

Medical Costs for Managing Chronic Kidney Disease and Related Complications in Patients With Chronic Kidney Disease and Type 2 Diabetes

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Introduction

Chronic kidney disease (CKD) is prevalent, and it is estimated that it will affect about 15% of adults or 37 million people in the United States in 2021.¹ Diabetes is one of the leading causes of CKD and kidney failure. About 1 in 3 US adults with diabetes has CKD, and CKD with diabetes accounts for approximately 39% of end-stage renal disease (ESRD) cases in the United States.¹ Moreover, CKD is associated with an increased risk of cardiovascular (CV) diseases and all-cause mortality.² The risk of heart failure, atrial fibrillation, stroke, and coronary heart disease is approximately double in patients with CKD.³⁻⁷ The adjusted mortality is also twice as high among Medicare beneficiaries with CKD compared with those without CKD.⁸

CKD poses a substantial economic burden. Medicare spending for all beneficiaries who had CKD exceeded \$120 billion in 2017, representing 33.8% of total Medicare fee-for-service spending.⁹ On an individual level, annual Medicare spending was \$16,112 per patient for those with CKD and increased to \$19,739 per patient for those with CKD and diabetes.⁹ In addition to general CKD management, addressing CV complications can be costly. Approximately 29% of the total inpatient hospitalization spending for those with CKD resulted from admissions to treat CV complications.⁹ Heart failure was associated with an incremental per-person per-year Medicare cost of \$19,944 among patients with CKD.⁸ Hyperkalemia is another complication that is common among patients with CKD, and it is associated with substantial health care costs.^{10,11} Specifically, hyperkalemia was associated with an increased 1-year cost of \$21,857 in patients with CKD and \$20,657 in patients with diabetes.¹⁰

Current treatment strategies for patients with CKD and type 2 diabetes (T2D) focus on CV risk reduction, blood pressure control, glycemic control, and lipid-lowering therapy.¹² For example, the current Kidney Disease: Improving Global Outcomes (KDIGO) guidelines recommend the use of renin-angiotensin-aldosterone system-blocking agents including angiotensin-converting enzyme inhibitors (ACEis) or angiotensin II receptor blockers (ARBs) in patients with CKD and diabetes who have hypertensive symptoms.¹³ Available evidence strongly indicates that the use of ACEis or ARBs yields a significant renal protective effect, reducing albuminuria and

ABSTRACT

Objective: To provide cost estimates for chronic kidney disease (CKD) management and major CKD complications among patients with CKD and type 2 diabetes (T2D).

Study Design: A retrospective cohort study of 52,599 adults with CKD and T2D using Optum Clinformatics claims data from 2014 to 2019.

Methods: Medical costs associated with CKD management, renal replacement therapies (RRTs), major CKD complications (eg, myocardial infarction, stroke, heart failure, atrial fibrillation, and hyperkalemia), and death were estimated using generalized estimating equations adjusting for baseline demographics, complications, and medical costs. Costs for CKD management, RRT, and major CKD complications were assessed in 4-month cycles. Mortality costs were assessed in the month before death.

Results: The estimated 4-month CKD management costs ranged from \$7725 for stage I to II disease to \$11,879 for stage V (without RRT), with high additional costs for dialysis and kidney transplantation (\$87,538 and \$124,271, respectively). The acute event costs were \$31,063 for heart failure, \$21,087 for stroke, and \$21,016 for myocardial infarction in the first 4 months after the incident event, which all decreased substantially in subsequent 4-month cycles. The acute event costs of atrial fibrillation and hyperkalemia were \$30,500 and \$31,212 with hospitalization, and \$5162 and \$1782 without. The costs associated with cardiovascular-related death, renal-related death, and death from other causes were \$17,031, \$12,605, and \$9900, respectively.

Conclusions: Management of CKD and its complications incurs high medical costs for patients with CKD and T2D. Results from this study can be used to quantify the economic profile of emerging treatments and inform decision-making.

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the risk of ESRD in this patient group.¹² Several emerging treatments, such as finerenone and sodium-glucose cotransporter-2 inhibitors (SGLT2is), have demonstrated clinical benefits in terms of preventing CV diseases in patients with CKD and T2D, slowing down the progression of kidney disease, and reducing the risk of death.¹⁴⁻¹⁸

To evaluate whether these clinical benefits translate to real-world economic benefit (ie, cost-effectiveness), it is essential to quantify the key cost components associated with the management of CKD and related complications in patients with CKD and T2D. However, knowledge gaps exist regarding the health care costs associated with general CKD management at different disease stages and major complications (including myocardial infarction [MI], heart failure, stroke, atrial fibrillation, and hyperkalemia) in patients with CKD and T2D. This study aims to provide the most up-to-date estimates of cost components related to general CKD management and major CKD complications using a regression-based approach. Results will facilitate the parameterization of economic models and quantify the economic burden in this population using the most recent data.

Methods

Study Design and Population

This retrospective cohort study identified adult patients with T2D and CKD using Optum Clinformatics claims data from 2014 to 2019. The Optum claims database is a single-payer source of administrative health claims with approximately 15 to 20 million annual covered enrollees across all states in the United States. Enrollees may be covered by commercial health plans or Medicare Advantage. The administrative claims were submitted for payment by providers and pharmacies and were verified, adjudicated, and de-identified.

T2D was identified using a modified version of the Electronic Medical Records and Genomics algorithm, developed to identify patients with T2D in electronic medical records with high specificity.¹⁹ Patients without observed insulin use were required to have at least 1 medical claim with a T2D diagnosis and at least 1 prescription claim for antidiabetic medication. Patients with observed insulin use were required to have (1) at least 1 medical claim with a T2D diagnosis and at least 1 prescription claim for antidiabetic therapy prior to the first insulin prescription; or (2) at least 2 T2D diagnoses on different dates among those without antidiabetic prescription claims. Patients with records of other types of diabetes (including type 1 diabetes, diabetes due to underlying conditions, drug- or chemical-induced diabetes, and other specified diabetes) were excluded.

CKD was identified using at least 1 inpatient or at least 2 outpatient CKD claims on distinct dates. Evidence of CKD included having diagnosis codes for CKD or ESRD, or procedure codes for renal replacement therapies (RRT), including dialysis and kidney transplantation. Only patients with known CKD stage based on diagnosis codes were included.

The study index date was defined as the first date when both T2D and CKD definitions were met. Patients were required to have continuous enrollment for 1 year before (baseline period) and at least 4 months after the index date. Patients covered by health maintenance organizations during the baseline or study period were excluded from the study sample because their recorded health care expenditures may not accurately reflect their medical care usage.

Study Outcomes

This study assessed medical costs from the payer's perspective, from the patient's index date to disenrollment, death, or end of data availability. Cost components included CKD management, RRT, major CKD complications, and death. The costs for CKD management, RRT, and major CKD complications were reported in 4-month cycles, which was a commonly evaluated cycle length in clinical trials in this population.^{15,17} Mortality costs were assessed in the month prior to death.

The costs of general CKD management were estimated by CKD stage, classified as stage I to II, stage III, stage IV, and stage V without RRT.²⁰ The costs of RRT were assessed separately, including dialysis costs and kidney transplantation costs. Major CKD complications included MI, heart failure (with hospitalization), stroke, hyperkalemia (with and without hospitalization), and atrial fibrillation (with and without hospitalization). Death was classified as CV-related, renal-related, or from other causes based on the primary diagnosis or procedure codes during hospitalization in the month of death because direct information on the cause of death was not available.

Events of interest were identified using *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)* and *International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM)* diagnosis codes, and Current Procedural Terminology, Healthcare Common Procedure Coding System, and *ICD-9-CM* or *ICD-10* Procedure Coding System procedure codes. All medical costs were inflated to 2020 US\$ using the medical care component of the Consumer Price Index.

Statistical Analysis

Descriptive analyses were performed for patient characteristics during baseline. Mean and standard deviation were reported for continuous variables, and frequency counts and percentages were used for categorical variables. Median and interquartile range were calculated for baseline medical costs.

A generalized estimating equation (GEE) regression with a normal distribution and an exchangeable correlation structure was used to model the monthly costs associated with the management of CKD, RRT, major CKD complications, and death, adjusting for age at index date, sex, baseline complications, and baseline medical costs (detailed model specification information is displayed in

FIGURE 1. Generalized Estimating Equation Model

$$\begin{aligned}
 \text{Monthly cost}_{ij} = & \underbrace{\beta_0 + \beta_1 \text{age}_i + \beta_2 \text{sex}_i + \beta_3 \text{BL_MI}_i + \beta_4 \text{BL_stroke}_i + \beta_5 \text{BL_HF}_i + \beta_6 \text{BL_hyperkalemia}_i + \beta_7 \text{BL_AFib}_i + \beta_8 \text{BL_costs}_i}_{\text{BL characteristics (time-invariant)}} \\
 & + \underbrace{\beta_9 \text{CKD_stage3}_{ij} + \beta_{10} \text{CKD_stage4}_{ij} + \beta_{11} \text{CKD_stage5_without_RRT}_{ij}}_{\text{CKD stage (time-varying)}} \\
 & + \underbrace{(\beta_{12} \text{P1_MI}_{ij} + \beta_{13} \text{P2_MI}_{ij} + \beta_{14} \text{P3_MI}_{ij}) + (\beta_{15} \text{P1_stroke}_{ij} + \beta_{16} \text{P2_stroke}_{ij} + \beta_{17} \text{P3_stroke}_{ij}) + (\beta_{18} \text{P1_HF}_{ij} + \beta_{19} \text{P2_HF}_{ij} + \beta_{20} \text{P3_HF}_{ij})}_{\text{Complications with acute and postacute costs (time-varying)}} \\
 & + \underbrace{(\beta_{21} \text{P1_dialysis}_{ij} + \beta_{22} \text{P2_dialysis}_{ij} + \beta_{23} \text{P3_dialysis}_{ij}) + (\beta_{24} \text{P1_KT}_{ij} + \beta_{25} \text{P2_KT}_{ij} + \beta_{26} \text{P3_KT}_{ij})}_{\text{RRT (time-varying)}} \\
 & + \underbrace{(\beta_{27} \text{P1_hyperkalemia}_{ij} + \beta_{28} \text{P2_hyperkalemia}_{ij}) + (\beta_{29} \text{P1_AFib}_{ij} + \beta_{30} \text{P2_AFib}_{ij})}_{\text{Complications with acute costs only (time-varying)}} \\
 & + \underbrace{\beta_{31} \text{CV_death}_{ij} + \beta_{32} \text{renal_death}_{ij} + \beta_{33} \text{other_death}_{ij}}_{\text{Death (time-varying)}}
 \end{aligned}$$

AFib, atrial fibrillation; BL, baseline; CKD, chronic kidney disease; CV, cardiovascular; HF, heart failure; KT, kidney transplantation; MI, myocardial infarction; RRT, renal replacement therapy.
 i, patient i; j, month j
 P1: in the month of the event
 P2: in the next 3 months after the incident month
 P3: after the first 4-month cycle

Figure 1). A GEE regression model is a technique for obtaining regression estimates in multilevel data. It was used to account for the within-subject correlations in our longitudinal claims data with repeated measurements. CKD management costs (excluding costs associated with RRT, major CKD complications, and death) were estimated on a monthly basis and were summarized in a 4-month period for CKD stages I to II through V without RRT. The costs for major CKD complications (eg, MI, heart failure, stroke), dialysis, and kidney transplantation were estimated for 2 phases. Acute costs included the costs occurring during the month of the event onset and the subsequent 3 months (ie, 4 months in total); postacute costs included costs during subsequent follow-up and were reported in 4-month cycles. Similar to Kähm et al, these later months were assumed to reflect the ongoing impact of the complication, regardless of whether the particular event recurred following the incident month.²¹ Only acute costs were estimated for hyperkalemia and atrial fibrillation due to their relatively short-term impact on costs.

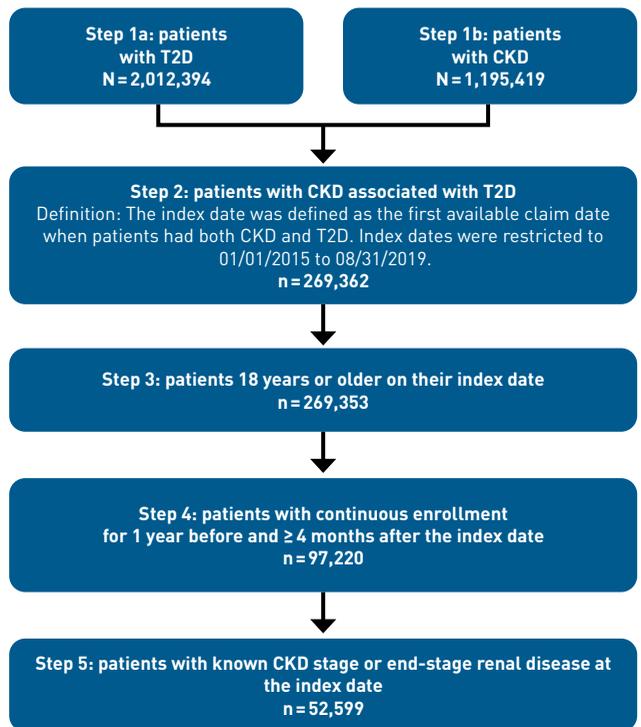
SAS 9.4 software (SAS Institute, Cary, NC) was used for all statistical analyses.

Results

Sample and Patient Characteristics

The study sample included 52,599 adult patients with T2D and CKD (**Figure 2**). **Table 1** describes patients' baseline demographics

Figure 2. Sample Selection



CKD, chronic kidney disease; T2D, type 2 diabetes.

TABLE 1. Patient Baseline Characteristics

Patients with T2D and CKD N = 52,599	
Demographic information at index date	
Age (years), mean (SD)	71.38 (9.78)
Female, n (%)	25,533 (48.54%)
Race, n (%)	
White	31,332 (59.57%)
Black	8173 (15.54%)
Hispanic	6291 (11.96%)
Asian	1645 (3.13%)
Unknown	5158 (9.81%)
Region, n (%)	
South	28,419 (54.03%)
Midwest	12,844 (24.42%)
Northeast	5977 (11.36%)
West	5342 (10.16%)
Other/unknown	17 (0.03%)
Insurance type, n (%)	
Medicare Advantage	42,249 (80.32%)
Commercial	10,369 (19.71%)
CKD stage, n (%)	
CKD stage I	2796 (5.32%)
CKD stage II	10,955 (20.83%)
CKD stage III	35,696 (67.86%)
CKD stage IV	2420 (4.60%)
CKD stage V and ESRD	732 (1.39%)
Comorbidities, n (%)	
Hypertension	48,639 (92.47%)
Hyperlipidemia	44,364 (84.34%)
Diabetes-related microvascular complications	16,695 (31.74%)
Ischemic heart diseases	15,720 (29.89%)
Myocardial infarction	3687 (7.01%)
Anemia	14,420 (27.41%)
Obesity	12,590 (23.94%)
Chronic pulmonary diseases	11,746 (22.33%)
Peripheral vascular diseases	9103 (17.31%)
Heart failure	8157 (15.51%)
Edema	7628 (14.50%)
Atrial fibrillation	6893 (13.10%)
Hyperkalemia	3181 (6.05%)
Stroke	2443 (4.64%)
Health care costs (2020 US\$)	
Medical costs	
Mean ± SD	16,995 ± 45,670
Median	4786
IQR	(1675, 14,684)

CKD, chronic kidney disease; ESRD, end-stage renal disease; IQR, interquartile range; SD, standard deviation; T2D, type 2 diabetes.

and clinical characteristics. Patients were 71 years of age on average; 49% were female and 60% were White. The majority of patients were covered by Medicare Advantage (80%). Most patients had a CKD diagnosis at index date indicating CKD stage III (68%), followed by stage II (21%). Diagnoses of hypertension (92%) and hyperlipidemia (84%) were very common in the study sample, which also had a relatively high prevalence of recorded microvascular complications (32%), ischemic heart diseases (30%), and anemia (27%). For the major CKD complications of interest, the prevalence was moderate to low during the 1-year baseline period: heart failure (16%), atrial fibrillation (13%), MI (7%), hyperkalemia (6%), and stroke (5%). Baseline all-cause medical costs were \$16,995 annually on average.

Cost Estimates

Table 2 shows the cost estimates for CKD management, RRT, major CKD complications, and death. The estimated 4-month CKD management costs for stage I to II were \$7725 and increased to \$11,879 for stage V (without RRT), with the largest increase (+\$1881) from stage III to IV. The estimated acute event costs for dialysis and kidney transplantation were \$87,538 and \$124,271, respectively. The costs decreased substantially to \$49,573 and \$7079 in the subsequent 4-month cycles, respectively.

For major CKD complications, the estimates of acute cost in the first 4 months after the incident event were \$21,016 for MI, \$21,087 for stroke, and \$31,063 for heart failure. For patients who experienced a hospitalization with atrial fibrillation, their acute costs were nearly 6 times higher than those without a hospitalization (\$30,500 vs \$5162). Similarly, the acute cost of hyperkalemia was \$31,212 with hospitalization and \$1782 without. In subsequent 4-month cycles, the cost of major CKD complications decreased to \$4931 for heart failure, \$2327 for stroke, and \$1941 for MI. In the month before death, the costs associated with CV-related death, renal-related death, and death from other causes were \$17,031, \$12,605, and \$9900, respectively.

Discussion

This study summarizes the real-world economic impact associated with CKD management, RRT, major CKD complications, and death in patients with CKD and T2D, using a large US administrative claims database. The results show that costs associated with CKD management increase with disease severity, and the costs were substantially higher with RRT. CKD complications were associated with high costs during the initial months, with acute costs nearly double or triple the amount associated with regular CKD management without RRT. In addition, both CV-related and renal-related death incurred high costs in this patient population.

Given the rising prevalence of T2D and the high prevalence of CKD among patients with T2D, slowing down CKD progression and

preventing these costly complications can substantially reduce the economic burden associated with this population.^{1,22} For example, by reducing the incidence of heart failure by 1 percentage point among patients with T2D and CKD, a Medicare Advantage plan of 1 million enrollees could save more than \$18.6 million in acute costs (using the estimated acute cost for heart failure [\$31,063]).^{23,24} Similarly, if a treatment can yield a percentage point reduction in the incidence of patients progressing to dialysis, the health care plan can save approximately \$52 million in dialysis initiation costs and \$30 million in each subsequent 4-month cycle.

This study found acute costs of major complications commonly seen in CKD and T2D to be much higher than postacute costs, which is largely consistent with results reported in published studies. For example, a retrospective analysis of 2002 to 2009 Medicare claims data among older MI survivors reported a mean health care cost of \$21,416 during the calendar quarter of the MI and \$3574 for each calendar quarter post MI.²⁵ A systematic literature review of journal articles published between 2014 and 2020 on heart failure–related costs reported a mean cost of \$11,315 during the first month after a heart failure event, and a mean monthly cost during the entire first year post heart failure of \$2427.²⁶ Another retrospective analysis assessed the cost of hyperkalemia using the MarketScan claims database; the 1-month cost after a hyperkalemia event was \$5994 and the average monthly cost within the first year was \$2654.¹⁰ Our results were largely in line with these previous findings in patients with CKD and T2D after controlling for patients' baseline demographics and complications.

Patients with CKD and T2D should be treated with a comprehensive strategy to reduce the risk of kidney disease progression and CV disease; the strategy usually includes blood pressure control by ACEis or ARBs, glycemic control by metformin and other antihyperglycemics, antiplatelet therapy with aspirin in those with established CV disease, and various lifestyle interventions.¹³ Several emerging treatments demonstrated promising efficacy in preventing CV- and renal-related events in recent trials. Canagliflozin, dapagliflozin, and empagliflozin, the first 3 SGLT2is approved by the United States Food and Drug Administration (FDA), were shown to decrease the risk of renal and CV outcomes in patients with CKD and T2D.^{14–16,18} Finerenone, a first-in-class nonsteroidal, selective mineralocorticoid receptor antagonist recently approved by the FDA in adults with CKD and T2D, was also shown to lower the risk of renal and CV outcomes in this patient population in the FIDELIO-DKD trial (NCT02540993).^{17,27} To formally evaluate the different roles that these emerging treatments can fill in the management of CKD and T2D, rigorous economic models are needed to systematically assess their cost-effectiveness, especially potential cost reductions in the setting of common CKD complications. The current study provides accurate estimates for the key cost components relevant to managing

TABLE 2. Cost Estimates for CKD Management, RRT, Major CKD Complications, and Death

Unit cost (2020 US\$)	All patients N = 52,599	
	4-month acute (SE)	4-month ongoing/postacute (SE)
CKD management		
CKD stage I and II	N/A	\$7725 (\$597)
CKD stage III	N/A	\$8928 (\$640)
CKD stage IV	N/A	\$10,809 (\$668)
CKD stage V (without RRT)	N/A	\$11,879 (\$937)
Dialysis	\$87,538 (\$6691)	\$49,573 (\$2476)
Kidney transplantation	\$124,271 (\$37,052)	\$7079 (\$1422)
Major CKD complications		
Myocardial infarction	\$21,016 (\$811)	\$1941 (\$367)
Heart failure	\$31,063 (\$823)	\$4931 (\$347)
Stroke	\$21,087 (\$975)	\$2327 (\$505)
Hyperkalemia		
Hyperkalemia with hospitalization	\$31,212 (\$2135)	N/A
Hyperkalemia without hospitalization	\$1782 (\$378)	N/A
Atrial fibrillation		
Atrial fibrillation with hospitalization	\$30,500 (\$1388)	N/A
Atrial fibrillation without hospitalization	\$5162 (\$666)	N/A
1-month (SE)		
Death costs		
CV-related	\$17,031 (\$1782)	N/A
Renal-related	\$12,605 (\$2380)	N/A
Other causes	\$9900 (\$504)	N/A

CKD, chronic kidney disease; CV, cardiovascular; N/A, not applicable; RRT, renal replacement therapy; SE, standard error.

patients with CKD and T2D from a US payer's perspective, which can be used to facilitate the parameterization of such cost-effectiveness models.

Limitations

The findings of this study need to be seen in light of several limitations. First, although this study used GEE regression analysis to provide cost estimates, adjusting for patient demographics, baseline complications, and baseline medical costs, the model did not control for other chronic comorbidities, such as hypertension and hyperlipidemia. This is not expected to impact the results significantly, given that age is a strong predictor of comorbidities.²¹ Nonetheless, there may be remaining confounding due to clinical characteristics (eg, disease duration and smoking status)

that cannot be observed in retrospective claims data.²¹ Second, this study was subject to the typical limitations of retrospective studies based on health care claims data, such as possible errors or omissions of claims. Certain comorbidities may be underestimated due to coding incompleteness, inaccuracies, or misclassification. CV-related or renal-related death was assigned based on the primary diagnosis or procedure codes during the hospitalization in the month of death, given that the cause of death cannot be evaluated directly in claims data. In addition, the cost items in this study reflect the adjudicated reimbursement rate, instead of actual cost. It is possible that some medical items were not claimed and thus not captured in the data. Third, the Optum Clinformatics claims data used in this study were from a single payer source (eg, UnitedHealth Group). Formularies of this specific payer may have impacted health care resource utilization and medical costs incurred. Future studies are needed to evaluate whether results of this study would be transferable to other payers. Fourth, patients in this study were enrolled in commercial plans or Medicare Advantage, and were required to have a known CKD stage based on diagnosis codes. The cost estimates may only apply to patients meeting the study criteria.

Conclusions

CKD incurs high health care costs in adult patients with T2D, which increase with more severe disease stages. RRT and management of major CKD complications, especially during the acute period immediately after the onset of the complications, are the most expensive components. The results demonstrate the imminent need for appropriate monitoring and treatment to avoid downstream costs in this patient population. The cost estimates from this study may also support the parametrization of economic models and help clinicians, payers, and other health care decision-makers determine the cost-effectiveness of interventions for CKD and T2D. ■

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