Supplementary Appendix

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This appendix has been provided by the authors to give readers additional information about the work.

Supplement

Cystatin C-Based Equation to Estimate GFR without the Inclusion of Race and Sex

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Table S1: Patient and method characteristics of the different validation cohorts

Name	Country	Cohort	n	Method mGFR	Age median [IQR]	mGFR median [IQR]	Crea/Q median [IQR]	CysC/Q' median [IQR]	% men
EKFC (White)			**7,727**		**62.0 [53.0 – 73.9]**	**70.8 [43.4 – 90.6]**	**1.13 [0.94 – 1.65]**	**1.28 [0.97 – 2.02]**	**53.4**
Berlin	Germany	BIS-study [1]	657	PC / iohexol	77.0 [73.6 – 82.5]	57.9 [43.4 – 70.0]	1.18 [1.00 – 1.52]	1.33 [1.12 – 1.72]	58.3
Kent#	UK	GFR in old adults study [2]	394	PC / 51Cr-EDTA	80.0 [77.0 – 83.0]	53.4 [35.3 – 67.8]	1.34 [1.08 – 2.02]	1.44 [1.19 – 2.26]	48.0
Lund#	Sweden	CAPA-study [3]	2,847	PC / iohexol	63.0 [50.0 – 72.0]	56.4 [31.2 – 81.6]	1.34 [1.01 – 2.15]	1.75 [1.27 – 2.72]	51.5
Lyon	France	Referrals*	914	PC/RC inulin/iohexol	51.6 [37.9 – 62.5]	79.6 [55.6 – 99.0]	1.10 [0.92 – 1.45]	1.13 [0.94 – 1.59]	54.9
Saint-Etienne	France	HIV-study [4]	203	RC / inulin	48.0 [42.0 – 56.0]	95.9 [80.3 – 107.7]	0.97 [0.87 – 1.09]	1.04 [0.92 – 1.16]	81.8
Stockholm	Sweden	Referrals*	577	PC / iohexol	75.0 [72.0 – 79.0]	42.2 [24.7 – 62.9]	1.65 [1.18 – 2.44]	1.99 [1.43 – 3.00]	52.5
Tromsö	Norway	RENIS-T6 study [5]	1,627	PC / iohexol	58.7 [54.7 – 61.4]	91.5 [82.9 – 101.2]	0.94 [0.85 – 1.04]	0.87 [0.79 – 0.97]	49.2
Örebro	Sweden	Referrals*	508	PC / iohexol	58.1 [43.2 – 68.4]	71.5 [41.5 – 93.0]	1.31 [1.02 – 1.74]	1.29 [0.98 – 2.04]	61.8
USA (White)#	Rochester, Minnesota	GENOA / ECAC study [6]	**1,093**	**RC / iothalamate**	**66.1 [59.1 – 71.2]**	**80.0 [66.0 – 93.0]**	**1.04 [0.92 – 1.17]**	**0.96 [0.84 – 1.09]**	**43.4**
Africa (Black)#			**508**		**39.0 [30.0 – 53.0]**	**86.8 [71.7 – 99.2]**	**1.16 [1.02 – 1.41]**	**1.07 [0.95 – 1.28]**	**53.3**
	Côte d'Ivoire	eGFR-study [7]	285	PC / iohexol	34.0 [27.0 – 43.0]	89.1 [73.9 – 100.8]	1.18 [1.04 – 1.48]	1.05 [0.93 – 1.32]	57.9
	Congo	eGFR-study [8]	223	PC / iohexol	49.0 [37.5 – 60.0]	84.4 [65.2 – 97.3]	1.13 [1.01 – 1.35]	1.13 [0.99 – 1.22]	47.5
Paris (White and Black)#			**3,504**		**53.4 [42.0 – 63.0]**	**63.2 [44.3 – 84.5]**	**1.42 [1.12 – 1.90]**	**1.48 [1.11 – 2.07]**	**57.4**
	Paris White	Referrals*	2,646	PC / ^{51}Cr EDTA	54.2 [42.3 – 64.0]	62.7 [43.8 – 85.3]	1.42 [1.09 – 1.90]	1.49 [1.11 – 2.11]	56.1
	Paris Black	Referrals*	858	PC / ^{51}Cr EDTA	51.2 [41.0 – 60.4]	64.3 [45.9 – 81.7]	1.46 [1.19 – 1.94]	1.45 [1.12 – 1.96]	61.3

mGFR= measured glomerular filtration rate, IQR= interquartile range, PC= plasma clearance (only blood samples are required), RC= renal clearance (both blood and urine samples are required). Crea/Q = scaled creatinine, CysC/Q' = scaled cystatin C (both scaled markers equal '1' for the average healthy subject); Referrals*: subjects referred for measured GFR; # = Cohorts are true "external" validation cohorts

Table S2. Detailed description of origin of patients

Name of the cohort	Country and city if indicated	Age median	% men	Definition of race	Sample size and proportion of White/Black participants	Source population
BIS-study [1]	Germany, Berlin	77.0	58.3	Self-reported	657 (100/0)	Population-based cohort. Participants were members of one of the largest German statutory health insurance (AOK Nordost Die Gesundheitskasse), all living in Berlin with ≥70 years at baseline.
GFR in old adults study [2]	UK, East-Kent	80.0	48.0	Self-reported	394 (100/0)	Participants ≥74 years were either patients known to the Kent Kidney Care Centre or residents of the local population. The latter were recruited through a variety of means, including the researchers attending discussion groups in Age Concern centers, golf clubs, Rotary clubs, and residential care homes, and through advertising the study by media briefings in hospital newsletters, local newspapers, and radio stations. Overall, 38% of participants were recruited through nephrology clinics, and 62%, through other methods.
CAPA-study [3]	Sweden	63.0	51.5	Assumed by geography	2847 (100/0)	Referrals for CKD diagnosis or follow-up or measured GFR in kidney donors candidates.
Lyon	France, Lyon	51.6	54.9	Assumed by geography	914 (100/0)	Referrals for CKD diagnosis or follow-up or measured GFR in kidney donors candidates.
HIV-study [4]	France, Saint-Etienne	48.0	81.8	Determined by researcher	203 (100/0)	Patients ≥74 years with confirmed HIV status were recruited from the department of infectious diseases of the university hospital of Saint-Etienne (France)
Stockholm	Sweden, Stockholm	75.0	52.5	Assumed by geography	577 (100/0)	Referrals for CKD diagnosis or follow-up or measured GFR in kidney donors candidates.
RENIS-T6 study [5]	Norway, Tromsø	58.7	49.2	Assumed by geography	1627 (100/0)	Population-based survey in the municipality of Tromsø, North Norway. RENIS-T6 is an ancillary part of the sixth Tromsø study, a series of health surveys of whole age-groups or random samples of the general population. The participation rate of Tromsø 6 was 66%. RENIS-T6 included a representative sample of persons between 50 and 62 years without self-reported cardiovascular disease, kidney disease or diabetes.
Örebro	Sweden, Örebro	58.1	61.8	Assumed by geography	508 (100/0)	Referrals for CKD diagnosis or follow-up or measured GFR in kidney donors candidates.
GENOA / ECAC study [6]	USA, Rochester, Minnesota	66.1	43.4	Self-reported	1093 (100/0)	GENOA was adult hypertensive siblings and ECAC was general population adults.
eGFR-study [7]	Côte d'Ivoire	34.0	57.9	Assumed by geography	285 (0/100)	Healthy subjects were recruited from blood donors and healthy status was assessed by clinical and biological evaluation. Diabetes and hypertension were excluded, and subjects had normal biological results (HIV, hepatitis B or C, and GFR between 60 and 130 ml/min per 1.73 m²) and no albuminuria. Patients with CKD were recruited from patients followed by nephrologists at the university hospital of Abidjan.

eGFR-study [8]	Democratic Republic of Congo	49.0	47.5	Assumed by geography	223 (0/100)	Healthy persons were randomly selected from the general population. Healthy subjects were all those who did not have hypertension, diabetes mellitus, obesity, urinary abnormalities, and impaired renal function (GFR <60 or >130 ml/min per 1.73 m²). Patients with CKD were recruited from the general population and from the medical services (Renal Unit of Kinshasa University Hospital). They had a decrease in GFR (<60 ml/min per 1.73 m2) with or without albuminuria.
Paris	France, Paris	53.4	57.4	Self-reported	3504 (76/24)	Referrals for CKD diagnosis or follow-up or measured GFR in kidney donors candidates.

Five different cohorts were defined. **White Europeans were from the EKFC cohort** (n = 7,727) with median [IQR] age 62.0 [53.0 – 73.9], median mGFR 70.8 [43.4 – 90.6] mL/min/1.73m² and 53.4% were men. We augmented the data of White subjects with **White Europeans from the Paris cohort** (n = 2,646) with median age 54.2 [42.3 – 64.0] years, median mGFR 62.7 [43.8 – 85.3] mL/min/1.73m² and 56.1% were men and **White Americans from Rochester, Minnesota** (n = 1,093, previously described as the GENOA and ECAC cohorts) with median age 66.1 [59.1 – 71.2] years, median mGFR 80.0 [66.0 – 93.0] mL/min/1.73m² and 43.4% were men. Two other new datasets were added with **Black Europeans from the Paris cohort** (n = 858) with median age 51.2 [41.0 – 60.4] years and median mGFR 64.3 [45.9 – 81.7] mL/min/1.73m², and 61.3% were men and **Black Africans from Côte d'Ivoire (n = 285) and Congo (n = 223)** with median age 39.0 [30.0 – 53.0] years and median mGFR 86.8 [71.7 – 99.2] mL/min/1.73m², and 53.3% were men.

The study was approved by the Regional Ethical Board in Lund, Sweden (Registration No 2018/220 with an amendment 2021-04177 approved by the Swedish Ethical Review Authority) for the EKFC cohort.[9] For Africa, the study protocol was approved by the Ethics Committee of the Public Health School of the University of Kinshasa, DRC (N°ESP/CE/029/2015) [8] and the national ethnic committee under the number 039/MSLS/CNER-dkn in Côte d'Ivoire [7]. In Paris, France, the study was approved by the Institutional review board of Assistance-Publique Hôpitaux de Paris and Paris 7 University (IRB 00006477, study 14-051). The cohort from Rochester, Minnesota, has been described previously.[6]

Section S2. Development of the Serum creatinine based EKFC equation

Developing an eGFR-equation based on age, sex and the biomarker value (whether it is serum creatinine or cystatin C) requires knowledge of how GFR and the biomarkers change with age/sex.

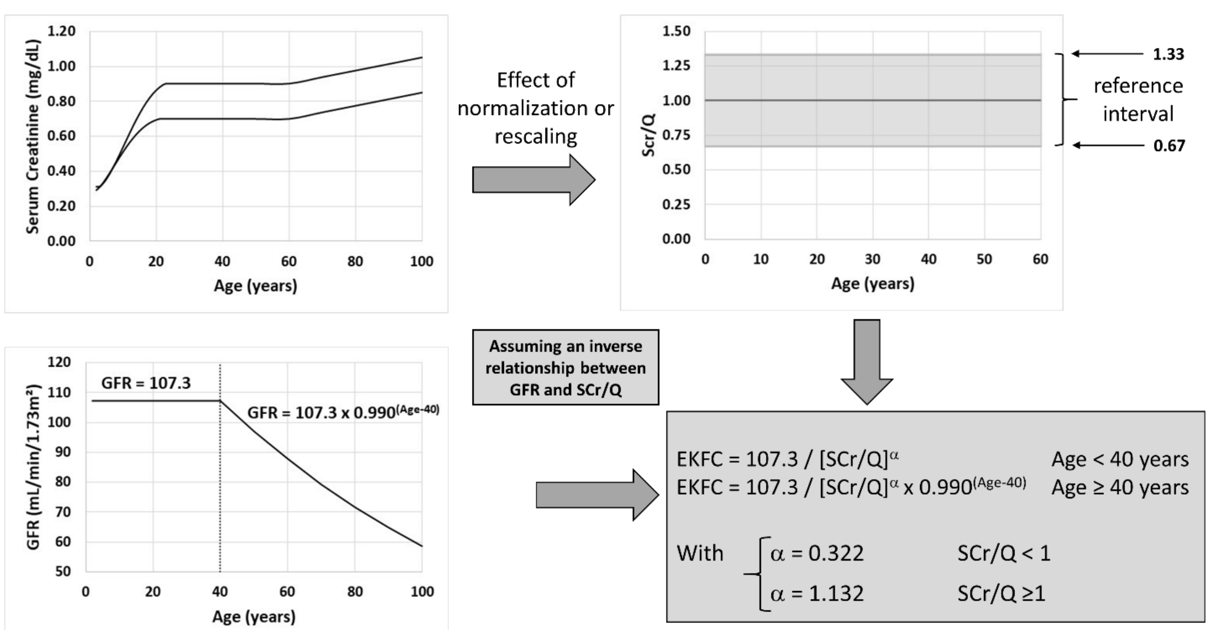
Serum creatinine increases during childhood when children gain muscle mass and this increase accelerates in boys during adolescence, becoming stable, on average, for both healthy (white) men and (white) women during adulthood, at values of 80 µmol/L (0.90 mg/dL) for men and 62 µmol/L (0.70 mg/dL) for women, until the age of 50-60 years, and beyond that age, serum creatinine starts to slightly increase again. [10]

As Glomerular Filtration Rate shows a totally different age-dependency (see Figure S1 [9]), this complicates the development of a SCr-based eGFR-equation. Indeed, for the average healthy subject, GFR remains stable starting at the age of 2-3 years (after maturation of the kidneys) around 105-110 mL/min/1.73m², until the age of about 40 years, and then starts to decrease. No evidence could be found for any difference between men and women. [11-12] To develop a formula that allows the calculation of GFR from SCr, this totally different age-dependency of GFR and SCr has to be taken into account.

To simplify the development of an eGFR-equation, a logical step was to normalize or rescale SCr. This rescaling was done by dividing each individual SCr-value by the age/sex specific median SCr-value for healthy subjects (the so-called Q-value). For adults (during the stable period), this Q-value equals 0.70 mg/dL for (White) women and 0.90 mg/dL for (White) men. By normalizing or rescaling SCr by this Q-value, SCr/Q becomes '1' for the average healthy adult person, independent of age and sex. It has been shown that – in healthy subjects - SCr/Q had a reference interval of [0.67 – 1.33], for children, adolescents, and adults, both for men and women. Note that for children, the Q-value was also dependent on age. Using a large dataset of apparently healthy children and adults, so-called creatinine growth curves could be established (see Figure S1, top left). Normalizing or rescaling SCr using so-called ‘creatinine growth curves’, simplified the development of a SCr-based eGFR-equation and also allowed to extend existing adult eGFR-equations (like the Lund-Malmö Revised and CKD-EPI equation) to become applicable in children [13-14].

The age-dependency of GFR could be described by GFR = 107.3 [x $0.990^{(Age-40)}$ if Age > 40 years].[9] To connect GFR with SCr, an inverse relationship between GFR and SCr/Q was proposed. It must be emphasized that SCr was not rescaled for the slight increase beyond the age of 60 years, so, the age-decline factor $0.990^{(Age-40)}$ also accounts for this slight increase in SCr. Note also that 0.70 and 0.90 are exactly the scaling factors for SCr used in the CKD-EPI-eGFR equation, and this was independently obtained from linear regression analysis (the CKD-EPI consortium did never refer to these scaling factors as the median SCr of healthy subjects, but it logically followed from their regression analysis). Rescaling SCr by 0.70 for women and 0.90 for men, makes it unnecessary to further adjust for differences between men and women at the GFR-level (not at all for EKFC-eGFR, and only by 1.018 (1.8%) for CKD-EPI).

Figure S1. Overview of building the SCr-based EKFC-eGFR equation [9]



The development of the SCr-based EKFC-eGFR equation thus comes down to the following steps:

1. We assume that the overarching equation for GFR is of the form GFR = A x [$C^{(Age-AgeCO)}$ if age > AgeCO years] and describes the GFR-age dependency. 'A' is the average GFR-value for children, adolescents and young adults, 'C' is the decline rate constant and the decline starts beyond the age threshold 'AgeCO'.
2. We further assume that SCr/Q is inversely related to GFR

Consequently, GFR can be described with an equation of the form:

$$GFR = A \times [SCr/Q]^{\alpha} \times [C^{(Age-AgeCO)} \text{ if age > AgeCO years}]$$

(where α is supposed to be negative). Taking the logarithm of both sides, we have

$$\log(GFR) = \log(A) + \alpha \log(SCr/Q) \qquad \text{for age} \leq \text{AgeCO}$$

$$\log(GFR) = \log(A) + \alpha \log(SCr/Q) + (Age - AgeCO) \times \log(C) \qquad \text{for Age > AgeCO}$$

By linear regression analysis we obtained A = 107.3, AgeCO = 40, C = 0.990 and α = - 0.322 if SCr/Q < 1 and α = - 1.132 if SCr/Q ≥ 1.

Section S2.1. Q-values for serum creatinine in White European subjects

The Q-values for White Europeans were modelled with fractional polynomials [9], making the SCr-based EKFC-eGFR equation a full age range equation.

Age	Gender	Q (µmol/L)
2-25	men	$\ln(Q) = 3.200 + 0.259 \times Age - 0.543 \times \ln(Age) - 0.00763 \times Age^2 + 0.0000790 \times Age^3$
	women	$\ln(Q) = 3.080 + 0.177 \times Age - 0.223 \times \ln(Age) - 0.00596 \times Age^2 + 0.0000686 \times Age^3$
> 25	men	80 (0.90 mg/dL)
	women	62 (0.70 mg/dL)

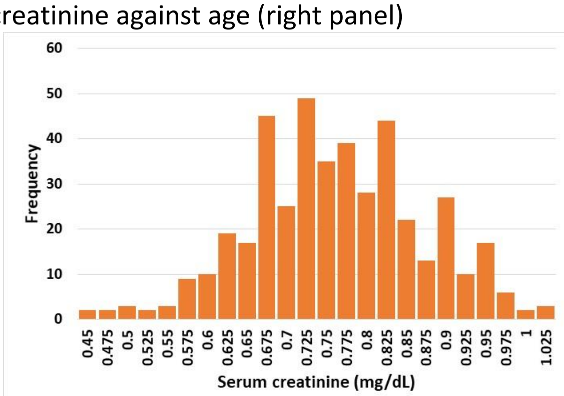
To convert from µmol/L to mg/dL, divide by 88.4

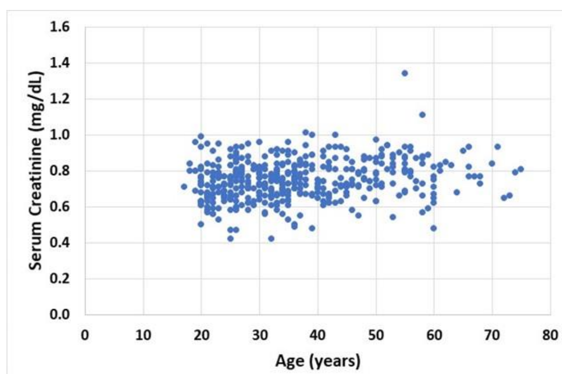
Section S2.2. Q-values for serum creatinine in African and Black European subjects

Section S2.2.1. African Q-values

Independent datasets from healthy habitants of République Démocratique de Congo (n = 616) and Côte d'Ivoire (n = 395) were used to define the median value, or Q-value, in men and women. The distribution of the female creatinine values (Roche Cobas, Roche Diagnostics, Mannheim, Germany) is shown in Figure S2.2.1.A, together with the plot of creatinine against age, showing no age-dependency. The median value of Q = 0.72 with 95%CI [0.704 – 0.732] was calculated from the participants aged 18-40 years.

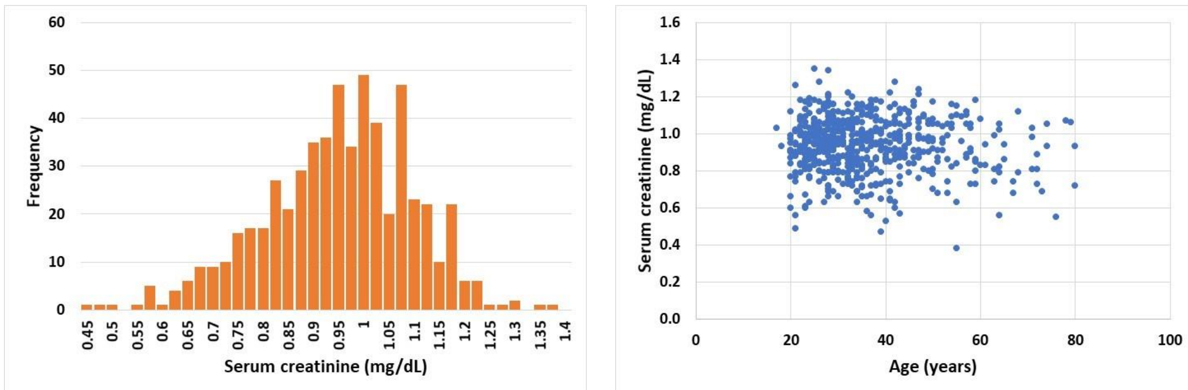
Figure S2.2.1.A. Distribution of serum creatinine in healthy African women (left panel) and serum creatinine against age (right panel)





The distribution of the creatinine values for men is shown in Figure S2.1.2.1.B, together with the plot of creatinine against age, showing no age-dependency. The median value of Q = 0.96 with 95%CI [0.946 – 0.977] was calculated from the participants aged 18-40 years.

Figure S2.2.1.B. Distribution of serum creatinine in healthy African men (left panel) and serum creatinine against age (right panel)



Section S2.2.2. Black European Q-values

The independent datasets from Black healthy kidney donors living in the environment of Paris to determine population-specific Q-values were much smaller (42 men and 48 women). SCr was measured with an enzymatic assay (Roche Creatinine Plus).

<u>Men</u>

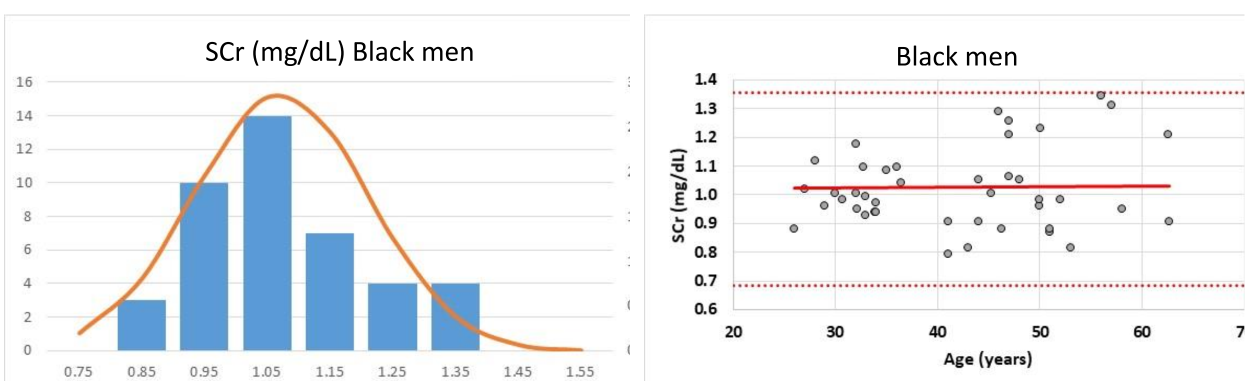
Min	0.79
Max	1.35
Count	42
Avg	1.02
Std	0.14
Median	0.99

We used 4 methods to evaluate normality of the data:

1. If the data are approximately normal, then IQR/SD = ± 1.34. We found IQR/SD = 1.26
2. The QQ-plot shows a straight line (not shown)
3. Lilliefors test: $p = 0.049$
4. Shapiro-Wilk test: $p < 0.05$

Conclusion: there is slight evidence of non-normality!

Figure S2.2.2.A. Distribution of SCr in healthy European Black male kidney donors and SCr vs age



Bootstrapping using 1000 resamples gives the following results:

	Mean	Median
Avg	1.021	0.994
Std	0.022	0.022
95%CI	0.978	0.950
	1.065	1.037

No age-dependency and all 42 subjects have SCr/Q within [0.67; 1.33]. We defined Q = 1.02 mg/dL.

Women

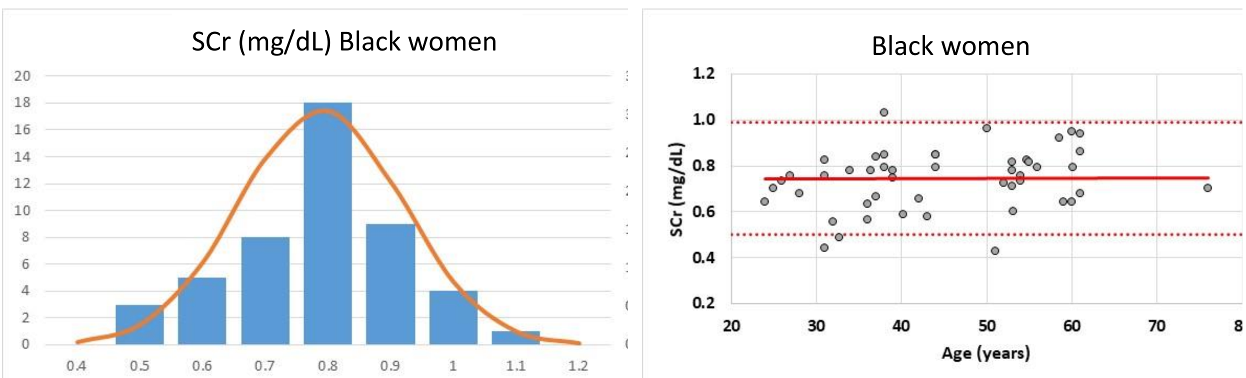
Min	0.43
Max	1.03
Count	48
Avg	0.74
Std	0.13
Median	0.76

We used 4 methods to evaluate normality of the data:

1. If the data are approximately normal, then IQR/SD = ± 1.34.
   We found IQR/SD = 1.346
2. The QQ-plot shows a straight line
3. Lilliefors test: $p > 0.1$
4. Shapriro-Wilk test: $p > 0.9$

Conclusion: there is no evidence of non-normality!

Figure S2.2.2.B. Distribution of SCr in healthy European Black female kidney donors and SCr vs age



Bootstrapping using 1000 resamples resulted in the following statistics for the SCr-values:

	Mean	Median
Avg	0.739	0.754
Std	0.020	0.025
95%CI	0.700	0.706
	0.777	0.802

No age-dependency and 44/48 = 92% of the subjects have SCr/Q between [0.67; 1.33]. We defined Q = 0.74 mg/dL.

Section S3. Matched cohort analysis

The aim of the matching analysis was to evaluate possible differences in the biomarker values at the same GFR-level between White and Black subjects, and between men and women. To avoid that observed differences were caused by differences in the measurement methods for the biomarkers and mGFR, we selected only patients from one hospital in Paris (Bichat Hospital) where the same methods for measuring creatinine (IDMS standardized enzymatic method), cystatin C (calibrated against the certified reference material ERM DA471/IFCC) and measured GFR (plasma clearance of ^{51}Cr EDTA) were used.

Using a SAS macro, we tried to match each Black patient (n = 697) with one unique White patient (n = 2,262) in a 1:1 setting, using the following matching criteria: age ± 3 years, sex, BMI ± 2.5 kg/m² and mGFR ± 3 mL/min/1.73m² to obtain subjects with similar demographic characteristics (age and sex), similar weight (BMI) and similar kidney function (mGFR). Table S3 presents the patient characteristics of the entire cohorts, used for the matching analysis.

Table S3. Patient characteristics of the entire cohorts used for the matching analysis (mean ± SD)

Ethnicity/Sex	N	Age (years)	BMI (kg/m²)	mGFR (mL/min/1.73m²)	SCr (mg/dL)	CysC (mg/L)
White Men	1296 (57%)	53.0 ± 14.6	26.2 ± 4.9	61.8 ± 26.0	1.52 ± 0.73	1.52 ± 0.68
Black Men	436 (63%)	50.7 ± 13.1	26.3 ± 4.5	62.0 ± 22.1	1.73 ± 0.81	1.41 ± 0.61
White Women	966 (43%)	52.5 ± 15.2	25.8 ± 6.2	62.8 ± 26.8	1.16 ± 0.61	1.38 ± 0.73
Black Women	261 (37%)	51.9 ± 15.2	27.4 ± 5.8	59.1 ± 25.6	1.40 ± 0.79	1.46 ± 0.76

In total, 577 Black subjects could successfully be matched with a White subject, 200 women (35%) and 377 men (65%), based on the predefined criteria. Table S4 gives an overview of the demographic and renal characteristics in the matched cohorts, demonstrating the successful matching. From the same Table it can be seen that there are differences in SCr between Black men and White men, and between Black women and White women, but not in Cystatin C, illustrating the race-independence of cystatin C.

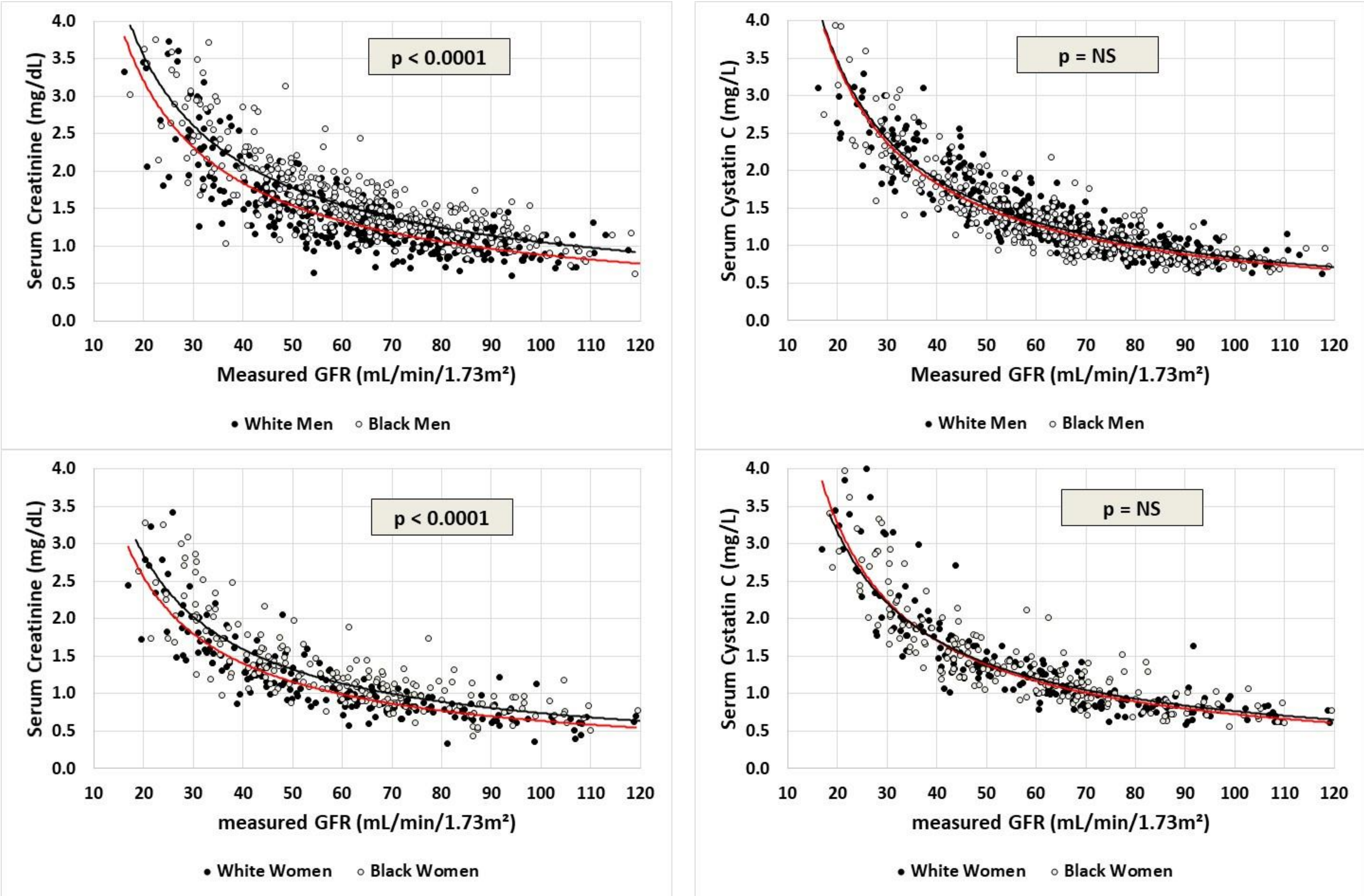
Moreover, there is also a clear difference in SCr between men and women, but not in cystatin C, illustrating the sex-independence of cystatin C.

Table S4. Demographic and renal characteristics of the matched White and Black subjects (mean ± SD)

Sex	N	Age (years)	BMI (kg/m²)	mGFR (mL/min/1.73m²)	SCr (mg/dL)	CysC (mg/L)
White Men	377	51.1 ± 12.2	25.7 ± 3.4	63.8 ± 21.0	1.43 ± 0.62	1.41 ± 0.56
Black Men	377	50.8 ± 12.3	25.8 ± 3.5	63.6 ± 21.0	1.65 ± 0.64	1.37 ± 0.59
White Women	200	53.4 ± 11.9	26.1 ± 4.6	59.7 ± 23.2	1.16 ± 0.53	1.40 ± 0.69
Black Women	200	53.3 ± 11.9	26.2 ± 4.6	59.8 ± 23.1	1.33 ± 0.61	1.41 ± 0.64

To further illustrate the differences in SCr and/or Cystatin C between Black and White subjects, we plotted serum creatinine and cystatin C versus measured GFR, separately for men and women, in Figure S2. The data were fitted with a power function separately for White and Black subjects, demonstrating a clear shift in the SCr vs mGFR curves between Black and White subjects for serum creatinine, while there is (nearly) no shift between the curves for cystatin C versus mGFR.

Figure S2. Serum creatinine (mg/dL) (left panel) and Cystatin C (mg/L) (right panel) versus measured GFR for the matched Black and White subjects from the same hospital in Paris. The black (for Black subjects) and red (for White subjects) curves are the fitted power functions ($y = a\ x^b$). P-values are obtained from the paired t-test.



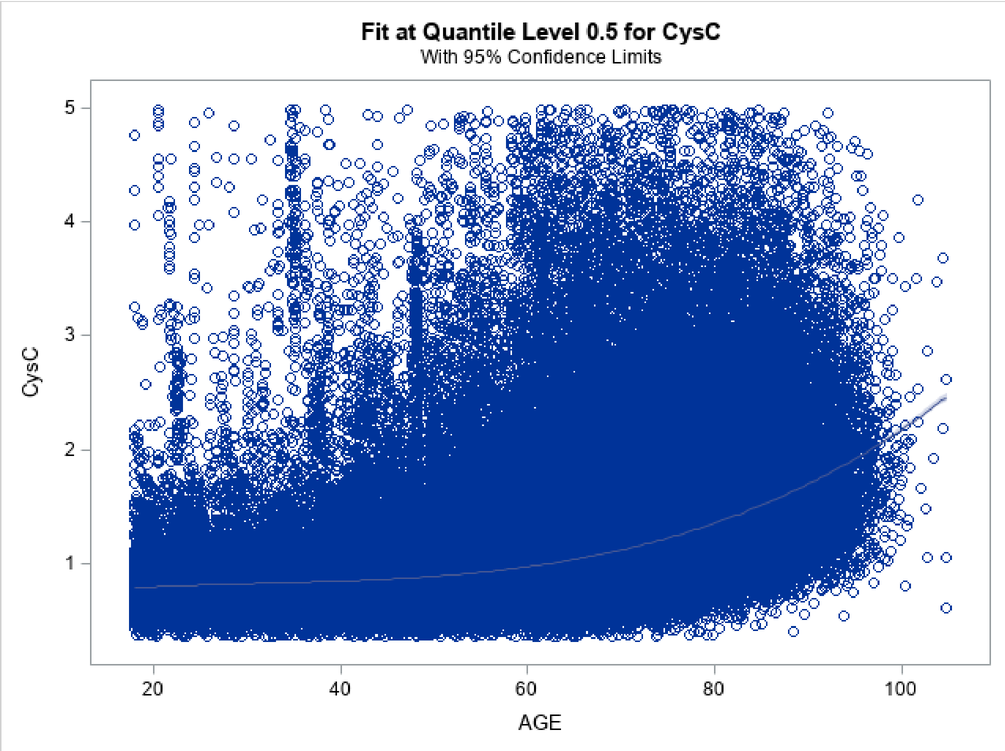
Section S4. Q-values for cystatin C

Like for SCr, the rescaling factor was defined as the average cystatin C value for healthy subjects. Based on a very large dataset for cystatin C, obtained from Uppsala University (Sweden), cystatin C versus age could be evaluated. Plasma concentrations of cystatin C between 2007 and 2020 were determined by an automated particle-enhanced immunoturbidimetric assay using cystatin PET-kit (Gentian, Moss, Norway) on an Architect Ci8200 analyser (Abbott Laboratories, Abbott Park, IL, USA) and calibrated against the international cystatin C reference material (ERM-DA471/IFCC). The procedure had a total coefficient of variation of 2.1%. The cystatin C method was monitored using internal controls and ten patient pools covering the cystatin C range from < 1 mg/L to > 6 mg/L with a batch acceptance criterion of a deviation of less than 3.0% [15]. These pools and the ERM-DA471/IFCC reference material were used to verify that the calibration of the instrument was correct when analysing patient samples for the CAPA equation [3]. The department of Clinical Chemistry and Pharmacology in Uppsala is participating in Equalis' (www.equalis.se) external quality assessment scheme for cystatin C and creatinine measurements.

Cystatin C measurements (153,827 in women and 229,661 in men) of Uppsala University Hospital, Sweden, were used to define rescaling values (Q'-values) for cystatin C in adults. The data were cleaned based on the following criteria: a) only clinics with at least 100 samples were included; and b) samples had a median cystatin C based eGFR (Caucasian Asian Pediatric Adult equation [3]) that was at least 70% of median creatinine based eGFR (EKFC-eGFR$_{Cr}$). Cleaning resulted in a final total number of included subjects of 227,643 (95,469 women and 132,174 men) (see Figure S3).

We calculated medians in one-year subgroups to evaluate the age- and sex-dependency of cystatin C (Figure S4). Median quantile regression using two linear splines with a knot at 50 years (as this was the age to get a flat first spline) was applied to determine a mathematical relationship between cystatin C and age. The simple mathematical model was to set Q' = 0.79 mg/L for women and 0.86 mg/L for men until age 50 years, and a linearly increasing model thereafter. Note however that creatinine also shows an increase after the age of 50 years and the decline rate coefficients in the FAS$_{Crea}$ [16] and EKFC-eGFR$_{Cr}$ [9] equations take this into account. Therefore, to keep the coefficients of EKFC-eGFR$_{Cr}$ in the EKFC-eGFR$_{Cys}$-equation, the acceleration rate of cystatin C after the age of 50 years should match the creatinine increase after 50 years (Figure S4.1). As cystatin C increases much faster than creatinine, we compensated this by using adjusted Q'-values after the age of 50 years, resulting in the following simple relationship: Q' = 0.79 mg/L until age 50 years, and Q' = 0.79 + 0.005 x (Age – 50) thereafter, for women, and Q' = 0.86 mg/L until age 50 years, and Q' = 0.86 + 0.005 x (Age – 50) thereafter for men.

Figure S3. Cystatin C versus age and the median quantile line for the 227,643 included subjects.



A simple sex-free relationship between cystatin C and age was obtained using Q' = 0.83 until the age of 50 years and Q' = 0.83 + 0.005 x (Age – 50) thereafter.

From Figure S4 it can be seen that a quadratic or cubic relationship between median cystatin C and age may give a better fit than the linear splines. Therefore, we investigated whether this more complex model would result in better eGFR-predictions.

The median cystatin C values were fitted against age with 3rd degree polynomials, as shown in figures S4.3a (women) and S4.3b (men). The SCr-age dependency is also shown in figure S4.2. In order to keep the same mathematical form of the EKFC equation (and the same coefficients), we had to compensate for the difference in acceleration rate of cystatin C compared to SCr. Therefore, we calculated the difference

(Difference = 3rd degree polynomial – SCr – 0.09), 0.09 being the shift at 18 years) (see Tables S4.1 and S4.2).

Figure S4. Median plasma cystatin C in one-year intervals against age for men and women. A mathematical model to define Q'-values is proposed (red solid line): for adults Q' = 0.79 mg/L (women, dashed line) and 0.86 mg/L (men, solid line) until 50 years and a linear increasing model thereafter.

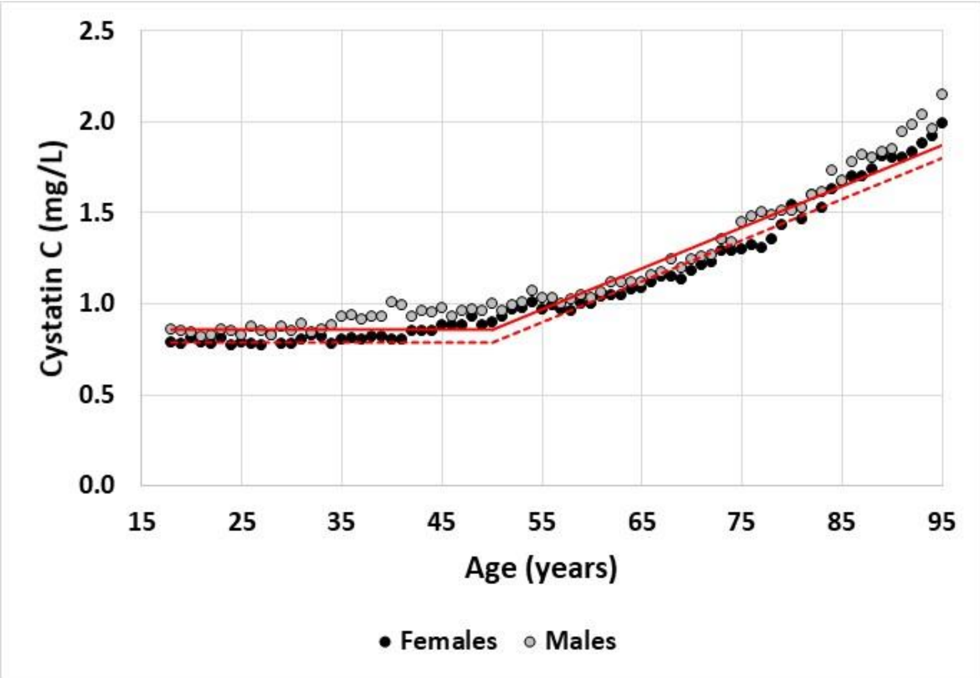


Figure S4.1. Simplified evolution of plasma/serum creatinine with age (red curves, right vertical axis) for men (upper line) and women (lower line). Evolution of plasma cystatin C (adult model) with age (black curves, left vertical axis) for men (upper line) and women (lower line). Modified evolution after 50 years for cystatin C (blue curve) to match the incline rate of creatinine. The dotted lines correspond to the Q'-values used in FAS_{CysC} (0.82 until age 70 years and 0.95 thereafter, respectively).

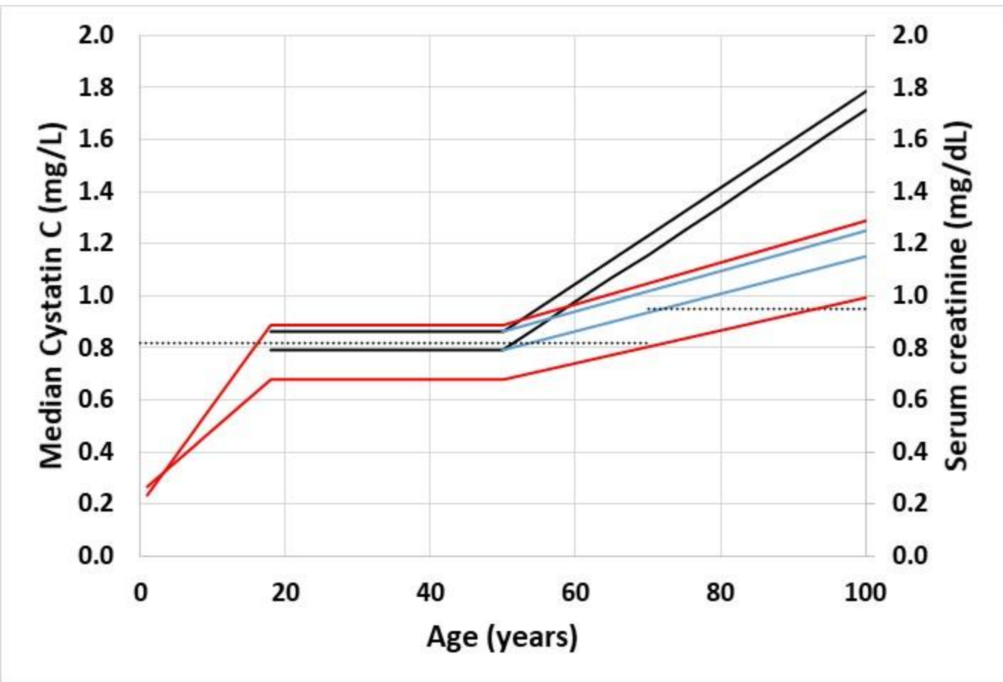


Table S4.1. Female data for the simplified SCr vs age model and the fitted 3rd degree polynomial for cystatin C. Difference = Polynomial - SCr – 0.09. Then this difference is subtracted from the 3rd degree polynomial and these data are fitted with a 2nd degree polynomial.

Age	SCr	3rd degree polynomial	Difference		3rd degree polynomial – Difference	Linear spline Q-values
18	0.70	0.79	0.00		0.79	0.79
25	0.70	0.79	0.00		0.79	0.79
30	0.70	0.80	0.01		0.79	0.79
35	0.70	0.81	0.02		0.79	0.79
40	0.70	0.83	0.04		0.79	0.79
45	0.70	0.86	0.07		0.79	0.79
50	0.70	0.90	0.11		0.79	0.79
55	0.71	0.96	0.14		0.82	0.82
60	0.74	1.02	0.17		0.85	0.84
65	0.77	1.11	0.22		0.88	0.87
70	0.81	1.21	0.29		0.92	0.89
75	0.84	1.32	0.38		0.95	0.92
80	0.87	1.46	0.48		0.98	0.94
85	0.90	1.62	0.61		1.01	0.97
90	0.93	1.80	0.76		1.04	0.99

Table S4.2. Male data for the simplified SCr vs age model and the fitted 3rd degree polynomial for cystatin C. Difference = Polynomial - SCr + 0.046 (0.046 is the shift at 18 years). Then this difference is subtracted from the 3rd degree polynomial and these data are fitted with a 2nd degree polynomial.

Age	SCr	3rd degree polynomial	Difference		3rd degree polynomial - Difference	Linear spline Q-values
18	0.90	0.854	0.000		0.854	0.86
25	0.90	0.861	0.008		0.854	0.86
30	0.90	0.871	0.017		0.854	0.86
35	0.90	0.886	0.032		0.854	0.86
40	0.89	0.908	0.055		0.854	0.86
45	0.89	0.939	0.085		0.854	0.86
50	0.89	0.980	0.126		0.854	0.86
55	0.93	1.033	0.139		0.894	0.89
60	0.97	1.099	0.165		0.934	0.91
65	1.01	1.180	0.206		0.974	0.94
70	1.05	1.278	0.264		1.014	0.96
75	1.09	1.393	0.340		1.054	0.99
80	1.13	1.529	0.435		1.094	1.01
85	1.17	1.685	0.552		1.134	1.04
90	1.21	1.865	0.691		1.174	1.06

The final 2nd degree polynomials were:

Q (women) = 0.85608594 – 0.00488212 x Age + 0.00007906 x Age^2

Q (men) = 0.93803213 – 0.00620726 x Age + 0.00010052 x Age^2

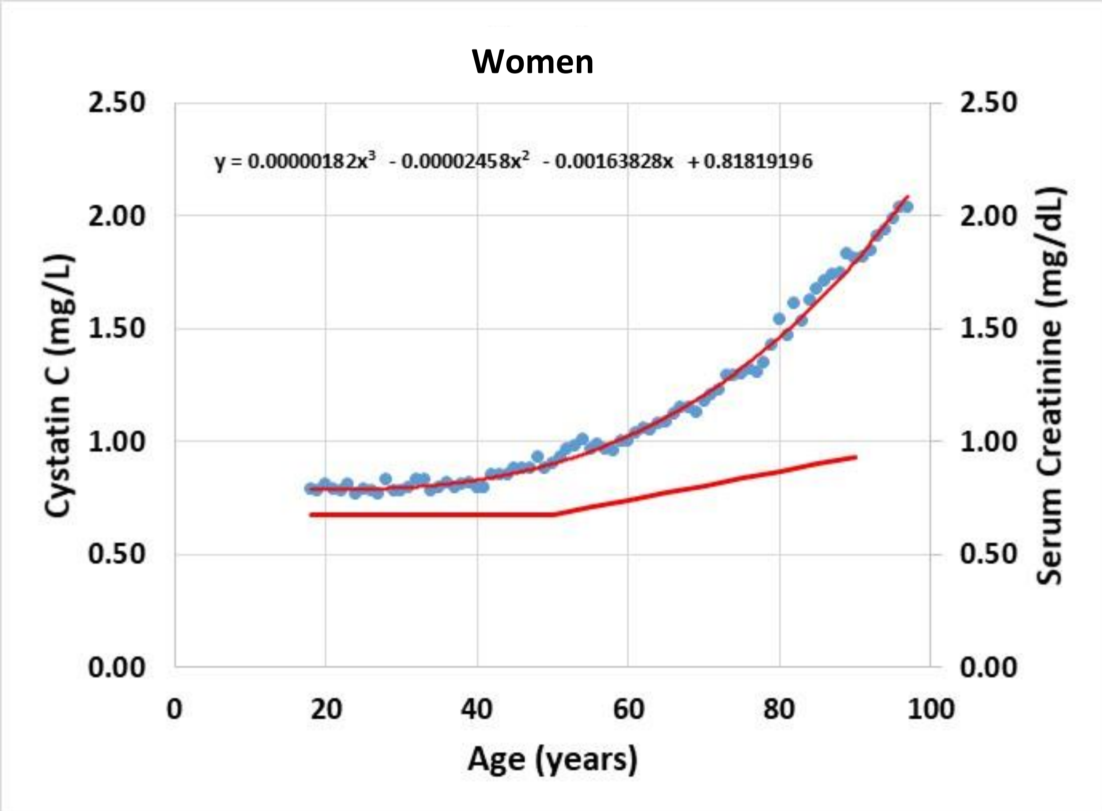


Figure S4.2a. Median cystatin C (and median serum creatinine (linear relationship)) versus age for women, fitted by a 3rd degree polynomial

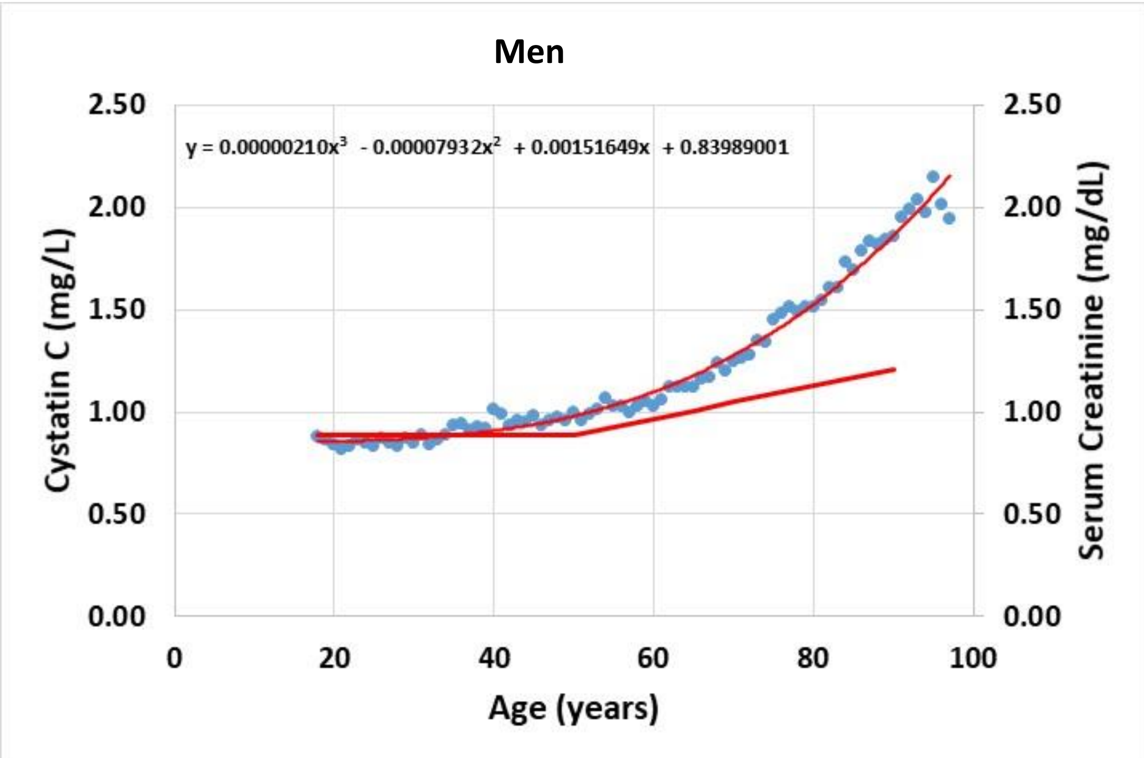


Figure S4.2b. Median cystatin C (and median serum creatinine (linear relationship)) versus age for men, fitted by a 3rd degree polynomial

Residual plots are shown in Figure S4.4 for the linear spline models and for the polynomial models.

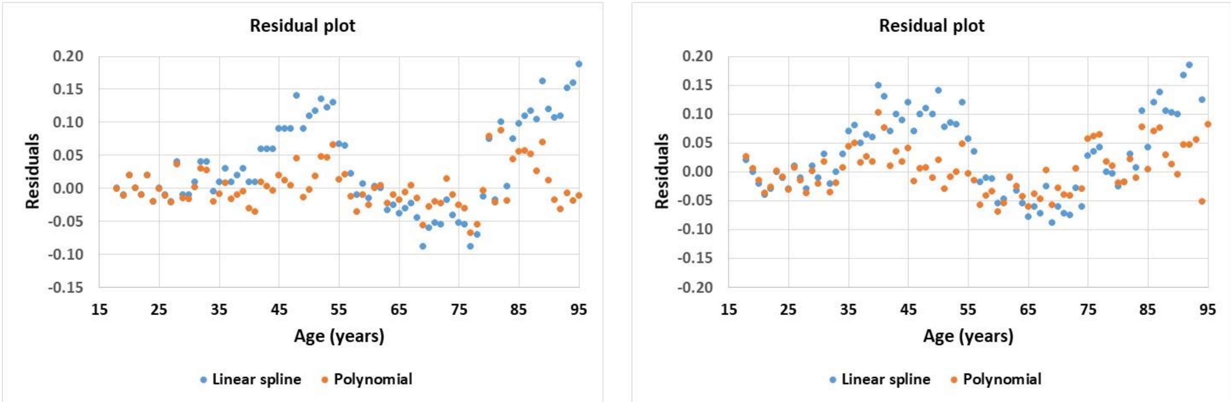


Figure S4.3. Residuals versus age for the linear spline and 3rd degree polynomial models for median cystatin C (left panel, women; right panel (men))

The final Q-values modelled as 2nd degree polynomials are shown in Figure S4.5 and the Q-values are presented in Table S4.3. for both the 2nd degree polynomial model and the simple linear splines model.

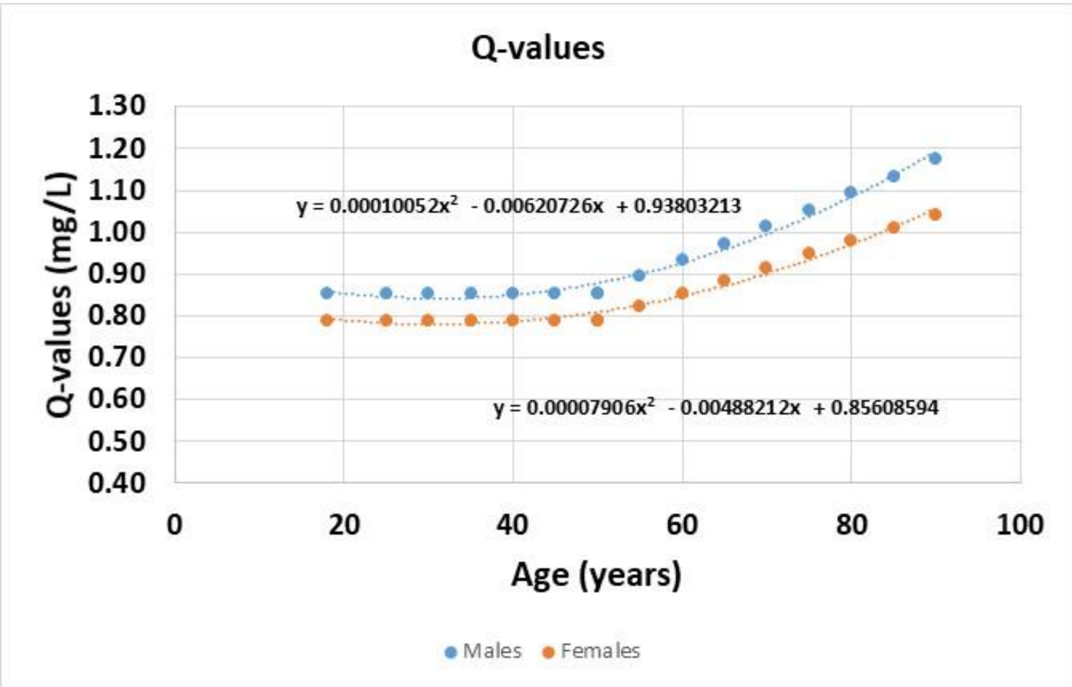


Figure S4.4. Q-values versus age modelled as 2nd degree polynomials

Based on the same reasoning, we also obtained a sex-independent 2nd degree polynomial for the Q-values:

Q = 0.00009180 x Age² - 0.00595997 x Age + 0.91672077

Then we compared, in the whole cohort, the performance of the $EKFC_{CysC}$-equation, using the Q-values obtained with the linear spline model and with the 2nd degree polynomial model. In Table S4.4 the results are shown for the sex-dependent and sex-independent Q-values. Because the Q values are obviously influenced by age, we showed the results according to three age categories. Table S4.4 shows a very similar bias and P30 in all subgroups independent of the way the Q values were calculated. For the sake of simplicity, we consider the Q values calculated from the linear splines in the rest of the manuscript.

Table S4.3. Q-values for cystatin C for men and women, based on the 2nd degree polynomials and on the linear spline model

	Men		Women	
Age	Q-linear	Q-polynomial	Q-linear	Q-polynomial
18	0.86	0.86	0.79	0.79
25	0.86	0.85	0.79	0.78
30	0.86	0.84	0.79	0.78
35	0.86	0.84	0.79	0.78
40	0.86	0.85	0.79	0.79
45	0.86	0.86	0.79	0.80
50	0.86	0.88	0.79	0.81
50	0.86	0.88	0.79	0.81
55	0.89	0.90	0.82	0.83
60	0.91	0.93	0.84	0.85
65	0.94	0.96	0.87	0.87
70	0.96	1.00	0.89	0.90
75	0.99	1.04	0.92	0.93
80	1.01	1.08	0.94	0.97
85	1.04	1.14	0.97	1.01
90	1.06	1.19	0.99	1.06

Table S4.4. Performance statistics of the cystatin C based EKFC-eGFR equation, using different Q-values

		Cystatin C based EKFC-eGFR			
Age		Q = linear splines	Q = sex-independent linear splines	Q = 2nd degree polynomial	Q = sex-independent 2nd degree polynomial
All	Bias	0.19 [-0.05; 0.39]	0.25 [0.02; 0.49]	1.06 [0.81; 1.30]	1.06 [0.84; 1.30]
(n = 12,832)	IQR	14.79 [-7.66; 7.14]	15.08 [-7.70; 7.39]	14.87 [-6.83; 8.04]	15.03 [-6.85; 8.18]
	P10	41.8 [40.9; 42.6]	40.9 [40.0; 41.7]	41.9 [41.1; 42.8]	41.0 [40.2; 41.9]
	P30	86.3 [85.7; 86.9]	86.3 [85.7; 86.9]	85.8 [85.2; 86.4]	85.7 [85.1; 86.3]
18-40	Bias	3.81 [3.03; 4.47]	3.91 [3.18; 4.61]	2.96 [2.11; 3.37]	3.54 [2.78; 4.18]
(n = 1,829)	IQR	18.21 [-5.65; 12.56]	18.59 [-5.51; 13.07]	18.23 [-6.52; 11.72]	18.55 [-5.89; 12.66]
	P10	41.3 [39.0; 43.5]	40.6 [38.3; 42.8]	42.0 [39.7; 44.3]	40.7 [38.4; 42.9]
	P30	86.1 [84.5; 87.7]	86.1 [84.5; 87.7]	86.9 [85.4; 88.5]	86.4 84.9; 88.0]
40-65	Bias	0.05 [-0.32; 0.37]	0.17 [-0.15; 0.50]	0.66 [0.34; 1.06]	0.78 [0.44; 1.05]
(n = 6,444)	IQR	15.64 [-8.10; 7.54]	16.13 [-8.25; 7.88]	15.61 [-7.40; 8.21]	15.99 [-7.57; 8.42]
	P10	45.0 [43.8; 46.3]	44.1 [42.9; 45.3]	45.3 [44.0; 46.5]	44.5 [43.3; 45.7]
	P30	88.7 [87.9; 89.4]	88.3 [87.5; 89.1]	88.6 [87.8; 89.4]	88.3 [87.5; 89.0]
≥ 65	Bias	-0.74 [-1.15; -0.38]	-0.73 [-1.11; -0.40]	0.88 [0.52; 1.30]	0.76 [0.37; 1.16]
(n = 4,559)	IQR	12.42 [-7.54; 4.88]	12.71 [-7.58; 5.13]	12.72 [-6.11; 6.61]	12.61 [-6.08; 6.53]
	P10	37.4 [35.9; 38.8]	36.5 [35.1; 37.9]	37.2 [35.8; 38.6]	36.6 [34.9; 37.7]
	P30	83.0 [82.0; 84.1]	83.4 [82.3; 84.5]	81.5 [80.3; 82.6]	81.7 [80.6; 82.9]

Section S5. External validation of EKFC-eGFR$_{Cr}$ and EKFC-eGFR$_{Cys}$ in the data from Kent and Lund

As the power coefficients of the creatinine based EKFC-eGFR-equation were partially derived from the data used to validate the EKFC-eGFR$_{Cys}$, it could be argued that the current validation is not a true external validation, as some datasets were part of the development/internal validation of the EKFC-eGFR$_{Cr}$-equation. We therefore also restricted the current validation to those datasets that were used for the external validation of the EKFC-eGFR$_{Cr}$-equation. The results are presented in Table S5. The external validation datasets are from Lund and Kent.

Table S5. Median bias [95%CI], interquartile range (IQR), P10 [95%CI] and P30 [95%CI] accuracy for different cystatin C based equations in the **external** EKFC-validation dataset. CKD-EPI-eGFR$_{Cr}$ (ASR) or (AS) and CKD-EPI-eGFR$_{Cys}$ serve as a benchmark (as the KDIGO recommended equations).

18 ≤ age < 40y, n = 368	CKD-EPI-eGFR$_{Cr}$ (ASR)	CKD-EPI-eGFR$_{Cr}$ (AS)	EKFC-eGFR$_{Cr}$	CKD-EPI-eGFR$_{Cys}$	EKFC-eGFR$_{Cys}$	CKD-EPI-eGFR$_{Cr+Cys}$	EKFC-eGFR$_{Cr+Cys}$
Median bias [95%CI]	13.2 [10.4; 14.6]	14.7 [12.8; 16.4]	5.2 [4.0; 7.7]	-3.1 [-4.8; -1.9]	-1.5 [-2.9; -0.5] / -1.9 [-3.2; 0.0]*	3.0 [1.6; 4.4] / 3.7 [2.3; 5.7]**	2.3 [0.8; 3.5] / 2.8 [0.9; 4.0]*
IQR [Pct25; Pct75]	23.6 [1.9; 25.5]	23.4 [3.6; 27.0]	18.5 [-2.6; 15.9]	16.0 [-12.2; 3.7]	16.3 [-11.1; 5.2] / 16.6 [-10.8; 5.7]*	15.8 [-4.1; 11.6] / 16.0 [-3.6; 12.4]**	14.3 [-5.5; 8.8] / 15.0 [-5.6; 9.4]*
P10 [95%CI]	32.1 [27.3; 36.9]	29.9 [25.2; 34.6]	41.3 [36.3; 46.4]	43.8 [38.7; 48.8]	47.3 [42.2; 52.4] / 45.7 [40.5; 50.8]*	49.7 [44.6; 54.9] / 48.4 [43.2; 53.5]**	50.8 [45.7; 55.9] / 50.0 [44.9; 55.1]*
P30 [95%CI]	72.6 [68.0; 77.1]	69.6 [64.8; 74.3]	81.8 [77.8; 85.8]	89.4 [86.2; 92.6]	88.9 [85.6; 92.1] / 89.9 [86.9; 93.0]*	92.4 [89.7; 95.1] / 92.4 [89.7; 95.1]**	91.0 [88.1; 94.0] / 90.5 [87.5; 93.5]*
40 ≤ age < 65y, n = 1194							
Median bias [95%CI]	5.2 [4.4; 5.8]	8.1 [7.4; 9.1]	3.6 [3.0; 4.6]	-6.0 [-6.7; -5.3]	-4.1 [-4.9; -3.4] / -3.6 [-4.5; -2.9]*	-1.2 [-1.7; -0.7] / 0.4 [-0.1; 0.8]**	0.3 [-0.2; 1.0] / 0.6 [-0.1; 1.0]*
IQR [Pct25; Pct75]	14.7 [-1.4; 13.3]	16.0 [1.1; 17.1]	14.2 [-2.8; 11.4]	14.1 [-13.8; 0.3]	14.9 [-12.7; 2.2] / 14.6 [-12.1; 2.6]*	10.3 [-6.4; 3.9] / 10.9 [-4.8; 6.0]**	11.5 [-6.2; 5.2] / 11.3 [-6.0; 5.3]*
P10 [95%CI]	39.5 [36.8; 42.3]	32.6 [29.9; 35.2]	41.0 [38.2; 43.8]	33.6 [30.9; 36.3]	39.2 [36.4; 42.0] / 41.0 [38.2; 43.7]*	50.3 [47.5; 53.2] / 50.5 [47.7; 53.3]**	49.8 [47.0; 52.7] / 49.0 [46.2; 51.8]*
P30 [95%CI]	79.8 [77.5; 82.1]	73.8 [71.3; 76.3]	81.2 [78.9; 83.4]	83.7 [81.6; 85.8]	84.4 [82.4; 86.5] / 85.4 [83.4; 87.4]*	94.1 [92.7; 95.4] / 93.6 [92.2; 95.0]**	90.8 [89.1; 92.4] / 91.1 [89.5; 92.7]*
Age ≥ 65y, n = 1679							
Median bias [95%CI]	3.1 [2.4; 3.6]	6.3 [5.5; 6.9]	0.0 [-0.4; 0.5]	-5.2 [-5.7; -4.5]	-2.7 [-3.2; -2.1] / -2.6 [-3.0; -2.0]*	-1.4 [-1.8; -1.1] / 0.2 [-0.2; 0.6]**	-1.2 [-1.5; -0.8] / -1.1 [-1.5; -0.6]*
IQR [Pct25; Pct75]	11.7 [-2.0; 9.7]	13.3 [0.6; 13.9]	11.0 [-5.3; 5.7]	12.1 [-11.8; 0.3]	12.3 [-9.8; 2.5] / 12.0 [-9.3; 2.7]*	8.8 [-5.8; 3.1] / 9.6 [-4.1; 5.5]**	9.1 [-6.1; 3.1] / 9.1 [-5.9; 3.2]*
P10 [95%CI]	36.8 [34.5; 39.1]	30.1 [27.9; 32.3]	39.0 [36.6; 41.3]	28.6 [26.5; 30.8]	34.9 [32.6; 37.2] / 33.9 [31.6; 36.2]*	42.5 [40.1; 44.8] / 42.9 [40.5; 45.3]**	45.0 [42.6; 47.3] / 44.8 [42.4; 47.2]*
P30 [95%CI]	78.0 [76.0; 80.0]	69.8 [67.6; 72.0]	82.5 [80.7; 84.3]	76.4 [74.4; 78.4]	80.6 [78.7; 82.5] / 82.0 [80.1; 83.8]*	87.6 [86.0; 89.2] / 87.2 [85.6; 88.8]**	88.7 [87.2; 90.3] / 89.0 [87.5; 90.5]*

Pct = percentiles; *using the sex-independent EKFC-eGFR$_{Cys}$; **using CKD-EPI-eGFR$_{Cr}$ (AS)

Section S6. Overview of eGFR-equations

Table S6. Overview of eGFR-equations used in this study

Name	Age	Sex			eGFR-Equation
CKD-EPI-eGFR$_{Cr}$(ASR) [17]	≥ 18	Female	SCr ≤ 0.70		144 x $(SCr/0.70)^{-0.329}$ x 0.9929^{Age} x 1.159 [if Black]
			SCr > 0.70		144 x $(SCr/0.70)^{-1.209}$ x 0.9929^{Age} x 1.159 [if Black]
		Male	SCr ≤ 0.90		141 x $(SCr/0.90)^{-0.411}$ x 0.9929^{Age} x 1.159 [if Black]
			SCr > 0.90		141 x $(SCr/0.90)^{-1.209}$ x 0.9929^{Age} x 1.159 [if Black]
CKD-EPI-eGFR$_{Cr}$ AS) [17]	≥ 18	Female	SCr ≤ 0.70		143 x $(SCr/0.70)^{-0.241}$ x 0.9938^{Age}
			SCr > 0.70		143 x $(SCr/0.70)^{-1.200}$ x 0.9938^{Age}
		Male	SCr ≤ 0.90		142 x $(SCr/0.90)^{-0.302}$ x 0.9938^{Age}
			SCr > 0.90		142 x $(SCr/0.90)^{-1.200}$ x 0.9938^{Age}
CKD-EPI-eGFR$_{Cys}$ [17]	≥ 18	Female	ScysC ≤ 0.80		133 x $(SCysC/0.80)^{-0.499}$ x 0.9962^{Age} x 0.932
			ScysC > 0.80		133 x $(SCysC/0.80)^{-1.328}$ x 0.9962^{Age} x 0.932
		Male	ScysC ≤ 0.80		133 x $(SCysC/0.80)^{-0.499}$ x 0.9962^{Age}
			ScysC > 0.80		133 x $(SCysC/0.80)^{-1.328}$ x 0.9962^{Age}
CKD-EPI-eGFR$_{Cr+Cys}$(ASR)	≥ 18	Female	SCr ≤ 0.70	ScysC ≤ 0.80	130 x $(SCr/0.70)^{-0.248}$ x $(ScysC/0.80)^{-0.375}$ x 0.9952^{Age}
[17]			SCr ≤ 0.70	ScysC > 0.80	130 x $(SCr/0.70)^{-0.248}$ x $(ScysC/0.80)^{-0.711}$ x 0.9952^{Age}
			SCr > 0.70	ScysC ≤ 0.80	130 x $(SCr/0.70)^{-0.601}$ x $(ScysC/0.80)^{-0.375}$ x 0.9952^{Age}
			SCr > 0.70	ScysC > 0.80	130 x $(SCr/0.70)^{-0.601}$ x $(ScysC/0.80)^{-0.711}$ x 0.9952^{Age}
	≥ 18	Male	SCr ≤ 0.90	ScysC ≤ 0.80	135 x $(SCr/0.90)^{-0.207}$ x $(ScysC/0.80)^{-0.375}$ x 0.9952^{Age}
			SCr ≤ 0.90	ScysC > 0.80	135 x $(SCr/0.90)^{-0.207}$ x $(ScysC/0.80)^{-0.711}$ x 0.9952^{Age}
			SCr > 0.90	ScysC ≤ 0.80	135 x $(SCr/0.90)^{-0.601}$ x $(ScysC/0.80)^{-0.375}$ x 0.9952^{Age}
			SCr > 0.90	ScysC > 0.80	135 x $(SCr/0.90)^{-0.601}$ x $(ScysC/0.80)^{-0.711}$ x 0.9952^{Age}
CKD-EPI-eGFR$_{Cr+Cys}$(AS)	≥ 18	Female	SCr ≤ 0.70	ScysC ≤ 0.80	130 x $(SCr/0.70)^{-0.219}$ x $(ScysC/0.80)^{-0.323}$ x 0.9961^{Age}
[17]			SCr ≤ 0.70	ScysC > 0.80	130 x $(SCr/0.70)^{-0.219}$ x $(ScysC/0.80)^{-0.778}$ x 0.9961^{Age}
			SCr > 0.70	ScysC ≤ 0.80	130 x $(SCr/0.70)^{-0.544}$ x $(ScysC/0.80)^{-0.323}$ x 0.9961^{Age}
			SCr > 0.70	ScysC > 0.80	130 x $(SCr/0.70)^{-0.544}$ x $(ScysC/0.80)^{-0.778}$ x 0.9961^{Age}
	≥ 18	Male	SCr ≤ 0.90	ScysC ≤ 0.80	135 x $(SCr/0.90)^{-0.144}$ x $(ScysC/0.80)^{-0.323}$ x 0.9961^{Age}
			SCr ≤ 0.90	ScysC > 0.80	135 x $(SCr/0.90)^{-0.144}$ x $(ScysC/0.80)^{-0.778}$ x 0.9961^{Age}
			SCr > 0.90	ScysC ≤ 0.80	135 x $(SCr/0.90)^{-0.544}$ x $(ScysC/0.80)^{-0.323}$ x 0.9961^{Age}
			SCr > 0.90	ScysC > 0.80	135 x $(SCr/0.90)^{-0.544}$ x $(ScysC/0.80)^{-0.778}$ x 0.9961^{Age}
EKFC-eGFR$_{Cr}$ [9]	18 - 40	Female	SCr/Q < 1.0		107.3 x $(SCr/Q)^{-0.322}$
			SCr/Q ≥ 1.0		107.3 x $(SCr/Q)^{-1.132}$
		Male	SCr/Q < 1.0		107.3 x $(SCr/Q)^{-0.322}$
			SCr/Q ≥ 1.0		107.3 x $(SCr/Q)^{-1.132}$
	> 40	Female	SCr/Q < 1.0		107.3 x $(SCr/Q)^{-0.322}$ x $0.990^{(Age-40)}$
			SCr/Q ≥ 1.0		107.3 x $(SCr/Q)^{-1.132}$ x $0.990^{(Age-40)}$
		Male	SCr/Q < 1.0		107.3 x $(SCr/Q)^{-0.322}$ x $0.990^{(Age-40)}$
			SCr/Q ≥ 1.0		107.3 x $(SCr/Q)^{-1.132}$ x $0.990^{(Age-40)}$
EKFC-eGFR$_{Cys}$	18 - 40		ScysC/0.83 < 1.0		107.3 x $(SCysC/0.83)^{-0.322}$
			ScysC/0.83 ≥ 1.0		107.3 x $(SCysC/0.83)^{-1.132}$
	> 40		ScysC/0.83 < 1.0		107.3 x $(SCysC/0.83)^{-0.322}$ x $0.990^{(Age-40)}$
			ScysC/0.83 ≥ 1.0		107.3 x $(SCysC/0.83)^{-1.132}$ x $0.990^{(Age-40)}$
	> 50		ScysC/Q < 1.0 Q = 0.83+0.005x(Age – 50)		107.3 x $(SCysC/Q)^{-0.322}$ x $0.990^{(Age-40)}$

			ScysC/Q ≥ 1.0 Q = 0.83+0.005x(Age – 50)	107.3 x $(SCysC/Q)^{-1.132}$ x $0.990^{(Age-40)}$
FAS_{Crea} [11]	≤ 40	Female		107.3 / [SCr/0.70]
	> 40			107.3 / [SCr/0.70] x $0.988^{(Age-40)}$
	≤ 40	Male		107.3 / [SCr/0.90]
	> 40			107.3 / [SCr/0.90] x $0.988^{(Age-40)}$
FAS_{CysC} [18]	≤ 40			107.3 / [SCysC/0.82]
	40-75			107.3 / [SCysC/0.82] x $0.988^{(Age-40)}$
	> 75			107.3 / [SCysC/0.95] x $0.988^{(Age-40)}$
LMREV [19]		Female	< 150 (in µmol/L)	X = 2.5 + 0.0121 x (150 – SCr) (SCr in µmol/L)
			≥ 150	X = 2.5 – 0.926 x log(SCr/150)
		Male	< 180	X = 2.56 + 0.00968 x (180 – SCr)
			≥ 180	X = 2.56 – 0.926 x log(SCr/180)
				GFR = exp(X – 0.0158 x age + 0.438 x log(age))
CAPA [10]				130 x $ScysC^{-1.069}$ x $age^{-0.117}$ - 7

Q = rescaling factor for the biomarker which are population-specific for SCr, but not for CysC.

To make a more continuous transition from the paediatric EKFC-$eGFR_{Cr}$-equation to the adult EKFC-$eGFR_{Cr}$-equation, the Q-values for children, adolescents and young adults (up to 25 years) can be calculated from (note that the Q-value obtained from these equations is expressed in µmol/L):

- Men, age ≤ 25: ln(Q) = 3.200 + 0.259 x age - 0.543 x log(age) - 0.00763 x age^2 + 0.0000790 x age^3
- Women, age ≤ 25 ln(Q) = 3.080 + 0.177 x age - 0.223 x log(age) - 0.00596 x age^2 + 0.0000686 x age^3

Q can be obtained in mg/dL using exp(Q)/88.4!
For White subjects, age > 25 years, use

- Men: Q = 0.90 mg/dL
- Women: Q = 0.70 mg/dL

In the next section, we present tables according to age-subgroups (18-40, 40-65 and > 65 years) for the five different cohorts. Graphs for bias versus age are based on median quantile regression using 4th degree polynomials. Likewise, the P30(%) accuracy against age graphs are based on cubic splines with three free knots using 3rd degree polynomials.

Section S7. Validation results in the five different cohorts, according to age-subgroups

Table S7.1. Performance in the **White EKFC Cohort** (n = 7,727) according to age subgroups. Median bias [95%CI] (mL/min/1.73m²), imprecision (interquartile range, IQR), P10(%) [95%CI] and P30(%) [95%CI] accuracy are presented.

18 ≤ age < 40 y, n = 805	CKD-EPI-eGFR$_{Cr}$ (ASR)	CKD-EPI-eGFR$_{Cr}$ (AS)	EKFC-eGFR$_{Cr}$	CKD-EPI-eGFR$_{Cys}$	EKFC-eGFR$_{Cys}$	CKD-EPI-eGFR$_{Cr+Cys}$	EKFC-eGFR$_{Cr+Cys}$
Median bias [95%CI]	10.9 [9.5; 12.8]	13.2 [11.7; 14.8]	4.2 [3.2; 5.2]	2.1 [1.0; 3.6]	1.6 [0.5; 2.6] / 2.4 [0.9; 3.2]*	6.2 [5.1; 7.3] / 7.7 [6.2; 8.6]**	3.1 [1.9; 4.2] / 3.3 [2.4; 4.3]*
IQR [Pct25; Pct75]	23.8 [0.4; 24.2]	23.9 [2.1; 25.9]	19.6 [-5.6; 14.0]	22.2 [-8.0; 14.2]	18.6 [-8.2; 10.4] / 18.4 [-8.1; 10.3]*	18.1 [-2.5; 15.6] / 18.1 [-1.1; 16.9]**	16.2 [-5.2; 11.0] / 15.9 [-5.3; 10.7]*
P10 [95%CI]	30.7 [27.5; 33.9]	29.9 [26.8; 33.1]	39.9 [36.5; 43.3]	37.3 [33.9; 40.6]	43.9 [40.4; 47.3] / 42.7 [39.3; 46.2]*	42.0 [38.6; 45.4] / 40.1 [36.7; 43.5]**	47.1 [43.6; 50.5] / 46.1 [42.6; 49.5]*
P30 [95%CI]	74.2 [71.1; 77.2]	71.7 [68.6; 74.8]	84.5 [82.0; 87.0]	84.5 [82.0; 87.0]	87.3 [85.0; 89.6] / 87.5 [85.2; 89.7]*	87.7 [85.4; 90.0] / 87.1 [84.8; 89.4]**	90.2 [88.1; 92.2] / 89.2 [87.0; 91.3]*
40 ≤ age < 65y, n = 3,716							
Median bias [95%CI]	3.2 [2.8; 3.7]	6.8 [6.3; 7.3]	0.4 [-0.1; 0.9]	4.7 [4.0; 5.6]	-0.0 [-0.4; 0.4] / 0.2 [-0.4; 0.6]*	5.3 [4.6; 6.0] / 8.7 [8.0; 9.4]**	0.4 [0.0; 0.8] / 0.5 [0.1; 0.9]**
IQR [Pct25; Pct75]	16.3 [-4.5; 11.9]	16.8 [-1.0; 15.8]	16.3 [-7.7; 8.6]	22.8 [-6.2; 16.6]	16.3 [-8.1; 7.4] / 16.4 [-8.7; 7.7]*	16.8 [-2.6; 14.2] / 18.5 [-0.3; 18.3]**	13.7 [-7.0; 6.7] / 13.8 [-6.9; 6.9]*
P10 [95%CI]	46.8 [45.2; 48.4]	41.7 [40.1; 43.3]	47.6 [46.0; 49.2]	31.9 [30.4; 33.4]	46.9 [45.3; 48.5] / 46.3 [44.7; 47.9]*	42.4 [40.8; 43.9] / 36.5 [35.0; 38.1]**	53.9 [52.3; 55.5] / 52.9 [51.3; 54.5]*
P30 [95%CI]	86.8 [85.7; 87.9]	83.1 [81.9; 84.3]	88.6 [87.5; 89.6]	81.5 [80.3; 82.8]	89.2 [88.2; 90.2] / 89.1 [88.1; 90.1]*	89.9 [88.9; 90.8] / 84.8 [83.7; 86.0]**	92.4 [91.6; 93.3] / 92.6 [91.7; 93.4]*
Age ≥ 65y, n = 3,206							
Median bias [95%CI]	3.7 [3.2; 4.0]	7.1 [6.7; 7.6]	0.3 [-0.0; 0.7]	-2.6 [-2.9; -2.2]	-0.6 [-1.0; -0.1]/ -0.6 [-1.0; -0.1]*	0.2 [-0.1; 0.5] / 2.2 [1.8; 2.5]**	-0.1 [-0.4; 0.2] / -0.2 [-0.4; 0.2]*
IQR [Pct25; Pct75]	12.9 [-2.0; 10.9]	14.4 [0.8; 15.2]	11.4 [-5.3; 6.1]	12.6 [-9.2; 3.4]	12.0 [-7.3; 4.6]	10.8 [-4.7; 6.1] / 12.0 [-2.7; 9.3]**	9.5 [-5.1; 4.5] / 9.5 [-4.9; 4.5]*
P10 [95%CI]	35.1 [33.4; 36.7]	27.8 [26.2; 29.3]	39.1 [37.5; 40.8]	30.8 [29.2; 32.4]	36.6 [35.0; 38.3] / 36.1 [34.5; 37.8]*	40.5 [38.8; 42.2] / 37.3 [35.7; 39.0]**	44.9 [43.1; 46.6] / 44.9 [43.2; 46.7]*
P30 [95%CI]	77.5 [76.1; 79.0]	68.2 [66.6; 69.8]	82.8 [81.5; 84.2]	79.1 [77.7; 80.5]	81.7 [80.4; 83.0] / 82.5 [81.2; 83.8]*	86.6 [85.4; 87.8] / 82.7 [81.4; 84.0]**	88.2 [87.1; 89.3] / 88.3 [87.2; 89.4]*

Pct = percentiles; *using the sex-free EKFC-eGFR$_{Cys}$; **using CKD-EPI-eGFR$_{Cr}$(AS)

Table S7.1 cont'd

18 ≤ age < 40 y, n = 805	FAS_{Crea}	FAS_{CysC}	$FAS_{Crea+CysC}$	LMR	CAPA	LMR+CAPA
Median bias [95%CI]	11.3 [9.8; 12.3]	6.3 [5.2; 7.3]	8.0 [7.0; 9.0]	-1.0 [-2.5; 0.1]	-0.7 [-1.7; 0.3]	-0.20 [-1.2; 0.8]
IQR [Pct25; Pct75]	22.1 [0.8; 23.0]	19.9 [-4.8; 15.1]	17.5 [-1.1; 16.4]	19.9 [-11.8; 8.1]	21.6 [-11.6; 10.0]	17.6 [-9.6; 8.0]
P10 [95%CI]	28.9 [25.8; 32.1]	37.6 [34.3; 41.0]	39.3 [35.9; 42.6]	43.2 [39.8; 46.7]	39.1 [35.8; 42.5]	47.5 [44.0; 50.9]
P30 [95%CI]	72.3 [69.2; 75.4]	80.5 [77.8; 83.2]	83.4 [80.8; 85.9]	86.7 [84.4; 89.1]	84.6 [82.1; 87.1]	92.0 [90.2; 93.9]
40 ≤ age < 65y, n = 3,716						
Median bias [95%CI]	3.2 [2.7; 3.7]	1.1 [0.5; 1.6]	1.9 [1.4; 2.3]	-2.9 [-3.3; -2.3]	2.6 [1.8; 3.4]	0.6 [0.1; 1.0]
IQR [Pct25; Pct75]	17.7 [-5.6; 12.1]	19.7 [-9.0; 10.7]	14.8 [-6.0; 8.8]	17.0 [-11.7; 5.3]	25.4 [-8.1; 17.3]	15.4 [-6.8; 8.6]
P10 [95%CI]	43.0 [41.4; 44.6]	38.8 [37.2; 40.3]	49.2 [47.6; 50.8]	44.1 [42.5; 45.7]	31.9 [30.4; 33.4]	48.4 [46.8; 50.0]
P30 [95%CI]	84.4 [83.2; 85.5]	83.9 [82.7; 85.1]	90.3 [89.4; 91.3]	90.0 [89.1; 91.0]	78.2 [76.9; 79.6]	92.5 [91.6; 93.3]
Age ≥ 65y, n = 3,206						
Median bias [95%CI]	0.5 [0.1; 0.7]	-2.0 [-2.5; -1.6]	-1.3 [-1.7; -1.0]	-0.8 [-1.1; -0.4]	-1.9 [-2.3; -1.5]	-1.2 [-1.5; -0.8]
IQR [Pct25; Pct75]	11.5 [-5.5; 6.0]	13.1 [-9.2; 3.8]	10.7 [-7.3; 3.4]	11.2 [-6.4; 4.7]	12.5 [-8.3; 4.2]	9.6 [-6.0; 3.6]
P10 [95%CI]	37.9 [36.2; 39.5]	33.3 [31.6; 34.9]	41.2 [39.5; 42.9]	38.6 [36.9; 40.2]	33.0 [31.4; 34.6]	43.6 [43.1; 46.6]
P30 [95%CI]	82.0 [80.7; 83.3]	80.3 [78.9; 81.7]	86.4 [85.2; 87.6]	84.2 [82.9; 85.4]	79.9 [78.6; 81.3]	88.5 [87.4; 89.6]

Table S7.2. Performance in the **White Paris Cohort** (n = 2,646) according to age subgroups. Median bias [95%CI] (mL/min/1.73m²), imprecision (interquartile range, IQR), P10(%) [95%CI] and P30(%) [95%CI] accuracy are presented.

18 ≤ age < 40 y, n = 564	CKD-EPI-eGFR$_{Cr}$ (ASR)	CKD-EPI-eGFR$_{Cr}$ (AS)	EKFC-eGFR$_{Cr}$	CKD-EPI-eGFR$_{Cys}$	EKFC-eGFR$_{Cys}$	CKD-EPI-eGFR$_{Cr+Cys}$	EKFC-eGFR$_{Cr+Cys}$
Median bias [95%CI]	5.8 [4.5; 7.4]	8.0 [6.7; 10.0]	3.2 [1.8; 4.4]	2.6 [1.5; 4.4]	4.8 [3.7; 6.0] / 5.0 [3.7; 6.3]*	3.8 [2.3; 5.2] / 5.5 [3.8; 7.0]**	4.7 [3.8; 5.8] / 4.8 [4.1; 6.0]*
IQR [Pct25; Pct75]	20.5 [-2.7; 17.8]	20.4 [-0.6; 19.8]	16.9 [-9.5; 7.2]	21.1 [-6.3; 14.8]	16.8 [-3.2; 13.6] / 17.3 [-3.2; 14.2]*	16.4 [-3.1; 13.3] / 17.8 [-2.0; 15.8]**	13.8 [-2.1; 11.8] / 14.5 [-2.2; 12.3]*
P10 [95%CI]	36.3 [32.4; 40.3]	34.9 [31.0; 38.9]	42.6 [38.5; 46.6]	37.4 [33.4; 41.4]	37.8 [33.8; 41.8] / 37.9 [33.9; 42.0]*	43.8 [39.7; 47.9] / 40.8 [36.7; 44.8]**	45.0 [40.9; 49.2] / 44.9 [40.7; 49.0]*
P30 [95%CI]	79.1 [75.7; 82.4]	77.1 [73.7; 80.6]	84.6 [81.6; 87.6]	83.7 [80.6; 86.7]	85.8 [82.9; 88.7] / 84.9 [82.0; 87.9]*	89.2 [86.6; 91.8] / 87.2 [84.5; 90.0]**	91.3 [89.0; 93.6] / 91.0 [88.6; 93.3]*
40 ≤ age < 65y, n = 1,477							
Median bias [95%CI]	-0.6 [-1.2; 0.1]	2.4 [1.9; 3.1]	-1.2 [-2.0; -0.5]	-2.8 [-3.5; -2.1]	-1.2 [-1.9; -0.7] / -1.2 [-1.9; -0.5]*	-1.8 [-2.4; -1.1] / 0.5 [-0.3; 1.1]**	-0.9 [-1.4; -0.4] / -0.8 [-1.3; -0.4]*
IQR [Pct25; Pct75]	14.9 [-7.7; 7.1]	15.4 [-4.9; 10.5]	14.4 [-8.5;5.9]	16.1 [-10.6; 5.5]	14.1 [-8.4; 5.7] / 14.8 [-8.8; 5.9]*	12.6 [-7.9; 4.7] / 14.0 [-6.3; 7.7]**	11.6 [-6.9; 4.8] / 11.9 [-7.1; 4.8]*
P10 [95%CI]	42.0 [39.5; 44.5]	40.1 [37.6; 42.6]	42.3 [39.8; 44.8]	36.0 [33.6; 38.5]	42.0 [39.5; 44.6] / 40.0 [37.5; 42.5]*	47.1 [44.5; 49.6] / 44.7 [42.1; 47.2]**	50.6 [48.0; 53.1] / 48.2 [45.7; 50.8]*
P30 [95%CI]	86.5 [84.8; 88.3]	84.7 [82.9; 86.5]	87.5 [85.9; 89.2]	85.5 [83.7; 87.3]	90.3 [88.7; 91.8] / 89.4 [87.9; 91.0]*	91.1 [89.6; 92.5] / 90.5 [89.0; 92.0]**	93.5 [92.2; 94.8] / 93.4 [92.1; 94.6]*
Age ≥ 65y, n = 605							
Median bias [95%CI]	-1.6 [-2.4; -0.4]	1.9 [1.0; 2.7]	-3.7 [-4.9; -2.8]	-6.4 [-7.1; -5.3]	-3.6 [-4.2; -2.7] / -3.9 [-4.5; -3.0]*	-4.5 [-5.1; -3.7] / -2.5 [-3.1; -1.5]**	-3.7 [-4.5; -2.9] / -3.6 [-4.2; -2.8]*
IQR [Pct25; Pct75]	12.3 [-7.4; 4.9]	13.1 [-4.5; 8.6]	11.9 [-9.9; 2.0]	12.1 [-11.6; 0.4]	11.6 [-9.2; 2.4] / 11.4 [-9.1; 2.3]*	10.5 [-8.7; 1.9] / 11.0 [-6.8; 4.2]**	9.8 [-8.3; 1.6] / 10.1 [-8.8; 1.3]*
P10 [95%CI]	36.5 [32.7; 40.4]	36.7 [32.8; 40.5]	35.7 [31.9; 39.5]	26.9 [23.4; 30.5]	37.5 [33.7; 41.4] / 34.2 [30.4; 38.0]*	36.2 [32.4; 40.0] / 37.7 [33.8; 41.6]**	41.7 [37.7; 45.6] / 40.7 [36.7; 44.6]*
P30 [95%CI]	84.5 [81.6; 87.4]	82.3 [79.3; 85.4]	85.6 [82.8; 88.4]	75.0 [71.6; 78.5]	86.8 [84.1; 89.5] / 85.6 [92.8; 88.4]*	86.8 [84.1; 89.5] / 87.9 [85.3; 90.5]**	91.1 [88.8; 93.4] / 90.1 [87.7; 92.5]*

Pct = percentiles; *using the sex-free EKFC-eGFR$_{Cys}$; **using CKD-EPI-eGFR$_{Cr}$ (AS)

Table S7.2. Cont'd

18 ≤ age < 40 y, n = 564	FAS_{Crea}	FAS_{CysC}	$FAS_{Crea+CysC}$	LMR	CAPA	LMR+CAPA
Median bias [95%CI]	7.9 [6.7; 9.1]	8.6 [7.2; 10.1]	8.3 [7.3; 9.2]	-1.9 [-3.2; -0.5]	0.5 [-1.6; 2.1]	-0.0 [-1.3; 1.0]
IQR [Pct25; Pct75]	18.2 [0.0; 18.2]	18.0 [-0.4; 17.6]	14.4 [1.2; 15.6]	16.7 [-9.5; 7.2]	18.5 [-8.6; 10.0]	14.8 [-7.3; 7.5]
P10 [95%CI]	35.3 [31.3; 39.2]	30.1 [26.3; 33.9]	35.5 [31.5; 39.4]	41.0 [36.9; 45.0]	37.8 [33.8; 41.8]	47.7 [43.6; 51.8]
P30 [95%CI]	78.4 [75.0; 81.8]	75.5 [72.0; 79.1]	83.9 [80.8; 86.9]	89.7 [87.2; 92.2]	85.3 [82.4; 88.2]	93.8 [91.8; 95.8]
40 ≤ age < 65y, n = 1,477						
Median bias [95%CI]	0.8 [-0.0; 1.5]	-1.1 [-1.8; -0.4]	-0.6 [-1.1; -0.1]	-4.5 [-5.0; -3.7]	-4.1 [-4.9; -3.5]	-3.7 [-4.3; -3.3]
IQR [Pct25; Pct75]	14.9 [-6.5; 8.4]	16.3 [-9.9; 6.4]	13.1 [-7.4; 5.7]	14.4 [-11.8; 2.6]	15.5 [-11.8; 3.7]	12.0 [-10.0; 2.0]
P10 [95%CI]	42.0 [39.5; 44.5]	37.6 [35.1; 40.0]	44.8 [42.2; 47.3]	38.1 [35.6; 40.5]	36.7 [34.2; 39.2]	45.3 [42.8; 47.8]
P30 [95%CI]	86.5 [84.7; 88.2]	87.1 [85.4; 88.8]	91.9 [90.5; 93.3]	86.6 [84.9; 88.3]	85.1 [83.3; 86.9]	92.6 [91.2; 93.9]
Age ≥ 65y, n = 605						
Median bias [95%CI]	-4.0 [-4.8; -3.1]	-5.1 [-6.1; -4.4]	-4.7 [-5.4; -3.9]	-5.4 [-6.0; -4.5]	-5.8 [-6.5; -4.8]	-5.1 [-5.8; -4.4]
IQR [Pct25; Pct75]	12.3 [-9.9; 2.3]	12.5 [-11.9; 0.6]	10.4 [-10.5; -0.1]	12.5 [-11.4; 1.1]	12.5 [-11.2; 1.3]	9.9 [-9.9; 0.0]
P10 [95%CI]	34.9 [31.1; 38.7]	30.6 [26.9; 34.3]	37.4 [33.5; 41.2]	30.4 [26.7; 34.1]	28.6 [25.0; 32.2]	33.7 [29.9; 37.5]
P30 [95%CI]	87.4 [84.8; 90.1]	84.0 [81.0; 86.9]	89.4 [87.0; 91.9]	81.3 [78.2; 84.4]	78.8 [75.6; 82.1]	86.3 [83.5; 89.0]

Table S7.3. Performance in the **White US Cohort** (n = 1,093) according to age subgroups. Median bias [95%CI] (mL/min/1.73m²), imprecision (interquartile range, IQR), P10(%) [95%CI] and P30(%) [95%CI] accuracy are presented. In this cohort, there were only 5 subjects aged < 40 years.

18 ≤ age < 65 y, n = 498	CKD-EPI-eGFR$_{Cr}$ (ASR)	CKD-EPI-eGFR$_{Cr}$ (AS)	EKFC-eGFR$_{Cr}$	CKD-EPI-eGFR$_{Cys}$	EKFC-eGFR$_{Cys}$	CKD-EPI-eGFR$_{Cr+Cys}$	EKFC-eGFR$_{Cr+Cys}$
Median bias [95%CI]	2.8 [1.4; 4.3]	7.1 [5.9; 8.6]	-1.3 [-2.5; 0.6]	14.1 [12.4; 16.0]	5.1 [3.8; 6.2] / 5.4 [4.1; 6.9]*	10.7 [9.0; 12.2] / 15.2 [13.8; 16.7]**	2.4 [0.7; 3.8] / 3.0 [1.1; 4.5]*
IQR [Pct25; Pct75]	20.4 [-6.6; 13.8]	20.1 [-2.6; 17.5]	19.2 [-10.4; 8.9]	22.1 [3.0; 25.1]	19.5 [-5.3; 14.2] / 20.4 [-5.1; 15.4]*	19.5 [1.2; 20.7] / 18.2 [6.5; 24.7]**	18.7 [-7.6; 11.2] / 18.1 [-7.2; 11.0]
P10 [95%CI]	43.0 [38.6; 47.3]	42.4 [38.0; 46.7]	44.4 [40.0; 48.8]	30.3 [26.3; 34.4]	42.6 [38.2; 46.9] / 42.2 [37.8; 46.5]*	38.6 [34.3; 42.8] / 27.3 [23.4; 31.2]**	48.8 [44.4; 53.2] / 47.2 [42.8; 51.6]*
P30 [95%CI]	86.7 [83.8; 89.7]	82.3 [79.0; 85.7]	89.6 [86.9; 92.3]	70.7 [66.7; 74.7]	82.9 [79.6; 86.2] / 82.3 [79.0; 85.7]*	78.7 [75.1; 82.3] / 71.3 [67.3; 75.3]**	89.2 [86.4; 91.9] / 88.2 [85.3; 91.0]*
Age ≥ 65 y, n = 595							
Median bias [95%CI]	2.9 [1.2; 3.6]	7.1 [5.9; 8.3]	-3.8 [-4.8; -2.6]	10.1 [8.3; 12.1]	3.0 [1.6; 4.1] / 3.1 [2.3; 4.4]*	8.5 [7.4; 9.5] / 13.1 [12.1; 14.4]**	-0.6 [-1.7; 0.8] / -0.1 [-1.3; 0.9]*
IQR [Pct25; Pct75]	17.4 [-6.6; 10.8]	17.2 [-1.8; 15.4]	17.5 [-12.7; 4.8]	19.6 [0.5; 20.2]	17.7 [-6.5; 11.2] / 16.4 [-5.5; 11.0]*	16.4 [-0.3; 16.1] / 17.3 [4.5; 21.8]**	16.6 [-9.4; 7.2] / 16.6 [-9.2; 7.5]**
P10 [95%CI]	41.0 [37.0; 45.0]	37.0 [33.1; 40.9]	39.0 [35.1; 42.9]	28.6 [24.9; 32.2]	41.5 [37.5; 45.5] / 41.0 [37.0; 45.0]*	36.0 [32.1; 39.8] / 28.7 [25.1; 32.4]**	44.4 [40.4; 48.4] / 44.4 [40.4; 48.4]*
P30 [95%CI]	85.4 [82.5; 88.2]	79.8 [76.6; 83.1]	89.1 [86.6; 91.6]	74.8 [71.3; 78.3]	85.4 [82.5; 88.2] / 85.2 [82.3; 88.1]*	80.2 [77.0; 83.4] / 72.8 [69.2; 76.4]**	89.1 [86.6; 91.6] / 89.2 [86.7; 91.7]*

Pct = percentiles; *using the sex-free EKFC$_{CysC}$; **using CKD-EPI$_{Crea}$ (AS)

Table S7.3. Cont'd

18 ≤ age < 65 y, n = 498	FAS$_{Crea}$	FAS$_{CysC}$	FAS$_{Crea+CysC}$	LMR	CAPA	LMR+CAPA
Median bias [95%CI]	0.4 [-1.3; 1.7]	6.8 [3.6; 8.6]	2.9 [1.5; 4.3]	-4.7 [-6.1; -3.2]	13.1 [11.3; 15.3]	4.8 [2.5; 6.5]
IQR [Pct25; Pct75]	20.5 [-9.8; 10.7]	23.7 [-5.2; 18.5]	19.3 [-6.8; 12.6]	20.0 [-14.6; 5.4]	25.3 [1.7; 26.9]	19.8 [-4.8; 15.0]
P10 [95%CI]	42.6 [38.2; 46.9]	37.8 [33.5; 42.0]	47.4 [43.0; 51.8]	40.4 [36.0; 44.7]	31.5 [27.4; 35.6]	44.6 [40.2; 49.0]
P30 [95%CI]	88.8 [86.0; 91.5]	79.9 [76.4; 83.5]	88.0 [85.1; 90.8]	89.4 [86.6; 92.1]	70.1 [66.0; 74.1]	85.5 [82.4; 88.6]
Age ≥ 65y, n = 595						
Median bias [95%CI]	-5.5 [-6.4; -4.2]	1.4 [0.3; 2.9]	-2.1 [-3.3; -0.9]	-5.2 [-6.6; -4.1]	9.8 [8.4; 11.8]	3.2 [1.5; 4.1]
IQR [Pct25; Pct75]	17.6 [-13.6; 4.0]	18.0 [-7.5; 10.5]	16.2 [-10.6; 5.6]	17.9 [-14.7; 3.2]	22.0 [-0.2; 21.8]	16.2 [-5.4; 10.8]
P10 [95%CI]	35.3 [31.4; 39.1]	39.5 [35.6; 43.4]	45.7 [41.7; 49.7]	36.0 [32.1; 39.8]	29.6 [25.9; 33.3]	42.9 [38.9; 46.8]
P30 [95%CI]	87.6 [84.9; 90.2]	82.9 [79.8; 85.9]	89.4 [86.9; 91.9]	87.9 [85.3; 90.5]	73.1 [69.5; 76.7]	86.4 [83.6; 89.1]

Table S7.4. Performance in the **Black Paris Cohort** (n = 858) according to age subgroups. Median bias [95%CI] (mL/min/1.73m²), imprecision (interquartile range, IQR), P10(%) [95%CI] and P30(%) [95%CI] accuracy are presented.

18 ≤ age < 40 y, n = 197	CKD-EPI-eGFR$_{Cr}$ (ASR)	CKD-EPI-eGFR$_{Cr}$ (AS)	EKFC-eGFR$_{Cr}$	CKD-EPI-eGFR$_{Cys}$	EKFC-eGFR$_{Cys}$	CKD-EPI-eGFR$_{Cr+Cys}$	EKFC-eGFR$_{Cr+Cys}$
Median bias [95%CI]	6.0 [3.0; 9.9]	-1.9 [-4.9; 0.3]	0.4 [-1.4; 2.4]	4.0 [1.2; 7.6]	5.5 [3.9; 8.0] / 5.5 [3.6; 7.7]*	4.5 [2.2; 7.9] / 0.9 [-1.0; 4.7]**	2.6 [1.4; 5.1] / 3.0 [0.6; 5.1]*
IQR [Pct25; Pct75]	24.3 [-11.6; 7.9]	19.4 [-11.6; 7.9]	17.8 [-8.6; 9.2]	20.2 [-5.0; 15.3]	15.9 [-1.9; 14.0] / 16.6 [-2.3; 14.3]*	20.5 [-4.1; 16.4] / 17.4 [-6.1; 11.3]**	13.5 [-2.8; 10.7] / 13.9 [-3.2; 10.7]*
P10 [95%CI]	35.5 [28.8; 42.3]	41.1 [34.2; 48.0]	44.7 [37.7; 51.7]	36.0 [29.3; 42.8]	37.1 [30.3; 43.9] / 38.1 [31.2; 44.9]*	37.1 [30.3; 43.9] / 38.1 [31.2; 44.9]**	48.2 [41.2; 55.3] / 48.7 [41.7; 55.8]*
P30 [95%CI]	75.6 [69.6; 81.7]	86.3 [81.4; 91.1]	88.3 [83.8; 92.8]	82.7 [77.4; 88.1]	84.3 [79.1; 89.4] / 86.8 [82.0; 91.6]*	88.3 [83.8; 92.8] / 91.4 [87.4; 95.3]**	93.9 [90.5; 97.3] / 93.4 [89.9; 96.9]*
40 ≤ age < 65y, n = 548							
Median bias [95%CI]	-0.6 [-1.4; 0.4]	-5.5 [-6.5; -4.5]	-2.6 [-3.6; -1.5]	-0.9 [-2.0; 0.0]	1.2 [0.2; 2.1] / 0.8 [0.0; 1.9]*	-0.7 [-1.7; 0.5] / -2.3 [-3.1; -1.3]**	-0.4 [-1.0; 0.5] / -0.7 [-1.5; 0.3]*
IQR [Pct25; Pct75]	18.0 [-8.2; 9.8]	15.9 [-12.7; 3.2]	14.7 [-9.4; 5.3]	17.0 [-7.9; 9.1]	14.0 [-5.5; 8.5] / 13.4 [-5.6; 7.9]*	14.6 [-6.6; 8.1] / 13.5 [-8.0; 5.5]**	11.7 [-5.9; 5.8] / 11.8 [-6.3; 5.6]*
P10 [95%CI]	35.9 [31.9; 40.0]	30.5 [26.6; 34.3]	36.3 [32.3; 40.4]	37.2 [33.2; 41.3]	42.9 [38.7; 47.0] / 42.3 [38.2; 46.5]*	38.0 [33.9; 42.0] / 38.7 [34.6; 42.8]**	51.1 [46.9; 55.3] / 49.1 [44.9; 53.3]*
P30 [95%CI]	81.8 [78.5; 85.0]	81.4 [78.1; 84.7]	85.9 [83.0; 88.9]	81.4 [78.1; 84.7]	88.0 [85.2; 90.7] / 87.8 [85.0; 90.5]*	87.8 [85.0; 90.5] / 89.6 [87.0; 92.2]**	91.1 [88.7; 93.5] / 92.0 [89.7; 94.3]*
Age ≥ 65y, n = 113							
Median bias [95%CI]	-2.6 [-5.5; -0.6]	-5.8 [-9.5; -4.3]	-5.9 [-9.5; -4.2]	-5.3 [-7.0; -2.5]	-2.7 [-4.0; -0.2] / -2.2 [-4.2; -0.6]*	-4.1 [-5.4; -1.8] / -4.4 [-6.1; -2.3]**	-3.7 [-5.5; -3.0] / -3.7 [-4.9; -2.7]*
IQR [Pct25; Pct75]	14.2 [-10.8; 3.4]	13.6 [-13.1; 0.5]	12.6 [-13.5; -0.9]	12.7 [-10.8; 1.9]	11.9 [-8.2; 3.7] / 10.3 [-7.1; 3.2]*	9.6 [-8.9; 0.7] / 9.1 [-9.5; -0.4]**	8.4 [-8.7; -0.3] / 8.4 [-8.5; -0.1]*
P10 [95%CI]	32.7 [24.0; 41.5]	31.0 [22.3; 39.6]	31.0 [22.3; 39.6]	31.9 [23.1; 40.6]	39.8 [30.7; 49.0] / 39.8 [30.7; 49.0]*	45.1 [35.8; 54.4] / 41.6 [32.4; 50.8]**	47.8 [38.4; 57.1] / 43.4 [34.1; 52.6]*
P30 [95%CI]	77.9 [70.1; 85.6]	79.6 [72.1; 87.2]	78.8 [71.1; 86.4]	79.6 [72.1; 87.2]	88.5 [82.5; 94.5] / 86.7 [80.4; 93.1]*	87.6 [81.4; 93.8] / 86.7 [80.4; 93.1]**	90.3 [84.7; 95.8] / 89.4 [83.6; 95.1]*

Pct = percentiles; *using the sex-free EKFC-eGFR$_{Cys}$; **using CKD-EPI-eGFR$_{Cr}$(AS); Note: EKFC-eGFR$_{Cr}$ is calculated using Q = 1.02 mg/dL for men and 0.74 mg/dL for women

Table S7.4. Cont'd

18 ≤ age < 40 y, n = 197	FAS_{Crea}	FAS_{CysC}	$FAS_{Crea+CysC}$	LMR	CAPA	LMR+CAPA
Median bias [95%CI]	-1.5 [-3.2; 1.1]	8.3 [6.0; 10.9]	3.6 [1.4; 5.1]	-11.3 [-12.8; -8.2]	-1.0 [-2.9; 2.6]	-4.3 [-6.4; -2.6]
IQR [Pct25; Pct75]	19.8 [-11.8; 8.0]	16.0 [1.3; 17.4]	14.9 [-4.8; 10.2]	17.9 [-20.4; -2.4]	16.9 [-6.6; 16.9]	14.9 [-11.6; 3.3]
P10 [95%CI]	45.7 [38.7; 52.7]	36.0 [29.3; 42.8]	47.7 [40.7; 54.8]	34.0 [27.3; 40.7]	45.2 [38.2; 52.2]	41.6 [34.7; 48.6]
P30 [95%CI]	88.3 [83.8; 92.8]	79.2 [73.5; 84.9]	92.4 [88.6; 96.1]	80.2 [74.6; 85.8]	84.3 [79.1; 89.4]	92.9 [89.3; 96.5]
40 ≤ age < 65y, n = 548						
Median bias [95%CI]	-5.6 [-6.8; -4.3]	1.01 [-0.0; 2.2]	-2.4 [-3.6; -1.6]	-10.6 [-11.5; -9.3]	-2.5 [-3.4; -1.7]	-6.2 [-7.2; -5.6]
IQR [Pct25; Pct75]	15.2 [-13.2; 2.0]	13.7 [-5.9; 7.8]	12.0 [-8.9; 3.0]	16.3 [-18.5; -2.2]	14.0 [-9.3; 4.7]	12.5 [-11.9; 0.6]
P10 [95%CI]	29.7 [25.9; 33.6]	41.2 [37.1; 45.4]	46.0 [41.8; 50.2]	21.9 [18.4; 25.4]	39.2 [35.1; 43.3]	36.1 [32.1; 40.2]
P30 [95%CI]	87.6 [84.8; 90.4]	86.3 [83.4; 89.2]	92.0 [89.7; 94.3]	73.2 [69.5; 76.9]	82.5 [79.3; 85.7]	89.6 [87.0; 92.2]
Age ≥ 65y, n = 113						
Median bias [95%CI]	-9.1 [-11.7; -6.7]	-4.7 [-5.5; -3.0]	-7.9 [-9.9; -6.0]	-10.9 [-13.8; -8.7]	-4.4 [-5.8; -1.7]	-7.3 [-8.9; -5.8]
IQR [Pct25; Pct75]	13.2 [-17.5; -4.3]	10.2 [-10.7; -0.4]	10.6 [-13.8; -3.2]	13.7 [-19.3; -5.6]	11.0 [-8.9; 2.2]	9.2 [-12.6; -3.4]
P10 [95%CI]	23.0 [15.1; 30.9]	38.1 [29.0; 47.1]	27.4 [19.1; 35.8]	19.5 [12.1; 26.9]	32.7 [24.0; 41.5]	26.5 [18.3; 34.8]
P30 [95%CI]	71.7 [63.2; 80.1]	85.0 [78.3; 91.6]	85.8 [79.3; 92.4]	61.9 [52.9; 71.0]	83.2 [76.2; 90.2]	80.5 [73.1; 87.9]

Note: FAS_{Crea} and LMR are calculated with the original formulas (no population specific adjustments!!)

Table S7.5. Performance in the **Black African Cohort** (n = 508) according to age subgroups. Median bias [95%CI] (mL/min/1.73m²), imprecision (interquartile range, IQR), P10(%) [95%CI] and P30(%) [95%CI] accuracy are presented. Because there are only 40 subjects aged ≥ 65 years, we used 18-40 years and ≥ 40 years as age-subgroups.

18 ≤ age < 40 y, n = 258	CKD-EPI-eGFR$_{Cr}$ (ASR)	CKD-EPI-eGFR$_{Cr}$ (AS)	EKFC-eGFR$_{Cr}$	CKD-EPI-eGFR$_{Cys}$	EKFC-eGFR$_{Cys}$	CKD-EPI-eGFR$_{Cr+Cys}$	EKFC-eGFR$_{Cr+Cys}$
Median bias [95%CI]	17.6 [14.3; 20.8]	5.0 [2.2; 7.8]	0.8 [-2.3; 4.0]	7.9 [5.1; 11.8]	4.5 [3.5; 6.9] / 5.40 [3.2; 8.2]*	13.6 [10.8; 16.8] / 8.2 [4.8; 11.3] **	2.4 [0.4; 4.4] / 1.9 [0.6; 4.7]*
IQR [Pct25; Pct75]	30.7 [0.2; 30.8]	24.8 [-8.3; 16.6]	21.3 [-11.0; 10.4]	22.6 [-2.5; 20.1]	19.4 [-3.9; 15.5] / 20.3 [-4.8; 15.6]*	24.5 [0.4; 24.8] / 21.9 [-2.8; 19.1]**	18.6 [-6.1; 12.5] / 18.3 [-5.3; 13.0]*
P10 [95%CI]	17.1 [12.4; 21.7]	34.1 [28.3; 39.9]	39.1 [33.2; 45.1]	32.6 [26.8; 38.3]	44.6 [38.5; 50.7] / 41.5 [35.4; 47.5]*	25.6 [20.2; 30.9] / 32.6 [26.8; 38.3]**	45.3 [39.2; 51.5] / 45.0 [38.9; 51.1]*
P30 [95%CI]	62.4 [56.5; 68.4]	76.7 [71.6; 81.9]	81.4 [76.6; 86.2]	78.7 [73.7; 83.7]	84.1 [79.6; 88.6] / 83.7 [79.2; 88.3]*	74.8 [69.5; 80.1] / 80.6 [75.8; 85.5]**	86.4 [82.2; 90.6] / 86.8 [82.7; 91.0]*
Age ≥ 40 y, n = 250							
Median bias [95%CI]	7.5 [5.7; 11.6]	0.5 [-2.7; 2.6]	-2.7 [-4.2; -0.8]	-2.7 [-4.3; 0.4]	-2.2 [-3.4; -0.4] / -1.50 [-3.4; 0.2]*	3.5 [1.7; 6.3] / 1.1 [-0.7; 2.5]**	-1.9 [-3.3; -0.6] / -1.4 [-3.0; -0.2]*
IQR [Pct25; Pct75]	26.7 [-5.3; 21.4]	20.3 [-9.3; 11.0]	17.5 [-10.1; 7.4]	20.3 [-11.4; 8.9]	13.9 [-8.3; 5.6] / 15.7 [-8.6; 7.2]*	21.6 [-7.7; 13.9] / 18.8 [-8.9; 10.0]**	15.0 [-9.3; 5.7] / 15.3 [-9.3; 6.1]*
P10 [95%CI]	22.0 [16.8; 27.2]	34.8 [28.9; 40.7]	36.8 [30.8; 42.8]	33.6 [27.7; 39.5]	41.2 [35.1; 47.3] / 39.6 [33.5; 45.7]*	32.0 [26.2; 37.8] / 36.0 [30.0; 42.0]**	43.6 [37.4; 49.8] / 42.0 [35.8; 48.2]*
P30 [95%CI]	64.8 [58.8; 70.8]	72.0 [66.4; 77.6]	76.4 [71.1; 81.7]	76.0 [70.7; 81.3]	84.4 [79.9; 88.9] / 83.2 [78.5; 87.9]*	75.2 [69.8; 80.6] / 74.4 [69.0; 79.8]**	81.6 [76.8; 86.4] / 81.6 [76.8; 86.4]*

Pct = percentiles; *using the sex-free EKFC$_{CysC}$; **using CKD-EPI$_{Crea}$ (AS)

Table S7.5. Cont'd

18 ≤ age < 40 y, n = 258	FAS$_{Crea}$	FAS$_{CysC}$	FAS$_{Crea+CysC}$	LMR	CAPA	LMR+CAPA
Median bias [95%CI]	-0.9 [-2.8; 1.4]	9.8 [7.2; 11.4]	2.9 [0.7; 5.6]	-10.2 [-11.4; -7.6]	3.2 [0.9; 5.2]	-3.3 [-5.9; -1.3]
IQR [Pct25; Pct75]	22.7 [-12.5; 10.2]	21.2 [-1.7; 19.4]	18.2 [-5.1; 13.2]	20.1 [-19.8; 0.3]	22.3 [-9.3; 13.0]	17.2 [-11.4; 5.8]
P10 [95%CI]	39.5 [33.5; 45.5]	34.1 [28.3; 39.9]	44.6 [38.5; 50.7]	34.1 [28.3; 39.9]	39.1 [33.2; 45.1]	46.1 [40.0; 52.2]
P30 [95%CI]	83.3 [78.8; 87.9]	80.6 [75.8; 85.5]	87.6 [83.5; 91.6]	81.0 [76.2; 85.8]	82.9 [78.3; 87.6]	87.6 [83.5; 91.6]
age ≥ 40 y, n = 250						
Median bias [95%CI]	-4.2 [-5.3; -2.4]	-3.0 [-4.5; -0.9]	-2.7 [-4.5; -1.2]	-8.2 [-10.4; -6.6]	-4.6 [-6.6; -3.3]	-6.5 [-8.0; -5.0]
IQR [Pct25; Pct75]	17.5 [-11.7; 5.8]	17.2 [-10.0; 7.1]	14.2 [-10.0; 4.2]	16.2 [-15.8; 0.4]	17.3 [-12.9; 4.4]	13.8 [-12.8; 1.1]
P10 [95%CI]	35.6 [29.6; 41.6]	34.0 [28.1; 39.9]	40.4 [34.3; 46.5]	28.4 [22.8; 34.0]	34.8 [28.9; 40.7]	40.0 [33.9; 46.1]
P30 [95%CI]	77.2 [72.0; 82.4]	84.4 [79.9; 88.9]	82.8 [78.1; 87.5]	74.4 [69.0; 79.8]	74.4 [69.0; 79.8]	79.2 [74.1; 84.3]

Section S8.Effect of sex-dependent vs. sex-free rescaling factors for cystatin C

Table S8.1. Median bias [95%CI] (mL/min/1.73m²), imprecision (interquartile range, IQR), root mean square error (rmse), P10(%) [95%CI] and P30(%) [95%CI] accuracy for different creatinine and cystatin C based equations in the EKFC-validation dataset, and the White Paris, White North American, Black Paris and Black African cohorts. CKD-EPI-eGFR$_{Cr}$(ASR), CKD-EPI-eGFR$_{Cr}$(AS) and CKD-EPI-eGFR$_{Cys}$ serve as a benchmark (as the KDIGO recommended equations). (ASR=age, sex and race factors, AS = age and sex but no race factor)

White EKFC cohort n = 7,727	**CKD-EPI-eGFR$_{Cys}$**	**EKFC-eGFR$_{Cys}$**	**EKFC-eGFR$_{Cys}$ (sex-free)**
Median bias [95%CI]	0.28 [-0.02; 0.64]	-0.14 [-0.39; 0.17]	0.00 [-0.37; 0.27]
IQR [Pct25; Pct75]	19.1 [-7.9; 11.2]	14.4 [-8.0; 6.3]	14.4 [-7.9; 6.5]
RMSE	15.8 [15.5; 16.1]	13.1 [12.8; 13.4]	13.5 [12.9; 14.1]
P10 [95%CI]	32.0 [31.0; 33.0]	42.3 [41.2; 43.4]	41.7 [40.6; 42.8]
P30 [95%CI]	80.8 [79.9; 81.7]	85.9 [85.1; 86.6]	86.2 [85.4; 87.0]
White Paris cohort n = 2,646			
Median bias [95%CI]	- 2.85 [-3.35; -2.21]	-0.81 [-1.23; -0.20]	-0.79 [-1.26; -0.31]
IQR [Pct25; Pct75]	16.4 [-10.3; 6.1]	14.6 [-8.1; 6.5]	15.3 [-8.5; 6.7]
RMSE	14.5 [13.9; 15.1]	13.2 [12.5; 13.8]	13.5 [12.9; 14.1]
P10 [95%CI]	34.2 [32.4; 36.0]	40.1 [38.2; 42.0]	38.2 [36.4; 40.1]
P30 [95%CI]	82.7 [81.3; 84.2]	88.5 [87.3; 89.7]	87.6 [86.3; 88.9]
White North American cohort n = 1,093			
Median bias [95%CI]	12.1 [11.1; 13.3]	3.98 [3.21; 4.65]	4.26 [3.33; 5.08]
IQR [Pct25; Pct75]	21.5 [1.5; 23.0]	18.7 [-6.1; 12.6]	18.3 [-5.3; 13.0]
RMSE	21.3 [20.3; 22.2]	16.7 [15.5; 17.7]	16.8 [15.7; 17.9]
P10 [95%CI]	29.4 [26.7; 32.1]	42.0 [39.1; 44.9]	41.5 [38.6; 44.5]
P30 [95%CI]	72.9 [70.3; 75.6]	84.3 [82.1; 86.4]	83.9 [81.7; 86.1]
Black Paris cohort n = 858			
Median bias [95%CI]	-0.62 [-1.71; 0.28]	1.58 [0.80; 2.38]	1.40 [0.38; 2.23]
IQR [Pct25; Pct75]	17.9 [-8.1; 9.8]	14.4 [-5.3; 9.1]	14.3 [-5.6; 8.8]
RMSE	15.4 [14.0; 16.6]	13.5 [12.1; 14.8]	13.5 [12.1; 14.7]
P10 [95%CI]	36.2 [33.0; 39.5]	41.1 [37.8; 44.4]	41.0 [37.7; 44.3]
P30 [95%CI]	81.5 [78.9; 84.1]	87.2 [84.9; 89.4]	87.4 [85.2; 89.6]
Black African cohort n = 508			
Median bias [95%CI]	2.82 [1.43; 4.48]	1.55 [-0.21; 3.04]	1.74 [0.28; 3.25]
IQR [Pct25; Pct75]	23.7 [-7.7; 16.0]	18.4 [-7.2; 11.2]	19.5 [-7.4; 12.1]
RMSE	18.5 [17.1; 19.8]	15.9 [14.5; 17.2]	16.0 [14.7; 17.2]
P10 [95%CI]	33.1 [29.0; 37.2]	42.9 [38.6; 47.2]	40.6 [36.3; 44.8]
P30 [95%CI]	77.4 [73.7; 81.0]	84.3 [81.1; 87.4]	83.5 [80.2; 86.7]

Pct=percentiles;

Table S8.2. Median bias [95%CI] (mL/min/1.73m²), imprecision (interquartile range, IQR), P10(%) [95%CI] and P30(%) [95%CI] accuracy for the combined creatinine and cystatin C based equations in the EKFC-validation dataset, and the White Paris, White North American, Black Paris and Black African cohorts. CKD-EPI-eGFR$_{Cr+Cys}$ (ASR), CKD-EPI-eGFR$_{Cr+Cys}$(AS) serve as a benchmark (as the KDIGO recommended equations). (ASR = age, sex and race factors, AS = age and sex but no race factor)

White EKFC cohort n = 7,727	**CKD-EPI-eGFR$_{Cr+Cys}$ (ASR)**	**CKD-EPI-eGFR$_{Cr+Cys}$ (AS)**	**EKFC-eGFR$_{Cr+Cys}$**	**EKFC-eGFR$_{Cr+Cys}$ (sex-free)**
Median bias [95%CI]	2.50 [2.17; 2.76]	5.04 [4.69; 5.36]	0.36 [0.13; 0.59]	0.37 [0.14; 0.66]
IQR [Pct25; Pct75]	14.8 [-3.6; 11.2]	16.7 [-1.8; 14.9]	12.0 [-6.0; 6.0]	12.0 [-5.9; 6.1]
RMSE	13.1 [12.8; 13.4]	14.7 [14.4; 15.0]	11.2 [10.9; 11.5]	11.3 [11.0; 11.6]
P10 [95%CI]	41.5 [40.4; 42.6]	37.2 [36.2; 38.3]	49.4 [48.3; 50.5]	48.9 [47.8; 50.0]
P30 [95%CI]	88.3 [87.6; 89.0]	84.2 [83.4; 85.0]	90.4 [89.8; 91.1]	90.4 [89.8; 91.1]
White Paris cohort n = 2,646				
Median bias [95%CI]	-1.35 [-1.82; -0.97]	0.64 [0.16; 1.15]	-0.70 [-1.12; -0.30]	-0.65 [-1.06; -0.23]
IQR [Pct25; Pct75]	13.4 [-7.5; 5.8]	14.1 [-5.8; 8.3]	12.1 [-6.8; 5.3]	12.4 [-6.8; 5.6]
RMSE	12.1 [11.6; 12.7]	12.6 [12.0; 13.1]	11.6 [11.0; 12.2]	11.8 [11.2; 12.4]
P10 [95%CI]	43.9 [42.0; 45.8]	42.3 [40.4; 44.1]	47.4 [45.5; 49.3]	45.8 [43.9; 47.7]
P30 [95%CI]	89.7 [88.5; 90.8]	89.2 [88.0; 90.4]	92.5 [91.5; 93.5]	92.1 [91.1; 93.1]
White North American cohort n = 1,093				
Median bias [95%CI]	9.23 [8.45; 10.1]	13.9 [13.1; 14.9]	0.72 [-0.28; 1.83]	0.97 [0.01; 2.12]
IQR [Pct25; Pct75]	18.4 [0.5; 18.8]	18.1 [5.1; 23.3]	17.1 [-8.4; 8.6]	17.4 [-8.2; 9.2]
RMSE	18.1 [17.1; 19.1]	21.0 [20.1; 22.0]	15.5 [14.2; 16.6]	15.5 [14.3; 16.7]
P10 [95%CI]	37.1 [34.3; 40.0]	28.1 [25.4; 30.8]	46.4 [43.4; 49.3]	45.7 [42.7; 48.6]
P30 [95%CI]	79.5 [77.1; 81.9]	72.1 [69.4; 74.8]	89.1 [87.3; 91.0]	88.7 [86.9; 90.6]
Black Paris cohort n = 858				
Median bias [95%CI]	-0.37 [-1.06; 0.57]	-2.08 [-2.71; -1.32]	-0.33 [-0.91; 0.26]	-0.65 [-1.23; 0.11]
IQR [Pct25; Pct75]	15.2 [-6.4; 8.8]	14.0 [-7.9; 6.1]	12.2 [-8.9; 3.3]	12.4 [-6.2; 6.2]
RMSE	13.3 [11.9; 14.6]	12.6 [11.2; 13.9]	11.6 [10.0; 13.1]	11.6 [10.0; 13.0]
P10 [95%CI]	38.7 [35.4; 42.0]	38.9 [35.7; 42.2]	50.0 [46.6; 53.4]	48.3 [44.9; 51.6]
P30 [95%CI]	87.9 [85.7; 90.1]	89.0 [87.0; 91.1]	91.6 [89.7; 93.5]	92.0 [90.1; 93.8]
Black African cohort n = 508				
Median bias [95%CI]	8.55 [6.87; 10.3]	4.08 [2.37; 5.78]	0.05 [-1.25; 1.58]	0.42 [-1.03; 1.51]
IQR [Pct25; Pct75]	24.7 [-4.5; 20.1]	22.0 [-7.4; 14.7]	16.7 [-7.1; 9.7]	17.1 [-7.2; 10.0]
RMSE	19.7 [18.2; 21.1]	17.2 [15.8; 18.5]	14.7 [13.3; 16.0]	14.7 [13.3; 16.0]
P10 [95%CI]	28.7 [24.8; 32.7]	34.3 [30.1; 38.4]	44.5 [40.2; 48.8]	43.5 [39.2; 47.8]
P30 [95%CI]	75.0 [71.2; 78.8]	77.6 [73.9; 81.2]	84.1 [80.9; 87.2]	84.3 [81.1; 87.4]

Pct = Percentiles; EKFC-eGFR$_{Cr+Cys}$ is the arithmetic mean of EKFC-eGFR$_{Cr}$ and EKFC-eGFR$_{Cys}$

Section S9. Performance statistics according to mGFR-level, sex and age subgroups

Table S9.1a. Comparison of Bias for mGFR < 60 mL/min/1.73m²

	Men			Women		
BIAS [95%CI]	age 18-40	age 40-65	age ≥ 65	age 18-40	age 40-65	age ≥ 65
N	223	1008	1556	184	741	1197
EKFC-eGFR$_{Cr}$	4.3 [2.2; 5.1]	2.5 [1.7; 3.2]	0.8 [0.4; 1.4]	4.3 [1.8; 6.6]	2.7 [1.9; 3.5]	0.6 [0.1; 1.3]
CKD-EPI-eGFR$_{Cr}$ (AS)	6.5 [4.3; 8.1]	3.4 [2.5; 4.4]	4.8 [4.3; 5.5]	6.6 [3.8; 8.8]	4.6 [3.5; 5.4]	5.5 [5.0; 6.3]
EKFC-eGFR$_{Cys}$ (S)	5.7 [4.3; 6.7]	1.1 [0.5; 1.6]	0.9 [0.5; 1.3]	4.0 [2.4; 5.5]	0.8 [0.1; 1.3]	0.3 [-0.3; 0.8]*
EKFC-eGFR$_{Cys}$	3.6 [2.6; 5.1]	-0.4 [-1.0; 0.2]*	-0.2 [-0.7; 0.2]*	6.5 [4.6; 7.8]	2.6 [2.1; 3.3]	2.0 [1.4; 2.4]
CKD-EPI-eGFR$_{Cys}$	-0.0 [-1.4; 1.3]*	-3.5 [-4.3; -2.9]	-2.8 [-3.3; -2.3]	-0.2 [-1.9; 1.4]*	-2.7 [-3.4; -2.1]	-2.6 [-3.1; -2.0]
EKFC-eGFR$_{Cr+Cys}$(S)	5.6 [4.1; 6.5]	2.1 [1.6; 2.7]	1.2 [0.8; 1.6]	5.0 [4.0; 6.2]	1.8 [1.2; 2.3]	0.5 [-0.1; 1.0]*
EKFC-eGFR$_{Cr+Cys}$	4.6 [3.4; 5.6]	1.4 [0.9; 2.0]	0.6 [0.3; 1.1]	6.1 [5.0; 7.8]	2.8 [2.2; 3.2]	1.3 [0.8; 1.8]
CKD-EPI-eGFR$_{Cr+Cys}$(AS)	1.7 [0.4; 2.6]	-0.7 [-1.3; 0.1]*	0.7 [0.4; 1.2]	2.0 [0.3; 4.1]	0.0 [-0.8; 0.8]*	0.8 [0.3; 1.3]

Table S9.1b. Comparison of Bias for mGFR ≥ 60 mL/min/1.73m²

	Men			Women		
BIAS [95%CI]	age 18-40	age 40-65	age ≥ 65	age 18-40	age 40-65	age ≥ 65
n	782	2452	858	640	2243	948
EKFC-eGFR$_{Cr}$	2.3 [0.6; 3.5]	-3.9 [-4.6; -3.4]	-5.0 [-6.0; -4.0]	3.1 [1.1; 4.5]	-0.0 [-0.8; 0.5]*	-3.7 [-4.5; -2.7]
CKD-EPI-eGFR$_{Cr}$ (AS)	8.8 [7.0; 10.4]	2.7 [2.0; 3.4]	6.0 [4.9; 7.4]	10.9 [9.0; 12.9]	7.5 [6.8; 8.3]	8.1 [7.2; 9.3]
EKFC-eGFR$_{Cys}$ (S)	3.2 [2.1; 4.5]	-1.9 [-2.5; -1.1]	-4.5 [-5.3; -3.4]	2.9 [1.5; 4.6]	0.7 [0.1; 1.5]	-4.5 [-5.5; -3.3]
EKFC-eGFR$_{Cys}$	0.2 [-1.0; 1.8]*	-3.8 [-4.3; -3.0]	-6.0 [-6.9; -5.2]	6.8 [5.4; 8.4]	3.4 [2.7; 4.1]	-2.0 [-3.2; -1.0]
CKD-EPI-eGFR$_{Cys}$	4.8 [3.0; 6.6]	5.2 [4.0; 6.2]	-0.1 [-2.0; 0.8]*	6.6 [5.0; 8.1]	8.1 [7.3; 9.0]	0.6 [-1.0; 2.2]*
EKFC-eGFR$_{Cr+Cys}$(S)	1.9 [1.0; 3.2]	-2.6 [-3.2; -2.0]	-4.5 [-5.6; -3.6]	3.6 [2.2; 4.7]	0.3 [-0.4; 0.8]*	-4.1 [-4.9; -3.5]
EKFC-eGFR$_{Cr+Cys}$	0.5 [-0.2; 1.8]*	-3.5 [-4.2; -3.0]	-5.5 [-6.4; -4.6]	5.1 [4.1; 6.6]	1.5 [0.9; 2.2]	-3.0 [-3.7; -2.3]
CKD-EPI-eGFR$_{Cr+Cys}$(AS)	7.0 [5.6; 8.0]	6.6 [5.7; 7.4]	5.3 [4.3; 6.6]	10.1 [8.8; 11.5]	11.8 [11.0; 12.5]	7.6 [6.5; 8.8]

EKFC-eGFR$_{Cys}$ (S) = Sex-dependent EKFC-eGFR$_{Cys}$-equation; CKD-EPI-eGFR$_{Cr}$ (AS) = race-independent CKD-EPI equation; EKFC-eGFR$_{Cr+Cys}$(S) = SCr/ sex-free CysC combined EKFC equation. As a rule of thumb, one may consider an absolute bias less than 5 mL/min/1.73m² as "clinically" non-significant.
* means unbiased.

Table S9.2a. Interquartile range (IQR) for mGFR < 60 mL/min/1.73m²

	Men			Women		
IQR [P25-P75]	age 18-40	age 40-65	age ≥ 65	age 18-40	age 40-65	age ≥ 65
n	223	1008	1556	184	741	1197
EKFC-eGFR$_{Cr}$	14.8 [-2.0; 12.8]	14.2 [-3.3; 10.9]	10.3 [-3.8; 6.5]	15.9 [-1.9; 14.0]	13.4 [-2.9; 10.5]	11.4 [-4.8; 6.6]
CKD-EPI-eGFR$_{Cr}$ (AS)	17.8 [-1.2; 16.6]	16.1 [-3.3; 12.9]	12.8 [-0.4; 12.5]	20.0 [-2.0; 18.0]	15.0 [-1.6; 13.4]	14.0 [-0.6; 13.4]
EKFC-eGFR$_{Cys}$ (S)	10.3 [0.5; 10.8]	10.5 [-4.4; 6.1]	9.5 [-4.1; 5.5]	10.3 [-0.1; 10.2]	11.3 [-5.0; 6.3]	11.0 [-5.6; 5.4]
EKFC-eGFR$_{Cys}$	9.9 [-1.2; 8.7]	10.7 [-6.0; 4.7]	9.5 [-5.2; 4.3]	11.6 [1.6; 13.3]	11.6 [-3.1; 8.5]	11.2 [-4.0; 7.1]
CKD-EPI-eGFR$_{Cys}$	10.5 [-5.2; 5.3]	11.1 [-9.2; 1.8]	10.0 [-8.1; 1.9]	11.6 [-4.6; 6.9]	11.6 [-8.4; 3.2]	11.5 [-8.8; 2.7]
EKFC-eGFR$_{Cr+Cys}$(S)	10.2 [0.3; 10.5]	9.4 [-2.3; 7.1]	8.3 [-3.1; 5.2]	10.7 [0.8; 11.5]	9.5 [-2.5; 7.0]	9.2 [-4.0; 5.2]
EKFC-eGFR$_{Cr+Cys}$	10.2 [-0.6; 9.7]	9.4 [-3.2; 6.3]	8.1 [-3.6; 4.6]	11.1 [1.9; 13.1]	9.6 [-1.5; 8.1]	9.5 [-3.2; 6.3]
CKD-EPI-eGFR$_{Cr+Cys}$(AS)	11.5 [-3.5; 8.0]	9.9 [-5.5; 4.4]	9.3 [-3.6; 5.8]	11.5 [-3.0; 8.5]	10.9 [-4.9; 6.0]	11.0 [-3.8; 7.3]

Table S9.2b. Interquartile range **(**IQR) for mGFR ≥ 60 mL/min/1.73m²

	Men			Women		
IQR [P25-P75]	age 18-40	age 40-65	age ≥ 65	age 18-40	age 40-65	age ≥ 65
n	782	2452	858	640	2243	948
EKFC-eGFR$_{Cr}$	21.2 [-9.8; 11.4]	17.4 [-12.4; 5.0]	15.9 [-13.5; 2.4]	19.4 [-6.5; 12.9]	16.4 [-8.3; 8.1]	14.6 [-11.4; 3.2]
CKD-EPI-eGFR$_{Cr}$ (AS)	25.2 [-4.9; 20.3]	18.7 [-6.8; 11.9]	17.8 [-3.0; 14.8]	22.3 [0.2; 22.4]	17.3 [-1.3; 16.0]	15.6 [-0.1; 15.6]
EKFC-eGFR$_{Cys}$ (S)	21.3 [-7.7; 13.6]	18.2 [-11.3; 6.9]	16.8 [-12.9; 3.9]	21.2 [-8.2; 13.1]	17.9 [-8.2; 9.7]	18.2 [-14.5; 3.7]
EKFC-eGFR$_{Cys}$	21.7 [-10.7; 11.0]	18.6 [-13.5; 5.1]	16.8 [-14.3; 2.5]	21.4 [-4.5; 16.9]	17.7 [-5.7; 11.9]	17.8 [-11.9; 5.8]
CKD-EPI-eGFR$_{Cys}$	25.5 [-8.0; 17.6]	24.6 [-7.7; 16.9]	22.5 [-11.7; 10.8]	24.2 [-6.3; 17.9]	22.7 [-4.0; 18.7]	24.5 [-12.3; 12.2]
EKFC-eGFR$_{Cr+Cys}$(S)	17.8 [-6.6; 11.3]	15.0 [-10.3; 4.6]	13.3 [-11.7; 1.6]	17.7 [-5.7; 12.0]	14.4 [-7.0; 7.5]	13.8 [-11.3; 2.5]
EKFC-eGFR$_{Cr+Cys}$	18.0 [-8.0; 10.0]	15.0 [-11.3; 3.6]	13.1 [-12.5; 0.7]	18.1 [-4.4; 13.8]	14.4 [-5.8; 8.7]	13.6 [-9.9; 3.6]
CKD-EPI-eGFR$_{Cr+Cys}$(AS)	20.1 [-3.5; 16.7]	19.0 [-2.9; 16.1]	17.8 [-3.1; 14.8]	19.0 [0.5; 19.5]	18.7 [1.9; 20.6]	19.0 [-1.9; 17.1]

Table S9.3a. P10-accuracy (% of subjects with eGFR within 10% of mGFR). for mGFR < 60 mL/min/1.73m².

P10 [95%CI]	Men			Women		
	age 18-40	age 40-65	age ≥ 65	age 18-40	age 40-65	age ≥ 65
N	223	1008	1556	184	741	1197
EKFC-eGFR$_{Cr}$	36.3 [30.0; 42.7]	30.5 [27.6; 33.3]	33.7 [31.3; 36.0]	27.7 [21.2; 34.2]	32.5 [29.1; 35.9]	32.7 [30.1; 35.4]
CKD-EPI-eGFR$_{Cr}$ (AS)	29.1 [23.1; 35.2]	26.3 [23.6; 29.0]	26.0 [23.8; 28.2]	23.4 [17.2; 29.5]	26.5 [23.3; 29.6]	24.7 [22.3; 27.2]
EKFC-eGFR$_{Cys}$ (S)	32.3 [26.1; 38.5]	36.6 [33.6; 39.6]	34.0 [31.6; 36.4]	32.1 [25.3; 38.9]	35.8 [32.3; 39.2]	31.7 [29.1; 34.4]
EKFC-eGFR$_{Cys}$	34.5 [28.2; 40.8]	35.9 [32.9; 38.9]	33.4 [31.1; 25.8]	26.6 [20.2; 33.1]	33.1 [29.7; 36.5]	30.3 [27.7; 32.9]
CKD-EPI-eGFR$_{Cys}$	39.5 [33.0; 45.9]	29.7 [26.8; 32.5]	29.2 [27.0; 31.5]	37.5 [30.4; 44.6]	29.0 [25.7; 32.3]	26.5 [24.0; 29.0]
EKFC-eGFR$_{Cr+Cys}$(S)	34.5 [28.2; 40.8]	39.8 [36.8; 42.8]	39.9 [37.5; 42.3]	34.8 [27.8; 41.7]	42.1 [38.5; 45.7]	38.0 [35.3; 40.8]
EKFC-eGFR$_{Cr+Cys}$	38.6 [32.1; 45.0]	40.1 [37.0; 43.1]	40.2 [37.7; 42.6]	28.3 [21.7; 34.8]	39.5 [36.0; 43.1]	37.6 [34.8; 40.3]
CKD-EPI-eGFR$_{Cr+Cys}$(AS)	39.9 [33.4; 46.4]	38.0 [35.0; 41.0]	35.9 [33.5; 38.2]	34.8 [27.8; 41.7]	37.7 [34.2; 41.1]	32.3 [29.7; 35.0]

Table S9.3b. P10-accuracy (% of subjects with eGFR within 10% of mGFR) for mGFR ≥ 60 mL/min/1.73m²

P10 [95%CI]	Men			Women		
	age 18-40	age 40-65	age ≥ 65	age 18-40	age 40-65	age ≥ 65
N	782	2452	858	640	2243	948
EKFC-eGFR$_{Cr}$	43.6 [40.1; 47.1]	47.2 [45.2; 49.2]	44.2 [40.8; 47.5]	43.8 [39.9; 47.6]	52.7 [50.6; 54.7]	48.3 [45.1; 51.5]
CKD-EPI-eGFR$_{Cr}$ (AS)	34.9 [31.6; 38.3]	48.0 [46.0; 49.9]	38.1 [34.9; 41.4]	35.8 [32.1; 39.5]	42.4 [40.4; 44.5]	37.3 [34.3; 40.4]
EKFC-eGFR$_{Cys}$ (S)	45.5 [42.0; 49.0]	48.7 [46.7; 50.7]	45.1 [41.8; 48.4]	41.9 [38.0; 45.7]	47.9 [45.9; 50.0]	42.9 [39.8; 46.1]
EKFC-eGFR$_{Cys}$	44.4 [40.9; 47.9]	47.3 [45.3; 49.2]	43.0 [39.7; 46.3]	42.0 [38.2; 45.9]	48.0 [45.9; 50.0]	43.4 [40.2; 46.5]
CKD-EPI-eGFR$_{Cys}$	34.9 [31.6; 38.3]	35.1 [33.2; 37.0]	34.3 [31.1; 37.4]	37.0 [33.3; 40.8]	34.3 [32.4; 36.3]	31.6 [28.7; 34.6]
EKFC-eGFR$_{Cr+Cys}$(S)	49.4 [45.8; 52.9]	54.9 [52.9; 56.9]	51.6 [48.3; 55.0]	50.2 [46.3; 54.0]	58.4 [56.3; 60.4]	52.6 [49.5; 55.8]
EKFC-eGFR$_{Cr+Cys}$	50.1 [46.6; 53.6]	53.5 [51.6; 55.5]	49.5 [46.2; 52.9]	48.3 [44.4; 52.2]	56.4 [54.4; 58.5]	53.7 [50.5; 56.9]
CKD-EPI-eGFR$_{Cr+Cys}$(AS)	40.7 [37.2; 44.1]	41.5 [39.5; 43.4]	41.5 [38.2; 44.8]	37.8 [34.0; 41.6]	34.2 [32.2; 36.2]	37.0 [33.9; 40.1]

Table S9.4a. P30-accuracy (% of subjects with eGFR within 30% of mGFR) for mGFR < 60 mL/min/1.73m²

P30 [95%CI]	Men			Women		
	age 18-40	age 40-65	age ≥ 65	age 18-40	age 40-65	age ≥ 65
N	223	1008	1556	184	741	1197
EKFC-eGFR$_{Cr}$	69.5 [63.4; 75.6]	70.6 [67.8; 73.5]	77.2 [75.1; 79.3]	65.2 [58.3; 72.2]	72.2 [69.0; 75.4]	76.4 [74.0; 78.8]
CKD-EPI-eGFR$_{Cr}$ (AS)	62.8 [56.4; 69.2]	66.4 [63.4; 69.3]	63.2 [60.8; 65.6]	56.5 [49.3; 63.8]	66.7 [63.3; 70.1]	62.4 [59.7; 65.2]
EKFC-eGFR$_{Cys}$ (S)	77.1 [71.6; 82.7]	80.3 [77.8; 82.7]	78.9 [76.8; 80.9]	69.0 [62.3; 75.8]	76.1 [73.0; 79.2]	76.7 [74.3; 79.1]
EKFC-eGFR$_{Cys}$	80.7 [75.5; 85.9]	81.9 [79.6; 84.3]	80.5 [78.5; 82.4]	65.2 [58.3; 72.2]	74.9 [71.8; 78.0]	75.5 [73.1; 78.0]
CKD-EPI-eGFR$_{Cys}$	80.7 [75.5; 85.9]	78.8 [76.2; 81.3]	77.3 [75.2; 79.4]	72.8 [66.3; 79.3]	74.0 [70.8; 77.1]	71.6 [69.0; 74.2]
EKFC-eGFR$_{Cr+Cys}$(S)	78.0 [72.6; 83.5]	81.2 [78.7; 83.6]	84.4 [82.6; 86.2]	74.5 [68.1; 80.8]	80.2 [77.3; 83.0]	82.7 [80.6; 84.9]
EKFC-eGFR$_{Cr+Cys}$	79.8 [74.5; 85.1]	82.5 [80.2; 84.9]	85.3 [83.5; 87.0]	70.1 [63.4; 76.8]	79.6 [76.7; 82.5]	81.5 [79.2; 83.7]
CKD-EPI-eGFR$_{Cr+Cys}$(AS)	85.2 [80.5; 89.9]	83.3 [81.0; 85.6]	81.0 [79.1; 83.0]	75.0 [68.7; 71.3]	79.9 [77.0; 82.8]	78.1 [75.8; 80.5]

Table S9.4b. P30-accuracy (% of subjects with eGFR within 30% of mGFR) for mGFR ≥ 60 mL/min/1.73m²

P30 [95%CI]	Men			Women		
	age 18-40	age 40-65	age ≥ 65	age 18-40	age 40-65	age ≥ 65
N	782	2452	858	640	2243	948
EKFC-eGFR$_{Cr}$	89.5 [87.4; 91.7]	93.3 [92.3; 94.3]	94.1 [92.5; 95.6]	89.2 [86.8; 91.6]	94.6 [93.7; 95.5]	95.0 [93.7; 96.4]
CKD-EPI-eGFR$_{Cr}$ (AS)	80.6 [77.8; 83.3]	89.4 [88.1; 90.6]	86.8 [84.6; 89.1]	79.8 [76.7; 83.0]	88.5 [87.2; 89.8]	84.8 [82.5; 87.1]
EKFC-eGFR$_{Cys}$ (S)	89.0 [86.8;91.2]	92.4 [91.3; 93.4]	91.3 [89.4; 93.2]	90.6 [88.4; 92.9]	92.5 [91.4; 93.6]	90.5 [88.6; 92.4]
EKFC-eGFR$_{Cys}$	91.0 [89.0; 93.1]	91.7 [90.6; 92.8]	90.2 [88.2; 92.2]	88.0 [85.4; 90.5]	91.9 [90.8; 93.1]	92.0 [90.3; 93.7]
CKD-EPI-eGFR$_{Cys}$	84.9 [82.4; 87.4]	83.5 [92.1; 85.0]	83.8 [81.3; 86.3]	85.2 [82.4; 87.9]	82.7 [81.1; 84.2]	81.9 [79.4; 84.3]
EKFC-eGFR$_{Cr+Cys}$(S)	94.5 [92.9; 96.1]	95.4 [94.6; 96.2]	95.8 [94.5; 97.1]	94.4 [92.6; 96.2]	97.0 [96.3; 97.7]	96.6 [95.5; 97.8]
EKFC-eGFR$_{Cr+Cys}$	94.8 [93.2; 96.3]	95.7 [94.9; 96.5]	95.5 [94.1; 96.9]	93.1 [91.2; 95.1]	96.3 [95.5; 97.1]	96.9 [85.8; 98.0]
CKD-EPI-eGFR$_{Cr+Cys}$(AS)	89.6 [87.5; 91.8]	88.9 [87.7; 90.2]	87.1 [84.8; 89.3]	87.0 [84.4; 89.6]	83.3 [81.8; 84.9]	84.7 [82.4; 87.0]

Section S10. Performance statistics according to Body Mass Index (BMI) category

Table S10.1. Comparison of Bias according to body mass index category

	Body Mass Index					
BIAS [95%CI]	< 18 kg/m²	18-25 kg/m²	25-30 kg/m²	30-35 kg/m²	35-40 kg/m²	≥ 40 kg/m²
N	285	4908	4659	2093	617	270
EKFC-eGFR$_{Cr}$	7.2 [4.8; 9.7]	0.9 [0.5; 1.2]	-1.1 [-1.4; -0.7]	-1.4 [-1.9; -0.8]	-1.0 [-2.0; 0.2]*	-1.6 [-3.3; 0.1]*
CKD-EPI-eGFR$_{Cr}$ (AS)	13.1 [10.2; 16.4]	6.9 [6.5; 7.4]	4.8 [4.4; 5.2]	4.4 [3.7; 5.1]	4.3 [2.9; 5.7]	3.1 [1.6; 4.7]
EKFC-eGFR$_{Cys}$ (S)	1.6 [0.5; 4.0]	0.8 [0.5; 1.2]	0.4 [0.1; 0.9]	-0.7 [-1.3; -0.3]	-2.0 [-3.0; -0.8]	-4.9 [-6.5; -3.1]
EKFC-eGFR$_{Cys}$	2.8 [1.0; 4.5]	1.0 [0.6; 1.4]	0.4 [-0.1; 0.8]*	-0.9 [-1.5; -0.3]	-0.9 [-2.2; -0.0]	-4.6 [-5.9; -2.9]
CKD-EPI-eGFR$_{Cys}$	0.9 [-2.1; 2.5]*	1.0 [0.6; 1.5]	1.1 [0.7; 1.6]	-0.9 [-1.4; -0.3]	-2.8 [-4.0; -1.7]	-6.6 [-8.6; -4.8]
EKFC-eGFR$_{Cr+Cys}$(S)	5.2 [3.8; 6.6]	0.8 [0.5; 1.2]	0.0 [-0.4; 0.3]*	-0.9 [-1.3; -0.4]	-1.3 [-2.5; -0.5]	-2.9 [-4.5; -2.1]
EKFC-eGFR$_{Cr+Cys}$	5.6 [4.6; 7.0]	0.8 [0.5; 1.1]	-0.2 [-0.4; 0.2]*	-0.8 [-1.2; -0.3]	-1.1 [-2.0; -0.2]	-2.3 [-3.8; -1.3]
CKD-EPI-eGFR$_{Cr+Cys}$(AS)	5.7 [4.1; 7.9]	5.0 [4.5; 5.5]	4.5 [4.0; 5.0]	2.8 [2.2; 3.4]	1.3 [0.4; 2.4]	-2.0 [-3.7; -0.5]

Considering an absolute bias of 5 mL/min/1.73m² as clinically meaningful, both equations perform equally well and within acceptable limits for the bias (except for CKD-EPI in extreme BMI > 40 kg/m²).

Table S10.2. Comparsion of interquartile range (IQR) according to body mass index category

	Body Mass Index					
IQR [P25-P75]	< 18 kg/m²	18-25 kg/m²	25-30 kg/m²	30-35 kg/m²	35-40 kg/m²	≥ 40 kg/m²
N	285	4908	4659	2093	617	270
EKFC-eGFR$_{Cr}$	19.4 [-1.6; 17.8]	15.4 [-6.6; 8.8]	14.4 [-8.3; 6.1]	15.2 [-9.2; 6.0]	16.4 [-9.0; 7.4]	15.5 [-9.4; 6.1]
CKD-EPI-eGFR$_{Cr}$ (AS)	25.6 [1.5; 27.1]	17.5 [-1.0; 16.4]	16.3 [-2.8; 13.5]	17.6 [-3.8; 13.8]	16.8 [-3.4; 13.5]	17.0 [-4.0; 12.9]
EKFC-eGFR$_{Cys}$ (S)	16.8 [-7.0; 9.8]	15.4 [-7.2; 8.2]	14.4 [-7.1; 7.3]	14.0 [-8.5; 5.4]	15.5 [-10.8; 4.7]	15.9 [-13.0; 2.8]
EKFC-eGFR$_{Cys}$	17.2 [-6.7; 10.5]	15.8 [-7.1; 8.7]	14.5 [-7.3; 7.3]	14.2 [-8.6; 5.6]	15.2 [-9.9; 5.3]	16.9 [-13.1; 3.8]
CKD-EPI-eGFR$_{Cys}$	17.8 [-8.0; 9.7]	21.1 [-7.8; 13.2]	19.3 [-7.0; 12.3]	18.4 [-9.0; 9.4]	17.7 [-11.3; 6.4]	15.1 [-13.9; 1.2]
EKFC-eGFR$_{Cr+Cys}$(S)	14.2 [-1.7; 12.5]	12.7 [-5.4; 7.3]	12.1 [-6.4; 5.7]	12.1 [-7.5; 4.7]	13.8 [-8.6; 5.2]	12.7 [-9.6; 3.1]
EKFC-eGFR$_{Cr+Cys}$	14.4 [-1.4; 13.0]	12.7 [-5.2; 7.5]	12.4 [-6.8; 5.6]	12.1 [-7.4; 4.8]	13.2 [-8.2; 5.0]	13.4 [-9.4; 4.0]
CKD-EPI-eGFR$_{Cr+Cys}$(AS)	17.7 [-1.6; 16.1]	17.7 [-2.6; 15.2]	16.5 [-2.4; 14.1]	16.5 [-3.8; 12.7]	16.1 [-5.9; 10.2]	14.5 [-8.1; 6.5]

The IQR (a measure of imprecision) is smaller for EKFC$_{CysC}$ than for CKD-EPI$_{CysC}$, except in the most extreme BMI-classes (at both sides).

Table S10.3. Comparison of P10-accuracy according to body mass index category

	Body Mass Index					
P10 [95%CI]	< 18 kg/m²	18-25 kg/m²	25-30 kg/m²	30-35 kg/m²	35-40 kg/m²	≥ 40 kg/m²
N	285	4908	4659	2093	617	270
EKFC-eGFR$_{Cr}$	25.6 [20.5; 30.7]	42.4 [41.0; 43.8]	44.6 [43.2; 46.0]	40.1 [38.0; 42.2]	35.3 [31.6; 39.1]	38.1 [32.3; 44.0]
CKD-EPI-eGFR$_{Cr}$ (AS)	21.4 [16.6; 26.2]	34.1 [32.8; 35.5]	38.4 [37.0; 39.8]	35.2 [33.2; 37.3]	36.0 [32.2; 39.8]	34.8 [29.1; 40.5]
EKFC-eGFR$_{Cys}$ (S)	34.0 [28.5; 39.6]	41.1 [39.7; 42.5]	43.1 [41.7; 44.5]	43.1 [41.0; 45.2]	40.2 [36.3; 44.1]	33.3 [27.7; 39.0]
EKFC-eGFR$_{Cys}$	29.5 [24.1; 34.8]	40.3 [38.9; 41.7]	42.1 [40.7; 43.6]	42.4 [40.3; 44.5]	39.9 [36.0; 43.7]	33.0 [27.3; 38.6]
CKD-EPI-eGFR$_{Cys}$	29.5 [24.1; 34.8]	31.0 [29.7; 32.3]	34.2 [32.9; 35.6]	33.4 [31.4; 35.5]	31.9 [28.2; 35.6]	30.4 [24.9; 35.9]
EKFC-eGFR$_{Cr+Cys}$(S)	29.5 [24.1; 34.8]	48.5 [47.1; 49.9]	50.4 [49.0; 51.9]	49.4 [47.3; 51.5]	45.4 [41.4; 49.3]	39.6 [33.8; 45.5]
EKFC-eGFR$_{Cr+Cys}$	29.8 [24.5; 35.2]	48.2 [46.7; 49.5]	49.3 [47.9; 50.7]	47.9 [45.8; 50.1]	43.4 [39.5; 47.4]	40.0 [34.1; 45.9]
CKD-EPI-eGFR$_{Cr+Cys}$(AS)	28.1 [22.8; 33.3]	36.2 [34.9; 37.6]	38.9 [37.5; 40.3]	38.2 [36.1; 40.3]	38.6 [34.7; 42.4]	37.0 [31.2; 42.8]

Table S10.4. Comparison of P30-accuracy according to body mass index category

	Body Mass Index					
P30 [95%CI]	< 18 kg/m²	18-25 kg/m²	25-30 kg/m²	30-35 kg/m²	35-40 kg/m²	≥ 40 kg/m²
N	285	4908	4659	2093	617	270
EKFC-eGFR$_{Cr}$	67.7 [62.3; 73.2]	85.0 [84.0; 86.0]	88.4 [87.4; 89.3]	86.3 [84.8; 87.8]	83.1 [80.2; 86.1]	83.3 [78.9; 87.8]
CKD-EPI-eGFR$_{Cr}$ (AS)	55.1 [49.3; 60.9]	76.4 [75.3; 77.6]	80.9 [79.8; 82.0]	78.6 [76.8; 80.4]	75.7 [72.3; 79.1]	79.3 [74.4; 84.1]
EKFC-eGFR$_{Cys}$ (S)	75.8 [70.8; 80.8]	85.8 [84.8; 86.8]	87.2 [86.2; 88.1]	87.9 [86.5; 89.3]	84.3 [81.4; 87.2]	83.3 [78.9; 87.8]
EKFC-eGFR$_{Cys}$	75.4 [70.4; 80.5]	85.7 [84.7; 86.6]	87.5 [86.5; 88.4]	87.2 [85.8; 88.6]	84.8 [81.9; 87.6]	83.7 [79.3; 88.1]
CKD-EPI-eGFR$_{Cys}$	73.0 [67.8; 78.2]	79.5 [78.3; 80.6]	81.6 [80.5; 82.7]	81.7 [80.0; 83.4]	80.6 [77.4; 83.7]	75.9 [70.8; 81.1]
EKFC-eGFR$_{Cr+Cys}$(S)	74.0 [68.9; 79.2]	90.1 [89.3; 91.0]	92.2 [91.4; 93.0]	91.2 [89.9; 92.4]	88.2 [85.6; 90.7]	88.9 [85.1; 92.7]
EKFC-eGFR$_{Cr+Cys}$	73.7 [68.5; 78.8]	90.2 [89.3; 91.0]	92.1 [91.4; 92.9]	91.0 [89.7; 92.2]	87.8 [85.3; 90.4]	88.1 [84.3; 92.0]
CKD-EPI-eGFR$_{Cr+Cys}$(AS)	74.4 [69.3; 79.5]	83.5 [82.5; 84.6]	85.2 [84.2; 86.3]	84.8 [83.3; 86.3]	85.4 [82.6; 88.2]	84.8 [80.5; 89.1]

Section S11. Cohort specific performance

Table S11. Median bias and P30(%) accuracy for the EKFC-equations in the different cohorts. # refers to external validation cohorts. Referrals*: subjects referred for measured GFR.

Center	Country	Cohort	n	Bias EKFC-eGFR$_{Cr}$	Bias EKFC-eGFR$_{Cys}$	Bias EKFC-eGFR$_{Cr+Cys}$	P30 EKFC-eGFR$_{Cr}$	P30 EKFC-eGFR$_{Cys}$	P30 EKFC-eGFR$_{Cr+Cys}$
Berlin	Germany	BIS-study	657	1.70	3.65	2.94	90.4	89.3	92.4
Kent#	UK	GFR in old adults study	394	-3.22	0.55	-1.26	85.5	90.9	91.1
Lund#	Sweden	CAPA-study	2,847	2.39	-3.74	-0.21	81.4	83.2	89.8
Lyon	France	Referrals*	914	1.92	1.29	2.00	80.6	82.7	85.0
Rochester#	USA	ECAC/GENOA study	1,093	-2.69	3.98	0.72	89.3	83.9	88.7
Saint-Etienne	France	HIV-study	203	0.24	-1.15	-0.01	84.7	85.2	85.2
Stockholm	Sweden	Referrals*	577	-0.04	-0.70	-0.36	80.6	81.5	87.2
Tromsö	Norway	RENIS-T6 study	1,627	-2.63	2.74	0.28	97.3	95.3	96.9
Örebro	Sweden	Referrals*	508	-0.81	4.20	1.55	82.9	78.1	86.0
Abidjan#	Côte d’Ivoire	eGFR-study	285	-5.11	3.97	-0.96	76.1	80.0	82.1
Kinshasa#	Congo	eGFR-study	223	-3.77	-0.78	-2.37	83.4	89.7	88.3
Paris#	France	White Referrals*	2,646	-1.24	-0.81	-0.70	86.5	87.6	92.1
Paris#	France	Black Referrals*	858	-2.58	1.58	-0.33	85.5	87.4	92.0

Section S12. Graphs of bias and P30 against age

Section S12.1. Graphs of bias and P30 against age in the White and Black cohorts

Figure S5. Bias versus age for EKFC-eGFR$_{Cr}$ (black solid line), EKFC-eGFR$_{Cys}$ (red solid line), EKFC-eGFR$_{Cr+Cys}$ (green solid line), CKD-EPI-eGFR$_{Cr}$(ASR) (Black dotted line), CKD-EPI-eGFR$_{Cr}$(AS) (black dashed line), CKD-EPI-eGFR$_{Cys}$ (red dotted line) and CKD-EPI-eGFR$_{Cr+Cys}$ (AS) (green dotted line) in the pooled White cohorts (EKFC, Paris, Rochester).

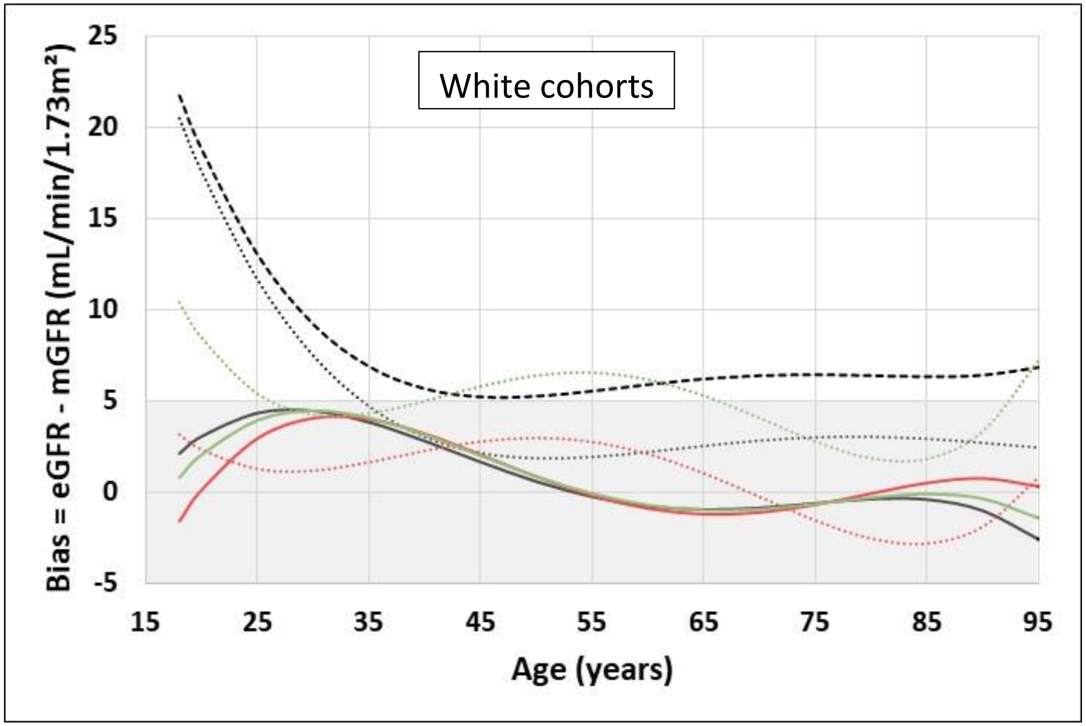


Figure S6. P30(%) versus age for the sex-dependent and sex-free EKFC-eGFR$_{Cys}$ and CKD-EPI-eGFR$_{Cys}$ in the pooled White cohorts (EKFC, Paris, Rochester). The grey area indicates P30 > 75%.

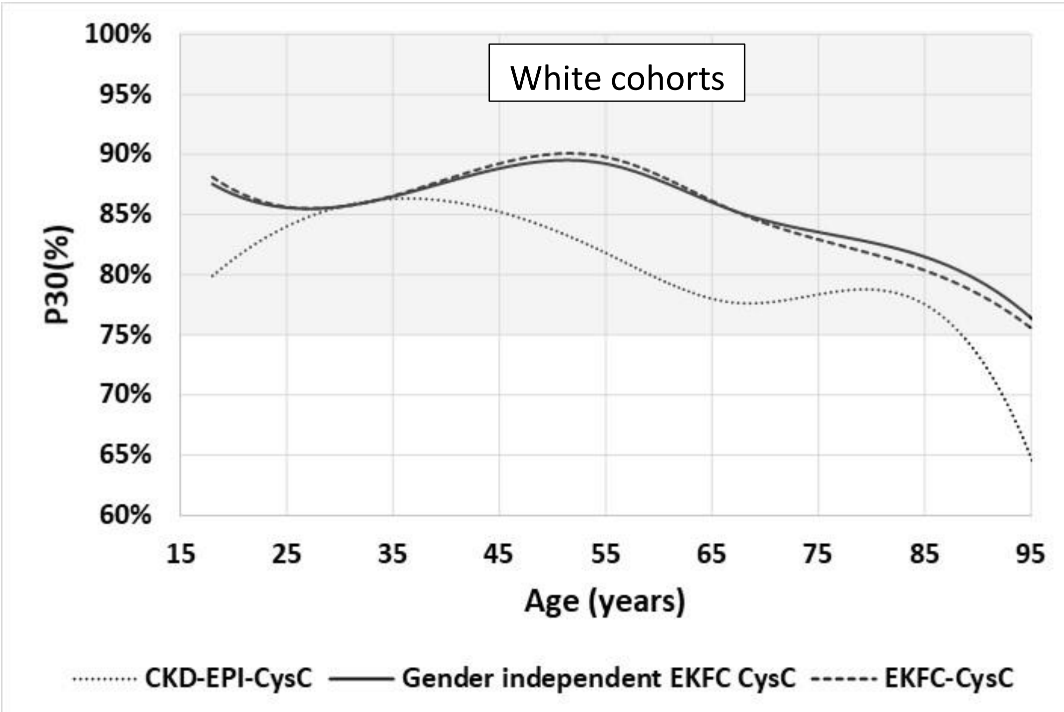


Figure S7. Bias versus age for EKFC-eGFR$_{Cr}$ (black solid line), EKFC-eGFR$_{Cys}$ (red solid line), EKFC-eGFR$_{Cr+Cys}$ (green solid line), CKD-EPI-eGFR$_{Cr}$ (ASR) (Black dotted line), CKD-EPI-eGFR$_{Cr}$ (AS) (black dashed line), CKD-EPI-eGFR$_{Cys}$ (red dotted line) and CKD-EPI-eGFR$_{Cr+Cys}$ (AS) (green dotted line) in the pooled Black cohorts (Paris, Côtes d'Ivoire, Congo).

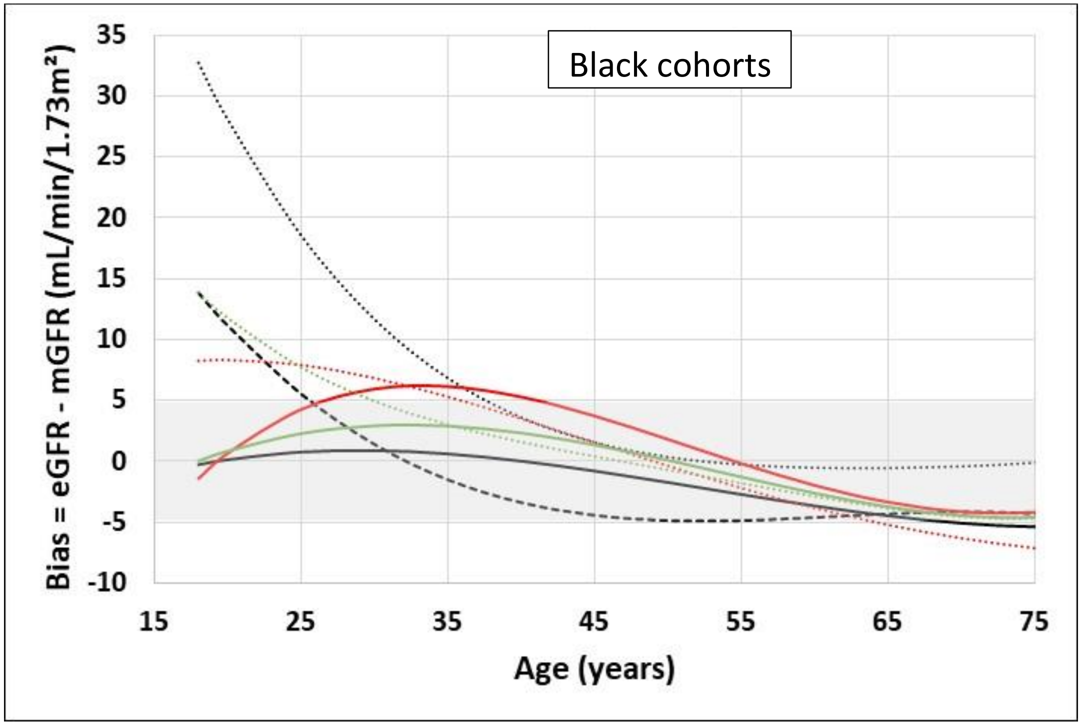
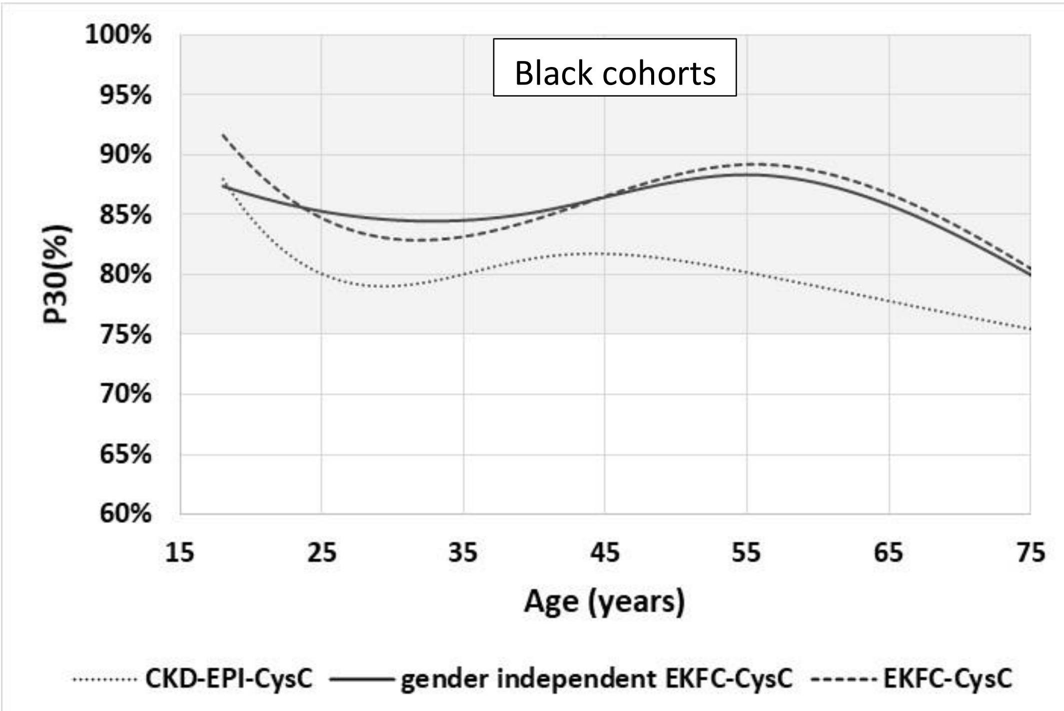


Figure S8. P30(%)-accuracy versus age for the sex-dependent, sex-free EKFC-eGFR$_{Cys}$ and CKD-EPI-eGFR$_{Cys}$ in the pooled Black cohorts (Paris, Côtes d'Ivoire, Congo).



Section S12.2. Graphs of bias and P30 against age in men and women

Figure S9. Bias versus age for EKFC-eGFR$_{Cys}$ for men and women using the sex-specific Q-values, and the sex-free Q-value (SF) for all cohorts pooled.

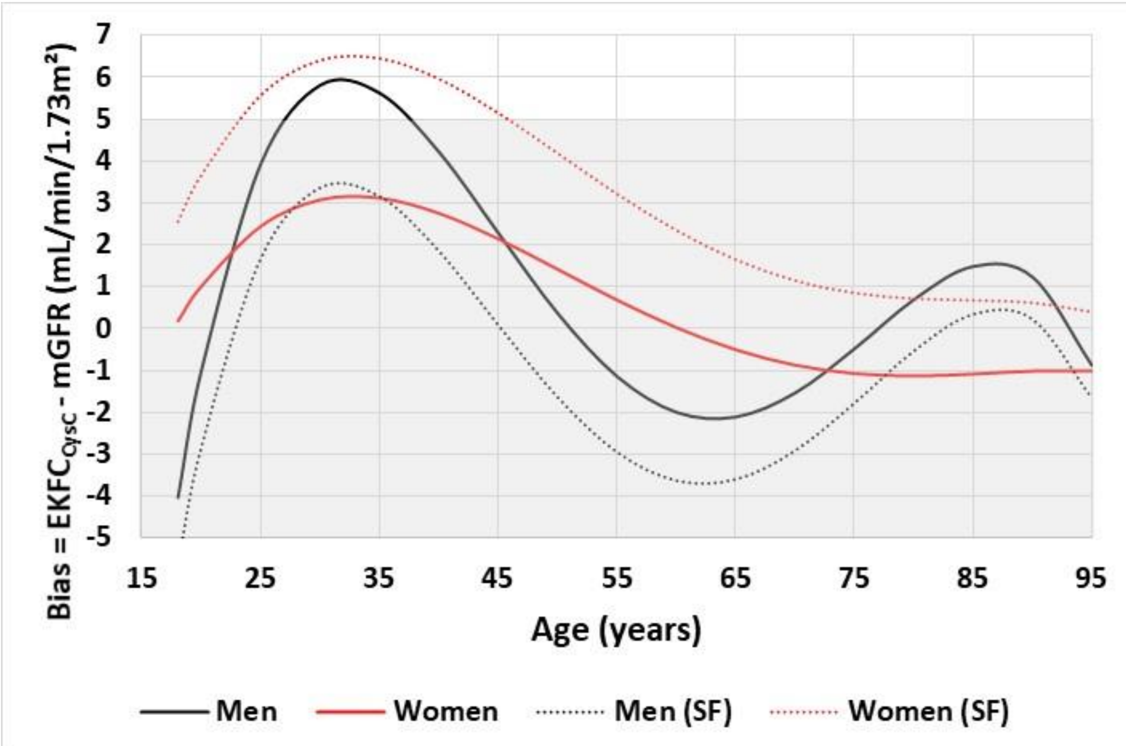
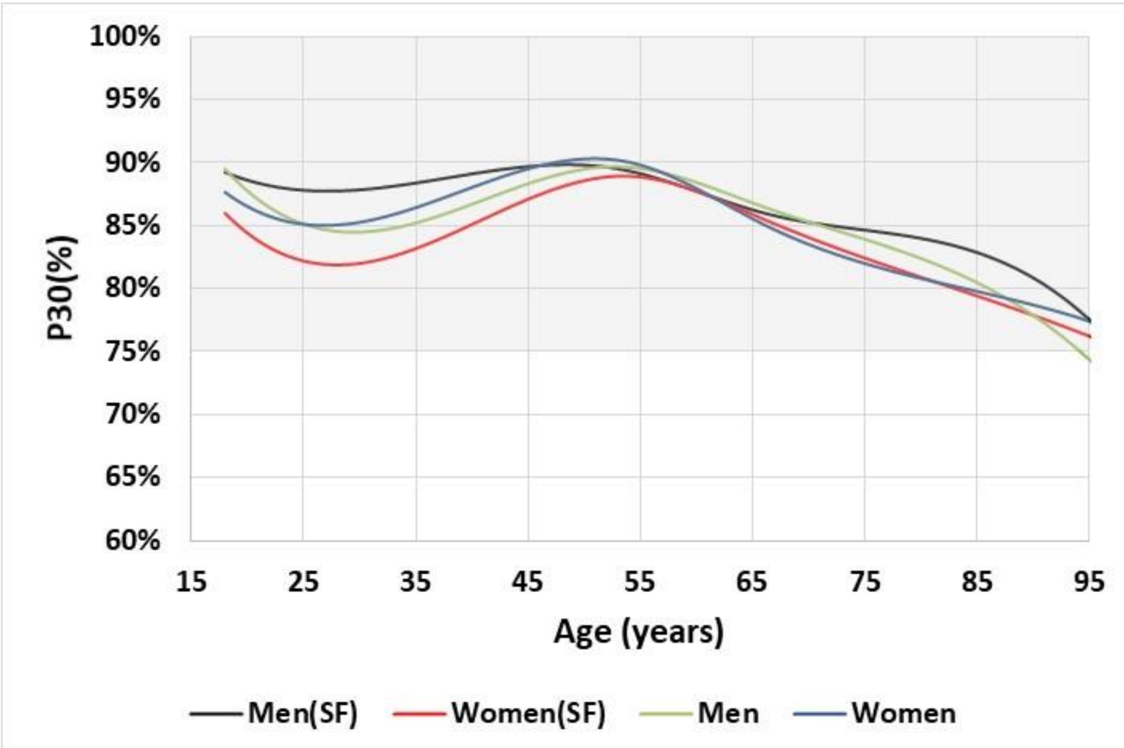
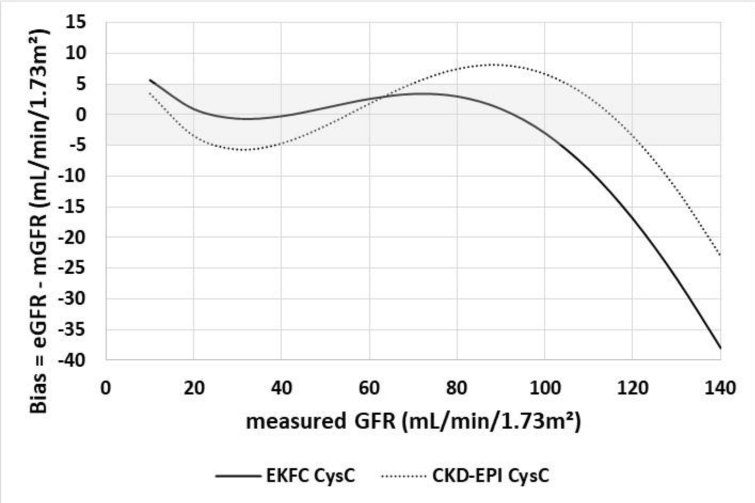


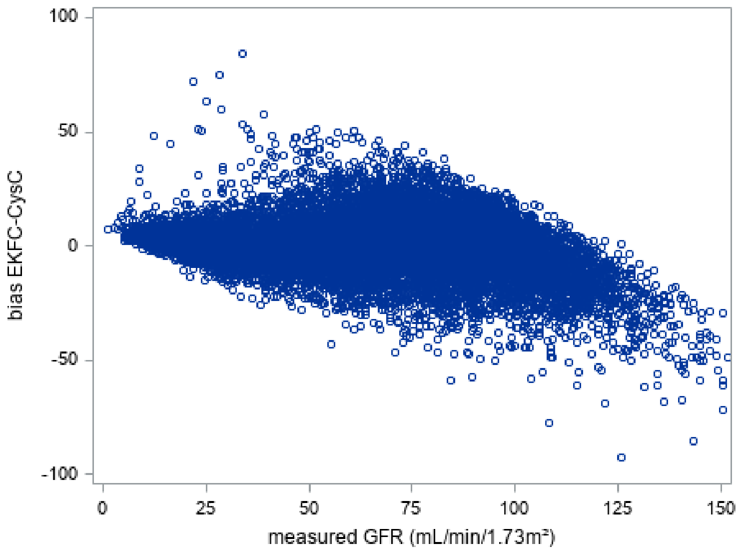
Figure S10. P30(%)-accuracy versus age for EKFC-eGFR$_{Cys}$ for men and women using the sex-specific Q-values, and the sex-free Q-value (SF) for all cohorts pooled.

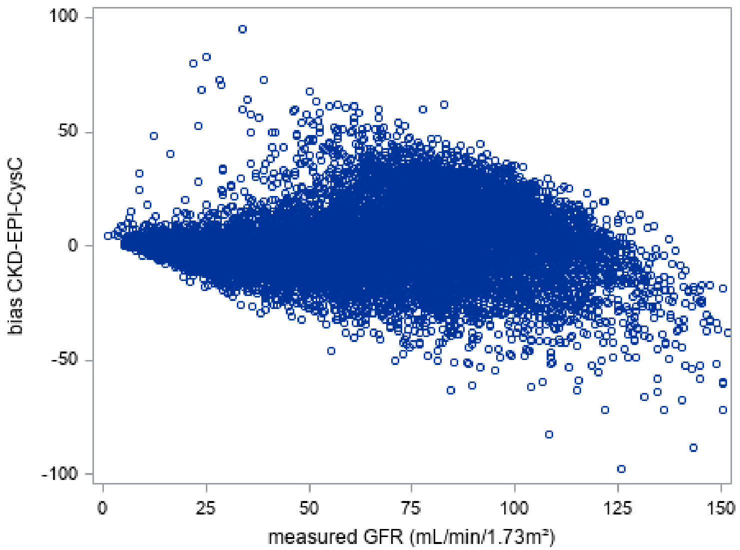


Section S12.3. Graphs of bias against mGFR

Figure S11. Median quantile line for bias of EKFC-eGFR$_{Cys}$ and CKD-EPI-eGFR$_{Cys}$ against measured GFR for all cohorts pooled (top graph) and scatter plots of bias against mGFR (bottom graphs).







Section S12.4. Accuracy diagram

Figure S12. Accuracy diagram [22]: measured GFR against estimated GFR (EKFC: EKFC-eGFR$_{Cr}$ = green, EKFC-eGFR$_{Cys}$ = blue, EKFC-eGFR$_{Cr+Cys}$ = red). The curved solid colored lines are the quantiles Q_{10}, Q_{50} and Q_{90}. The middle straight dotted line is the identity line. When Q_{50} coincides with the identity line, then median bias is zero. The V-shape area constrained by the dotted lines indicate the P30-region. When the Q_{10}-Q_{90} curves are within this V-shape area, then P30 > 80%.
At an estimated EKFC-eGFR$_{Cr}$ of 60mL/min/1.73m², measured GFR is within 46 to 79 mL/min/1.73m² with 80% probability. At an estimated EKFC-eGFR$_{Cys}$ of 60 mL/min/1.73m², measured GFR is within 49 to 80 mL/min/1.73m² with 80% probability. At an estimated EKFC-eGFR$_{Cr+Cys}$ of 60 mL/min/1.73m², measured GFR is within 49 to 74 mL/min/1.73m² with 80% probability.

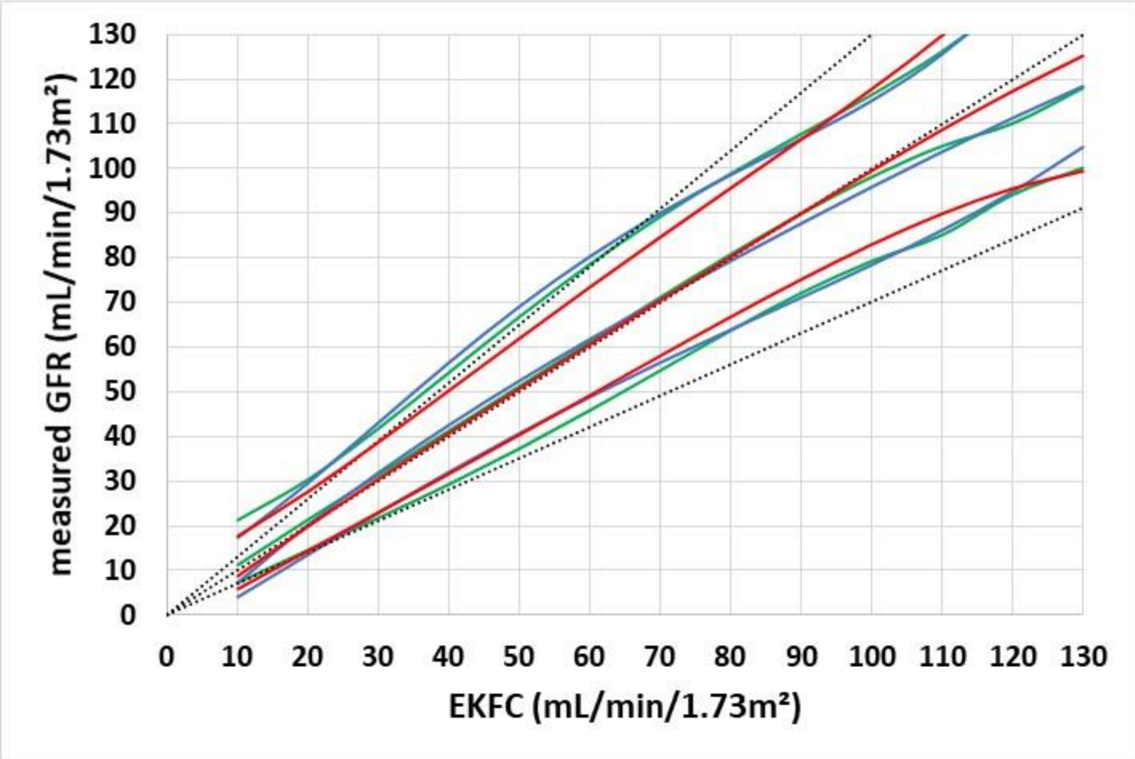


Figure S13. Scatterplot of mGFR against eGFR, with identity line and P30-lines, for the sex-free cystatin C based EKFC (P30 = 86.3% [85.7-86.9], left panel) and cystatin C based CKD-EPI equation (P30 = 80.4% [79.8-81.1], right panel) in the entire dataset (n = 12.832).

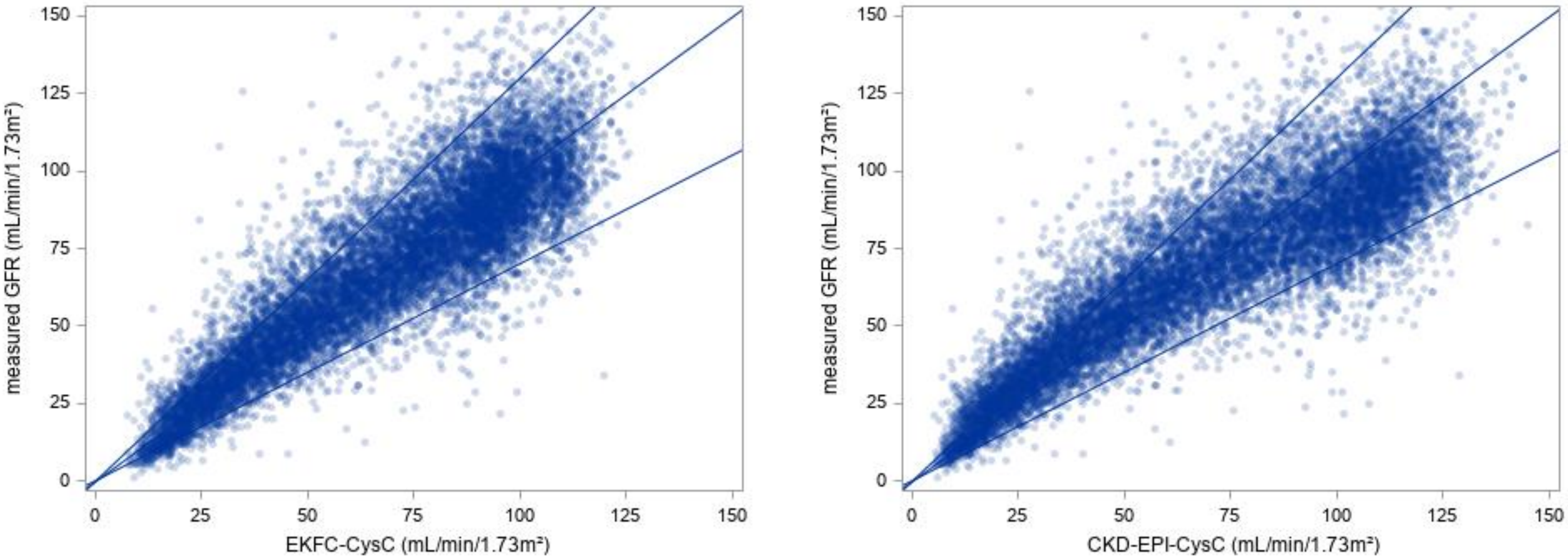
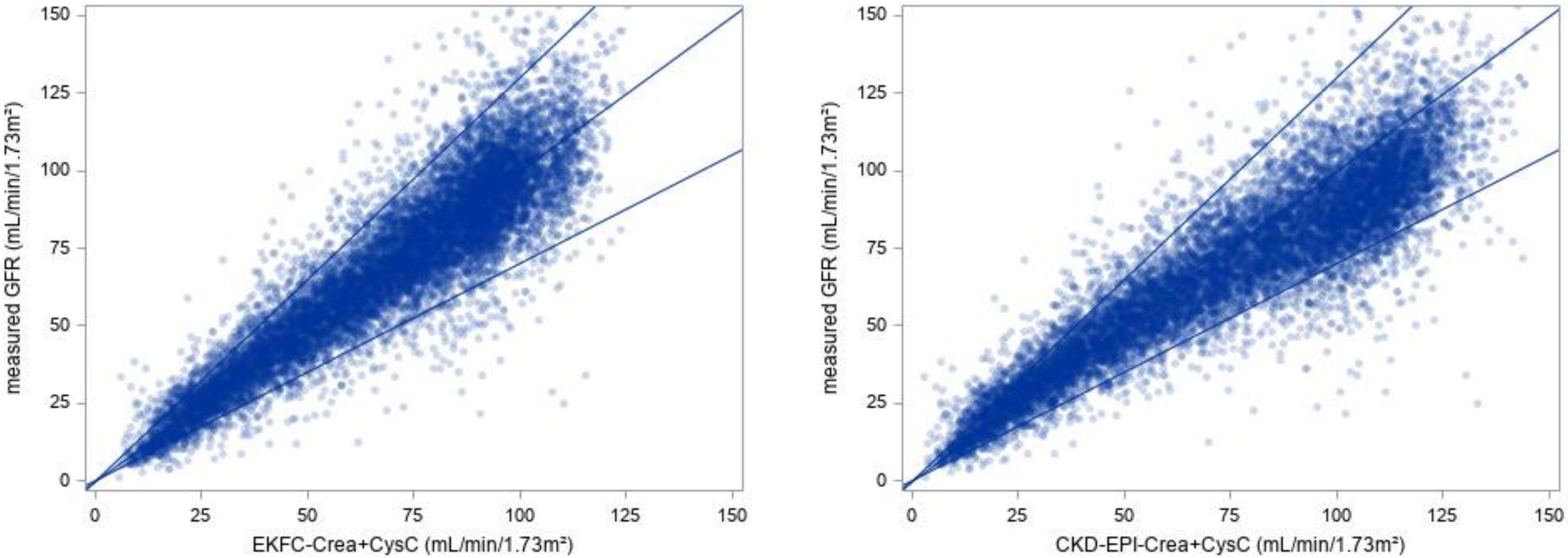


Figure S14. Scatterplot of mGFR against eGFR, with identity line and P30-lines, for the creatinine/cystatin C based EKFC (P30 = 90.5% [90.0-91.0], left panel) and CKD-EPI equation (P30 = 84.3% [83.6-84.9], right panel) in the entire dataset (n = 12.832).



Section S13. Author's Contributions

HP, JB, AR, UN and PD contributed to the conception and design, analysis and interpretation of the data. HP, AR, and PD drafted the manuscript. JB, UN, AR, AL, BOE and TM revised it critically for important intellectual content. All co-authors were involved in the acquisition of data [NE, ES (Berlin), LD (Lyon), AR (Rochester), EJL (Kent), CM (Saint-Etienne), TM, BOE (Tromsø), KAM, KL, MH (Stockholm), AG, AA (Lund), AL (Uppsala), POS (Örebro), JBB, EKS, EC (Congo), EY, DM, EC (Côtes d'Ivoire)] and revised the manuscript, before giving final approval of the version to be published.

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