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CKD intercept

U.S. Pharmacy Organizations Endorse Transition from Cockcroft-Gault Estimated Creatinine Clearance to the 2021 CKD-EPI Equation for Estimated Glomerular Filtration Rate to Improve Medication-related Decision-making in Adults Across Healthcare Settings

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Approximately 70% of healthcare decisions are based on laboratory tests, making standardized testing methodologies and results critically important to care quality. Accurate assessment of kidney filtration is essential for medication management because it directly affects medication clearance, dosing safety, treatment effectiveness, and toxicity risk. Historically, the Cockcroft-Gault estimated creatinine clearance (C-G eCrCL) equation guided medication dosing, while estimated glomerular filtration rate (eGFR) informed diagnosis and staging of chronic kidney disease (CKD). Transitioning from C-G eCrCL to the race-agnostic 2021 CKD-EPI eGFR equation for medication decisions aligns with standardized testing practices and advances care quality.

The C-G eCrCL was developed with data from 249 white males, employing an estimated 15% adjustment for females, and validated using measured creatinine clearance - which is known to overestimate measured GFR (mGFR). Current eGFR equations have been validated against mGFR, the current standard for assessing kidney filtration, and in thousands of people representing broader, more diverse patient populations. In addition, the C-G eCrCL equation was developed at a time when serum creatinine assays were not standardized. By 2011 most serum creatinine assays had been standardized to an isotope dilution mass spectrometry (IDMS) reference measurement, with the average serum creatinine value decreasing by 12% and large variability in impact between laboratories. Consequently, today's C-G eCrCL values (on average) are higher than those obtained during the pharmacokinetic studies used to create dosing recommendations prior to 2011.

In addition to these limitations, consideration must also be given to modifications employed to adapt C-G eCrCL for current practice:

- The average body weight of the U.S. population has increased since its introduction. As a result, application of total body weight or any single body weight parameter across the current body size or weight spectrum has been shown to reduce C-G eCrCL accuracy.
- Body weight parameters are inconsistently applied among clinicians, institutions, and across practice settings, leading to significant variability in results and interpretation.
- Recent data show the 2021 CKD-EPIcr eGFR equation adjusted for body surface area (BSA) more accurately predicts clearance of four medications predominantly cleared by kidneys (i.e. vancomycin, cefepime, meropenem, aminoglycosides) than C-G eCrCL using total body weight or a variable dosing weight.
- Many pharmacists incorporate adaptations for older age. These commonly include use of highly variable criteria to empirically inflate a patient's serum creatinine when it is below normal range (although clear evidence refutes this empiric adjustment). This also contributes to the variability observed in C-G eCrCL results across the U.S.

- Increasingly, pharmaceutical companies are using eGFR in pharmacokinetic studies, resulting in an increase in eGFR-based dosing recommendations. The U.S. Food and Drug Administration (FDA) final 2024 guidance for industry recommending "use of eGFR to determine renal function in pharmacokinetic (PK) studies... over eCLcr [eCrCL]" and the use of BSA-adjusted results in mL/min will likely accelerate the transition.

Transitioning from C-G eCrCL to BSA-adjusted eGFR provides pharmacists across all practice settings with a consistent, accurate, and equitable foundation for kidney-related medication decisions. It can also enhance collaboration with other prescribers, simplify patient counseling, improve chronic disease management, and ultimately advance safe and effective medication use.

Consensus:

The pharmacy community noted below supports transitioning from the Cockcroft-Gault eCrCL equation to the race-agnostic 2021 CKD-EPIcr eGFR equation (with results adjusted for body surface area) as the preferred creatinine-only equation for estimating kidney function in adults for medication-related decisions. During this transition, exceptions may be warranted for ongoing clinical trials with narrow therapeutic index medications, where protocols specify an alternate, required method for estimation of GFR. This transition will align with standardized testing practices, improve dosing accuracy, reduce variability, and enhance patient safety and care quality across healthcare settings.

- ***American Association of Colleges of Pharmacy (AACP)***
- ***American College of Clinical Pharmacy (ACCP)***
- ***American Pharmacists Association (APhA)***
- ***American Society of Health-System Pharmacists (ASHP)***
- ***Hematology/Oncology Pharmacy Association (HOPA)***

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