

# Drug Dosage Adjustment Using Renal Estimation Equations: A Review of the Literature

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## Abstract

**Purpose:** To examine the factors affecting drug clearance and the available evidence for drug dosing based on the Cockcroft-Gault (CG) equation and the abbreviated Modification of Diet in Renal Disease (abbrMDRD) equation. Factors that would distort the accuracy of these formulas and the affect of this distortion on the use of either formula in drug dosage adjustment were reviewed.

**Methods:** An updated review of the literature was performed that pertained to the accuracy of the CG and abbrMDRD equations and their use in drug dosage adjustment. *MEDLINE* was searched using the OVIDSP database, from the inception of the database (1950) through June 2008.

**Discussion:** To cover the major issues concerning the use of renal estimation equations in drug dosing adjustment, various areas were examined. Topics included the accuracy of the CG and abbrMDRD formulas, variability in these equations because of patient and laboratory factors, the isotope dilution–mass spectrometry standardization initiative, and the applicability of each formula to modifying medication doses.

**Conclusion:** Although the abbrMDRD equation has many advantages as compared with the CG equation, too little research has been completed at this time to recommend the clinical use of the abbrMDRD equation in pharmacy practice.

**Key Words**—Cockcroft-Gault, creatinine clearance, glomerular filtration rate, MDRD

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stages of CKD and equivalent GFR. Data from the National Health and Nutrition Examination Survey (NHANES IV) show that approximately 16.8% of those in the US population who are 20 years of age or older are living with CKD.<sup>2</sup> This is compared with 14.5% from the NHANES III data.<sup>2</sup> In addition, the quickly expanding elderly population has age-specific reductions in GFR.<sup>1,4</sup> Fortunately, national recognition of CKD has increased over the past decade and has yielded a new renal estimation equation, which has been incorporated into CKD practice guidelines.<sup>1</sup> These guidelines clearly express how and why clinicians should use the abbreviated Modification of Diet in Renal Disease equation (abbrMDRD) to stage CKD, but they do not describe how the equation should be used for drug dosage initiation and adjustment.<sup>1</sup> In fact, the guidelines state that “clinical conditions in which it may be necessary to measure GFR by using clearance methods include ... calculation of the dose of potentially toxic drugs that are excreted by the kidneys.”<sup>1</sup> Clearance methods are defined as measuring the urinary clearance of

## INTRODUCTION

Chronic kidney disease (CKD) has become a rapidly growing epidemic in the United States and around the world.<sup>1,2</sup> The National Kidney Foundation defines CKD as

“either the presence of kidney damage or glomerular filtration rate (GFR) less than 60 mL/min/1.73 m<sup>2</sup> for 3 or more months and can be diagnosed without knowledge of its cause.”<sup>3</sup> Table 1 illustrates the

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**Table 1. National Kidney Foundation Kidney Disease Outcomes Quality Initiative Classification**

Stage	Description	GFR (mL/min/1.73 m <sup>2</sup> )
	At increased risk	60 or greater (with chronic kidney disease risk factors)
1	Kidney damage with normal or increased GFR	90 or greater
2	Kidney damage with mildly decreased GFR	60 to 89
3	Moderately decreased GFR	30 to 59
4	Severely decreased GFR	15 to 29
5	Kidney failure	Less than 15 (or dialysis)

GFR = glomerular filtration rate. (Adapted with permission from the American College of Physicians. Levey AS, Coresh J, Balk ET, et al; National Kidney Foundation. National Kidney Foundation practice guidelines for chronic kidney disease: evaluation, classification, and stratification. *Ann Intern Med.* 2003;139[2]:137-147.)

exogenous filtration markers such as ethylenediaminetetraacetic acid, inulin, iothalamate, diethylene triamine pentaacetic acid, or iothalamate.<sup>5,6</sup> Clinicians may view this as an unrealistic goal because of its complexity and cost and, thus, are confronted with the dilemma of using either the commonly utilized Cockcroft-Gault (CG) equation or the abbrMDRD equation for drug dosage adjustment.<sup>5</sup>

The purpose of this review is to examine the factors affecting drug clearance and the available evidence for drug dosing based on the CG and the abbrMDRD equations. The important differences and clinical utility of these equations should be appreciated before their use, and these are discussed. Because of the scope of this article, recommendations for patients with chronic renal failure or end-stage renal disease on hemodialysis are not reviewed.

**BACKGROUND**  
**Renal Estimation Equations**

Published in 1976, the CG equation was developed to estimate creatinine clearance (CrCl) and was derived from a group of 249 men

between 18 and 92 years of age.<sup>7</sup> Cockcroft and Gault determined their patient's CrCl by measuring the 24-hour urinary clearance of creatinine.<sup>7</sup> The designation of milliliters per minute, rather than milliliters per minute per 1.73 m<sup>2</sup>, is used because the calculation is not corrected for body surface area (BSA).<sup>7</sup> It should also be noted that the authors had no intention of predicting GFR; rather, they intended

to calculate CrCl.<sup>8</sup> The CG formula is shown in Equation 1.<sup>7</sup>

The abbrMDRD equation, published in 2000, estimates GFR and was derived from 1,070 patients and then validated in a separate sample of 558 patients, all of whom had CKD.<sup>9,10</sup> Their patient's GFR was determined by measuring the renal clearance of <sup>125</sup>I-iothalamate, as well as a spot SCr and 24-hour urine collection.<sup>9</sup> It has been demonstrated that the renal clearance of <sup>125</sup>I-iothalamate corroborates closely with the true GFR; thus, it is the gold standard for this measurement.<sup>3</sup> The abbrMDRD and original MDRD formulas are shown in Equations 2 and 3.<sup>10</sup>

**METHODS**

An updated narrative review of the literature was performed, which pertained to the accuracy of the CG and abbrMDRD equations and their use in drug dosage adjustment.

**Inclusion and Exclusion Criteria**

One unblinded reviewer performed electronic searches and screened the initial results. MED-

**Equation 1** CG CrCl (mL/min)  

$$= \frac{(140 - \text{age}) \times (\text{lean body weight [kg]})}{\text{serum creatinine (SCr) (mg/dL)} \times 72}$$
 × 0.85 (if female)

**Equation 2** abbrMDRD GFR (mL/min/1.73 m<sup>2</sup>)  

$$= 186 \times (\text{SCr})^{-1.154} \times (\text{age})^{-0.203}$$
 × 0.742 (if female)  
 × 1.210 (if African American)

**Equation 3** Original 6-variable MDRD GFR (mL/min/1.73 m<sup>2</sup>)  

$$= 170 \times (\text{SCr})^{-0.999} \times (\text{age})^{-0.176}$$
 × 0.762 (if female)  
 × 1.18 (if African American)  
 × (blood urea nitrogen [BUN])<sup>-0.170</sup> × (albumin)<sup>0.318</sup>

LINE was searched using the OVIDSP database, from the inception of the database (1950) through June 2008. Searches of the literature used combinations of the following terms: MDRD, MDRD equation, Modification of Diet in Renal Disease, Cockcroft-Gault, Cockcroft-Gault equation, glomerular filtration rate, creatinine clearance, creatinine, Jaffe reaction, alkaline picrate, chronic kidney disease, gender, age, ethnicity, renal function estimation, medication, drug, and dose adjustment. Only articles published in English and pertaining to humans were analyzed.

### Accuracy of Renal Estimation Equations

The abbrMDRD was studied in a population consisting entirely of patients with CKD.<sup>9</sup> It has been shown that the abbrMDRD is not accurate when the GFR is expressed above 90 mL/min/m<sup>2</sup> because it is derived from patients with CKD.<sup>7</sup> Levey et al conducted a study evaluating patients with CKD in which it was determined that the abbrMDRD had 90% of its estimations within 30% of the measured GFR as determined by the renal clearance of <sup>125</sup>I-iothalamate.<sup>9</sup> This accuracy did not hold true with estimated GFR values above 90 mL/min/m<sup>2</sup>. The CG had 83% and 60% of its estimations within 30% of the measured GFR as determined by the renal clearance of <sup>125</sup>I-iothalamate, with and without correction for bias, respectively.<sup>9</sup> Levey et al showed that the 6-variable and, likewise, the abbrMDRD equations demonstrated less bias and greater precision for GFR prediction compared with CrCl estimation equations such as the CG formula.<sup>9</sup> The original MDRD study also used a validation sample that was different from the cohort used to derive the equa-

tion (training sample), which contributed to the accuracy of the equation.<sup>9</sup> Froissart et al conducted a retrospective study of 2,095 European patients, of which 1,933 had CKD, and found the least precision with the abbrMDRD in patients who were underweight and younger than 65 years of age and had a measured GFR of at least 60 mL/min/1.73 m<sup>2</sup>.<sup>11</sup> The CG equation showed the least precision in patients who were overweight and younger than 65 years of age and had a measured GFR of at least 60 mL/min/1.73 m<sup>2</sup>.<sup>11</sup> Poggio et al conducted a retrospective study of 1,285 patients in which 457 were healthy kidney donors and 828 had CKD.<sup>12</sup> This study found that the abbrMDRD performed significantly better than the CG formula in the CKD group, whereas the CG formula consistently overestimated measured GFR through all GFR ranges.<sup>12</sup>

### Variability in Renal Estimation Equations

Serum creatinine is an endogenous amino acid creatine derivative that is derived from muscle stores and freely filtered by the glomerulus.<sup>3,5,13</sup> This measurement has been used since the determination that it is more accurate than measuring blood urea level, urea clearance, or timed collection of urine for CrCl more than 50 years ago.<sup>14</sup> However, the use of SCr still poses some problems,<sup>14</sup> which can be cumulative when compounded by multiple factors that alter and skew the value of SCr. These factors include proximal tubular secretion and extrarenal elimination of SCr, age-related changes in SCr and GFR, gender-related differences, body size, ethnic differences, critical illness, and SCr assay variance. It must be understood that SCr has a nonlinear correlation with GFR,

and because of the multitude of factors that affect SCr, the GFR must lower to approximately half before the concentration of SCr increases above the upper limit of the normal range.<sup>3,15</sup> These factors, discussed in the following sections, should be considered before a renal estimation equation is applied to a patient case.

### Proximal Tubular Secretion and Extrarenal Elimination of Creatinine

Proximal tubular secretion of creatinine in humans is estimated as approximately 28% but can vary considerably within an individual, as well as between individuals.<sup>5,8</sup> Variability in proximal tubular secretion can cause overestimation in CrCl by 10% to 40% in healthy patients and even more unpredictable variations in those with CKD.<sup>13</sup> Serum creatinine concentration also can be affected by medications that alter proximal tubular secretion, such as cimetidine, cefoxitin, and trimethoprim.<sup>5,8</sup>

### Effect of Age on Serum Creatinine and Glomerular Filtration Rate

It is well known that GFR declines with age.<sup>5,13</sup> This decline is on the order of about 10 mL/min/1.73 m<sup>2</sup> every decade and starts at about 30 years of age.<sup>5,13</sup> For example, a 65-year-old woman may have a mean GFR of 85 mL/min/1.73 m<sup>2</sup> or possibly lower if she has a CKD risk factor such as diabetes.<sup>5,7,13</sup> With already-reduced kidney function, elderly patients are at a higher risk for drug toxicity than any other adult age-group. Thus, it is vital that the estimation equation used for drug dosage adjustment in elderly patients be as accurate as possible, particularly with narrow therapeutic drugs. Verhave et al and Cirillo et al found that the accuracy of the CG predic-

tion decreased in older patients and was best suited for those younger than 65 years of age, whereas the abbrMDRD prediction was best suited for low GFR (less than 60 mL/min/1.73 m<sup>2</sup>), which primarily occurs in elderly patients, and was recommended as such by Verhave et al.<sup>16,17</sup> Pedone et al recommended using the CG equation rather than the abbrMDRD for dose adjustment in elderly patients, and their study demonstrated that the CG and abbrMDRD estimations are farthest apart at low levels of SCr.<sup>18</sup> Laroche et al determined that the CG equation tended to underestimate true GFR, whereas the abbrMDRD tended to overestimate the true GFR, in patients of at least 65 years of age.<sup>19</sup>

#### ***Gender-Related Differences in Serum Creatinine and Glomerular Filtration Rate***

Because of the difference in muscle mass between men and women, both equations include a variable for adjustment.<sup>5,7,10</sup> This difference pertains to the fact that, on average, women have a lower muscle mass than men.<sup>5</sup> A lower muscle mass can then be interpreted into a lower SCr and, thus, elevated GFR. This does not imply that the female GFR is improved or better than the male counterpart.<sup>5</sup> Cirillo et al found that the CG prediction was relatively accurate but that the abbrMDRD overestimated GFR in the female population.<sup>17</sup>

#### ***Effects of Body Mass on the Serum Creatinine and Glomerular Filtration Rate***

To allow for direct comparison of data in patients with varying body size and to define normal GFR values, the GFR is indexed for BSA.<sup>20</sup> This is appropriate for a patient with a normal body mass index (BMI) of 18.5 to 25 kg/m<sup>2</sup>,

for which Delanaye et al showed that the absolute GFR (unadjusted to BSA) is not statistically significant ( $P = 0.067$ ) or clinically different ( $1.09 \pm 3.66$  mL/min) from the indexed GFR (adjusted to 1.73 m<sup>2</sup>).<sup>20</sup> Contrarily, in a patient with a BMI of greater than 30, the mean difference between the absolute GFR and indexed GFR was  $18.2 \pm 12.1$  ( $P < 0.0001$ ).<sup>20</sup> This difference is likely attributable to factors other than creatinine generation because patients who are obese have extra fat mass that does not contribute to creatinine generation.<sup>3,5</sup> It was determined in 1916 that the average BSA is 1.73 m<sup>2</sup>.<sup>21</sup> This average is likely no longer valid in the United States, considering the steady rise in obesity.<sup>22-24</sup> The abbrMDRD, however, incorporates the 1.73 m<sup>2</sup> average BSA into its value for GFR.<sup>9</sup> This could potentially be a factor when using the abbrMDRD equation for drug dosage adjustments in those who are obese or cachectic, which is the reasoning behind recommendations to unadjust for BSA in these situations.<sup>3,22</sup> The CG equation, which incorporates weight into its calculation, has similar issues with regard to body size. In patients who are obese, the equation may overestimate CrCl if total body weight is used or underestimate CrCl if ideal body weight (IBW) is used.<sup>20,22,25</sup> Adjusted body weight (adjBW) is commonly used in the CG equation to improve the accuracy of the estimate, although agreement with regard to when to use adjBW (ie, cutoff of 20%, 30%, or 40% over IBW) is still under debate. The abbrMDRD does not use weight in its equation and, thus, remains standardized to the average BSA of 1.73 m<sup>2</sup>. Verhave et al and Cirillo et al found a large overestimation in CG CrCl with patients who are obese (BMI  $\geq 30$ ) and an underesti-

mation in abbrMDRD GFR irrespective of BMI.<sup>16,17</sup>

In addition to the implications of patient weight, muscle mass plays a large role in measuring SCr and estimating GFR. In patients who are emaciated and severely malnourished, it is expected that SCr will be reduced.<sup>3,5,13</sup> This situation can be compared with that of elderly patients who have reduced muscle mass as a result of the aging process.<sup>3,5,13</sup> Alternatively, it is expected that patients with increased muscle mass, such as body builders (especially those on creatine supplementation), and those on a primarily meat diet will have an elevated SCr.<sup>3,5,13</sup> Because patients who have amputations also are viewed as having reduced muscle mass contributing to the SCr, consideration of subtracting the weight that is missing may be warranted.<sup>3,25</sup> Most importantly, whether the SCr is elevated or reduced in each situation, it must be understood that the CrCl and/or GFR may not necessarily be altered, and thus, misinterpretation when values are underestimated or overestimated should be avoided.<sup>3,5,8,13,25</sup>

#### ***Effects of Ethnicity and Various Groups on Serum Creatinine and Glomerular Filtration Rate***

The abbrMDRD has been validated in various ethnic populations, and it has been shown that this equation is similar to or more accurate than the CG formula.<sup>5</sup> Study groups have included Caucasian, African American, Asian, and European patients with nondiabetic CKD. Ethnic groups that have not been studied include Hispanic, Indian, Arab, Native American, and non-Chinese Asian populations.<sup>3</sup> It has been shown that the GFRs of patients with different ethnic backgrounds vary substantially, primarily because of variance in creatinine production.<sup>3,5</sup> The abbr-

**Equation 4** Chinese abbrMDRD GFR (mL/min/1.73 m<sup>2</sup>)  
 $= 186 \times (\text{SCr})^{-1.154} \times (\text{age})^{-0.203}$   
 $\times 0.742$  (if female)  
 $\times 1.233$  (if Chinese)

**Equation 5** Reexpressed abbrMDRD GFR (mL/min/1.73 m<sup>2</sup>)  
 $= 175 \times (\text{SCr})^{-1.154} \times (\text{age})^{-0.203}$   
 $\times 0.742$  (if female)  
 $\times 1.212$  (if African American)

MDRD equation includes a variable that accounts for African American race because of increased muscle mass and, thus, increased creatinine production when compared with the Caucasian population.<sup>3,10,13</sup> Hispanic and Asian patients have reduced creatinine production when compared with the Caucasian population.<sup>5</sup> Ma et al published a modification of the MDRD that includes a Chinese variable, but like the abbrMDRD, it has not yet been validated for drug dosage adjustment.<sup>26</sup> The authors also do not know if this equation is accurate for other Asian populations.<sup>26</sup> The revised abbrMDRD with the Chinese component is shown in Equation 4.<sup>26</sup>

Like the abbrMDRD was initially, the Chinese abbrMDRD is still untested in various groups, and thus, it should not be used until further validation of the formula is completed. Studies of other ethnic groups also must be conducted to determine how accurate the abbrMDRD equation is for them and whether or not an adjustment should be made, as was done for the African American and Chinese populations.<sup>27</sup>

#### *Critical Illness and Fluctuations in Serum Creatinine and Glomerular Filtration Rate*

Patients being hospitalized likely present the most complicated instances because their unstable

situations involve multiple variables that may potentially alter SCr and GFR. In fact, in patients with acute kidney injury, the CG and abbrMDRD equations overestimate CrCl and GFR, respectively, because of a delayed rise in the SCr level and vice versa when the SCr is falling.<sup>3,25</sup> This constitutes a non-steady-state SCr level, which causes grossly inaccurate calculations from all estimation equations.<sup>3,25</sup> A general rule of thumb is that when the SCr doubles within 24 hours, the GFR will be near 0.<sup>3</sup>

Patients with various comorbidities, such as chronic heart failure (CHF) and liver failure, may have altered SCr levels because of changes in physiology.<sup>25,28</sup> These changes, such as altered renal blood flow in CHF and altered creatinine production in liver failure, should be taken into account when assessing CrCl or GFR.<sup>17,25</sup> Poggio et al found that, in patients with a high BUN-SCr ratio, the original 6-variable MDRD equation performed better than the abbrMDRD equation, but it still performed poorly in patients being hospitalized and was not a reliable predictor of renal function.<sup>28</sup>

#### **Isotope Dilution–Mass Spectrometry Standardization Program**

The isotope dilution–mass spectrometry (ID-MS) assay is a more accurate method for determining SCr when compared with the Jaffe

and enzymatic methods, which have a positive bias because of interference from noncreatinine chromogens (NCCs).<sup>3,6,25</sup> NCCs are endogenous substances that are interpreted by the Jaffe and enzymatic method as SCr.<sup>3,6,25</sup> This interpretation leads to a 0.1 to 0.3 mg/dL positive bias in SCr values.<sup>3,6</sup> ID-MS is considered the method of choice for determining the actual SCr because of its high level of specificity and small standard deviation (less than 0.3%).<sup>6</sup> Standardization across laboratories would help reduce inter- and intralaboratory variability.<sup>6</sup> The switch to ID-MS would lower the SCr reference interval because of an overall reduction in SCr values (approximately 5% to 20% lower).<sup>6,29</sup> Standardization also would pose new problems for the CG formula because although adjustments have been made to the abbrMDRD for this change, the CG equation has no such adjustment.<sup>25</sup> With the introduction of the ID-MS assay, lowering of the SCr as the result of a more accurate analysis of SCr may cause an overestimation of the CG CrCl. The abbrMDRD, which has a reexpressed formula to correct for this change, does not have this problem.

The reexpressed abbrMDRD for use with the ID-MS SCr assay is shown in Equation 5.<sup>3</sup>

If the laboratory switches to the ID-MS method, the change should be reported to the pharmacy department or inquired about in advance so that appropriate education and practice changes are implemented.<sup>6,29</sup> If no changes are made when using the CG equation, CG values will regularly calculate CrCl with a 10% to 20% higher value.<sup>29</sup> If the ID-MS method is used in the laboratory, consideration as to the proper use of the CG equation should be reevaluated by

the clinical team until further studies can assess the clinical significance of this change.

### Cockcroft-Gault Versus Abbreviated Modification of Diet in Renal Disease Estimations for Manufacturer Dose Adjustment Recommendations and Narrow Therapeutic Drugs

During the past 10 years, much effort has been devoted to determining how accurate the abbrMDRD equation is in various patient populations when compared with the CG formula.<sup>11,12,18,26,28,30-32</sup>

On the contrary, very little research has been conducted regarding application of the abbrMDRD in drug dosage adjustment.<sup>18,22,27,33,34</sup> Questions that must be asked include the following:

- In what population should the abbrMDRD be used for dose adjustment?
- Should any special adjustments be made to the abbrMDRD equation?
- Can the abbrMDRD be applied to pharmacokinetic principles?

The following are studies that conducted comparisons between the CG and abbrMDRD equations with regard to drug dosage adjustment. Whether or not the abbrMDRD can be applied to pharmacokinetic principles will not be determined until further studies are conducted.

Gill et al conducted a study of 180 patients from a long-term care facility in which the CG (BSA adjusted) was compared with the abbrMDRD (ID-MS formula). The authors determined what percentage of digoxin and amantadine doses would be adjusted downward based on the estimated CrCl or GFR. In the amantadine group, 70% of patients for whom the abbrMDRD was used would have required a downward adjustment compared with 91.2% in those for

whom the CG was used. In the digoxin group, 26% of patients for whom the abbrMDRD was used would have required a downward adjustment compared with 58% in those for whom the CG was used. This study had 2 major limitations. The percentages were only based on estimation equations with no comparison to measured GFR (ie, inulin) or drug levels. The ID-MS reexpressed abbrMDRD was used, whereas the CG only had an adjustment for BSA and, thus, may have added more bias to this comparison.<sup>27</sup>

Wargo et al conducted a study of 409 patients from a tertiary care facility in which the CG (using IBW or adjBW) was compared with the 6-variable MDRD or the abbrMDRD if variables were missing (both were BSA unadjusted). The purpose of the study was to determine if there was a difference between estimates when making antimicrobial dosage adjustments as per recommendations in the package insert (PI). The authors found an overall discordance rate of 20% to 36% ( $P < 0.001$ ) between the CG, MDRD, and PI. The authors also noted that the 6-variable MDRD mirrored the overall discordance rate, whereas the abbrMDRD had more variation when compared with the CG. These overall variations implied a possible overdose with the MDRD equation for 18% to 30% of the cases when using the CG as the correct value with the PI recommendations. Because the outcome cannot be determined as a result of making these switches, ascertaining which equation was more accurate than the other is not possible.<sup>33</sup>

Golik et al conducted a study of 207 patients who were hospitalized but not in the intensive care unit and who had an estimated GFR of less than 90 mL/min/m<sup>2</sup> as determined by the 4- and 6-variable

MDRD equation. Using 2 MDRD and 4 CG equations, discordance in drug dosing was determined with cefepime, levofloxacin, meropenem, and piperacillin-tazobactam. The average patient age was 63.6 years ( $\pm 15.9$  years), and 56.5% of patients were men. One-third of patients had diabetes mellitus, and most were Caucasian. Using the abbrMDRD unadjusted for BSA and the CG based on IBW and SCr adjusted up to 1, the authors found a discordance rate of 22.8% to 36.3% of the time when dosing antimicrobials. Thus, the 2 equations would have led clinicians to recommending different doses and/or frequencies for the antibiotics based on which equation had been used. The 2 equations showed a mean CrCl discordance rate of 16.5 mL/min between them. The authors concluded that in almost every situation, the abbrMDRD would have resulted in a higher total daily dose being prescribed.<sup>34</sup>

### CONCLUSION

At this time, neither the National Kidney Disease Education Program (NKDEP) nor the authors of this review can recommend the use of the abbrMDRD in drug dosage adjustment.<sup>29</sup> Although some researchers have advocated the use of the abbrMDRD in drug dosage adjustment,<sup>15</sup> the NKDEP and others<sup>33-36</sup> believe that more studies must be conducted regarding the performance of the abbrMDRD equation in the dosing of medications.<sup>29</sup> If drug PIs contained recommendations for drug dosage adjustments based on pharmacokinetic studies with the abbrMDRD, clinicians would be able to appropriately modify their patients' therapy using this method. As it stands currently, all PI recommendations for medication dosage adjustments are based on the CG estimation of

renal function. Until further studies are conducted, this should be followed for drug dosing.

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