Performance of the CKD-EPI equation in estimating glomerular filtration rate change over time in people with diabetes

Dr Digsu Koye
Senior Research Fellow
Melbourne School of Population and Global Health
University of Melbourne, Australia
✉ digsu.koye@unimelb.edu.au

Kidney function measurement

- Glomerular filtration rate (GFR) is an important indicator of kidney function[1]
- GFR can be measured by clearance of exogenous filtration markers (inulin or iohexol) or indirectly by estimation of clearance of endogenous markers (serum creatinine or cystatin C)
- Direct measurement of kidney function – impractical, invasive, expensive and not routinely performed.
- More than 60 creatinine or cystatin C based eGFR measurements[2]
- eGFR is the commonly used in clinical practice and current guidelines recommend the 2021 CKD-EPI equation[3]

1. Kwok R et al. Diabetes Australia 2022
2. Porrini E *Nature Reviews Nephrology 2109; 15(3): 177-90*
3. Inker LA et al. N Engl J Med. 385(19): 1737-1749

CKD-EPI Equations

CKD-EPI 2009 equation

- Developed in 2009 to address the limitations of the Modification of Diet in Renal Disease (MDRD) equation
- Wide demographic and large pooled populations from multiple studies
- 10 studies (developmental) and 16 studies (validation)
- GFR is estimated using age, sex, race and serum creatinine levels

CKD-EPI 2021 equation (race free)

- Race is considered a social not a biological construct
- 10 studies (developmental) and 13 studies (validation)

Levey AS et al. Ann Intern Med. 2009;150(9):604-12; Inker LA et al. N Engl J Med. 385(19): 1737-1749

SYSTEMATIC REVIEW OR META-ANALYSIS

Evaluation of the diagnostic performance of the creatinine-based Chronic Kidney Disease Epidemiology Collaboration equation in people with diabetes: A systematic review

N. Zafari, L. Churilov, L. Y.-L. Wong, M. Lotfaliany, M. Hachem, K. V. Kiburg, L. Kong, N. Torkamani, H. Baxter, R. J. MacIsaac, E. I. Ekinci

Key findings

- 29 papers identified (2009 – 2019)
- CKD-EPI underperforms in people with diabetes
- Inconsistency in the literature regarding measures to evaluate the diagnostic performance of the CKD-EPI 2009 equation

Individual participant data meta-analysis

		Agreement	Bias (CKD-EPI* - mGFR)	Precision	Accuracy	
Study	**N**	**ICC (95% CI)**	**Mean difference (95% CI)**	**SD**	**P10**	**P30**
DCCT, USA	1,339	0.35 (0.32, 0.38)	1.82 (1.07, 2.57)	13.61	46%	89%
Germany	173	0.85 (0.80, 0.87)	9.06 (7.33, 10.79)	8.22	24%	71%
Spain	605	0.84 (0.82, 0.86)	5.31 (3.76, 6.85)	13.68	24%	65%
Korea	850	0.79 (0.76, 0.81)	2.71 (1.38, 4.04)	14.02	28%	70%
Australia	2,167	0.81 (0.79, 0.82)	15.24 (14.70, 15.79)	12.29	22%	59%
Overall	3,795	0.82 (0.79, 0.84)	12.04 (11.55, 12.53)	17.6	23%	61%

DCCT – Diabetes Control and Complications Trial; ICC – Intraclass correlation coefficient
mGFR – measured GFR; P30 – percentage of estimated GFR within 30% of measured GFR
*CKD-EPI 2021 equation

Aims

To evaluate the performance of CKD-EPI GFR estimation equations (2009 and the race free 2021) compared to direct measures of GFR over time in people with diabetes.

Methods

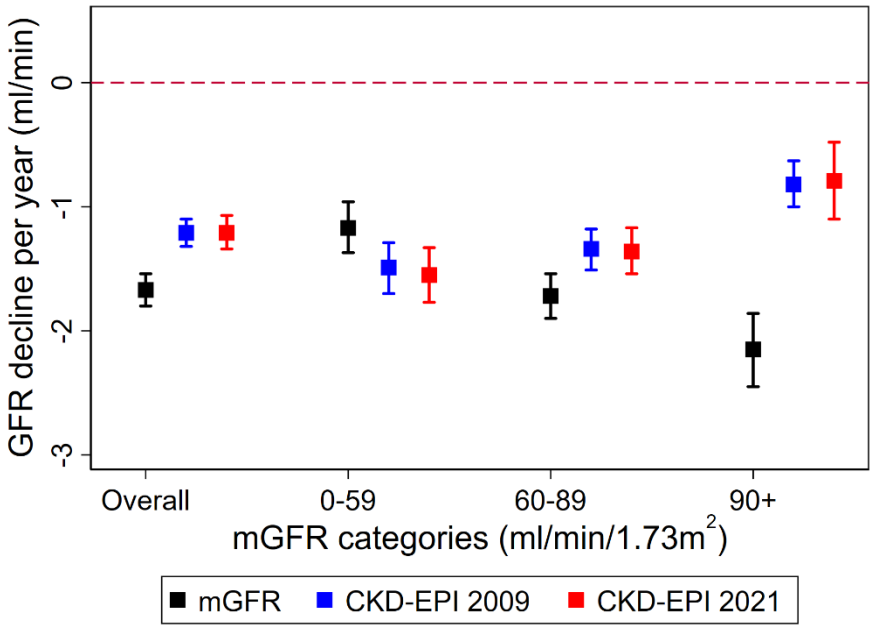
- Participants with type 1 and type 2 diabetes attending Austin Health in Melbourne, Australia.
- With at least two or more GFR measurements between July 2002 and September 2022.
- Measured GFR (mGFR) was calculated using the plasma disappearance rate of diethylene-triamine-penta-acetic acid (DTPA).
- Estimated GFR was calculated using both the 2009 and 2021 CKD-EPI equations.
- Absolute GFR slopes for mGFR, CKD-EPI 2009 and CKD-EPI 2021 were calculated for the overall population and stratified by clinically relevant mGFR categories using mixed-effects linear regression models.

Baseline characteristics

	N = 786
Age (years)	61 (13)
Male sex	476 (61%)
BMI(kg/m^2)	30 (26-34)
HbA1c (%)	7.4 (6.8-8.2)
Systolic blood pressure (mmHg)	133 (22)
Type 2 diabetes	637 (81%)
CKD-EPI eGFR 2009 ($ml/min/1.73m^2$)	78 (62-94)
CKD-EPI eGFR 2021 ($ml/min/1.73m^2$)	83 (66-99)
Measured GFR ($ml/min/1.73m^2$)	68 (51-85)

- Participants had a median of 3 (IQR: 2-4) repeated mGFR measurements
- Over a median follow-up of 5.1 (IQR: 2.5-8.5) years.

Rate of GFR decline



Rate of GFR decline (ml/min/1.73m^2 per year) by mGFR categories at baseline. Error bars corresponds to the 95%CI

Conclusion

- Both the 2009 and 2021 CKD-EPI equations consistently underestimated the rate of GFR decline over time in people with diabetes.
- When considering clinically relevant mGFR categories, both the 2009 and 2021 CKD-EPI equations tended to overestimate GFR slopes at lower mGFR values and underestimate at higher GFR values.
- There is a need for research on development of more precise methods to estimate kidney function for people with diabetes.

RenoTrue™

A clinical decision support tool empowering clinicians with precise estimation of kidney function for people living with diabetes

- **6 international collaborators**
- **>10,000 datapoints**
- **Direct measurements of kidney function**
- **Machine learning algortihm**

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Co-authors

- Rodney Kwok
- Kartik Kishore
- Tina Zafari
- Richard MacIsaac
- Leonid Churilov
- Elif Ekinci