## Current Status Of Reporting Estimated Glomerular Filtration Rate (eGFR)

Chronic kidney disease (CKD) is usually asymptomatic until substantial kidney damage has occurred. CKD is primarily diagnosed by an eGFR <60 mL/min/1.73m<sup>2</sup> or a urine albumin:creatinine ratio >30 mg/g. Creatinine has been shown to be a sensitive indicator of kidney function and to appropriately track disease progression even at low concentrations found within a typical reference interval (1). For example, doubling of serum creatinine from 0.6 to 1.2 mg/dL indicates significant kidney damage but because the concentrations are within typical reference intervals, the extent of kidney damage may not be recognized. There is evidence that physicians do not consider the possibility of kidney damage until creatinine exceeds the reference interval (2, 3). Because an eGFR value is more easily related to a patient's kidney disease condition than is a creatinine concentration, the National Kidney Disease Education Program (NKDEP) recommends to report eGFR along with serum (or plasma or whole blood) creatinine. The public health goal of the NKDEP is to improve identification of patients with CKD so they can be put on treatment to slow progression and reduce complications of the disease.

The general chemistry C-B Survey, June 2010, included questions regarding practices for reporting estimated glomerular filtration rate (eGFR) from serum creatinine results for adult patients. Of those responding, 80% were reporting eGFR (Figure 1). Figure 2 shows that 83% reported eGFR with all creatinine results as recommended by the NKDEP and 12% reported eGFR only when requested.



The NKDEP web site cautions that there are clinical conditions when the rate of production of creatinine is affected which makes it less reliable as an indicator of kidney function. These conditions include: extremes of body size, muscle mass, nutritional status (e.g. meat increases and vegan decreases, blood concentration), clinical conditions which decrease muscle mass (e.g. cancer, paraplegia, amputation), pregnancy which increases GFR and decreases creatinine concentration, and patients with serious comorbid conditions or with metabolically unstable kidney function. However, if a computer reporting system cannot identify patients for whom reporting eGFR is appropriate, laboratories should report eGFR for all patients and allow the clinician to determine the suitability of a result for a patient's condition.





Figure 3 shows the upper numeric limit of the eGFR value reported by laboratories. The NKDEP recommends not to report a numeric value for eGFR >60 mL/min/1.73m<sup>2</sup> using the MDRD Study equation because several factors combine to make the values more variable and biased lower than true GFR measured values. However, 27% of laboratories were reporting higher numeric values. The reasons for reporting eGFR values >60 mL/min/1.73m<sup>2</sup> were not gathered in the survey.

Figure 4 shows the equations used by laboratories to calculate eGFR. A large number of laboratories (81%) used the NKDEP recommended 4-parameter MDRD Study equation. Of these, 1.7% used a 3-parameter version by not including the coefficient for race. It is very important that a laboratory use the isotope dilution mass spectrometry (IDMS) traceable version of the MDRD 4-variable equation (4) because essentially all creatinine methods in use are now calibrated to have results traceable to an IDMS reference measurement procedure (5).

A new equation has been developed by the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) to estimate GFR (6). The CKD-EPI equation was based on aggregated data from a large number of investigations which included measured GFR and creatinine with calibration adjusted to be traceable to IDMS. The equation uses the same variables as the MDRD equation and was reported to have greater accuracy compared to measured GFR especially for values >60 mL/min/1.73m<sup>2</sup>. The NKDEP has not made a recommendation to change or not to change to this equation because the values are nearly the same below 60 mL/min/1.73m<sup>2</sup> and the educational efforts to identify patients are currently focused on Stage 3 CKD which has eGFR <60 mL/min/1.73m<sup>2</sup> should consider the CKD-EPI equation.

It is important to note that there is not a version of the MDRD 6-variable, the Cockcroft-Gault or any other estimating equation suitable for use with creatinine methods that have calibration traceable to IDMS. For most methods, IDMS traceable calibration caused a 10-20% reduction in creatinine concentration compared to older calibration schemes, which will cause an erroneously high estimate of GFR with older estimating equations. Laboratories using these equations should change to either the IDMS traceable version of the MDRD equation or the newer CKD-EPI equation.

Additional information on reporting eGFR is available at the NKDEP web site: http://www.nkdep.nih.gov/.

References:

- Spanaus K-S, Kollerits B, Ritz E, et al. Serum Creatinine, Cystatin C, and β-Trace Protein in Diagnostic Staging and Predicting Progression of Primary Nondiabetic Chronic Kidney Disease. Clin Chem 2010;56:740-9.
- 2. Coresh J, Byrd-Holt D, Astore BC, et al. Chronic Kidney Disease Awareness, Prevalence, and Trends among U.S. Adults, 1999 to 2000. J Am Soc Nephrol 2005;16:180-8.
- 3. Hemmelgarn BR, Zhang J, Manns BJ, et al. Nephrology Visits and Health Care Resources Use Before and After Reporting Estimated Glomerular Filtration Rate. JAMA 2010;303:1151-8.
- 4. Levey AS, Coresh J, Greene T, et al. Expressing the Modification of Diet in Renal Disease Study Equation for Estimating Glomerular Filtration Rate with Standardized Serum Creatinine Values. Clin Chem 2007;53:766-72.
- 5. Participant Summary Report, CAP 2010 C-A Survey.
- 6. Levey AS, Stevens LA, Schmidet CH, al. A New Equation to Estimate Glomerular Filtration Rate. Ann Intern Med. 2009;150:604-12.

Greg Miller, Ph.D. Chemistry Resource Committee