Nephrology comanagement and the quality of antibiotic prescribing in primary care for patients with chronic kidney disease: a retrospective cross-sectional study

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ABSTRACT

Background. In primary care, patients with chronic kidney disease (CKD) are frequently prescribed excessive doses of antibiotics relative to their kidney function. We examined whether nephrology comanagement is associated with improved prescribing in primary care.

Methods. In a retrospective propensity score-matched cross-sectional study, we studied the appropriateness of antibiotic prescriptions by primary care physicians to Ontarians ≥ 66 years of age with CKD Stages 4 and 5 (estimated glomerular filtration rate < 30 mL/min/1.73 m² not receiving dialysis) from 1 April 2003 to 31 March 2014. Comanagement was defined as having at least one outpatient visit with a nephrologist within the year prior to antibiotic prescription date. We compared the rate of appropriately dosed antibiotics in primary care between 3937 patients who were comanaged by a nephrologist and 3937 patients who were not.

Results. Only 1184 (30%) of 3937 noncomanaged patients had appropriately dosed antibiotic prescriptions prescribed by a primary care physician. Nephrology comanagement was associated with an increased likelihood that an appropriately dosed prescription was prescribed by a primary care physician; however, the magnitude of the effect was modest [1342/3937 (34%); odds ratio 1.20 (95% confidence interval 1.09–1.32); $P < 0.001$].

Conclusion. The majority of antibiotics prescribed by primary care physicians are inappropriately dosed in CKD patients, whether or not a nephrologist is comanaging the patient. Nephrologists have an opportunity to increase awareness of appropriate dosing of medications in primary care through the patients they comanage.

Keywords: chronic renal failure, chronic renal insufficiency, comanagement, medication dosing, medication error

INTRODUCTION

Patients with chronic kidney disease (CKD) have higher risks of mortality and morbidity than the general population [1, 2]. While most patients with early CKD (i.e. Stages 1–3) are solely managed by primary care physicians, patients with more advanced CKD (i.e. Stages 4 and 5) are frequently comanaged with nephrologists. The addition of nephrologists to advanced CKD care improves guideline adherence and has been associated with better outcomes, including lower mortality, decreased progression of disease and fewer hospitalizations [3–9].

Patients with CKD are at high risk of receiving medications inappropriately dosed relative to their kidney function [10]. Rates of inappropriately dosed medications have ranged from 30% to $> 50\%$ [11–13]. In a prior study we found that 64% of outpatient antibiotic prescriptions were dosed inappropriately in nondialysis patients with Stage 4 or 5 CKD [14].

In the face of the poor quality of antibiotic prescribing in patients with advanced CKD, the nephrology consultation note represents an opportunity to provide education to the primary care physician to increase awareness of the need to dose-adjust medications for a given patient's level of kidney function. We conducted this study to determine if the quality of antibiotic prescribing by primary care physicians in patients with advanced CKD was influenced by nephrology comanagement. We hypothesized that nephrology comanagement would positively impact primary care physicians' prescribing practices and have an association with appropriately dosed prescriptions.

MATERIALS AND METHODS

Study overview and setting

We conducted a population-based, propensity score-matched and retrospective cross-sectional study in the province

of Ontario, Canada from 1 April 2003 to 31 March 2014. Ontario currently has 13 million citizens and all residents have universal health care access, including physician services, hospital care and laboratory investigations. Ontario residents ≥ 65 years of age also have universal prescription drug coverage via the Ontario Drug Benefit program. This study was conducted at the Institute for Clinical Evaluative Sciences (ICES) Western site in London, Ontario, Canada. Our study was approved by the research ethics board at Sunnybrook Health Sciences Centre. The reporting of this study follows recommended guidelines for routinely collected health care data ([Supplementary data, Table S1](#)) [15].

Data sources

We ascertained baseline characteristics, physician visits and prescription data using eight linked health care databases. These datasets were linked using unique encoded identifiers. Demographic and vital status information on all Ontario residents who have ever been issued a health card is recorded in the Ontario Registered Persons Database. Detailed diagnostic and procedural information on all hospital admissions is recorded in the Canadian Institute for Health Information's Discharge Abstract Database and all emergency department (ED) visits in the National Ambulatory Care Reporting System database. Health claims for inpatient and outpatient physician services are recorded in the Ontario Health Insurance Plan database. Outpatient prescription drug information, including the dispensing date, quantity of pills and number of days supplied, is accurately recorded in the Ontario Drug Benefit database for all individuals ≥ 65 years of age, with an error rate of $<1\%$ [16]. Daily drug dose is calculated using the strength of medication multiplied by the quantity of tablets divided by the number of days supplied. The ICES Physician Database contains information on physicians in Ontario such as medical specialty, education, practice location and demographics. We obtained baseline serum creatinine values from two-linked laboratory databases: Dynacare, a large outpatient provincial laboratory provider, and Cerner (Kansas City, MO, USA), an electronic medical record database containing inpatient, outpatient and ED laboratory values for 12 hospitals in southwestern Ontario. These data sources have been used in previous population-based renal drug studies [5, 14, 17–24].

Identification of patients and study prescriptions

We identified all patients in Ontario ≥ 65 years of age who filled a prescription between 1 April 2003 and 31 March 2014 prescribed by a primary care physician for one of the following study antibiotics: cephalexin, ciprofloxacin, clarithromycin, nitrofurantoin, trimethoprim/sulfamethoxazole, levofloxacin, cefprozil, amoxicillin/clavulanic acid, cefixime, tetracycline or ofloxacin. It is recommended that the daily dose of these antibiotics be reduced in the presence of CKD (see 'Outcome' section). The date of prescription filling served as the index date (study entry date). To be eligible for this study, all patients were required to have a baseline value of renal function, and we identified patients' renal function using their estimated glomerular filtration rate (eGFR), calculated from their most recent outpatient serum

creatinine value in the 1 year prior to their index date [a median of 57 (25th–75th percentile 15–143) days prior to the index date] using the CKD Epidemiology Collaboration (CKD-EPI) formula [25].

The best equation to estimate kidney function for the purposes of drug adjustment continues to be controversial. The US Kidney Disease Education program indicates that equations that express results in mL/min/1.73 m² or mL/min are both appropriate for this purpose. In this study we estimated glomerular filtration rate (GFR) using the CKD-EPI equation, which when <30 mL/min/1.73 m² would also generally identify a patient with a Cockcroft–Gault result <30 mL/min. In addition, we found that outpatient serum creatinine tests in our region are generally stable [26]. Therefore we also allowed patients with only a single eligible outpatient serum creatinine in the study to prevent reductions to the sample.

We made the following exclusions: patients with missing key variables (age, gender, database ID, non-Ontario residents and patients who are deceased prior to prescription date); patients in the first year of eligibility for prescription drug coverage (age <66 years) were excluded to prevent incomplete medication records; patients with eGFR ≥ 30 mL/min/1.73 m² (to include only patients with Stage 4 or 5 CKD); patients discharged from the hospital or ED in the 7 days prior to the index date to ensure that prescriptions were new outpatient prescriptions; patients with any study medications in the 180 days prior to index date to ensure new antibiotic use and to eliminate prescriptions used for chronic infections; patients on chronic dialysis or with evidence of a prior kidney transplant; patients with multiple study prescriptions on the same date; or patients with prescriptions not prescribed by a primary care physician. If there were multiple eligible prescriptions available, we restricted to the first prescription (i.e. one prescription per patient).

Exposure

The primary exposure was comanagement, which was defined as having at least one outpatient visit with a nephrologist in the year prior to the index date (see [Supplementary data, Table S2](#)). In Ontario, a specialist consultation (including nephrology) will always result in a letter back to the referring physician. It is also common practice for specialists to send a copy of the assessment to a patient's primary care physician even when the referral is made by another type of physician involved in the patient's care. Patients were categorized into those with and without evidence of nephrology comanagement.

Outcome

Our primary outcome was whether the antibiotic prescription was appropriately dosed for a patient's given eGFR. Dosing recommendations were in accordance with UpToDate and the Compendium of Pharmaceuticals and Specialties (CPS) in November 2014, focusing specifically on Canadian recommendations. A prescription was labeled as inappropriate if the daily dose was above the acceptable cutoff as defined in [Table 1](#).

We included the following antibiotics in our study: cephalexin, ciprofloxacin, clarithromycin, nitrofurantoin, trimethoprim/sulfamethoxazole, levofloxacin, cefprozil, amoxicillin/

clavulanic acid, cefixime, tetracycline and ofloxacin. We selected common antibiotics across multiple classes that are prescribed in the outpatient setting [27]. These antibiotics have all been associated with side effects, which may be exacerbated in patients with decreased drug clearance [28].

Statistical analysis

Variables for baseline characteristics were identified *a priori* and were compared between noncomanaged and comanaged

Table 1. Antibiotic dosing recommendations for patients with eGFR <30 mL/min/1.73 m²

Drug name	Appropriate total daily dose
Cephalexin	Daily dose ≤1500 mg
Ciprofloxacin	Daily dose ≤500 mg
Clarithromycin	Daily dose ≤500 mg
Nitrofurantoin	Contraindicated
Trimethoprim (T)/Sulfamethoxazole (S) ^a	Daily dose T ≤160 mg/ S ≤ 800 mg
Levofloxacin	Daily dose ≤375 mg
Cefprozil	Daily dose ≤500 mg
Amoxicillin/clavulanic acid ^b	Daily dose ≤1000 mg
Cefixime	Daily dose ≤300 mg
Ofloxacin	Daily dose ≤400 mg
Tetracycline	Daily dose ≤1000 mg

Total daily appropriate and inappropriate doses of antibiotics were determined using UpToDate and CPS. Total daily doses less than the maximum recommended doses were deemed appropriate.

^aFormulations of sulfamethoxazole and trimethoprim include both chemicals in one pill or suspension.

^bFormulations include only the combination pill of amoxicillin/clavulanic acid. This excludes formulations with amoxicillin only.

groups using standardized differences. This metric describes differences between group means relative to the pooled standard deviation (SD) and is considered a meaningful difference if >10% [29]. Continuous variables were described as mean with SD and median with interquartile range (IQR). Categorical and binary variables were described as a proportion.

We used propensity score matching to achieve balance on a large number of measured baseline characteristics in the two groups defined by nephrology comanagement. A propensity score for the predicted probability of receiving nephrology comanagement was derived from a logistic regression model in which treatment status was regressed on >35 variables that were potentially associated with comanagement or the outcome (Supplementary data, Table S3) [29]. We used greedy matching to match each comanaged patient to a noncomanaged patient based on the following characteristics: the logit of the propensity score (± 0.2 SD), CKD stage (Stage 4 versus Stage 5) and year of index date (pre-2006 versus 1 January 2006 and onwards). We applied matching without replacement, where patients could only be selected once for inclusion in the study. Greedy matching without replacement has previously been demonstrated to produce less biased estimates than other algorithms [30]. We used conditional logistic regression to obtain the conditional odds ratio (OR) of the association between nephrology comanagement and appropriately dosed prescriptions, with noncomanaged patients as the referent group. As there may have been clustering by primary care physician, we addressed this in a sensitivity analysis. Specifically, we reran the logistic regression model, accounting for correlation by primary care physician using generalized estimating equations. Using model statistical interaction terms, we also performed subgroup analyses to determine whether the association between comanagement and appropriately dosed prescriptions was modified

FIGURE 1: Participant flow diagram.

Table 2. Baseline characteristics after propensity score matching

Characteristics	Noncomanaged (n = 3937)	Comanaged (n = 3937)	Standardized difference, %
Age (years)			
Mean $\pm$ SD	81 $\pm$ 7.3	81 $\pm$ 7.0	2
Median (IQR)	81 (75–86)	81 (76–86)	–
Female	2472 (63)	2467 (63)	0
Baseline eGFR (mL/min/1.73 m ²)			
Mean $\pm$ SD	24 $\pm$ 4.9	24 $\pm$ 4.9	2
Median (IQR)	25 (21–28)	25 (21–28)	–
15–<30, n (%)	3693 (94)	3693 (94)	0
<15, n (%)	244 (6)	244 (6)	0
Urinary ACR, n (%) with available values	1226 (31)	1241 (32)	1
Mean $\pm$ SD (mg/mmol) ^a	41 $\pm$ 109	47 $\pm$ 105	6
Hematuria, n (%) with available values	1713 (44)	1738 (44)	1
Negative for hematuria	1239 (72)	1259 (72)	1
Positive for hematuria ^b	474 (28)	479 (28)	1
Rural residence ^c	428 (11)	415 (11)	1
Income quintile ^d			
First (lowest)	883 (22)	890 (23)	0
Second	890 (23)	893 (23)	0
Third (middle)	821 (21)	814 (21)	0
Fourth	710 (18)	727 (19)	1
Fifth (highest)	633 (16)	613 (16)	1
Long-term care facility residence	367 (9.3)	373 (9.5)	1
Year of index prescription date			
2003–05	592 (15)	611 (16)	1
2006–08	1219 (31)	1159 (29)	3
2009–11	1150 (29)	1175 (30)	1
2012–14	976 (25)	992 (25)	1
Time since nephrology visit (days), mean $\pm$ SD	Not applicable	103 $\pm$ 85	
Health care visits in the last 1 year, mean $\pm$ SD			
No. of hospitalizations	0.5 $\pm$ 0.9	0.5 $\pm$ 0.9	1
No. of ED visits	1.0 $\pm$ 1.6	1.0 $\pm$ 1.6	1
No. of primary care visits	15.9 $\pm$ 14.0	15.9 $\pm$ 14.0	0
0–7 primary care visits, n (%)	871 (22)	877 (22)	0
>7 primary care visits, n (%)	3066 (78)	3060 (78)	0
No. of internal medicine visits	2.0 $\pm$ 4.5	2.0 $\pm$ 5.3	2
$\geq$ 1 internal medicine visits, n (%)	1739 (44)	1563 (40)	9
Comorbidities ^e			
Hypertension	3607 (92)	3608 (92)	0
Diabetes	2033 (52)	2004 (51)	1
Coronary artery disease (without angina)	1906 (48)	1898 (48)	0
Congestive heart failure	1571 (40)	1552 (39)	1
Myocardial infarction	382 (10)	380 (10)	0
Chronic lung disease	1377 (35)	1357 (35)	1
Major cancer	665 (17)	668 (17)	0
Atrial fibrillation/flutter	642 (16)	613 (16)	2
Stroke	232 (6)	218 (6)	2
Chronic liver disease	195 (5)	189 (5)	1
Peripheral vascular disease	182 (5)	187 (5)	0
Charlson comorbidity score ^f			
Mean $\pm$ SD	2.0 $\pm$ 2.3	2.0 $\pm$ 2.2	1
Median (IQR)	1 (0–3)	1 (0–3)	
0	1777 (45)	1732 (44)	2
1	380 (10)	331 (8)	5
2	446 (11)	538 (13)	6
$\geq$ 3	1334 (34)	1346 (34)	1
Polypharmacy ^g			
No. of concurrent medications, mean $\pm$ SD	12.5 $\pm$ 6.0	12.5 $\pm$ 5.8	1
Antihypertensive medications	3680 (94)	3673 (93)	1
Diabetes medications	1398 (36)	1380 (35)	1
Immunosuppressive medications	16 (0.4)	23 (0.6)	3
Primary care physician characteristics			
Number of unique physicians	2282	2494	n/a
Prescriber age (years), mean $\pm$ SD	53 $\pm$ 10.8	53 $\pm$ 10.8	1

Continued

Table 2. Continued

Characteristics	Noncomanaged (n = 3937)	Comanaged (n = 3937)	Standardized difference, %
Male prescriber	2943 (75)	2943 (75)	0
Rural practice location	379 (10)	369 (9)	1
Canadian medical graduate	2923 (74)	2914 (74)	0
Time since graduation (years), mean $\pm$ SD	27 $\pm$ 11.1	27 $\pm$ 11.1	2

Results reported as n (%) unless otherwise specified.

n/a, not applicable.

^aTo convert mg/mmol to mg/g, multiply by 8.85.

^bIncludes trace, small, moderate and large hematuria on urinalysis.

^cDenotes municipality with population <10 000. Missing data were categorized as urban residence.

^dPeople with missing income quintile were input into the middle category.

^eComorbidities were assessed in the 5 years prior to the index date.

^fCharlson comorbidity score was assessed with an algorithm using diagnosis codes from hospitalizations in the 5 years prior; patients with no hospitalizations during this period were given a value of zero.

^gPolypharmacy denotes the total number of unique medications dispensed in the 180 days prior to the index date.

Table 3. Number of antibiotic prescriptions by exposure group

Study medication	Noncomanaged (n=3937)	Comanaged (n=3937)	Standardized difference
Cephalexin	799	844	3
Ciprofloxacin	744	708	2
Clarithromycin	609	674	4
Nitrofurantoin	618	482	10 ^b
Trimethoprim/ sulfamethoxazole	374	344	1
Levofloxacin	298	293	1
Cefprozil	251	297	4
Amoxicillin and clavulanate	177	211	4
Cefixime or ofloxacin ^a	31	51	5
Tetracycline	36	33	1

^aValues merged due to small numbers.

^bDenotes significant standardized difference.

by the introduction of mandatory eGFR reporting in Ontario (pre-2006 versus post-2006) or CKD stage [Stage 4 (eGFR 15–<30 mL/min/1.73 m²) versus Stage 5 (eGFR <15 mL/min/1.73 m²)].

The studied variables included age, gender, eGFR, albumin:creatinine ratio (ACR) (where available), hematuria (where available), rural residence (population <10 000), neighborhood income quintile, long-term care placement and year of index prescription date; the number of health care encounters in the last year, including hospitalizations, ED visits, primary care physician visits and internal medicine visits; time since last nephrology visit; number of unique medications within the last 180 days; prescriptions within the previous 180 days, including antihypertensive medications, diabetic medications and immunosuppressive medications; primary care prescriber characteristics, including age, gender, practice location, country of graduation and time since graduation; and patient comorbidities in the past 5 years, including Charlson comorbidity index, hypertension, diabetes, coronary artery disease, congestive heart failure, myocardial infarction, chronic lung disease, major cancers, atrial fibrillation, stroke, chronic liver disease and peripheral vascular disease. See [Supplementary data, Table S3](#) for administrative codes used to define baseline characteristics.

All statistical analyses were performed using Statistical Analysis Software (SAS) version 9.4 (SAS Institute, Cary, NC, USA). A two-sided P-value <0.05 was defined as statistically significant.

RESULTS

Study patients and baseline characteristics

After exclusions there were 13 875 eligible patients with a study antibiotic prescription from a primary care physician. Of these, 5961 (43%) patients were comanaged by a nephrologist. In the comanaged group, the most recent nephrologist visit was a median of 72 (25th–75th percentile 34–135) days prior to the antibiotic prescription date.

After matching, we retained 3937 unique patients in each group for a total of 7874 patients. Patient selection is presented in [Figure 1](#). The two groups were well balanced across baseline characteristics after matching ([Table 2](#)). Patients had a median age of 81 (25th–75th percentile 76–86) years and 63% were female. Patients had a median eGFR of 25 (25th–75th percentile 21–28) mL/min/1.73 m² and 94% of the patients had Stage 4 CKD. The number of patients with two or more serum creatinine measurements in the year prior to the index date was 6049 of 7874 patients (76.8%). Approximately 11% of patients resided in a rural location and 9% of patients were in a long-term care facility.

Antibiotic prescriptions

Of the 11 study antibiotics, cephalexin, ciprofloxacin and clarithromycin accounted for 55% of all prescriptions (21, 18 and 16%, respectively). There were no differences in terms of frequency of antibiotic prescriptions between noncomanaged and comanaged groups except for nitrofurantoin ([Table 3](#)). Nitrofurantoin (which is contraindicated in advanced CKD) was more frequently prescribed in patients in the noncomanaged group.

In total, the overall percentage of appropriately dosed prescriptions for the study cohort was 32% (2526/7874). [Figure 2](#) depicts the number of inappropriately dosed prescriptions by the type of antibiotic. Cefixime and ofloxacin were grouped together due to small numbers and accounted for 1% of total prescriptions.

FIGURE 2: Number and percentage of appropriately and inappropriately dosed prescriptions by antibiotic type. Percentages above each bar denote the percentage of appropriately dosed prescriptions for that antibiotic.

Table 4. Association between nephrology comanagement and an appropriately dosed prescription by a primary care physician

Exposure status	n	Appropriately dosed prescriptions, n (%)	Conditional OR (95% CI)	P-value
Noncomanaged	3937	1184 (30)	1.00 (reference)	< 0.001
Comanaged	3937	1342 (34)	1.20 (1.09–1.32)	

Association of comanagement and appropriately dosed prescriptions

In the absence of nephrology comanagement, 1184/3937 (30%) patients had appropriate doses of an antibiotic. Nephrology comanagement was associated with an increase in the chance that an appropriate dose of an antibiotic was prescribed by a primary care physician, although the effect was modest [1342/3937 [34%]; OR 1.20 [95% confidence interval (CI) 1.09–1.32]; $P < 0.001$] (Table 4). This corresponded to an absolute difference of 4.0% (95% CI 2.0–6.1) between the groups.

Additional analyses: effects of mandatory eGFR reporting or the degree of renal dysfunction

Mandatory eGFR reporting on laboratory reports (instituted in January 2006 in Ontario) did not significantly modify the association between comanagement and appropriately dosed prescriptions (interaction $P = 0.08$) (Table 5). The prevalence of total inappropriate antibiotic prescriptions in both groups combined was 66% pre-2006 and continued to be high post-2006 (69%).

A second subgroup analysis was performed to examine if the association of comanagement with appropriately dosed prescriptions was modified by stage of CKD: CKD Stage 4 (eGFR 15–<30 mL/min/1.73 m²) versus CKD Stage 5 (eGFR <15 mL/min/1.73 m²) (Table 5). There was no evidence

of interaction by CKD stage with a conditional OR of 1.19 (95% CI 1.08–1.31) in Stage 4 CKD and 1.37 (95% CI 0.96–1.97) in Stage 5 CKD (interaction $P = 0.5$) (Table 5).

Additional analyses: accounting for prescriptions by the same physician

A total of 7874 patients were under the care of 3461 unique primary care physicians. Of 3461 physicians, 1315 cared for patients belonging to both comanaged and noncomanaged groups, yielding a total of 2494 in the comanaged group and 2282 in the noncomanaged group. In additional analyses, accounting for the correlation of patients followed by the same primary care physician, the results were the same to two decimal points. The 3937 patients were comanaged by 220 unique nephrologists.

DISCUSSION

We conducted this study to assess the quality of CKD antibiotic prescribing in primary care and to determine whether patient comanagement with a nephrologist improved prescribing patterns. In approximately two-thirds of cases, the primary care dosing of antibiotics was against recommended practice. Nephrology comanagement improved the quality of primary care antibiotic prescribing in advanced CKD by a modest 4%.

After completing a detailed search of MEDLINE and other bibliographic databases through March 2017, we confirm that this appears to be the first study to examine the effects of nephrology comanagement on the prescribing practices of primary care physicians in CKD. Our study's strength lies in the use of Ontario's broadly inclusive, linked health care databases, which provided us with a large representative sample of patients. We included a large number of relevant variables in our propensity score-matched data to minimize significant biases between the groups to achieve a more representative analysis on the effects of comanagement.

Table 5. Subgroup analyses by eGFR reporting year or stage of CKD

Subgroup	No. of appropriate/No. prescribed (% appropriate)		Conditional OR (95% CI)	Interaction P-value
	Noncomanaged	Comanaged		
Pre- and post-eGFR reporting (2006)				
Pre-2006	215/688 (31)	272/688 (40)	1.44 (1.15–1.79)	0.08
Post-2006	969/3249 (30)	1070/3249 (33)	1.16 (1.04–1.28)	
Stage of CKD				
IV: eGFR 15–≤30 mL/min/1.73 m ²	1086/3693 (29)	1225/3693 (33)	1.19 (1.08–1.31)	0.5
V ^a : eGFR <15 mL/min/1.73 m ²	98/244 (40)	117/244 (48)	1.37 (0.96–1.97)	

^aPatients receiving dialysis or those with a prior kidney transplant were excluded from the study.

Despite our robust databases, there are some limitations to our study. While we studied prescription patterns, we did not have information on actual drug intake or detailed information on the indications for the antibiotics. Furthermore, we limited our study to the appropriateness of prescription doses, as associated clinical outcomes are beyond the study objectives. Clinical outcomes related to antibiotic use/misuse, such as treatment efficacy or adverse events, may be difficult to study due to multiple factors such as noncompliance, resistant organisms, immunosuppression and drug–drug interactions. The results of observational studies are subject to confounding. Better estimates of the effects nephrologists could have on primary care prescribing may come from future randomized controlled trials comparing different types of education and support provided by nephrology to primary care, possibly with tips provided in the consultation note.

By demonstrating a high prevalence of inappropriately dosed prescriptions, our study highlights an opportunity for quality improvement in CKD primary care. In the literature, many other studies highlight the high prevalence of potentially inappropriate medications in patients with CKD. Most recently, Chang *et al.* [11] reported that ~30% of US veterans with Stages 3 and 4 CKD are prescribed at least one potentially inappropriate medication. This rate increased to >50% when isolated to patients with Stage 4 CKD [11]. Jones and Bhandari [13] reported that 56% of inpatients with CKD at a British hospital had at least one potentially inappropriate medication prescribed. Additionally, Doody *et al.* [12] published a retrospective chart review that looked at rates of potentially inappropriate medications in a tertiary hospital in Australia. They found that 32% of inpatients with CKD had at least one potentially inappropriate medication, 16% had a contraindicated medication and 21% had an inappropriately dosed medication in an inpatient setting.

There is a paucity of published literature testing strategies to reduce medication errors in CKD patients. Our results suggest that simply involving a nephrologist in the care of advanced CKD patients is not associated with a dramatic improvement in dosing medications among advanced CKD patients. Instead, perhaps nephrologists should be, through their consult notes to primary care physicians, educating/reinforcing the importance of choosing appropriate medications and doses in patients with advanced CKD. There might also be opportunities for the nephrologist to educate patients and their families about reminding prescribers and pharmacists that they have reduced kidney

function and the doses of medications should be adjusted. These strategies warrant testing in future studies.

SUPPLEMENTARY DATA

Supplementary data are available at ndt.oxfordjournals.org online.

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AUTHORS' CONTRIBUTIONS

J.X.G.Z., A.X.G. and A.K.J. proposed the research idea. All authors contributed to the study design and development of the study plan, interpretation of results and writing of the

manuscript. E.M. contributed data/statistical analysis. A.X.G. and A.K.J. supervised or provided mentorship. Each author contributed important intellectual content during manuscript drafting or revision and accepts accountability for the overall work by ensuring that questions pertaining to the accuracy or integrity of any portion of the work are appropriately investigated and resolved.

CONFLICT OF INTEREST STATEMENT

The results in this article have not been published previously in whole or part, except in abstract format.

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