Annual Out-of-Pocket Costs and Productivity Loss Among Patients with Diabetic Kidney Disease Compared to Type 2 Diabetes Mellitus

Ashley Soojin Cha

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Committee:
Ryan N. Hansen
Josh J. Carlson

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Abstract

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Ashley Cha

Chair of the Supervisory Committee:

Associate Professor, Ryan N. Hansen, PharmD, PhD

School of Pharmacy

Background

Type II diabetes mellitus (T2DM) is a chronic disease of impaired glucose homeostasis characterized by both insulin resistance and a decrease in insulin production. Disease progression may lead to multisystem complications including the development of diabetic kidney disease (DKD). Though the association of T2DM and DKD with poor health outcomes and increased health care costs has been studied, there remains a paucity of literature assessing the incremental impact of DKD versus T2DM on outcomes and costs.

Objective

The objective of this study was to compare total annual out-of-pocket costs and workplace productivity loss measured by absenteeism and short-term disability between patients with T2DM compared to patients with DKD.

Methods

Data from the IBM/Watson MarketScan Commercial Claims and Encounters (CCAE) and Health and Productivity Management (HPM) Databases were used to conduct this retrospective cohort study (2013-2018). Adult patients ≥18 years with ≥2 unique service claims with a principal or secondary diagnosis for

T2DM within 6-months during the enrollment period were assigned to the T2DM cohort. Among the T2DM cohort, a subset of patients with an additional ≥2 unique service claims for CKD during the enrollment period were selected and assigned to the DKD cohort. All patients were continuously enrolled for 12-months prior to the index date, beginning at the date of first T2DM claim. Inclusion in either cohort was mutually exclusive. Patients with incident DKD after the index date were followed in the T2DM cohort until the second CKD claim and were then followed in the DKD cohort thereafter. Individuals also present in the HPM databases were included in the sub-populations for the workplace absence or short-term disability outcomes. We used the Kaplan-Meier Sample Average approach to estimate outcomes using 1-month intervals during the follow-up period. To evaluate uncertainty, we performed a nonparametric bootstrap with 1000 replicates to generate 95% credible intervals (CIs).

Results

In the primary population (N=411,887), the mean annual out-of-pocket cost was significantly higher among patients with DKD ($151 [95% CI: $147, $153]) compared to those with T2DM ($118 [95% CI: $114, $124]), with a mean difference of $327.5 (95% CI: $326.8, $328.2). The mean annual productivity loss due to workplace absenteeism was found to be similar between those with DKD (227 hours [219 hours, 236 hours]) and T2DM (217 hours [187 hours, 226 hours]), with a mean difference of 21.7 hours (95% CI: 21.0 hours, 22.3 hours). Significantly higher mean annual short-term disability was observed among those with DKD (4.6 days [4.4 days, 4.8 days]) compared to those with T2DM (2.8 days [2.3 days, 3.4 days]), with a mean difference of 1.78 days (95% CI: 1.76 days, 1.80 days).

Conclusions

Patients with DKD were found to have higher mean annual OOP costs and experience more days with short-term disability claims compared to patients with T2DM. These results quantify the economic burden of T2DM and DKD from a patient and employer perspective and may be useful in economic evaluations to inform health care decision-making.

Acknowledgments

The completion of this thesis would not have been possible without the guidance and mentorship of the faculty members of my committee, Dr. Ryan N. Hansen and Dr. Josh J. Carlson. I am especially grateful to Dr. Hansen for providing detailed, constructive feedback throughout each step of this process and for answering all my questions with his methodological and technical expertise. Further, I would like to acknowledge the faculty, staff, and students of the CHOICE Department for their support and encouragement, especially during these unprecedented times. My sincere thanks goes to Dr. Sheldon Kong and the Data Generation and Observational Studies team at Bayer Pharmaceuticals for their continued interest in my research and for the opportunity to join them in the following year of my fellowship.

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1. Background

Diabetes mellitus is a chronic, multisystem disease marked by impaired glucose homeostasis. In type II diabetes mellitus (T2DM), initial insulin resistance is often followed by subsequent decline in insulin production and further altered glucose metabolism. The progression of T2DM is associated with various etiologic pathways causing multiorgan dysfunction, including macrovascular and microvascular complications.[1] In 2018, the prevalence of diabetes mellitus among the US adult population of ages 18 or older was 13.0%. Of the nearly 34 million individuals affected by diabetes mellitus, T2DM accounts for 90-95% of all cases.[2] Diabetic kidney disease (DKD) is one such microvascular complication and is characterized by clinical markers including albuminuria and impaired renal function, both of which have been associated with increased morbidity, mortality, and health care costs.[3] It is estimated that over one-third of US adults with diabetes mellitus have DKD, as defined by the development of comorbid chronic kidney disease (CKD stages I-IV) secondary to diabetes. T2DM is a leading cause of CKD worldwide, and DKD accounts for nearly half of the incident cases of end-stage renal disease (CKD stage V or ESRD) in the US.[2,4]

Both diabetes mellitus and kidney disease were among the ten leading causes of death in the US in 2017[5] On an absolute scale, an additive interaction in all-cause mortality between diabetes mellitus and kidney disease has been observed, further suggesting that patients with both comorbid conditions are at a particularly high risk for poor health outcomes.[6-8] Beyond the clinical endpoints of morbidity and mortality, the economic burden of T2DM and DKD on health care spending has also been well characterized.[9,10] Among patients with T2DM, available studies have mainly explored associations between presence of kidney disease and increases in total health care costs and direct medical costs.[10-12] In 2017, it was estimated that 1 in 4 US healthcare dollars was spent on diagnosed diabetes care, and patients with diabetes had approximately 2.3 times higher medical expenditures compared to those without diabetes.[12] The high overall healthcare spending for DKD is largely due to its association with comorbid cardiovascular disease and progression to ESRD.[13] ESRD is defined by irreversible loss of kidney function (CKD stage V, < 15 mL/min/1.73m^2), often requiring exogenous renal replacement therapy. Development of this disease is most commonly attributed to the clinical precursors diabetes mellitus and hypertension. Historically, the increase in ESRD care spending was due to the development of treatments with demonstrated mortality benefits among patients with ESRD; however, recent trends of continued increases in ESRD care spending are due to increases in per-patient per-year spending. Although ESRD affects less than 1% of the total US population, the US Renal Data System showed that in

2016 alone, ESRD care accounted for 7.2% of overall Medicare fee-for-service spending equivalent to 35.4 billion dollars.[3] There is no shortage of evidence to suggest that the cost burden of T2DM and its comorbid conditions, including DKD, weigh heavy on the US health care system.

Current clinical guidelines for the treatment of T2DM emphasize prevention of disease progression and maintenance of quality of life as the main goals of therapy. Early detection of disease onset and timely initiation of interventions are key for the prevention of complications secondary to T2DM.[1,14,15] Failure to prevent microvascular complications such as DKD places a substantial cost burden on patients and employers. Compared to patients with T2DM, patients with DKD often require higher time costs from greater frequency of interaction with the health care system as well as higher economic costs from increased health care resource utilization.[16] Further, greater workplace productivity loss has been observed among patients with T2DM compared to the general population measured as higher work-loss days and reduced performance in the workplace due to frequent sick leave, period of inactivity, among other reasons.[16,17] Patients with DKD are likely to have a significant drop in perceived quality of life due to the effects of additional kidney function loss on physical functioning, activity of daily living including workplace productivity.[18]

Set against the backdrop of the continued push to lower health care spending and drug prices in the US, the burden of patient out-of-pocket costs and indirect expenses consequent to illness such as loss in workplace productivity may be more meaningful from the patient and employer perspectives.[19-21] The financial vulnerability of patients with diabetes mellitus, regardless of type or presence of comorbid DKD, was made evident by the wide public response to the dramatic, three-fold increase in the cost of insulin between 2002 and 2013.[21-23] To our knowledge, a quantified comparison of patient cost burden among those with T2DM versus DKD has not been performed. We sought to better understand the financial burden of T2DM and DKD from a societal perspective. The primary objective of this study was to assess the difference in total annual out-of-pocket costs between patients with T2DM compared to patients with DKD among a commercially insured population in the United States (US). The secondary objectives were to compare the incremental difference in annual workplace productivity loss measured by absenteeism and short-term disability among patients with T2DM compared to patients with DKD.

2. Methods

2.1 Study Design and Data Source

Administrative claims data for this retrospective cohort study were obtained from the IBM/Watson MarketScan® Research Databases between January 1, 2013 through December 31, 2018. We utilized the IBM MarketScan® Commercial Claims and Encounters (CCAE) and the Health Productivity Management (HPM) data sets. The CCAE data set serves as a representative sample of the commercially insured population in the US. Within the CCAE data set, the enrollment, inpatient services, and outpatient services data tables were used to capture health care utilization and costs longitudinally. The HPM database contains fully integrated information regarding workplace productivity for a subset of individuals from the CCAE database who receive commercial coverage from participating employers. Within the HPM data set, absence and short-term disability data tables were used to assess the indirect costs associated with a certain medical condition and to estimate workplace productivity loss longitudinally over time.

Patient-level data were de-identified and compliant with the Health Insurance Portability and Accountability Act of 1996 (HIPAA). A self-determination of non-human subjects research was conducted as specified by the Human Subjects Division at the University of Washington.

2.2 Sample Selection

The T2DM cohort included adult individuals who were at least 18 years old at index date with at least two unique nondiagnostic inpatient or outpatient medical claims with a principal or secondary diagnosis for T2DM [International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) or Tenth Revision (ICD-10-CM)] on unique service dates during the 12-month pre-index enrollment period [Appendix A]. Individuals included in the T2DM cohort had at least two, unique inpatient or outpatient service claims with a principal or secondary diagnosis for T2DM within 6 months of each other during the pre-index enrollment period. A second medical claim within six months of the first claim was required to confirm the presence of chronic disease. The index date was the date 1-year following the first T2DM claim, and index dates ranged between January 1, 2014 and December 31, 2018. The DKD population included individuals who met the inclusion criteria of the T2DM population and additionally had at least two, unique medical claims with a principal or secondary diagnosis for chronic kidney disease (CKD) on unique service dates during the 12-month pre-index enrollment period (ICD-9-CM or ICD-10-CM) [Appendix A]. Two CKD medical claims were required to exclude isolated cases of acute disease or injury. This analysis assumed that CKD claims in patients with a preceding T2DM claim or

claims represented presence DKD. Laboratory data at the patient-level was not available from the data source. Throughout the duration of the 12-month pre-index enrollment period, continuous enrollment in a health plan was required for inclusion in the primary population, as reported by the CCAE annual summary enrollment data table.

Individuals were followed for up to 12-months in the post-index follow-up period. Censoring occurred if a patient was lost to follow-up due to any interruption or discontinuation of continuous enrollment in insurance coverage. Those who developed incident cases of DKD during the post-index follow-up period among the T2DM cohort transitioned from the T2DM cohort to the DKD cohort on the date of the second CKD claim during the follow-up period (censoring them in the T2DM cohort). Subsequently, contribution of follow-up time in the DKD population ended at the censor date. Individuals in the absence or short-term disability data tables were included in the populations used to evaluate those outcomes. Figure 1 provides a visual depiction of the predefined study enrollment criteria.

2.3 Study Measures and Outcomes

Baseline demographic characteristics of all eligible individuals were assessed during the pre-index enrollment period. Information regarding age, index year, sex, Charlson comorbidity index (CCI), region, union status, employment status, and insurance plan type were collected. Age was measured as a continuous variable and further divided into the following age categories: 18-34 years, 35-44 years, 45-54 years, and 55+ years.

The primary outcome of interest in this study was mean annual out-of-pocket (OOP) cost for patients with T2DM compared to patients with DKD incurred during the post-index follow-up period. Out-of-pocket cost was defined as the sum of coinsurance, copay, and deductible amounts associated with an inpatient service, outpatient service, or outpatient prescription drug claim.

The secondary outcome of interest was incremental mean annual workplace productivity loss, defined as the aggregate measure of days missed at work due to absenteeism and short-term disability between an individual's index date and censor date. Reported reasons for absence included incidental illness, occupational and nonoccupational disability, leave, recreational time off, and other. Workplace absence due to occupational and nonoccupational disability were excluded from mean annual productivity loss due to absenteeism to avoid double counting of workdays missed due to short-term disability. Workdays missed due to short-term disability were reported as case-level records and were collected by

employers offering disability benefits. The associated mean indirect cost of workplace productivity loss was calculated assuming an 8-hour work day and using the seasonally adjusted, median hourly wage rate of $27.54 for all employees on private nonfarm payrolls in December 2018, as reported by the US Bureau of Labor Statistics.[24] All costs were reported in 2018 US dollars using the medical care component of the Consumer Price Index for all urban consumers.[25]

2.4 Statistical Analysis

To characterize baseline demographics in each of the study cohorts, continuous variables were summarized by mean and standard deviation (SD) and categorical variables were summarized by counts and proportions of individuals in each category. Differences between the two cohorts was reported using standardized mean differences (SMD). For categorical variables, SMD were calculated for the aggregate variable.[26]

Differences in the primary outcome and secondary outcomes of interest were estimated using a naïve Kaplan-Meier sample average (KMSA) to account for participants who were censored during follow-up due to an interruption or discontinuation in insurance coverage. The KMSA measures the mean of an outcome over the post-index follow-up period by multiplying the probability of remaining in follow-up at a given time interval with the mean measure of the outcome among patients who remain in follow-up to the beginning of the respective time interval.[27] The Kaplan-Meier estimator of the survival probability of (*P*) from the index date to a given month interval (*i*) can be expressed as:

$$P_i = \prod_{i:t_i \leq t} \frac{N_i - L_i}{N_i}$$

where N_i is the number of subjects at risk at time *i* and L_i is the number of individuals who are censored at time *i*. For the purposes of this analysis, patients in the cohort are not censored by events of death; rather, patients are censored at the event of any interruption or discontinuation in private health insurance coverage. Therefore, the equation for P_i above calculates the probability of remaining in follow-up with continuous enrollment.

In this analysis, KMSA naïve estimates were used to calculate the mean annual OOP costs, work productivity loss due to absenteeism, and work productivity loss due to short-term disability for patients with T2DM compared to DKD across the 12-month post-index follow-up period, divided into 1-month intervals. For each outcome and respective cohort, nonparametric bootstrapping methods were used to

generate 95% credible intervals (CI) to estimate the uncertainty in outcomes. We sampled 1,000 replicates and using a sample size of approximately 5% of the overall population for each outcome.

The difference in mean outcomes was calculated using a t-test for two independent samples. The test of equality of variances showed high significance; therefore, Satterthwaite confidence intervals were used assuming unequal variances. All statistical analyses were performed using RStudio version 1.2.5042 (RStudio Inc., Boston, MA) and SAS version 9.4 (SAS Institute, Cary, NC).

3. Results

3.1 Baseline Characteristics

Primary Population

Across the inpatient services and outpatient services tables of MarketScan® CCAE database, 16.9 million individuals were identified between January 1, 2013 and December 31, 2018. A total of 411,887 patients met the prespecified sample selection criteria for the primary outcome and were included in the analysis, denoted as the primary objective population (Figure 2). On average, patients in the DKD cohort were older (mean age of 54.20 ± 9.24) and had a greater proportion of individuals in the highest age category of greater than 55 years (57.6%) compared to patients in the T2DM cohort (mean age of 52.12 ± 9.82, 47.8% in age category of greater than 55 years). The DKD cohort had a greater proportion of individuals with a CCI score of 3 or greater compared to patients in the T2DM cohort (86.6% vs. 23.5%). The T2DM and DKD cohorts were similar in proportion female (47.7% vs. 41.9%) and full-time employment status (55.4% vs. 53.0%). In both cohorts, more patients were in the South geographical region than any other region, had similar proportions of union members, and the majority were enrolled in preferred provider organization (PPO) plans than any other insurance plan type (Table 1).

Secondary Populations

A total of 9,423 patients were included in the analysis for the secondary objective population assessing absenteeism and a total of 52,990 patients were included in the analysis for the secondary objective population assessing short-term disability (Figure 2). Similar to the primary population, patients in the DKD cohorts had a higher mean age compared to patients in the T2DM cohorts when assessing absenteeism (51.93 ± 8.13 vs. 51.75 ± 8.45) and when assessing short-term disability (50.75 ± 8.51 vs. 51.46 ± 8.58). In both secondary populations, majority of individuals were male gender and the DKD

cohorts had a greater proportion of individuals with a CCI score of 3 or greater compared to the T2DM cohorts. The absenteeism population and the short-term disability population had a similar distribution of geographic region, union status, employment status, and insurance plan type between the T2DM and DKD cohorts. (Table 1).

3.2 Primary Objective

Censored data in this analysis is assumed to be missing completely at random; therefore, naïve Kaplan-Meier estimates were used rather than a multivariate regression. Prior to conducting the KMSA analysis, negative costs representative of claim reversals were removed. The Kaplan-Meier survival shows the proportion of individuals remaining enrolled with continuous follow-up among the DKD and T2DM cohorts (Figure 3). The mean (95% CI) annual OOP cost was significantly higher among patients in the DKD cohort ($1,078 [95% CI: $1062, $1090]) compared to those in the T2DM cohort ($751 [95% CI: $733, $767]) (Table 2). The calculated difference in mean (95% CI) annual OOP cost in the 12-month post-index follow-up period among patients in the DKD cohort compared to the T2DM cohort was $327.5 (95% CI: $326.8, $328.2). Given the observed data, the mean annual OOP cost for patients in the DKD cohort has a 95% probability of falling within a range of $1062 to $1090 and the mean annual OOP cost for patients in the T2DM cohort has a 95% probability of falling within a range of $733 to $767 (Table 2).

3.3 Secondary Objectives

No patients were censored between month 1 through month 11 of follow-up in either secondary populations. A very small proportion of patients were censored at month 12 for the populations assessed for absenteeism (3.8% in the DKD cohort, 2.3% in the T2DM cohort) and short-term disability (3.0% in the DKD cohort, 2.2% in the T2DM cohort).

In the secondary population assessing absenteeism, the mean (95% CI) annual hours of work missed due to absence in the 12-month post-index follow-up period was similar among the DKD cohort (227 hours [95% CI: 219 hours, 236 hours]) and the T2DM cohort (206 hours [95% CI: 187 hours, 226 hours]) as evidenced by the overlapping confidence intervals around the respective point estimates. The mean difference (95% CI) in annual hours of work missed due to absence was 21.7 hours (95% CI: 21.0 hours,

22.3 hours). It is further estimated that the mean annual indirect cost of productivity loss from absenteeism was $6,263 for the DKD cohort and $5,670 for the T2DM cohort (Table 3A).

In the secondary population assessing short-term disability, the mean (95% CI) annual days of work missed due to short-term disability in the 12-month post-index follow-up period was statistically significantly higher among patients in the DKD cohort (4.6 days [95% CI: 4.4 days, 4.8 days]) compared to patients in the T2DM cohort (2.8 days [95% CI: 2.3 days, 3.4 days]). The mean difference (95% CI) in annual days of work missed due to short-term disability was 1.78 days (95% CI: 1.76 days, 1.80 days). This finding Assuming an 8-hour workday, the mean annual indirect cost of productivity loss from short-term disability was $1,016 for the DKD cohort and $624 for the T2DM cohort. The lack of overlap in the credible intervals provides evidence of a statistically significant difference in the naïve KMSA estimates of the means (Table 3B).

4. Discussion

In this study we sought to quantify the economic burden of T2DM compared to DKD as measured by mean annual out-of-pocket costs and mean annual workplace productivity loss from absenteeism and short-term disability. Our findings suggest that patients with DKD have higher mean annual OOP costs compared to patients with T2DM. No significant difference in mean annual hours missed due to workplace absenteeism was observed between the two cohorts; however, there was an observed significant difference between mean annual days missed at work due to short-term disability between the DKD cohort and the T2DM cohort. Using the naïve estimates from the KMSA, productivity loss estimates were converted from respective units of time to indirect costs. Patients with T2DM incurred indirect costs of $5,670 from absenteeism and $557 from short-term disability per annum. In contrast, patients with DKD incurred indirect costs of $6262 from absenteeism and $1029 from short-term disability. These results suggest that among commercially insured patients with T2DM, those with consequent renal impairment incur greater out-of-pocket costs and experience greater loss in workplace productivity.

It is important to consider the scope of disease prevalence when interpreting the results of this analysis. The American Diabetes Association estimated that over $245 billion was spent on diabetes care in 2012. This estimate is a sum of direct health care expenditures ($176 billion), including patient OOP costs, and lost productivity due to absenteeism, reduced productivity, disability, and premature mortality ($69 billion).[12] Though the numerical estimates in this analysis may not present a dramatic cost burden at the

individual level, the implications of these findings are more substantial when calculated at a health system or societal level. As a chronic disease that affects multiple organ systems, T2DM may progress to several burdensome macrovascular complications and microvascular complications, including nephropathy, retinopathy, and neuropathy. As reflected by recent updates to clinical practice guidelines, research efforts have been focused on stratifying treatment recommendations by presence of comorbid cardiovascular or other macrovascular disease in recent years.[28] However, specific treatments in patients with comorbid microvascular disease may be on the horizon. With an improved understanding of the economic burden of diabetic kidney disease, the possible policy implications include greater support of current research efforts to develop renoprotective therapies in patients with T2DM.[29]

These findings may be helpful in informing the broader impacts of these diseases outside the formal health care system. The outcomes measured in this study may serve as useful inputs in economic evaluations which consider the societal perspective. The Second Panel on Cost-Effectiveness in Health Medicine recommends the inclusion of an impact inventory in cost-effectiveness analysis studies (CEA) to details the effects of health improvements experience beyond the formal health care sector.[30] This inventory explicitly patient out-of-pocket costs and effects on productivity and consumption among other health and non-health related consequences such as time costs of receiving care and transportation costs. By adding to the currently body of evidence, our results may be used to generate more transparent CEA conducted from a societal perspective to inform health policy decision making.[31]

There are several limitations to consider when evaluating our study outcomes. First, naïve KMSA estimates of the outcomes were calculated without controlling for possible confounders. Namely, patients in the DKD population were found to be older in age with more comorbid conditions. Previous studies have established the association between the presence of multiple chronic conditions and higher out-of-pocket costs and health care costs overall.[32,33] Therefore, the reported results may be biased due imbalanced baseline characteristics between cohorts. Second, only patients with commercial insurance were accounted for in the data source. Since Medicare pays for the cost of chronic renal replacement therapy, the use of this data source excluded a large portion of individuals with ESRD. Hallab and Wish estimated that at the time of dialysis initiation, only 23-24% of patients reported employment compared to 81-85% population employment rate over an 18-year study period.[34] Therefore, since individuals with ESRD are less likely to have reported employment, the use of the MarketScan® database is expected to have minimal bias on the estimate of indirect costs attributed to workplace productivity loss. However,

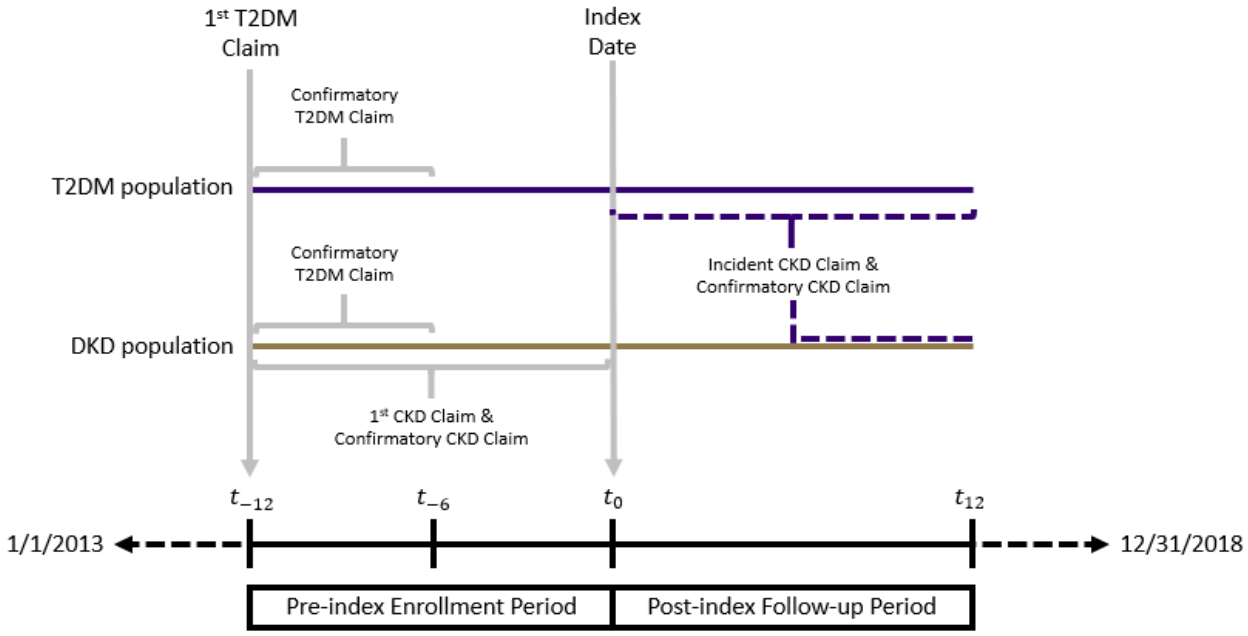
it is plausible to suspect the exclusion of patients with the greatest impairments in kidney function could bias our results towards lower values, particularly in the estimates of OOP costs.[34,35] The populations to assess outcomes of productivity loss were further restricted to a subset of patients who were eligible for the HPM dataset. Therefore, the use of this convenience sample may limit the generalizability of our findings to a larger population. Lastly, the use of administrative codes to identify the presence of disease may not have accurately captured all cases of T2DM or DKD. Specifically, studies document the difficulty of capturing cases of DKD and CKD in claims databases.[36,37] Possible contributing factors include low rates of diagnosis and laboratory testing among milder disease, heterogeneity in disease presentation, among other real-world applications to best practices.[38-40] Though clinical guidelines for best practices present clearly define diagnostic criteria for DKD, there remains no gold standard to identify these cases for retrospective analyses.[15]

5. Conclusion

People with DKD were found to have higher mean annual OOP costs and experience greater losses in mean annual workplace productivity due to short-term disability compared to patients with T2DM. These results quantify the cost burden of T2DM and DKD from the patient and employer perspectives, which may be useful in economic evaluations such as CEA studies which may inform health care decision-making.

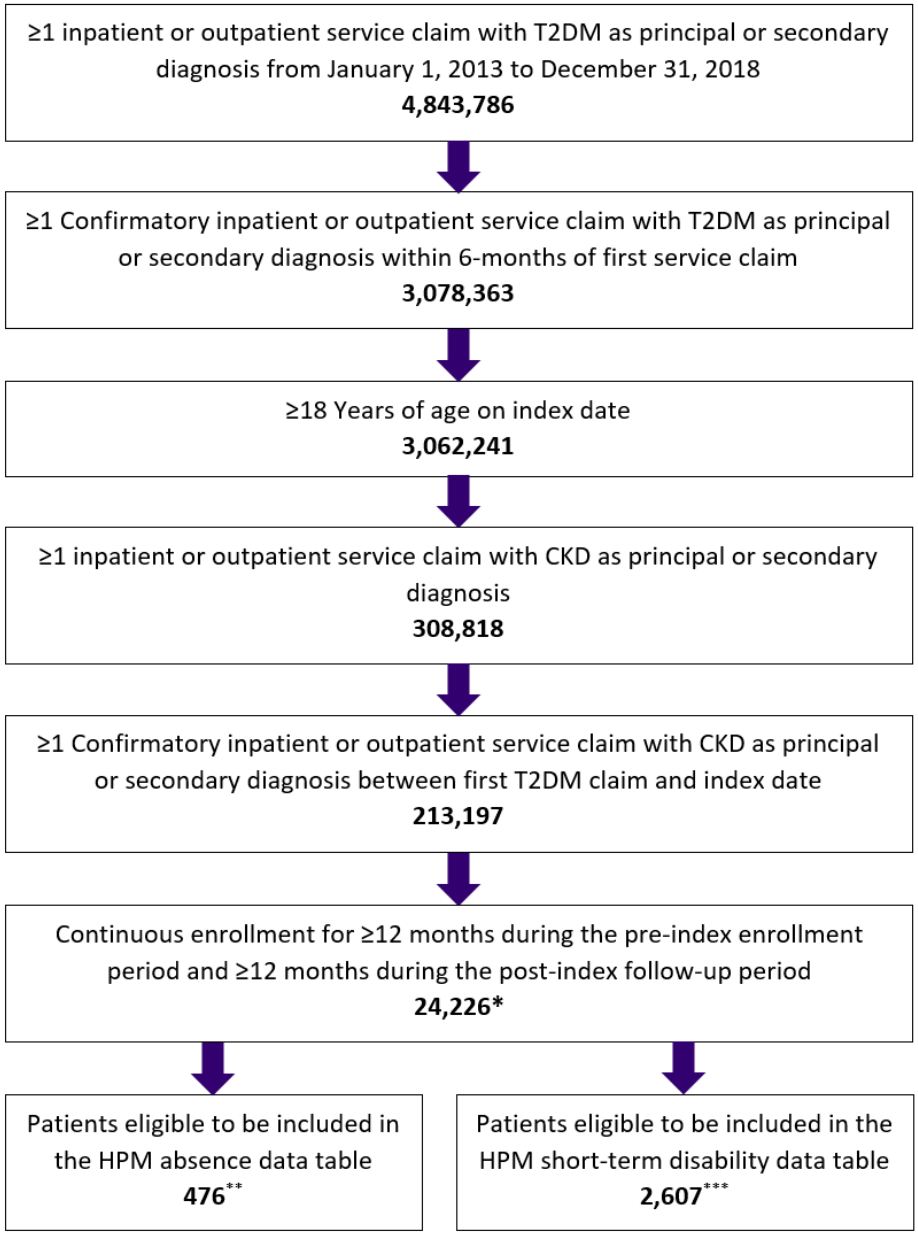
6. Figures

6.1 [Figure 1] Study Enrollment Criteria



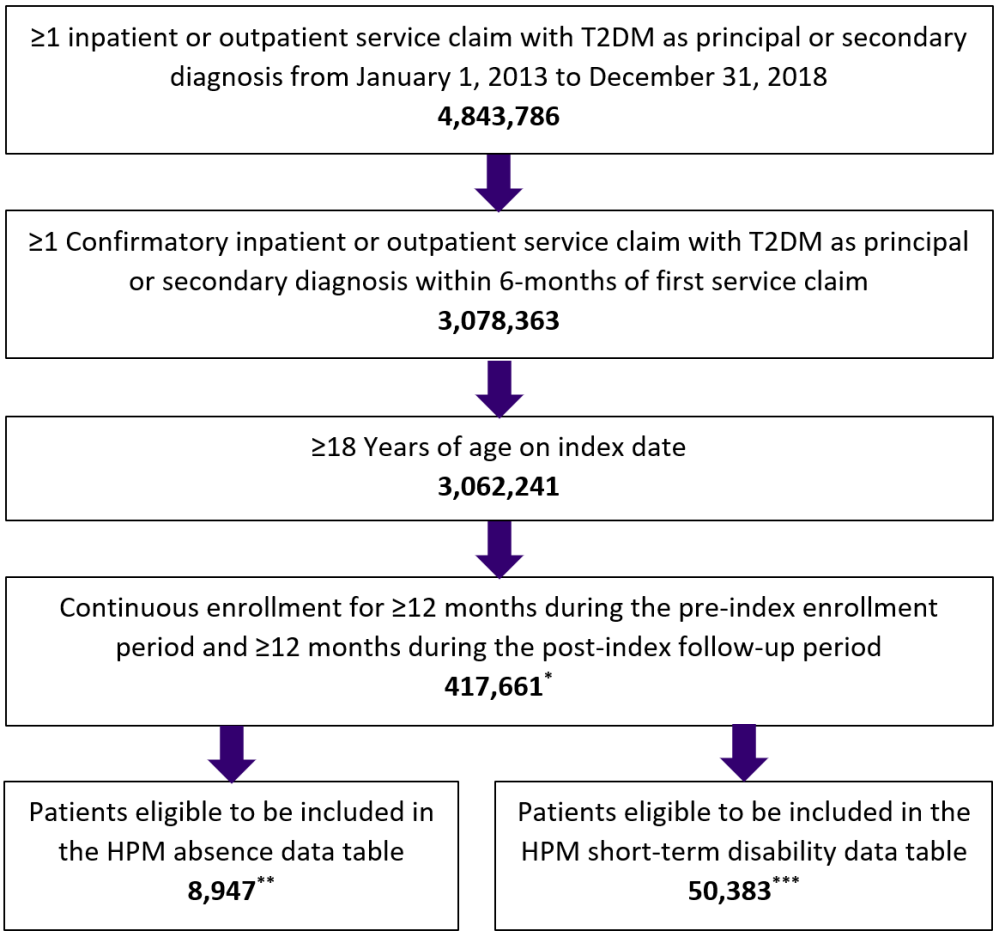
6.2 [Figure 2] Sample Attrition Figures

(A) Diabetic Kidney Disease (DKD) Population



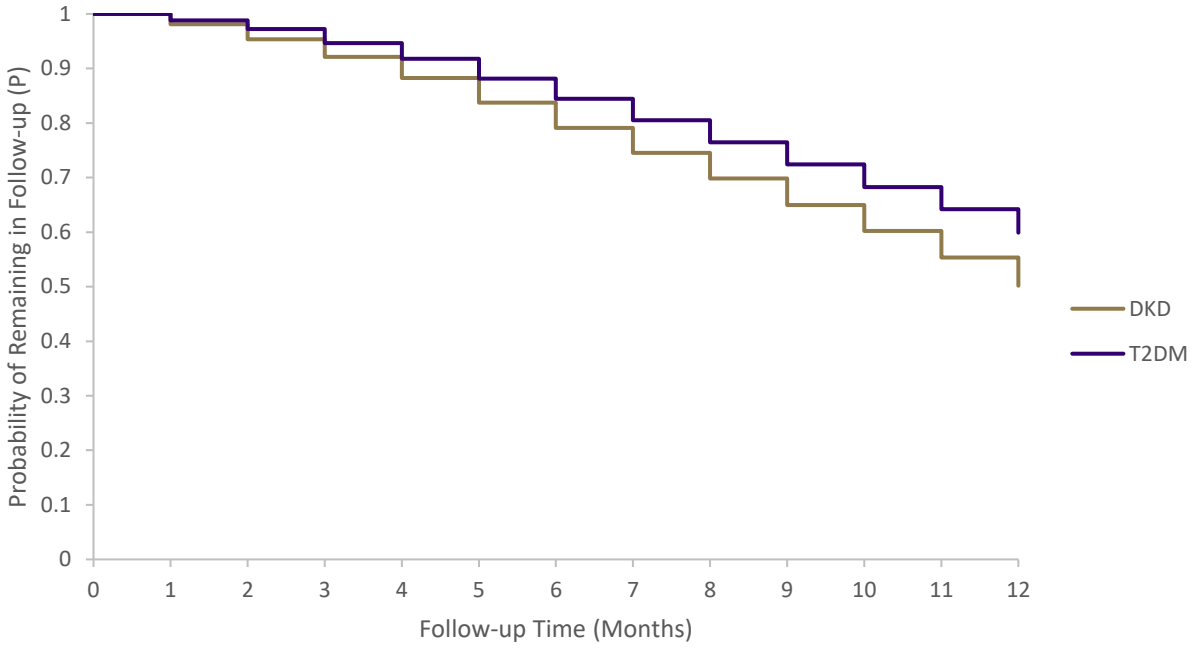
**Primary objective population*
***Secondary objective population, absenteeism*
****Secondary objective population, short-term disability*

(B) Type 2 Diabetes Mellitus (T2DM) Population



**Primary objective population*
***Secondary objective population, absenteeism*
****Secondary objective population, short-term disability*

6.3 [Figure 3] Monthly Probability of Remaining in Follow-up with Continuous Enrollment for the Commercial Claims Population



7. Tables

7.1 [Table 1] Baseline Characteristics of Study Populations

	Primary Population N = 441,887			Secondary Population, Absenteeism N = 9,423			Secondary Population, Short-term Disability N = 52,990		
Characteristic	T2DM	DKD	SMD	T2DM	DKD	SMD	T2DM	DKD	SMD
N	417661	24226		8947	476	--	50383	2607	--
Age at index date, mean (SD)	52.12 (9.82)	54.20 (9.24)	0.218	51.93 (8.13)	51.75 (8.45)	0.021	50.75 (8.51)	51.46 (8.58)	0.084
Index year, mean (SD)	2016.14 (1.12)	2016.37 (1.13)	0.197	2015.92 (0.87)	2016.13 (0.90)	0.245	2015.87 (0.86)	2016 (0.88)	0.208
Age category (%)			0.206			0.075			0.091
18 – 34	25012 (6.0)	983 (4.1)		334 (3.7)	20 (4.2)		2481 (4.9)	123 (4.7)	
35 – 44	61623 (14.8)	2709 (11.2)		1323 (14.8)	81 (17.0)		9106 (18.1)	433 (16.6)	
45 – 54	131480 (47.8)	6572 (27.1)		3279 (36.6)	162 (34.0)		19094 (37.9)	915 (35.1)	
55+	199546 (47.8)	13962 (57.6)		4011 (44.8)	213 (44.7)		19702 (39.1)	1136 (43.6)	
Female gender (%)	199260 (47.7)	10140 (41.9)	0.118	2104 (23.5)	92 (19.3)	0.102	18529 (36.8)	801 (30.7)	0.128
Charlson comorbidity index score (%)			1.655			1.771			1.740
0	909 (0.2)	11 (0.0)		24 (0.3)	0 (0.0)		123 (0.2)	0 (0.0)	
1	23177 (55.5)	1756 (7.2)		5412 (60.5)	46 (9.7)		30555 (60.6)	247 (9.5)	
2	86665 (20.8)	1482 (6.1)		1776 (19.9)	23 (4.8)		9803 (19.5)	144 (5.5)	
3+	983101 (23.5)	20977 (86.6)		1735 (19.4)	407 (85.5)		9902 (19.7)	2216 (85.0)	
Region (%)			0.066			0.067			0.092
Northeast	72983 (17.5)	3939 (16.3)		1083 (12.1)	60 (12.6)		6817 (13.5)	294 (11.3)	
North Central	78861 (18.9)	4404 (18.2)		1744 (19.5)	86 (18.1)		11875 (23.6)	596 (22.9)	
South	200536 (48.0)	11980 49.5)		3788 (42.3)	196 (41.2)		22732 (45.1)	1188 (45.6)	
West	60805 (14.6)	3750 (15.5)		2327 (26.0)	134 (28.2)		8872 (17.6)	520 (19.9)	
Unknown	4476 (1.1)	153 (0.6)		5 (0.1)	0 (0.0)		87 (0.2)	9 (0.3)	
Union Status (%)			0.099			0.057			0.068
Union	61497 (14.7)	4236 (17.5)		2117 (23.7)	124 (26.1)		11196 (22.2)	634 (24.3)	
Non-Union	151526 (36.3)	9019 (37.2)		3692 (41.3)	193 (40.5)		28593 (56.8)	1485 (57.0)	
Other/Unknown	204638 (49.7)	10971 (45.3)		3138 (35.1)	159 (33.4)		10594 (21.0)	488 (18.7)	
Employment Status (%)			0.159			0.025			0.097
Full Time	231211 (55.4)	12851 (53.0)		7378 (82.5)	397 (83.4)		45564 (90.4)	2278 (87.4)	
Non-Full Time	186450 (44.6)	11375 (47.0)		1569 (17.5)	79 (16.6)		4819 (9.6)	329 (12.6)	
Insurance Plan Type (%)			0.076			0.130			0.048
Comprehensive	13096 (3.2)	998 (4.2)		12 (0.1)	0 (0.0)		1831 (3.7)	94 (3.6)	
EPO	4752 (1.2)	255 (1.1)		189 (2.1)	11 (2.3)		360 (0.7)	19 (0.7)	
HMO	45334 (11.0)	2863 (12.0)		1037 (11.6)	44 (9.3)		4741 (9.5)	271 (10.5)	
POS	29366 (7.1)	1698 (7.1)		252 (2.8)	11 (2.3)		1696 (3.4)	93 (3.6)	
PPO	246011 (59.8)	13676 (57.4)		4011 (4.8)	236 (49.7)		27367 (54.6)	1382 (53.3)	
POS with capitation	5074 (1.2)	381 (1.6)		0 (0.0)	0 (0.0)		91 (0.2)	2 (0.1)	
CDHP	446637 (10.9)	2669 (11.2)		3059 (34.2)	150 (31.6)		9593 (19.1)	503 (19.4)	
HDHP	23013 (5.6)	1287 (5.4)		386 (4.3)	23 (4.8)		4422 (8.8)	228 (8.8)	

T2DM = type 2 diabetes mellitus, DKD = diabetic kidney disease, SMD = standardized mean differences, SD = standard deviation, EPO = exclusive provider organization, HMO – health maintenance organization, POS = point of service, PPO = preferred provider organization, CDHP = consumer-driven health plan, HDHP = high-deductible health plan

7.2 [Table 2] Kaplan-Meier Sample Average Naïve Estimates of Mean Annual Out-of-Pocket Costs

Type 2 Diabetes Cohort												
Month	1	2	3	4	5	6	7	8	9	10	11	12
P	0.989	0.974	0.949	0.920	0.885	0.847	0.808	0.768	0.728	0.687	0.647	0.604
Cost ($)*	83.83	78.04	78.50	72.76	74.99	73.97	71.98	74.01	74.80	76.77	76.89	82.12
Weighted Cost ($)*	82.89	76.01	74.53	66.93	66.38	62.64	58.13	56.87	54.44	52.76	49.73	49.62
Mean Annual OOP Cost (95% CI): $751 ($733, $767)												
Diabetic Kidney Disease Cohort												
Month	1	2	3	4	5	6	7	8	9	10	11	12
P	0.981	0.954	0.921	0.882	0.838	0.793	0.746	0.700	0.651	0.603	0.554	0.502
Cost ($)*	157.50	124.80	124.00	113.47	112.46	109.51	105.08	108.07	108.86	112.37	106.24	115.42
Weighted Cost ($)*	154.47	118.99	114.15	100.05	94.27	86.81	78.35	75.61	70.87	67.74	58.86	57.97
Mean Annual OOP Cost (95% CI): $1,078 ($1,062, $1,090)												
Mean Difference (95% CI): 327.5 (326.8, 328.2), p < 0.0001												

P = probability of remaining in follow-up with continuous enrollment, OOP = out-of-pocket, CI = credible interval

*Reported in 2018 US dollars

7.3 [Table 3] Kaplan-Meier Sample Average Naïve Estimates of Mean Annual Workplace Productivity Loss from Absenteeism and Short-Term Disability

(A) Mean Annual Productivity Loss from Absenteeism

Type 2 Diabetes Cohort												
Month	1	2	3	4	5	6	7	8	9	10	11	12
P	1	1	1	1	1	1	1	1	1	1	1	0.977
Hours	16.59	17.07	17.59	16.84	17.84	17.27	17.04	17.81	17.27	17.88	17.87	15.16
Weighted Hours	16.59	17.07	17.59	16.84	17.84	17.27	17.04	17.81	17.27	17.88	17.87	14.81
Mean Annual ABS Hours Missed (95% CI): 206 (187, 226)												
Indirect Cost of Annual ABS Productivity Loss: $5,670												
Diabetic Kidney Disease Cohort												
Month	1	2	3	4	5	6	7	8	9	10	11	12
P	1	1	1	1	1	1	1	1	1	1	1	0.962
Hours	18.88	18.95	19.61	18.37	21.10	18.86	17.21	18.18	18.72	20.94	20.22	17.06
Weighted Hours	18.88	18.95	19.61	18.37	21.10	18.86	17.21	18.18	18.72	20.94	20.22	16.41
Mean Annual ABS Hours Missed (95% CI): 227 (219, 236)												
Indirect Cost of Annual ABS Productivity Loss: $6,263.42												
Mean Difference (95% CI): 21.7 (21.0, 22.3), p < 0.0001												

P = probability of remaining in follow-up with continuous enrollment, ABS = absenteeism, CI = credible interval

(B) Mean Annual Productivity Loss from Short-Term Disability

Type 2 Diabetes Cohort												
Month	1	2	3	4	5	6	7	8	9	10	11	12
P	1	1	1	1	1	1	1	1	1	1	1	0.978
Days	0.349	0.343	0.329	0.294	0.318	0.284	0.273	0.216	0.175	0.149	0.082	0.014
Weighted Days	0.349	0.343	0.329	0.294	0.318	0.284	0.273	0.216	0.175	0.149	0.082	0.014
Mean Annual STD Days Missed (95% CI): 2.8 (2.3, 3.4)												
Indirect Cost of STD Productivity Loss: $624												
Diabetic Kidney Disease Cohort												
Month	1	2	3	4	5	6	7	8	9	10	11	12
P	1	1	1	1	1	1	1	1	1	1	1	0.971
Days	0.632	0.600	0.437	0.762	0.358	0.512	0.389	0.315	0.249	0.214	0.082	0.025
Weighted Days	0.632	0.600	0.437	0.762	0.358	0.512	0.389	0.315	0.249	0.214	0.082	0.024
Mean Annual STD Days Missed (95% CI): 4.6 (4.4, 4.8)												
Indirect Cost of STD Productivity Loss: $1,016												
Mean Difference (95% CI): 1.78 (1.76, 1.80), p < 0.0001												

P = probability of remaining in follow-up with continuous enrollment, STD = short-term disability, CI = credible interval

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9. Appendices

9.1 [Appendix A] International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) and Tenth Revision (ICD-10-CM) diagnosis codes used to identify eligible patients with T2DM and CKD

Condition	ICD-9 Codes	ICD-10 Codes
Chronic Kidney Disease	2494, 24940, 24941, 2504, 25040, 25042, 2714, 2741, 4401, 4421, 5724, 581, 5810, 5811, 5812, 5813, 5818, 58181, 58189, 5819, 582, 5820, 5821, 5822, 5824, 5828, 58281, 58289, 5829, 583, 5830, 5831, 5832, 5834, 5836, 5837, 5838, 58381, 58389, 5839, 591, 6421, 6462, 75312, 75313, 75314, 75315, 75316, 75317, 75319, 7532, 7944, 28521, 403, 4030, 40300, 40301, 4031, 40310, 40311, 4039, 40390, 40391, 404, 4040, 40400, 40401, 40402, 40403, 4041, 40410, 40411, 40412, 40413, 4049, 40490, 40491, 40492, 40493, 585, 5851, 5852, 5853, 5854, 5855, 5856, 5859	C64, C641, C642, C649, C689, D300, D3000, D3001, D3002, D410, D4100, D4101, D4102, D412, D4120, D4121, D4122, D631, E082, E0821, E0822, E0829, E092, E0921, E0922, E0929, E102, E1021, E1022, E1029, E112, E1121, E1122, E1129, E132, E1321, E1322, E1329, I12, I120, I129, I13, I130, I131, I132, I1310, K767, M103, M1030, M1031, M10311, M10312, M10319, M3214, M3215, N01, N010, N012, N0123, N014, N016, N017, N018, N019, N02, N020, N021, N022, N023, N024, N025, N026, N027, N028, N029, N03, N031, N032, N033, N034, N035, N036, N037, N038, N039, N04, N040, N041, N042, N043, N044, N045, N046, N047, N048, N049, N05, N051, N052, N053, N054, N055, N056, N057, N058, N059, N06, N061, N062, N063, N064, N065, N066, N067, N068, N069, N07, N070, N071, N072, N073, N074, N075, N076, N077, N078, N079, N08, N131, N132, N1330, N1339, N14, N140, N141, N142, N143, N144, N150, N158, N159, N16, N17, N170, N171, N172, N178, N179, N18, N181, N182, N183, N184, N185, N186, N189, N19, N25, N250, N251, N2581, N2589, N259, N261, N269, O9089, Q6102, Q611, Q6111, Q6119, R944
Type 2 Diabetes Mellitus	2494, 24940, 24941, 25000, 25002, 25010, 25012, 25020, 25022, 25030, 25032, 2504, 25040, 25042, 25050, 25052, 25060, 25062, 25070, 25072, 25080, 25082, 25090, 25092	E08, E082, E0821, E0822, E0829, E09, E092, E0921, E0922, E0929, E11, E110, E1100, E1101, E111, E1110, E1111, E112, E1121, E1122, E1129, E113, E1131, E11311, E11319, E1132, E11321, E113211, E113212, E113213, E113219, E11329, E113291, E113292, E113293, E113299, E1133, E113311, E113312, E113313, E113319, E11339, E113391, E113392, E113393, E113399, E1134,

		E11341, E113411, E113412, E113413, E113419, E11349, E113491, E113492, E113493, E113499, E1135, E11351, E113511, E113512, E113513, E113519, E11352, E113521, E113522, E113523, E113529, E11353, E113531, E113532, E113533, E113539, E11354, E113541, E113542, E113543, E113549, E11355, E113551, E113552, E113553, E113559, E11359, E113591, E113592, E113593, E113599, E1136, E1137, E1137x1, E1137x2, E1137x3, E1137x9, E1139, E114, E1140, E1141, E1142, E1143, E1144, E1149, E115, E1151, E1152, E1159, E116, E1161, E11610, E11618, E1162, E11620, E11621, E11622, E11628, E1163, E11630, E11638, E1164, E11641, E11649, E1165, E1169, E118, E119