Impact of the 2021 CKD-EPI eGFR Equation on Kidney Care Referral Criteria in Ontario, Canada: A Population-based Cross-sectional Study

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Abstract

Background: In some jurisdictions, individuals become eligible or recommended for referral for different types of kidney care using criteria based on their estimated glomerular filtration rate (eGFR). Historically, GFR was estimated with an equation developed in 2009, which included a Black race term. An updated, race-free equation was developed in 2021. It is unclear how adoption of the 2021 equation will influence the number of individuals meeting referral criteria to receive different types of kidney care.

Objective: To develop population-based estimates on how the number of individuals meeting the eGFR-based referral criteria to receive three different types of kidney care (nephrologist consultation, care in a multi-care specialty clinic, kidney transplant evaluation) changes when the 2021 versus 2009 equation is used to calculate eGFR.

Design: Population-based, cross-sectional study.

Setting: Ontario, Canada's most populous province with 14.2 million residents as of 2021. Less than 5% of Ontario's residents self-identify as being of Black race.

Patients: Adults with at least one outpatient serum creatinine measurement in the 2 years prior to December 31, 2021.

Measurements: Referral criteria to 3 different types of kidney care: nephrologist consultation, multi-care specialty clinic, and evaluation for a kidney transplant. The eGFR thresholds used to define referral eligibility or recommendation for these kidney health services were based on guidelines from Ontario's provincial renal agency.

Methods: The number of individuals meeting referral criteria for the 3 different healthcare services was compared between the 2009 and 2021 equations, restricted to individuals not yet receiving that level of care. As individual-level race data were not available, estimates were repeated, randomly assigning a Black race status to 1%, 5%, and 10% of the population.

Results: We had an outpatient serum creatinine measurement available for 1 048 110 adults. Using the 2009 equation, 37 345 individuals met the criteria to be referred to a nephrologist, 10019 met the criteria to receive care in a multi-care specialty clinic, and 10178 met the criteria to be referred for kidney transplant evaluation. Corresponding numbers with the 2021 equation (and the percent relative to the 2009 equation) were 26 645 (71.3%), 9009 (89.9%), and 8615 (84.6%) individuals, respectively. These numbers were largely unchanged when Black race was assumed in up to 10% of the population.

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Limitations: Referral criteria based solely on urine albumin-to-creatinine ratio were not assessed. Self-reported race data were unavailable.

Conclusions: For healthcare planning, in regions where a minority of the population is Black, a substantial number of individuals may no longer meet referral criteria for different types of kidney healthcare following adoption of the new 2021 eGFR equation.

Abrégé

Contexte: Dans certaines régions, les individus sont dirigés vers différents types de soins rénaux, ou y deviennent admissibles, selon des critères fondés sur le débit de filtration glomérulaire estimé (DFGe). Historiquement, le DFG était estimé avec une équation développée en 2009 comportant un terme qui tenait compte du fait d'être une personne de race noire. Une nouvelle équation sans mention de la race a été développée en 2021. Il est difficile de savoir comment l'adoption de l'équation de 2021 influencera le nombre de personnes qui répondront aux critères pour recevoir divers types de soins rénaux.

Objectifs: Établir des estimations populationnelles de la variation du nombre de personnes qui répondent aux critères d'orientation fondés sur le DFGe pour recevoir trois différents types de soins rénaux (consultation avec un néphrologue, soins dans une clinique multidisciplinaire spécialisée, évaluation pour une transplantation rénale) selon que le DFGe est calculé avec l'équation de 2021 ou de 2009.

Conception: Étude populationnelle transversale rétrospective.

Cadre: L'Ontario, la province la plus peuplée du Canada avec 14,2 millions d'habitants en 2021. Moins de 5 % des résidents de l'Ontario s'identifient comme étant de race noire.

Sujets: Des adultes avec au moins une mesure de la créatinine sérique en ambulatoire au cours des deux ans précédant le 31 décembre 2021.

Mesures: Les critères d'orientation vers trois différents types de soins rénaux : consultation avec un néphrologue, soins en clinique multidisciplinaire spécialisée et évaluation pour une transplantation rénale. Les seuils de DFGe utilisés pour définir l'admissibilité à — ou l'orientation vers — ces services de santé rénale étaient fondés sur les lignes directrices de l'agence provinciale de soins rénaux de l'Ontario.

Méthodologie: On a comparé les nombres d'individus répondant aux critères d'orientation pour les trois différents services de santé, calculés avec les équations de 2009 et de 2021, en se limitant aux personnes qui ne recevaient pas encore de tels soins. Les données individuelles sur la race n'étant pas disponibles, les estimations ont été répétées en attribuant aléatoirement un statut de race noire à 1 %, à 5 % et à 10 % de la population étudiée.

Résultats: Une mesure de la créatinine sérique en ambulatoire était disponible pour un total de 1 048 110 adultes. Avec l'équation de 2009, 37 345 personnes répondaient aux critères pour être dirigées vers un néphrologue, 10 019 répondaient aux critères pour recevoir des soins dans une clinique multidisciplinaire spécialisée et 10 178 répondaient aux critères pour être évaluées pour une transplantation rénale. Avec l'équation de 2021, ces mêmes nombres de personnes (pourcentage par rapport à l'équation de 2009) étaient respectivement 26 645 (71,3 %), 9 009 (89,9 %) et 8 615 (84,6 %). Des chiffres qui sont demeurés majoritairement inchangés même en assumant une proportion de jusqu'à 10 % de personnes de race noire dans la population.

Limites: Les critères d'orientation fondés uniquement sur le rapport albumine/créatinine urinaire n'ont pas été évalués. Les données autodéclarées sur la race n'étaient pas disponibles.

Conclusion: Pour la planification des soins de santé, dans les régions où une minorité de la population est noire, un nombre important de personnes pourraient ne plus répondre aux critères d'orientation vers différents types de soins rénaux après l'adoption de l'équation de 2021 pour le calcul du DFGe.

Keywords

CKD (chronic kidney disease), clinical guidelines, health services research, referral, estimated glomerular filtration rate

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Introduction

Estimating glomerular filtration rate is important for many reasons, including the planning of healthcare delivery in individuals with chronic kidney disease (CKD). The eGFR equation developed by the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) has been almost universally used to estimate an individual's kidney function since its creation in 2009.¹ However, the inclusion of Black race in this equation has been increasingly scrutinized in recent years as it inflates eGFR for those with Black race, which could delay access to treatment in these individuals.²⁻⁴ As a result, a revised race-free equation was developed in 2021 by the CKD-EPI group that only used patient age, sex, and serum creatinine.⁵ This new equation was advanced with a focus on diversity and equity, with observed differences between measured glomerular filtration rate and eGFR now better balanced between Black and non-Black individuals (measured GFR underestimated by 3.6 mL/min/1.73 m² in Black participants and overestimated by 3.9 mL/min/1.73 m² in non-Black participants).⁵

Many organizations worldwide, including the National Kidney Foundation, American Society of Nephrology, and UK Kidney Association, have recommended universal adoption of this new equation.⁶⁻⁸ In Ontario, Canada's largest province, this equation is expected to replace the race-based equation, with the Ontario Renal Network and the Ontario Association of Medical Laboratories already transitioning to this updated calculation.⁹ Member laboratories of the Ontario Association of Medical Laboratories currently perform more than 95% of all community-based laboratory testing in the province, so their adoption of this new equation will impact nearly all community-based serum creatinine measurements in Ontario.¹⁰

Within Ontario, the Ontario Renal Network is a provincial agency that manages the funding and delivery of nephrology care across the province, including referral eligibility criteria for pre-end-stage kidney disease multidisciplinary clinic (also known as Multi-Care Kidney Clinic [MCKC]) and guidelines for when it is recommended to refer for nephrologist consultation and kidney transplantation assessment. While individuals will not be funded for care at an MCKC unless they meet the specific referral eligibility criteria, the criteria for nephrologist consultation and kidney transplantation serve as a recommendation from the Ontario Renal Network, with referral to these two settings being made solely at the referring physician's discretion. For the purposes of this article, we use the common language of referral criteria across all three settings. In Ontario, the guidelines on referral for nephrologist consultation by a primary care physician, MCKC, and kidney transplant evaluation currently all contain eGFR components. What impact universal adoption of the new eGFR equation would have on the population meeting the referral criteria in Ontario is currently unknown. Using population-based laboratory data, we sought to estimate how many individuals would experience a change in meeting the eGFR-based referral criteria using the 2021 CKD-EPI equation compared to the 2009 CKD-EPI equation. Given that the 2021 equation results in slightly higher values in non-Black individuals and lower values in Black individuals than the 2009 equation,¹¹ we expected that some non-Black individuals would no longer meet the criteria for referral once their eGFR was re-calculated with the new equation, while some Black individuals would newly meet the criteria.

Methods

Design and Setting

We conducted a retrospective, population-based cross-sectional study in Ontario, Canada. In Ontario, the Ontario Renal Network's KidneyWise Clinical Toolkit provides indications for referral to nephrologist consultation from primary care.¹² Individuals with advanced CKD who are approaching the need for dialysis are referred to and receive specialized, multidisciplinary care at MCKCs.13 Multi-Care Kidney Clinics aim to provide person-centred care from a multidisciplinary team consisting of nurses, nephrologists, pharmacists, dietitians, and social workers to prepare eligible individuals for end-stage kidney disease. Individuals will not be funded for care at an MCKC unless they meet the referral eligibility criteria. Similar to nephrologist consultation, there is guidance on when an individual is recommended to be referred as a candidate for kidney transplantation.¹⁴ Referral to nephrologist consultation and kidney transplantation do not have the same rigid eligibility criteria tied to patient funding as with MCKC. Referrals to nephrologist consultation and kidney transplantation are made at the referring physician's discretion, with the aforementioned criteria serving as the recommendation by the Ontario Renal Network. For the purposes of this article, we use the common language of referral criteria across all three settings.

Data Sources

We used individual-level data from health administrative databases in Ontario, and these datasets were linked using unique, encoded identifiers and analyzed at ICES. ICES is an independent, non-profit research institute whose legal status under Ontario's health information privacy law allows it to collect and analyze healthcare and demographic data, without consent, for health system evaluation and improvement. The use of data in this project was authorized under section 45 of Ontario's Personal Health Information Protection Act, which does not require review by a Research Ethics Board. This study followed the Reporting of Studies Conducted Using Observational Routinely-Collected Health Data (RECORD) guidelines (Supplemental Table 1).¹⁵ Laboratory data were obtained using the Ontario Laboratories Information System (OLIS) database. OLIS is a provincial repository of data from hospital-based and community laboratories across Ontario. As of 2020, 144 hospitals and all major community laboratories in the province were contributing to OLIS, with >95% of community laboratory records in Ontario expected to be linked to the repository.^{10,16,17} Demographics and vital status were obtained from the Registered Persons Database. Baseline characteristics were ascertained using physician billings in the Ontario Health Insurance Plan database, emergency department visits in the

Canadian Institute for Health Information's National Ambulatory Care Reporting System, the Ontario Mental Health Reporting System, the Ontario Cancer Registry, and the ICES-derived databases of the Ontario Diabetes Database, the Chronic Obstructive Pulmonary Disease database, the Ontario Dementia Database, the Ontario Hypertension database, and the Congestive Heart Failure database. Physician specialty was determined using the ICES Physician Database. The Ontario Renal Reporting System was used to identify prior visits to an MCKC. The list of codes used to identify variables for the cohort build and baseline characteristics is in the online appendix (Supplemental Table 2).

Population

We included all adults with a valid, non-missing patient identifier and sex, with an outpatient serum creatinine measurement in the 2 years prior to and including December 31, 2021. Individuals were excluded if they had an invalid age (>105), were non-Ontario residents, or had evidence of a death date on or prior to their serum creatinine date. The most recent serum creatinine measurement was used in individuals with multiple values in the 2 years prior to December 31, 2021. The date of the serum creatinine measurement served as an individual's index date. We calculated eGFR values using the 2009 CKD-EPI equation, excluding the Black race multiplier due to the absence of race in our laboratory data. In the 2021 Inker et al article, this approach is referred to as the Age, Sex, Race-Non-Black (ASR-NB) equation since it was developed using age, sex, and race, but with the Black race multiplier ignored (everyone assumed non-Black).⁵ This approach has historically been used for population-based studies in Ontario¹⁸⁻²⁰ and aligns with what would typically be given as the result by the laboratory, with the onus on the physician to apply the Black multiplier, when appropriate.²¹ We compared these eGFR values to eGFR values re-calculated using the new 2021 CKD-EPI equation that was developed using just age and sex, in addition to serum creatinine. These two different eGFR equations were used to assess referral criteria and estimate the potential impact the new equation would have on the population meeting the referral criteria in the province. To best approximate an individual's baseline kidney function for all referral criteria, we only considered outpatient laboratory values.

Individuals met the criteria to be recommended for referral by primary care to nephrologist consultation if they had evidence of any of the following on their index date: (1) an outpatient eGFR <30 mL/min/1.73 m², (2) an outpatient eGFR <45 mL/min/1.73 m² with evidence of a >5 mL/ min/1.73 m² decline in the 180 days prior, or (3) a 5-year Kidney Failure Risk Equation (KFRE) predicted probability of \geq 5%.²² Individuals were also required to have evidence of an eGFR <60 mL/min/1.73 m² in the 90 to 365 days preceding the aforementioned criteria. An individual was excluded from this cohort if they had evidence of a prior kidney transplant, receipt of maintenance dialysis in the 1 year prior to their serum creatinine measurement, or any evidence of a prior visit with a nephrologist.

The eligibility criteria for referral to MCKC were any of the following on their index date: (1) an outpatient eGFR <15 mL/min/1.73 m² with an additional outpatient eGFR <15 mL/min/1.73 m² in the 90 to 365 days prior or (2) a 2-year KFRE predicted probability of \geq 10%, with an additional 2-year KFRE \geq 10% in the 90 to 365 days prior to the index date.²³ Individuals were excluded from this cohort if they had evidence of a prior kidney transplant, receipt of maintenance dialysis in the 1 year prior to their serum creatinine measurement, any prior specialty clinic or MCKC visit, or no evidence of an outpatient visit with a nephrologist in the prior 15 months (since individuals are referred to MCKC by a nephrologist).

Recommendation for kidney transplant evaluation referral was defined as at least one of the following on their index date: (1) an outpatient eGFR < 15 mL/min/1.73 m^2 with an additional outpatient eGFR <15 mL/min/1.73 m² in the 90 to 365 days prior or (2) a 2-year KFRE predicted probability of $\geq 25\%$. Individuals were excluded from this cohort if they had evidence of a prior kidney transplant, receipt of maintenance dialysis in the 1 year prior, or no evidence of an outpatient visit with a nephrologist in the prior 15 months (since individuals are referred to kidney transplant evaluation by a nephrologist). When calculating the KFRE, urine albumin-to-creatinine ratio values had to occur in the 30 days prior to or on the same day as the eGFR value. eGFR was categorized into CKD categories based on Kidney Disease Improving Global Outcomes guidelines.²⁴

Statistical Analysis

Continuous variables are presented as mean (standard deviation [SD]) or median (interguartile range [IQR]), as appropriate. Categorical variables are presented as frequency (percentage). We compared baseline characteristics of individuals meeting the referral criteria with both the 2009 and 2021 equations to those of individuals who only met the criteria with the 2009 equation but not with the 2021 equation. Baseline characteristics were estimated as of the individual's serum creatinine test date and were compared using standardized differences, with a standardized difference >0.10 considered a meaningful difference.²⁵ The slope of eGFR decline over the previous 3 years was presented as a baseline characteristic, calculated using linear mixed models with a random intercept for individuals that accounted for the correlation present within individuals with multiple measurements. As a sensitivity analysis, and because Ontario's population is not 100% non-Black, we also estimated the number of individuals meeting the

referral criteria after randomly applying the Black race multiplier to 1%, 5%, and 10% of the study population when calculating eGFR with the 2009 equation. According to the 2016 Census, 4.7% of Ontario's population identifies as Black.²⁶ All analyses used SAS version 9.4 (SAS Institute Inc., Cary, NC, USA).

Results

After data cleaning exclusions and restricting to the most recent available record, we had 1048110 individuals included in our study with an eGFR $<60 \text{ mL/min}/1.73 \text{ m}^2$ using the 2009 equation, as of December 31, 2021 (Figure 1). When re-calculated with the 2021 equation, eGFR increased by a median (IQR) of 3.5 (2.9-3.9) mL/ min/1.73 m². As a result of this increase in eGFR, 36.4% of individuals were re-categorized to a less-severe category of CKD. With the new equation, 299056 (28.5%) individuals no longer had an eGFR $<60 \text{ mL/min}/1.73 \text{ m}^2$. The change in eGFR value differed by CKD category, with more severe categories of CKD having a smaller absolute change in mL/min/1.73 m² but a larger relative change as a percentage of their 2009 eGFR value (Table 1). As a result, more severe categories of CKD were also less likely to experience a change in category when using the 2021 equation (10.2% in those with 2009 eGFR <15 mL/ min/1.73 m² compared to 40.4% in those with 2009 eGFR $45 - (60 \text{ mL/min}/1.73 \text{ m}^2)$.

Of the 1048110 individuals with eGFR values included in the study, 37345 met recommended criteria for referral for nephrologist consultation by primary care when using the 2009 equation. When eGFR was re-calculated using the 2021 equation, 26645 (71.3%) still met the criteria for referral to nephrologist consultation (Table 2). The proportion of individuals continuing to meet the referral criteria was largely consistent across the different criteria for nephrologist consultation (67.9% for eGFR <30 mL/min/1.73 m², 72.4% for eGFR <45 mL/min/1.73 m² with evidence of a >5 mL/ min/1.73 m² decline, and 73.5% for 5-year KFRE \geq 5%). Individuals no longer meeting the criteria for referral to nephrology (vs those continuing to meet the criteria) had higher eGFR (mean 2021 eGFR of 41.9 vs 33.6 mL/min/1.73 m²), lower urine albumin-to-creatinine ratio (mean 19.1 vs 34.6 mg/mmol), fewer prior visits with primary care (mean 11.0 vs 12.9), fewer emergency department visits (mean 1.1 vs 1.4), and less congestive heart failure (24.6% vs 33.6%) (Table 3). Individuals no longer meeting the criteria for referral to nephrology had an average eGFR decline of -5.0 mL/ min/1.73 m² (95% confidence interval [CI]: -5.2, -4.8) per year based on all serum creatinine measurements in the 3 years prior. Considering this rate of eGFR decline and the median (IQR) increase in eGFR with the 2021 equation of 3.5 (2.9-3.9) mL/min/1.73 m², we would expect many individuals to meet the referral criteria again in less than 1 year. When

we randomly included the Black multiplier in the 2009 eGFR calculation for up to 10% of individuals to simulate the potential prevalence of the Black population in Ontario, the number of individuals still meeting the referral criteria did not substantially change (25943 with 10% Black vs 26645 with 0% Black). In addition, when we simulated a 10% Black prevalence, 838 Black individuals who did not meet the referral criteria with the 2009 equation now met the criteria with the 2021 equation.

We identified 10019 individuals eligible for referral to MCKC using the 2009 eGFR equation. When we re-calculated eGFR using the 2021 equation, 9009 (89.9%) remained eligible for MCKC referral (Table 2). The proportion of individuals remaining eligible for referral appeared higher in those meeting the KFRE criterion (92.2% for 2-year KFRE $\geq 10\%$ vs 80.2% for eGFR <15 mL/min/1.73 m²). Individuals who were no longer eligible for referral to MCKC (vs those still eligible for referral) were older (mean 76.7 vs 71.7), had higher eGFR (mean 2021 eGFR of 21.0 vs 16.1 mL/min/1.73 m²), lower urine albumin-to-creatinine ratio (mean 74.0 vs 151.6 mg/mmol), fewer visits with a nephrologist (mean 3.5 vs 4.5), more congestive heart failure (38.8% vs 29.9%), chronic obstructive pulmonary disease (29.7% vs 25.0%), and cancer (28.1% vs 22.5%) (Table 3). As with nephrologist consultation, the number of individuals still meeting the criteria for referral did not substantially change when we simulated a >0% Black prevalence in the population (8933 with 10% Black vs 9009 with 0% Black). In addition, when we simulated a 10% Black prevalence, 76 Black individuals who were not eligible for referral with the 2009 equation now became eligible with the 2021 equation.

We identified 10178 individuals who met recommended criteria for referral for kidney transplant evaluation using the 2009 eGFR equation. When we re-calculated eGFR using the 2021 equation, 8615 (84.6%) continued to meet the criteria for referral (Table 2). The proportion of individuals still meeting the referral criteria appeared higher in those meeting the KFRE criterion (88.1% for 2-year KFRE $\geq 25\%$ vs 78.4% for eGFR <15 mL/min/1.73 m²). Individuals who were no longer meeting criteria for referral to transplant (vs those still meeting criteria for referral) were older (mean 76.3 vs 71.0), had higher eGFR (mean 2021 eGFR of 18.4 vs 14.2 mL/min/1.73 m²), lower urine albumin-to-creatinine ratio (mean 107.9 vs 197.3 mg/ mmol), fewer visits with a nephrologist (mean 3.7 vs 4.7), and more congestive heart failure (36.7% vs 30.0%) (Table 3). The number of individuals still meeting referral criteria did not substantially change as we increased the Black prevalence in the population (8490 with 10% Black vs 8615 with 0% Black). With a 10% Black prevalence, 126 Black individuals who did not meet the criteria for referral to transplant with the 2009 equation now met the criteria with the 2021 equation.



Figure 1. Cohort selection process.

Note. eGFR = estimated glomerular filtration rate, CKD-EPI = Chronic Kidney Disease Epidemiology Collaboration.

Table I.	Change in eGFR	Values and CKD	Category Using	g the 2021 v	vs 2009 Equation.
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		Change in eGFR, 202	21 vs 2009 equation		
CKD category (eGFR in mL/ min/1.73 m²)	Number in CKD category (2009 equation)	Absolute change (mL/min/1.73 m²), median (IQR)	Percentage change, median (IQR)	Number in CKD category (2021 equation)	% in CKD category using 2021 equation vs 2009
Overall, CKD G2-G5ND (<60)	048 0	3.5 (2.9-3.9)	7.1% (6.4%-7.8%)	749054	71.5%
CKD G3a (45-<60)	739336	3.7 (3.3-4.1)	6.9% (6.2%-7.5%)	440 280	59.6%
CKD G3b (30-<45)	213937	2.9 (2.6-3.2)	7.6% (7.0%-8.2%)	150682	70.4%
CKD G4 (15-<30)	70730	1.9 (1.6-2.2)	8.1% (7.4%-8.7%)	53839	76.1%
CKD G5ND (<15)	24107	0.7 (0.5-1.0)	8.4% (7.6%-9.2%)	21656	89.8%

Note. eGFR = estimated glomerular filtration rate; CKD = chronic kidney disease; IQR = interquartile range.

			Met referral criteria	with 2021 equation	
	Met referral criteria	0% Black	I % Black	5% Black	10% Black
Referral service	with 2009 equation	n (%)	n (%)	n (%)	n (%)
Nephrologist consultation	37 345	26645 (71.3%)	26576 (71.3%)	26321 (71.1%)	25 943 (70.7%)
Multi-Care Kidney Clinic (MCKC)	10019	9009 (89.9%)	8995 (89.9%)	8965 (89.9%)	8933 (89.8%)
Kidney transplant evaluation	10178	8615 (84.6%)	8598 (84.6%)	8561 (84.6%)	8490 (84.5%)

 Table 2.
 Number of Individuals Meeting Referral Criteria With the 2009 and 2021 eGFR Equations, Varying the Prevalence of Black Race.

Note. eGFR = estimated glomerular filtration rate.

Discussion

We quantified the potential healthcare resource and referral utilization of switching from the 2009 to 2021 eGFR equation on eGFR-based referral recommendations and eligibility in Ontario. As expected, the overall change in eGFR value between the two equations was modest, with a median increase of 3.5 mL/min/1.73 m² when using the 2021 equation. However, the impact of this marginal increase in eGFR is that some individuals will no longer meet the criteria for referral to nephrologist consultation, MCKC, or kidney transplant evaluation when the referral criteria are assessed with this new eGFR value. Our various scenarios showed that upwards of 10000 individuals may no longer meet the criteria recommended for nephrologist referral, and similarly 1000 and 1500 for MCKC and kidney transplant evaluation, respectively. It should be noted that this is likely just a temporary delay in meeting the referral criteria for many of these individuals. Conversely, we would expect to see earlier, more appropriate referrals among Black individuals. With the 2021 equation, assuming a Black prevalence of 10% in Ontario, an additional 838, 76, and 126 Black individuals would meet the criteria for nephrologist referral, MCKC, and kidney transplant evaluation, respectively. In our group of individuals who no longer met the recommended criteria for nephrologist referral with the 2021 equation, the average eGFR decline per year was -5.0 mL/min/1.73 m². Considering the average increase in eGFR using the 2021 equation in this group compared to the 2009 equation was only 3.0 mL/min/1.73 m², we would expect most individuals to meet the criteria for nephrology referral in less than 1 year. Care providers and healthcare organizations may want to consider using the 2021 equation to assess referral criteria only in individuals who have not yet been referred, to ensure that access to care is not taken away from individuals who already met the criteria and were referred based on the older equation. It is also important to emphasize that this new equation was developed with equity in mind and will enable

earlier, more appropriate referrals for hundreds of Black individuals in Ontario.

The median increase in eGFR of 3.5 mL/min/1.73 m² we observed in adults in Ontario when using the 2021 equation is comparable to that observed in other studies, including the original Inker et al.⁵ article (mean eGFR increase in non-Black individuals of 3.4 mL/min/1.73 m²), a study in living kidney donors (median eGFR increase of 2.4 mL/min/1.73 m²), and individuals in a study based on National Health and Nutrition Examination Survey (NHANES) data in the United States (median increase 4.0 mL/min/1.73 m²).

We observed that 28.5% of individuals with CKD using the 2009 equation would no longer have an eGFR <60 mL/ $min/1.73 m^2$ when using the 2021 equation, which is very similar to a Danish study that found a 24.2% reduction in the prevalence of CKD in their predominantly non-Black population.²⁹ However, this differs from the aforementioned study that used 2001 to 2018 NHANES data, where they estimated a 12.1% reduction in the prevalence of CKD.²⁸ This variance may be due to age differences, as our study population was considerably older (median 75 vs 47), and differences in eGFR between the two equations are more pronounced in older age.¹¹ A similar discrepancy is seen in the Inker et al.⁵ article where they estimated a 16% relative decreased CKD prevalence in non-Black individuals using 1999 to 2002 NHANES data (mean age 46).⁵ While the kidney transplant referral criteria in the Diao et al²⁸ study were slightly different (eGFR < 20 mL/min/1.73 m²), the potential decrease in the eligibility prevalence was comparable to what we observed (12.9% decrease vs 15.4% in our study).

A strength of our study is that we were able to evaluate these eGFR equations using population-based data, with near-universal capture of outpatient laboratory results across the province. Our jurisdiction is likely comparable to several others nationally and internationally where a small minority of the population is Black, making the interpretation of our study findings particularly relevant. Quantifying the potential number of individuals both gaining and losing

Variahles		Continu criteria for referral //	r nephrologist • nephrologist • = 76.6451	No longer for nephro /N =	meets criteria vlogist referral		Remains elig	gible for MCKC (NI = 9009)	No longe MCK(er eligible for C referral ≡ 1010		Continue criteria fo	es to meet r transplant N = 8615)	No longer r for transp	neets criteria lant referral	
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Description	Value	z	%	z	%	diff.	z	%	z	%	diff.	z	%	z	%	diff.
Age	Mean ± SD	80.69	10.4	79.75	10.01	0.09	71.7	14.25	76.74	11.34	0.39	70.98	15.09	76.3	12.71	0.38
	Median (IQR)	82	(74-88)	8	(73-87)		74	(64-82)	78	(70-85)		73	(62-82)	78	(70-85)	
	< 65	1061	7.1%	768	7.2%	0.00	2374	26.4%	140	13.9%	0.32	2516	29.2%	249	15.9%	0.32
	65-<75	4948	18.6%	2262	21.1%	0.06	2324	25.8%	229	22.7%	0.07	2128	24.7%	346	22.1%	0.06
	75-<85	9082	34.1%	3957	37.0%	0.06	2610	29.0%	374	37.0%	0.17	2291	26.6%	531	34.0%	0.16
	85+	10714	40.2%	3713	34.7%	0.11	1701	18.9%	267	26.4%	0.18	1680	19.5%	437	28.0%	0.20
Sex	Female	16050	60.2%	5990	56.0%	0.09	3571	39.6%	410	40.6%	0.02	3628	42.1%	670	42.9%	0.02
	Male	10595	39.8%	4710	44.0%	0.09	5438	60.4%	600	59.4%	0.02	4987	57.9%	893	57.1%	0.02
Rurality	Missing	83	0.3%	23	0.2%	0.02	24	0.3%	0	0.0%	0.08	*		*		
	Urban	22 25 2	83.5%	9043	84.5%	0.03	8009	88.9%	902	89.3%	0.01	7686	89.2%	1402	89.7%	0.02
	Rural	4310	16.2%	1634	15.3%	0.02	976	10.8%	108	10.7%	0.00	929	10.8%	161	10.3%	0.02
Income quintile	Missing	104	0.4%	30	0.3%	0.02	31	0.3%	0	0.0%	0.08	#		#		
	_	6262	23.5%	2444	22.8%	0.02	2332	25.9%	265	26.2%	0.01	2304	26.7%	379	24.3%	0.05
	2	5927	22.2%	233 I	21.8%	0.01	2031	22.5%	204	20.2%	0.06	1963	22.8%	377	24.1%	0.03
	e	5342	20.0%	2145	20.0%	0.00	1695	18.8%	206	20.4%	0.04	1670	19.4%	310	19.8%	0.01
	4	4650	17.5%	1923	18.0%	0.01	1571	17.4%	175	17.3%	0.00	1473	17.1%	274	17.5%	0.01
	5	4360	16.4%	1827	17.1%	0.02	1349	15.0%	160	15.8%	0.02	1205	14.0%	223	14.3%	0.01
Index year	2020	5337	20.0%	1061	17.8%	0.06	1068	11.9%	129	12.8%	0.03	1257	14.6%	232	14.8%	0.01
	202	21 308	80.0%	8799	82.2%	0.06	7941	88.1%	881	87.2%	0.03	7358	85.4%	1331	85.2%	0.01
Baseline	$Mean \pm SD$	161.49	56.85	131.86	39.62	09.0	347.47	138.56	258.1	75.71	0.80	380.79	144.61	278.46	61.53	0.92
SCr, µmol/L	Median (IQR)	150	(129-177)	131	(109-142)		315	(254-404)	246	(205-295)		347	(287-433)	265	(239-314)	
Baseline eGFR	$Mean \pm SD$	31.2	7.74	38.96	6.75	I.07	14.99	5.84	19.48	6.38	0.73	13.16	4.88	17.09	4.73	0.82
(2009 CKD-EPI	Median (IQR)	32	(26-38)	43	(31-44)		4	(61-11)	8	(14-24)		<u>8</u>	(10-16)	15	(14-20)	
no race), mL/min	/ 60+	0	0.0%	0	0.0%	0.00	0	0.0%	0	0.0%	0.00	0	0.0%	0	0.0%	0.00
l.73 m⁴	45-<60	96 1 7 7 1	0.4%	7010	1.4%	0.11	0 5	0.0%	0 [%0.0 %	0.00	0 [0.0%	0 -	0.0%	0.00
	00 / 31	10001	%4.7C %c oc	0147	%0.47	00.0	C0	0.7%	6/1	0.0% 5.2 2%	00.0	C1 C1	0.7% 21.1%	217	%0.1 47 0%	01.0
	SI >	777	2.9%	35	0.3%	0.21	4910	54.5%	402	39.8%	0.30	5919	68.7%	813	52.0%	0.35
Baseline eGFR	Mean ± SD	33.62	8.23	41.91	7.14	I.08	16.14	6.20	21.02	6.78	0.75	14.17	5.15	18.44	4.96	0.84
(202 I CKD-EPI),	Median (IQR)	35	(28-41)	46	(33-47)		15	(12-20)	20	(15-26)		4	(11-17)	16	(15-22)	
mL/min/1.73 m ²	+09	0	0.0%	4-			0	0.0%	0	0.0%	0.00	0	0.0%	0	0.0%	0.00
	45-<60	206	0.8%	6638	62.0%	1.75	0	0.0%	0	0.0%	0.00	0	0.0%	0	0.0%	0.00
	30-<45	17010	63.8%	3898	36.4%	0.57	183	2.0%	129	12.8%	0.42	30	0.3%	39	2.5%	0.19
	15-<30	8836	33.2%	134	1.3%	0.93	4476	49.7%	721	71.4%	0.46	3198	37.1%	1236	79.1%	0.94
	∧ 5	593	2.2%	30	0.3%	0.17	4350	48.3%	160	15.8%	0.74	5387	62.5%	288	18.4%	10.1
Difference in	Mean ± SD	2.43	0.56	2.95	0.5	0.97	1.15	0.41	1.54	0.44	0.92	10.1	0.33	1.36	0.3	Ξ.
baseline eGFR	Median (IQR)	2	(2-3)	c	(3-3)		_	(1-1)	_	(1-2)		_	(1-1)	_	(1-2)	
(2021 vs. 2009), mL/min/1.73 m ²																

(continued)

Table 3. Baseline Characteristics by Referral Status.

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Variables		Conti criteria f referral	nues to meet or nephrologist (N = 26645)	No longe for nephr (N	r meets criteria ologist referral = 10700)		Remains e referra	ligible for MCKC II (N = 9009)	No lon MC MC	ger eligible for KC referral I = 1010)	, S	Contil criteria referra	nues to meet for transplant il (N = 8615)	No longe for tran (N	er meets criteria Isplant referral = 1563)	
Description	Value	z	%	z	%	diff.	z	%	z	%	diff.	z	%	z	%	diff.
eGFR slope, per year (2021 CKD- EPI), mL/min/ 1.73 m ²	Estimate (95% CI)	-5.98	(-6.10 to -5.87)	-4.99	(-5.15 to -4.83)		-4.17	(-4.31 to -4.03)	-2.97	(-3.34 to -2.60)		-5.12	(-5.28 to -4.95)	-4.	(-4.45 to -3.77)	
Baseline urine	Mean ± SD	34.6	92.24	19.08	64.99	0.19	151.62	173.8	74	112.84	0.53	197.33	203.37	107.93	138.62	0.51
ACR, mg/mmol	Median (IQR)	2	(2-22)	m	(1-12)		94	(36-199)	34	(12-92)		133	(54-270)	60	(15-146)	
	Missing	13737	51.6%	5416	50.6%	0.02	216	2.4%	35	3.5%	0.07	343	4.0%	73	4.7%	0.03
	ų	4919	I 8.5%	2555	23.9%	0.13	113	1.3%	62	6.1%	0.26	140	1.6%	87	5.6%	0.22
	3-<30	5261	19.7%	2044	19.1%	0.02	1761	19.5%	409	40.5%	0.47	1148	13.3%	443	28.3%	0.38
	30-60	176	3.6%	307	2.9%	0.04	1381	15.3%	171	16.9%	0.04	934	10.8%	215	13.8%	0.09
	>60	1757	6.6%	378	3.5%	0.14	5538	61.5%	333	33.0%	09.0	6050	70.2%	745	47.7%	0.47
Eligible for referral	Yes	1121	4.2%	222	2.1%	0.12	N/A	N/A	N/A	N/A		N/A	N/A	N/A	N/A	
using urine ACR- only criteria																
Visits with a family	$Mean \pm SD$	12.89	13.97	10.98	12.13	0.15	10.47	13.15	8.II	14.96	0.09	11.36	14.36	12.34	15.92	0.06
doctor	Median (IQR)	6	(4-16)	8	(4-13)		9	(3-13)	7	(3-15)		7	(3-14)	7	(3-15)	
ED visits	Mean ± SD	1.39	2.25	1.12	2.04	0.13	1.17	2.21	1.19	I.83	0.01	Г. З	2.08	1.31	2.08	0.00
	Median (IQR)	_	(0-2)	0	(0-2)		0	(0-2)	0	(0-2)		_	(0-2)	_	(0-2)	
Visits with a	Mean ± SD	N/A	N/A	N/A	N/A		4.46	3.97	3.53	3.02	0.26	4.73	4.46	3.73	3.26	0.26
nephrologist	Median (IQR)						4	(2-5)	m	(2-4)		4	(2-5)	m	(2-4)	
Diabetes	Yes	14412	54.1%	5537	51.7%	0.05	5974	66.3%	688	68.1%	0.04	5628	65.3%	1055	67.5%	0.05
Mental illness	Yes	187	0.7%	74	0.7%	00.00	70	0.8%	7	0.7%	0.01	75	0.9%	12	0.8%	0.01
(previous 5 vears)																
CHF	Yes	8958	33.6%	2628	24.6%	0.20	2695	29.9%	392	38.8%	0.19	2581	30.0%	574	36.7%	0.14
Hypertension	Yes	23694	88.9%	9257	86.5%	0.07	8141	90.4%	930	92.1%	0.06	7710	89.5%	1426	91.2%	0.06
Dementia	Yes	3522	13.2%	1160	10.8%	0.07	556	6.2%	86	8.5%	0.09	593	6.9%	140	9.0%	0.08
COPD	Yes	8335	31.3%	3047	28.5%	0.06	2250	25.0%	300	29.7%	0.11	2092	24.3%	440	28.2%	0.09
Cancer diagnosis	Yes	8784	33.0%	3409	31.9%	0.02	2028	22.5%	284	28.1%	0.13	1919	22.3%	398	25.5%	0.08
(anytime prior)																
Note. MCKC = Mult	i-Care Kidney (Clinic; SD	= standard deviati	on; IQR =	= interquartile rang	e; eGFR	= estimat	ed glomerular filtrat	ion rate;	CKD-EPI = Chron	ic Kidne	y Disease	Epidemiology Coll	aboratior	ו; Cl = confidence	

interval; SCr = serum creatinine; ACR = albumin-to-creatinine ratio; ED = emergency department; CHF = congestive heart failure; COPD = chronic obstructive pulmonary disease; Stan. diff. = Standardized difference; MIA = not applicable. *Missing values were imputed as "Urban" to comply with privacy requirements. #Missing values were imputed as "Ur to comply with privacy requirements.

eligibility at 3 key points of referral can be used for planning purposes by physicians and policymakers. While the specific referral criteria examined in this study are Ontariospecific, analogous criteria likely apply in other jurisdictions, and so this study may have broader relevance, nationally and internationally. As with all research using administrative data, our study is not without limitations. While we did limit our analyses to outpatient tests, we do not know the indications for the serum creatinine tests, and the values used may not truly represent an individual's baseline kidney function. However, a previous study in Ontario found that outpatient serum creatinine values were generally chronic, stable values.³⁰ Similarly, we were unable to determine individuals that may have been already referred (but never completed) or denied referral for unknown reasons. As such, the true underlying proportion that is still naïve to referral may be overrepresented in our study. However, we also only assessed the eGFR equations among those who had laboratory testing during our study period of 2020 to 2021. If fewer individuals received laboratory testing during this period due to the COVID-19 pandemic, we would be undercapturing the number of individuals potentially impacted. We focused only on the referral criteria that were eGFRbased. The criteria for referral to nephrology and MCKC both contain components that are based on urine albuminto-creatinine ratio, and some individuals we classified as no longer meeting the referral criteria may still meet the criteria based on their urine albumin-to-creatinine ratio. Our study was also limited by the lack of self-reported race data. The availability of this data would have allowed for an evaluation of the potential impact of the 2021 equation in both Black and non-Black individuals within Ontario. Given that <5% of Ontario's population self-identifies as Black and our results were largely unchanged when we simulated up to a 10% Black population, it is unlikely that significantly different results would have been observed in our study if race was available. Our results may not be generalizable to jurisdictions with a more prevalent Black population or where referral criteria significantly differ from those used in Ontario.31

Conclusions

Our study provides estimates into the potential impact on the population recommended or eligible for nephrologist consultation, MCKC, and kidney transplant evaluation in Ontario. Physicians should ensure that Black individuals have their eGFR re-calculated with the race-free equation to ensure more timely, appropriate access to care, and non-Black individuals who do not meet the referral criteria should continue to be monitored. To safeguard against marginalized non-Black populations potentially being negatively impacted by this change, those who are already receiving these services but who will no longer meet referral criteria based on the new formula should be managed sensitively and not have their care disrupted. In the case of MCKCs where funding of this care is directly dependent on eligibility, mitigation using a "grandfathering in" process may be desirable and is already being planned by the Ontario Renal Network.

Ethics Approval and Consent to Participate

ICES is an independent, non-profit research institute whose legal status under Ontario's health information privacy law allows it to collect and analyze healthcare and demographic data, without consent, for health system evaluation and improvement. The use of data in this project was authorized under section 45 of Ontario's Personal Health Information Protection Act, which does not require review by a Research Ethics Board.

Consent for Publication

Consent for publication was obtained from all authors.

Availability of Data and Materials

The dataset from this study is held securely in coded form at ICES. While legal data sharing agreements between ICES and data providers (e.g., healthcare organizations and government) prohibit ICES from making the dataset publicly available, access may be granted to those who meet prespecified criteria for confidential access, available at www.ices.on.ca/DAS (email: das@ices.on.ca). The full dataset creation plan and underlying analytic code are available from the authors upon request, understanding that the computer programs may rely upon coding templates or macros that are unique to ICES and are therefore either inaccessible or may require modification.

Declaration of Conflicting Interests

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Supplemental Material

Supplemental material for this article is available online.

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