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A. Complete methods for GFR measurement

GFR Measurement Protocol

Approximately one week prior to the study visit, each participant was contacted. Medications were reviewed with the participant. Participants were asked to avoid changes in medications that influence GFR (e.g. anti-inflammatory agents, diuretics, renin-angiotensin blocking agents). Participants taking medications that interfere with creatinine secretion (e.g. cimetidine or trimethoprim) were requested to consult with their physician to determine whether or not it is safe to discontinue medications affecting creatinine levels, and if so, were asked to stop the medications two days prior to the visit. An instruction sheet with details and pictures of the medications to stop were also provided. In addition, the study physicians obtained verbal permission from the subjects to call their physicians to confirm this. Non-diabetic subjects were asked to have a light meal the evening before and fast overnight before the morning of their study visit. Participants with diabetes were asked to eat a light breakfast the morning of the study visit. All participants were verbally instructed to pass urine into the container provided on the morning of their GFR study visit at home and bring it to the study center for measurement of albuminuria. All subjects were asked to drink two to three glasses of non-alcoholic, non-caffeinated beverages prior to arrival for the study visit.

On the day of the GFR visit, two intravenous lines (Optiva 2 venflon, gauge size 20) were inserted at two different sites. After taking the baseline blood sample, 5 mL of iohexol (Omnipaque 300; 300 mg/mL of organic iodine)[1] was administered by a nurse at the Icelandic Heart Association over a period of approximately 60 seconds through one of the IV ports, followed by a flush with approximately 10 mL of 0.9% normal saline solution.[2-6] A physician was present at the time of the iohexol injection. The IV line through which the iohexol was administered was removed. The syringe was weighted to the nearest tenth gram on the same scale before and after injection. Blood samples for plasma clearance measurements were obtained from the second IV line, which remained in place throughout the course of the study visit. Normal saline was administered through the second IV line after each blood draw to maintain patency. Before each blood draw, a small sample of blood was drawn and discarded before sample collection.

The administration of iohexol was considered time 0. Following the iohexol administration, blood samples were collected at approximately 120, 180, 240 and 300 minutes from the second IV line. The exact time of the sample was recorded. Participants were fed a standard lunch and were free to move around during the GFR test. The study nurse assessed study subjects approximately 1 hour following administration of the iohexol for the presence of adverse events (AE). Physician co investigators then determined whether the AE was related to the GFR protocol. After the final blood sample, the second IV line was removed; participants were observed for approximately 30 minutes before they returned home.

The iohexol dose was calculated from the difference in the syringe weights before and after administration of the iohexol multiplied by the concentration of iohexol divided by the density at room temperature (1.345 g/cm^3). GFR was calculated from plasma clearance of iohexol using the Brochner Mortensen equation[7]. GFR= 0.990778*(I/(expA/α))-(0.001218*(I/(expA/α))^2 where I is dose of the iohexol (mg), exp A is the intercept of the curve and α is its corresponding slope. GFR was multiplied by the ratio of 1.73 m^2/body surface area (BSA) in order to correct to 1.73 m^2 of BSA.

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6. Nilsson-Ehle, P, Grubb, A: New markers for the determination of GFR: iohexol clearance and cystatin C serum concentration. *Kidney Int Suppl,* 47**:** S17-19, 1994.
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B. Supplementary Tables

Table S1 Comparison of the median bias in eGFRcr for the CKD-EPI, Japanese and BIS equations by subgroups

	Age group			Sex		Diabetes		BMI group				mGFR category			
	< 80	**80-84**	**≥ 85**	**male**	**female**	**No**	**Yes**	**< 20**	**20-24**	**25-29**	**≥ 30**	**< 30**	**30-59**	**60-89**	**≥ 90**
N	402	279	124	355	450	615	190	10	185	457	153	28	286	458	33
CKD-EPI	-2.5 (-3.7, 1.6)	-2.7 (-3.9,-1.5)	-2.7 (-5.0,-1.7)	-1.4 (-2.3,-0.1)	-3.7 (-4.7,-2.7)	-2.8 (-3.8,-2.2)	-2.1 (-3.1,0.4)	-3.1 (-4.3,-2.0)	-2.5 (-3.3,-1.6)	-2.8 (-4.2,-1.7)	-1.8 (-3.8,1.8)	-2.2 (-4.1, 1.7)	-3.2 (-4.5, -2.1)	-3.0 (-4.2, -2.2)	9.1 (5.1, 11.1)
Japanese equation	12.6 (11.5,13.7)	9.9 (8.9,11.0)	6.9 (5.2,8.1)	10.9 (9.8,12.2)	10.0 (9.2,11.2)	10.6 (9.8,11.6)	10.0 (8.7,11.9)	10.4 (8.2,11.6)	10.8 (9.8, 1.9)	10.1 (8.9,12.8)	1.9 (0.6, 5.4)	1.9 (0.5, 4.4)	7.3 (6.7, 8.1)	13.5 (12.8, 14.3)	21.6 (17.4, 26.1)
BIS	6.6 (5.3,7.7)	5.7 (5.0,6.7)	4.3 (3.0,5.9)	7.9 (6.5, 9.3)	4.7 (3.4, 5.4)	5.8 (5.0, 6.8)	5.4 (3.6, 7.1)	6.1 (4.7, 7.9)	5.9 (4.9, 6.9)	5.3 (3.3, 7.1)	-3.8 (-4.7, -1.0)	-3.9 (-5.3, -1.1)	2.1 (1.3, 2.8)	9.2 (8.3, 10.4)	19.1 (16.7, 22.5)
Not different from CKD-EPI						Better than CKD-EPI					Worse than CKD-EPI				

Non-overlapping confidence intervals were considered to represent differences. Bias was calculated as mGFR-eGFR. Units for GFR and bias are ml/min/1.73 m^2.

To convert GFR from mL/min/1.73 m^2 to mL/s/1.73 m^2, multiply by 0.0167.

Table S2 Comparison of the median bias in eGFRcys for the CKD-EPI, Japanese and CAPA equations by subgroups

	Age group			Sex		Diabetes		BMI group				mGFR category			
	< 80	**80-84**	**≥ 85**	**male**	**female**	**No**	**Yes**	**< 20**	**20-24**	**25-29**	**≥ 30**	**< 30**	**30-59**	**60-89**	**≥ 90**
N	402	279	124	355	450	615	190	10	185	457	153	28	286	458	33
CKD-EPI	1.4 (0.0, 2.2)	3.2 (1.5, 4.6)	2.5 (0.7, 4.4)	1.7 (1.1, 3.0)	2.0 (0.8, 3.2)	1.4 (0.5, 2.2)	3.3 (2.1, 5.0)	-3.7 (-6.7, 4.0)	-0.8 (-2.5, 1.2)	1.7 (0.8, 2.7)	5.0 (3.9, 7.7)	2.1 (0.0, 4.0)	1.2 (0.0, 2.3)	2.4 (1.4, 3.4)	6.4 (-0.1, 11.8)
Japanese equation	4.1 (3.4, 5.3)	5.4 (4.0, 6.7)	4.8 (2.8, 6.5)	3.6 (2.8, 4.2)	5.7 (4.6, 6.5)	4.1 (3.4, 5.2)	6.1 (4.2, 7.4)	-0.8 (-7.1, 5.8)	2.8 (1.3, 4.0)	4.3 (3.5, 5.5)	8.3 (6.3,10.0)	3.5 (1.5, 5.3)	3.6 (2.6, 5.0)	5.7 (4.2, 6.8)	4.5 (-0.4, 16.6)
CAPA	-0.6 (-1.6, 0.5)	1.3 (0.1, 2.4)	-1.1 (-2.1, 0.4)	2.4 (1.3, 3.0)	-2.0 (-3.0, -1.1)	-0.6 (-1.5, 0.3)	1.4 (0.0, 2.6)	-4.7 (-8.6, 3.3)	-2.2 (-3.8, -1.3)	0.1 (-0.7, 1.0)	2.7 (1.1, 4.2)	0.3 (-2.9, 1.9)	-2.0 (-3.1, -0.7)	0.9 (0.0, 1.6)	5.4 (1.0, 11.5)
No difference than CKD-EPI						Better than CKD-EPI						Worse than CKD-EPI			

Non-overlapping confidence intervals were considered to represent differences. Bias was calculated as mGFR-eGFR. Units for GFR and bias are ml/min/1.73 m^2.

To convert GFR from mL/min/1.73m^2 to mL/s/1.73m^2, multiply by 0.0167.

Table S3 Comparison of the median bias in eGFRcr-cys for the CKD-EPI, Japanese, and BIS equations by subgroups

	Age group			Sex		Diabetes		BMI group				mGFR category			
	< 80	**80-84**	**≥ 85**	**male**	**female**	**No**	**Yes**	**< 20**	**20-24**	**25-29**	**≥ 30**	**< 30**	**30-59**	**60-89**	**≥ 90**
N	402	279	124	355	450	615	190	10	185	457	153	28	286	458	33
CKD-EPI	-1.2 (-2.0,-0.3)	0.4 (-0.5, 1.3)	-0.6 (-2.0, 0.9)	-0.1 (-1.0, 0.5)	-0.9 (-1.9, 0.0)	-0.9 (-1.7, -0.1)	0.5 (-0.4, 1.4)	-5.8 (-8.3,-0.1)	-2.0 (-3.5,-1.3)	-0.2 (-1.1, 0.4)	1.6 (0.5, 3.1)	1.4 (-1.0, 2.9)	-0.6 (-1.6, 0.4)	-1.1 (-1.9, -0.1)	4.9 (0.9, 7.9)
Japanese equation	8.7 (8.0,9.5)	8.2 (7.3, 9.1)	6.4 (5.8, 8.1)	8.0 (7.1, 8.8)	8.4 (7.8, 9.2)	8.1 (7.6, 8.7)	8.7 (7.4, 9.8)	2.8 (0.4, 6.1)	6.4 (5.6, 8.0)	8.4 (7.9, 8.9)	9.7 (8.4, 11.4)	3.8 (2.4, 5.2)	6.4 (5.8, 7.3)	9.8 (8.9, 10.3)	15.4 (9.5, 19.3)
BIS	6.0 (5.1, 6.9)	5.3 (4.6, 6.6)	4.3 (2.3, 5.5)	5.9 (5.3, 6.8)	4.8 (4.0, 6.0)	5.3 (4.8, 6.1)	5.7 (4.5, 7.5)	0.4 (-1.4, 5.5)	4.3 (3.2, 6.0)	5.4 (4.9, 6.2)	7.4 (5.3, 8.6)	-1.5 (-3.1, -0.3)	2.2 (1.5, 2.8)	8.0 (7.3, 8.8)	16.0 (13.3, 20.0)
No difference than CKD-EPI						Better than CKD-EPI						Worse than CKD-EPI			

Non-overlapping confidence intervals were considered to represent differences. Bias was calculated as mGFR-eGFR. Units for GFR and bias are ml/min/1.73 m^2.

To convert GFR from mL/min/1.73m^2 to mL/s/1.73m^2, multiply by 0.0167.

Table S4 Comparison the performance of CKD-EPI equations in the entire cohort

Equations	Bias Median Difference (95% CI)	Precision IQR (95% CI)	Accuracy P_{30} (95% CI)	Accuracy RMSE (95% CI)
eGFRcr-cys	-0.6 (-1.2, 0.1)	10.2 (9.0, 11.1)	96.1 (94.8, 97.4)	0.137 (0.128, 0.145)
eGFRcr	-2.7 (-3.3, -2.1)	12.1 (11.2, 13.4)	91.7 (89.8, 93.4)	0.165 (0.154, 0.177)
eGFRcys	1.9 (1.3, 2.8)	11.4 (10.7, 12.5)	93.7 (91.9, 95.3)	0.167 (0.157, 0.178)

Not different from eGFRcr-cys   Better than eGFRcr-cys   Worse than eGFRcr-cys

Non-overlapping confidence intervals were considered to represent differences. Bias was calculated as the median value of (mGFR-eGFR). IQR, interquartile range of the difference between mGFR and eGFR. P_{30}, percentage of eGFR within 30% of mGFR. RMSE, the root mean squared error for the regression of log mGFR on log eGFR. Units for GFR, bias and IQR are mL/min/1.73 m^2.

To convert GFR from mL/min/1.73m^2 to mL/s/1.73m^2, multiply by 0.0167.

Table S5 Comparison the performance of the Japanese equations in the entire cohort

Equations	Bias Median Difference (95% CI)	Precision IQR (95% CI)	Accuracy P_{30} (95% CI)	Accuracy RMSE (95% CI)
eGFRcr-cys	8.2 (7.7, 8.7)	9.0 (8.2, 10.0)	93.0 (91.2, 94.8)	0.204 (0.195, 0.212)
eGFRcr	10.5 (9.8, 11.2)	10.9 (9.7, 12.1)	86.3 (83.9, 88.6)	0.251 (0.241, 0.263)
eGFRcys	4.6 (3.8, 5.6)	11.2 (10.2, 12.3)	92.8 (90.9, 94.5)	0.189 (0.179, 0.200)

Not different from eGFRcr-cys | Better than eGFRcr-cys | Worse than eGFRcr-cys

Non-overlapping confidence intervals were considered to represent differences. Bias was calculated as the median value of (mGFR-eGFR). IQR, interquartile range of the difference between mGFR and eGFR. P_{30}, percentage of eGFR within 30% of mGFR. RMSE, the root mean squared error for the regression of log mGFR on log eGFR. Units for GFR, bias and IQR are mL/min/1.73 m^2.

To convert GFR from mL/min/1.73m^2 to mL/s/1.73m^2, multiply by 0.0167.

Table S6 Comparison the performance of the BIS equations in the entire cohort

Equations	Bias Median Difference (95% CI)	Precision IQR (95% CI)	Accuracy P_{30} (95% CI)	Accuracy RMSE (95% CI)
eGFRcr-cys	5.3 (4.9, 6.1)	9.6 (8.6, 10.4)	97.9 (96.8, 98.8)	0.152 (0.145, 0.158)
eGFRcr	5.7 (5.1, 6.4)	11.9 (10.6, 12.7)	95.8 (94.4, 97.1)	0.178 (0.169, 0.187)

Not different from eGFRcr-cys	Better than eGFRcr-cys	Worse than eGFRcr-cys

Non-overlapping confidence intervals were considered to represent differences. Bias was calculated as the median value of (mGFR-eGFR). IQR, interquartile range of the difference between mGFR and eGFR. P_{30}, percentage of eGFR within 30% of mGFR. RMSE, the root mean squared error for the regression of log mGFR on log eGFR. Units for GFR, bias and IQR are mL/min/1.73 m^2.

To convert GFR from mL/min/1.73m^2 to mL/s/1.73m^2, multiply by 0.0167.

Table S7 Comparison the performance of all equations to the CKD-EPI creatinine-cystatin C equation in the entire cohort by research groups

	Bias Median Difference (95% CI)	Precision IQR (95% CI)	Accuracy P_{30} (95% CI)	Accuracy RMSE (95% CI)
CKD-EPI				
eGFRcr-cys	-0.6 (-1.2, 0.1)	10.2 (9.0, 11.1)	96.1 (94.8, 97.4)	0.137 (0.128, 0.145)
eGFRcr	-2.7 (-3.3, -2.1)	12.1 (11.2, 13.4)	91.7 (89.8, 93.4)	0.165 (0.154, 0.177)
eGFRcys	1.9 (1.3, 2.8)	11.4 (10.7, 12.5)	93.7 (91.9, 95.3)	0.167 (0.157, 0.178)
Japanese equation				
eGFRcr-cys	8.2 (7.7, 8.7)	9.0 (8.2, 10.0)	93.0 (91.2, 94.8)	0.204 (0.195, 0.212)
eGFRcr	10.5 (9.8, 11.2)	10.9 (9.7, 12.1)	86.3 (83.9, 88.6)	0.251 (0.241, 0.263)
eGFRcys	4.6 (3.8, 5.6)	11.2 (10.2, 12.3)	92.8 (90.9, 94.5)	0.189 (0.179, 0.200)
BIS				
eGFRcr-cys	5.3 (4.9, 6.1)	9.6 (8.6, 10.4)	97.9 (96.8, 98.8)	0.152 (0.145, 0.158)
eGFRcr	5.7 (5.1, 6.4)	11.9 (10.6, 12.7)	95.8 (94.4, 97.1)	0.178 (0.169, 0.187)
CAPA				
eGFRcys	0.1 (-0.7, 0.6)	11.8 (10.8, 12.9)	94.4 (92.8, 95.9)	0.157 (0.147, 0.168)

No difference than CKD-EPI eGFRcr-cys	Better than CKD-EPI eGFRcr-cys	Worse than CKD-EPI eGFRcr-cys

Non-overlapping confidence intervals were considered to represent differences. Bias was calculated as the median value of (mGFR-eGFR). IQR, interquartile range of the difference between mGFR and eGFR.P_{30}, percentage of eGFR within 30% of mGFR. RMSE, the root mean squared error for the regression of log mGFR on log eGFR. Units for GFR, bias and IQR are mL/min/1.73 m^2.To convert GFR from mL/min/1.73m^2 to mL/s/1.73m^2, multiply by 0.0167.

Table S8 GFR estimation equations

Research group	GFR Measurement Method	Endogenous Filtration markers	Equation
CKD-EPI	Urinary clearance of ^{125}I-iothalamate	Creatinine	eGFR= 141 $\times$ min(Scr/κ, 1)$^{\alpha}$ $\times$ max(Scr/κ, 1)$^{-1.209}$ $\times$ 0.993^{Age} [$\times$ 1.018 if female] [$\times$ 1.159 if black] where Scr is serum creatinine, κ is 0.7 for females and 0.9 for males, α is −0.329 for females and −0.411 for males, min is the minimum of Scr/κ or 1, and max is the maximum of Scr/κ or 1.
		Cystatin C	eGFR= 133 $\times$ min(Scys/0.8, 1)$^{-0.499}$ $\times$ max(Scys/0.8, 1)$^{-1.328}$ $\times$ 0.996^{Age} [$\times$ 0.932 if female] where Scys is serum cystatin C, min indicates the minimum of Scr/κ or 1, and max indicates the maximum of Scys/κ or 1.
		Creatinine and Cystatin C	eGFR= 135 $\times$ min(Scr/κ, 1)$^{\alpha}$ $\times$ max(Scr/κ, 1)$^{-0.601}$ $\times$ min(Scys/0.8, 1)$^{-0.375}$ $\times$ max(Scys/0.8, 1)$^{-0.711}$ $\times$ 0.995^{Age} [$\times$ 0.969 if female] [$\times$ 1.08 if black] where Scr is serum creatinine, Scys is serum cystatin C, κ is 0.7 for females and 0.9 for males, α is −0.248 for females and −0.207 for males, min indicates the minimum of Scr/κ or 1, and max indicates the maximum of Scr/κ or 1.
Japanese	Urinary clearance of inulin	Creatinine	eGFR= 194 $\times$ Creatinine$^{-1.094}$ $\times$ Age$^{-0.287}$ $\times$ 0.739 [if female]
		Cystatin C	eGFR= 96 $\times$ Cystatin C$^{-1.324}$ $\times$ 0.996^{Age} $\times$ 0.894 [if female]
		Creatinine and Cystatin C	eGFR= 92 $\times$ Cystatin C$^{-0.575}$ $\times$ Creatinine$^{-0.670}$ $\times$ 0.995^{Age} $\times$ 0.784 [if female]
BIS	Plasma clearance of iohexol	Creatinine	eGFR= 3736 $\times$ Creatinine$^{-0.87}$ $\times$ Age$^{-0.95}$ $\times$ 0.82 [if female]
		Creatinine and cystatin C	eGFR= 767 $\times$ Cystatin C$^{-0.61}$ $\times$ Creatinine$^{-0.40}$ $\times$ Age$^{-0.57}$ $\times$ 0.87 [if female]

CAPA	Plasma clearance of iohexol, plasma clearance of ^{51}Cr-EDTA, urinary clearance of inulin	Cystatin C	eGFR= $130 \times \text{Cystatin C}^{-1.069} \times \text{Age}^{-0.117} - 7$

Units for eGFR, serum creatinine and cystatin C are mL/min/1.73m^2, mg/dL and mg/L, respectively.