=estimated glomerular filtration rate. RRT=renal replacement therapy.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

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

* adam.shardlow@nhs.net

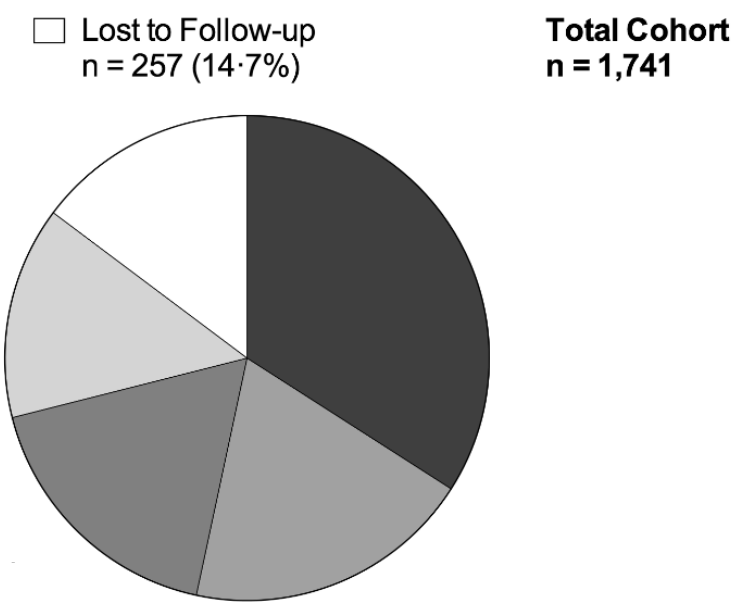
2016 PLOS Medicine | DOI:10.1371/

CrossMark click for updates

- 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/1.73m² 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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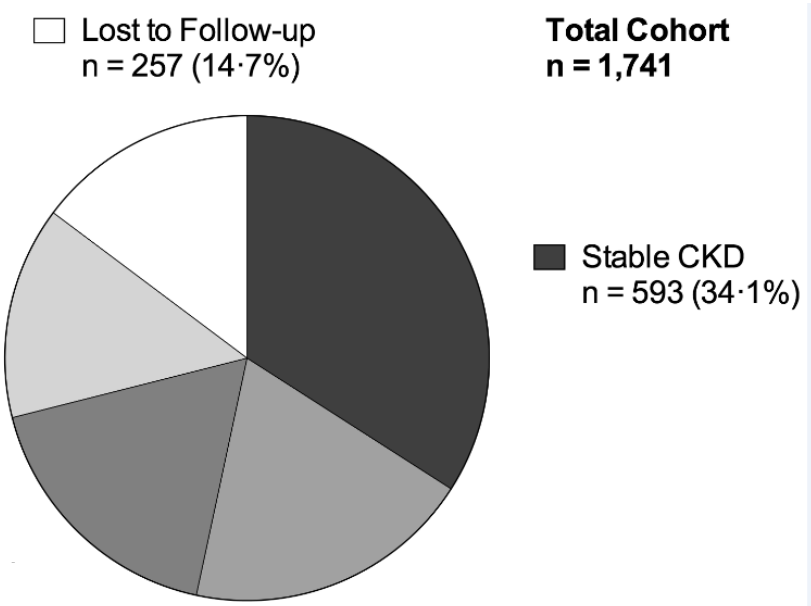

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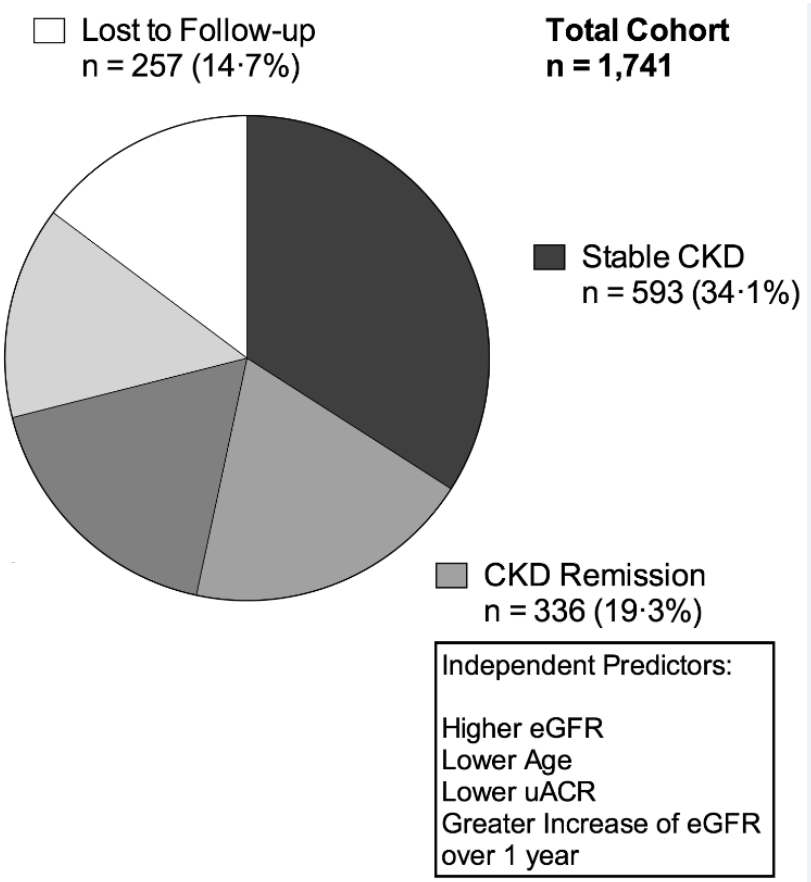

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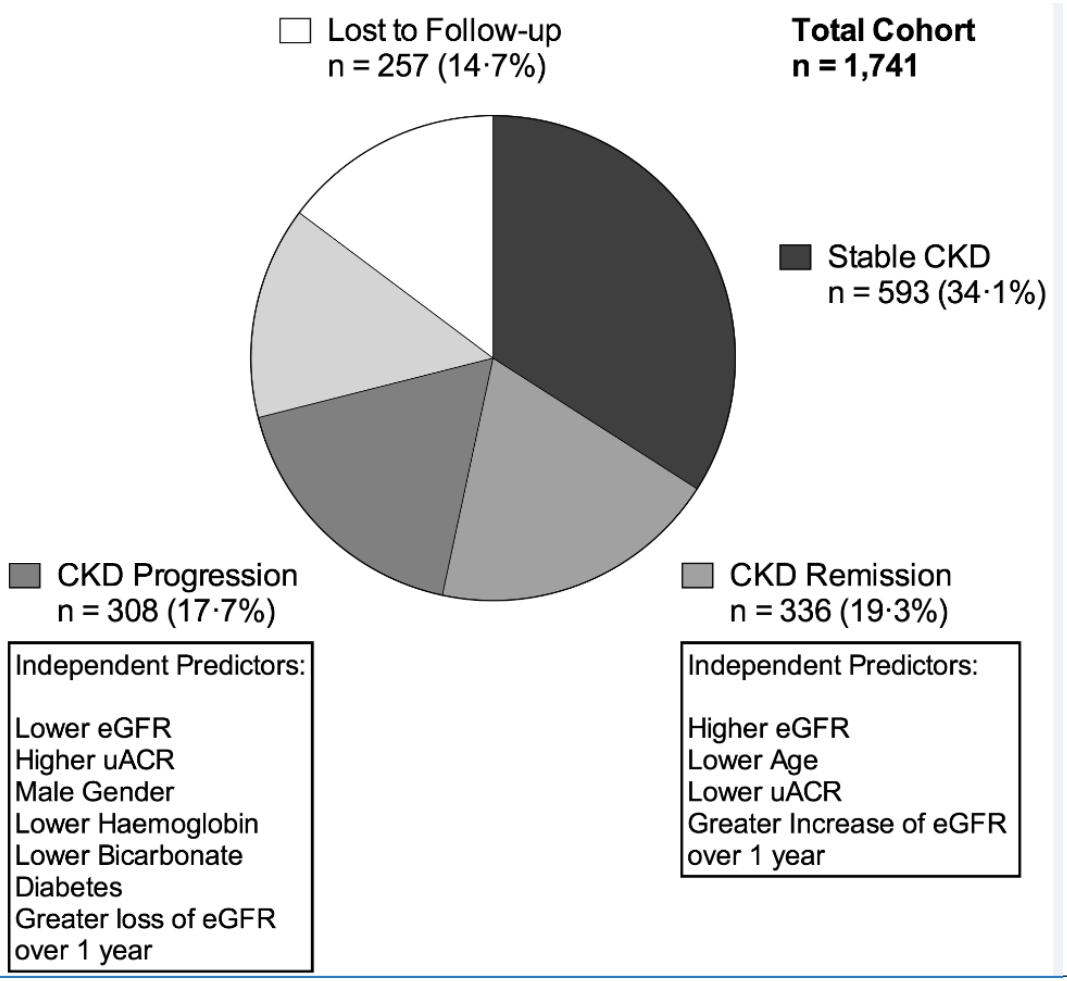
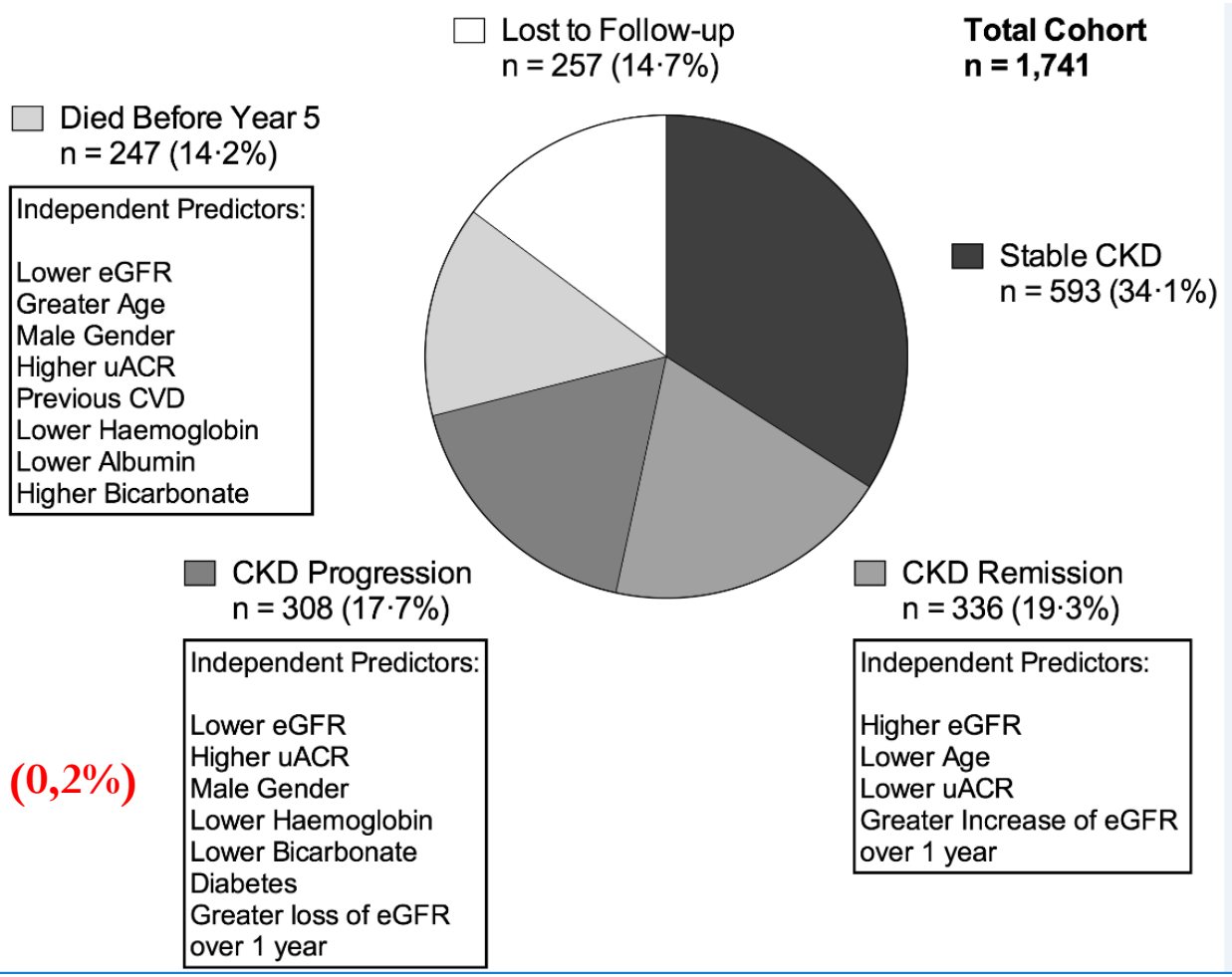


ESRD: n=4 (0,2%)

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



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

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 other kidney damage) is not CKD in the elderly

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

So...

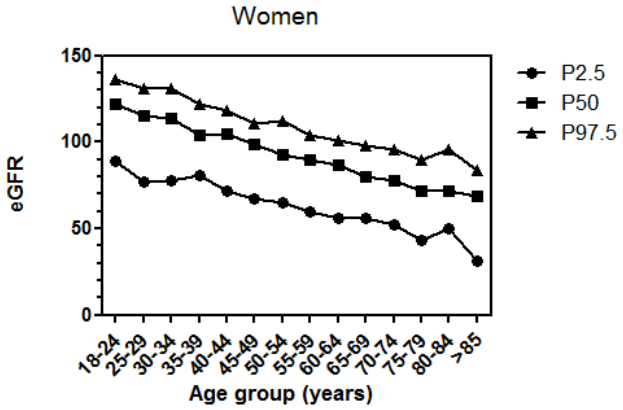
- A single absolute threshold of eGFR overestimates CKD in the healthy elderly

But…

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

Alternative 1

- Percentiles (like pediatrics)



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

https://www.kuleuven-kulak.be/egfr_calculator/ by Pr Hans Pottel

Patient characteristics

Patient id

Age (years) 75

Sex
- (•) Male
- ( ) Female

Race
- ( ) Afr. Am.
- (•) Caucasian
- ( ) Other

Scr (mg/dL) 1.1

Cystatin C (mg/L)

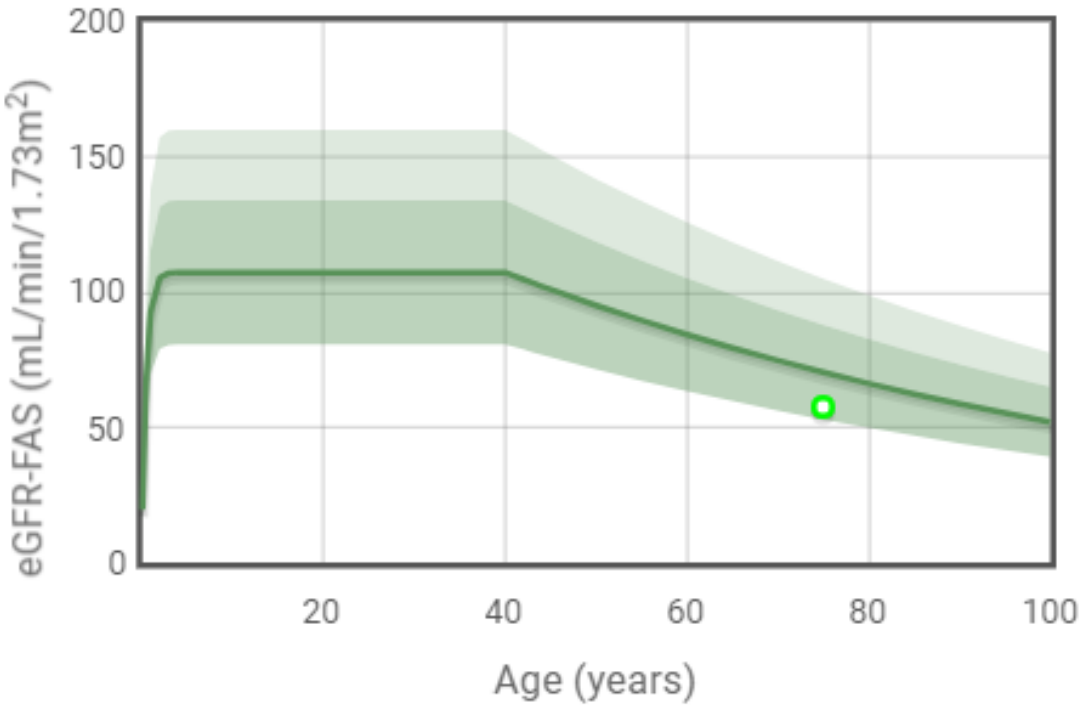
Height (cm) 175

Weight (kg) 75

BSA (m^2) 1.90

CALCULATE RESET

FAS prediction



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

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

Prognosis of CKD by GFR and albuminuria category

Prognosis of CKD by GFR and Albuminuria Categories: KDIGO 2012

GFR categories (ml/min/1.73 m²) Description and range				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
	G1	Normal or high	≥90			
	G2	Mildly decreased	60-89			
	G3a	Mildly to moderately decreased	45-59	>65 y / ≤65 y		
	G3b	Moderately to severely decreased	30-44			
	G4	Severely decreased	15-29			
	G5	Kidney failure	<15			

Green: low risk (if no other markers of kidney disease, no CKD); Yellow: moderately increased risk; Orange: high risk; Red, very high risk.

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

So...

- 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?

Is it relevant or purely semantic?

CKD prevalence: 11.5%

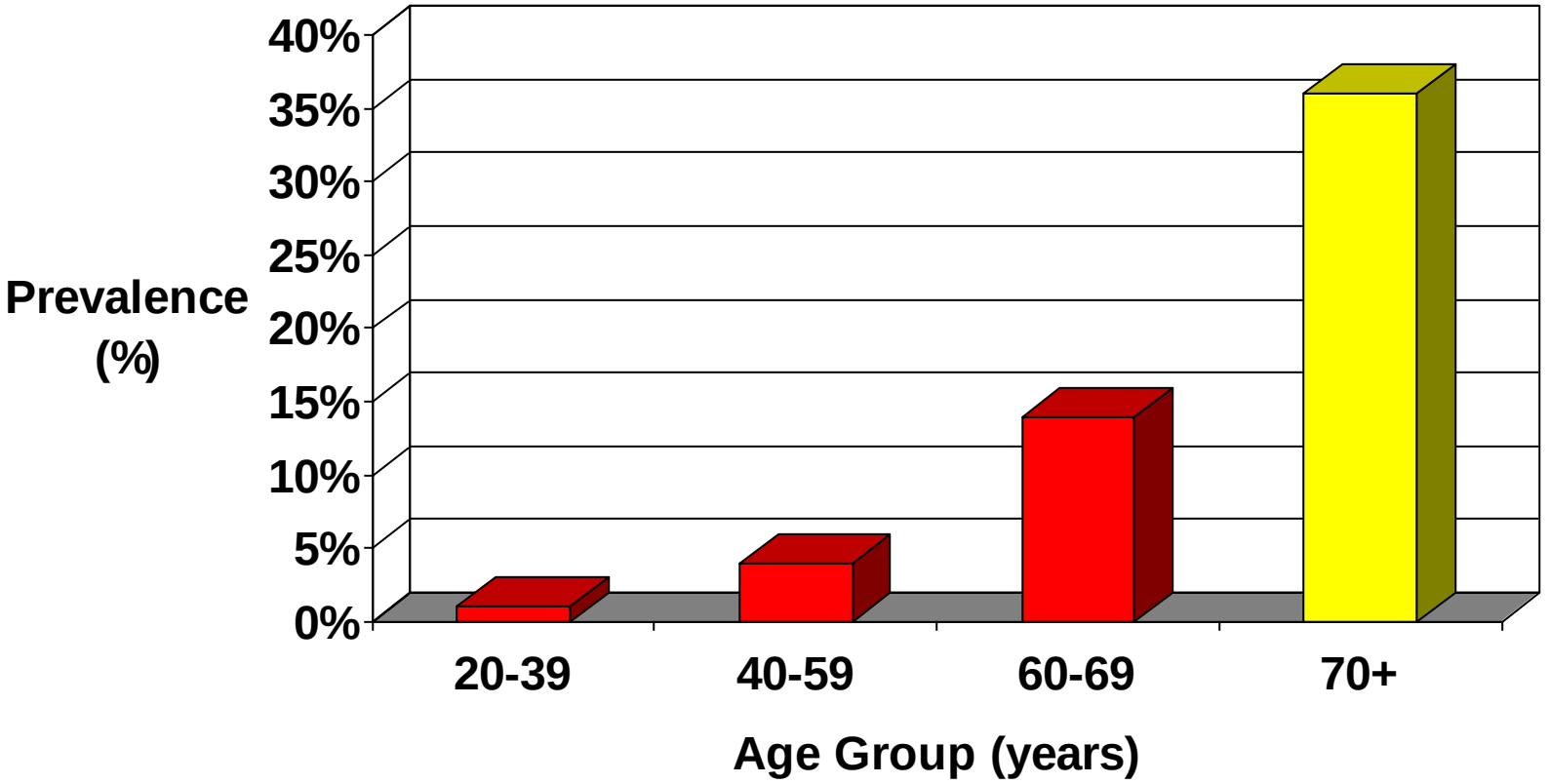
CKD prevalence based on eGFR only: 4.8%

Percentage of US Population by eGFR and Albuminuria Category: KDIGO 2012 and NHANES 1999-2006

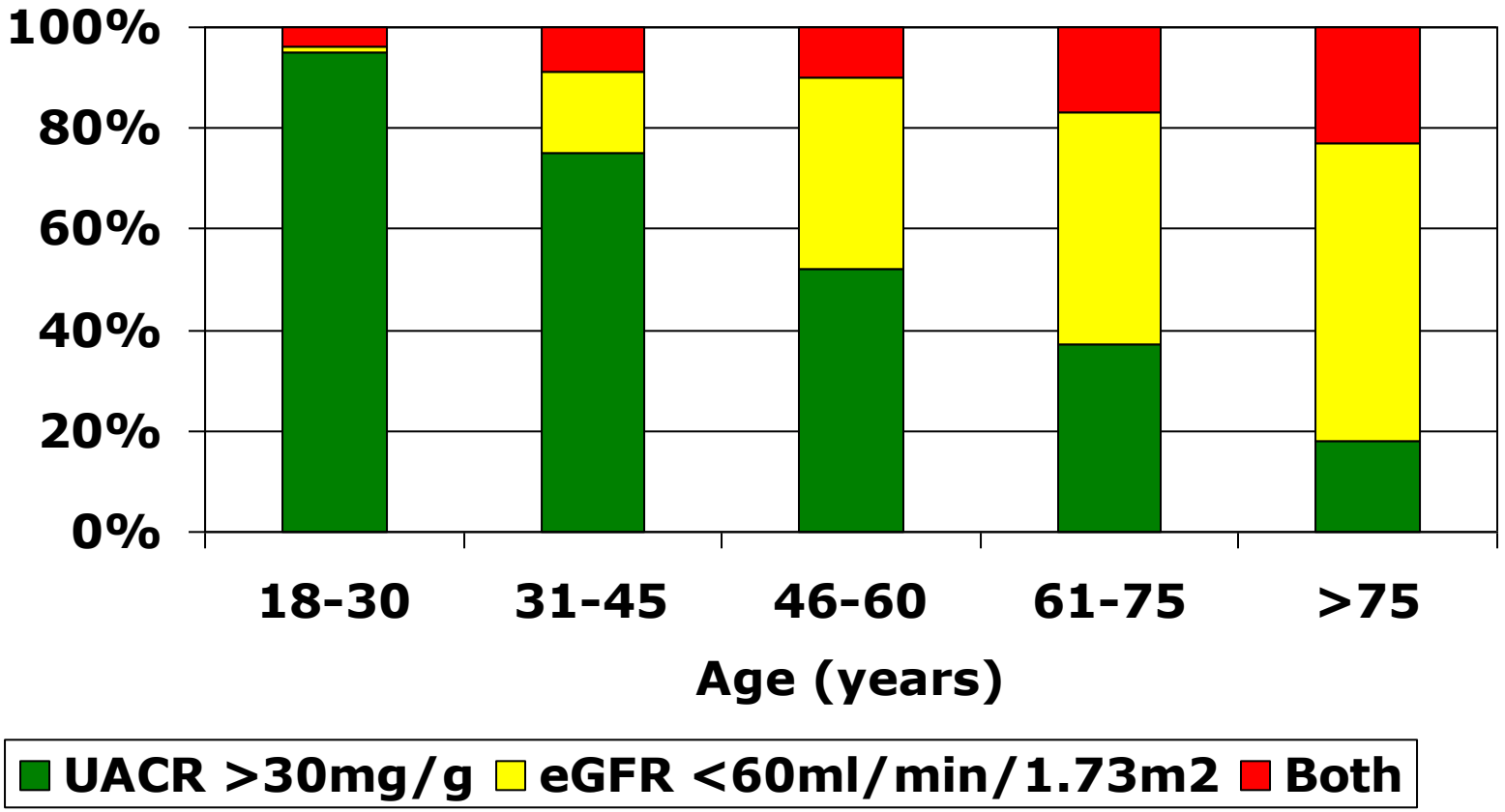
GFR categories (ml/min/ 1.73m^2) Description and range				Persistent albuminuria categories Description and range			
				A1	A2	A3	
				Normal to mildly increased	Moderately increased	Severely increased	
				<30 mg/g <3 mg/mmol	30-300 mg/g 3-30 mg/mmol	>300 mg/g >30mg/mmol	
	G1	Normal or high	≥90	55.6	1.9	0.4	57.9
	G2	Mildly decreased	[illegible]	[illegible]	[illegible].2	0.3	35.4
	G3a	Mildly to moderately decreased	45-59	3.6	[illegible].8	0.2	4.6
	G3b	Moderately to severely decreased	[illegible]	[illegible].0	[illegible].4	0.2	1.6
	G4	Severely decreased	15-29	0.2	0.1	0.1	0.4
	G5	Kidney failure	<15	0.0	0.0	0.1	0.1
				93.2	5.4	1.3	100.0

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

- Stage 3a/A1 is not disease in the elderly
- Stage 3a is the majority of CKD
- Most subjects in stage 3a are older than 65 years
- Most subjects in stage 3a are A1
- Among the 3,6% of « CKD3a », an important proportion is old people without kidney damage

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

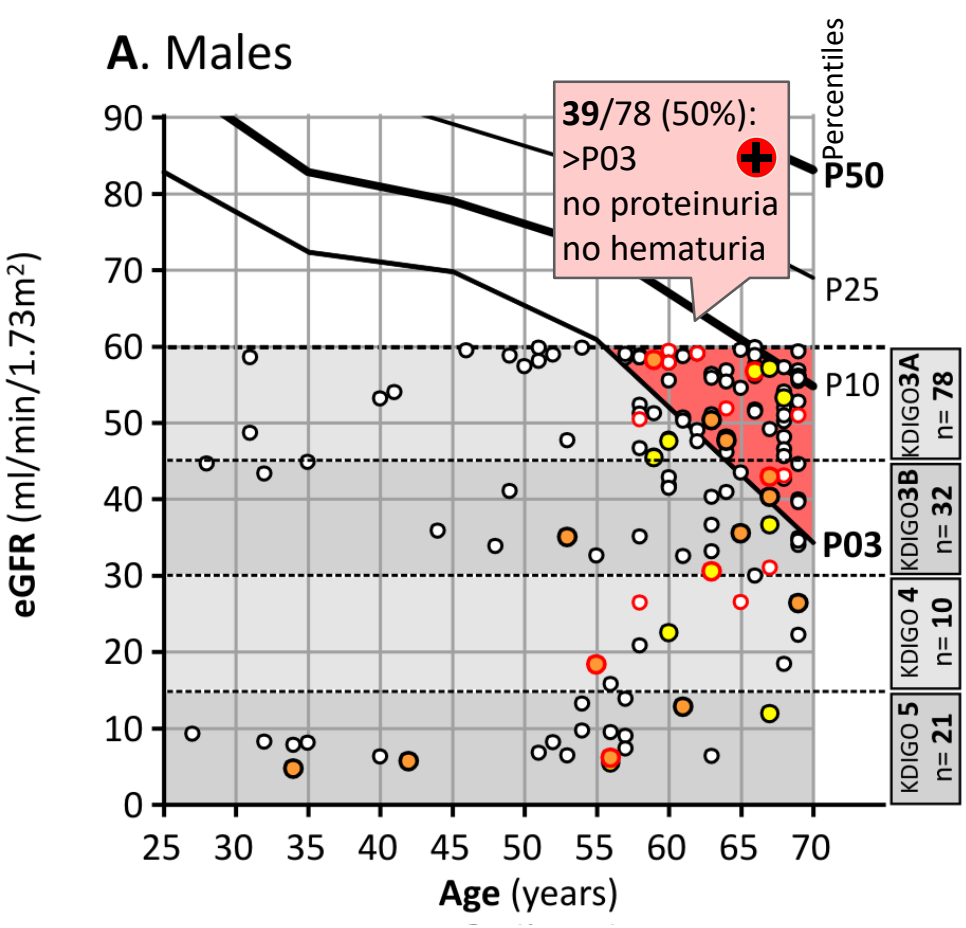
Mohammed Benghanem Gharbi[1,6], Monique Elseviers[2,6], Mohamed Zamd[1], Abdelali Belghiti Alaoui[3], Naïma Benahadi[3], El Hassane Trabelssi[3], Rabia Bayahia[4], Benyounès Ramdani[1] and Marc E. De Broe[5,6]

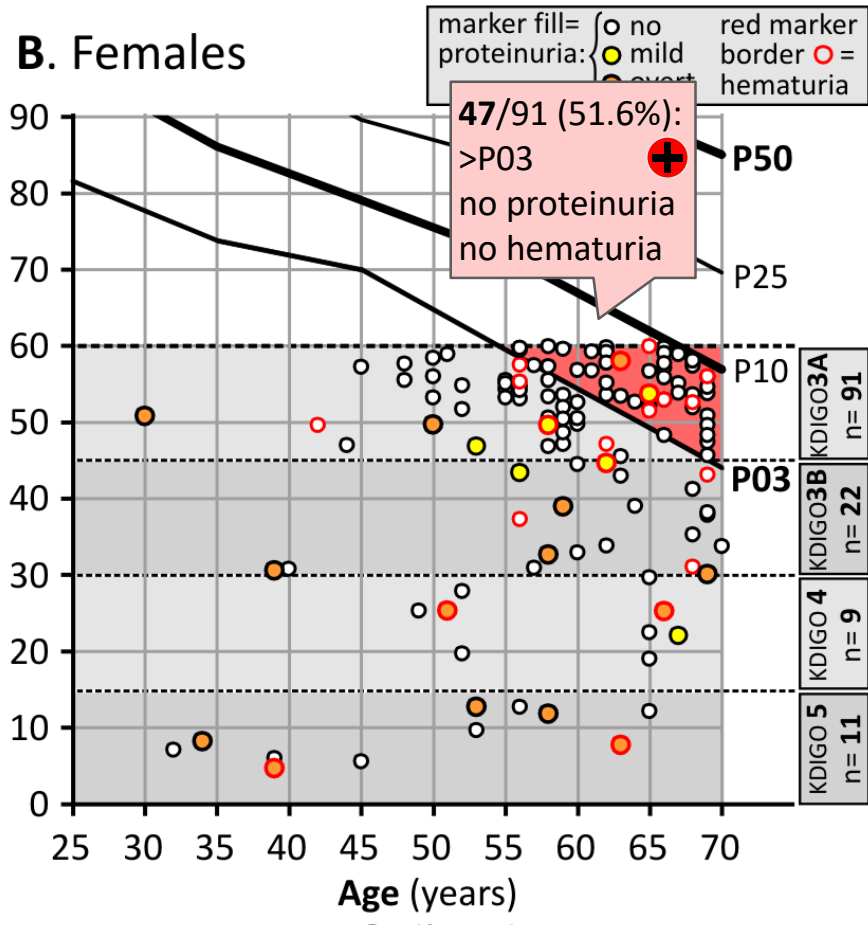
[1]Faculty of Medicine and Pharmacy, University Hassan II, Casablanca, Morocco; [2]Department of Biostatistics, Center for Research and Innovation in Care, University of Antwerp, Antwerp, Belgium; [3]Ministry of Health, Rabat, Morocco; [4]Faculty of Medicine and Pharmacy, University Mohammed V, Rabat,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

Kidney Int, 2016, 89, 1363-1371

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

Alternative 1





Alternative 2
Examples from Belgium and Italy

Delanaye *et al. BMC Nephrology* 2013, **14**:57
http://www.biomedcentral.com/1471-2369/14/57

BMC Nephrology

RESEARCH ARTICLE Open Access

Creatinine-or cystatin C-based equations to estimate glomerular filtration in the general population: impact on the epidemiology of chronic kidney disease

Pierre Delanaye[1*], Etienne Cavalier[2], Olivier Moranne[3], Laurence Lutteri[2], Jean-Marie Krzesinski[1] and Olivier Bruyère[4]

CKD screening (bus) on a voluntary basis
>50 y
n=4189
Mean age:63±7 y

Prevalence of CKD in Northeastern Italy: Results of the INCIPE Study and Comparison with NHANES

Giovanni Gambaro,*† Tewoldemedhn Yabarek,* Maria Stella Graziani,‡ Alessandro Gemelli,§ Cataldo Abaterusso,* Anna Chiara Frigo,‖ Nicola Marchionna,* Lorenzo Citron,§ Luciana Bonfante,§ Francesco Grigoletto,‖ Salvatore Tata,§ Pietro Manuel Ferraro,† Angelo Legnaro,§ Gina Meneghel,¶ Piero Conz,** Paolo Rizzotti,‡a Angela D'Angelo,§ and Antonio Lupo,* for the INCIPE Study Group

Clin J Am Soc Nephrol 5: 1946–1953, 2010.

Random Selection
>40 y
n=3870
Mean age:60y

Unpublished data

- If CKD is defined as eGFR<60 mL/min/1.73 m², CKD prevalence is 9.8%/4,6%

- If CKD is defined as eGFR<60 mL/min/1.73 m² for younger than 65 y AND eGFR<45 mL/min/1.73 m² for older than 65 y, CKD prevalence is 4.4%/1,5%

To Pr Gambaro, Verona, Italy: Grazie Mille !!

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 impact on the epidemiology of CKD is high!

Two topics

- Age and CKD definition
- Chronicity

Nephrol Dial Transplant (2015) 30: iv6–iv16
doi: 10.1093/ndt/gfv131

ndt
Nephrology Dialysis Transplantation

Original Article

Methodology used in studies reporting chronic kidney disease prevalence: a systematic literature review

Katharina Brück[1], Kitty J. Jager[1], Evangelia Dounousi[2], Alexander Kainz[3], Dorothea Nitsch[4], Johan Ärnlöv[5], Dietrich Rothenbacher[6], Gemma Browne[7], Vincenzo Capuano[8], Pietro Manuel Ferraro[9], Jean Ferrieres[10], Giovanni Gambaro[9], Idris Guessous[11], Stein Hallan[12], Mika Kastarinen[13], Gerjan Navis[14], Alfonso Otero Gonzalez[15], Luigi Palmieri[16], Solfrid Romundstad[17], Belinda Spoto[18], Benedicte Stengel[19], Charles Tomson[20], Giovanni Tripepi[18], Henry Völzke[21], Andrzej Więcek[22], Ron Gansevoort[23], Ben Schöttker[24], Christoph Wanner[25], Jose Vinhas[26], Carmine Zoccali[18], Wim Van Biesen[27] and Vianda S. Stel[1] on behalf of the European CKD Burden Consortium

Table 1. Description of the method of general population sample selection per study

Author (Ref.)	Study name	Country	Time period	Number of subjects, *N*	Age range	Sampling frame	Sample design	Response, %
Aumann *et al.* [10]	SHIP	Germany	2001–6	2830	25–88	Not specified[a]	Multistage sampling	69
Bongard *et al.* [11]	MONA LISA	France	2006–7	4727	35–75	Electoral rolls	Age and sex stratified	Not given
Browne *et al.* [12]	SLAN	Ireland	2007	1098	45+	Other (Geo directory)	Multistage random sampling: by area and region	66
Capuano *et al.* [13]	VIP	Italy	1998–99 and 2008–9	2400	25–74	Electoral rolls	Age and sex stratified	Not given
Christensson *et al.* [14]	GAS	Sweden	2001–4	2815	60–93	Census	Stratified, age, sex and urban/rural location	60
Chudek *et al.* [15]	PolSenior	Poland	2007–11	3793	65+	Not specified[a]	Not specified[a]	32
Cirillo *et al.* [16]	Gubbio Population Study	Italy	Not specified	4574	18–95	Not specified[a]	Not specified[a]	Not given[a]
Codreanu *et al.* [17]	Early Detection and Intervention Program for Chronic Renal and Cardiovascular Disease in the Rep Moldova	Moldova	2006–7	973	18–77	Not specified	Not specified	Not given
De Nicola *et al.* [18]	CARHES	Italy	2008	4077	35–79	Electoral rolls	Age and sex stratified	45
Delanaye *et al.* [19]		Belgium	2008–9	1992	45–75	Not specified	Voluntary nature	Not given
Donfrancesco *et al.* [20]	MATISS	Italy	1993–96	2924	20–79	Electoral rolls	Age- and sex-stratified random sample	60
Formiga *et al.* [21]	Octabaix	Spain	2009	328	85	Not specified[a]	Not specified[a]	Not given
Fraser *et al.* [22]	HSE	England	2009–10	5799	16+	Other (address list)	Random two-stage sample	Not given[a]
Gambaro *et al.* [23]	INCIPE	Italy	2006	3629	40+	General practitioner list	Random sample	62
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible] given
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible] given
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible] given
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible] men
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible] women
Otero *et al.* [35]	EPIRCE	Spain	2004–8	2746	20+	Census	Age-, sex- and region-stratified random sample	43
Pani *et al.* [36]	SardiNIA study	Italy	2001–	4471	14–102	Not specified[a]	Not specified[a]	56
Pattaro *et al.* [37]	MICROS	Italy	2002–3	1199	18+	Not specified[a]	Not specified[a]	Not given
Ponte *et al.* [38]	CoLaus	Switzerland	2003–6	5921	35–75	Population registry	Random sample	41
Redon *et al.* [39]	PREV-ICTUS	Spain	2005	6419	60+	General practitioner lists	Random sample	72
Robles *et al.* [40]	HERMEX	Spain	Not specified	2813	25–79	Other (health-care system database)	Age- and sex-stratified random sample	83
Roderick *et al.* [41]	MRC Older Age Study	UK	1994–99	13 179	75+	General practitioner list	Practices stratified by mortality score and deprivation score	73
Rothenbacher *et al.* [42]	ActiFE Ulm	Germany	2009–10	1471	65+	Census	Random sample	20
Rutkowski *et al.* [43]	PolNef	Poland	2004–5	2476	n/a	Other (address list)	Random sample	26
Sahin *et al.* [44]		Turkey	2005	1079	18–95	Not specified	Age, sex and region stratified	Not given
Schaeffner *et al.* [45]	BIS	Germany	2011	570	70+	Not specified[a]	Not specified[a]	Not given
Stengel *et al.* [48]	3C	France	1991–2001	8705	65+	Electoral rolls	Random sample	37
Suleymanlar *et al.* [49]	CREDIT	Turkey	Not specified	10 056	18+	Not specified	Age, sex and region stratified	Not given
Tavira *et al.* [50]	RENASTUR	Spain	2010–12	592	55–85	Not specified	Random sample	Not given
Van Pottelbergh *et al.* [51]	Crystal	Russia	2009	611	65–91	General practitioner list	All registered on list	66
Viktorsdottir *et al.* [52]	RHS	Iceland	1967–96	19 256	33–85	Not specified	All in birth cohort	Not given
Vinhas *et al.* [53]	PREVADIAB	Portugal	2008–9	5167	20–79	Other (universal health card)	Age, sex and region stratified	84
Wasen *et al.* [54]		Finland	1998–99	1246	64–100	Not specified	All residents born ≤1933	83
Wetmore *et al.* [55]		Iceland	2001–3	1630	18+	Not specified	Random sample	71
Zambon *et al.* [56]	ProV.A.	Italy	1995–97	3063	65+	Other (health district registries)	Age- and sex-stratified random sample	77 in men 64 in women
Zhang *et al.* [57]	ESTHER	Germany	2000–2	9806	50–74	General practitioners	All participants who underwent a general health check-up	Not given

N, Number of subjects with [illegible] measurement; n/a, not applicable;

The chronicity criterion is not applied in all these studies !!

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, 89, 1363-1371

- Chronicity confirmed at 3 months in 78.9% of CKD (n=285)
- Stage 3A: 32% were found with eGFR>60 ml/min/1.73m²
- Stage 3B: 7,4% were found with eGFR>60 ml/min/1,73m²

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

* adam.shardlow@nhs.net

Shardlow A et al, Plos Med, 2016

- "Confirmed" was at least 2 previous eGFR results of 30 to 59 ml/min per 1.73 m2 in the course of clinical care
- Then serum creatinine is re-measured at baseline for the study

=> 29% had eGFR>60 mL/min/1.73m²

Other (few) data in brief…

- NHANES III: random sample of 98 patients with an eGFR<60 mL/min/1.73 m² (stage 3A), a second examination (in a median period of only 2 weeks)

⇒ 23% moved to eGFR>60mL/min/1.73m²

- Tasmania: n=369,098 (retrospective lab's data in 2007):

  eGFR<60 mL/min/1.73m²: ♂: 12,1% ♀: 15,6%

  => 60,4% had second test: ♂: 5,8% ♀: 8%

- VA: n=26,080 with two serum creatinine in 2005 available 3-6 months apart

  first eGFR>60 mL/min/1.73m² => 93% were confirmed

  first eGFR stage 3 => 20% eGFR>60 mL/min/1.73m²

- Tromsø study: One lab in the city, n=38,241 measurement, n=6,863 in Stage 3A, among them, 5,337 with second creatinine 3 months apart or more

  =>40.8% had eGFR>60 mL/min/1.73m²

Coresh J, Am J Kdiney Dis, 2003, p1
Jose MD, Nephrology, 2009, p743
Shahinian VD, AJKD, 2013, p930
Eriksen BO, Kidney Int, 2006, p375

Clin Kidney J, 2017, 10, 370-374

EDITORIAL COMMENT

Epidemiology of chronic kidney disease: think (at least) twice!

Pierre Delanaye[1], Richard J. Glassock[2] and Marc E. De Broe[3]

[1]Department of Nephrology Dialysis Transplantation, CHU Sart Tilman, University of Liège, Liège, Belgium, [2]Department of Medicine, David Geffen School of Medicine at UCLA, Laguna Niguel, CA, USA and [3]Laboratory of Pathophysiology, University of Antwerp, Antwerp, Belgium

Correspondence and offprint requests to: Pierre Delanaye; E-mail: pierre_delanaye@yahoo.fr

20 to 40% of stage 3a are not confirmed CKD !!

…also true for albuminuria

Conclusions

- The current prevalence of CKD is overstated by most epidemiological studies
- Methodological reasons
- Absence of CHRONICITY confirmation
- Absence of an age-calibrated definition

=> CKD prevalence is lower (by HALF) than currently stated

As a conclusion…

Too much Nephrology?

The CKD epidemics is overstated

- The title is a bit misleading
- Even if I consider that CKD epidemics is overstated, I don't say that CKD prevalence is negligible

Epidemiology must help for « Better » nephrology (not always « More »)

Focus on hypertension

Focus on diabetes

Focus on albuminuria

Focus on specific patients etc (low birth weight, familial CKD, AKI etc)

Thank you for your attention