Nephrology Visits and Health Care Resource Use Before and After Reporting Estimated Glomerular Filtration Rate

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Context Laboratory reporting of estimated glomerular filtration rate (GFR) has been widely implemented, with limited evaluation.

Objective To examine trends in nephrologist visits and health care resource use before and after estimated GFR reporting.

Design, Setting, and Patients Community-based cohort study (N=1 135 968) with time-series analysis. Participants were identified from a laboratory registry in Alberta, Canada, and followed up from May 15, 2003, to March 14, 2007 (with estimated GFR reporting implemented October 15, 2004).

Main Outcome Measure Nephrologist visits and patient management.

Results Following estimated GFR reporting, the rate of first outpatient visits to a nephrologist for patients with chronic kidney disease (CKD; estimated GFR <60 mL/min/1.73 m²) increased by 17.5 (95% confidence interval [CI], 16.5-18.6) visits per 10 000 CKD patients per month, corresponding to a relative increase from baseline of 68.4% (95% CI, 65.7%-71.2%). There was no association between estimated GFR reporting and rate of first nephrologist visit among patients without CKD. Among patients with an estimated GFR of less than 30 mL/min/1.73 m², the rate of first nephrologist visits increased by 134.4 (95% CI, 60.0-208.7) visits per 10 000 patients per month. This increase was predominantly seen in women, patients aged 46 to 65 years as well as those aged 86 years or older, and those with hypertension, diabetes, and comorbidity. Reporting of estimated GFR was not associated with increased rates of internal medicine or general practitioner visits or increased use of angiotensin-converting enzyme inhibitors/angiotensin II receptor blockers among patients with CKD and proteinuria or the subgroup limited to patients with diabetes.

Conclusions Reporting of estimated GFR was associated with an increase in first nephrologist visits, particularly among patients with more severe kidney dysfunction, women, middle-aged and very elderly patients, and those with comorbidities. Any effect on outcomes remains to be shown.

For editorial comment see p 1201.
NEPHROLOGY VISITS AND ESTIMATED GFR REPORTING

CKD and overwhelming limited health care resources) have been raised.\textsuperscript{13,14} Despite lack of evidence, automated reporting of estimated GFR is widely used.\textsuperscript{15}

In a large community-based cohort, we evaluated the association of estimated GFR reporting with nephrologist visits, health care resource use, and management of patients with CKD. Specifically, we aimed to determine whether estimated GFR reporting increased the rate of outpatient visits to a nephrologist. We also evaluated whether estimated GFR reporting was associated with health care resource use (internal medicine specialist and general practitioner visits) and use of drugs commonly recommended in this patient population.

METHODS

Study Design and Data Sources

We used administrative health care and laboratory data from the province of Alberta, Canada. The study population included adults aged 18 years or older who had at least 1 outpatient serum creatinine measurement between May 15, 2002, and February 15, 2007, in the Capital Health Region or between July 1, 2003, and February 15, 2007, in the Calgary Health Region (period to define prevalent CKD), as determined from the Alberta Kidney Disease Network database.

Estimated GFR Reporting

Reporting of estimated GFR was implemented in outpatient settings as of October 15, 2004. Prior to implementation, a Physician Information Sheet was mailed to physicians describing the rationale for estimated GFR reporting, basic recommendations for referral and management, and a Web site link for further information (http://www.akdn.info). The abbreviated Modification of Diet in Renal Disease (MDRD) equation\textsuperscript{17} was used to estimate and report estimated GFR throughout the study period for the Capital Health Region, and for the Calgary Health Region until November 29, 2006, when the laboratory switched to an isotope dilution mass spectroscopy (IDMS)–calibrated reference standard, at which point the IDMS-traceable MDRD study equation was used to calculate and report the estimated GFR.\textsuperscript{18} Estimates of GFR using the 2 equations were compared and yielded similar results. Although data on race were not available, misclassification of estimated GFR was expected to be minimal because less than 1% of the Alberta population is black.\textsuperscript{19}

For patients with estimated GFR of at least 60 mL/min/1.73m\textsuperscript{2}, the calculated estimated GFR was not reported and instead a comment appeared: “Chronic kidney disease is defined by estimated GFR which is persistently <60 mL/min/1.73 m\textsuperscript{2}. See www.akdn.info for more information.” For patients with estimated GFR of less than 60 mL/min/1.73 m\textsuperscript{2}, the calculated estimated GFR was reported with the following comment: “In patients with stable kidney function, estimated GFR is a more accurate marker of kidney function than serum creatinine. Chronic kidney disease is defined by estimated GFR <60 mL/min/1.73 m\textsuperscript{2} for more than 3 months. Published guidelines recommend that patients with estimated GFR <30 mL/min/1.73 m\textsuperscript{2} be referred to a nephrologist (see www.akdn.info).”

Identification of Patients

The study observation period (May 15, 2003, to March 14, 2007) was divided into monthly intervals before and after the introduction of estimated GFR reporting. Outpatient-estimated GFR measurements were used to define monthly cohorts of patients with CKD (defined as mean estimated GFR <60 mL/min/1.73 m\textsuperscript{2} in the prior year based on all available measurements). A total of 46 consecutive monthly cohorts were thus created (17 before and 29 after estimated GFR reporting). Patients receiving dialysis or with a renal transplant prior to May 15, 2003, were excluded, as were those identified at the beginning of each monthly interval as having developed end-stage renal disease.\textsuperscript{16,20} For each monthly interval, we recategorized patients by CKD stage using investigator-calculated estimated GFR measurements before, and laboratory reported measurements after, the implementation of estimated GFR reporting.

Study Outcomes

The primary outcome was the monthly rate of first outpatient visits to a nephrologist, as recorded in the Alberta Health and Wellness physician claims database, among patients with prevalent CKD (estimated GFR <60 mL/min/1.73 m\textsuperscript{2}) as well as in the subgroup with more severe kidney disease (estimated GFR <30 mL/min/1.73 m\textsuperscript{2}). Outpatient appointments with nephrologists were considered first visits if the patient had not visited a nephrologist in at least 4 years preceding the index visit. Secondary outcomes (reflecting health care resource use) included monthly rates of first outpatient visits to internal medicine specialists and all outpatient visits to a general practitioner. For participants aged 66 years or older (population eligible for universal drug coverage in Alberta), we also analyzed monthly rates of angiotensin-converting enzyme (ACE) inhibitor and angiotensin II receptor blocker (ARB) use for 4 subgroups of patients: all patients with CKD irrespective of diabetes status or proteinuria; patients with CKD and diabetes irrespective of proteinuria; and the former 2 groups each with overt proteinuria. Drug use was classified as new use (no prescriptions for an ACE inhibitor or an ARB in the prior year) or any use (irrespective of prior use). We also analyzed monthly rates of new and any drug use for cholesterol-lowering agents (both statin and nonstatin agents) for patients with and without CKD. Finally, we evaluated the association between estimated GFR reporting and hospitalization with a primary discharge diagnosis of acute myocardial infarction, stroke, or congestive heart failure.
Measurement of Covariates
Diabetes and hypertension were identified from hospital discharge records and physician claims following validated algorithms. Other comorbid conditions based on the Deyo classification of Charlson comorbidities were identified using validated International Classification of Diseases, Ninth Revision, Clinical Modification and International Statistical Classification of Diseases, 10th Revision coding algorithms applied to physician claims and hospitalization data, with weights applied to each condition to obtain a summary score for each participant. Proteinuria was categorized based on the Kidney Disease Outcomes Quality Initiative guidelines, with overt proteinuria defined as 24-hour urine protein greater than 300 mg/d, protein-creatinine ratio greater than 200 mg/g, and albumin-creatinine ratio greater than 250 mg/g for men and greater than 355 mg/g for women. A participant was defined as having overt proteinuria if at least 1 measurement in the year prior to the monthly interval met the definition.

Statistical Analysis
The association between estimated GFR reporting and outcomes was examined using segmented linear regression analysis of interrupted time series with 17 months before and 29 months after implementation of estimated GFR reporting, providing adequate data points for the study. Segmented linear regression takes into account pre-estimated GFR reporting trends and potential autocorrelation or seasonal influences that may be present. We first used a generalized linear model for each of the monthly count outcomes while adjusting for potential confounders (age, sex, hypertension, diabetes, Charlson comorbidity score, and socioeconomic status). We corrected for overdispersion by including a scale parameter in the model and for intraclass correlation using generalized estimating equations in conjunction with the Huber-White sandwich robust estimator of variance. We used the generalized linear model framework with generalized estimating equations to calculate adjusted monthly event rates for each of the outcomes and to examine month-to-month patterns in these rates using time-series analyses.

For the primary outcome, a 3-month period after initiation of estimated GFR reporting was used to account for delay between referral submission and nephrologist visit (based on provincial estimates of wait times for first nephrologist visits). Visits occurring within this 3-month period were not included in the time-series analysis; rather, all visits after the 3-month period to study end (March 14, 2007) were considered. A transition period was not implemented for other study outcomes. Reporting of estimated GFR was evaluated by assessing the change in the level and/or trend of the outcome before and after estimated GFR reporting. A change in level, eg, an abrupt increase or decrease in the outcome after the intervention, constitutes an intervention effect. A change in trend (or slope) is defined by an increase or decrease in the slope of the segment after the intervention compared with the segment preceding the intervention and represents a long-term intervention effect. When assessing change in level and/or slope, we took the baseline trend into account and corrected for autocorrelation effects by incorporating terms in the segmented regression model for the lagged residuals, if necessary. The Durbin-Watson statistic and the autocorrelation, inverse autocorrelation, and partial autocorrelation functions were used to check for autocorrelation and seasonality. The adequacy of the model was tested by standard methods of residual analysis. Results were also stratified by age, sex, baseline estimated GFR, diabetes mellitus, hypertension, and Charlson comorbidity score. Analyses were conducted with SAS software, version 9.2 (SAS Institute Inc, Cary, North Carolina), and Stata, version 10.1 (Stata Corp, College Station, Texas). P<.05 indicates statistical significance. The institutional review boards of the Universities of Calgary and Alberta approved the study and granted a waiver of patient consent.

RESULTS
Overall, 1,135,968 participants were included in the cohort. The median numbers of adults with and without CKD in each monthly cohort for the 46 months were 77,437 (interquartile range, 70,054-80,837) and 472,218 (interquartile range, 399,527-503,161), respectively. Demographic characteristics of participants were similar across the 2 periods, as were the prevalences of diabetes and hypertension and the Charlson comorbidity score (Table 1).

Physician Visits
After a 3-month transition period following estimated GFR reporting, the rate of first outpatient visits to a nephrologist for patients with CKD (estimated GFR <60 mL/min/1.73 m²) increased significantly by 17.5 (95% confidence interval [CI], 16.5%-18.6%) visits per 10,000 CKD patients per month (P<.001), corresponding to a relative increase from baseline of 68.4% (95% CI, 65.7%-71.2%) (Figure 1). There was a small but significant decrease in the slope (the rate of change in new visits over time) following estimated GFR reporting (P=.02), suggesting that the magnitude of increase in referrals declined over time. Despite this decline, there was a sustained increase compared with the expected rate in the absence of estimated GFR reporting. Specifically, the increase in first nephrologist visits at 2 years following introduction of reporting was 13.3 (95% CI, 9.1%-17.4%) visits per 10,000 CKD patients per month, corresponding to a 61.7% (95% CI, 30.7%-92.7%) relative increase. There was no association between estimated GFR reporting and rate of first outpatient nephrologist visits among patients without CKD (Figure 1). The rate of all outpatient nephrologist visits for patients with CKD following estimated GFR reporting (including visits among individuals with
and without prior nephrologist visits) also increased significantly by 19.8 (95% CI, 9.5%-30.2%) visits per 10 000 CKD patients per month (P < .001) (Figure 2). Compared with the pre–estimated GFR reporting period, there was a significant increase in the slope for the monthly nephrology visit rate after estimated GFR reporting (P = .007), suggesting that the magnitude of increase in visits increased over time.

Findings were similar in a subgroup with estimated GFR of less than 30 mL/min/1.73 m²: the rate of first outpatient nephrologist visits increased significantly by 134.4 (95% CI, 60.0-208.7) visits per 10 000 patients per month.

### Table 1. Characteristics of Study Participants Before and After Estimated GFR Reporting Among Select Monthly Cohorts

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Before Estimated GFR Reporting</th>
<th>After Estimated GFR Reporting</th>
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<tbody>
<tr>
<td></td>
<td>May 2003 (n = 236 749)</td>
<td>Nov 2003 (n = 367 589)</td>
</tr>
<tr>
<td></td>
<td>May 2004 (n = 497 734)</td>
<td>May 2005 (n = 557 130)</td>
</tr>
<tr>
<td></td>
<td>May 2006 (n = 585 774)</td>
<td>Nov 2005 (n = 572 732)</td>
</tr>
<tr>
<td></td>
<td>May 2006 (n = 585 774)</td>
<td>May 2006 (n = 585 774)</td>
</tr>
<tr>
<td>Age, mean (SD), y</td>
<td>53.7 (17.2)</td>
<td>53.9 (17.3)</td>
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<tr>
<td>Female</td>
<td>58.8</td>
<td>58.4</td>
</tr>
<tr>
<td>Aboriginal</td>
<td>1.8</td>
<td>1.6</td>
</tr>
<tr>
<td>Socioeconomic status</td>
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<td></td>
</tr>
<tr>
<td>Low</td>
<td>22.0</td>
<td>21.4</td>
</tr>
<tr>
<td>Low with subsidy</td>
<td>3.3</td>
<td>3.0</td>
</tr>
<tr>
<td>Diabetes</td>
<td>10.4</td>
<td>10.4</td>
</tr>
<tr>
<td>Hypertension</td>
<td>26.2</td>
<td>26.7</td>
</tr>
<tr>
<td>Charlson comorbidity score</td>
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<td>64.9</td>
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<td>≥5</td>
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<td>3.2</td>
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<tr>
<td>Estimated GFR, mL/min/1.73 m²</td>
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<td></td>
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<tr>
<td>≥60</td>
<td>82.3</td>
<td>82.4</td>
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<td>30-59.9</td>
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<tr>
<td>&lt;30</td>
<td>0.9</td>
<td>1.0</td>
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</table>

Abbreviation: GFR, glomerular filtration rate.

Data are expressed as percentages of participants unless otherwise indicated. Totals do not always add to 100% because of rounding.

Socioeconomic status was categorized as high (annual adjusted taxable family income ≥Can $39 250), low (annual adjusted taxable family income <Can $39 250), and low with subsidy (receiving social assistance) based on government of Alberta health care insurance records.

Comorbidities in the Charlson comorbidity score include cerebrovascular disease, peripheral vascular disease, congestive heart failure, cancer, chronic obstructive pulmonary disease, dementia, diabetes with complications, diabetes without complications, AIDS/human immunodeficiency virus, metastatic solid tumor, myocardial infarction, mild liver disease, moderate/severe liver disease, paralysis, peptic ulcer disease, renal disease, and rheumatic disease.

**Figure 1.** Time Series of Monthly Adjusted Rates of First Outpatient Nephrology Visits per 10 000 Population Aged 18 Years or Older

GFR indicates glomerular filtration rate. Fitted trend lines show predicted values from the segmented regression model. Rates are adjusted for age, sex, diabetes, hypertension, Charlson comorbidity score, and socioeconomic status.

Each month corresponds to the period spanning from the 15th day of that month to the 14th day of the next month (eg, May 2003 corresponds to May 15 to June 14, 2003).
(P < .004) (eFigure; available at http://www.jama.com). Participants with an estimated GFR of 30 to 44.9 mL/min/1.73 m² and 45 to 59.9 mL/min/1.73 m² also experienced a significant but less pronounced increase in first visits (eTable).

Among participants with an estimated GFR of less than 30 mL/min/1.73 m², women experienced a greater increase in the rate of first visits to a nephrologist, while there was no increase for men (TABLE 2). The increase in the rate of first visits to a nephrologist was predominantly seen in patients aged 46 to 65 and those aged 86 years or older as well as those with hypertension, diabetes, and comorbidity (Charlson comorbidity score >0) (Table 2).

Other Outcomes

There was no association between estimated GFR reporting and increase in the monthly rate of first outpatient visits to internal medicine specialists or the monthly rate of total visits (irrespective of prior visits) to general practitioners for patients with estimated GFR of less than 60 mL/min/1.73 m² (TABLE 3).

A large proportion of CKD patients aged 66 years or older were already taking an ACE inhibitor or ARB prior to the introduction of estimated GFR reporting (77.5% of participants with diabetes and proteinuria; 61.4% of participants with nondiabetic proteinuria). Reporting of estimated GFR was not associated with an increase in the monthly rate of ACE inhibitor or ARB use (either new use or any use) among all patients with CKD (Table 3) or those with diabetes, proteinuria, or diabetes and proteinuria combined. While the rate of prescriptions for several medications (ACE inhibitors, ARBs, and cholesterol-lowering agents) decreased slightly following the introduction of estimated GFR reporting, the decrease was similar in both CKD and non-CKD patients. Finally, there was no association between estimated GFR reporting and hospitalization rates for acute myocardial infarction, stroke, or congestive heart failure (Table 3).

COMMENT

In this large community-based cohort, we found that estimated GFR reporting was associated with a significant increase in the rate of first outpatient visit to a nephrologist for patients with CKD, an increase that was sustained over at least a 2-year period. The increase was most pronounced among the subgroup with estimated GFR of less than 30 mL/min/1.73 m², the group for whom current practice guidelines emphasize the value of timely nephrological referral. In addition, referral of participants who were at increased risk of late detection of CKD (such as older or female patients) and those at highest risk of adverse outcomes (people with hypertension, diabetes, and other comorbidity) increased to a greater extent than those without these characteristics. However, reporting of estimated GFR was not associated with an increase in ACE inhibitor or ARB use, even among the subgroup with a proven clinical indication; namely, those with diabetes and proteinuria.

While estimated GFR reporting was associated with an increased rate of nephrology visits, as demonstrated in prior studies, we did not find an association between estimated GFR reporting and other aspects of health care resource use, including visits to internal medicine specialists or to general practitioners. Also similar to other studies that showed minimal effect, we did not find an increase in ACE inhibitor or ARB use, medications that interrupt the renin-angiotensin system and slow the
progression of nondiabetic and diabetic CKD. We speculate that this finding was due to 2 factors. First, a large proportion of CKD patients aged 66 years or older with diabetes and proteinuria (77.5%) and those with non-diabetic proteinuria (61.4%) were already taking an ACE inhibitor or ARB prior to estimated GFR reporting. Second, our educational intervention was general in nature and did not specifically direct physicians to consider use of these medications. However, given that evidence supporting ACE inhibitor and ARB use in CKD is weaker in older than in younger adults, the significance of this finding is unclear at present.

A variety of interventions have been advocated to improve recognition of CKD and guide physician management. We chose a multipronged approach (estimated GFR reporting with mailed and Web-based instruction) be-

<table>
<thead>
<tr>
<th>Table 2. Interrupted Time-Series Regression Analysis of Monthly Adjusted Rates of First Outpatient Visit to Nephrologist per 10 000 Population Aged 18 Years or Older With Estimated GFR of Less than 30 mL/min/1.73 m² per Month by Patient Demographics and Comorbidities</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Characteristics</strong></td>
</tr>
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<td>Sex</td>
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<tr>
<td>Male</td>
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<td>Hypertension</td>
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<tr>
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<td>1-4</td>
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<td>≥5</td>
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Table 3. Interrupted Time-Series Regression Analysis of Monthly Adjusted Rates for Secondary Outcomes per Population Aged 18 Years or Older With Estimated GFR of Less Than 60 mL/min/1.73 m² per Month

<table>
<thead>
<tr>
<th>Table 3. Interrupted Time-Series Regression Analysis of Monthly Adjusted Rates for Secondary Outcomes per Population Aged 18 Years or Older With Estimated GFR of Less Than 60 mL/min/1.73 m² per Month</th>
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</thead>
<tbody>
<tr>
<td><strong>Characteristics</strong></td>
</tr>
<tr>
<td>Internal medicine visits</td>
</tr>
<tr>
<td>New visits (per 10 000 population)</td>
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<tr>
<td>General practitioner visits</td>
</tr>
<tr>
<td>ACE inhibitor or ARB use</td>
</tr>
<tr>
<td>New use (per 10 000 population)</td>
</tr>
<tr>
<td>Any use (per 100 population)</td>
</tr>
<tr>
<td>Cholesterol-lowering agents</td>
</tr>
<tr>
<td>New use (per 10 000 population)</td>
</tr>
<tr>
<td>Any use (per 100 population)</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; GFR, glomerular filtration rate.

aAdjusted for age, sex, diabetes, hypertension, Charlson comorbidity score, and socioeconomic status.
bData not applicable (NA); nonsignificant variables were removed using a backward elimination strategy to achieve the most parsimonious model.
cause single educational interventions are generally insufficient to change practice behavior.39-41 Although didactic teaching sessions have been shown to increase CKD recognition,12 the sustainability of such a resource-intensive intervention and its effect on patient outcomes have not been assessed.

Laboratory reporting of estimated GFR has also resulted in considerable debate,42-44 with concern for potential mislabeling of patients with CKD, which, in itself, has been shown to negate any potential benefit in cost-effectiveness of reporting due to associated decreases in quality of life.44 This mislabeling is most common among those with an estimated GFR of 45 to 59.9 mL/min/1.73 m² and among older individuals.13,45,46 However, considering that cardiovascular disease is the leading cause of mortality in CKD7 that even mild reductions in estimated GFR have been associated with excess cardiovascular risk,47 and that proven treatments are available, earlier referral of these individuals to nephrologists may improve their outcomes.

Our study has many novel contributions, including measures of both kidney function and proteinuria, the ability to examine nephrology visits by patient characteristics and level of estimated GFR (including a control group with estimated GFR ≥60 mL/min/1.73 m²), and inclusion of other measures of resource use, such as internal medicine and general practitioner visits. In addition to our study’s large size and community-based nature, an additional strength was the interrupted time-series design, in which the effect of an intervention is assessed accounting for underlying trend or seasonal influences.26 In a nonrandomized setting, the interrupted time-series design with a concomitant comparison group (in this case, patients without CKD) is the strongest quasi-experimental approach for evaluating longitudinal effects of interventions.27,28

Our study also has limitations. First, participants may have been misclassified with respect to kidney function or CKD status, as the laboratory prompts relied on a single measure of estimated GFR. If correct classification were the goal, multiple direct measurements of estimated GFR (separated by ≥3 months)24 would have been preferable. However, given the objective of the study (to determine the association with estimated GFR reporting on nephrology visits), this potential misclassification would not have biased the results. Second, since our study was conducted primarily in urban areas, our results may not be generalizable to persons in more rural regions. Third, our data did not allow us to evaluate other important clinical outcomes, including development of end-stage kidney disease or death or quality of the referrals, which may decrease following estimated GFR reporting.35 Finally, we did not have information on blood pressure measurements for patients with hypertension and, thus, cannot exclude the possibility of residual confounding. However, given the magnitude of the trends obtained, it is unlikely that further stratification for severity of these covariates would negate the observed associations.

In conclusion, reporting of estimated GFR was associated with a significant increase in the rate of first outpatient visits to a nephrologist, particularly for those with estimated GFR of less than 30 mL/min/1.73 m²; middle-aged, older, or female participants; and those with comorbidities. The association with estimated GFR reporting and long-term patient outcomes, as well as economic consequences, remains to be determined.

Author Contributions: Dr Hemmelgarn had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Hemmelgarn, Zhang, Manns, Ravani, Klarenbach, Culleton, Thorlacius, Tonelli.

Acquisition of data: Hemmelgarn, James, Krause, Thorlacius.

Analysis and interpretation of data: Hemmelgarn, Zhang, Manns, James, Quinn, Ravani, Klarenbach, Krause, Thorlacius, Jain, Tonelli.

Drafting of the manuscript: Hemmelgarn, Zhang.

Critical revision of the manuscript for important intellectual content: Hemmelgarn, Zhang, Manns, James, Quinn, Ravani, Klarenbach, Krause, Thorlacius, Jain, Tonelli.

Statistical analysis: Hemmelgarn, Zhang, James, Ravani, Jain.

Obtained funding: Hemmelgarn, Zhang, Manns, Culleton.

Administrative, technical, or material support: Hemmelgarn, Zhang, James, Krause, Thorlacius.

Study supervision: Hemmelgarn.

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Role of the Sponsor: The funding organizations had no role in the design and conduct of the study; in the collection, analysis, and interpretation of the data; or in the preparation, review, or approval of the manuscript.

Online-Only Material: The eFigure and eTable are available at http://www.jama.com.

REFERENCES


