KI REPORTS
KIReports.org
CLINICAL RESEARCH

Discordant Results Between Creatinine- and Cystatin C-based Equations for Estimating GFR

Pierre Delanaye[1,2], Martin Flamant[3], Emmanuelle Vidal-Petiot[3], Jonas Björk[4,5], Ulf Nyman[6], Anders Grubb[7], Stephan J.L. Bakker[8], Martin H. de Borst[8], Marco van Londen[8], Laurence Derain-Dubourg[9], Andrew D. Rule[10], Björn O. Eriksen[11], Toralf Melsom[11], Per-Ola Sundin[12], Natalie Ebert[13], Elke Schaeffner[13], Magnus Hansson[14], Karin Littmann[15], Anders Larsson[16], Thomas Stehlé[17,18], Etienne Cavalier[19], Justine B. Bukabau[20], Ernest K. Sumaili[20], Eric Yayo[21], Christophe Mariat[22], Olivier Moranne[2], Anders Christensson[23], Antoine Lanot[24,25,26,27] and Hans Pottel[27]

[1]Department of Nephrology-Dialysis-Transplantation, University of Liège, CHU Sart Tilman, Liège, Belgium; [2]Department of Nephrology-Dialysis-Apheresis, Hôpital Universitaire Carémeau, Université de Montpellier, Nîmes, France; [3]Assistance Publique-Hôpitaux de Paris, Bichat Hospital, INSERM U1148, Université Paris Cité and Université Sorbonne Paris Nord, LVTS, Center, Paris, France; [4]Division of Occupational and Environmental Medicine, Lund University, Lund, Sweden; [5]Clinical Studies Sweden, Forum South, Skåne University Hospital, Lund, Sweden; [6]Department of Translational Medicine, Division of Medical Radiology, Lund University, Malmö, Sweden; [7]Department of Clinical Chemistry, Skåne University Hospital, Lund University, Lund, Sweden; [8]Division of Nephrology, Department of Internal Medicine, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands; [9]Néphrologie, Dialyse, Hypertension et Exploration Fonctionnelle Rénale, Hôpital Edouard Herriot, Hospices Civils de Lyon, Lyon, France; [10]Division of Nephrology and Hypertension, Mayo Clinic, Rochester, Minnesota, USA; [11]Section of Nephrology, University Hospital of North Norway and Metabolic and Renal Research Group, UiT The Arctic University of Norway, Tromsø, Norway; [12]Karla Healthcare Centre, Faculty of Medicine and Health, Örebro University, Örebro, Sweden; [13]Charité Universitätsmedizin Berlin, Institute of Public Health, Berlin, Germany; [14]Function Area Clinical Chemistry, Karolinska University Laboratory, Department of Laboratory Medicine, Karolinska University Hospital Huddinge, Karolinska Institute, Stockholm, Sweden; [15]Division of Medicine Huddinge (MedH), Karolinska Institute, Stockholm, Sweden; [16]Department of Medical Sciences, Clinical Chemistry, Uppsala University, Uppsala, Sweden; [17]Université Paris Est Créteil, INSERM, Institut Mondor de Recherche Biomédicale, Créteil, France; [18]Assistance Publique-Hôpitaux de Paris, Hôpitaux Universitaires Henri Mondor, Service de Néphrologie et Transplantation, Fédération Hospitalo-Universitaire, Innovative therapy for immune disorders, Créteil, France; [19]Department of Clinical Chemistry, University of Liège, CHU Sart Tilman, Liège, Belgium; [20]Renal Unit, Department of Internal Medicine, Kinshasa University Hospital, University of Kinshasa, Kinshasa, Democratic Republic of the Congo; [21]Département de Biochimie, UFR Sciences Pharmaceutiques et Biologiques, Université Felix Houphouët Boigny, Abidjan, Côte d'Ivoire; [22]Service de Néphrologie, Dialyse et Transplantation Rénale, Hôpital Nord, CHU de Saint-Etienne, France; [23]Department of Nephrology, Skåne University Hospital, Lund University, Malmö, Sweden; [24]Normandie Université, Unicaen, CHU de Caen Normandie, Néphrologie, Côte de Nacre Caen, France; [25]Normandie Université, Unicaen, UFR de médecine, Caen, France; [26]ANTICIPE" U1086 INSERM-UCN, Center François Baclesse, Caen, France; and [27]Department of Public Health and Primary Care, KU Leuven Campus Kulak Kortrijk, Kortrijk, Belgium

Introduction: Discordant results between cystatin C and creatinine in estimating glomerular filtration rate (GFR) are an important medical issue. However, the equation that should be used when GFR estimates are discordant remains unclear.

Methods: This cross-sectional analysis included 15,485 participants with GFR measured by the clearance of an exogenous marker, serum creatinine, and cystatin C. We studied the proportion of discordant results defined as an absolute ($>$ 15 ml/min per 1.73 m^2) or relative ($>$ 20%) difference between creatinine-based estimated GFR (eGFR, $eGFR_{crea}$) and cystatin C–based eGFR ($eGFR_{cys}$) using different equations (Chronic Kidney Disease Epidemiology Collaboration [CKD-EPI], European Kidney Function Consortium [EKFC], and reexpressed Lund-Malmö [r-LMR]). We also researched for the best estimating equations to be used in subjects with concordant or discordant results to estimate measured GFR (mGFR).

Results: In the total cohort, the proportion of subjects with discordant results (absolute or relative) was larger for CKD-EPI (35.1 and 40.6%) than for EKFC (21.9 and 31.7%) or r-LMR (22.8 and 32.8%) equations. Among discrepant results, the proportion of $eGFR_{cys} < eGFR_{crea}$ was significantly higher than the proportion of $eGFR_{crea} < eGFR_{cys}$ for the CKD-EPI equations, whereas the occurrence of discrepancy was

Correspondence: Pierre Delanaye, Service de Dialyse, CHU Sart Tilman 4000 Liège, Belgium. E-mail: pdelanaye@chuliege.be

Received 22 December 2024; revised 17 January 2025; accepted 21 January 2025; published online 29 January 2025

similar in the 2 discrepant groups for EKFC or r-LMR. For the EKFC and r-LMR equations, but not for the CKD-EPI, the equation combining creatinine and cystatin C was consistently the closest to the mGFR in the discrepant groups.

Conclusion: Based on the lower discrepancy proportion, better balance between $eGFR_{crea}$ and $eGFR_{cys}$, and better concordance with mGFR, the EKFC, and r-LMR equations should be preferred over the CKD-EPI to estimate GFR.

Kidney Int Rep (2025) **10,** 1248–1259; https://doi.org/10.1016/j.ekir.2025.01.030
KEYWORDS: creatinine; cystatin C; glomerular filtration rate

The new Kidney Disease Improving Global Outcomes (KDIGO) guidelines for the evaluation and management of chronic kidney disease (CKD) support the wide spread use of cystatin C to estimate GFR.[1] Although $eGFR_{cys}$ does not outperform $eGFR_{crea}$,[2,3] equations combining both biomarkers ($eGFR_{crea+cys}$) perform significantly better. Because cystatin C is more commonly used, it must be anticipated that some results between $eGFR_{cys}$ and $eGFR_{crea}$ will be discordant. The proportion of discordant results has been found to be between 10% and 55% depending on the population considered and the definition for discrepancy. In all studies, the number of discordant results with $eGFR_{cys} < eGFR_{crea}$ was much higher than the number of discordant results with $eGFR_{crea} < eGFR_{cys}$,[4-11] although no clear explanation for this observation has been provided. Several studies have shown that discrepancies between the 2 biomarkers were associated with worse outcomes (mortality and frailty).[4,10,12-14] In terms of estimating GFR, there is still a debate about which results, creatinine- and/or cystatin C-based, should be used when eGFR estimations are discordant.[6,7,15] However, it must be emphasized that the vast majority of studies have been performed with the CKD-EPI equations[3,16]; whereas new equations such as the EKFC[2,17] or the r-LMR equations,[18] both based on rescaled biomarkers, are also considered as valid to estimate GFR, and have been shown to better perform for estimating GFR.[1,19,20] In the current analysis, we aimed to study the proportion of discordant results between $eGFR_{crea}$ and $eGFR_{cys}$ according to both the definition of discrepancy and the equations used to estimate GFR. We also studied the characteristics of patients with discordant results compared with those with concordant results. Finally, using the available mGFR, we studied the performance of the following different equations in 3 groups: subjects with concordant results, subjects with discordant results and $eGFR_{cys} < eGFR_{crea}$, and subjects with discordant results and $eGFR_{crea} < eGFR_{cys}$.

METHODS

Design Overview and Participants

The dataset used to validate the EKFC cystatin C-based equation has been augmented with additional data from The Netherlands and France.[2] Only adult subjects (aged $\geq$ 18 years) were included. The cohorts are described in Supplementary Table S1.

Covariates

Briefly, in all cohorts, creatinine was directly measured using an isotope dilution mass spectrometry traceable assay, and cystatin C was measured using standardized assays.[17,21,22] GFR was measured using validated reference methods (Supplementary Table S1).[23-25]

The CKD-EPI, r-LMR, and EKFC equations are described in Supplementary Table S2.[2,16-18] We used the race-free CKD-EPI equation for the entire cohort and race-free Q value for the US cohort.[16,22,26]

Outcomes

Discrepancy was defined by different thresholds and using either the relative or the absolute (the term absolute is used in the meaning of opposite to "relative," not in the meaning of an absolute number, because we kept the signs "+" or "−") difference between $eGFR_{cys}$ and $eGFR_{crea}$. The absolute difference (in ml/min per 1.73 m^2) is thus calculated as $eGFR_{cys} - eGFR_{crea}$, and the relative difference (in%) is calculated as $([eGFR_{cys} - eGFR_{crea}]/ eGFR_{crea}] * 100)$. As thresholds, we considered absolute differences of 5, 10, 15, 20, and 30 ml/min per 1.73 m^2 and relative differences of 5%, 10%, 20%, and 30%. The proportion of discordant results was also calculated in subgroups according to the population (White Europeans, White Americans, Black Europeans, and Black Africans). Owing to the limited sample size in other subgroups, subanalyses according to sex assigned at birth, age, mGFR, and body mass index (BMI) were performed only in White Europeans. The absolute and relative differences between the mGFR and the respective eGFR equations were graphically represented (the x-axis being the mGFR and the y-axis

being the [absolute or relative] difference between $eGFR_{cys}$ and $eGFR_{crea}$).

Thereafter, we considered the 2 most used thresholds in the literature and those proposed in the KDIGO guidelines, that is, an absolute difference of 15 ml/min per 1.73 m^2 and a relative difference of 20%.[1,5,6,8] We compared the EKFC, r-LMR, and CKD-EPI equations. The following 3 groups were defined accordingly: (i) the group of subjects with concordant results (GFR_C) between $eGFR_{crea}$ and $eGFR_{cys}$, (ii) the group of subjects with discordant results and $eGFR_{cys} < eGFR_{crea}$ (GFR_{DCys}, the group with an absolute or relative difference >-15 ml/min per 1.73 m^2 or -20%), (iii) the group of subjects with discordant results and $eGFR_{crea} < eGFR_{cys}$ (GFR_{DCrea}, the group with an absolute or relative difference over $+15$ ml/min per 1.73 m^2 or $+20\%$). We compared the characteristics of the different groups and the performance of all equations ($eGFR_{crea}$, $eGFR_{cys}$, and eGFR combined with creatinine and cystatin C [$eGFR_{crea+cys}$]) to estimate the GFR in the 3 groups relative to the mGFR (focusing on accuracy results).

Statistical Analysis

Analyses and calculations were performed using SAS 9.4 (SAS Institute Inc., Cary, NC) and R (version 4.2.0; R Foundation for Statistical Computing, Vienna, Austria) software. Data are presented as medians and interquartile ranges.

The association between characteristics and belonging to one of the discrepant groups was modeled using multivariate multinomial logistic regression, allowing the assessment of relative risk ratios. The covariates included were age, sex, BMI, and mGFR, and were included *a priori*. The reference group exhibited concordant results. Collinearity was evaluated by calculating the variance inflation factor, which measures multicollinearity among the predictor variables in a regression model. A variance inflation factor > 5 suggests moderate multicollinearity, whereas a variance inflation factor > 10 indicates a high level that may affect model reliability.

The performance of eGFR equations was compared with usual metrics: median bias (i.e., eGFR $-$ mGFR) with 95% CI, imprecision (interquartile range), as well as P30 and P20 accuracy (percentage of eGFR values within $\pm 30\%$ or 20% of mGFR) with 95% CI. An absolute bias < 5 ml/min per 1.73 m^2 was considered reasonable.[2,17] Imprecision should be as low as possible.[27] To test if an equation is different from another equation in the same population, we did not use statistical tests to avoid numerous *P*-value calculations; however, the reader may consider an equation as different when the 95% CI between equations was not overlapping, which is a more conservative criterion.[2,17]

We also repeated the subgroup analyses according to sex, age, mGFR, and BMI in the White European subgroup. Linear regression of the (relative or absolute) differences against mGFR (note that $eGFR_{cys} - eGFR_{crea}$ and mGFR were independent) and age is graphically represented.

RESULTS

Characteristics of Participants

mGFR, serum creatinine, and cystatin C were available in 15,485 individuals. Among them, the population of White Europeans was the largest ($n = 13{,}022$), with smaller sample sizes in other populations (White Americans, $n = 1093$; Black Europeans, $n = 862$; and Black Africans, $n = 508$). In the entire study population, the median age was 60 years (range: 49–69 years), and 47% were women. Median BMI was 26.0 (23.1–29.5) kg/m^2. The median mGFR, serum creatinine, and serum cystatin C were 70 (47–90) ml/min per 1.73 m^2, 0.98 (0.77–1.39) mg/dl, and 1.07 (0.83–1.57) mg/l, respectively. The median serum creatinine was 1.13 (0.90–1.58) in men and 0.83 (0.69–1.12) mg/dl in women. Descriptions of the populations and every single cohort are presented in Supplementary Table S1.

Percentage of Discordant Results According to the Equations and the Definition

The percentage of discordant results was, as expected, higher if a more stringent definition of discrepancy was considered (Table 1). We observed that the proportion of discordant results was systematically and significantly lower when the EKFC or r-LMR equations were used than when the CKD-EPI equations were used. The proportions of the discrepancies were similar for the EKFC and r-LMR equations. For the commonly used thresholds (15 ml/min per 1.73 m^2 and 20%), the percentages of discordant results with the EKFC equations (21.9% and 31.7%, respectively) were 13% and 9% lower than those with the CKD-EPI equations (35.1% and 40.6%, respectively) (Table 1).

In Figure 1, we show the association between absolute (15 ml/min per 1.73 m^2, 1a [CKD-EPI] and 1b [EKFC]) or relative (20%, 1c [CKD-EPI] and 1d [EKFC]) differences and mGFR. The figure shows a higher discordance of results with the CKD-EPI equations (Figure 1a and c) than with the EKFC equations (Figure 1b and d). Moreover, we observed a more balanced distribution of discordant results for the EKFC and r-LMR equations than for the CKD-EPI equations. With CKD-EPI, the proportion of discordant results with $eGFR_{cys} < eGFR_{Crea}$ was much higher than the proportion of discordant results with $eGFR_{Crea} < eGFR_{cys}$, that is, 25.4% versus 9.7% (absolute difference) and 30.5% versus 10.2% (relative difference).

Table 1. Percentage of discordant results between creatinine- and cystatin C-based equations according to the equations and the definitions

	Absolute difference ($eGFR_{crea}$-$eGFR_{cys}$) of more than					Relative difference ([$eGFR_{crea}$-$eGFR_{cys}$]/$eGFR_{crea}$) of more than			
All results in %	±5 ml/min per 1.73 m^2	±10 ml/min per 1.73 m^2	±15 ml/min per 1.73 m^2	±20 ml/min per 1.73 m^2	±30 ml/min per 1.73 m^2	±5%	±10%	±20%	±30%
All $N = 15,485$									
CKD-EPI	73.7	51.8	35.1	23.1	9.4	82.1	66.1	40.6	23.8
EKFC	62.7	37.2	21.9	12.7	3.9	75.0	56.4	31.7	16.3
r-LMR	65.8	40.5	22.8	12.2	3.5	80.0	61.4	32.8	16.3
White Europeans $n = 13,022$									
CKD-EPI	74.0	52.5	35.8	23.7	9.8	82.5	66.9	42.0	24.8
EKFC	62.7	37.4	22.0	13.0	4.1	75.7	57.5	32.5	16.6
r-LMR	65.4	40.4	22.9	12.6	3.8	80.3	62.1	33.5	16.9
Black Europeans $n = 862$									
CKD-EPI	72.0	48.7	32.5	23.9	9.5	84.1	70.8	45.0	28.9
EKFC	68.7	41.9	27.5	16.7	4.8	80.4	63.3	39.7	23.7
r-LMR	68.4	43.4	26.9	14.3	3.7	83.5	65.8	40.1	21.0
White Americans $n = 1093$									
CKD-EPI	72.6	48.0	29.5	16.5	4.0	75.8	54.3	23.5	10.1
EKFC	56.4	29.0	13.6	5.2	0.7	62.8	38.7	16.0	5.8
r-LMR	67.2	41.0	18.3	7.2	0.7	74.1	52.7	19.7	6.3
Africans $n = 508$									
CKD-EPI	70.9	48.6	33.1	21.5	8.9	80.7	61.8	34.3	18.9
EKFC	67.7	40.2	26.4	16.1	4.1	72.4	55.1	31.3	18.7
r-LMR	67.5	38.0	22.8	11.6	3.5	77.6	55.1	29.7	15.6

CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; $eGFR_{crea}$, creatinine-based estimation of glomerular filtration rate; $eGFR_{cys}$, cystatin C–based estimation of glomerular filtration rate; EKFC, European Kidney Function Consortium; r-LMR, re-expressed Lund-Malmö.

Using the EKFC equations, the proportion of discordant results was 11.7% versus 10.1% (for the absolute difference) and 14.7% versus 17% (for the relative difference) (the results for r-LMR were very similar to those for EKFC; Tables 2 and 3). Finally, the differences between $eGFR_{cys}$ and $eGFR_{crea}$ were not dependent on mGFR or age for the EKFC and r-LMR equations, whereas the difference was significantly influenced by mGFR and age when the CKD-EPI equations were used (Figure 1 and Supplementary Figure S1).

Similar findings of a lower proportion of discordant results with the EKFC and r-LMR equations were observed when stratified by population (Table 1). In the cohort of White Europeans, we repeated the analyses and obtained the same observations in subgroups according to age, sex, mGFR, and BMI (Supplementary Table S3).

Comparison of Characteristics of the Subjects With Concordant (GFR_C) or Discordant Results (GFR_{DCys} and GFR_{DCrea})

In the current paragraph, we only report the analyses performed in the European White cohort (because the sample size in other populations was too small) comparing CKD-EPI and EKFC equations and using the thresholds of 15 ml/min per 1.73 m^2 and 20%. The characteristics (age, sex, mGFR, and BMI) of the participants in the concordant and discordant groups are shown in Supplementary Table S4. Using multivariable multinomial logistic regression models (Table 4), we showed that males were less likely to have a discrepant result, with $eGFR_{crea}$ lower than $eGFR_{cys}$ using the EKFC equation (both relative and absolute differences). In contrast, no association was observed between sex and discrepancy as assessed using the CKD-EPI equation. For both equations, age was significantly associated with the risk of belonging to one of the 2 discrepant groups (the younger the participant, the higher the risk of belonging to one discrepant group). Increasing BMI was associated with a lower risk of having a lower $eGFR_{crea}$ according to the EKFC equation, with the discrepancy defined by absolute or relative thresholds, but only when considering the relative threshold for the CKD-EPI equation. Results concerning mGFR were conflicting with an increased risk of a lower $eGFR_{crea}$ with EKFC and an absolute difference with the threshold of 15 ml/min per 1.73 m^2; however, a decrease in this risk with the CKD-EPI equation and with EKFC when considering the relative difference of 20%. The variance inflation factor for sex, age, BMI, and mGFR were all < 1.3, indicating the absence of collinearity.

Performance of the Different Equations in the 3 Groups With Concordant (GFR_C) or Discordant Results (GFR_{DCys} and GFR_{DCrea}) to Estimate mGFR

In White Europeans, the results are shown for the 3 equations ($eGFR_{crea}$, $eGFR_{cys}$, and $eGFR_{crea+cys}$) in

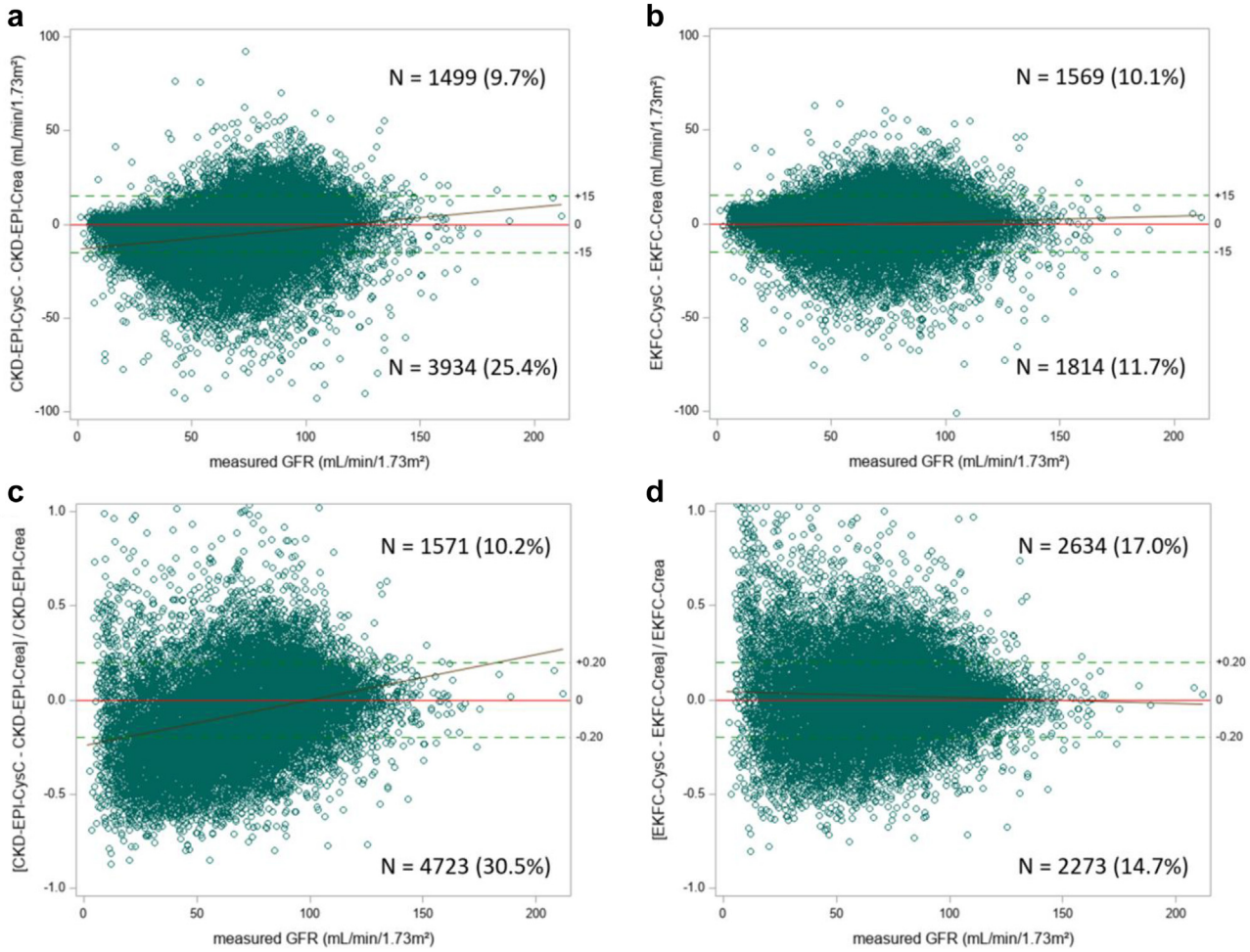

Figure 1. Association between differences in creatinine and cystatin C-based equations and measured GFR. CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration (1a and c); crea, creatinine; cys, cystatin C; EKFC, European Kidney Function Consortium (1b and 1d). The absolute differences are shown in Figures 1a and b. The green dashed lines are corresponding to the interval of 15 ml/min per 1.73 m^2. The relative differences are shown in Figures 1c and d. The green dashed lines correspond to the intervals of 20%. Redlines are the zero-bias line. The grey line corresponds to the regression line. The *n* values are the number of results beyond the thresholds of 15 ml/min per 1.73 m^2 or 20%.

Table 2 and Supplementary Table S5 for the criteria of 20% and 15 ml/min per 1.73 m^2, respectively. Considering the entire White European population (first column of Table 2 and Supplementary Table S5), P30 and P20 were better ([a] in Table 2 and Supplementary Table S5) for the combined equations, and this was shown for both the EKFC, r-LMR, and CKD-EPI equations.

In each of the 3 groups (concordant and 2 discordant), we analyzed and compared the P20 and P30 results ([a] in Table 2 and Supplementary Table S5 assigned to the best results in each group). Considering the EKFC and r-LMR equations, the combined $eGFR_{crea+cys}$ equations were systematically the best (or among the best), regardless of the threshold used. However, using the CKD-EPI equations, the results were not systematically better for the combined $eGFR_{crea+cys}$ equation. Indeed, considering the threshold of 15 ml/min per 1.73 m^2, P20 was better for $eGFR_{crea}$ both in the GFR_C and $GFR_{DCrea.}$ groups. Considering a threshold of 20%, P20 and P30 were better for $eGFR_{crea}$ and $eGFR_{cys}$ in GFR_C. The P30 was also better for $eGFR_{crea}$ than in the GFR_{DCrea} groups.

In other populations (Table 3 and Supplementary Table S6), the same results were observed, because the combined $eGFR_{crea+cys}$ equation was systematically among the best equations in the concordant and discordant groups, at least when the EKFC and r-LMR equations were considered (although this was not systematically the case for the CKD-EPI equations, notably in White American populations).

In White Europeans, this type of analysis was repeated in subgroups according to sex, age, mGFR, and BMI (Supplementary Tables S7–S10) with a threshold of 20% and only for the EKFC and CKD-EPI equations, leading to the same global conclusions.

DISCUSSION

In the current study, we showed that using the EKFC or r-LMR instead of the CKD-EPI equations led to a lower prevalence of discrepant results between the

Table 2. Performance of the different equations in the concordant and discordant groups in White Europeans (relative difference)

Performance	Whole	GFR_{DCys}	GFR_{C}	GFR_{DCrea}
		CKD-EPI and 20%		
n (%)	13,022	4444 (34.1)	7547 (58.0)	1031 (7.9)
Bias (ml/min per 1.73 m^2) $eGFR_{crea}$	5.40 [5.14;5.65]	11.31 [10.87;11.82]	3.46 [3.16;3.79]	−6.04 [−6.75;−5.20]
Bias (ml/min per 1.73 m^2) $eGFR_{cys}$	−1.59 [−1.82;−1.31]	−9.11 [−9.43;−8.84]	2.31 [1.99;2.61]	12.69 [11.10;14.11]
Bias (ml/min per 1.73 m^2) $eGFR_{crea+cys}$	3.14 [2.90;3.35]	−0.26 [−0.60;0.14]	5.79 [5.50;6.18]	5.42 [4.49;6.46]
IQR (ml/min per 1.73 m^2) $eGFR_{crea}$	16.6 [−2.1;14.5]	16.7 [4.0;20.7]	15.1 [−3.3;11.8]	13.1 [−13.3;−0.2]
IQR (ml/min per 1.73 m^2) $eGFR_{cys}$	17.7 [−9.3;8.4]	12.9 [−16.3;−3.4]	16.8 [−4.9;11.9]	18.9 [3.4;22.2]
IQR (ml/min per 1.73 m^2) $eGFR_{crea+cys}$	15.9 [−3.4;12.5]	11.6 [−5.9;5.6]	17.5 [−1.6;15.9]	16.8 [−1.5;15.3]
P20 (ml/min per 1.73 m^2) $eGFR_{crea}$	63.5 [62.7;64.3]	41.8 [40.4;43.3]	74.9 [74.0;75.9][a]	73.0 [70.3;75.7][a]
P20 (ml/min per 1.73 m^2) $eGFR_{cys}$	62.9 [62.1;63.8]	47.0 [45.5;48.5]	73.8 [72.8;74.8][a]	52.0 [48.9;55.5]
P20 (ml/min per 1.73 m^2) $eGFR_{crea+cys}$	70.1 [69.3;70.9][a]	71.6 [70.3;73.0][a]	69.0 [68.0;70.1]	71.0 [68.2;73.8][a]
P30 (ml/min per 1.73 m^2) $eGFR_{crea}$	78.7 [78.0;79.4]	58.6 [57.1;60.0]	88.9 [88.2;89.6][a]	90.4 [88.6;92.2][a]
P30 (ml/min per 1.73 m^2) $eGFR_{cys}$	82.7 [82.0;83.3]	73.0 [71.6;74.3]	89.7 [89.0;90.3][a]	73.3 [70.6;76.0]
P30 (ml/min per 1.73 m^2) $eGFR_{crea+cys}$	86.5 [85.9;87.1][a]	87.1 [86.1;88.1][a]	86.1 [85.3;86.9]	86.4 [84.3;88.5]
		EKFC and 20%		
n (%)	13,022	2118 (16.3)	8789 (67.5)	2115 (16.2)
Bias (ml/min per 1.73 m^2) $eGFR_{crea}$	−0.51 [−0.74;−0.27]	9.81 [9.23;10.36]	−0.79 [−1.08;−0.56]	−7.06 [−7.45;−6.53]
Bias (ml/min per 1.73 m^2) $eGFR_{cys}$	−0.46 [−0.69;−0.20]	−8.39 [−8.94;−7.82]	−0.56 [−0.82;−0.31]	6.77 [6.40;7.33]
Bias (ml/min per 1.73 m^2) $eGFR_{crea+cys}$	−0.30 [−0.48;−0.11]	0.77 [0.23;1.38]	−0.70 [−0.92;−0.46]	0.22 [−0.21;0.66]
IQR (ml/min per 1.73 m^2) $eGFR_{crea}$	15.1 [−8.0;7.1]	15.2 [3.1;18.4]	13.7 [−7.8;5.9]	12.2 [−13.7;−1.5]
IQR (ml/min per 1.73 m^2) $eGFR_{cys}$	14.8 [−8.2;6.5]	14.5 [−16.4;−1.9]	13.7 [−7.7;6.0]	11.9 [1.6;13.5]
IQR (ml/min per 1.73 m^2) $eGFR_{crea+cys}$	12.5 [−6.7;5.8]	12.8 [−5.6;7.2]	12.9 [−7.2;5.6]	10.1 [−5.2;4.9]
P20 (ml/min per 1.73 m^2) $eGFR_{crea}$	71.4 [70.6;72.2]	46.9 [44.8;49.1]	79.8 [78.9;80.6]	61.2 [59.2;63.3]
P20 (ml/min per 1.73 m^2) $eGFR_{cys}$	71.1 [70.3;71.9]	51.3 [49.2;53.5]	79.0 [78.2;79.9]	58.1 [56.0;60.2]
P20 (ml/min per 1.73 m^2) $eGFR_{crea+cys}$	78.7 [78.0;79.4][a]	67.7 [65.7;69.7][a]	81.8 [81.0;82.6][a]	76.7 [74.9;78.5][a]
P30 (ml/min per 1.73 m^2) $eGFR_{crea}$	86.3 [85.7;86.9]	62.3 [60.2;64.3]	92.3 [91.8;92.9][a]	85.5 [84.0;87.0]
P30 (ml/min per 1.73 m^2) $eGFR_{cys}$	87.2 [86.6;87.8]	75.9 [74.1;77.7]	92.7 [92.2;93.2][a]	75.6 [73.8;77.4]
P30 (ml/min per 1.73 m^2) $eGFR_{crea+cys}$	91.2 [90.7;91.7][a]	84.1 [82.5;85.6][a]	93.3 [92.8;93.8][a]	89.6 [88.3;90.9][a]
		r-LMR and 20%		
n (%)	13,022	2186 (16.8)	8655 (66.6)	2181 (16.7)
Bias (ml/min per 1.73 m^2) $eGFR_{crea}$	−3.14 [−3.38;−2.94]	7.47 [6.89;8.02]	−3.67 [−4.01;−3.41]	−9.59 [−10.13;−9.10]
Bias (ml/min per 1.73 m^2) $eGFR_{cys}$	−3.11 [−3.34;−2.85]	−10.80 [−11.41;−10.19]	−3.25 [−3.56;−3.02]	4.70 [4.30;5.00]
Bias (ml/min per 1.73 m^2) $eGFR_{crea+cys}$	−2.96 [−3.17;−2.79]	−1.57 [−1.94;−1.10]	−3.50 [−3.74;−3.28]	−2.13 [−2.68;−1.75]
IQR (ml/min per 1.73 m^2) $eGFR_{crea}$	15.1 [−10.9;4.2]	14.5 [1.1;15.6]	13.7 [−11.0;2.8]	12.8 [−16.4;−3.6]
IQR (ml/min per 1.73 m^2) $eGFR_{cys}$	15.0 [−11.0;3.9]	14.4 [−18.8;−4.4]	13.9 [−10.7;3.3]	11.6 [−0.9;10.6]
IQR (ml/min per 1.73 m^2) $eGFR_{crea+cys}$	12.6 [−9.6;3.0]	12.6 [−7.7;4.9]	12.9 [−10.4;2.6]	10.9 [−8.1;2.7]
P20 (ml/min per 1.73 m^2) $eGFR_{crea}$	70.0 [69.2;70.8]	54.4 [52.3;56.5]	77.9 [77.1;78.8]	54.2 [52.2;56.3]
P20 (ml/min per 1.73 m^2) $eGFR_{cys}$	70.0 [69.2;70.8]	41.9 [39.8;43.9]	77.6 [76.7;78.5]	68.3 [66.4;70.3]
P20 (ml/min per 1.73 m^2) $eGFR_{crea+cys}$	78.2 [77.5;78.9][a]	70.7 [68.8;72.6][a]	80.2 [79.4;81.1][a]	77.6 [75.9;79.4][a]
P30 (ml/min per 1.73 m^2) $eGFR_{crea}$	87.3 [86.7;87.8]	70.4 [68.5;72.3]	92.9 [92.4;93.5][a]	81.7 [80.1;83.3]
P30 (ml/min per 1.73 m^2) $eGFR_{cys}$	87.1 [86.5;87.6]	69.2 [67.3;71.1]	92.5 [91.9;93.1][a]	83.4 [81.8;85.0]
P30 (ml/min per 1.73 m^2) $eGFR_{crea+cys}$	91.9 [91.5;92.4][a]	86.5 [85.1;87.9][a]	93.5 [93.0;94.0][a]	91.2 [90.0;92.4][a]

CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; $eGFR_{crea}$, creatinine-based estimating glomerular filtration rate; $eGFR_{crea+cys}$, estimating glomerular filtration rate combining creatinine and cystatin C; $eGFR_{cys}$, cystatin C-based estimating glomerular filtration rate; EKFC, European Kidney Function Consortium; GFR_{C}, group of subjects with concordant estimating glomerular filtration rate results; GFR_{DCrea}, group of subjects with discordant estimating glomerular filtration rate results and with creatinine-based results lower than cystatin C-based results; GFR_{DCys}, group of subjects with discordant estimating glomerular filtration rate results and with cystatin C-based results lower than creatinine-based results; IQR: interquartile range; P20: accuracy within 20%;P30, accuracy within 30%; r-LMR: re-expressed Lund-Malmö.
[a]The best P20 and P30 results within each group.

$eGFR_{crea}$ and $eGFR_{cys}$ equations. With the release of the recent KDIGO guidelines, it can be anticipated that cystatin C will be increasingly used in the future to estimate GFR.[1,4,6–8] If cystatin C is concomitantly ordered with creatinine, it is important to help clinicians interpret eGFR results in cases where they are discordant for the 2 biomarkers.[1,20] It is known that the proportion of discordant results could differ according to the population studied, and this was confirmed here by the different percentages of discrepancy observed in the different cohorts included in the current analysis (Supplementary Table S1). This is probably explained by our multivariate logistic regression analysis showing that the proportion of discrepancies is influenced by sex, age, BMI, and, to a lesser extent, mGFR. We found that sex influenced the risk of discrepancies with EKFC and non-not with CKD-EPI. This can probably be explained, at least in part, by the fact that the variable "sex" is not included in the EKFC $eGFR_{cys}$ equation. Indeed, using the version of $EKFC_{cys}$ with the

Table 3. Performance of the different equations in the concordant and discordant groups in other populations (relative difference)

Performance	Whole	GFR_{DCys}	GFR_{C}	GFR_{DCrea}
Black Europeans		CKD-EPI and 20%		
n (%)	862	125 (14.5)	474 (55.0)	263 (30.5)
Bias (ml/min per 1.73 m^2) $eGFR_{crea}$	−5.09 [−5.70;−4.20]	6.30 [4.12;8.82]	−3.12 [−4.20;−2.04]	−13.26 [−14.82;−12.06]
Bias (ml/min per 1.73 m^2) $eGFR_{cys}$	−1.19 [−2.27;−0.31]	−10.12 [−12.20;−8.94]	−2.46 [−3.31;−1.26]	7.55 [5.51;10.00]
Bias (ml/min per 1.73 m^2) $eGFR_{crea+cys}$	−2.08 [−2.73;−1.32]	−3.39 [−5.35;−2.31]	−1.52 [−2.58;−0.44]	−1.57 [−3.13;0.15]
IQR (ml/min per 1.73 m^2) $eGFR_{crea}$	16.7 [−12.7;4.0]	14.1 [−0.5;13.6]	14.2 [−9.1;5.1]	12.3 [−19.3;−7.0]
IQR (ml/min per 1.73 m^2) $eGFR_{cys}$	17.4 [−3.3;9.0]	11.6 [−16.7;−5.1]	14.6 [−9.0;5.6]	19.4 [−0.6;18.9]
IQR (ml/min per 1.73 m^2) $eGFR_{crea+cys}$	14.0 [−7.9;6.1]	11.6 [−8.6;3.0]	15.0 [−7.9;7.1]	13.4 [−7.1;6.3]
P20 (ml/min per 1.73 m^2) $eGFR_{crea}$	62.1 [58.8;65.3]	58.4 [49.8;67.0][a]	71.5 [67.5;75.6][a]	46.8 [40.7;52.8]
P20 (ml/min per 1.73 m^2) $eGFR_{cys}$	60.9 [57.6;64.2]	39.2 [30.6;47.8]	68.8 [64.6;72.9][a]	57.0 [51.1;63.0]
P20 (ml/min per 1.73 m^2) $eGFR_{crea+cys}$	70.0 [66.9;73.0][a]	68.0 [59.8;76.2][a]	70.5 [66.4;74.6][a]	79.1 [74.2;84.0][a]
P30 (ml/min per 1.73 m^2) $eGFR_{crea}$	82.3 [79.7;84.8]	73.6 [65.9;81.3]	88.2 [85.3;91.1][a]	75.7 [70.5;80.9]
P30 (ml/min per 1.73 m^2) $eGFR_{cys}$	81.3 [78.7;83.9]	64.0 [55.6;72.4]	87.8 [84.8;90.7][a]	77.9 [72.9;83.0]
P30 (ml/min per 1.73 m^2) $eGFR_{crea+cys}$	89.1 [87.0;91.2][a]	89.6 [84.2;95.0][a]	88.2 [85.3;91.1][a]	90.5 [86.9;94.0][a]
		EKFC and 20%		
n (%)	862	101 (11.7)	520 (60.3)	241 (28.0)
Bias (ml/min per 1.73 m^2) $eGFR_{crea}$	−2.43 [−3.24;−1.37]	10.13 [7.27;13.56]	−0.73 [−1.56;0.10]	−9.47 [−10.79;−8.41]
Bias (ml/min per 1.73 m^2) $eGFR_{cys}$	1.40 [0.38;2.21]	−7.42 [−9.43;−4.70]	0.15 [−0.41;0.96]	7.19 [5.46;9.04]
Bias (ml/min per 1.73 m^2) $eGFR_{crea+cys}$	−0.49 [−1.15;0.27]	1.68 [−1.23;3.47]	−0.50 [−1.18;0.42]	−1.26 [−2.42;0.27]
IQR (ml/min per 1.73 m^2) $eGFR_{crea}$	14.8 [−9.4;5.4]	15.9 [2.5;18.4]	13.5 [−7.3;6.2]	11.7 [−16.0;−4.3]
IQR (ml/min per 1.73 m^2) $eGFR_{cys}$	14.3 [−5.5;8.8]	13.0 [−13.9;−0.9]	12.5 [−5.7;6.8]	14.6 [1.1;15.7]
IQR (ml/min per 1.73 m^2) $eGFR_{crea+cys}$	12.4 [−6.0;6.4]	13.3 [−5.1;8.2]	12.5 [−6.1;6.4]	10.3 [−6.0;4.2]
P20 (ml/min per 1.73 m^2) $eGFR_{crea}$	67.7 [64.6;70.9]	43.6 [33.9;53.2]	77.3 [73.7;80.9][a]	57.3 [51.0;63.5]
P20 (ml/min per 1.73 m^2) $eGFR_{cys}$	70.2 [67.1;73.2]	55.4 [45.8;65.1][a]	77.5 [73.9;81.1][a]	60.6 [54.4;66.8]
P20 (ml/min per 1.73 m^2) $eGFR_{crea+cys}$	78.7 [75.9;81.4][a]	69.3 [60.3;78.3][a]	79.6 [76.2;83.1][a]	80.5 [75.5;85.5][a]
P30 (ml/min per 1.73 m^2) $eGFR_{crea}$	85.5 [83.1;87.8]	60.4 [50.9;69.9]	91.7 [89.4;94.1][a]	82.6 [77.8;87.4]
P30 (ml/min per 1.73 m^2) $eGFR_{cys}$	87.5 [85.3;89.7]	82.2 [74.7;89.6][a]	92.1 [89.8;94.4][a]	79.7 [74.6;84.7]
P30 (ml/min per 1.73 m^2) $eGFR_{crea+cys}$	91.9 [90.1;93.7][a]	83.2 [75.9;90.5][a]	93.1 [90.9;95.3][a]	92.9 [89.7;96.2][a]
		r-LMR and 20%		
n (%)	862	108 (12,5)	516 (59.9)	238 (27.6)
Bias (ml/min per 1.73 m^2) $eGFR_{crea}$	−5,46 [−6,21;−4,51]	7,85 [2,70;9,92]	−3,40 [−4,59;−2,46]	−12,18 [−13,68;−11,04]
Bias (ml/min per 1.73 m^2) $eGFR_{cys}$	−2,11 [−3,19;−1,23]	−11,00 [−13,87;−8,80]	−3,40 [−4,19;−2,57]	2,74 [1,33;4,30]
Bias (ml/min per 1.73 m^2) $eGFR_{crea+cys}$	−3,61 [−4,49;−3,01]	−2,24 [−5,47;0,27]	−3,26 [−4,34;−2,46]	−4,96 [−6,21;−3,79]
IQR (ml/min per 1.73 m^2) $eGFR_{crea}$	14,5 [−12,6;1,8]	17,3 [−2,1;15,2]	12,6 [−10,1;2,5]	11,9 [−18,8;−6,9]
IQR (ml/min per 1.73 m^2) $eGFR_{cys}$	13,2 [−8,7;4,5]	15,5 [−18,9;−3,3]	11,8 [−8,8;3,0]	12,4 [−2,0;10,4]
IQR (ml/min per 1.73 m^2) $eGFR_{crea+cys}$	11,4 [−9,1;2,3]	15,5 [−9,8;5,8]	11,0 [−8,6;2,5]	10,0 [−9,3;0,7]
P20 (ml/min per 1.73 m^2) $eGFR_{crea}$	65,0 [61,9;68,2]	56,5 [47,1;65,8][a]	78,4 [74,9;82,0][a]	39,9 [33,7;46,1]
P20 (ml/min per 1.73 m^2) $eGFR_{cys}$	72,7 [69,7;75,7]	39,8 [30,6;49,0]	80,0 [76,5;83,5][a]	71,8 [66,1;77,6][a]
P20 (ml/min per 1.73 m^2) $eGFR_{crea+cys}$	78,9 [76,1;81,6][a]	65,7 [56,8;74,7][a]	81,2 [77,8;84,5][a]	79,8 [74,7;84,9][a]
P30 (ml/min per 1.73 m^2) $eGFR_{crea}$	85,1 [82,8;87,5]	72,2 [63,8;80,7]	92,4 [90,1;94,7][a]	75,2 [69,7;80,7]
P30 (ml/min per 1.73 m^2) $eGFR_{cys}$	88,0 [85,9;90,2]	66,7 [57,8;75,6]	93,2 [91,0;95,4][a]	86,6 [82,2;90,9][a]
P30 (ml/min per 1.73 m^2) $eGFR_{crea+cys}$	92,5 [90,7;94,2][a]	88,0 [81,8;94,1][a]	93,8 [91,7;95,9][a]	91,6 [88,1;95,1][a]
White Americans		CKD-EPI and 20%		
n (%)	1093	95 (8.7)	836 (76.5)	162 (14.8)
Bias (ml/min per 1.73 m^2) $eGFR_{crea}$	7.11 [6.13;7.95]	17.47 [14.87;21.05]	7.19 [6.09;8.27]	−0.47 [−2.47;2.50]
Bias (ml/min per 1.73 m^2) $eGFR_{cys}$	10.89 [9.91;12.14]	−3.76 [−8.23;−1.55]	10.44 [9.08;11.58]	23.64 [21.22;26.03]
Bias (ml/min per 1.73 m^2) $eGFR_{crea+cys}$	13.89 [13.05;14.84]	9.30 [3.14;10.38]	14.17 [12.91;15.20]	17.35 [14.24;19.01]
IQR (ml/min per 1.73 m^2) $eGFR_{crea}$	18.7 [−2.2;16.5]	16.8 [8.2;25.0]	17.8 [−1.5;16.3]	18.3 [−9.2;9.1]
IQR (ml/min per 1.73 m^2) $eGFR_{cys}$	21.4 [0.4;21.8]	15.7 [−13.5;2.2]	18.9 [0.5;19.4]	17.8 [15.3;33.2]
IQR (ml/min per 1.73 m^2) $eGFR_{crea+cys}$	18.1 [5.1;23.2]	15.4 [−0.8;14.6]	18.4 [5.2;23.6]	18.7 [7.9;26.6]
P20 (ml/min per 1.73 m^2) $eGFR_{crea}$	65.9 [63.1;68.7][a]	36.8 [27.1;46.5]	67.7 [64.5;70.9][a]	73.5 [66.7;80.3][a]
P20 (ml/min per 1.73 m^2) $eGFR_{cys}$	57.3 [54.3;60.2]	67.4 [57.9;76.8][a]	61.8 [58.8;65.1][a]	27.8 [20.9;34.7]
P20 (ml/min per 1.73 m^2) $eGFR_{crea+cys}$	52.3 [49.4;55.3]	60.0 [50.1;69.9][a]	53.2 [49.8;56.6]	43.2 [35.6;50.8]
P30 (ml/min per 1.73 m^2) $eGFR_{crea}$	81.0 [78.6;83.3][a]	49.5 [39.4;59.5]	82.8 [80.2;85.3][a]	90.1 [85.5;94.7][a]
P30 (ml/min per 1.73 m^2) $eGFR_{cys}$	74.9 [72.4;77.5]	83.2 [75.6;90.7][a]	79.2 [76.4;81.9][a]	48.1 [40.5;55.8]
P30 (ml/min per 1.73 m^2) $eGFR_{crea+cys}$	72.1 [69.4;74.8]	81.1 [73.2;88.9][a]	72.5 [69.5;75.5]	64.8 [57.5;72.2]
		EKFC and 20%		
n (%)	1093	22 (2.0)	918 (84.0)	153 (14.0)
Bias (ml/min per 1.73 m^2) $eGFR_{crea}$	−0.62 [−1.60;0.45]	15.80 [3.98;19.40]	0.11 [−1.11;1.29]	−5.19 [−7.28;−2.66]

(Continued on following page)

Table 3. (Continued) Performance of the different equations in the concordant and discordant groups in other populations (relative difference)

Performance	Whole	GFR_{DCys}	GFR_{C}	GFR_{DCrea}
Bias (ml/min per 1.73 m^2) $eGFR_{cys}$	4.26 [3.32;5.02]	−4.21 [−13.36;1.16]	3.26 [2.33;4.24]	12.73 [10.01;15.15]
Bias (ml/min per 1.73 m^2) $eGFR_{crea+cys}$	2.23 [1.17;3.18]	5.14 [−5.82;12.14]	1.65 [0.82;2.62]	4.46 [1.54;5.60]
IQR (ml/min per 1.73 m^2) $eGFR_{crea}$	18.4 [−9.5;8.9]	17.9 [4.1;22.0]	18.6 [−9.2;9.4]	16.7 [−14.9;1.9]
IQR (ml/min per 1.73 m^2) $eGFR_{cys}$	18.3 [−5.3;13.0]	15.8 [−13.2;2.6]	17.8 [−6.3;11.5]	17.7 [4.1;21.8]
IQR (ml/min per 1.73 m^2) $eGFR_{crea+cys}$	17.5 [−7.2;10.3]	18.8 [−5.5;13.3]	17.8 [−7.6;10.2]	16.4 [−4.3;12.0]
P20 (ml/min per 1.73 m^2) $eGFR_{crea}$	73.6 [70.9;76.2][a]	40.9 [20.4;61.5][a]	75.6 [72.8;78.4][a]	66.0 [58.5;73.5][a]
P20 (ml/min per 1.73 m^2) $eGFR_{cys}$	69.9 [67.2;72.6][a]	59.1 [38.5;79.6][a]	73.6 [70.8;76.5][a]	49.0 [41.1;56.9]
P20 (ml/min per 1.73 m^2) $eGFR_{crea+cys}$	75.0 [72.5;77.6][a]	54.5 [33.7;75.4][a]	75.8 [73.0;78.6][a]	73.2 [66.2;80.2][a]
P30 (ml/min per 1.73 m^2) $eGFR_{crea}$	88.5 [86.6;90.4][a]	50.0 [29.1;70.9][a]	88.7 [86.6;90.7][a]	92.8 [88.7;96.9][a]
P30 (ml/min per 1.73 m^2) $eGFR_{cys}$	83.9 [81.7;86.1]	72.7 [54.1;91.3][a]	87.0 [84.9;89.2][a]	66.7 [59.2;74.1]
P30 (ml/min per 1.73 m^2) $eGFR_{crea+cys}$	87.0 [85.0;89.0][a]	72.7 [54.1;91.3][a]	87.9 [85.8;90.0][a]	83.7 [77.8;89.5][a]
		r-LMR and 20%		
n (%)	1,093	25 (16.8)	878 (80,3)	190 (17.4)
Bias (ml/min per 1.73 m^2) $eGFR_{crea}$	−3,16 [−4,20;−2,42]	14,90 [1,55;16,54]	−2,83 [−3,79;−1,88]	−6,22 [−8,67;−4,86]
Bias (ml/min per 1.73 m^2) $eGFR_{cys}$	2,06 [1,23;2,99]	−4,54 [−13,49;−2,41]	0,65 [−0,37;1,52]	11,62 [8,94;14,61]
Bias (ml/min per 1.73 m^2) $eGFR_{crea+cys}$	−0,41 [−1,25;0,67]	4,97 [−6,34;8,15]	−0,87 [−1,97;−0,06]	2,98 [0,09;4,79]
IQR (ml/min per 1.73 m^2) $eGFR_{crea}$	18,8 [−12,7;6,2]	17,7 [1,1;18,9]	18,6 [−11,8;6,7]	17,0 [−15,5;1,5]
IQR (ml/min per 1.73 m^2) $eGFR_{cys}$	18,5 [−7,4;11,1]	13,2 [−13,9;−0,7]	17,9 [−8,8;9,1]	17,5 [2,7;20,2]
IQR (ml/min per 1.73 m^2) $eGFR_{crea+cys}$	17,3 [−9,2;8,0]	16,9 [−6,4;10,5]	17,6 [−10,3;7,4]	16,7 [−6,1;10,5]
P20 (ml/min per 1.73 m^2) $eGFR_{crea}$	73,4 [70,8;76,0][a]	44,0 [24,5;63,5][a]	76,3 [73,5;79,1][a]	63,7 [56,8;70,5][a]
P20 (ml/min per 1.73 m^2) $eGFR_{cys}$	71,7 [69,1;74,4][a]	56,0 [36,5;75,5][a]	75,3 [72,4;78,1][a]	57,4 [50,3;64,4]
P20 (ml/min per 1.73 m^2) $eGFR_{crea+cys}$	76,4 [73,9;78,9][a]	64,0 [45,2;82,8][a]	77,0 [74,2;79,8][a]	75,3 [69,1;81,4][a]
P30 (ml/min per 1.73 m^2) $eGFR_{crea}$	89,6 [87,8;91,4][a]	64,0 [45,2;82,8][a]	90,1 [88,1;92,1][a]	90,5 [86,4;94,7][a]
P30 (ml/min per 1.73 m^2) $eGFR_{cys}$	85,9 [83,8;88,0]	68,0 [49,7;86,3][a]	89,4 [87,4;91,4][a]	72,1 [65,7;78,5]
P30 (ml/min per 1.73 m^2) $eGFR_{crea+cys}$	90,0 [88,3;91,8][a]	80,0 [64,3;95,7][a]	91,3 [89,5;93,2][a]	85,3 [80,2;90,3][a]
Black Africans		CKD-EPI and 20%		
n (%)	508	59 (11.6)	334 (65.7)	115 (22.6)
Bias (ml/min per 1.73 m^2) $eGFR_{crea}$	2.48 [0.73;4.11]	15.01 [8.40;20.04]	4.58 [2.57;6.75]	−10.35 [−14.66;−7.78]
Bias (ml/min per 1.73 m^2) $eGFR_{cys}$	2.24 [0.84;3.58]	−12.79 [−16.57;−9.24]	3.39 [1.81;5.08]	7.38 [2.59;13.75]
Bias (ml/min per 1.73 m^2) $eGFR_{crea+cys}$	4.08 [2.37;5.67]	−0.34 [−6.37;3.89]	6.77 [4.39;8.58]	−0.99 [−3.54;2.03]
IQR (ml/min per 1.73 m^2) $eGFR_{crea}$	23.2 [−8.9;14.3]	24.3 [1.6;25.9]	20.8 [−5.5;15.3]	17.9 [−18.6;−0.7]
IQR (ml/min per 1.73 m^2) $eGFR_{cys}$	23.4 [−8.2;15.3]	16.9 [−21.6;−4.6]	21.7 [−6.2;15.5]	28.8 [−6.6;22.2]
IQR (ml/min per 1.73 m^2) $eGFR_{crea+cys}$	21.9 [−7.3;14.6]	20.1 [−9.3;10.8]	20.6 [−3.8;16.8]	22.4 [−10.9;11.4]
P20 (ml/min per 1.73 m^2) $eGFR_{crea}$	59.6 [55.4;63.9][a]	47.5 [34.7;60.2]	68.6 [63.6;73.5][a]	40.0 [31.0;49.0][a]
P20 (ml/min per 1.73 m^2) $eGFR_{cys}$	58.9 [54.6;63.1][a]	59.3 [46.8;71.9][a]	65.6 [60.5;70.7][a]	39.1 [30.2;48.1][a]
P20 (ml/min per 1.73 m^2) $eGFR_{crea+cys}$	62.0 [57.8;66.2][a]	74.6 [63.5;85.7][a]	65.6 [60.5;70.7][a]	45.2 [36.1;54.3][a]
P30 (ml/min per 1.73 m^2) $eGFR_{crea}$	74.4 [70.6;78.2][a]	61.0 [48.6;73.5]	83.5 [79.6;87.5][a]	54.8 [45.7;63.9][a]
P30 (ml/min per 1.73 m^2) $eGFR_{cys}$	77.4 [73.7;81.0][a]	76.3 [65.4;87.1][a]	84.7 [80.9;88.6][a]	56.5 [47.5;65.6][a]
P30 (ml/min per 1.73 m^2) $eGFR_{crea+cys}$	77.6 [73.9;81.2][a]	86.4 [77.7;95.2][a]	82.9 [78.9;87.0][a]	57.4 [48.4;66.4][a]
		EKFC and 20%		
n (%)	508	32 (6.3)	349 (68.7)	127 (25.0)
Bias (ml/min per 1.73 m^2) $eGFR_{crea}$	−1.59 [−3.08;0.07]	14.11 [0.07;21.23]	2.33 [−0.63;4.41]	−13.21 [−15.23;−9.53]
Bias (ml/min per 1.73 m^2) $eGFR_{cys}$	1.74 [0.28;3.23]	−11.25 [−19.24;−9.60]	2.12 [0.70;3.79]	3.93 [0.18;7.21]
Bias (ml/min per 1.73 m^2) $eGFR_{crea+cys}$	0.28 [−1.05;1.42]	0.42 [−9.88;7.16]	2.24 [0.54;3.73]	−3.77 [−6.01;−1.93]
IQR (ml/min per 1.73 m^2) $eGFR_{crea}$	20.8 [−11.0;9.8]	23.8 [−0.8;23.0]	17.9 [−6.5;11.4]	14.0 [−18.2;−4.2]
IQR (ml/min per 1.73 m^2) $eGFR_{cys}$	19.3 [−7.4;11.9]	14.4 [−20.3;−5.9]	18.8 [−6.3;12.4]	19.4 [−6.0;13.4]
IQR (ml/min per 1.73 m^2) $eGFR_{crea+cys}$	17.3 [−7.4;9.9]	18.6 [−11.2;7.4]	17.3 [−5.2;12.1]	13.3 [−11.1;2.2]
P20 (ml/min per 1.73 m^2) $eGFR_{crea}$	63.8 [59.6;68.0]	46.9 [29.6;64.2][a]	74.2 [69.6;78.8][a]	39.4 [30.9;47.9][a]
P20 (ml/min per 1.73 m^2) $eGFR_{cys}$	66.7 [62.6;70.8][a]	59.4 [42.4;76.4][a]	72.8 [68.1;77.4][a]	52.0 [43.3;60.7][a]
P20 (ml/min per 1.73 m^2) $eGFR_{crea+cys}$	72.4 [68.6;76.3][a]	78.1 [63.8;92.4][a]	77.9 [73.6;82.3][a]	55.9 [47.3;64.5][a]
P30 (ml/min per 1.73 m^2) $eGFR_{crea}$	78.9 [75.4;82.5][a]	71.9 [56.3;87.5][a]	88.8 [85.5;92.1][a]	53.5 [44.9;62.2]
P30 (ml/min per 1.73 m^2) $eGFR_{cys}$	83.5 [80.2;86.7][a]	81.3 [67.7;94.8][a]	87.4 [83.9;90.9][a]	73.2 [65.5;80.9][a]
P30 (ml/min per 1.73 m^2) $eGFR_{crea+cys}$	84.3 [81.1;87.4][a]	90.6 [80.5;100.7][a]	90.0 [86.8;93.1][a]	66.9 [58.7;75.1][a]
		r-LMR and 20%		
n (%)	508	29 (5.7)	357 (70.3)	122 (20.4)
Bias (ml/min per 1.73 m^2) $eGFR_{crea}$	−6,21 [−7,69;−5,05]	11,35 [−0,62;18,46]	−5,02 [−6,24;−3,82]	−13,45 [−16,29;−10,49]
Bias (ml/min per 1.73 m^2) $eGFR_{cys}$	−4,28 [−5,60;−2,96]	−15,76 [−23,05;−9,53]	−4,89 [−6,18;−3,56]	0,52 [−2,12;2,83]
Bias (ml/min per 1.73 m^2) $eGFR_{crea+cys}$	−5,57 [−6,78;−4,61]	−2,27 [−12,00;4,26]	−5,15 [−6,77;−4,26]	−6,95 [−9,52;−5,39]
IQR (ml/min per 1.73 m^2) $eGFR_{crea}$	17,7 [−15,5;2,2]	26,4 [−6,0;20,4]	16,2 [−13,1;3,1]	16,3 [−20,6;−4,2]

(Continued on following page)

Table 3. (Continued) Performance of the different equations in the concordant and discordant groups in other populations (relative difference)

Performance	Whole	GFR_{DCys}	GFR_{C}	GFR_{DCrea}
IQR (ml/min per 1.73 m^2) $eGFR_{cys}$	17,2 [−12,1;5,1]	19,0 [−25,7;−6,7]	17,6 [−13,1;4,6]	15,4 [−7,5;7,9]
IQR (ml/min per 1.73 m^2) $eGFR_{crea+cys}$	15,2 [−12,0;3,2]	19,9 [−13,1;6,8]	15,1 [−11,7;3,3]	13,6 [−12,7;0,9]
P20 (ml/min per 1.73 m^2) $eGFR_{crea}$	64,0 [59,8;68,2][a]	48,3 [30,1;66,5][a]	77,3 [73,0;81,7][a]	28,7 [20,7;36,7]
P20 (ml/min per 1.73 m^2) $eGFR_{cys}$	71,1 [67,1;75,0][a]	55,2 [37,1;73,3][a]	78,2 [73,9;82,4][a]	54,1 [45,3;62,9][a]
P20 (ml/min per 1.73 m^2) $eGFR_{crea+cys}$	71,1 [67,1;75,0][a]	75,9 [60,3;91,4][a]	78,7 [74,5;83,0][a]	47,5 [38,7;56,4][a]
P30 (ml/min per 1.73 m^2) $eGFR_{crea}$	80,1 [76,6;83,6]	86,2 [73,7;98,8][a]	91,0 [88,1;94,0][a]	46,7 [37,9;55,6]
P30 (ml/min per 1.73 m^2) $eGFR_{cys}$	84,4 [81,3;87,6][a]	72,4 [56,1;88,7][a]	90,5 [87,4;93,5][a]	69,7 [61,5;77,8][a]
P30 (ml/min per 1.73 m^2) $eGFR_{crea+cys}$	86,6 [83,7;89,6][a]	93,1 [83,9;102,3][a]	93,0 [90,3;95,6][a]	66,4 [58,0;74,8][a]

CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; $eGFR_{crea}$, creatinine-based estimating glomerular filtration rate; $eGFR_{crea+cys}$: estimating glomerular filtration rate combining creatinine and cystatin C; $eGFR_{cys}$, cystatin C-based estimating glomerular filtration rate; EKFC, European Kidney Function Consortium; GFR_{C}, group of subjects with concordant estimating glomerular filtration rate results; GFR_{DCrea}, group of subjects with discordant estimating glomerular filtration rate results and with creatinine-based results lower than cystatin C-based results; GFR_{DCys}, group of subjects with discordant estimating glomerular filtration rate results and with cystatin C-based results lower than creatinine-based results; IQR, interquartile range; P20, accuracy within 20%; P30, accuracy within 30%; r-LMR: re-expressed Lund-Malmö.
[a]The best P20 and P30 results within each group.

sex variable makes the hazard ratio much closer to 1 (data not shown). However, in both males and females, all EKFC equations performed better than the respective CKD-EPI equations.

From our dataset, we showed that the proportion of discordant results was dependent on the definition and the choice of the threshold as well as on the eGFR equation considered. As expected, for more stringent thresholds, higher percentages of discrepancies are seen. The choice of the threshold is somewhat arbitrary but can be briefly discussed. First, as the KDIGO suggests,[1] we think it is of interest to consider both relative and absolute differences, because they might provide different information. However, we must keep in mind that an absolute threshold (e.g., 15 ml/min per 1.73 m^2) will have a different meaning at a low or high GFR level. In this view, the use of a relative difference maybe more relevant. The choice of 20% difference as the relevant threshold can be indirectly justified by exclusion. Indeed, 10% is probably a too stringent criterion because this value corresponds to the least significant change of measured GFR.[24,28] In contrast, a threshold of 30% is probably not strict enough, because this threshold is used when eGFR equations are compared with mGFR.

Table 4. Results of the multinomial logistic regression models assessing the association between subjects' characteristics and belonging to one of the discrepant group

Covariate	GFR_{DCrea}	GFR_{DCys}
CKD-EPI and absolute difference of 15 ml/min per 1.73 m^2		
Sex (ref: female)	0.98 [0.86;1.12]	1.04 [0.97;1.13]
Age (yrs)	0.99 [0.98;0.99][a]	0.995 [0.992;0.998][a]
BMI (kg/m^2)	0.98 [0.96;0.99][a]	1.00 [0.99;1.01]
mGFR (ml/min per 1.73 m^2)	1.02 [1.02;1.03][a]	0.999 [0.997;1.002]
CKD-EPI and relative difference of 20%		
Sex (ref: female)	0.94 [0.83;1.07]	1.11 [1.03;1.21][a]
Age (yrs)	0.98 [0.98;0.99][a]	1.00 [0.997;1.003]
BMI (kg/m^2)	0.99 [0.98;1.00]	1.01 [1.00;1.02][a]
mGFR (ml/min per 1.73 m^2)	0.99 [0.99;0.99][a]	0.97 [0.97;0.97][a]
EKFC and absolute difference of 15 ml/min per 1.73m^2		
Sex (ref: female)	0.45 [0.40;0.51][a]	1.34 [1.20;1.49][a]
Age (yrs)	0.97 [0.97;0.98][a]	0.98 [0.97;0.98][a]
BMI (kg/m^2)	0.98 [0.96;0.99][a]	0.99 [0.98;0.997][a]
mGFR (ml/min per 1.73 m^2)	1.007 [1.004 ;1.009][a]	0.999 [0.997;1.001]
EKFC and relative difference of 20%		
Sex (ref: female)	0.58 [0.52;0.63][a]	1.35 [1.23;1.50][a]
Age (yrs)	0.99 [0.98;0.99][a]	0.99 [0.98;1.00][a]
BMI (kg/m^2)	0.99 [0.98;0.997][a]	0.998 [0.99;1.01]
mGFR (ml/min per 1.73 m^2)	0.98 [0.97;0.98][a]	0.97 [0.97;0.98][a]

95%CI: 95% confidence interval; BMI, body mass index; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; EKFC, European Kidney Function Consortium; GFR_{DCrea}, group of subjects with discrepant estimated glomerular filtration rate results and with creatinine-based results lower than creatinine-based results; GFR_{DCys}, group of subjects with discrepant estimated glomerular filtration rate results and with cystatin C-based results lower than creatinine-based results; mGFR, measured glomerular filtration rate.
[a]$P < 0.05$.
The Relative Risk Ratio is the exponential of the coefficient of the multinomial logistic regression models.

To the best of our knowledge, this is the first time that a comparison has been made between the EKFC (and r-LMR) and CKD-EPI equations regarding the proportion of discrepancies between creatinine-and cystatin C–based equations. The 2 main results are the lower occurrence of discrepant results with EKFC or r-LMR compared with CKD-EPI and, among discrepant results, a much more balanced repartition between $eGFR_{cys} < eGFR_{crea}$ and $eGFR_{crea} < eGFR_{cys}$ with the EKFC and r-LMR equation than with the CKD-EPI equation (with this last equation, a much higher occurrence of $eGFR_{cys} < eGFR_{crea}$ is observed). First, a much lower proportion of discordant results with the EKFC and r-LMR equations was confirmed in the whole population, in our main group (White Europeans), and in all subgroup analyses according to age, sex, BMI, and mGFR. This is probably explained by the fact that the mathematical structures of the EKFC and r-LMR equations are the same for both creatinine and cystatin.[2,17] In contrast, age and sex were modelled mathematically differently in the 2 CKD-EPI equations.[3,16] Second, we observed a more balanced repartition in discordant results with the EKFC than with the CKD-EPI equations. Indeed, with the CKD-EPI

equations, the proportion of discordant results with $eGFR_{cys} < eGFR_{crea}$ was much higher than that with $eGFR_{crea} < eGFR_{cys}$, a phenomenon that has already been observed in other studies.[6,12] However, there is no well-known explanation for this observation, and it seems more logical to observe a more balanced repartition among discrepant results, similar to the EKFC equations. Indeed, with the EKFC equations, the percentage of discordant results with $eGFR_{cys}$ lower than that with $eGFR_{crea}$ was similar to the percentage of discordant results with $eGFR_{crea}$ lower than that with $eGFR_{cys}$. Moreover, we observed a clear but unexpected association between the differences in $eGFR_{crea}$ and $eGFR_{cys}$ and mGFR or age (Figure 1 and Supplementary Figure S1) when the CKD-EPI equations were used, whereas there was virtually no dependency on mGFR and age when the EKFC equations were considered. Even if indirect, these results are arguments for preferring the use of the EKFC equations over the CKD-EPI equations, as well as in subjects with discordant results between $eGFR_{crea}$ and $eGFR_{cys}$.

The current study confirms the better performance of the EKFC equations, which is, at least for European cohorts, explained by the fact that some of the cohorts considered were used for the partial development (determination of some of the coefficients) of the serum creatinine–based EKFC equation. However, a lower percentage of discordant results with the EKFC and a more balanced repartition of discordant results with the EKFC than with the CKD-EPI equations were confirmed when analyses were restricted to cohorts not used in the development of the EKFC creatinine-based equation (Supplementary Table S11).

Another important strategic question is which equation should be used, notably when eGFR with creatinine and cystatin C is discordant. The KDIGO suggests that the $eGFR_{crea+cys}$ CKD-EPI equation should be used in these cases. This is supported by some,[6,8,9,15,29] but not all data in the literature.[30,31] However, we have shown that the strategy of using $eGFR_{crea+cys}$ when the results based on each biomarker are discordant is only systematically true when the EKFC equations are considered, but not when the CKD-EPI equations are used (notably, in White Europeans, in the group of discordant results with $eGFR_{crea} < eGFR_{cys,}$ the best CKD-EPI equation is $eGFR_{crea}$, not $eGFR_{crea+cys}$). For the EKFC and r-LMR equations, $eGFR_{crea+cys}$ is the average of $eGFR_{crea}$ and $eGFR_{cys}$.

To the best of our knowledge, our dataset is the largest with creatinine, cystatin C, and mGFR levels available, allowing several subgroup analyses. However, this study has some limitations. First, our largest cohort was limited to White Europeans, and subanalyses could only be conducted in this cohort. We did not have data on Black US or Asian subjects. Moreover, in the subgroup analyses, the sample size may be limited; thus, the results must be interpreted with caution. Second, our analysis was restricted to the performance of eGFR equations to estimate GFR and not to predict outcomes such as mortality or cardiovascular mortality. This would be a totally different analysis; however, several studies have already shown the superiority of cystatin C to predict outcomes.[12,13,32] Third, the performance of the multinomial logistic regression models was suboptimal (accuracies of the models are between 0.64 and 0.78 for EKFC and CKD-EPI) because of the imbalance in the distribution of the 3 discrepancy groups. This imbalance limited the explanatory power of the model. Fourth, mGFR was measured using different techniques, which may have contributed to differences between cohorts. Finally, the discrepant results between the creatinine- and cystatin C–based equations may be explained, at least in part, by the non-GFR determinants of creatinine (muscular mass, protein intake, and creatinine tubular secretion) and cystatin C (dysthyroidism and high-dose steroids are the most well-defined), and most of these variables were not available in our study.[13,33] Therefore, if we observed a lower occurrence of discrepant results and a more balanced repartition among discrepant results with EKFC or r-LMR, further studies including more variables are required to explain why such results are found.

In conclusion, we have shown that the proportion of discordant results between $eGFR_{crea}$ and $eGFR_{cys}$ is significantly lower when the EKFC equations are used instead of the CKD-EPI equations. Moreover, the distribution of the discordant results is more balanced with the EKFC equations and less dependent on age and mGFR. The strategy of considering the combined $eGFR_{crea+cys}$ equations when the results are discordant between the biomarkers is valid, but only if the EKFC equations are used. However, all equations provide an estimation of the GFR. Even when $eGFR_{crea}$ and $eGFR_{cys}$ are fully concordant, the result is different of more than 30% of the measured GFR in approximately 10% of the cases using EKFC and 15% of the cases using the CKD-EPI equation. Moreover, in some subgroups (notably in patients with discordant results and extreme BMI or mGFR), the performance of all equations is insufficient and measuring GFR makes more sense.

DISCLOSURE

PD and EC are consultants for Nephrolyx. NE receives honoraria from Bayer Leverkusen. All the other authors declared no competing interests.

ACKNOWLEDGMENTS

We Thank Edmund J. Lamb from the Department of Clinical Biochemistry, East Kent Hospitals University NHS Foundation Trust, Canterbury, United Kingdom for sharing his data. The results presented in this paper have not been previously published, either in whole or in part.

Funding

Swedish Research Council (Vetenskapsrådet; grant no. 2019-00198). Professor J. Björk received funding from the Swedish Research Council (VR) to conduct large-scale epidemiological studies linked with registered healthcare data. This funding source was not involved in the design, analysis, presentation, or interpretation of the study results.

DATA AVAILABILITY STATEMENT

A short protocol is available to interested readers by contacting PD at pdelanaye@chuliege.be. SAS code is available to interested readers by contacting HP at hans.pottel@kuleuven.be. The EKFC dataset used in the present study is hosted by the Lund University Population Research Platform. Legal and ethical restrictions prevent public sharing of datasets. Data can be made available for collaborations upon request of interested researchers but would generally require new ethical permission and permission from each of the data owners. You can find contact information for the data host at https://www.lupop.lu.se/. The GENOA/ECAC, Paris, Créteil, Nîmes and Groningen data are not publicly available because of the confidential nature of patient information obtained for clinical care. Legal and ethical restrictions prevent public sharing of datasets. Data can be made available for collaborations upon request of interested researchers but would generally require new ethical permission and permission from each of the data owners.

SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Supplemental References.

Figure S1. Association between differences in creatinine and cystatin C-based equations and age.

Table S1. Description of the populations and cohorts.

Table S2. Creatinine- and/or cystatin C–based equations.

Table S3. Proportion of discrepant results between creatinine- and cystatin C–based equations in the White European population according to sex, age, mGFR and BMI.

Table S4. Characteristics of the population in concordant and discordant groups in White Europeans.

Table S5. Performance of the different equations in the concordant and discordant groups in White Europeans (absolute difference).

Table S6. Performance of the different equations in the concordant and discordant groups in other populations (absolute difference).

Table S7. Performance of the different equations in the concordant and discordant groups according to sex in White Europeans.

Table S8. Performance of the different equations in the concordant and discordant groups according to age in White Europeans.

Table S9. Performance of the different equations in the concordant and discordant groups according to mGFR in White Europeans.

Table S10. Performance of the different equations in the concordant and discordant groups according to BMI in White Europeans.

Table S11. Performance of the different equations in the concordant and discordant groups in White Europeans (relative difference) including cohorts not used for the development of the creatinine-based EKFC equation (Lyon, Créteil, Nîmes, Paris, Groningen).

STROBE Checklist.

REFERENCES

1. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2024 clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney Int Suppl*. 2024;105:S117–S314.
2. Pottel H, Björk J, Rule AD, et al. Cystatin C–based equation to estimate GFR without the inclusion of race and sex. *N Engl J Med*. 2023;388:333–343. https://doi.org/10.1056/NEJMoa2203769
3. Inker LA, Schmid CH, Tighiouart H, et al. Estimating glomerular filtration rate from serum creatinine and cystatin C. *N Engl J Med*. 2012;367:20–29. https://doi.org/10.1056/NEJMoa1114248
4. Carrero JJ, Fu EL, Sang Y, et al. Discordances between creatinine and cystatin C-based estimated GFR and adverse clinical outcomes in routine clinical practice. *Am J Kidney Dis*. 2023;82:534–542. https://doi.org/10.1053/j.ajkd.2023.04.002
5. Chen DC, Lu K, Scherzer R, et al. Cystatin C- and creatinine-based estimated GFR differences: Prevalence and predictors in the UK Biobank. *Kidney Med*. 2024;6:100796. https://doi.org/10.1016/j.xkme.2024.100796
6. Fu EL, Levey AS, Coresh J, et al. Accuracy of GFR estimating equations in patients with discordances between creatinine and cystatin C-based estimations. *J Am Soc Nephrol*. 2023;34:1241–1251. https://doi.org/10.1681/ASN.0000000000000128
7. Potok OA, Rifkin DE, Ix JH, et al. Estimated GFR accuracy when cystatin C and creatinine-based estimates are discrepant in older adults. *Kidney Med*. 2023;5:100628. https://doi.org/10.1016/j.xkme.2023.100628
8. Wang Y, Adingwupu OM, Shlipak MG, et al. Discordance between creatinine-based and cystatin C–based estimated GFR: Interpretation according to performance compared to measured GFR. *Kidney Med*. 2023;5:100710. https://doi.org/10.1016/j.xkme.2023.100710

9. Björk J, Grubb A, Larsson A, et al. Accuracy of GFR estimating equations combining standardized cystatin C and creatinine assays: A cross-sectional study in Sweden. *Clin Chem Lab Med*. 2015;53:403–414. https://doi.org/10.1515/cclm-2014-0578
10. Åkesson A, Lindström V, Nyman U, et al. Shrunken pore syndrome and mortality: A cohort study of patients with measured GFR and known comorbidities. *Scand J Clin Lab Investig*. 2020;80:412–422. https://doi.org/10.1080/00365513.2020.1759139
11. Rule AD, Glassock RJ. Cystatin C and the misdiagnosis of CKD in older adults. *Nat Rev Nephrol*. 2024;6:560–561. https://doi.org/10.1038/s41581-024-00852-y
12. Fu EL, Carrero JJ, Sang Y, et al. Association of low glomerular filtration rate with adverse outcomes at older age in a large population with routinely measured cystatin C. *Ann Intern Med Med*. 2024;177:269–279. https://doi.org/10.7326/M23-1138
13. Malmgren L, Öberg C, den Bakker E, et al. The complexity of kidney disease and diagnosing it – cystatin C, selective glomerular hypofiltration syndromes and proteome regulation. *J Intern Med*. 2023;293:293–308. https://doi.org/10.1111/joim.13589
14. Farrington D, Surapaneni A, Matsushita K, Seegmiller JC, Coresh J, Grams M. Discrepancies between cystatin C-based and creatinine-based estimated glomerular filtration rates. *Clin J Am Soc Nephrol*. 2023;18:1143–1152. https://doi.org/10.2215/CJN.0000000000000217
15. Grubb A. Non-invasive estimation of glomerular filtration rate (GFR). The Lund model: Simultaneous use of cystatin C- and creatinine-based GFR-prediction equations, clinical data and an internal quality check. *Scand J Clin Lab Investig*. 2010;70:65–70. https://doi.org/10.3109/00365511003642535
16. Inker LA, Eneanya ND, Coresh J, et al. New creatinine- and cystatin C–based equations to estimate GFR without race. *N Engl J Med*. 2021;385:1737–1749. https://doi.org/10.1056/NEJMoa2102953
17. Pottel H, Björk J, Courbebaisse M, et al. Development and validation of a modified full age spectrum creatinine-based equation to estimate glomerular filtration rate. A cross-sectional analysis of pooled data. *Ann Intern Med*. 2021;174:183–191. https://doi.org/10.7326/M20-4366
18. Nyman U, Björk J, Delanaye P, et al. Rescaling creatinine makes GFR estimation equations generally applicable across populations - validation results for the Lund-Malmö equation in a French cohort of sub-Saharan ancestry. *Clin Chem Lab Med*. 2023;62:421–427. https://doi.org/10.1515/cclm-2023-0496
19. Delanaye P, Cavalier E, Stehlé T, Pottel H. Glomerular filtration rate estimation in adults: Myths and promises. *Nephron*. 2024;148:408–414. https://doi.org/10.1159/000536243
20. Delanaye P, Pottel H, Cavalier E, Flamant M, Stehlé T, Mariat C. Diagnostic standard: Assessing glomerular filtration rate. *Nephrol Dial Transpl*. 2024;39:1088–1096. https://doi.org/10.1093/ndt/gfad241
21. Pottel H, Cavalier E, Björk J, et al. Standardization of serum creatinine is essential for accurate use of unbiased estimated GFR equations: Evidence from three cohorts matched on renal function. *Clin Kidney J*. 2022;15:2258–2265. https://doi.org/10.1093/ckj/sfac182
22. Delanaye P, Rule AD, Schaeffner ES, et al. Performance of the European Kidney Function Consortium (EKFC) creatinine-based equation in United States cohorts. *Kidney Int*. 2024;105:629–637. https://doi.org/10.1016/j.kint.2023.11.024
23. Soveri I, Berg UB, Björk J, et al. Measuring GFR: A systematic review. *Am J Kidney Dis*. 2014;64:411–424. https://doi.org/10.1053/j.ajkd.2014.04.010
24. Delanaye P, Ebert N, Melsom T, et al. Iohexol plasma clearance for measuring glomerular filtration rate in clinical practice and research: A review. Part 2: Why to measure glomerular filtration rate with iohexol? *Clin Kidney J*. 2016;9:682–699. https://doi.org/10.1093/ckj/sfw070
25. Apperloo AJ, de Zeeuw D, Donker AJ, de Jong PE. Precision of glomerular filtration rate determinations for long-term slope calculations is improved by simultaneous infusion of 125I-iothalamate and 131I-hippuran. *J Am Soc Nephrol*. 1996;7:567–572. https://doi.org/10.1681/ASN.V74567
26. Delgado C, Baweja M, Crews DC, et al. A unifying approach for GFR estimation: Recommendations of the NKF-ASN task force on reassessing the inclusion of race in diagnosing kidney disease. *J Am Soc Nephrol*. 2021;32:2994–3015. https://doi.org/10.1681/ASN.2021070988
27. Delanaye P, Pottel H, Botev R, Inker LA, Levey AS. Con: Should we abandon the use of the MDRD equation in favour of the CKD-EPI equation? *Nephrol Dial Transpl*. 2013;28:1396–1403. https://doi.org/10.1093/ndt/gft006
28. Delanaye P, Cavalier E, Depas G, Chapelle JP, Krzesinski JM. New data on the intraindividual variation of cystatin C. *Nephron Clin Pr*. 2008;108:246–249. https://doi.org/10.1159/000124327
29. Schei J, Stefansson VTN, Mathisen UD, et al. Residual associations of inflammatory markers with eGFR after accounting for measured GFR in a community-based cohort without CKD. *Clin J Am Soc Nephrol*. 2016;11:280–286. https://doi.org/10.2215/CJN.07360715
30. Rule AD, Bailey KR, Lieske JC, Peyser PA, Turner ST. Estimating the glomerular filtration rate from serum creatinine is better than from cystatin C for evaluating risk factors associated with chronic kidney disease. *Kidney Int*. 2013;83:1169–1176. https://doi.org/10.1038/ki.2013.7
31. Melsom T, Fuskevåg OM, Mathisen UD, et al. Estimated GFR is biased by non-traditional cardiovascular risk factors. *Am J Nephrol*. 2015;41:7–15. https://doi.org/10.1159/000371557
32. Shlipak MG, Matsushita K, Arnlov J, et al. Cystatin C versus creatinine in determining risk based on kidney function. *N Engl J Med*. 2013;369:932–943. https://doi.org/10.1056/NEJMoa1214234
33. Stehlé T, Delanaye P. Which is the best glomerular filtration marker : Creatinine, cystatin C or both? *Eur J Clin Investig*. 2024;54:e14278. https://doi.org/10.1111/eci.14278