Healthcare Costs Across Diabetic Kidney Disease Stages: A Veterans Affairs Study

Kibum Kim, Jacob Crook, Chao-Chin Lu, Heather Nyman, Jyotirmoy Sarker, Richard Nelson, and Joanne LaFleur

Background: In the United States, diabetic kidney disease (DKD) affects about one-third of individuals with type 2 diabetes, causing significant economic burdens on the health care system and affecting patients' quality of life.

Objective: The aim of the study was to quantify the burden of care in patients at different stages of DKD and to monitor shifts in healthcare costs throughout these stages.

Methods: This study used data from the Veterans Affairs National database, focusing on US veterans diagnosed with DKD between January 2016 and March 2022. Aggregated all-cause health care costs per month were summarized using descriptive statistics. We used a generalized linear model to calculate the cost of DKD patent care based on the stages, dialysis phase, and kidney replacement therapy.

Results: The cohort of 685,288 patients with DKD was predominantly male (96.51%), White (74.42%), and non-Hispanic (93.54%). The mean (SD) per-patient per-month costs were $1,597 ($3,178), $1,772 ($4,269), $2,857 ($13,072), $3,722 ($12,134), $5,505 ($14,639), and $6,999 ($16,901) for stages 1, 2, 3a, 3b, 4 and 5 respectively. The average monthly expenditure for patients receiving long-term dialysis was $12,299. Costs peaked sharply during the first month of kidney replacement therapy at $38,359 but subsequently decreased to $6,636 after 1 year.

Conclusions: The economic implications of DKD are profound, emphasizing the need for efficient early detection and disease management strategies. Preventing patients from progressing to advanced DKD stage will minimize the economic repercussions of DKD and will assist health care systems in optimizing resource allocation.

Complete author and article information provided before references.

Correspondence to K. Kim (kkim204@uic.edu)

Kidney Med. 6(9):100873. Published online July 18, 2024.

doi: 10.1016/j.xkme.2024.100873

Chronic kidney disease (CKD) represents a significant public health challenge in the United States, with approximately 35.5 million or 15% of US adults being affected.[1] Diabetic kidney disease (DKD) is a clinical term characterizing the onset of CKD as a complication of diabetes based on diagnostic criteria such as symptoms, signs, and laboratory data.[2] It is estimated that between 20% and 40% of individuals with type 2 diabetes (T2D) develop DKD.[3] Globally T2D stands as a primary contributor to CKD and eventual kidney failure necessitating dialysis and kidney replacement therapy (KRT).[2] DKD places significant economic burden on health care system and severely alters the quality of life of those diagnosed.[2,3] The increasing incidence of T2D and associated risk elements has led to an increasing prevalence of DKD, further intensifying health care demands and related financial implications.[3]

Some individuals with DKD will experience progression over time. Advanced stages of DKD are associated with an increased risk of cardiovascular complications as well as the development of kidney failure that requires long-term dialysis, leading to a significant increase in health care cost along with DKD progression.[4-6] According to a recent analysis of a commercial claims from 2014 through 2019, the estimated cost to payers in the United States was $7,725 per 4 months for stage 1 or 2 DKD patients, which increased to $11,879 with progression to stage 5.[7] T2D patients covered by commercial insurance, on average, incurred $24,209 of total cost annually since the onset of kidney disease.[3] However, study findings are not applicable for an economic burden calculation or health technology assessment in non-commercially insured or uninsured population primarily because of the variation in payment mechanisms in the United States. Further, with recent developments in DKD management and changes in nephroprotective agent use, it is warranted to analyze the recent cost of care for DKD patients.[8]

Kidney disease imposes a significant burden to the Veterans Health Administration (VHA), the largest integrated health care system in the United States. CKD affects 1 out of 6 veterans, and this number continues to increase as a result of the high prevalence of diabetes approaching 25% of the veterans affairs (VA) population. As a part of the efforts to alleviate the burden of care, the Department of Veterans Affairs issued the new VHA Directive 1053 in 2020 aiming to improve the prevention, early recognition and management of CKD in VA medical facilities.[9] A precise estimation of the cost incurred by DKD patients would place another stepping stone to propose action plans to mitigate costs, which is a part of the Directive 1053.

To close the aforementioned knowledge gap, we performed a retrospective cost of care study using the data obtained from VHA. Our primary aim was to estimate the cost of care incurred by patients with DKD, with a specific focus on stage-by-stage expenses within the VA community to inform and guide the development of cost-effective strategies that can be used to optimize the management of this condition within the US VHA.

PLAIN-LANGUAGE SUMMARY

Diabetic kidney disease (DKD) places a substantial burden on health care systems in the United States. In part of our effort to close the knowledge gap around the disease burden, care cost analysis for the patients with DKD was performed for US veterans. Along with stage progression, overall care costs per-patient per-month drastically increases from $1,597 (stage 1) to $6,999 (stage 5). Monthly costs exceeded $10,000 once veterans started to receive long-term dialysis. The quantitative summary will help health care systems efficiently allocate resources across various disease sectors.

METHODS

This is a retrospective cohort study using a secondary database obtained from the National VHA.

Overview of Data

VHA is the largest unified health care system in the United States and operates 172 hospitals and 1,138 outpatient facilities.[10] Using the Veteran Affairs Informatics and Computing Infrastructure, investigators had access to a comprehensive repository of various patient data types, including pharmacy records, laboratory results, clinical data, and procedural information. The cost information was abstracted from the VA Managerial Cost Accounting that relies on pre-existing VA databases for information on what care was provided and which patients used it. Data integrity within Veteran Affairs Informatics and Computing Infrastructure is maintained through the Veteran Affairs Surgical Quality Initiative Project, a quality assurance endeavor. The use of Veteran Affairs Informatics and Computing Infrastructure to obtain the limited VHA data used to perform this retrospective observational research was deemed exempt as a nonhuman subject research by the University of Utah and Salt Lake VA Institutional Review Boards.

Cohort Selection and Stage Classification

Our research focused on US veterans with DKD seen between January 2016 and March 2022. To qualify for our study, the individuals were required to have T2D confirmed by either 2 or more health care encounters (inpatient, outpatient, and emergency department services) with T2D diagnosis in different dates within 365 days or records of noninsulin antidiabetic agent use along with 1 or more T2D diagnosis within 365 days. Study individuals had at least 1 T2D encounter before the record of estimated glomerular filtration rate (eGFR) or microalbuminuria for DKD. Patients with type 1 diabetes or gestational diabetes during the cohort identification period were excluded from our study.

The analytic cohort includes patients with DKD with either eGFR less than 60 mL/min/1.73 m^2 or microalbuminuria (urinary albumin-creatinine ratio [uACR] ≥ 30 mg/g), indicating kidney function decline and kidney damage, respectively. For the patients with missing albuminuria records, we used urinary protein-creatinine ratio (uPCR) ≥ 15 mg/mmol or urinary protein ≥ 150 mg/day as an alternative indicator of the kidney damage. To confirm the chronic status, patients must have at least 2 eGFR or microalbuminuria (proteinuria) measurements on 2 different dates 90-365 days apart. We also included T2D patients with a record of long-term dialysis or KRT as defined by 2 or more relevant procedures in different dates within the 90 days. Individuals under the age of 18 years at the first record with abnormal eGFR or albuminuria were excluded from our study. The first of the multiple encounters was considered as a cohort entry date or index date for the DKD stage progression. Of note, we calculated eGFR based on the Modification of Diet in Renal Disease equation in which racial background is a regressor, considering that individual laboratories would have converted the eGFR values using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) 2012 or CKD-EPI 2021 equation at different times.[11-13]

We first defined the DKD stages based on the records at the cohort entry date.[8] To address the anticipated gradual decrease in the intensity of KRT over time, the follow-up period after transplant was segmented into 4 groups: first month, second and third months, fourth to 12th months, and after 1 year. All patients were reassessed over the follow-up period from the cohort entry date to either last encounter date, or March 2023, for the potential DKD stage reclassification. Once the stage progression was confirmed by the 2 or more laboratory test results or procedure records, we reassigned the patient to the newly advanced stage for the stage-specific cost assessment at the first date out of multiple laboratories meeting the stage criteria. In our analysis, patients were not allowed to move from advanced DKD stage to a less severe eGFR criteria.

Baseline Characteristics

Patient characteristics including clinical characteristics and demographics were collected from the structured electronic health care records during the 365 days before or at the cohort entry date, and reassessed at the 1-year baseline of each progression. Demographic information included age, sex (male or female), race, ethnicity, and smoking status. We also captured clinical characteristics, point-of-care measures and laboratory test results, body mass index (BMI), systolic blood pressure, and diastolic blood pressure as well as glycated hemoglobin (HbA1c), low-density lipoprotein, high-density lipoprotein, total cholesterol, and triglyceride levels. Further, we abstracted the diagnosis codes and VHA problem lists to identify comorbid conditions, including hypertension, dyslipidemia, malignancy, liver disorder, anemia, gout, connective tissue disorder, and substance abuse.

Outcome

All-cause health care costs covered by the VHA was the outcome of interest. Health care costs while the patient stayed in a specific stage were abstracted from the VHA's Managerial Cost Accounting. Therefore, the cost calculation was based on the information on the care provided and used within the VHA, and reflects the VA health care sector's perspective. All the costs were inflation adjusted to 2022 USD values using the Bureau of Labor Statistics Consumer Price Index for All Urban Consumers.[14] To adjust for the differential duration of DKD stages, we divided the aggregated stage-specific costs by the time and calculated per-patient per-month (PPPM) cost.

Patients could potentially qualify for the cost analysis on multiple occasions as their DKD advances into more severe stages. For instance, patients initially entering the analytic cohort with stage G3a DKD were suitable for the cost estimation for G3a, as long as their DKD did not progress further. If their DKD advanced to stage 3b or stage 4 with a reduction in eGFR, they re-entered the analytic cohort for the respective stage cost assessment.

Statistical Analysis

Descriptive statistics were used to present the number of patients at different DKD stages after the analytic cohort entry and subsequent stage transition. Continuous variables including age, BMI, and laboratory test values were summarized using means and standard deviations. Missing observations were excluded in the calculation of summary statistics for continuous variables. Age, BMI and A1c levels were categorized into 3 or 4 classes based on the distribution of the features and clinical risk thresholds. All the categorical variables were summarized using frequency and percentages out of the total number of eligible individuals, and missing records were categorized into the "unknown" category.

Mean (SD) and median (interquartile range) of the stage-specific PPPM expenditure were estimated. Given the skewed nature of cost data, a generalized linear model was applied employing a Gamma error distribution and a log-link function, in which the cost and its variance were correlated with stage progression. The adjusted costs were recalculated using the regression coefficients for each stage in reference to the intercept estimates for Stage G1. To determine the 95% confidence interval range for these adjusted cost predictions, a 5,000 semi-parametric bootstrap using the regression coefficients and their standard error was performed.

RESULTS

We identified 685,288 patients with 1,018,546 instances of various DKD stages (patients were counted multiple times if they progressed to a more advanced stage during the study period). Overall, stages G3a (50.16%) followed by G3b (25.03%) account for more than two-third of the study cohort. The analysis included 26,396 long-term dialysis and 1,970 kidney transplant cases. More than 95% of individuals in each stage in our cohort were males, and the age distribution in different groups varied. Although patients were predominantly White in every DKD stage, the proportion of African Americans was generally greater among the patients with advanced stages, with 15.0%, 15.2%, 20.7%, 33.8% and 40.6% in stages G3a, G3b, G4, and G5 of and long-term dialysis, respectively (Table 1).

On average, veterans with DKD carry elevated metabolic and cardiovascular risks (Table 2). The mean BMI was consistently above 30. However, there was a declining BMI pattern with higher DKD stages: stage 1 patients entered the cohort with an average BMI of 33, and KRT patients had the mean BMI of 30 at different stages of KRT. The average systolic blood pressure across the stages 1 to 4 ranged from 135 to 140 and was higher than 140 among patients with DKD at stage 5 or beyond. In general, A1c, diastolic blood pressure, low-density lipoprotein, high-density lipoprotein, total cholesterol, and triglyceride levels were also higher than the average values for the population. uACR, an indicator of kidney damage, generally increased with stage progression, with mean uACR values of 177.7 and 368.9 mg/gCr at stages G1 and G5, respectively.

Chronic conditions defined by discrete criteria and diagnosis codes across the stages of DKD are outlined in Table 3. The percentage of patients with overweight or obesity as defined by BMI > 25 kg/m^2 was consistently between 80% and 90% across all groups. In higher DKD stages, there was a higher proportion with HbA1c < 7%. Specifically, only 30.3% of patients in stage 1 had an A1c level below 7.0%, compared with 53.2% for those in stage 5 and 55.0% among patients undergoing dialysis. The prevalence of anemia was higher with more advanced stages of DKD. In stage 1, only 2.9% of patients exhibited anemia. However, this proportion was 45.1% among stage 5 patients and 58.6% among those undergoing dialysis. A small fraction of patients had connective tissue disease with the proportions ranging from 0.17% to 1.07%. The majority of patients with DKD had a diagnosis of hypertension, which also was higher in more advanced stages of DKD (67% of stage 1 patients had hypertension which increased to 73.9%, 73.9%, 77.1%, 80.8%, and 81.7% for stages 2, 3a, 3b, 4, and 5 respectively). The DKD patient cohort was dominated with dyslipidemia with a prevalence of 57.5% and 65.8% noted for at stages 1 and 5, respectively (Table 3).

The mean and median PPPM costs increased with disease progression. The mean (SD) PPPM costs were $1,597 ($3,178), $1,772 ($4,269), $2,857 ($13,072), $3,722 ($12,134), $5,505 ($14,639), and $6,999 ($16,901) for stages 1, 2, 3a, 3b, 4 and 5, respectively. The corresponding median costs were $795, $892, $1,036, $1.324, $2,040, and $2,271, respectively. The differences between the mean and median costs highlighted the right-skewed nature of cost data. Similarly, for patients undergoing

Table 1. Demographics at Baseline

Characteristic	DKD Stages							Kidney Replacement Therapy			
	G1 A2/A3	G2 A2/A3	G3a	G3b	G4	G5	Dialysis	First 30 d	31-90 d	91-365 d	After 1 y
N	18,833 (1.9)	96,700 (9.5)	508,026 (50.2)	253,508 (25.0)	85,581 (8.5)	21,786 (2.2)	26,369 (2.6)	1,970 (0.2)	1,965 (0.2)	1,948 (0.2)	1,860 (0.2)
Sex											
Female	771 (4.1)	2,996 (3.1)	18,854 (3.7)	8,693 (3.4)	2,686 (3.1)	588 (2.7)	693 (2.6)	69 (3.5)	69 (3.5)	69 (3.5)	66 (3.5)
Male	18,062 (95.9)	93,704 (96.9)	489,172 (96.3)	244,815 (96.6)	82,895 (96.9)	21,198 (97.3)	25,676 (97.4)	1,901 (96.5)	1,896 (96.5)	1,879 (96.5)	1,794 (96.5)
Age, y											
75+	1,832 (9.7)	17,894 (18.5)	147,320 (29.0)	99,340 (39.2)	31,218 (36.5)	5,459 (25.1)	4,781 (18.1)	93 (4.7)	93 (4.73)	92 (4.72)	83 (4.46)
65-74.9	7,236 (38.4)	45,860 (47.4)	260,145 (51.2)	114,699 (45.2)	38,614 (45.1)	10,261 (47.1)	12,484 (47.3)	864 (43.9)	863 (43.92)	857 (43.99)	817 (43.92)
45-64.9	8,473 (45.0)	30,970 (32.0)	98,072 (19.3)	38,742 (15.3)	15,390 (18.0)	5,917 (27.2)	8,857 (33.6)	938 (47.6)	934 (47.53)	925 (47.48)	889 (47.80)
<45	1,292 (6.9)	1,976 (2.0)	2,489 (0.5)	727 (0.3)	359 (0.4)	149 (0.7)	247 (0.9)	75 (3.8)	75 (3.82)	74 (3.80)	71 (3.82)
Race											
White	12,116 (64.3)	69,098 (71.5)	391,676 (77.1)	195,254 (77.0)	60,830 (71.1)	12,272 (56.3)	13,132 (49.8)	914 (46.4)	910 (46.3)	901 (46.3)	861 (46.3)
African American	4,073 (21.6)	17,210 (17.8)	75,980 (15.0)	38,411 (15.2)	17,744 (20.7)	7,367 (33.8)	10,717 (40.6)	848 (43.0)	847 (43.1)	841 (43.2)	802 (43.1)
Asian Pacific	537 (2.9)	2,684 (2.8)	9,488 (1.9)	4,850 (1.9)	1,828 (2.1)	629 (2.9)	807 (3.1)	72 (3.7)	72 (3.7)	72 (3.7)	70 (3.8)
Native American or Alaskan	432 (2.3)	1,488 (1.5)	5,049 (1.0)	2,443 (1.0)	944 (1.1)	296 (1.4)	362 (1.4)	26 (1.3)	26 (1.3)	26 (1.3)	25 (1.3)
Unknown	1,675 (8.9)	6,220 (6.4)	25,833 (5.1)	12,550 (5.0)	4,235 (4.9)	1,222 (5.6)	1,351 (5.1)	110 (5.6)	110 (5.6)	108 (5.5)	102 (5.5)
Ethnicity											
Non-Hispanic	16,472 (87.5)	87,447 (90.4)	479,186 (94.3)	239,154 (94.3)	79,830 (93.3)	19,837 (91.1)	23,979 (90.9)	1,744 (88.5)	1,741 (88.6)	1,725 (88.6)	1,646 (88.5)
Hispanic	2,361 (12.5)	9,253 (9.6)	28,840 (5.7)	14,354 (5.7)	5,751 (6.7)	1,949 (8.9)	2,390 (9.1)	226 (11.5)	224 (11.4)	223 (11.4)	214 (11.5)
Smoking											
Current	3,300 (17.5)	12,608 (13.0)	57,119 (11.2)	30,131 (11.9)	11,462 (13.4)	3,199 (14.7)	4,147 (15.7)	142 (7.2)	141 (7.2)	139 (7.1)	129 (6.9)
Former	3,283 (17.4)	15,972 (16.5)	101,901 (20.1)	57,648 (22.7)	20,361 (23.8)	4,973 (22.8)	6,167 (23.4)	439 (22.3)	439 (22.3)	437 (22.4)	412 (22.2)
Never	10,324 (54.8)	58,275 (60.3)	277,688 (54.7)	127,420 (50.3)	40,286 (47.1)	9,946 (45.7)	11,437 (43.4)	953 (48.4)	950 (48.3)	939 (48.2)	898 (48.3)
Unknown	1,926 (10.2)	9,845 (10.2)	71,318 (14.0)	38,309 (15.1)	13,472 (15.7)	3,668 (16.8)	4,618 (17.5)	436 (22.1)	435 (22.1)	433 (22.2)	421 (22.6)

Note: Each patient could contribute to multiple CKD stages over the course of follow-up on progression.

Table 2. Laboratory Test and Point-of-Care Clinical Measures of Metabolic and Cardiovascular Risks (Continuous Variables)

	DKD Stages							Kidney Replacement Therapy			
Characteristic	**G1 A2/A3**	**G2 A2/A3**	**G3a**	**G3b**	**G4**	**G5**	**Dialysis**	**First 30 d**	**31-90 d**	**91-365 d**	**After 1 y**
Age, y	62.4 (10.9)	67.1 (9.8)	70.7 (9.0)	72.8 (9.2)	72.1 (9.6)	69.1 (9.4)	67.3 (9.1)	62.5 (8.7)	62.5 (8.7)	62.5 (8.7)	62.4 (8.7)
uACR	177.7 (238.9)	161.9 (209.6)	164.7 (215.2)	162.6 (225.3)	208.6 (269.3)	288.3 (318.7)	368.9 (340.5)	372.5 (337.8)	-	-	-
	80.0 (45.0-193.2)	*82.1 (47.5-176.9)*	*80.9 (47.0-178.9)*	*72.0 (42.7-170.7)*	*94.1 (47.9-239.9)*	*165.0 (64.6-376.0)*	*251.6 (119.4-496.7)*	*258.6 (126.8-502.2)*	-	-	-
BMI	33.0 (6.9)	32.7 (6.5)	32.1 (6.4)	31.9 (6.6)	31.9 (6.8)	31.1 (6.6)	30.6 (6.7)	30.2 (5.1)	30.2 (5.1)	30.2 (5.1)	30.3 (5.1)
A1c	8.2 (2.0)	7.9 (1.8)	7.4 (1.6)	7.5 (1.6)	7.5 (1.6)	7.1 (1.6)	6.9 (1.6)	7.0 (1.6)	7.0 (1.6)	7.0 (1.6)	7.0 (1.6)
SBP	138.5 (17.8)	138.8 (18.5)	135.3 (19.7)	135.9 (21.4)	139.4 (23.5)	144.9 (24.9)	145.8 (25.7)	142.7 (23.0)	142.6 (23.1)	142.7 (23.1)	142.5 (23.0)
DBP	78.3 (10.8)	77.0 (10.9)	74.6 (11.2)	73.0 (11.6)	72.9 (12.4)	73.9 (12.9)	74.6 (13.4)	76.8 (12.1)	76.8 (12.1)	76.8 (12.1)	76.8 (12.1)
LDL	89.3 (36.2)	85.6 (35.3)	84.1 (33.7)	82.3 (34.0)	83.0 (36.2)	85.2 (39.1)	82.0 (39.2)	83.6 (35.8)	83.6 (35.8)	83.6 (35.7)	83.5 (35.5)
HDL	42.3 (13.3)	41.2 (12.2)	40.7 (12.3)	39.9 (12.3)	39.7 (12.8)	40.7 (13.7)	41.0 (14.3)	43.4 (14.9)	43.4 (14.9)	43.3 (14.8)	43.4 (14.9)
Total cholesterol	165.5 (48.0)	159.6 (44.8)	156.3 (41.8)	154.4 (43.0)	155.7 (46.9)	158.5 (50.3)	153.6 (50.1)	158.0 (46.2)	158.1 (46.2)	158.1 (46.2)	157.8 (45.5)
Triglyceride	186.6 (138.0)	184.5 (127.4)	177.9 (114.6)	180.9 (118.2)	181.8 (123.0)	173.8 (120.3)	164.7 (115.9)	172.0 (123.6)	172.1 (123.7)	172.4 (124.0)	172.1 (121.9)

Note: Summary statistics are presented as the mean (SD) or median (interquartile range). Each patient could contribute to multiple CKD stages over the course of follow-up on progression.
Abbreviations: A1c, glycated hemoglobin (%); BMI, body mass index; DBP, diastolic blood pressure; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SBP, systolic blood pressure; uACR, urine albumin-creatinine ratio (mg/g).

dialysis, the mean (SD) cost was \$12,299 (\$24,355), and the median was \$6,012. There is a high cost immediately after transplant in which the mean (SD) PPPM cost in the first month of KRT was \$38,360 (\$73,653) and median was \$4,926. The mean costs gradually decrease with time in which the PPPM costs were \$12,105 (\$112,488), \$9,892 (\$119,705), and \$6,636 (\$15,572) for months 2-3, months 4-12, and after 1 year of follow-up, respectively (Table 4).

The anticipated stage-specific costs and 95% confidence intervals calculated from the regression are projected in Figure 1. The PPPM all-cause health care costs associated among DKD patients exponentially increases from stage 1 to dialysis. There was no overlap of the confidence interval ranges, demonstrating a distinctive cost difference and escalation across the DKD stages. A gradual decrease in the monthly care cost over time was observed in patients receiving KRT (Fig 1).

DISCUSSION

Health care costs among patients with DKD sharply increased with progression to each stage, with the estimated cost exceeding \$5,000 per month in patients with stage 4 disease or in severe conditions. We summarized the real-world economic burden of health care among veterans with DKD in VHA, the largest integrated health care system in the United States. Using the data obtained from the nationwide health care system, this study includes more than 1,000,000 unique datapoints on DKD stage information from all DKD cases from recent VHA data. Therefore, the economic burden estimates from our study are generalizable to the national VA population, having the greatest influence on the US health care economy.

A correlation between advanced DKD stages and escalating health care costs was observed, and the pace of care cost escalation in the veterans with DKD increases with stage progression. Similar to the recent stage-specific estimates from Canadian population, the cost escalation trend from among veterans with DKD was particularly pronounced in the stages G4 or above, with the all-cause monthly health care costs exceeding \$10,000 once patient started long-term dialysis.[15] This exponential escalation of DKD patient care cost, coupled with a rate of DKD stage progression among veterans that exceeds the anticipated eGFR decline in general population, will impose a significant burden to the VHA.[16] Therefore, once a decrease in eGFR is identified, the recommended approach for cost containment, which also aligns with DKD management guidelines, is to focus on preventing further stage progression in patients.[17-19]

These findings echo the VHA Directive 1053, emphasizing the need for early CKD intervention in VA medical facilities.[9] Of the 9 million veterans under VA care, 11% meet the criteria for CKD, making it the fourth most common diagnosis in the VA.[9] The annual VHA costs associated with CKD can reach up to \$19 billion, with a

Table 3. Comorbid Conditions and Categorized Measures of Baseline Characteristics: Risk Factors in DKD Progression

Characteristic	Stage 1	Stage 2	Stage 3a	Stage 3b	Stage 4	Stage 5	Dialysis	Kidney Replacement Therapy			
								First 30 d	31-90 d	91-365 d	After 1 y
BMI											
30+	12,026 (63.9)	60,912 (63.0)	297953 (58.6)	144,802 (57.1)	48,648 (56.8)	11,403 (52.3)	12,906 (48.9)	991 (50.3)	989 (50.3)	980 (50.3)	943 (50.7)
25-29.9	4,877 (25.9)	26,689 (27.6)	155,186 (30.5)	76,882 (30.3)	24,930 (29.1)	6,656 (30.6)	8,076 (30.6)	678 (34.4)	676 (34.4)	670 (34.4)	634 (34.1)
Less than 25	1,904 (10.1)	9,023 (9.3)	54,435 (10.7)	31,595 (12.5)	11,929 (13.9)	3,712 (17.0)	5,364 (20.3)	301 (15.3)	300 (15.3)	298 (15.3)	283 (15.2)
Unknown	26 (0.1)	76 (0.1)	452 (0.1)	229 (0.1)	74 (0.1)	15 (0.1)	23 (0.1)	(0.0)	(0.0)	(0.0)	(0.0)
A1c											
8.0%+	8,719 (46.3)	37,028 (38.3)	138,938 (27.3)	76,995 (30.4)	26,096 (30.5)	4,914 (22.6)	4,928 (18.7)	422 (21.4)	421 (21.4)	417 (21.4)	401 (21.6)
7.0%-7.99%	4,250 (22.6)	24,855 (25.7)	129,259 (25.4)	66,880 (26.4)	21,925 (25.6)	4,784 (22.0)	5,020 (19.0)	396 (20.1)	396 (20.2)	392 (20.1)	375 (20.2)
Less than 7%	5,712 (30.3)	34,191 (35.4)	225,688 (44.4)	104,292 (41.1)	35,843 (41.9)	11,586 (53.2)	14,512 (55.0)	973 (49.4)	969 (49.3)	960 (49.3)	910 (48.9)
Unknown	152 (0.8)	626 (0.6)	14,141 (2.8)	5,341 (2.1)	1,717 (2.0)	502 (2.3)	1,909 (7.2)	179 (9.1)	179 (9.1)	179 (9.2)	174 (9.4)
Anemia	551 (2.9)	4,936 (5.1)	39,507 (7.8)	35,307 (13.9)	23,038 (26.9)	9,823 (45.1)	15,449 (58.6)	786 (39.9)	782 (39.8)	772 (39.6)	721 (38.8)
Connective tissue disease	49 (0.3)	165 (0.2)	2,179 (0.4)	916 (0.4)	278 (0.3)	55 (0.3)	115 (0.4)	21 (1.1)	21 (1.1)	21 (1.1)	21 (1.1)
Dyslipidemia	10,822 (57.5)	60,570 (62.6)	315,102 (62.0)	162,482 (64.1)	56,276 (65.8)	13,764 (63.2)	16,943 (64.3)	1,162 (59.0)	1,159 (59.0)	1,147 (58.9)	1,087 (58.4)
Gout	416 (2.2)	4,026 (4.2)	27,916 (5.5)	20,130 (7.9)	10,153 (11.9)	2,961 (13.6)	3,723 (14.1)	266 (13.5)	265 (13.5)	259 (13.3)	247 (13.3)
Hypertension	12,619 (67.0)	71,429 (73.9)	375,511 (73.9)	195,431 (77.1)	69,148 (80.8)	17,807 (81.7)	21,986 (83.4)	1,648 (83.7)	1,643 (83.6)	1,626 (83.5)	1,554 (83.5)
Liver disease	1,014 (5.4)	5,067 (5.2)	23,750 (4.7)	13,504 (5.3)	6,283 (7.3)	2,109 (9.7)	3,317 (12.6)	266 (13.5)	266 (13.5)	262 (13.4)	251 (13.5)
Malignancy	952 (5.1)	7,055 (7.3)	49,015 (9.6)	29,196 (11.5)	10,877 (12.7)	2,474 (11.4)	3,093 (11.7)	174 (8.8)	174 (8.9)	172 (8.8)	159 (8.5)

Note: Each patient could contribute to multiple CKD stages over the course of follow-up on progression.

significant impact of advanced stages of the disease and treatments like dialysis.[9] However, only 5% of veterans have been diagnosed, indicating limited awareness within the VA health care system about this financially and medically burdensome illness.[9] Given that CKD is frequently underdiagnosed, the VHA Directive 1053 highlights prevention, early detection, and robust management.[9] The VHA's Veteran Kidney Health Committee further reinforces this by addressing kidney care comprehensively, from preventive measures for high-risk groups to leveraging technological advancements, ensuring both enhanced care and efficient resource utilization.[9]

Our findings are noteworthy as the most recent care cost estimation for the patients with DKD. The burden of DKD care in the commercially insured population has been an interest to health economics and outcomes research. For example, the all-cause annual health care cost for patients with stage 3a to stage 5 DKD from 2009 to 2012 ranged from $1,732 to $20,210 based on the 2015 USD value.[20] Lately, a study using a laboratory data linked 2014-2019 commercial health plan claims calculated a 4-month all-cause DKD patient care costs of stages 1 through 5 of $7,700 to $12,000 in 2020 USD.[7] However, fluctuation around the cost estimates of DKD makes the application of the previous findings for the assessment of recently developed technologies challenging. The accuracy of adjusting for the historic estimates using the consumer price index could be influenced by the recent trends in gross health care expenditures, such as medical care price escalation not outpacing the general growth of economy with coronavirus disease <COVID) pandemic or a decrease in the overall share of the gross domestic product devoted to health care.[14,21,22] With respect to the scope of clinical pathways, the recent shift in the use of renal-protective agent use in early-stage DKD might lead to a significant shift in the DKD management strategy followed by changes in health care costs.[23,24] Such longitudinal changes, along with the diversity of population characteristics across various health care delivery systems, should be addressed by incorporating up-do-date epidemiological and economic data, particularly when a value assessment is performed before a health care system adapts an advanced treatment strategy or diagnostics. The comprehensive summary of the recent health care expenditures from our study will provide inputs in projecting the economic outcomes of new interventions in US veterans with DKD for the postpandemic era.

Understanding recent studies on the cost of DKD patient care will help to interpret and appreciate the value our findings. Nichols at al[25] analyzed the health care cost attributed to CKD care while controlling for cardiovascular conditions. In this assessment, CKD management in patients with diabetes is associated with an incremental health care cost ranging between $4,200 and $5,800 per-patient per-year in 2020 USD. Total health care costs varied from $13,000 to $34,000, depending on the presence of cardiovascular comorbid conditions alongside

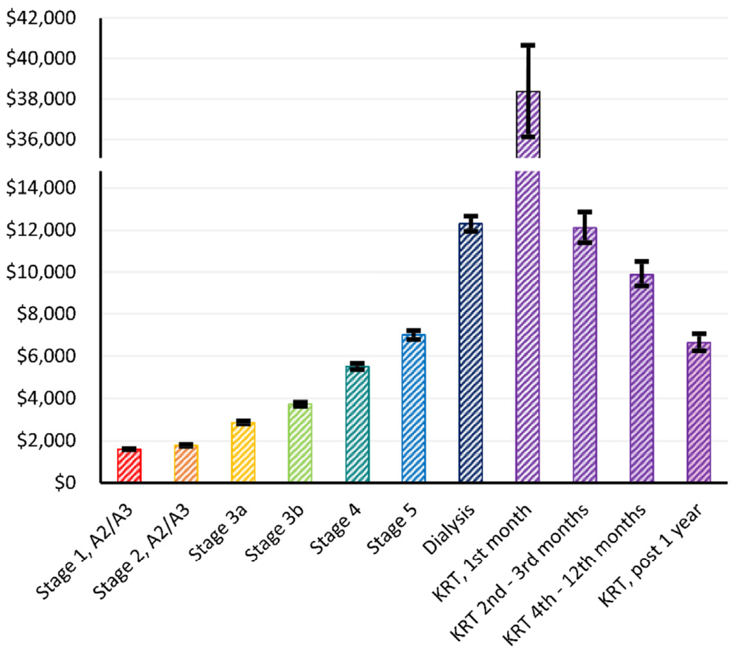
Table 4. Descriptive Summary of the Cost for DKD Patient Care

		n	Mean (SD)	Median (Interquartile Range)
Stage 1		18,833	1,597 (3,178)	795 (403-1,618)
Stage 2		96,700	1,772 (4,269)	892 (451-1,824)
Stage 3a		508,026	2,857 (13,072)	1,036 (472-2,432)
Stage 3b		253,508	3,722 (12,134)	1,324 (566-3,368)
Stage 4		85,581	5,505 (14,639)	2,040 (795-5,484)
Stage 5		21,786	6,999 (16,901)	2,271 (886-6,213)
Dialysis		26,369	12,299 (24,355)	6,012 (2,303-14,132)
Kidney Replacement Therapy	First month	1,970	38,360 (73,653)	4,926 (2,180-24,999)
	Second-Third month	1,965	12,105 (112,488)	2,965 (1,275-9,405)
	4th-12th month	1,948	9,892 (119,705)	3,551 (1,696-8,232)
	After 1 y	1,860	6,636 (15,572)	3,418 (1,672-7,689)

Note: Summary statistics are unadjusted mean and median of per-patient per-month costs.

diabetes and CKD. These annualized cost estimates align with our findings for the stages 1 through 3a DKD patients, after accounting for health care cost inflation.[25] The actual burden of DKD in the United States would be even greater from a broad societal perspective, considering the indirect impact of the disease and unrecognized progression to late-stage kidney disease that imposes a burden beyond health care sectors or payers.[26,27]

The use of various methods available to calculate eGFR would be interesting to consider when interpreting our study findings. We classified patient DKD stages based on the eGFR from the Modification of Diet in Renal Disease method, which factors race into the calculation.[11] Considering that the receiver operator characteristics are generally consistent across different methods, the average cost among a large number of patients in a specific stage would not be influenced by the selection of the eGFR calculation method.[12,28] On the other hand, several studies raised questions about the use of the Modification of Diet in Renal Disease method regarding potential eGFR underestimation, particularly in healthy populations or patients with true GFR ≥ 60 mL/min/1.73 m^2.[29,30] Considering that an underestimated eGFR due to the difference between the measured and estimated GFRs may classify a small subset of patients at a later DKD stage as having a lower grade DKD, our



DKD stages	Bootstrap Mean [95% CI]
Stage 1, A2/A3	$ 1,597 [1,570 – 1,625]
Stage 2, A2/A3	$ 1,772 [1,727 – 1,821]
Stage 3a	$ 2,857 [2,787 – 2,928]
Stage 3b	$ 3,722 [3,627 – 3,819]
Stage 4	$ 5,505 [5,363 – 5,652]
Stage 5	$ 6,999 [6,790 – 7,210]
Dialysis	$ 12,298 [11,940 – 12,661]
KRT, 1st month	$ 38,361 [36,125 – 40,650]
KRT, 2nd – 3rd months	$ 12,105 [11,406 – 12,854]
KRT, 4th – 12th months	$ 9,891 [9,322 – 10,513]
KRT, post 1 year	$ 6,636 [6,253 – 7,058]

Figure 1. Results from semi-parametric bootstrap cost estimation and 95% confidence intervals. Summary statistics are per-patient per-month costs calculated from generalized linear model using Gamma distribution of the data with a log-link function. Bar charts graphically present the cost estimate and 95% confidence interval from regression and semi-parametric bootstrap. DKD, diabetic kidney disease; KRT, kidney replacement therapy.

per-patient cost estimate has a small chance of per-patient cost over calculation.

Using 2 or more eGFR values as inclusion criteria may raise concerns about on underestimating patient count by excluding patients who would have been selected if 1 eGFR record had been implemented, particularly in identifying patients at a later DKD stage. However, the benefits of more specific patient identification criteria outweigh the disadvantage of reduced sensitivity. A restrictive patient selection ensures the accuracy of the patient-level burden of DKD care and minimize the chance of per-patient cost underestimation. All things considered, taking the cost estimates from our study would aid in making a conservative decision regarding the allocation of budget or resources for managing patients with DKD.

Our study estimates are derived from a larger sample size and are contemporary in nature compared with other observational studies. Nevertheless, future studies will provide better insights into the burden and care cost of DKD by addressing several key limitations. First, although the health care costs for patients diagnosed with DKD were assessed, our study did not employ a corresponding control group. Introducing a comparable non-DKD cohort will facilitate a top-down estimate of the incremental cost burden due to diabetes, kidney function decline, or comorbid conditions, separately. Future research should incorporate this comparative approach to better understand the specific financial impact of diabetes within the CKD population. Second, this research focused on the US veteran community only, offering significant insights about a subgroup with a notable occurrence of DKD. Though the VHA data enabled a thorough evaluation of laboratory metrics and extended monitoring, offering a deeper understanding of this group, the study findings might not apply to the general public, especially concerning the clinical characteristics and health care costs. Health care obtained outside the VA health system was not included, as some might have accessed care via other insurance, and sizable proportion of veterans with DK might look for their care outside of the VA.[31] This might have led to underestimation of the total costs associated with DKD, if the cost was incurred outside of VA health care networks. Regarding the analytic approach, current analysis did not specifically address the longitudinal changes in the treatment patterns. Future studies are warranted to address the limitation by incorporating advanced analytic approaches and accounting for the crucial factors, including longitudinal changes in the patient characteristics and recently advanced medications, such as GLP1RA, SGLT2I or finerenone. Lastly, it is important to consider general limitations of retrospective data analysis, such as selection bias and misclassification.

In conclusion, DKD represents a formidable clinical and economic burden in the United States. This study, based on a comprehensive analysis of the Veterans Affairs National database, provides a thorough understanding of the health care resource utilization linked to DKD progression. Over a million patients across varying DKD stages were studied, revealing that the majority were in stage 3a. It was evident that certain health complications, including anemia, gout, and hypertension, became more prevalent in more advanced DKD stages. Furthermore, there was a significant racial disparity, with African Americans being more present in advanced DKD stages. Health care costs, correspondingly, increased monotonically with higher DKD stages. The findings of this study could provide valuable insights for health care providers, policymakers, and stakeholders in optimizing care and resource allocation for DKD patients.

ARTICLE INFORMATION

Authors' Full Names and Academic Degrees: Kibum Kim, BPharm, PhD, Jacob Crook, MS, Chao-Chin Lu, PhD, Heather Nyman, PharmD, Jyotirmoy Sarker, MPharm, Richard Nelson, PhD, Joanne LaFleur, PharmD, MSPH

Authors' Affiliations: Department of Pharmacy Systems, Outcomes and Policy, University of Illinois Chicago, Chicago, IL (KK, JS); Department of Pharmacotherapy, University of Utah, Salt Lake City, UT (KK, HN, JL); Salt Lake City VA Health Care System, Salt Lake City, UT (KK, JC, C-CL, HN, RN, JL); and Division of Epidemiology, University of Utah, Salt Lake City (JC, RN).

Address for Correspondence: Kibum Kim, BPharm, PhD, Department of Pharmacy Systems, Outcomes and Policy, University of Illinois Chicago, 833 S. Wood Street, Rm 256, PHARM MC 871, Chicago, IL 60612. Email: kkim204@uic.edu

Authors' Contributions: Research idea and study design: KK, HN, JL, RN; data acquisition: KK, JC, C-CL, HN, RN, JL; analysis plan: all authors; data analysis/interpretation: all authors; statistical analysis: KK, JC, C-CL; supervision or mentorship: JL, RN, Each author contributed important intellectual content during article 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.

Support: This study was funded by Renalytix. Renalytix had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, or approval of the article; or decision to submit the article for publication.

Financial Disclosure: Dr Kim received research support from the Institute for Clinical and Economic Review and AstraZeneca outside the submitted work. The other authors declare that they have no relevant financial interests.

Acknowledgements: The authors were assisted by Michael Kim, Pharm D, who identified and reviewed recently published DKD cost of care studies.

Peer Review: Received January 10, 2024, as a submission to the expedited consideration track with 2 external peer reviews. Direct editorial input from the Statistical Editor and the Editor-in-Chief. Accepted in revised form April 30, 2024.

REFERENCES

1. Chronic kidney disease in the United States. Centers for Disease Control and Prevention; 2021. Accessed October 18, 2021. https://www.cdc.gov/kidneydisease/publications-resources/ckd-national-facts.html
2. Alicic R, Nicholas SB. Diabetic kidney disease back in focus: management field guide for health care professionals in the

21st Century. *Mayo Clin Proc*. 2022;97(10):1904-1919. doi:10.1016/j.mayocp.2022.05.003
3. Folkerts K, Petruski-Ivleva N, Kelly A, et al. Annual health care resource utilization and cost among type 2 diabetes patients with newly recognized chronic kidney disease within a large U.S. administrative claims database. *J Manag Care Spec Pharm*. 2020;26(12):1506-1516. doi:10.18553/jmcp.2020.26.12.1506
4. Shubrook JH, Neumiller JJ, Wright E. Management of chronic kidney disease in type 2 diabetes: screening, diagnosis and treatment goals, and recommendations. *Postgrad Med*. 2022;134(4):376-387. doi:10.1080/00325481.2021.2009726
5. Rangaswami J, Bhalla V, de Boer IH, et al. Cardiorenal protection with the newer antidiabetic agents in patients with diabetes and chronic kidney disease: a scientific statement from the American Heart Association. *Circulation*. 2020;142(17):e265-e286. doi:10.1161/cir.0000000000000920
6. Deng Y, Li N, Wu Y, et al. Global, regional, and national burden of diabetes-related chronic kidney disease from 1990 to 2019. *Front Endocrinol (Lausanne)*. 2021;12:672350. doi:10.3389/fendo.2021.672350
7. Betts KA, Song J, Faust E, et al. Medical costs for managing chronic kidney disease and related complications in patients with chronic kidney disease and type 2 diabetes. *Am J Manag Care*. 2021;27(20 Suppl):S369-S374. doi:10.37765/ajmc.2021.88807
8. Rossing P, Caramori ML, Chan JCN, et al. Executive summary of the KDIGO 2022 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease: an update based on rapidly emerging new evidence. *Kidney Int*. 2022;102(5):990-999. doi:10.1016/j.kint.2022.06.013
9. Chronic kidney disease prevention, early recognition, and management. Veterans Health Administration. U.S Department of Veteran Affairs; 2023. Accessed August 17, 2023. https://www.va.gov/vhapublications/ViewPublication.asp?pub_ID=8737
10. Veterans Health Administration. About VHA. Accessed August 10, 2023. https://www.va.gov/health/aboutVHA.asp
11. Levey AS, Coresh J, Greene T, et al. Using standardized serum creatinine values in the modification of diet in renal disease study equation for estimating glomerular filtration rate. *Ann Intern Med*. 2006;145(4):247-254. doi:10.7326/0003-4819-145-4-200608150-00004
12. Levey AS, Stevens LA, Schmid CH, et al. A new equation to estimate glomerular filtration rate. *Ann Intern Med*. 2009;150(9):604-612. doi:10.7326/0003-4819-150-9-200905050-00006
13. Inker LA, Eneanya ND, Coresh J, et al. New creatinine- and cystatin C-based equations to estimate GFR without race. *N Engl J Med*. 2021;385(19):1737-1749. doi:10.1056/NEJMoa2102953
14. Consumer price index. U.S. Bureau of Labor Statistics Division of Consumer Prices and Price Indexes. Accessed July 23, 2023. https://www.bls.gov/cpi/
15. Manns B, Hemmelgarn B, Tonelli M, et al. The cost of care for people with chronic kidney disease. *Can J Kidney Health Dis*. 2019;6:2054358119835521. doi:10.1177/2054358119835521
16. Kim K, Crook J, Lu C-C, Nyman H, Abdelaziz A, LaFleur J. Epidemiology of diabetic kidney disease among US Veterans. *Diabetes Metab Syndr Obes*. 2024;17:1585-1596.
17. Naaman SC, Bakris GL. Diabetic nephropathy: update on pillars of therapy slowing progression. *Diabetes Care*. 2023;46(9):1574-1586. doi:10.2337/dci23-0030
18. Kidney Disease: Improving Global Outcomes (KDIGO) Diabetes Work Group. KDIGO 2020 clinical practice guideline for diabetes management in chronic kidney disease. *Kidney Int*. 2020;98(4S):S1-S115.
19. Kidney Disease Improving Global Outcomes (KDIGO) consortium. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney Int*. 2013;3(1):1-163.
20. McQueen RB, Farahbakhshian S, Bell KF, Nair KV, Saseen JJ. Economic burden of comorbid chronic kidney disease and diabetes. *J Med Econ*. 2017;20(6):585-591. doi:10.1080/13696998.2017.1288127
21. National health expenditure data. Center for Medicare & Medicaid Services. Accessed November 1, 2023. https://www.cms.gov/files/document/highlights.pdf
22. Dunn A, Grosse SD, Zuvekas SH. Adjusting health expenditures for inflation: a review of measures for health services research in the United States. *Health Serv Res*. 2018;53(1):175-196. doi:10.1111/1475-6773.12612
23. Nishi L, Ghossein C, Srivastava A. Increasing sodium-glucose cotransporter 2 inhibitor use in CKD: perspectives and presentation of a clinical pathway. *Kidney Med*. 2022;4(5):100446. doi:10.1016/j.xkme.2022.100446
24. Yau K, Dharia A, Alrowiyti I, Cherney DZI. Prescribing SGLT2 inhibitors in patients with CKD: expanding indications and practical considerations. *Kidney Int Rep*. 2022;7(7):1463-1476. doi:10.1016/j.ekir.2022.04.094
25. Nichols GA, Ustyugova A, Deruaz-Luyet A, O'Keeffe-Rosetti M, Brodovicz KG. Health care costs by type of expenditure across eGFR stages among patients with and without diabetes, cardiovascular disease, and heart failure. *J Am Soc Nephrol*. 2020;31(7):1594-1601. doi:10.1681/ASN.2019121308
26. Spencer D, Dunning S, McPheeters J, St Clair Russell J, Hane C. Health care costs associated with unrecognized progression to late-stage kidney disease. *Am J Manag Care*. 2023;29(2):e64-e68. doi:10.37765/ajmc.2023.89323
27. Elshahat S, Cockwell P, Maxwell AP, Griffin M, O'Brien T, O'Neill C. The impact of chronic kidney disease on developed countries from a health economics perspective: A systematic scoping review. *PLOS ONE*. 2020;15(3):e0230512. doi:10.1371/journal.pone.0230512
28. Björk J, Grubb A, Sterner G, Nyman U. A new tool for predicting the probability of chronic kidney disease from a specific value of estimated GFR. *Scand J Clin Lab Invest*. 2010;70(5):327-333. doi:10.3109/00365513.2010.488699
29. Stevens LA, Coresh J, Feldman HI, et al. Evaluation of the modification of diet in renal disease study equation in a large diverse population. *J Am Soc Nephrol*. 2007;18(10):2749-2757. doi:10.1681/asn.2007020199
30. Rule AD, Larson TS, Bergstralh EJ, Slezak JM, Jacobsen SJ, Cosio FG. Using serum creatinine to estimate glomerular filtration rate: accuracy in good health and in chronic kidney disease. *Ann Intern Med*. 2004;141(12):929-937. doi:10.7326/0003-4819-141-12-200412210-00009
31. Zelaya CE, Nugent CN. Trends in health insurance and type among military veterans: United States, 2000-2016. *Am J Public Health*. 2018;108(3):361-367. doi:10.2105/ajph.2017.304212