CKD Prevalence Among Patients With and Without Type 2 Diabetes: Regional Differences in the United States

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Rationale & Objective: Regional variation in chronic kidney disease (CKD) prevalence in patients with or without type 2 diabetes mellitus (T2DM) has not been well characterized.

Study Design: Spatial and temporal comparative analysis.

Setting & Participants: MarketScan databases were used to identify patients with CKD overall and subgroups of patients with CKD with and without T2DM in the United States.

Outcomes: Spatial patterns in CKD prevalence based on year, regional clusters of CKD between years, and characteristics of patients in high-prevalence states.

Analytical Approach: Geomapping was used to visualize the state-level data of CKD prevalence generated from 2013 to 2018. We used univariate local indicators of spatial association (LISA) to evaluate geographic differences in prevalence, differential LISA for changes in CKD prevalence over time, and the χ^2 test to identify patient characteristics in the top-20th percentile states for the prevalence of CKD.

n 2019, roughly 15% of US adults, or approximately 37 million people, were living with chronic kidney disease (CKD).^{1,2} The prevalence and burden of CKD have steadily increased in the past decade and are likely to continue in an upward trajectory.^{3,4} Diabetes mellitus remains the leading cause of CKD, and approximately 30% to 40% of patients with type 2 diabetes (T2DM) have been estimated to have CKD.^{2,5,6} CKD with T2DM leads to a worse prognosis than T2DM alone, including higher risk of cardiovascular morbidity and cardiovascular and all-cause mortality.^{7,8} Compared with patients with T2DM without CKD, patients with the dual comorbid conditions of CKD and T2DM might have a 3-fold increase in all-cause mortality.⁹ Although T2DM is a major risk factor for CKD, CKD is often identified before the diagnosis of T2DM.¹⁰ Potential differences between these patient groups with regard to risk profile and therapeutic strategies remain poorly understood.

Studies have demonstrated that the relative prevalence of CKD and T2DM is not equally distributed across the United States. For example, a high prevalence of kidney disease in the United States over the years from 2013 to 2016 was observed in Hawaii, Arizona, Michigan, and West Virginia, whereas a low prevalence was observed in Alaska,

Results: In univariate LISA, low-low clusters, in which a state has a low CKD prevalence and the surrounding states have a below-average CKD prevalence, were observed in the northwest region throughout the study period, regardless of the T2DM status, indicating a consistently low prevalence of CKD clustered in these areas. High-high clusters were observed, regardless of the T2DM status, in the southeast region in more recent years, suggesting an increased CKD prevalence in this region.

Limitations: Health care insurance enrollment might not have been representative of the United States; the estimates were based on claims data that likely underestimated the true prevalence.

Conclusions: Geographic disparities in CKD prevalence appear increasingly magnified, with an increase in the southeastern region of the United States. This increase is especially problematic because patients with CKD in high-prevalence states experience a greater likelihood of chronic conditions than those in the rest of the United States.

Visual Abstract included

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Minnesota, Colorado, and New York.¹¹ A heterogeneous pattern of T2DM prevalence in the United States has also been well established, with a high prevalence of T2DM predominantly in the southern areas of the United States.^{12,13} Although these investigations have provided valuable insights into CKD and T2DM prevalence in the United States, we are not aware of any studies that have examined regional variations in the prevalence of CKD in relation to T2DM in the United States. In the current study, our primary objective was to understand differences in the prevalence of CKD (stages 1-5) with and without T2DM across the United States and variability over time. Our secondary objective was to examine differences in demographic and clinical characteristics that might help explain the regional variations in CKD prevalence.

METHODS

Data Source

Data were derived from the IBM MarketScan Commercial and Medicare supplemental databases. The MarketScan database contains paid outpatient and pharmaceutical claims generated by nearly 51 million employees and their



PLAIN-LANGUAGE SUMMARY

Diabetes mellitus is the leading cause of chronic kidney disease (CKD), and CKD with type 2 diabetes (T2DM) leads to a worse prognosis than T2DM alone. Regional variation in CKD prevalence in patients with or without T2DM has not been well characterized. We used geomapping and spatial analyses to evaluate CKD prevalence across the United States from 2013 to 2018. We found that the prevalence of CKD increased from 2013 to 2018 in patients with and without T2DM. A consistently low prevalence was observed in the northwest while high prevalence was observed in the southeast in more recent years. Patients with CKD living in high-prevalence states exhibited more chronic conditions compared with patients with CKD living in the rest of the United States.

dependents per year with employer-sponsored insurance who are enrolled in a variety of fee-for-service and managed care plans for 50 states, Puerto Rico, and US territories.

This research was exempted from Health and Human Services requirements for institutional review board approval and informed consent (45 CFR 46.104(d)).

Study Design

For objective 1, we performed a spatial and temporal comparative analysis using aggregated state-level data to examine variations in CKD prevalence. The overall study period was divided into 6 nonmutually exclusive calendar year cohorts representing the years 2013 through 2018 (Fig 1).

For objective 2, we performed a subanalysis comparing the demographic and clinical characteristics of patients living in high-prevalence states with those of patients living in the rest of the United States in 2018.

Study Population and Criteria

The eligible population within each calendar year cohort consisted of adults aged ≥ 18 years at the start of each calendar year and with continuous health plan enrollment during the calendar year. Eligible enrollees with CKD were segmented into 2 subgroups, representing enrollees with and without T2DM (ie, CKD with T2DM and CKD without T2DM). Additionally, enrollees missing from their state of residence were excluded from the analyses of regional differences for the secondary objective.

Measurements

Diagnosis of CKD With or Without T2DM

The presence of non–dialysis-dependent CKD (stages 1-5) and T2DM was defined using the International Classification of Diseases, 9th revision, clinical modification or International Classification of Diseases, 10th revision, clinical modification diagnostic codes, and this required at least 1 inpatient or 2 outpatient diagnoses ≥30 days apart during a calendar year cohort.^{14,15} All other enrollees were classified as without CKD or T2DM. Once CKD and/or T2DM were identified in an enrollee, they remained classified as with CKD and/or T2DM throughout subsequent calendar year cohorts.

Measurement of CKD Prevalence and Definition of High-Prevalence States

The prevalence of CKD overall (with or without T2DM) and among the subgroups (CKD with T2DM and CKD without T2DM) was calculated nationally and by state for the years 2013 through 2018. The prevalence of CKD was calculated as the number of incident and prevalent cases for each calendar year cohort divided by the enrolled population during that calendar year and multiplied by



Figure 1. Study design. Abbreviations: CKD, chronic kidney disease; T2DM, type 2 diabetes.



Figure 2. Prevalence of CKD overall, CKD with type 2 diabetes, and CKD without type 2 diabetes, 2013-2018. Abbreviations: CKD, chronic kidney disease; T2DM, type 2 diabetes.

100%. To address the secondary objective, we used 2018 data to define high-prevalence states, which were coded as such if they were in the top-20th percentile for the prevalence of CKD. All remaining states were combined and referred to as the rest of the United States.

Demographic and Clinical Characteristics

The demographic and clinical variables of each patient collected included age, sex, metropolitan statistical area, insurance coverage, comorbid conditions, medication use, and total number of drug classes. Comorbid conditions were defined as a medical claim with at least 1 International Classification of Diseases, 9th revision, clinical modification or International Classification of Diseases, 10th revision, clinical modification diagnosis code during each calendar year cohort. National drug codes were used to identify drug classes within the profile, including antiplatelet agents, antihyperlipidemic agents, antihypertensive agents, and glucose-lowering agents, and the total number of these drug classes taken within a calendar year cohort. Missing data for any demographic or clinical characteristic were reported.

Statistical Analysis

Geomapping

Geomapping was used to visualize the prevalence of CKD diagnoses overall and among those with and without T2DM at the state level for the years 2013 through 2018. In Fig 2, darker colors indicate a higher prevalence and lighter colors represent a lower prevalence. For CKD prevalence overall, the classification was as follows: $\leq 1\%$, >1% to $\leq 2\%$, >2% to $\leq 3\%$, >3% to ≤ 4 , and >4%. For the subgroups of patients with CKD with T2DM and those with CKD without T2DM, the classification from light to dark colors was as follows: $\leq 0.5\%$, >0.5% to <1%, $\geq 1\%$ to <2%, and $\geq 2\%$.

Spatial Analysis

Univariate local indicators of spatial association (LISA) were computed to evaluate spatial patterns in CKD prevalence for each calendar year cohort from 2013 through 2018. Spatial analyses were limited to patients with known state of residence from 48 adjoining US states because isolates (ie, the noncontiguous states of Hawaii and Alaska) could not be analyzed using LISA. The spatial patterns were identified. A high-high cluster indicates a state with an above-average prevalence of CKD. A low-low cluster indicates a state with a below-average prevalence of CKD surrounded by states with a below-average prevalence of CKD.

Differential LISA was used to explore differences in prevalence, identify potential clusters between the 2013 and 2018 cohorts, and depict temporal-spatial autocorrelation. In differential LISA, for example, a high-high cluster indicated a state with an above-average difference in the prevalence of CKD surrounded by other states with an above-average difference.

We used the queen contiguity weights matrix to define the neighbors of the states. Moran's I and a significance level at P < 0.05 were used to assess the spatial autocorrelation.^{16,17} GeoDA 1.14 and Adobe Illustrator software were used to visualize the prevalence of CKD and map the spatial patterns identified using univariate and differential LISA.

Demographics and Clinical Characteristics

The differences in the demographic and clinical characteristics of enrollees with CKD living in high-prevalence states versus those of enrollees with CKD living in the rest of the United States are presented as frequencies and percentages. The analyses were performed using data from the 50 US states plus Puerto Rico. Missing data were reported. χ^2 tests were performed, and P values were reported. In addition, absolute percent and standardized differences in each variable category between the high-prevalence states and the rest of the United States were presented. Standardized differences for continuous variables were calculated as the difference in means between

the 2 comparative groups divided by the pooled standard deviation of the 2 groups; for categorical variables, the formula was modified by replacing the difference in proportions between the 2 groups and dividing it by the pooled standard deviation based on proportions. Although P values were influenced by sample size because they rely on the standard deviation of each group separately, standardized differences were included because they rely on the pooled standard deviation of the groups being compared and are less biased by large sample sizes. Standardized difference scores of >10% are commonly used as a guide for identifying meaningful differences in demographic and clinical characteristics between high-prevalence states and the rest of the United States.¹⁸

RESULTS

Prevalence of CKD Overall and Within Subgroups

There were 26,737,790 enrollees in 2013 and 15,917,049 in 2018; they were aged ≥ 18 years and with continuous enrollment in the calendar year. The overall prevalence of non-dialysis-dependent CKD (stages 1-5) increased from 1.50% (95% confidence interval [CI], 1.50-1.51; N=401,135) in 2013 to 2.89% (95% CI, 2.88-2.90; N=460,408) in 2018. The prevalence of CKD with T2DM increased from 0.70% (95% CI, 0.70-0.70) in 2013 to 1.28% (95% CI, 1.28-1.29) in 2018. Similarly, the prevalence of CKD without T2DM increased from 0.80% (95% CI, 0.80-0.80) in 2013 to 1.61% (95% CI, 1.60-1.62) in 2018 (Fig 2). The top-3 states with the highest prevalence of CKD in 2013 were Hawaii (5.48%; 95% CI, 4.94-6.02), Michigan (2.73%; 95% CI, 2.70-2.76), and West Virginia (2.14%; 95% CI, 2.05-2.23); the top-3 states with the highest prevalence of CKD in 2018 were Hawaii (6.67%; 95% CI, 5.67-7.68), Florida (3.97%; 95% CI, 3.94-4.01), and Michigan (3.28%; 95% CI, 3.24-3.32). Among all the enrollees with a CKD diagnosis, 46.58% (95% CI, 46.42-46.73; N=186,844) of the patients were identified with CKD and T2DM in 2013; this proportion decreased slightly to 44.40% (95% CI, 44.25-44.54; N=204,404) in 2018.

Spatial Analysis

Figure 2 illustrates the maps of state-level CKD prevalence (stages 1-5) from 2013 to 2018. Given that the spatial analyses were performed in patients with known state of residence in the 48 adjoining US states, the average state-level prevalence of CKD was slightly lower than the national estimates presented above.

Univariate LISA

For CKD prevalence overall, the univariate global Moran's I was 0.14 (P = 0.06) in 2013, which kept increasing each year, and was estimated at 0.34 (P = 0.002) in 2018, which indicated an increasing geographic disparity during the observation period across the United States. A similar pattern of increase in global Moran's I was observed for



Figure 3. Spatial patterns of CKD overall, CKD with type 2 diabetes, and CKD without type 2 diabetes determined using univariate LISA, 2013-2018. Abbreviations: CKD, chronic kidney disease; LISA, local indicator for spatial analysis; T2DM, type 2 diabetes.

CKD prevalence among those with and without T2DM. Figure 3 illustrates the results of the estimation of univariate local Moran's I for CKD prevalence overall and among those with and without T2DM. Low-low clusters were observed in the northwest region of the United States for CKD prevalence overall, regardless of the T2DM status, indicating a consistently low prevalence of CKD clustered in these areas. For example, Wyoming, North Dakota, South Dakota, and Minnesota were identified as low-low clusters across all years. High-high clusters were also observed, regardless of the T2DM status, particularly in the southeast region (eg, Florida, Georgia, and Alabama) from 2017 to 2018, suggesting an emerging cluster in this region.

Differential LISA

For specific states, Fig 4 illustrates the results of the differential local Moran's I and the identified high-high clusters in the southeast region of the country, including Tennessee, Georgia, and Alabama, for CKD prevalence overall and among the subgroups of CKD with and without T2DM, suggesting that these states, with an above-average difference in prevalence from 2013 to 2018, were clustered in this region.

Figure 4. Temporal-spatial patterns of CKD with or without type 2 diabetes, CKD with type 2 diabetes, and CKD without type 2 diabetes determined using differential LISA, 2013-2018. Abbreviations: CKD, chronic kidney disease; LISA, local indicator for spatial analysis; T2DM, type 2 diabetes.

Demographic and Clinical Characteristics of High-Prevalence States

The demographic and clinical characteristics of the 13,888,585 (85.3%) enrollees with known states of residence reported in high-prevalence states versus those of enrollees in the rest of the United States are presented in Table 1. Patients with CKD living in high-prevalence states differed from those living in the rest of the United States. A greater proportion of patients with CKD in high-prevalence states were aged >65 years, women, and taking medication from \geq 1 drug classes in the profile, including antiplatelet, antihyperlipidemic, and antihypertensive agents.

Patients with CKD without T2DM in high-prevalence states (N=69,977), compared with those in the rest of the United States (N=128,096), were more likely to have hypertension, hyperlipidemia, obesity, coronary artery disease, and angina pectoris (Fig 5). Patients with CKD and T2DM in regions with a high prevalence of CKD (N=54,475), compared with those in the rest of the United States (N=96,334), were also likely to have the same comorbid conditions, although the standardized difference for some decreased to just below the prespecified 10% threshold. Among patients with CKD and T2DM, >60% used antihyperlipidemic agents and antihypertensive agents (Fig 6). The use of both the agents in patients with CKD was higher in high-prevalence states than in the rest of the United States, regardless of the T2DM status. However, according to the standardized difference, only the regional difference in antihyperlipidemic agent use in patients with CKD without T2DM was statistically significant.

DISCUSSION

The present study is the first to use spatial and temporal information to understand regional and time differences in CKD prevalence in patients with and/or without T2DM using a large claims database of commercially insured US patients. Overall, we observed a comparatively lower prevalence of CKD than that reported in previous literature, and the prevalence in the present study nearly doubled between 2013 (1.5%) and 2018 (2.9%) in the United States. We found significant geographic disparities and spatial-temporal variations in the prevalence of CKD with and without T2DM, including in areas with a consistently low prevalence of CKD and in clustered areas with an increasing prevalence of CKD, in recent years. Additionally, we discovered that patients with CKD living in highprevalence states, whether they had T2DM or not, exhibited a higher prevalence of several chronic conditions compared with patients with CKD living in the rest of the United States.

Specifically, the states with a CKD prevalence rate of >3% for at least 4 of the 6 study years included Hawaii, Michigan, Florida, Ohio, and Alabama. A low-low cluster of states was consistently identified in the northwest region of the United States using univariate LISA, regardless of the T2DM status. A high-high cluster of states was observed in the southeast region of the United States using differential LISA, indicating a cluster of increasing CKD prevalence from 2013 to 2018 in this region. This finding is consistent with that of the high-high clusters identified using univariate LISA in 2017 to 2018.

During the study period, the prevalence of CKD increased from <2% to 4% in Florida, which was second to that in Hawaii in terms of CKD prevalence in 2018. These findings are consistent with the 2018 United States Renal Data System report that noted a shift toward a higher prevalence of CKD in southeastern states in 2016 compared with that in previous years.¹¹ These findings highlight the increasing CKD diagnoses geographically clustered in Georgia, Alabama, and Florida, which warrant further investigation.

The increasing overall prevalence of CKD in the United States might have been due to a variety of factors, including aging of the population and increased burden of major risk factors such as diabetes and hypertension.^{1,4} Although insurance coverage in the database decreased during the study period, the increases in prevalence might have been influenced by the enactment of the Affordable Care Act, improving insurance coverage for minorities and

	CKD With T2DM					CKD Without T2DM			
	High- Prevalence States	Rest of the United States	Absolute	Standardized Difference (%)	High- Prevalence States	Rest of the United States	Absolute	Standardized Difference (%)	
Characteristic	N=54,475	N=96,334	Difference (%)		N=69,977	N=128,096	Difference (%)		
Age group, n (%), y									
18-34	817 (1.5)	1,913 (2.0)	-0.5	-3.8	5,527 (7.9)	13,107 (10.2)	-2.3	-8.0	
35-64	34,910 (64.1)	76,397 (79.3)	-15.2	-34.2	44,527 (63.6)	95,523 (74.6)	-11.0	-24.0	
65-74	7,037 (12.9)	6,746 (7.0)	5.9	19.8	6,038 (8.6)	5,385 (4.2)	4.4	18.1	
≥75	11,711 (21.5)	11,278 (11.7)	9.8	26.6	13,885 (19.8)	14,081 (11.0)	8.8	24.6	
Sex, n (%)									
Male	30,870 (56.7)	56,559 (58.7)	-2.0	-4.0	35,420 (50.6)	66,701 (52.1)	-1.5	-3.0	
Female	23,605 (43.3)	39,775 (41.3)	2.0	4.0	34,557 (49.4)	61,395 (47.9)	1.5	3.0	
MSA, n (%)ª		· · · · · · · · · · · · · · · · · · ·			· · · · · · · · · · · · · · · · · · ·				
Non-MSA	5,658 (10.4)	9,661 (10.0)	0.4	1.3	7,134 (10.2)	12,746 (10.0)	0.2	0.7	
MSA	39,782 (73.0)	74,867 (77.7)	-4.7	-10.9	53,036 (75.8)	100,569 (78.5)	-2.7	-6.4	
Unknown	9,035 (16.6)	11,806 (12.3)	4.3	12.3	9,807 (14.0)	14,781 (11.5)	2.5	7.5	
Payer type, n(%)									
Commercial	35,763 (65.7)	78,481 (81.5)	-15.8	-36.4	50,128 (71.6)	108,790 (84.9)	-13.3	-32.7	
Medicare	18,712 (34.3)	17,853 (18.5)	15.8	36.4	19,849 (28.4)	19,306 (15.1)	13.3	32.7	
Medication classes used									
Antiplatelet agents	7,419 (13.6)	12,187 (12.7)	-0.9	2.7	4,827 (6.9)	7,449 (5.8)	-1.1	4.5	
Antihyperlipidemic agents	37,342 (68.5)	64,370 (66.8)	-1.7	3.6	25,578 (36.6)	40,625 (31.7)	-4.9	10.3	
Antihypertensive agents	45,977 (84.4)	78,383 (81.4)	-3.0	8.0	44,518 (63.6)	76,289 (59.6)	-4.0	8.2	
Glucose-lowering agents	39,878 (73.2)	71,116 (73.8)	0.6	-1.4	1,615 (2.3)	3,697 (2.9)	0.6	-3.8	
Number of drug classes in profile, n (%)									
0	4,907 (9.0)	11,038 (11.5)	-2.5	-8.2	21,416 (30.6)	44,833 (35.0)	-4.4	-9.4	
1	5,170 (9.5)	8,646 (9.0)	0.5	1.7	24,903 (35.6)	45,395 (35.4)	0.2	0.4	
2	13,120 (24.1)	21,597 (22.4)	1.7	4.0	19,425 (27.8)	31,138 (24.3)	3.5	8.0	
3	25,906 (47.6)	45,996 (47.7)	-0.1	-0.2	4,147 (5.9)	6,531 (5.1)	0.8	3.5	
4	5,372 (9.9)	9,057 (9.4)	0.5	1.7	86 (0.1)	199 (0.2)	-0.1	-2.6	

Table 1. Sociodemographic and Clinical Characteristics of Enrollees With CKD in High-Prevalence States Versus in the Rest of the United States, 2018

Note: P < 0.001 for all χ^2 testing between high-prevalence states and the rest of the United States. Standardized differences rely on the pooled standard deviation of the groups being compared and are less biased by large sample sizes than by P values.

Abbreviations: CKD, chronic kidney disease; MSA, metropolitan statistical area; T2DM, type 2 diabetes.

^aMSA is defined as urban areas of >50,000 population or combined counties with an urban core area of >10,000 population.

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Comorbidities in CKD Patients with T2DM

Figure 5. Patient comorbid conditions in high-prevalence states versus in the rest of the United States in patients with CKD with and without type 2 diabetes.^a. ^aStandardized difference between high-prevalence states and the rest of the United States is shown in the figure. Comorbid conditions presented were identified as the most-prevalent conditions or those with the largest standardized difference. P < 0.001 for all listed conditions. Abbreviations: CKD, chronic kidney disease; T2DM, type 2 diabetes; US, United States.

low-income individuals, in whom the risk of CKD is higher, and this might explain the variation in regional prevalence.¹⁹⁻²¹ Moreover, the heterogeneous patterns of comorbid conditions, such as the "diabetes belt" seen in the southern region of the United States, might help explain the regional differences, as do other possibilities.¹² Regional or state differences in social determinants of health, such as health policy (ie, access to or quality of health care), access to quality education, economic stability (ie, affordable housing and rate of employment), and environment (ie, access to food and exposure to crime and violence), may contribute to regional differences in CKD prevalence.²² The higher prevalence of CKD among Black patients and native Hawaiians or Pacific Islanders and their regional variation might, in part, explain the regional differences in CKD prevalence.^{23,24}

The current study identified a lower CKD prevalence than that previously reported in the literature. General population estimates have suggested a prevalence closer to 15%.¹ Our CKD prevalence rates were based on health care insurance enrollment and might have been lower, in part, because of the study's design and incomplete nature of the health care claims data. First, general population estimates from databases such as the National Health and Nutrition Examination Survey are independent of insurance type and weighted to be nationally representative; however, the database used in this study contained only commercial health coverage enrollees. Second, this dataset was based

Medication Classes in CKD Patients without T2DM

Figure 6. Medication classes used in high-prevalence states versus in the rest of the United States in patients with CKD with and without type 2 diabetes.^a. ^aBoxed numbers represent standardized differences. P < 0.001 for all values presented. Abbreviations: CKD, chronic kidney disease; T2DM, type 2 diabetes; US, United States.

on claims from covered enrollees, which represent a younger employed population. Although this dataset includes Medicare supplemental data for retirees covered by previous employers, these represent a small proportion of enrollees and may not be representative of the US population of Medicare beneficiaries. Third, this study was designed to assess changes in CKD prevalence over years and, thus, required the enrollees to have 1 inpatient or at least 2 outpatient diagnoses within a calendar year. This criterion might have reduced the overall prevalence if enrollees with the relevant diagnosis coded were not seen twice in a calendar year.

Per our secondary objective, we found that patients with CKD living in high-prevalence states were more likely to be over the age of 65 years, women, and taking medication from ≥ 1 drug classes than patients with CKD in the rest of the United States. Comorbid conditions were also not similarly distributed, with hypertension, hyper-lipidemia, obesity, and osteoarthritis being more common in high-prevalence states than in the rest of the United States. Although many of these comorbid conditions are associated with diabetes mellitus, which is similarly high in the southern region of the United States, the rates for comorbid conditions in high-prevalence states were pronounced in both patients with and without T2DM.^{1,12}

These findings suggest that T2DM, as well as other comorbid conditions, explains some, but not all, differences in regional variation in prevalence.

Comorbid conditions can worsen kidney and heart outcomes and affect the prognosis of CKD.²⁵⁻²⁸ In addition, comorbid conditions might help explain the spatial and temporal changes in CKD prevalence across the United States. With higher concentrations of comorbid conditions in regions with CKD prevalence, it is imperative to identify and treat CKD and its associated comorbid conditions. This information will help identify areas in which targeted interventions may provide the highest level of benefit. Future work should determine whether the rates of these other comorbid conditions contribute to the high-high cluster in the southeast and increased CKD prevalence in this region.

Nonetheless, there are some limitations to note beyond those addressed, which might have affected the reported prevalence of CKD. The diagnosis of CKD and T2DM was based on requirements for diagnosis codes available within the claims data, which might not have reflected the true patient diagnoses; moreover, laboratory test results or chart data were not available for confirmation. Patient evaluation of urine albumin and glomerular filtration rate might not have been uniformly monitored by providers across the states, and this might have influenced the

reported prevalence rates. The database is limited to patients with commercial and Medicare supplemental insurances; as such, the population was generally younger and employed, which makes the results less generalizable to the US population. Furthermore, the analysis did not adjust for differences in patient demographic and clinical characteristics, such as age distribution of the patients or the proportion of Medicare patients within a given state, which might have influenced the reported regional and temporal trends and affected the generalizability of findings.

In 2015, coverage in insurance plans decreased and, thus, so did the sample of enrolled patients. Although the effect of these changes cannot be directly assessed, the estimates of prevalence were based on the denominator of enrolled patients at the time of the evaluation and, thus, should not be influenced by patients no longer included in the sample. In 2017, MarketScan databases implemented a process to protect patient anonymity, which provided additional confidentiality of information by masking geography in areas in which any 1 data source dominates the data pool. As a result, the number of enrollees with missing information in the states increased, which might have influenced the prevalence rates across the states if their data were missing systematically. We also noticed some changes in the cohorts over time, with the average age in the 2018 cohort (\sim 45 years) being lower than that in the previous cohorts (eg, ~ 47 years in 2013) and the proportion of patients with CKD and T2DM slightly decreasing from 46.7% in 2013 to 44.4% in 2018. The true prevalence of CKD overall likely increased if age and T2DM status were adjusted for the year 2018. In addition, risk factors, such as racial and ethnic distributions, could not be ascertained from the current data source, and thus, we were not able to adjust for these factors.

This study demonstrates regional variations in CKD prevalence in the United States and characterized variations in the prevalence of CKD with or without T2DM, based on the claims data. Regional disparities appear increasingly magnified, with a continually increasing prevalence in the southeastern region of the United States, in contrast with a consistently lower prevalence in the northwest region of the country, from 2013 to 2018. This finding highlights the potential need for CKD care improvement in high-prevalence states, especially because these regions also tend to have a higher prevalence of other chronic conditions that contribute to a high health care burden. Further exploration of the possible predictors underlying regional and temporal differences in CKD prevalence is warranted, including regional variations in commercial versus Medicare distributions. Further assessment of variation in CKD prevalence within smaller regional areas, such as counties or cities, which may drive prevalence rates within the state (ie, hot spots or high-prevalence communities), is also recommended. This study also highlights the need for a customized CKD treatment approach

across states based on differences observed in the prevalence as well as demographic and clinical characteristics of those with CKD.

ARTICLE INFORMATION

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Authors' Contributions: Research idea and study design: XF, RF, BBD, AG, SXK, JE, RS; data acquisition: FX, JE; data analysis/ interpretation: XF, RF, BBD, FX, AG, SXK, JE, SL, RS; statistical analysis: XF, RF, BBD, FX, RS; supervision or mentorship: SXK, JE, SL. Each author contributed important intellectual content during manuscript drafting and revision, accepts personal accountability for the author's own contributions, and agrees to ensure that questions pertaining to the accuracy or integrity of any portion of the work are appropriately investigated and resolved.

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