National Government Services, Inc.
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To the NGS Inc. Medical Directors:

In September 2021, the National Kidney Foundation and the American Society of Nephrology finalized a multi-year initiative to evaluate how race is used to diagnose to kidney disease. In finalizing its work, the Task Force recommended: (1) immediate implementation of reporting of estimated glomerular filtration rate (eGFR) using the 2021 CKD-EPI creatinine eGFR equation that was refit without the race variable by all clinical laboratories, (2) increased, routine, and timely use of cystatin C for confirmatory assessment of kidney function, and (3) increased research on GFR estimation with new endogenous filtration markers and on interventions to eliminate race and ethnic disparities. **We are writing today to request that NGS Inc. align its medical policies with recommendation two regarding increased use of cystatin C as confirmatory assessment of kidney function.**

The NKF-ASN Task Force on Reassessing the Inclusion of Race in Diagnosing Kidney Diseases was launched on July 2, 2020, in response to a recognition of the need to improve health equity by addressing the use of race in clinical algorithms, including the equations used to calculate eGFR, assess kidney function, and diagnose and stage kidney disease. Glomerular filtration rate (GFR) cannot be easily measured in clinical practice, so numerous approaches have been developed to estimate its value. The most widely utilized approach is based on the concentration of serum creatinine, which is routinely measured as part of basic and comprehensive metabolic profiles. While creatinine-based estimation of kidney function is generally reliable, the relationship between serum creatinine and kidney function may be altered by numerous factors including increased or decreased muscle mass, malnutrition, acute and chronic illness, diet and medications. Thus, attention has focused on finding alternative markers of kidney function including cystatin C, beta-2-microglobulin and beta-trace protein. Of these, calculation of eGFR based on serum cystatin C or serum cystatin C and serum creatinine are most readily applicable in clinical practice. In fact, clinical practice guidelines recognize that the most accurate estimation of kidney function is a function of creatinine and cystatin, C.[1]

Demand for cystatin C testing is increasing and will continue to increase in the wake of the Task Force recommendations. During the debate over the future of creatinine-based estimating equations, it was noted that unlike serum creatinine, the relationship between cystatin C and kidney function is independent of race. While the Task Force ultimately recommended the expeditious adoption of a new race-neutral creatinine-based estimating equation (CKD-EPI 2021), there are numerous scenarios in which the ordering of cystatin C is in the patient's best interest. Cystatin C is used to either confirm or rule out kidney disease when a patient's GFR is on the margin between chronic kidney disease (CKD) stages.

[1] https://kdigo.org/wp-content/uploads/2017/02/KDIGO_2012_CKD_GL.pdf

Cystatin C is also ordered when a patient's condition could affect the accuracy of estimation based on creatinine, which is influenced by diet, body composition, medications that inhibit creatinine secretion and activity level. In individuals that are critically ill or with amputations, spinal cord injury, neurodegenerative diseases, cachexia and malnutrition, creatinine generation may be severely reduced and creatinine-based values of eGFR will overestimate the true GFR and underestimate the severity of kidney dysfunction. Conversely, in individuals with increased muscle mass, such as, bodybuilders, elite athletes, and others who vigorously exercise, individuals with high dietary red meat consumption and individuals taking dietary supplements that contain creatine, serum creatinine-based eGFR calculations will underestimate the true GFR, potentially leading to the diagnosis of kidney disease in individuals with normal kidney function. In addition, cystatin C assay and calculation of cystatin C -based eGFR may be clinically indicated at specific thresholds of kidney function where more precise estimates of kidney function are needed for medication management (e.g., metformin at an eGFR of 30 mL/min/1.73 m^2) or referral for kidney transplant evaluation. The foundation underpinning the work of the NKF-ASN Task Force was that nephrologists must determine the most accurate method of estimating kidney function based on the unique circumstances of their patients. **NKF and ASN request that NGS Inc. approach cystatin C policies with the same regard for the nephrologist's clinical judgement by expanding the circumstances under which cystatin C is considered "medically reasonable and necessary."**

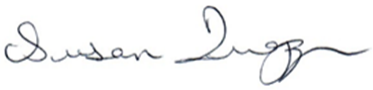
Kidney disease disproportionally affects people from racially and ethnically diverse populations. Black/African American, Native American, and Hispanic individuals make up the majority of the prevalent population with kidney failure.[2] The main causes of kidney disease, diabetes, and hypertension, disproportionally affect non-White populations. Black/African American and Hispanic people with CKD lose kidney function more quickly, in part the result of Social Determinants of Health such as low socioeconomic status and inadequate access to healthcare. Implementation of the NKF-ASN Task Force recommendations will end the systematic overestimation of kidney function leading to delayed and inequitable care for self-identified Black/African American patients. Clearing the path for all clinicians, not only nephrologists, to order cystatin C more easily is an essential step in realizing the health equity promise of the Task Force's work. We look forward to NGS Inc.'s partnership in this endeavor. Please contact Miriam Godwin, Health Policy Director, at miriam.godwin@kidney.org to set up time to discuss the requests made herein.

Sincerely,

[2] https://adr.usrds.org/2021/end-stage-renal-disease/1-incidence-prevalence-patient-characteristics-and-treatment-modalities

NATIONAL KIDNEY FOUNDATION®

ASN American Society of Nephrology



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