Implementation of the 2021 CKD-EPI GFR equations

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Please check back <u>here</u> for updated information and text as we develop more tools

Contents

Background	2
Equations to be programmed into your laboratory information system	
2021 CKD-EPI Creatinine equation	2
2021 CKD-EPI Creatinine-cystatin C equation	3
Equations in statistical code	3
Prior equations	3
eGFR reporting by clinical laboratories	4
Educational material for health care providers or laboratories	4
How should differences in a patient's eGFR be interpreted during the transition from the old to the new equations?	
Educational material for patients	5
Approach to GFR evaluation	5
Annendix: Testing programmed equations	6

Background

Glomerular filtration rate (GFR) is most commonly estimated from serum creatinine using estimating equations. In 2021, the NKF-ASN Task Force on Reassessing the Inclusion of Race in Diagnosing Kidney Diseases concluded that race should not be included in GFR estimating equations, and recommended use of the 2021 CKD-EPI creatinine equation that includes factors for age and sex but not race group for immediate implementation by clinical laboratories. They also recommended more frequent measurement of cystatin C to confirm estimated GFR from creatinine when the clinical need requires, because combining creatinine and cystatin C gives a more accurate eGFR. The Task Force recommended the 2021 CKD-EPI creatinine-cystatin C equation as that does not include a term for race group.

Equations to be programmed into your laboratory information system

2021 CKD-EPI Creatinine equation

Expressed as a single equation eGFR= 142 X min(S_{cr}/κ ,1)^{α} X max(S_{cr}/κ ,1)^{α} X 0.9938^{Age} X 1.012 [if female]

Abbreviations/Units

eGFR (estimated glomerular filtration rate) = mL/min/1.73 m² S_{cr} (standardized serum creatinine) = mg/dL; divide by 88.4 for creatinine in μ mol/L κ = 0.7 (females) or 0.9 (males) α = -0.241 (females) or -0.302 (males) min = indicates the minimum of S_{cr}/κ or 1 max = indicates the maximum of S_{cr}/κ or 1 age = years

OR

CKD-EPI Equation for Estimating GFR on the Natural Scale Expressed for Specified Sex, Standardized Serum Creatinine and Standardized Serum Cystatin C (From New Eng J Med 2021)

Serum Creatinine	Equation				
(mg/dL)					
≤0.7	GFR= 142 x (Scr/0.7) ^{-0.241} x 0.9938 ^{Age} x 1.012				
>0.7	GFR= 142 x (Scr/0.7) ^{-1.200} x 0.9938 ^{Age} x 1.012				
≤0.9	GFR= 142 x (Scr/0.9) ^{-0.302} x 0.9938 ^{Age}				
>0.9	GFR= 142 x (Scr/0.9) ^{-1.200} x 0.9938 ^{Age}				
	(mg/dL) ≤0.7 >0.7 ≤0.9				

The appendix include creatinine inputs and expected eGFRcr outputs that cover a range of values suitable for verifying correct calculations using the CKD-EPI 2021 equation. Values were selected to be below, at and above the knots.

2021 CKD-EPI Creatinine-cystatin C equation

Expressed as a single equation eGFR= 135 X min(S_{cr}/κ ,1) $^{\alpha}$ X max(S_{cr}/κ ,1) $^{-0.544}$ X min($S_{cys}/0.8$,1) $^{-0.323}$ X max($S_{cys}/0.8$,1) $^{-0.778}$ X 0.9961 Age X 0.963 [if female]

Abbreviations/Units

eGFR (estimated glomerular filtration rate) = mL/min/1.73 m² S_{cr} (standardized serum creatinine) = mg/dL divide by 88.4 for creatinine in μ mol/L S_{cys} (standardized serum cystatin C) = mg/L κ = 0.7 (females) or 0.9 (males) α = -0.219 (females) or -0.144 (males) min = indicates the minimum of S_{cr}/κ or 1 max = indicates the maximum of S_{cr}/κ or 1

OR

age = years

CKD-EPI Equation for Estimating GFR on the Natural Scale Expressed for Specified Sex, Standardized Serum Creatinine and Standardized Serum Cystatin C (From New Eng J Med 2021)

Sex	Serum	Serum	Equation				
	Creatinine	Cystatin C					
	(mg/dL)	(mg/L)					
Female	≤0.7	≤0.8	GFR= 135 x (Scr/0.7)-0.219 x (Scys/0.8)-0.323 x 0.9961 ^{Age} x 0.963				
Female	≤0.7	>0.8	GFR= 135 x (Scr/0.7)-0.219 x (Scys/0.8)-0.778 x 0.9961 ^{Age} x 0.963				
Female	>0.7	≤0.8	GFR= 135 x (Scr/0.7)-0.544 x (Scys/0.8)-0.323 x 0.9961Age x 0.963				
Female	>0.7	>0.8	GFR= 135 x (Scr/0.7)-0.544 x (Scys/0.8)-0.778 x 0.9961Age x 0.963				
Male	≤0.9	≤0.8	GFR= 135 x (Scr/0.9)-0.144 x (Scys/0.8)-0.323 x 0.9961Age				
Male	≤0.9	>0.8	GFR= 135 x (Scr/0.9)-0.144 x (Scys/0.8)-0.778 x 0.9961Age				
Male	>0.9	≤0.8	GFR= 135 x (Scr/0.9)-0.544 x (Scys/0.8)-0.323 x 0.9961Age				
Male	>0.9	>0.8	GFR= 135 x (Scr/0.9)-0.544 x (Scys/0.8)-0.778 x 0.9961 Age				

The appendix include creatinine and cystatin C inputs and expected eGFRcr-cys outputs that cover a range of values suitable for verifying correct calculations using the CKD-EPI 2021 equation. Values were selected to be below, at and above the knots.

Equations in statistical code

Formulas in R and SAS

Prior equations

Formulas for 2009 and 2012 CKD-EPI equations

eGFR reporting by clinical laboratories

Please see the NKF website for tools for laboratories:

<u>Laboratory Implementation of the NKF-ASN Task Force Reassessing the Inclusion of Race in Diagnosing Kidney Diseases | National Kidney Foundation</u>

Key points to consider:

- 1. Use the CKD-EPI 2021 equations for all people 18 years of age and older. For people less than 18 years of age, the Bedside Schwartz equation is recommended for use Pediatric GFR Calculator National Kidney Foundation.
- 2. Using the CKD-EPI 2021 equation, specific values throughout the GFR range can be reported. That is, numeric values above and below 60 should be reported.
- 3. Age can be computed as differences in date from date of birth, which would give more precision than if used as a whole number. However, if only age in whole years is available, that is acceptable.
- 4. Creatinine results should be reported to 2 decimals in mg/dL or 1 decimal in μmol/L, and cystatin C to 2 decimals in mg/L, to avoid rounding errors when calculating eGFR.Methods for assay of serum creatinine and cystatin C should be traceable to higher order references; IDMS reference measurement procedures for creatinine and the ERM-DA471/IFCC certified reference material for cystatin C.
- 5. The nomenclature recommended by KDIGO is eGFRcr for the creatinine-based estimate, eGFRcr-cys for the combined creatinine-cystatin C-based estimate and eGFRcys for the cystatin C alone estimate. eGFR calculated using CKD-EPI 2021 equations should not be allowed to trend with values calculated using older equations

Educational material for health care providers or laboratories

ASN-NKF Task Force Report NKF GFR Calculator

How should differences in a patient's eGFR be interpreted during the transition from the old to the new equations?

The rationale for the development of the 2021 CKD-EPI equations was to avoid need to specify race in our multiracial and diverse population. On average, for patients who previously identified as Black, eGFR using the 2021 equations will be lower than eGFR using the 2009 creatinine or 2012 creatinine –cystatin C equation. On average, for patients who previously identified as non-Black, eGFR using the 2021 equations will be higher than eGFR using the 2009 creatinine or 2012 creatinine-cystatin C equations. The magnitude of the difference will depend on age, sex, the level of GFR (Table). These differences may impact a diagnosis of CKD, the CKD G stages, medication use and dosing, the need for interdisciplinary care and decisions about kidney replacement therapy planning and initiation. Given the uncertainty of the eGFR estimated by the equations, small differences in eGFR may not be clinically important. If there

is uncertainty about clinical decision-making using the 2021 creatinine equations, it is recommended to measure serum cystatin C and use the 2012 cystatin C equation and the 2021 creatinine-cystatin C equation. For the 2021 creatinine-cystatin C equation, the difference in eGFR compared to the 2012 creatinine-cystatin C equation is smaller than the difference between the 2021 and 2009 creatinine equations. There is no difference using the 2012 cystatin C equation.

The table below provides comparison of eGFR values from the new 2021 equations to the 2009 CKD-EPI creatinine equations for select ages and creatinine values.

Race	Age Creatinine (mg/dl)		50 years				75 years			
groups			0.6	1	1.5	2	0.6	1	1.5	2
Black		2009 eGFRcr	136	101	62	44	114	85	52	37
	Male	2021 eGFRcr	118	92	56	40	101	78	48	34
		Difference	18	9	6	4	13	7	4	3
	Female	2009 eGFRcr	123	76	47	33	103	64	39	28
		2021 eGFRcr	109	69	42	30	94	59	36	26
		Difference	14	7	5	3	9	5	3	2
NonBlack	Male	2009 eGFRcr	117	87	54	38	98	73	45	32
		2021 eGFRcr	118	92	56	40	101	78	48	34
		Difference	-1	-5	-2	-2	-3	-5	-3	-2
	Female	2009 eGFRcr	106	66	40	28	89	55	34	24
		2021 eGFRcr	109	69	42	30	94	59	36	26
		Difference	-3	-3	-2	-2	-5	-4	-2	-2

Educational material for patients

NKF newsletter to patients Sept 2021

Approach to GFR evaluation

Click on any of these to learn more about our approach to GFR evaluation.

Measurement and estimation of GFR for use in clinical practice: Core Curriculum, *Inker and Titan AJKD* 2021

Measured and estimated glomerular filtration rate: current status and future directions *Levey, Coresh and Tighiouart et al Nat Rev Nephrol 2020*

KDIGO clinical practice guidelines on the evaluation and management of CKD

Tufts Medical Center's Kidney Function Evaluation Center

Appendix: Testing programmed equations

id		In	put	eGFRcr	eGFRcys	eGFRcr-cys		
	age	female	Scr	Scys	2021	2012	2021	
1	27	0	0.68	0.78	131	121	128	
2	27	0	0.90	0.80	120	119	121	
3	27	0	0.91	0.81	118	117	120	
4	27	0	1.0	1.0	106	89	96	
5	27	1	0.68	0.78	122	113	119	
6	27	1	0.70	0.80	121	111	117	
7	27	1	0.71	0.81	119	109	115	
8	27	1	1.0	1.0	79	83	81	
9	54	0	0.68	0.78	110	108	115	
10	54	0	0.90	0.80	101	107	109	
11	54	0	0.91	0.81	100	105	108	
12	54	0	1.0	1.0	89	80	87	
13	54	1	0.68	0.78	103	101	107	
14	54	1	0.70	0.80	103	100	105	
15	54	1	0.71	0.81	101	98	103	
16	54	1	1.0	1.0	67	74	73	

Scr, creatinine in mg/dL. Scys, cystatin C in mg/L