Implementation of the 2021 CKD-EPI eGFR$_{cr}$ Equation Re-fit without Race Co-efficient
M.J. Lewis
Senior Project Director, CKDintercept
National Kidney Foundation
Email: MJ.Lewis@kidney.org

April 13, 2023
Kidney Disease in the United States

• An estimated 37 million adults have CKD but nearly 90% are unaware
  – < 30% with diabetes & only 10% with hypertension receive guideline-concordant assessment

• CKD is a disease multiplier - nearly 50% with CKD die from CVD before reaching ESRD
  – Adverse outcomes: heart failure, coronary artery disease & premature cardiovascular death

• Diabetes, hypertension & CKD disproportionately impact communities of color
  – Lower access to nephrology care, home dialysis & kidney transplant

Szczech et al. Primary Care Detection of Chronic Kidney Disease in Adults with Type-2 Diabetes: The ADD-CKD Study (Awareness, Detection and Drug Therapy in Type 2 Diabetes and Chronic Kidney Disease). PLoS ONE 9(11): e110535.


CDC CKD Surveillance System

In 2020, the National Kidney Foundation (NKF) & the American Society of Nephrology (ASN) created a task force to reassess inclusion of race in the estimation of glomerular filtration rate (eGFR)

**September 23, 2021**
Task Force Recommendations published in *American Journal of Kidney Disease*
Getting from Recommendations to Implementation

The Laboratory Engagement Work Group created guidance to facilitate laboratory implementation of Task Force Recommendations.

Guidance included:

- Communications
- Assay
- Programming
- Results
- Complementary testing
Getting from Recommendations to Implementation

Educational materials & tools for professionals & patients were uploaded to www.kidney.org

The NKF would like to thank its Laboratory Engagement Initiative Workgroup for their efforts to develop tools to support laboratories implementing this new approach to calculating eGFR.

1. Position Statement: U.S. Pathology & Laboratory Society Leadership Endorse Use of CKD-EPI 2021 Race-free Equations for eGFR
2. eGFR summary for ordering clinicians
3. Not by Muscle, Race or Ethnicity: Practical use of Cystatin C to estimate GFR
4. eGFR Results Messages
5. eGFR 2021 CKD EPI creatinine equation that estimates kidney function without a race variable in NEJM paper
6. NKF-ASN Task Force final report
7. FAQs About GFR Estimates
8. Laboratory guidance for implementing CKD-EPI 2021 race-free eGFR equations
9. Patient information about kidney disease and eGFR testing

https://www.kidney.org/content/laboratory-implementation-nkf-asn-task-force-reassessing-inclusion-race-diagnosing-kidney
### Getting from Recommendations to Implementation

#### Laboratory Organizations

<table>
<thead>
<tr>
<th>Organization</th>
<th>Organization</th>
</tr>
</thead>
<tbody>
<tr>
<td>Academy of Clinical Laboratory Physicians &amp; Scientists (ACLPS)</td>
<td>Clinical Laboratory Management Association (CLMA)</td>
</tr>
<tr>
<td>American Association for Clinical Chemistry (AACC)</td>
<td>COLA Inc</td>
</tr>
<tr>
<td>American Association of Bioanalysts (AAB)</td>
<td>College of American Pathologists (CAP)</td>
</tr>
<tr>
<td>American Society for Clinical Pathology (ASCP)</td>
<td>National Independent Laboratory Association (NILA)</td>
</tr>
<tr>
<td>Association of Pathology Chairs (APC)</td>
<td>Society of American Federal Medical Laboratory Scientists (SAFMLS)</td>
</tr>
</tbody>
</table>

**U.S. Pathology & Laboratory Societies Endorse 2021 CKD-EPI eGFR Equations**

https://www.cap.org/publications/cap-today
Getting from Recommendations to Implementation

- NKF organized Pharmacy Engagement Workgroup to address medication-related decisions associated with the 2021 CKD-EPI eGFRcr Race-free Equation
- “Laboratory Implementation of Recommendations from the NKF-ASN Task Force Reassessing the Inclusion of Race in Diagnosing Kidney Disease” presented at the annual 2022 AACC Scientific Assembly
- NKF collaboration with American Association for Clinical Chemistry Academy on in-depth guidance on 2021 CKD-EPI eGFR Implementation

S2344 Why Should Pathologists Care About the CKD-EPI 2021 Race-Free eGFR Equations?
Getting from Recommendations to Implementation

- In collaboration with ASCP & APC, NKF surveyed their members September – October, 2022:
  - Most aware of the new equation
  - Nearly all commercial reference labs & some HHS labs had implemented the new equation
  - Roughly 30 – 50% planning implementation 7/1 – 12/31, 2022
  - Approximately 25 – 44% planning implementation in 2023
- Survey findings align directionally with those of CAP’s survey published in November (JAMA November 22/29, 2022 Vol 328, No 20: 2060-2062)
• It is a starting point to drive kidney health equity
• It is an opportunity to standardize to a single equation, eliminating differences in eGFR due to different equations used by different laboratories
• Clinicians and their patients are best served when labs report standardized results across all communities regardless of where patients are tested
• Use of a standardized eGFR equation is important in clinical practice, research, and public health
THANK YOU
Implementation of the CKD-EPI 2021 eGFR Equation Refit without the Race Coefficient

Jonathan Genzen, MD, PhD

Professor (Clinical), University of Utah
Chief Medical Officer, ARUP Laboratories
About the Presenter

- **Professor**, University of Utah, Department of Pathology
- **Chief Medical Officer**, ARUP Laboratories
- **Participant**, National Kidney Foundation Laboratory Engagement Workgroup
- **Chair**, Clinical Chemistry Committee, College of American Pathologists

ARUP is a non-profit clinical laboratory enterprise of the University of Utah Department of Pathology
Estimated Glomerular Filtration Rate (eGFR)

- Based on creatinine (Cr) measurement (a waste product of muscle breakdown)
- Filtered by the kidney
- Cr assays are often standardized to IDMS*-traceable methods (comparable across labs)

*Isotope dilution mass spectrometry
Estimated Glomerular Filtration Rate (eGFR)

https://www.kidney.org/atoz/content/gfr
Estimated Glomerular Filtration Rate (eGFR)

- eGFR is a **calculation**

**Example**
- 2009 CKD Epidemiology Collaboration (CKD-EPI)¹

\[
eGFR = 141 \times \min \left( \frac{Scr}{\kappa}, 1 \right) \alpha \times \max \left( \frac{Scr}{\kappa}, 1 \right) - 1.209 \times 0.993 \text{Age} \times 1.018 \text{[if female]} \times 1.159 \text{[if black]}
\]

**Impact of the Equation**

<table>
<thead>
<tr>
<th>↑ Cr</th>
<th>↑ Age</th>
<th>Female</th>
<th>Black</th>
</tr>
</thead>
<tbody>
<tr>
<td>↓ eGFR</td>
<td>↓ eGFR</td>
<td>↓ eGFR</td>
<td>↑ eGFR</td>
</tr>
</tbody>
</table>

Race Adjustment Factors

• Originally incorporated to account for increased average plasma Cr concentrations in individuals who self-identified or were categorized as Black / African American.

• These populations have a 3.7-fold greater prevalence of end stage renal disease

• Race is a social, not a biological construct

Implications

• Classification of CKD Stage
• Organ Transplant Donor / Recipient Eligibility
• Medication Dosing
• Treatment Options

Source: 2021 CAP Position Statement on eGFR
A Push for Race-Free Equations

• 2020

• National Kidney Foundation (NKF) and American Society of Nephrology (ASN) Task Force was formed to develop future recommendations.

2021

New Equations Developed and Published\(^1\)

‘2021 CKD-EPI Creatinine’
‘2021 CKD-EPI Creatinine-Cystatin C’

• 2021

• NKF/ASN Task Force Recommendations Published\(^2\)
  • Implement ‘2021 CKD-EPI creatinine’ equation in all laboratories
  • Facilitate use of cystatin C in individuals at increased risk of CKD
  • Further research on eGFR with new markers to eliminate race and ethnic disparities


3. 2021 CAP Position Statement on eGFR
Survey of New Equation Adoption

College of American Pathologists
  » Clinical Chemistry Committee
  » Instrumentation Committee

Educational Questionnaire in Proficiency Testing Survey
  » Survey included in March 2022 CAP Chemistry A Survey
  » Distributed to 6,317 clinical laboratories
  » Final dataset include 4,298 surveys
  » 86.5% US, 13.5% international

JAMA. 2022 Nov 22;328(20):2060-2062
Genzen JR, Souers RJ, Pearson LN, Manthei DM, Chambliss AB, Shajani-Yi Z, Miller WG.

College of American Pathologists, University of Utah/ARUP Laboratories, University of Michigan, University of Southern California, LabCorp, Virginia Commonwealth University
Questions

1. Is your laboratory aware of the 2021 CKD-EPI equations for eGFR that do not include race adjustment factors?

<table>
<thead>
<tr>
<th>US Laboratories No. (%)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>2859 (76.9)</td>
</tr>
<tr>
<td>No</td>
<td>859 (23.1)</td>
</tr>
<tr>
<td>Total</td>
<td>3718</td>
</tr>
</tbody>
</table>

Questions

2. Has your laboratory adopted the 2021 CKD-EPI creatinine equation for eGFR reporting?

<table>
<thead>
<tr>
<th></th>
<th>US Laboratories No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>1124 (30.3)</td>
</tr>
<tr>
<td>No</td>
<td>2059 (55.5)</td>
</tr>
<tr>
<td>Unsure</td>
<td>525 (14.2)</td>
</tr>
<tr>
<td>Total</td>
<td>3708</td>
</tr>
</tbody>
</table>

3. **When** does your laboratory plan to adopt the 2021 CKD-EPI creatinine equation for eGFR reporting?

<table>
<thead>
<tr>
<th></th>
<th>US Laboratories No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before July 1, 2022</td>
<td>440 (21.6)</td>
</tr>
<tr>
<td>Between July 1 and December 31, 2022</td>
<td>218 (10.7)</td>
</tr>
<tr>
<td>2023 or later</td>
<td>45 (2.2)</td>
</tr>
<tr>
<td>Unsure</td>
<td>1187 (58.4)</td>
</tr>
<tr>
<td>Not applicable; do not plan to implement this equation</td>
<td>144 (7.1)</td>
</tr>
<tr>
<td>Total</td>
<td>2034</td>
</tr>
</tbody>
</table>
4. Does your laboratory plan to adopt the 2021 CKD-EPI creatinine-cystatin C equation for eGFR reporting?

<table>
<thead>
<tr>
<th>Response</th>
<th>US Laboratories No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>292 (8.0)</td>
</tr>
<tr>
<td>No</td>
<td>1174 (32.0)</td>
</tr>
<tr>
<td>Unsure</td>
<td>2082 (56.7)</td>
</tr>
<tr>
<td>Not applicable; we have already implemented this equation</td>
<td>123 (3.4)</td>
</tr>
<tr>
<td>Total</td>
<td>3671</td>
</tr>
</tbody>
</table>

5. Are there any **barriers** impacting your laboratory’s consideration or adoption of the 2021 CKD-EPI creatinine-cystatin C equation for eGFR reporting (multiple responses allowed)?

<table>
<thead>
<tr>
<th>US Laboratories No. (%)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Limited cystatin C testing options</td>
<td>1310 (58.5)</td>
</tr>
<tr>
<td>Cost of testing</td>
<td>523 (23.4)</td>
</tr>
<tr>
<td>Staffing resources</td>
<td>519 (23.2)</td>
</tr>
<tr>
<td>Patient population</td>
<td>257 (11.5)</td>
</tr>
<tr>
<td>Other</td>
<td>448 (20.0)</td>
</tr>
<tr>
<td>Total respondents</td>
<td>2239</td>
</tr>
</tbody>
</table>

Conclusions

- **New equations** are available that eliminate the race adjustment factor from eGFR
  - 2021 CKD-EPI Creatinine
  - 2021 CKD-EPI Creatinine-Cystatin C
- **Adoption** of these equations is occurring widely across clinical laboratory settings
- **Practical guidance** exists to facilitate adopting the equations
- A **repeat survey** is currently being conducted to assess further increase in adoption since March 2022.

Questions?

jonathan.genzen@aruplab.com