

Estimated GFR Reporting Influences Recommendations for Dialysis Initiation

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ABSTRACT

Automated reporting of estimated GFR (eGFR) with serum creatinine measurement is now common. We surveyed nephrologists in four countries to determine whether eGFR reporting influences nephrologists' recommendations for dialysis initiation. Respondents were randomly allocated to receive a survey of four clinical vignettes that included either serum creatinine concentration only or serum creatinine and the corresponding eGFR. For each scenario, the respondent was asked to rank his or her likelihood of recommending dialysis initiation on a modified 8-point Likert scale, ranging from 1 ("definitely not") to 8 ("definitely would"). Analysis of the 822 eligible responses received showed that the predicted likelihood of recommending dialysis increased by 0.55 points when eGFR was reported (95% confidence interval, 0.33 to 0.76), and this effect was larger for eGFRs >5 ml/min per 1.73 m² ($P < 0.001$). Subgroup analyses suggested that physicians who had been in practice ≥ 13 years were more affected by eGFR reporting ($P = 0.03$). These results indicate that eGFR reporting modestly increases the likelihood that dialysis is recommended, and physicians should be aware of this effect when assessing patients with severe CKD.

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Serum creatinine concentration is commonly used to calculate the estimated GFR (eGFR). The eGFR can identify patients with significant CKD even when the serum creatinine level is not markedly abnormal. As such, clinical practice guidelines recommend using eGFR, rather than serum creatinine, to identify, risk stratify, and manage patients with CKD.^{1–3}

Automatically reporting eGFR when serum creatinine is measured is becoming commonplace to enhance the identification of patients with CKD.⁴

Observational studies have demonstrated that eGFR reporting improved CKD detection and increased referrals of patients with early CKD to nephrologists.^{5–8} Furthermore, eGFR reporting is associated with increased appropriate treatment in patients with CKD.⁹ However, the effects of eGFR reporting on nephrologists' practices are uncertain.

Whether eGFR reporting influences the decision to initiate dialysis is important to patients, physicians, and health care systems. We conducted a

randomized survey to determine whether eGFR reporting influences the likelihood that a nephrologist will recommend the initiation of dialysis. The survey randomly allocated half of the recipients to receive only serum creatinine information for clinical vignettes of CKD and half to receive both serum creatinine and eGFR information.

Of the 5576 surveys distributed, 579 were returned to the sender, leaving 4997 potential respondents. Of the 938 surveys (19%) that were returned, 822 (16%) were analyzed (Figure 1). Respondents were similar between groups (Table 1). The majority of respondents were from the United States, predominantly worked in CKD and ESRD, and worked in an academic setting.

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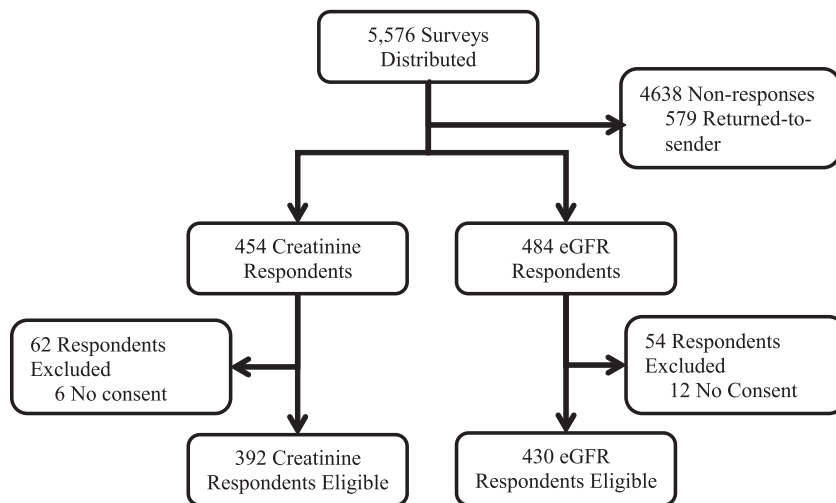


Figure 1. Flow of surveys and respondents throughout the study.

Table 1. Respondent characteristics

Characteristic	Creatinine (n=392)	eGFR (n=430)
Years in practice	13 (7–23)	13 (6–23)
Country		
Australia	76 (19.4)	80 (18.6)
Canada	58 (14.8)	61 (14.2)
New Zealand	16 (4.1)	14 (3.3)
United Kingdom	33 (8.4)	41 (9.5)
United States	185 (47.2)	209 (48.6)
Missing	24 (6.1)	25 (5.8)
Clinical practice		
CKD/ESRD	275 (70.2)	287 (66.7)
Transplant	11 (2.8)	23 (5.4)
Both	82 (20.9)	95 (22.1)
Missing	24 (6.1)	25 (5.8)
Academic practice		
Yes	222 (56.6)	252 (62.2)
No	144 (36.7)	153 (35.6)
Missing	26 (6.6)	25 (5.8)

Data are presented as the median (interquartile range) or n (%).

RESULTS

Effect of eGFR Reporting on Likelihood to Recommend Initiating Dialysis

The likelihood of recommending dialysis increased with lower kidney function, with a mean increase of 1.14 points (95% confidence interval [95% CI], 1.12 to 1.16) for each decrement in eGFR of 2.5 ml/min per 1.73 m² (Figure 1). Overall,

33%, 50%, 76%, and 93% of responses were ≥ 6 of 8 for the 12.5, 10, 7.5, and 5 ml/min per 1.73 m² eGFR categories, respectively.

At all levels of kidney function, the eGFR group was more likely to recommend initiating dialysis (Table 2, Figure 2). The effect of eGFR reporting was smaller at the lowest level of kidney function compared with other levels ($P < 0.001$). We therefore analyzed responses for eGFR of 5 ml/min per 1.73 m² separately. In scenarios with an eGFR > 5 ml/min per 1.73 m², the eGFR group was 0.62 points (95% CI, 0.37 to 0.87; $P < 0.001$) more likely to recommend initiating dialysis, an effect size of 0.27. In scenarios with patients with an eGFR of 5 ml/min per 1.73 m², the eGFR group was 0.32 points (95% CI, 0.17 to 0.48; $P < 0.001$) more likely to recommend initiating dialysis, also an effect size of 0.27.

These effects were consistent with the sensitivity analysis in which the outcome was a score ≥ 6 . The odds ratio for a score ≥ 6 was 2.62 (95% CI, 1.73 to 3.96; $P < 0.001$) for the eGFR group in scenarios in which the eGFR was > 5 ml/min per 1.73 m², and 2.21 (95% CI, 1.60 to 3.06; $P < 0.001$) in patients with an eGFR of 5 ml/min per 1.73 m².

Effect of Symptom Severity on Survey Responses

The presence of moderate compared with mild uremic symptoms was associated with a 1.7-point increase in the

modified Likert scale score (95% CI, 1.64 to 1.79; $P < 0.001$). The effect size for moderate versus mild symptoms was 0.74.

Effect of Respondent Characteristics

There was no evidence of a subgroup effect by the respondents' country, whether they were in an academic practice, or whether their practice was classified as mostly CKD/ESRD (Figure 3). There was evidence of an interaction by the number of years the respondent reported being in practice ($P = 0.03$). eGFR reporting appeared to have less of an effect on respondents below the median of 13 years in practice (0.29 points different between groups; 95% CI, -0.03 to 0.61) compared with respondents in practice ≥ 13 years (0.77 points different between groups; 95% CI, 0.46 to 1.05).

DISCUSSION

In this study, we found that eGFR reporting increased the likelihood that nephrologists recommended initiating dialysis in patients with advanced CKD in all studied countries and practice types and across the entire range of advanced CKD. The effect was slightly larger in patients with an eGFR of ≥ 7.5 ml/min per 1.73 m² and in nephrologists that were in practice ≥ 13 years.

Dialysis was initiated at progressively higher levels of kidney function over the last decade.^{10,11} This trend has, in part, been explained by observational evidence suggesting improved outcomes with earlier dialysis initiation.^{12,13} However, the trend of earlier dialysis initiation parallels the utilization of automated eGFR reporting. For example, only 33% of patients in the United States started dialysis with an eGFR > 10 ml/min per 1.73 m² in 2000, whereas $> 50\%$ of patients started dialysis with an eGFR > 10 ml/min per 1.73 m² in 2009, the period when eGFR reporting became widespread.¹⁰ Our study suggests that automated eGFR reporting could have contributed to earlier dialysis initiation. This possibility is consistent with the

Table 2. Difference in mean score on an 8-point modified Likert scale for likelihood to recommend initiating dialysis and proportion of responses that scored ≥ 6 to by group

eGFR Category (ml/min per 1.73 m ²)	Creatinine (n=392)		eGFR (n=430)	
	Mean Score	Proportion with Score ≥ 6 (%)	Mean Score	Proportion with Score ≥ 6 (%)
12.5	3.8 (2.2)	28	4.4 (2.3)	37
10	4.8 (2.2)	42	5.5 (2.1)	57
7.5	6.2 (1.9)	70	6.8 (1.6)	82
5	7.3 (1.4)	90	7.6 (1.0)	95

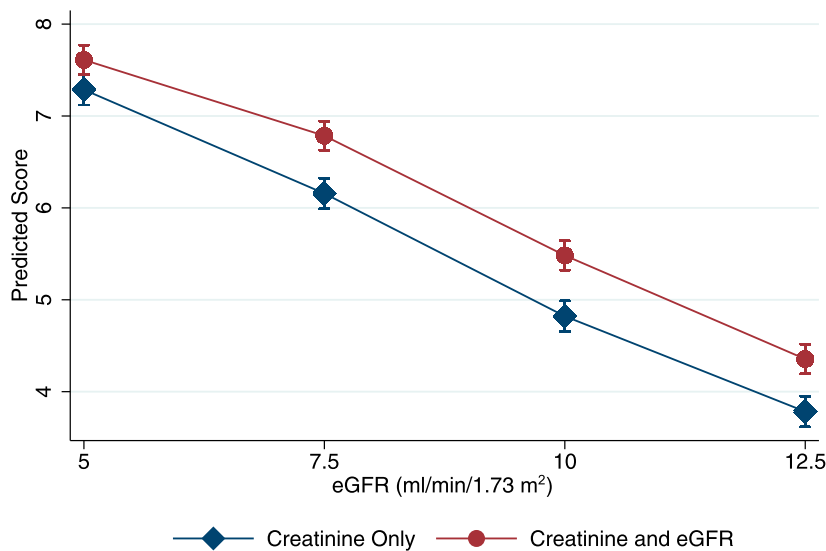


Figure 2. Effect of eGFR reporting in addition to creatinine on modified Likert scale scores for likelihood to recommend initiation of dialysis.

effect of automated eGFR reporting seen in primary care, where it results in increased nephrology referrals likely by enhancing the identification of poor renal function compared with creatinine alone.

One of the major difficulties with studies like ours is gauging the importance of the effect. An effect size of 0.3–0.5, as observed for eGFR reporting in our study, is typically considered to be between small and moderate in psychology research.¹⁴ Consistent with this, uremic symptoms, generally considered the most important reason to initiate dialysis, had a large effect size in our study. In relative terms, the effect size of eGFR reporting was approximately one third of the effect of moderate (versus mild) symptoms and half as large as the effect of a 2.5 ml/min per 1.73 m² reduction in

eGFR. By comparison, the Initiating Dialysis Early and Late (IDEAL) trial randomized patients to either early or late initiation of dialysis, resulting in a 2.2-ml/min difference and 5.6-month difference in eGFR at initiation between groups.¹⁵ Extrapolating from the IDEAL data, our effect size suggests that the initiation of dialysis would occur approximately 3 months earlier with eGFR reporting compared with creatinine reporting alone. Given that >100,000 patients commence dialysis every year in the United States,¹⁶ this would suggest that automated eGFR reporting could result in 25,000 patient-years of extra dialysis in the United States alone.

Our study has several strengths. This study is relatively large, allowing us to estimate the effect of eGFR reporting with precision. We surveyed a broad

sample of nephrologists, including academic and community practitioners from several countries, which improves the generalizability of our findings. The results were consistent across subgroups and in sensitivity analyses, which suggests that the observed effect is robust. Finally, our results are consistent with the known effects of eGFR reporting in primary care, which also suggests a true effect.

However, our results must be considered in the context of our study's limitations. The survey asked nephrologists about their intent, which may not translate to real-life practices. Our overall response rate was low and the results may reflect a response bias. However, the demographics of the respondents were quite broad, which suggests that the results are generalizable. Furthermore, contact lists contained numerous ineligible contacts (*i.e.*, not practicing nephrologists) that were unlikely to respond to the Email invitation. The respondents likely represent a much larger fraction of the eligible population than our reported response rate suggests. Response bias was also minimized by concealing the nature of the randomized groups in the cover letter.

In conclusion, automated eGFR reporting increased the likelihood of nephrologists recommending initiation of dialysis in patients with advanced CKD. This finding may partially explain the observation that initiation of dialysis with a higher eGFR compared with eras when eGFR reporting was not widespread. Studies comparing eGFR at initiation of dialysis before and after the introduction of automated eGFR reporting may clarify this. Nephrologists should be aware of the potential influence that eGFR reporting may have on their recommendations to initiate dialysis, particularly in light of the lack of evidence supporting benefits for earlier dialysis initiation.

CONCISE METHODS

We constructed a survey to assess the likelihood that nephrologists would recommend

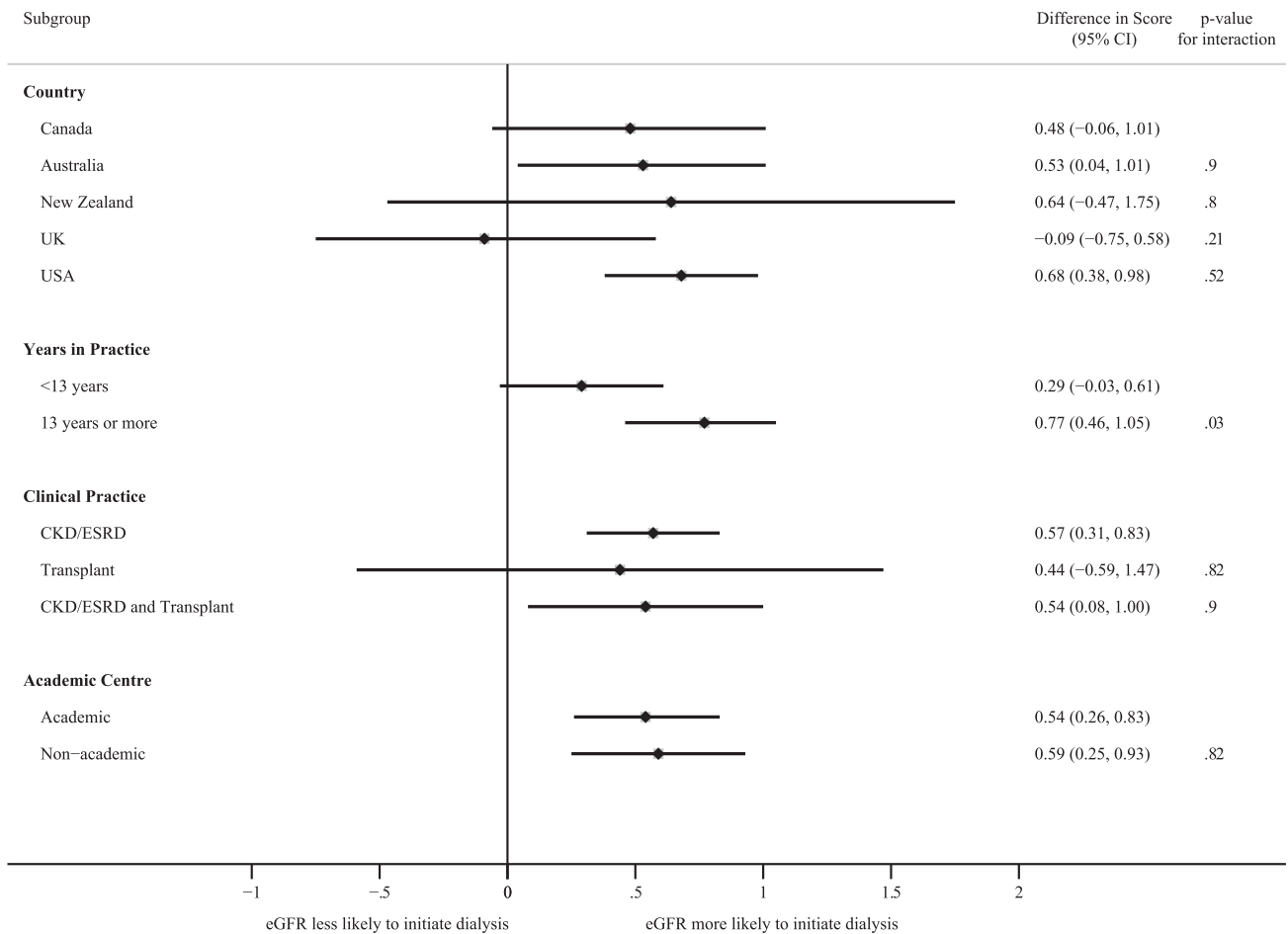


Figure 3. Effect of eGFR reporting in addition to creatinine on modified Likert scale scores for likelihood to recommend initiation of dialysis by subgroups.

patients initiate dialysis. This study was approved by the St. Joseph's Healthcare Research Ethics Board in Hamilton, Ontario, Canada, and the John F. Wolf, M.D. Human Subjects Committee at the Los Angeles Biomedical Research Institute in Torrance, California.

Development of the Survey Instrument

The survey was designed through multiple iterations and piloted by five nephrologists not involved in its design. The pilot assessed the survey for face validity, content validity, clarity, utility, discriminability, and item redundancy. Before final modifications, the survey was also reviewed by investigators from each target country for clarity.

The survey consisted of three scenarios in which a patient with CKD developed moderate symptoms of uremia (see the

Supplemental Material).¹⁷ Scenarios differed only in terms of the level of comorbidity for the described patient (mild, moderate, or severe).¹⁸ For each scenario, four levels of renal function were provided as both a creatinine concentration and eGFR based on that creatinine using the 4-variable Modification of Diet in Renal Disease equation.¹⁹ Renal function corresponded to an eGFR of 5 ml/min per 1.73 m², 7.5 ml/min per 1.73 m², 10 ml/min per 1.73 m², and 12.5 ml/min per 1.73 m². Respondents were then asked to rate the likelihood they would recommend initiation of dialysis from 1 ("definitely not") to 8 ("definitely would") on a modified Likert scale with only numeric indicators between these points. One additional scenario assessed the degree to which uremic symptoms altered the likelihood of recommending dialysis. Two versions of the survey were then constructed, one that included serum creatinine only (creatinine

version) and one that included both serum creatinine and its corresponding eGFR (eGFR version) for each question. Respondents were not informed that there were two versions of the survey and they explicitly consented to the use of their responses in research studies.

Survey Sample

Lists of Email addresses of potentially eligible nephrologists were assembled by liaising with a professional society in each target country. Email addresses on each list were randomly allocated to either the creatinine version or the eGFR version of the survey using a randomly permuted blocks stratified by country and generated independently of the Email list manager.

Survey Administration

Surveys were distributed by Email using Survey Monkey (www.surveymonkey.com)

and were completed online. Reminder Emails were distributed twice after the initial distribution. Before beginning the survey, respondents were asked to verify eligibility criteria and consented to the use of their results for research purposes. Eligible respondents were required to be practicing nephrologists in one of the target countries (Canada, United States, United Kingdom, Australia, or New Zealand), and had to complete at least one question from one clinical vignette.

Outcomes

The primary outcome was the difference in the modified Likert scale scores between the two groups using the first three clinical vignettes (*i.e.*, those that varied comorbidity and renal function). We assessed the subgroups of nephrologists by country of practice, number of years in practice (< or \geq the median), type of clinical practice (focused on CKD/ESRD, focused on transplantation, or both), and whether the respondent practiced at an academic or community hospital.

Statistical Analyses

Continuous variables were described as means \pm SDs or medians (25th to 75th percentiles) and categorical variables were expressed as frequencies (%). Between-group differences in the modified Likert scale scores were calculated using random-effects models to account for the multiple questions answered by each respondent. *A priori* we evaluated whether there was an interaction between survey version and the level of eGFR for each question hypothesizing that eGFR reporting would be less important at the extremes of renal function. There was a significant quantitative interaction at the $P < 0.001$ level for the lowest eGFR group (eGFR = 5 ml/min per 1.73 m²) compared with the highest eGFR group (eGFR = 12.5 ml/min per 1.73 m²) but not for any other groups. We therefore reported the primary outcome results separately for questions in which the eGFR was 5 ml/min per 1.73 m² while combining responses for all other eGFR values. We calculated the effect size as the mean difference between groups divided by the pooled SD.¹⁴ We conducted sensitivity analyses in which we dichotomized the modified Likert scale scores as ≥ 6 or < 6 and used a multi-level logistic regression model to assess the relative odds of a score ≥ 6 for the

eGFR group compared with the creatinine group.

The sample size was determined by convenience with the goal of obtaining a broad cross-section of nephrologists from each target country. We estimated that under the assumption of moderate autocorrelation, we would be able to detect a difference in scores of 0.7 with 90% power and a two-sided α of 0.025 if we received only 200 responses and we would be able to detect a difference of 0.3 if we received 1000 responses under the same assumptions (PASS software, version 11; NCSS LLC, Kaysville, UT).

All analyses were conducted with Stata software (version 11 MP; StataCorp, College Station, TX). A P value < 0.05 was considered statistically significant.

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K.B.S. and M.W. had full access to the study data and take responsibility for the integrity of the data and the analysis.

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DISCLOSURES

None.

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FULL METHODS

We constructed a survey to assess the likelihood that nephrologists would recommend patients initiate dialysis. Two versions of the survey were created that were identical except one version included only serum creatinine values (Creatinine version) and the other included both serum creatinine values and eGFR (eGFR version). Potential respondents were randomly allocated to receive either the Creatinine or eGFR version. Respondents were not informed that there were two versions of the survey and they explicitly consented to the use of their responses in research studies. The study was approved by the St. Josephs Healthcare Research Ethics Board in Hamilton, Ontario, Canada and the John F. Wolf, M.D. Human Subjects Committee at the Los Angeles Biomedical Research Institute in Torrance, California, U.S.A.

Development of survey instrument

The survey was designed by four practicing nephrologists and after multiple iterations amongst the designers the survey was piloted by five nephrologists not involved in its design. The pilot assessed the survey for face validity, content validity, clarity, utility, discriminability and item redundancy. After final modifications, the survey was also reviewed by investigators from each target country for clarity.

We constructed a hypothetical scenario in which a patient with chronic kidney disease developed moderate symptoms of uremia¹⁰. For each scenario 4 levels of renal function were provided as both a creatinine concentration and eGFR based on that creatinine using the 4 variable Modification of Diet in Renal Disease equation¹¹. Renal function corresponded to an eGFR of 5 ml/min/1.73 m², 7.5 ml/min/1.73 m², 10 ml/min/1.73 m², and 12.5 ml/min/1.73 m². Respondents were then asked to rate the likelihood they would recommend initiation of dialysis.

A response was recorded on a modified 8-point Likert scale anchored at “Definitely Not”=1 and “Definitely Would”=8. The scenario was then repeated with the patient’s comorbidities adjusted to reflect moderate and severe levels¹². Two versions of the survey were then constructed, one that included serum creatinine only (Creatinine version) and one that included both serum creatinine and its corresponding eGFR (eGFR version) for each question.

To assess the relative importance of eGFR reporting we developed an additional scenario in which the degree of uremic symptoms were modified from moderate to mild (i.e. fatigue only) with an eGFR of 10 ml/min/1.73 m². Respondents were asked the likelihood of recommending dialysis on the same modified Likert scale as the other scenarios.

Survey Sample

Lists of email addresses of potentially eligible nephrologists were assembled by liaising with a professional society in each target country (the Canadian Society of Nephrology in Canada, the National Kidney Foundation in the USA, the Renal Registry in the UK, and the Australian and New Zealand Society of Nephrology for Australia and New Zealand). These membership lists include non-nephrologists, nephrologists practicing outside the target countries, and nephrologists that do not routinely treat hemodialysis patients. Email addresses on each list were randomly allocated to either the Creatinine version or the eGFR version of the survey using a randomly permuted blocks stratified by country and generated independently of the email list manager.

Survey Administration

Surveys were distributed by email using Survey Monkey© (www.surveymonkey.com) and were completed online. Reminder emails were distributed twice after the initial distribution.

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Statistical Analysis

Continuous variables were described as means and standard deviations (SD) or medians and interquartile ranges (25th to 75th percentile) and categorical variables were expressed as frequencies (%).

Differences in the modified Likert scale scores were calculated using random-effects regression to account for the multiple questions answered by each respondent. Respondents were considered a random intercept and the allocated survey version was considered a fixed effect. Initial modeling did not indicate improved model fit when respondents were treated as a random slope and the random slope component was dropped. *A priori* we evaluated whether there was an interaction between survey version and the level of eGFR for each question hypothesizing that

eGFR reporting would be less important at the extremes of renal function. There was a significant quantitative interaction at the $p < 0.001$ level for the lowest eGFR group (eGFR = 5 ml/min/1.73m²) compared to the highest eGFR group (eGFR = 12.5 ml/min/1.73m²) but not for any other groups. We therefore reported the primary outcome results separately for questions in which the eGFR was 5 ml/min/1.73m² while combining responses for all other eGFR values. We calculated the effect size as the mean difference between groups divided by the pooled standard deviation¹³. We conducted sensitivity analyses in which we converted the modified Likert scale scores to “Highly Likely” (score ≥ 6) or “Not Highly Likely” (score < 6) and used a multi-level logistic regression model to assess the relative odds of a “Highly Likely” score for the eGFR Group compared to the Creatinine Group.

The sample size was determined by convenience with the goal of obtaining a broad cross-section of nephrologists from each target country. We estimated that under the assumption of moderate autocorrelation, we would be able to detect a difference in scores of 0.7 with 90% power and a two-sided alpha of 0.025 if we received only 200 responses and we would be able to detect a difference of 0.3 if we received 1000 responses under the same assumptions (PASS version 11, Kaysville, Utah, USA).

All analyses were conducted with Stata version 11 MP (College Station, Texas, USA). A p-value < 0.05 was considered statistically significant.

