

Health Care Resource Utilization Among Patients With T2D and Cardiovascular-, Heart Failure-, or Renal-Related Hospitalizations

Srinivas Annavarapu, MBBS, PhD; Sabyasachi Ghosh, MS; Yong Li, PhD; Chad Moretz, ScD, MS; Sharashchandra Shetty, PhD; and Todd Prewitt, MD

D iabetes is a major public health concern in the United States; the American Diabetes Association (ADA) estimates that 24.7 million patients had a diagnosis of diabetes in the United States in 2017.¹ Type 2 diabetes (T2D) accounts for 90% to 95% of all cases.² Poorly controlled diabetes can cause macrovascular (eg, stroke, myocardial infarction) and microvascular (eg, neuropathy, nephropathy) complications.³⁻⁵ In addition to higher morbidity and mortality, diabetes is associated with direct health care costs of \$237 billion in the United States, 29.4% of which are due to inpatient hospitalizations.¹ In fact, of the projected 162 million hospital inpatient days in 2017, 22.6 million could be attributed to diabetes.¹ The prevalence and economic burden of diabetes are increasing for patients 65 years and older, resulting in a greater financial burden to these patients and economic cost to the Medicare program.^{1,6}

Patients with diabetes frequently experience comorbid conditions.^{3,7-11} The prevalence of these conditions was examined using data from the National Health and Nutrition Examination Survey (1999-2006), and the report revealed that for patients 60 years or older with diabetes, the proportions with comorbid coronary heart disease, stroke, congestive heart failure, and chronic kidney disease were 29.9%, 14.0%, 15.6%, and 40.0%, respectively.¹² The high rate of comorbidities was expected because diabetes frequently occurs in multimorbidity (2 or more coexisting chronic conditions) clusters including hypertension, arthritis, and ischemic heart disease.^{13,14} For example, patients with comorbid diabetes and renal disease have a higher risk of cardiovascular (CV) mortality.¹⁵ Interestingly, the number of comorbid conditions has been reported to be higher for hospitalized patients with diabetes (2.6) compared with those without diabetes (1.3).^{6,16} As expected, management of patients with multimorbidity is challenging for a number of reasons, including low health system support, lack of guidance for health care professionals, impairment of patients' overall health, and financial burden.¹⁷

One way to address the challenge of multimorbidity in patients with diabetes is through monitoring and early interventions to achieve glycemic control and treat comorbid conditions. This may be effective in reducing morbidity, mortality, and health care

ABSTRACT

OBJECTIVES: In patients with type 2 diabetes (T2D), comorbidity-related hospitalizations can have significant impact on longitudinal care. This study aimed to estimate incremental all-cause health care resource utilization (HCRU) and costs between patients with T2D who experienced cardiovascular (CV)-, heart failure (HF)-, or renal-related hospitalizations vs those who did not.

STUDY DESIGN: This was a retrospective cohort study using data from a large national health plan.

METHODS: Patients with T2D aged 18 to 90 years with CV, HF, or renal hospitalizations were identified from the Humana claims database from October 1, 2009, to September 30, 2015, and separated into CV, HF, and renal cohorts. Patients had 12 months of continuous enrollment prior to the date of first hospitalization (index) and were followed for up to 12 months. Per-patient per-month (PPPM) all-cause HCRU and costs for hospitalized patients were compared with those of no-CV, no-HF, and no-renal cohorts. Differences in baseline characteristics between cohorts were controlled for using generalized linear models.

RESULTS: A total of 221,229, 68,126, and 120,105 patients were included in the CV, HF, and renal cohorts, respectively; these patients were older and had higher Deyo-Charlson Comorbidity Index scores than patients in the no-CV, no-HF, and no-renal cohorts. Adjusted for baseline covariates, they had higher mean PPPM inpatient stays, outpatient visits, emergency department visits, and total health care costs.

CONCLUSIONS: Among patients with T2D, concurrent CV, HF, or renal events present significant disease burden leading to poor quality of life. This information can be used to guide disease management strategies and interventions aimed at reducing comorbidity-related hospitalizations and health care costs, thus providing improved quality of life for these patients.

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resource utilization (HCRU)¹⁸⁻²⁰; however, real-world evidence is lacking in current literature regarding patient characteristics and HCRU for patients with T2D experiencing hospitalizations due to comorbid conditions such as CV-, heart failure (HF)-, or renal-related events. With the understanding that resource use and, therefore, likely costs will be higher in this population, the intent of the current study was to quantify the incremental HCRU and costs of specific comorbidity-related hospitalizations in patients with T2D in a primarily Medicare population.

METHODS

Study Design and Data Source

This was a retrospective cohort study using existing administrative claims data. The study was conducted using the Humana Inc health insurance claims database. The database contains integrated medical, pharmacy, behavioral, and laboratory-related claims, representing more than 12 million current and former Humana Medicare beneficiaries and commercially insured patients. The deidentified patient-level data include detailed use, outcomes, and cost data for health care services performed in inpatient and outpatient settings, prescription drug claims, and information on patient enrollment. The claims are linked through a patient identifier that remains constant regardless of benefit design, gap in coverage, or change of employer. These data have information for patients enrolled in commercial, Medicare Advantage, and prescription drug plans. The database has national coverage, with high proportions of members from Texas, Florida, and Ohio.

Study Population

The study period was from October 1, 2008, to September 30, 2016. Patients aged 18 to 90 years were identified during the 6-year identification period from October 1, 2009, to September 30, 2015 (Figure 1). Three separate cohorts of patients with at least 1 CV-, HF-, or renal-related hospitalization during the identification period were identified using *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)* diagnosis codes (eAppendix Table 1 [eAppendix available at ajmc.com]). The codes for CV events and HF were mutually exclusive. The date of first observed CV-, HF-, or renal-related hospitalization (index hospitalization) was defined as the index date; the month was defined as the index month.

The comparator cohort was defined based on random selection of 1 comparison patient from a pool of all patients who had any medical claims during the index month but did not experience any CV hospitalization during the identification period, including the index month, for each patient with at least 1 CV hospitalization. Patients without CV hospitalizations could have HF- or renal-related hospitalizations. This process was repeated for all patients in the CV

TAKEAWAY POINTS

This study aimed to estimate incremental all-cause health care resource utilization and costs (total, medical, and pharmacy) between patients with type 2 diabetes who experienced cardiovascular (CV)-, heart failure (HF)-, or renal-related hospitalizations vs those did not.

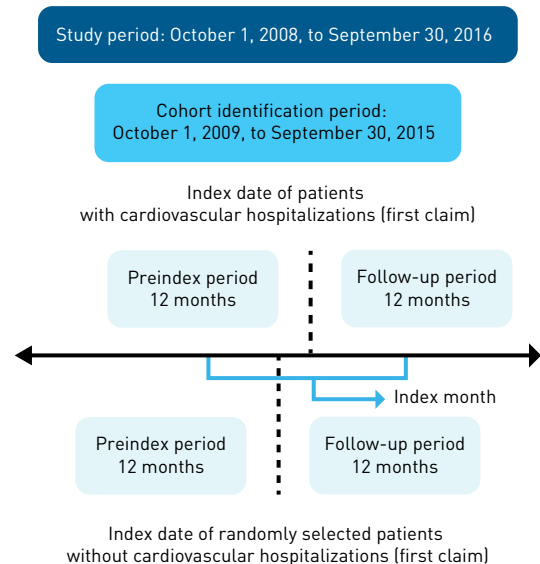
- ▶ Patients in the CV, HF, and renal cohorts were older and had higher Deyo-Charlson Comorbidity Index scores compared with patients in the no-CV, no-HF, and no-renal cohorts.
- ▶ Per-member per-month hospitalizations, office visits, emergency department visits, and health care costs were significantly higher in the CV, HF, and renal cohorts.
- ▶ Concurrent CV-, HF-, or renal-related hospitalization presents significant disease burden leading to poor quality of life.

cohort, without replacement, until a ratio of 1:1 was achieved. The date of the first medical claim during the index month was defined as the index date for each patient within the comparator cohort.

Similarly, comparator cohorts of patients without HF- and renal-related hospitalizations were identified for the cohort of patients with HF-related hospitalizations and the cohort of patients with renal-related hospitalizations, respectively.

Patients with T2D were identified by having at least 1 prescription claim for insulin or an oral hypoglycemic or antihyperglycemic drug (eAppendix Table 1); at least 2 outpatient visits or a nonacute inpatient stay with a diagnosis code for T2D (*ICD-9-CM* codes 250.x0 or 250.x2) in any position; or at least 1 acute inpatient stay or emergency department (ED) visit with a diagnosis code for T2D in any position in the 12-month period preceding the index date (preindex period). Included patients were required to be continuously enrolled in a Medicare Advantage or commercial health plan during the 12-month preindex period.

FIGURE 1. Patient Sample Selection Timeline*



*Design was repeated for selection of heart failure- and renal-related hospitalization cohorts and corresponding comparator cohorts.

Patients with gestational diabetes (*ICD-9-CM* 648.8x), pregnancy (*ICD-9-CM* V22.2), type 1 diabetes (*ICD-9-CM* 250.x1 or 250.x3), or polycystic ovary syndrome (*ICD-9-CM* 256.4) during the study period were excluded. In addition, patients with dual eligibility (patients enrolled in a Medicare plan who are also eligible for Medicaid) and residents of Puerto Rico were excluded. Patients in each cohort were followed for a minimum of 30 days post index date, including the index date, up to a maximum of 12 months.

Patient Characteristics

The following patient characteristics were evaluated in the 1-year preindex period for all cohorts: demographic, clinical, HCRU, and cost variables. Demographic characteristics included age, sex, race/ethnicity, line of business, geographical location, low-income subsidy status, and health plan type (health maintenance organization, preferred provider organization, fee-for-service or Medicare Advantage, or Part D). Clinical characteristics included mean count of pharmacy claims for oral antidiabetic medications, glucagon-like peptide-1 (GLP-1) agonists, insulins ([eAppendix Table 2](#)), and cardiovascular medications ([eAppendix Table 3](#)); Diabetes Complications Severity Index (DCSI) score ([eAppendix Table 4](#)); Deyo-Charlson Comorbidity Index (DCI) score ([eAppendix Table 5](#))²¹; number of claims for glycated hemoglobin (A1C) tests ([eAppendix Table 6](#)); and baseline comorbid conditions ([eAppendix Table 7](#)).

Outcomes

Key outcome measures were incremental HCRU and costs (total, medical, and pharmacy) among CV, HF, and renal cohorts in the pre- and postindex periods. Patients were censored at the end of the follow-up period (12 months), disenrollment, or death, whichever occurred first.

Statistical Analyses

Baseline demographics, clinical, HCRU, and costs were reported (mean, SD, median, and interquartile range) and compared using *t* tests and χ^2 tests between the following cohorts with T2D: CV cohort vs no-CV cohort, HF cohort vs no-HF cohort, and renal cohort vs no-renal cohort. All-cause HCRU was assessed during the pre- and postindex periods by type of service—namely, inpatient, outpatient, and ED visits. All-cause pharmacy, medical (inpatient, outpatient, and ED), and total (medical and pharmacy) costs were assessed during the pre- and postindex periods.

All costs were inflation adjusted to 2016 US dollars using the medical component of the US Consumer Price Index. HCRU and costs were reported on a per-patient per-month (PPPM) basis. Age-adjusted descriptive statistics were reported for all cost measures. Data from the CDC Behavioral Risk Factor Surveillance System were used to estimate the age distribution of the US population of patients with T2D. Sample statistics were weighted to reflect this distribution, providing more generalizable cost estimates.

Separate multivariate regression models within a generalized linear model framework were used to estimate the difference in all-cause

HCRU and costs adjusted for differences in patient characteristics between the CV cohort vs the no-CV cohort, between the HF cohort vs the no-HF cohort, and between the renal cohort vs the no-renal cohort. The following demographic characteristics were used as covariates in the model: age, gender, race, region (Northeast, West, South, and Midwest), low-income subsidy eligibility, and population density (urban vs rural). The following clinical characteristics were used as covariates in the model: number of classes of oral antidiabetic medications, number of prescriptions for GLP-1 agonists, number of prescriptions for insulins, number of classes of CV medications, number of A1C tests, DCI score, prescribing physician specialty (primary care vs specialist), and common comorbidities. Gamma link was used for cost outcomes, whereas Poisson link was used for HCRU. HCRU by type (office visit, ED, inpatient, and total) and costs by type (medical, pharmacy, and total) were reported. SAS Enterprise Guide version 7.11 (SAS Institute) was used to conduct the analysis. Statistics with a *P* value of .05 or less were considered statistically significant.

RESULTS

Sample Characteristics

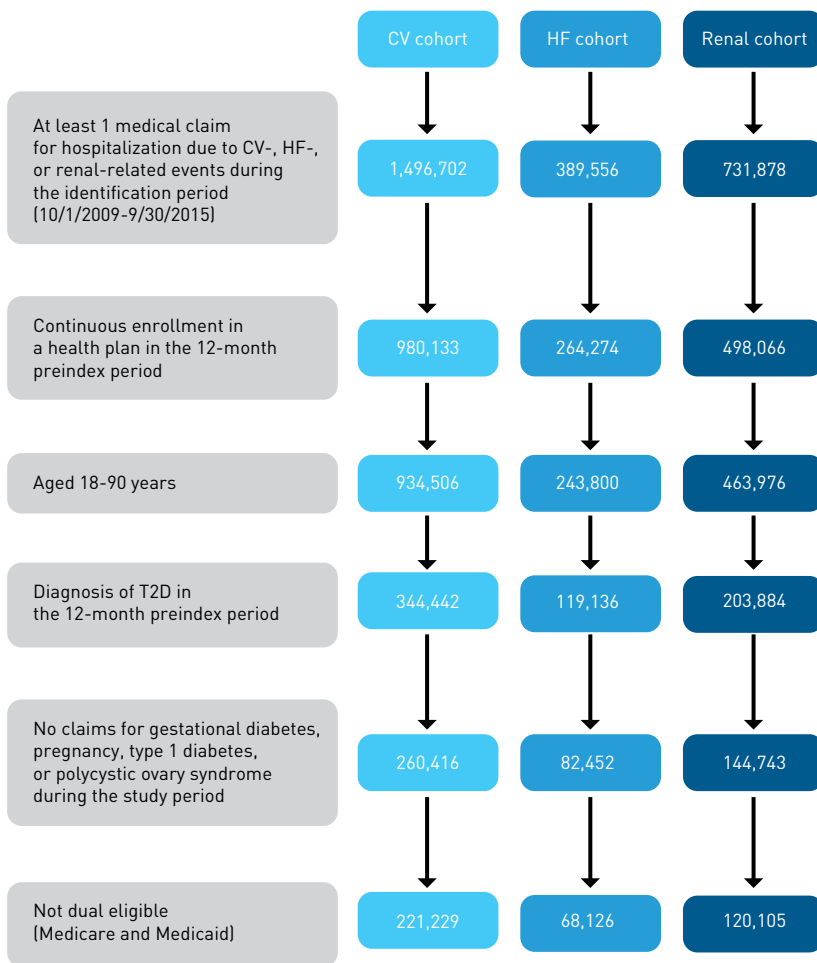
A total of 221,229 (92.4% Medicare), 68,126 (96.3% Medicare), and 120,105 (95.0% Medicare) patients met the criteria for inclusion in the CV, HF, and renal cohorts, respectively. [Figure 2](#) indicates the number of included and excluded patients with T2D and with CV-, HF-, or renal-related hospitalizations as each step of inclusion and exclusion criteria was applied.

Baseline Demographic Characteristics

Baseline demographic characteristics were compared between the cohorts and their respective comparator cohorts ([eAppendix Tables 8, 9, and 10](#)). The CV, HF, and renal cohorts had higher mean ages (71.4, 73.5, and 73.1 years vs 67.5, 69.7, and 69.0 years, respectively; $P < .0001$) and had lower proportions of women compared with the no-CV, no-HF, and no-renal cohorts. A smaller proportion of patients in the CV, HF, and renal cohorts lived in the Southern region of the United States during the study time period compared with the no-CV, no-HF, and no-renal cohorts.

Baseline Clinical Characteristics

Baseline clinical characteristics were compared between the cohorts and their respective comparator cohorts ([eAppendix Tables 11, 12, and 13](#)). Mean DCSI and mean DCI scores were higher in the CV, HF, and renal cohorts compared with the no-CV, no-HF, and no-renal cohorts (DCSI: 2.35, 3.73, and 3.12 vs 1.38, 1.97, and 1.77, respectively; $P < .0001$; DCI: 2.50, 3.78, and 3.36 vs 1.81, 2.41, and 2.18, respectively; $P < .0001$). The mean count of A1C tests was lower in the CV, HF, and renal cohorts compared with the no-CV, no-HF, and no-renal cohorts (1.84, 1.81, and 1.85 vs 1.95, 2.03, and 2.02, respectively; $P < .0001$). Most comorbidities were higher in the CV, HF, and renal cohorts compared with the no-CV, no-HF, and no-renal cohorts.

FIGURE 2. Attrition Diagram for Patient Selection

CV, cardiovascular; HF, heart failure; T2D, type 2 diabetes.

Baseline HCRU and Cost Characteristics

Baseline HCRU and cost characteristics were compared between the cohorts and their respective comparator cohorts (eAppendix Tables 14, 15, and 16). All measures of HCRU and cost were significantly higher in the CV, HF, and renal Medicare cohorts compared with the no-CV, no-HF, and no-renal cohorts except outpatient visits; inpatient stays and ED visits were higher in the CV, HF, and renal cohorts compared with their counterpart cohorts (inpatient: 18.7%, 51.0%, and 40.6% vs 5.1%, 20.3%, and 16.4%, respectively; $P < .0001$; ED: 40.9%, 60.7%, and 54.8% vs 18.8%, 30.6%, and 27.3%, respectively; $P < .0001$). Mean health care cost PPPM was higher in the CV, HF, and renal cohorts compared with the no-CV, no-HF, and no-renal cohorts (\$936.70, \$2046.30, and \$1582.10 vs \$548.90, \$948.70, and \$809.70, respectively; $P < .0001$). Mean medical and pharmacy costs PPPM were also higher in the CV, HF, and renal cohorts compared with their counterpart cohorts (eAppendix Tables 14, 15, and 16).

All-Cause HCRU and Costs Adjusted for Covariates in Postindex Period

CV vs no-CV cohorts. During follow-up among all patients, mean numbers of inpatient stays, outpatient visits, and ED visits PPPM, adjusted for covariates, were higher in the CV cohort compared with the no-CV cohort (inpatient: 0.10 vs 0.01; $P < .0001$; outpatient: 1.44 vs 0.82; $P < .0001$; ED: 0.17 vs 0.02; $P < .0001$) (Table 1). Adjusted mean health care costs PPPM were approximately 5-fold higher in the CV cohort compared with the no-CV cohort (\$2686 vs \$510; $P < .0001$). Medical costs, the major contributor to health care costs, were higher in the CV cohort compared with the no-CV cohort after adjusting for covariates (\$2642 vs \$366 PPPM; $P < .0001$). Adjusted pharmacy costs PPPM were also higher in the CV cohort compared with the no-CV cohort (\$138 vs \$98; $P < .0001$).

HF vs no-HF cohorts. Similar to the CV and no-CV cohorts, mean numbers of inpatient stays, outpatient visits, and ED visits PPPM, adjusted for covariates, were higher in the HF cohort compared with the no-HF cohort (inpatient: 0.17 vs 0.03; $P < .0001$; outpatient: 1.73 vs 1.00; $P < .0001$; ED: 0.25 vs 0.04; $P < .0001$) (Table 2). Adjusted mean health care costs PPPM were 4-fold higher in the HF cohort compared with the no-HF cohort (\$4111 vs \$930; $P < .0001$). As in the CV and no-CV cohorts, medical costs, the major contributor to health care costs, were higher in the HF cohort compared with the no-HF cohort after adjusting for covariates (\$3940 vs \$753 PPPM; $P < .0001$). Adjusted pharmacy costs PPPM were also higher in the HF cohort compared with the no-HF cohort (\$177 vs \$131; $P < .0001$).

Renal vs no-renal cohorts. Findings in the renal and no-renal cohorts were similar to those from the CV, no-CV, HF, and no-HF cohorts. Mean number of inpatient stays, outpatient visits, and ED visits PPPM, adjusted for covariates, were higher in the renal cohort compared with the no-renal cohort (inpatient: 0.14 vs 0.02; $P < .0001$; outpatient: 1.61 vs 0.93; $P < .0001$; ED: 0.21 vs 0.03; $P < .0001$) (Table 3). Further, adjusted mean health care costs PPPM were approximately 4-fold higher in the renal cohort compared with the no-renal cohort (\$3703 vs \$774; $P < .0001$). Medical costs were higher in the renal cohort compared with the no-renal cohort after adjusting for covariates (\$3612 vs \$614 PPPM; $P < .0001$) and, as in the CV and HF cohorts, were the major contributor to health care costs. Similar to the other comparisons, adjusted pharmacy costs PPPM were higher in the renal cohort compared with the no-renal cohort (\$171 vs \$117; $P < .0001$).

CLINICAL

TABLE 1. All-Cause HCRU and Costs Among All Patients With and Without CV-Related Hospitalizations^a

Measure	CV (n = 221,229)	No CV (n = 221,229)	P
HCRU and costs, PPPM, mean (95% CI)			
Inpatient stays	0.10 (0.09-0.11)	0.01 (0.01-0.01)	<.0001
Outpatient visits	1.44 (1.41-1.47)	0.82 (0.81-0.84)	<.0001
ED visits	0.17 (0.16-0.18)	0.02 (0.02-0.02)	<.0001
Health care cost ^b	2686 (2617-2756)	510 (497-523)	<.0001
Medical cost	2642 (2567-2720)	366 (355-377)	<.0001
Inpatient cost	1342 (1283-1403)	48 (46-51)	<.0001
Outpatient cost	408 (397-419)	175 (170-180)	<.0001
ED cost	159 (154-165)	29 (28-30)	<.0001
Pharmacy cost	138 (135-142)	98 (95-100)	<.0001

CV, cardiovascular; ED, emergency department; HCRU, health care resource utilization; PPPM, per patient per month.

^aData from patients with type 2 diabetes in the postindex period were used for this table and adjusted for covariates.

^bMedical plus pharmacy cost PPPM.

TABLE 2. All-Cause HCRU and Costs Among All Patients With and Without HF-Related Hospitalizations^a

Measure	HF (n = 68,126)	No HF (n = 68,126)	P
HCRU and costs, PPPM, mean (95% CI)			
Inpatient stays	0.17 (0.15-0.19)	0.03 (0.03-0.03)	<.0001
Outpatient visits	1.73 (1.69-1.77)	1.00 (0.97-1.03)	<.0001
ED visits	0.25 (0.24-0.27)	0.04 (0.04-0.05)	<.0001
Health care cost ^b	4111 (3956-4271)	930 (894-967)	<.0001
Medical cost	3940 (3774-4113)	753 (720-786)	<.0001
Inpatient cost	2084 (1950-2228)	282 (264-302)	<.0001
Outpatient cost	494 (475-515)	252 (241-262)	<.0001
ED cost	200 (191-210)	46 (44-49)	<.0001
Pharmacy cost	177 (171-184)	131 (126-136)	<.0001

ED, emergency department; HCRU, health care resource utilization; HF, heart failure; PPPM, per patient per month.

^aData from patients with type 2 diabetes in the postindex period were used for this table and adjusted for covariates.

^bMedical plus pharmacy cost PPPM.

TABLE 3. All-Cause HCRU and Costs Among All Patients With and Without Renal-Related Hospitalizations^a

Measure	Renal (n = 120,105)	No renal (n = 120,105)	P
HCRU and costs, PPPM, mean (95% CI)			
Inpatient stays	0.14 (0.13-0.15)	0.02 (0.02-0.02)	<.0001
Outpatient visits	1.61 (1.58-1.64)	0.93 (0.91-0.95)	<.0001
ED visits	0.21 (0.20-0.22)	0.03 (0.03-0.03)	<.0001
Health care cost ^b	3703 (3596-3814)	774 (752-798)	<.0001
Medical cost	3612 (3495-3734)	614 (593-635)	<.0001
Inpatient cost	1943 (1843-2048)	210 (199-221)	<.0001
Outpatient cost	442 (429-456)	210 (203-216)	<.0001
ED cost	176 (170-183)	39 (37-40)	<.0001
Pharmacy cost	171 (166-175)	117 (113-120)	<.0001

ED, emergency department; HCRU, health care resource utilization; PPPM, per patient per month.

^aData from patients with type 2 diabetes in the postindex period were used for this table and adjusted for covariates.

^bMedical plus pharmacy cost PPPM.

This finding suggests that amid the burden of T2D and competing interests in effectively managing modifiable metabolic risk factors, patients may be receiving more insulin compared with other antidiabetic agents. Future research should look into insulin prescribing in these groups over a longer time window and assess whether there is a greater increase in prescribing in one group over another.

Similar to our findings, results reported by the ADA and others have shown rising HCRU and costs in patients with diabetes.^{1,7,22} This may be expected because patients with T2D have a high comorbidity burden^{2,6,16} and are at higher risks of hospitalization and death.³ Our results reflect these facts and are in agreement with studies that have reported increases in HCRU and costs between patients with and without comorbid HF or CV disease.²³⁻²⁵ Bogner et al, using data from a Medicare claims database, reported that patients with comorbid diabetes and HF had higher annual average total costs (\$32,676) compared with patients with diabetes and without HF (\$10,566) and higher average lengths of inpatient stays (26.6 days vs 9.9 days).²³ Other studies focused on increases in resource utilization and costs due to comorbid CV disease or HF during the last months of life.^{24,25} A large proportion of these costs are expected to be borne by patients 65 years and older enrolled in Medicare health plans.¹

Besides the direct cost of treating comorbid conditions, higher HCRU and costs in patients with diabetes and concurrent comorbidities may be due to several reasons. Existence of multiple comorbidities presents great challenges to physicians treating patients with diabetes, when screening and treatment needs can far exceed the limited time available during a typical office visit.^{17,26} Comorbidities can also directly or indirectly hamper self-management when they take a toll on the patient's functional ability and/or mental health, resulting in lower quality of life and less desirable health outcomes.²⁷⁻³⁰ On a positive note, the comorbid conditions studied in this research—namely, CV disease, HF, and renal disease—are considered “concordant” with diabetes under the typology proposed by Piette and Kerr, meaning they share

DISCUSSION

Our study contributes to the current literature by examining real-world evidence for patients with T2D with regard to comorbid conditions resulting in incremental HCRU and subsequent costs. We found that, after adjusting for covariates, cohorts with comorbidity-related hospitalizations had approximately 6- to 10-fold higher inpatient hospitalizations, 1.7-fold higher outpatient visits, and 6- to 9-fold higher ED visits. Total health care costs were 4- to 5-fold higher in patients with comorbidity-related hospitalizations; a large proportion of these costs stemmed from medical expenses.

Interestingly, the CV, HF, and renal cohorts had lower mean numbers of classes of oral antidiabetic medications and of prescriptions for GLP-1 agonists but higher mean numbers of prescriptions for insulins.

common parts of the same overall pathophysiologic risk profile and thus are more likely to be addressed concurrently within the same disease management plan.¹⁷ Given the burden of these comorbidities and their concordant nature, there are opportunities to prioritize the comanagement of these conditions and improve health outcomes in patients with T2D. In fact, frameworks have been proposed to identify points of intervention and improve care for patients with multiple chronic conditions,³¹ specifically for those with concurrent diabetes and comorbidities.¹⁷ This work will be important to build out, in particular for health plans and health care stakeholders to continue to support and promote care coordination activities.

Limitations

This study has several limitations, including that this was a retrospective observational study using administrative claims data. Therefore, all information captured assumes completeness of the record of medical visits. Also, lack of laboratory values in the claims data limits the study in determining the incremental cost burden while adjusting for certain clinical factors relevant to the population with diabetes, such as A1C and estimated glomerular filtration rate. Additionally, this study utilized data with a Medicare-rich member population, so the results may not be generalizable, particularly to commercial plans, although these plans are provided to large numbers of members with diverse characteristics who reside in a broad array of geographic regions. No causal inference can be ascertained from this study because it is an observational study utilizing retrospective claims data. Finally, relationships between inpatient hospitalization status and outcomes were established based on statistical associations and temporal relationships; as such, causal inference may not be directly determined.

CONCLUSIONS

After controlling for baseline differences in patient characteristics, patients with T2D experiencing CV-, HF-, or renal-related hospitalizations incurred higher HCRU and costs compared with those not experiencing these hospitalizations. Such information could help multiple health care stakeholders develop targeted disease management plans leading to improved outcomes for these patients. ■

Author Affiliations: Humana Healthcare Research Inc (SA, YL, CM), Louisville, KY; Boehringer Ingelheim Pharmaceuticals Inc (SG, SS), Ridgefield, CT; Humana Inc (TP), Louisville, KY.

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Authorship Information: Concept and design (SA, SG, YL, CM, SS, TP); acquisition of data (SG, YL); analysis and interpretation of data (SA, SG, YL, CM); drafting of the manuscript (SA, YL, CM, SS); critical revision of the manuscript for important intellectual content (YL, CM, SS, TP); statistical analysis (YL); obtaining funding (SG); and supervision (SG, YL, TP).

Address Correspondence to: Yong Li, PhD, Humana Healthcare Research Inc, 515 Market St, Louisville, KY 40202. Email: yli4@humana.com.

REFERENCES

- American Diabetes Association. Economic costs of diabetes in the U.S. in 2017. *Diabetes Care*. 2018;41(5):917-928. doi:10.2337/dci18-0007
- National diabetes statistics report, 2017. American Diabetes Association. 2017. Accessed May 31, 2019. <https://dev.diabetes.org/sites/default/files/2019-06/cdc-statistics-report-2017.pdf>
- Cavender MA, Steg PG, Smith SC Jr, et al. Impact of diabetes mellitus on hospitalization for heart failure, cardiovascular events, and death: outcomes at 4 years from the Reduction of Atherothrombosis for Continued Health (REACH) registry. *Circulation*. 2015;132(10):923-931. doi:10.1161/CIRCULATIONAHA.114.014796
- National Diabetes Data Group. *Diabetes in America*. 2nd ed. National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases; 1995.
- Campbell RK. Type 2 diabetes: where we are today: an overview of disease burden, current treatments, and treatment strategies. *J Am Pharm Assoc* (2003). 2009;49(suppl 1):S3-S9. doi:10.1331/JAPhA.2009.09077
- Costantino ME, Stacy JN, Song F, Xu Y, Bouchard JR. The burden of diabetes mellitus for Medicare beneficiaries. *Popul Health Manag*. 2014;17(5):272-278. doi:10.1089/pop.2013.0097
- Fraze T, Jiang HJ, Burgess J. Hospital stays for patients with diabetes, 2008. Agency for Healthcare Research and Quality. August 2010. Accessed May 31, 2019. <https://www.hcup-us.ahrq.gov/reports/statbriefs/sb93.pdf>
- Murphy D, McCulloch CE, Lin F, et al; Centers for Disease Control and Prevention Chronic Kidney Disease Surveillance Team. Trends in prevalence of chronic kidney disease in the United States. *Ann Intern Med*. 2016;165(7):473-481. doi:10.7326/M16-0273
- Stratton IM, Adler AI, Neil HA, et al. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. *BMJ*. 2000;321(7258):405-412. doi:10.1136/bmj.321.7258.405
- Iribarren C, Karter AJ, Go AS, et al. Glycemic control and heart failure among adult patients with diabetes. *Circulation*. 2001;103(22):2668-2673. doi:10.1161/01.cir.103.22.2668
- Williams R, Van Gaal L, Lucioni C, CODE-2 Advisory Board. Assessing the impact of complications on the costs of type 1 diabetes. *Diabetologia*. 2002;45(7):S13-S17. doi:10.1007/s00125-002-0859-9
- Kalyani RR, Saudek CD, Brancati FL, Selvin E. Association of diabetes, comorbidities, and A1C with functional disability in older adults: results from the National Health and Nutrition Examination Survey (NHANES), 1999-2006. *Diabetes Care*. 2010;33(5):1055-1060. doi:10.2337/dc09-1597
- Ward BW, Schiller JS. Prevalence of multiple chronic conditions among US adults: estimates from the National Health Interview Survey, 2010. *Prev Chronic Dis*. 2013;10:E65. doi:10.5888/pcd10.120203
- Schäfer I, von Leitner EC, Schön G, et al. Multimorbidity patterns in the elderly: a new approach of disease clustering identifies complex interrelations between chronic conditions. *PLoS One*. 2010;5(12):e15941. doi:10.1371/journal.pone.0015941
- Fox CS, Matsushita K, Woodward M, et al; Chronic Kidney Disease Prognosis Consortium. Associations of kidney disease measures with mortality and end-stage renal disease in individuals with and without diabetes: a meta-analysis. *Lancet*. 2012;380(9854):1662-1673. doi:10.1016/S0140-6736(12)61350-6. Published correction appears in *Lancet*. 2013;381(9864):374. doi:10.1016/S0140-6736(13)60172-5
- Dall TM, Mann SE, Zhang Y, et al. Distinguishing the economic costs associated with type 1 and type 2 diabetes. *Popul Health Manag*. 2009;12(2):103-110. doi:10.1089/pop.2009.12203
- Piette JD, Kerr EA. The impact of comorbid chronic conditions on diabetes care. *Diabetes Care*. 2006;29(3):725-731. doi:10.2337/diacare.29.03.06.dc05-2078
- Ware MG, Flavell CM, Lewis EF, Nohria A, Warner-Stevenson L, Givertz MM. Heart failure and diabetes: collateral benefit of chronic disease management. *Congest Heart Fail*. 2006;12(3):132-136. doi:10.1111/j.1527-5299.2005.05354.x
- Zimman B, Wanner C, Lachin JM, et al; EMPA-REG OUTCOME Investigators. Empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes. *N Engl J Med*. 2015;373(22):2117-2128. doi:10.1056/NEJMoa1504720
- Wanner C, Inzucchi SE, Lachin JM, et al; EMPA-REG OUTCOME Investigators. Empagliflozin and progression of kidney disease in type 2 diabetes. *N Engl J Med*. 2016;375(4):323-334. doi:10.1056/NEJMoa1515920
- Deyo RA, Cherkin DC, Ciol MA. Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. *J Clin Epidemiol*. 1992;45(6):613-619. doi:10.1016/0895-4356(92)90133-8
- McDermott KW, Elixhauser A, Sun R. Trends in hospital inpatient stays in the United States, 2005-2014. Agency for Healthcare Research and Quality. June 2017. Accessed May 31, 2019. <https://www.hcup-us.ahrq.gov/reports/statbriefs/sb225-Inpatient-US-Stays-Trends.jsp>
- Bogner HR, Miller SD, de Vries HF, Chhatre S, Jayadevappa R. Assessment of cost and health resource utilization for elderly patients with heart failure and diabetes mellitus. *J Card Fail*. 2010;16(6):454-460. doi:10.1016/j.cardfail.2010.01.007
- Shetty S, Stafkey-Mailey D, Yue B, et al. The cost of cardiovascular-disease-related death in patients with type 2 diabetes mellitus. *Curr Med Res Opin*. 2018;34(6):1081-1087. doi:10.1080/03007995.2018.1445620
- Obi EN, Swindle JP, Turner SJ, Russo PA, Altan A. Health care costs for patients with heart failure escalate nearly 3-fold in final months of life. *J Manag Care Spec Pharm*. 2016;22(12):1446-1456. doi:10.18553/jmcp.2016.22.12.1446
- Yarnall KS, Pollak KI, Ostbye T, Krause KM, Michener JL. Primary care: is there enough time for prevention? *Am J Public Health*. 2003;93(4):635-641. doi:10.2105/ajph.93.4.635
- Ciechanowski PS, Katon WJ, Russo JE. Depression and diabetes: impact of depressive symptoms on adherence, function, and costs. *Arch Intern Med*. 2000;160(21):3278-3285. doi:10.1001/archinte.160.21.3278
- Krein SL, Heisler M, Piette JD, Makkfi F, Kerr EA. The effect of chronic pain on diabetes patients' self-management. *Diabetes Care*. 2005;28(1):65-70. doi:10.2337/diacare.28.1.65
- Schoenberg NE, Drungle SC. Barriers to non-insulin dependent diabetes mellitus (NIDDM) self-care practices among older women. *J Aging Health*. 2001;13(4):443-466. doi:10.1177/089826430101300401
- Glasgow RE, Ruggiero L, Eakin EG, Dryfoos J, Chobanian L. Quality of life and associated characteristics in a large sample of adults with diabetes. *Diabetes Care*. 1997;20(4):562-567. doi:10.2337/diacare.20.4.562
- About the Multiple Chronic Conditions Initiative. HHS. September 2011. Accessed May 31, 2019. <https://www.hhs.gov/ash/about-ash/multiple-chronic-conditions/about-mcc/index.html>

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eAppendix methods

eAppendix Table 1. Diagnosis Codes for Identification of Patients with Cardiovascular, Heart Failure or Renal Related Hospitalizations

Diagnosis Codes for Identification of Cardiovascular Related Hospitalizations

Cardiovascular, Cerebrovascular and Peripheral Vascular Disease	ICD-9 Diagnosis Code
Cardiovascular Disease	
Aortic and other aneurysms	441, 442
Hypotension	458
Angina	413
Conduction disorders and cardiac dysrhythmias	426–427
Arteriosclerotic cardiovascular disease	429.2
Cardiomegaly	429.3
Cardiomyopathy	425
Other acute and subacute forms of ischemic heart disease	411
Diabetes with peripheral circulatory disorders	250.7
Myocardial degeneration	429.1
Myocardial infarction	410, 412
Other chronic ischemic heart disease	414
Hypertension	401–405
Peripheral Vascular Disease	
Atherosclerosis	440
Embolism and thrombosis, structure of artery	444, 447.1
Other peripheral vascular disease	443
Other disorders of circulatory system	459
Phlebitis and thrombophlebitis, portal vein thrombosis, thrombolism, and venous thrombolism	451, 452
Other venous embolism and thrombolism	453
Varicose veins of lower extremities	454
Gangrene and amputations	785.4, 885–887, 895–897
Chronic ulcer of skin	707
Cerebrovascular Disease	
Occlusion of cerebral arteries	434
Hemorrhagic stroke	430–432
Late effects of cerebrovascular disease	438
Occlusion of stenosis of precerebral arteries	433
Other and ill-defined cerebrovascular disease	437
Acute, but ill-defined, cerebrovascular disease	436
Transient ischemic attacks	435

Reference: American Diabetes Association. Economic costs of diabetes in the U.S. in 2012. Diabetes Care. 2013 Apr;36(4):1033-46.

Diagnosis Codes for Identification of Heart Failure Related Hospitalizations

Heart Failure	ICD-9 Diagnosis Code
Heart Failure	428

Reference: American Diabetes Association. Economic costs of diabetes in the U.S. in 2012. Diabetes Care. 2013 Apr;36(4):1033-46.

Diagnosis Codes for Identification of Renal Related Hospitalizations

Renal Complications	ICD-9 Diagnosis Code
Infections of kidney	590
Other disorders of bladder	596
Cystitis	595
Renal sclerosis, unspecified	587
Glomerulonephritis, nephrotic syndrome, nephritis, and nephropathy	580-583
Proteinuria	791.0
Renal failure and its sequelae	584, 586, 588
Other disorders of kidney and ureter	593
Urinary tract infection	599.0
Diabetes and renal complications	250.4
Chronic renal failure (ESRD)	585

Reference: American Diabetes Association. Economic costs of diabetes in the U.S. in 2012. Diabetes Care. 2013 Apr;36(4):1033-46.

eAppendix Table 2. GPI codes for Insulin and non-insulin glucose-lowering medications

Antidiabetic Class	Drugs in class	GPI code
Oral Antidiabetic Medications		
Biguanides *	metformin	2725
Sulfonylureas	chlorpropamide, glimepiride, glipizide, glyburide, tolazamide, tolbutamide	2720
Thiazolidinediones (TZDs)	Actos (pioglitazone), Avandia (rosiglitazone)	2760
Amylin agonists	Symlin (pramlintide)	2715
Meglitinides	Prandin (repaglinide), Starlix (nateglinide)	2723, 2728
Alpha-glucosidase inhibitors	Precose (acarbose), Glyset (miglitol)	2750
Dipeptidyl peptidase-4 (DPP-4) inhibitors	Januvia (sitagliptin), Onglyza (saxagliptin), Tradjenta (linagliptin), Nesina (alogliptin)	2755
SGLT-2 Inhibitors	Invokana (canagliflozin), Farxiga (dapagliflozin), Jardiance (empagliflozin)	2770
Bile acid sequestrants	Welchol (colesevelam)	3910001610
Dopamine-2 agonists	Cycloset (bromocriptine)	2757
Glucagon		2730001010, 2730001015
Oral fixed dose combinations	All combinations	2799
Glucagon-like peptide-1 (GLP-1) receptor agonists	Byetta (exenatide), Victoza (liraglutide), Bydureon (exenatide), Tanzeum (albiglutide), Trulicity (dulaglutide)	2717
Insulin	All insulins	2710

eAppendix Table 3. GPI Codes for Cardiovascular Medications

GPI-2 Code	Cardiovascular Medication Class
31*	Cardiotonics
32*	Antianginal Agents
33*	Beta Blockers
34*	Calcium Channel Blockers
35*	Antiarrhythmics
36*	Antihypertensives
37*	Diuretics
38*	Vasopressors
39*	Antihyperlipidemics
40*	Cardiovascular Agents-Misc.

Reference: Feldman SR, Zhao Y, Shi L, Tran MH. Economic and Comorbidity Burden Among Patients with Moderate-to-Severe Psoriasis. *J Manag Care Spec Pharm.* 2015 Oct;21(10):874-88.

eAppendix Table 4. Diabetes Complications Severity Index Diagnosis Codes

Complication	ICD-9 Diagnosis	ICD9	Weight *
Retinopathy	Diabetic ophthalmologic disease	250.5x	1
Retinopathy	Background retinopathy	362.01	1
Retinopathy	Other retinopathy	362.1	1
Retinopathy	Retinal edema	362.83	1
Retinopathy	Cystoid macular edema/degeneration	362.53	1
Retinopathy	Other retinal disorders	362.81, 362.82	1
Retinopathy	Proliferative retinopathy	362.02	2
Retinopathy	Retinal detachment	361.xx	2
Retinopathy	Blindness	369.xx .00-.99	2
Retinopathy	Vitreous hemorrhage	379.23	2
Nephropathy	Diabetic nephropathy	250.4	1
Nephropathy	Acute glomerulonephritis	580	1
Nephropathy	Nephrotic syndrome	581	1
Nephropathy	Hypertension, nephrosis	581.81	1
Nephropathy	Chronic glomerulonephritis	582	1
Nephropathy	Nephritis/nephropathy	583	1
Nephropathy	Chronic renal failure	585	2
Nephropathy	Renal failure, not otherwise specified	586	2
Nephropathy	Renal insufficiency	593.9	2
	Urine protein >30 mg/g of creatinine, or (+) dipstick protein or serum creatinine >1.5 mg/dL		1
	Serum creatinine >2.0 mg/dL		2
Neuropathy	Diabetic neuropathy	356.9, 250.6	1
Neuropathy	Amyotrophy	358.1	1
Neuropathy	Cranial nerve palsy	951.0, 951.1, 951.3	1
Neuropathy	Mononeuropathy	354.0-355.9	1
Neuropathy	Charcot's arthropathy	713.5	1
Neuropathy	Polyneuropathy	357.2	1
Neuropathy	Neurogenic bladder	596.54	1
Neuropathy	Autonomic neuropathy	337.0, 337.1	1
Neuropathy	Gastroparesis/diarrhea	564.5, 536.3	1
Neuropathy	Orthostatic hypotension	458	1
Cerebrovascular	Transient ischemic attack	435	1
Cerebrovascular	Stroke	431, 433, 434, 436	2

Complication	ICD-9 Diagnosis	ICD9	Weight *
Cardiovascular	Atherosclerosis	440.xx	1
Cardiovascular	Other ischemic heart disease	411	1
Cardiovascular	Angina pectoris	413	1
Cardiovascular	Other chronic IHD	414	1
Cardiovascular	Myocardial infarction	410	2
Cardiovascular	Ventricular fibrillation, arrest	427.1, 427.3	2
Cardiovascular	Atrial fibrillation, arrest	427.4, 427.5	2
Cardiovascular	Other atherosclerotic cardiovascular disease	429.2	1
Cardiovascular	Old myocardial infarction	412	2
Cardiovascular	Heart failure	428	2
Cardiovascular	Atherosclerosis, severe	440.23, 440.24	2
Cardiovascular	Aortic aneurysm/dissection	441	2
PVD	Diabetic peripheral vascular disease	250.7	1
PVD	Other aneurysm	442.3	1
PVD	PVD	443.81, 443.9	1
PVD	Foot wound + complication	892.1	1
PVD	Claudication, intermittent	443.9	1
PVD	Embolism/thrombosis (lower extremity)	444.22	2
PVD	Gangrene	785.4	2
PVD	Gas gangrene	040.0	2
PVD	Ulcer of lower limbs	707.1	2
Metabolic	Ketoacidosis	250.1	2
Metabolic	Hyperosmolar	250.2	2
Metabolic	Other coma	250.3	2

* Bessie Ann Young and Elizabeth Lin et al. Diabetes Complications Severity Index and Risk of Mortality, Hospitalization, and Healthcare Utilization. Am J Manag Care. 2008 January ; 14(1): 15–23.

eAppendix Table 5. Deyo Charlson Comorbidity Categories and Associated Diagnosis Codes and Weights

Enhanced (Quan, 2005) Coding Algorithm for Charlson Comorbidities

Number	Comorbidity	ICD-9-CM Codes	Weight
1	Myocardial Infarction	410.x, 412.x	1
2	Congestive Heart Failure	398.91, 402.01, 402.11, 402.91, 404.01, 404.03, 404.11, 404.13, 404.91, 404.93, 425.4–425.9, 428.x	1
3	Peripheral Vascular Disease	093.0, 440.x, 441.x, 443.1–443.9, 557.1, 557.9, V43.4	1
4	Cerebrovascular Disease	362.34, 430.x–438.x	1
5	Dementia	290.x, 294.1, 331.2	1
6	Chronic Pulmonary Disease	416.8, 416.9, 490.x–505.x, 506.4, 508.1, 508.8	1
7	Connective Tissue Disease	446.5, 710.0–710.4, 714.0–714.2, 714.8, 725.x	1
8	Peptic Ulcer Disease	531.x–534.x	1
9	Mild Liver Disease	070.22, 070.23, 070.32, 070.33, 070.44, 070.54, 070.6, 070.9, 570.x, 571.x, 573.3, 573.4, 573.8, 573.9, V42.7	1
10	Diabetes without Complications	250.0–250.3, 250.8, 250.9	1
11	Diabetes with Complications	250.4–250.7	2
12	Paraplegia and Hemiplegia	334.1, 342.x, 343.x, 344.0–344.6, 344.9	2
13	Renal Disease	403.01, 403.11, 403.91, 404.02, 404.12, 404.92, 582.x, 583.0–583.7, 585.x, 586.x, 588.0, V42.0, V45.1, V56.x	2
14	Cancer (Including Leukemia and Lymphoma)	140.x–172.x, 174.x–195.8, 200.x–208.x, 238.6	2
15	Moderate or Severe Liver Disease	456.0–456.2, 572.2–572.8	3
16	Metastatic Carcinoma	196.x–199.x	6
17	Acquired Immunodeficiency Syndrome (AIDS)	042.x–044.x	6

*ICD-9-CM Procedural Code

References

- ¹Deyo RA, Cherkin DC, and Ciol MA. Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. *Journal of Clinical Epidemiology* 1992; 45: 613-619.
- ²Quan H, Sundararajan V, Halfon P, Fong A, Burnand B, Luthi J-C, Saunders LD, Beck CA, Feasby TE, Ghali WA. Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. *Medical Care* 2005;43(11):1130-1139.
- ³Klabunde CN, Potosky AL, Legler JM, and Warren JL. Development of a comorbidity index using physician claims data. *Journal of Clinical Epidemiology*. 2000; 53:1258-1267.

eAppendix Table 6. CPT codes for Identification of HbA1c Testing

Code	Description	Code Type	Code Category
3044F	Most recent hemoglobin A1c (HbA1c) level less than 7.0% (DM)	CPT	HbA1C
3045F	Most recent hemoglobin A1c (HbA1c) level 7.0-9.0% (DM)	CPT	HbA1C
3046F	Most recent hemoglobin A1c level greater than 9.0% (DM)	CPT	HbA1C
83036	Hemoglobin A1c (glycosylated hemoglobin)	CPT	HbA1C
83037	Hemoglobin A1c (glycosylated hemoglobin)	CPT	HbA1C

eAppendix Table 7. ICD Codes for Comorbid Conditions

Comorbid Conditions	ICD 9 CM Codes
Acute heart failure	398.91, 402.01, 402.11, 402.91, 404.01, 404.03, 404.11, 404.13, 404.91, 404.93, 428.0, 428.1, 428.20, 428.21, 428.22, 428.23, 428.30, 428.31, 428.32, 428.33, 428.40, 428.41, 428.42, 428.43, 428.9
Acute myocardial infarction	410.00, 410.01, 410.02, 410.10, 410.11, 410.12, 410.20, 410.21, 410.22, 410.30, 410.31, 410.32, 410.40, 410.41, 410.42, 410.50, 410.51, 410.52, 410.60, 410.61, 410.62, 410.70, 410.71, 410.72, 410.80, 410.81, 410.82, 410.90, 410.91, 410.92
Alcohol use	303.00, 303.01, 303.02, 303.03, 303.90, 303.91, 303.92, 303.93, 305.00, 305.01, 305.02, 305.03
Amputations	895.0, 895.1, 896.0, 896.1, 896.2, 896.3, 897.0, 897.1, 897.2, 897.3, 897.4, 897.5, 897.6, 897.7, V49.71, V49.72, V49.73, V49.74, V49.75, V49.76
Amputations (procedure codes)	84.11, 84.12, 84.13, 84.14, 84.15
Chronic kidney disease	249.40, 249.41, 250.40, 250.41, 250.42, 250.43, 285.21, 403.00, 403.01, 403.10, 403.11, 403.90, 403.91, 404.00, 404.01, 404.02, 404.03, 404.10, 404.11, 404.12, 404.13, 404.90, 404.91, 404.92, 404.93, 405.01, 405.11, 405.91, 458.21, 581.81, 582.0, 582.1, 582.2, 582.4, 582.81, 582.89, 582.9, 583.0, 583.1, 583.2, 583.4, 583.6, 583.7, 583.81, 583.89, 583.9, 585.1, 585.2, 585.3, 585.4, 585.5, 585.6, 585.9, 587, 588.0, 588.81, 588.89, 588.9, 590.00, 590.01, 590.80, 590.81, 593.71, 593.72, 593.73, 792.5, 996.56, 996.68, 996.73, 996.81, V42.0, V45.11, V45.12, V56.0, V56.1, V56.2, V56.31, V56.32, V56.8
Coronary artery disease	414.01
Erectile dysfunction or male impotence	607.84
Gastrointestinal autonomic dysfunction	536.3, 564.5, 564.81, 564.89

Hyperlipidemia	272.0, 272.1, 272.2, 272.3, 272.4
Hypertension	401.0, 401.1, 401.9
Ischemic heart disease	410.00, 410.01, 410.02, 410.10, 410.11, 410.12, 410.20, 410.21, 410.22, 410.30, 410.31, 410.32, 410.40, 410.41, 410.42, 410.50, 410.51, 410.52, 410.60, 410.61, 410.62, 410.70, 410.71, 410.72, 410.80, 410.81, 410.82, 410.90, 410.91, 410.92, 411.0, 411.1, 411.81, 411.89, 412, 413.0, 413.1, 413.9, 414.00, 414.01, 414.02, 414.03, 414.04, 414.05, 414.06, 414.07, 414.10, 414.11, 414.12, 414.19, 414.2, 414.3, 414.4, 414.8, 414.9, 429.71, 429.79, V45.81, V45.82
Ischemic stroke or transient ischemic attack	346.60, 346.61, 346.62, 346.63, 362.34, 362.35, 433.01, 433.11, 433.21, 433.31, 433.81, 433.91, 434.01, 434.11, 434.91, 435.0, 435.1, 435.2, 435.3, 435.8, 435.9, 436
Lower limb abscess or ulcer	454.0, 454.2, 680.6, 680.7, 681.10, 681.9, 682.6, 682.7, 682.9, 707.00, 707.01, 707.02, 707.03, 707.04, 707.05, 707.06, 707.07, 707.09, 707.10, 707.11, 707.12, 707.13, 707.14, 707.15, 707.19, 707.20, 707.21, 707.22, 707.23, 707.24, 707.25, 707.8, 707.9, 730.06, 730.07, 730.08, 730.09, 785.4, 997.60, 997.61, 997.62, 997.69
Neuropathy	249.60, 249.61, 250.60, 250.61, 337.1, 357.2, 357.4, 354.0, 354.1, 354.2, 354.3, 354.4, 354.5, 354.8, 354.9, 355.0, 355.1, 355.2, 355.3, 355.4, 355.5, 355.6, 355.71, 355.79, 355.8, 355.9, 358.1, 536.3, 713.5
Peripheral vascular arterial surgery	250.70, 250.71, 250.72, 250.73, 440.20, 440.21, 440.22, 440.23, 440.24, 440.29, 440.30, 440.31, 440.32, 440.4, 440.8, 440.9, 442.0, 442.2, 442.3, 442.81, 442.82, 442.89, 442.9, 443.22, 443.29, 443.89, 443.9, 444.21, 444.22, 444.81, 444.89, 444.9, 445.01, 445.02, 445.89
Diabetic retinopathy and other eye complications	249.50, 249.51, 250.50, 250.51, 250.52, 250.53, 362.01, 362.02, 362.03, 362.04, 362.05, 362.06, 362.07, 362.10, 362.14, 362.16, 362.30, 362.31, 362.32, 362.33, 362.40, 362.41, 362.42, 362.43, 362.81, 362.82, 362.83, 362.84, 362.85, 362.89, 364.22, 365.00, 365.01, 365.02, 365.03, 365.04, 365.05, 365.06, 365.10, 365.11, 365.12, 365.13, 365.14, 365.15, 365.44, 365.60, 365.63, 365.81, 365.89, 365.9, 366.31, 366.41, 366.8, 366.9, 377.14, 379.23, 369.00, 369.01, 369.02, 369.03, 369.04, 369.05, 369.06, 369.07, 369.08, 369.10, 369.11, 369.12, 369.13, 369.14, 369.15, 369.16, 369.17, 369.18, 369.20, 369.21, 369.22, 369.23, 369.24, 369.25, 369.3, 369.4, 369.60, 369.61, 369.62, 369.63, 369.64, 369.65, 369.66, 369.67, 369.68, 369.69, 369.70, 369.71, 369.72, 369.73, 369.74, 369.75, 369.76, 369.8, 369.9.
Skin complications	681.00, 681.01, 681.02, 681.10, 681.11, 681.9, 682.0, 682.1, 682.2, 682.3, 682.4, 682.5, 682.6, 682.7, 682.8,

	682.9, 707.00, 707.01, 707.02, 707.03, 707.04, 707.05, 707.06, 707.07, 707.09, 707.10, 707.11, 707.12, 707.13, 707.14, 707.15, 707.19, 707.20, 707.21, 707.22, 707.23, 707.24, 707.25, 707.8, 707.9, 785.4
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eAppendix Table 8. Baseline Demographic Characteristics of CV and no CV Cohorts

Measure	Medicare Cohorts			Commercial Cohorts		
	CV	no CV	P-value	CV	no CV	P-value
n	204,398	184,325		16,831	36,904	
Age, mean (SD)	72.59 (\pm 8.53)	70.30 (\pm 7.97)	<.0001	57.35 (\pm 9.94)	53.65 (\pm 9.85)	<.0001
Gender = female (vs. male), n (%)	96900 (47.4%)	94771 (51.4%)	<.0001	7565 (44.9%)	19004 (51.5%)	<.0001
Race/ethnicity, n (%)						
White	167925 (82.2%)	145007 (78.7%)	<.0001			
Black	27113 (13.3%)	27978 (15.2%)				
Hispanic	3201 (1.6%)	3057 (1.7%)				
Other	4719 (2.3%)	6598 (3.6%)				
Unknown	1440 (0.7%)	1685 (0.9%)				
Geographic region, n (%)						
Northeast	5179 (2.5%)	4794 (2.6%)	<.0001	30 (0.2%)	60 (0.2%)	<.0001
Midwest	49337 (24.1%)	40452 (21.9%)		4914 (29.2%)	9705 (26.3%)	
South	130981 (64.1%)	118721 (64.4%)		11414 (67.8%)	25666 (69.5%)	
West	18901 (9.2%)	20358 (11.0%)		473 (2.8%)	1472 (4.0%)	
Low Income Subsidy recipients, n (%)	24669 (12.1%)	18722 (10.2%)	<.0001			
Population density						
Urban	127448 (62.4%)	113077 (61.3%)	<.0001	12952 (77.0%)	27987 (75.8%)	0.0364
Suburban	51716 (25.3%)	47600 (25.8%)		2867 (17.0%)	6632 (18.0%)	
Rural	23763 (11.6%)	22254 (12.1%)		860 (5.1%)	1925 (5.2%)	
Unknown	1471 (0.7%)	1394 (0.8%)		152 (0.9%)	360 (1.0%)	

SD: standard deviation.

Note: Race/ethnicity and Low Income Subsidy status not available for patients enrolled in commercial health plans.

eAppendix Table 9. Baseline Demographic Characteristics of HF and no HF Cohorts

Measure	Medicare Cohorts			Commercial Cohorts		
	HF		P-value	HF		P-value
n	65,582	60,656		2,544	7,470	
Age, mean (SD)	73.99 (±8.57)	71.53 (±8.26)	<.0001	60.93 (±10.61)	55.21 (±9.92)	<.0001
Gender = female (vs. male), n (%)	28572 (43.6%)	31056 (51.2%)	<.0001	1004 (39.5%)	3872 (51.8%)	<.0001
Race/ethnicity, n (%)						
White	54485 (83.1%)	48742 (80.4%)	<.0001			
Black	8552 (13.0%)	8754 (14.4%)				
Hispanic	902 (1.4%)	1014 (1.7%)				
Other	1225 (1.9%)	1793 (3.0%)				
Unknown	418 (0.6%)	353 (0.6%)				
Geographic region, n (%)						
Northeast	1676 (2.6%)	1431 (2.4%)	<.0001	5 (0.2%)	17 (0.2%)	<.0001
Midwest	16665 (25.4%)	13327 (22.0%)		878 (34.5%)	1994 (26.7%)	
South	41740 (63.6%)	40086 (66.1%)		1611 (63.3%)	5147 (68.9%)	
West	5501 (8.4%)	5812 (9.6%)		50 (2.0%)	312 (4.2%)	
Low income subsidy recipients, n (%)	9635 (14.7%)	6251 (10.3%)	<.0001			
Population density						
Urban	40321 (61.5%)	38263 (63.1%)	<.0001	1983 (77.9%)	5707 (76.4%)	0.2707
Suburban	17045 (26.0%)	15135 (25.0%)		426 (16.7%)	1312 (17.6%)	
Rural	7782 (11.9%)	6844 (11.3%)		118 (4.6%)	379 (5.1%)	
Unknown	434 (0.7%)	414 (0.7%)		17 (0.7%)	72 (1.0%)	

SD: standard deviation.

Note: Race/ethnicity and Low Income Subsidy status not available for patients enrolled in commercial health plans.

eAppendix Table 10. Baseline Demographic Characteristics of Renal and no Renal Cohorts

Measure	Medicare Cohorts			Commercial Cohorts		
	Renal	no Renal	P-value	Renal	no Renal	P-value
n	114,136	105,461		5,969	14,644	
Age, mean (SD)	73.82 (±8.49)	70.99 (±8.16)	<.0001	59.25 (±10.96)	54.78 (±9.72)	<.0001
Gender = female (vs. male), n (%)	53706 (47.1%)	53778 (51.0%)	<.0001	2729 (45.7%)	7601 (51.9%)	<.0001
Race/ethnicity, n (%)						
White	93286 (81.7%)	84834 (80.4%)	<.0001			
Black	15956 (14.0%)	15063 (14.3%)				
Hispanic	1727 (1.5%)	1729 (1.6%)				
Other	2471 (2.2%)	3145 (3.0%)				
Unknown	696 (0.6%)	690 (0.7%)				
Geographic region, n (%)						
Northeast	2708 (2.4%)	2542 (2.4%)	<.0001	7 (0.1%)	28 (0.2%)	<.0001
Midwest	28484 (25.0%)	23191 (22.0%)		1872 (31.4%)	3861 (26.4%)	
South	72685 (63.7%)	69331 (65.7%)		3913 (65.6%)	10198 (69.6%)	
West	10259 (9.0%)	10397 (9.9%)		177 (3.0%)	556 (3.8%)	
Low income subsidy recipients, n (%)	15707 (13.8%)	10615 (10.1%)	<.0001			
Population density						
Urban	72563 (63.6%)	65312 (61.9%)	<.0001	4712 (78.9%)	11179 (76.3%)	0.0009
Suburban	28301 (24.8%)	26959 (25.6%)		934 (15.6%)	2564 (17.5%)	
Rural	12452 (10.9%)	12367 (11.7%)		272 (4.6%)	748 (5.1%)	
Unknown	820 (0.7%)	823 (0.8%)		51 (0.9%)	153 (1.0%)	

SD: standard deviation.

Note: Race/ethnicity and Low Income Subsidy status not available for patients enrolled in commercial health plans.

eAppendix Table 11. Baseline Clinical Characteristics of CV and Cohorts

Measure	Medicare Cohorts			Commercial Cohorts		
	CV		P-value	CV		P-value
n	204398	184325		16831	36904	
Classes of oral antidiabetic medications, mean (SD)	0.92 (±0.87)	1.03 (±0.86)	<.0001	0.97 (±0.92)	1.15 (±0.84)	<.0001
GLP-1 agonists, mean (SD)	0.04 (±0.49)	0.05 (±0.59)	<.0001	0.16 (±1.10)	0.21 (±1.23)	<.0001
Insulins, mean (SD)	0.83 (±2.71)	0.69 (±2.46)	<.0001	0.85 (±2.71)	0.69 (±2.50)	<.0001
Classes of cardiovascular medications, mean (SD)	3.07 (±1.94)	2.67 (±1.70)	<.0001	2.49 (±1.86)	2.00 (±1.56)	<.0001
Diabetes complications severity index, mean (SD)	2.44 (±2.05)	1.54 (±1.69)	<.0001	1.24 (±1.62)	0.58 (±1.05)	<.0001
Deyo Charlson comorbidity index, mean (SD)	2.57 (±2.25)	1.96 (±1.73)	<.0001	1.57 (±1.84)	1.08 (±1.14)	<.0001
Count of HbA1c tests, mean (SD)	1.88 (±1.36)	2.01 (±1.24)	<.0001	1.42 (±1.26)	1.64 (±1.16)	<.0001
Specialty of prescribing physician, n (%)						
Cardiology	417 (0.2%)	257 (0.1%)	<.0001	42 (0.2%)	77 (0.2%)	<.0001
Endocrinology	< 10	< 10		< 10	57 (0.2%)	
Gastroenterology	118 (0.1%)	144 (0.1%)		12 (0.1%)	91 (0.2%)	
Primary care	116585 (57.0%)	119117 (64.6%)		9593 (57.0%)	25910 (70.2%)	
Other	9108 (4.5%)	9082 (4.9%)		878 (5.2%)	2653 (7.2%)	
Unknown	78167 (38.2%)	55719 (30.2%)		6301 (37.4%)	8116 (22.0%)	
Comorbid conditions, n (%)						
Acute heart failure	19323 (9.5%)	5915 (3.2%)	<.0001	640 (3.8%)	287 (0.8%)	<.0001
Acute myocardial infarction	1203 (0.6%)	313 (0.2%)	<.0001	100 (0.6%)	52 (0.1%)	<.0001
Alcohol use	1573 (0.8%)	807 (0.4%)	<.0001	161 (1.0%)	100 (0.3%)	<.0001
Amputations	526 (0.3%)	189 (0.1%)	<.0001	33 (0.2%)	10 (0.0%)	<.0001
Chronic kidney disease	40665 (19.9%)	25014 (13.6%)	<.0001	1386 (8.2%)	1296 (3.5%)	<.0001
Coronary artery disease	24872 (12.2%)	10618 (5.8%)	<.0001	1192 (7.1%)	940 (2.5%)	<.0001
Erectile dysfunction or male impotence	3082 (1.5%)	3204 (1.7%)	<.0001	198 (1.2%)	460 (1.2%)	0.4933
Gastrointestinal autonomic dysfunction	857 (0.4%)	352 (0.2%)	<.0001	76 (0.5%)	58 (0.2%)	<.0001
Hyperlipidemia	110259 (53.9%)	104382 (56.6%)	<.0001	7676 (45.6%)	17562 (47.6%)	<.0001

Hypertension	137358 (67.2%)	114012 (61.9%)	<.0001	9796 (58.2%)	17675 (47.9%)	<.0001
Ischemic heart disease	35440 (17.3%)	16108 (8.7%)	<.0001	1419 (8.4%)	1157 (3.1%)	<.0001
Ischemic stroke or transient ischemic attack	5757 (2.8%)	2401 (1.3%)	<.0001	247 (1.5%)	195 (0.5%)	<.0001
Lower limb abscess or ulcer	9410 (4.6%)	3553 (1.9%)	<.0001	665 (4.0%)	513 (1.4%)	<.0001
Neuropathy	27788 (13.6%)	19822 (10.8%)	<.0001	1097 (6.5%)	1545 (4.2%)	<.0001
Peripheral vascular arterial surgery	24380 (11.9%)	12823 (7.0%)	<.0001	754 (4.5%)	578 (1.6%)	<.0001
Diabetic retinopathy and other eye complications	24215 (11.8%)	22903 (12.4%)	<.0001	990 (5.9%)	1877 (5.1%)	0.0001
Skin complications	2951 (1.4%)	1589 (0.9%)	<.0001	262 (1.6%)	305 (0.8%)	<.0001

SD: standard deviation.

eAppendix Table 12. Baseline Clinical Characteristics of HF and Cohorts

Measure	Medicare Cohorts			Commercial Cohorts		
	HF		<i>P</i> -value	HF		<i>P</i> -value
n	65582	60656		2544	7470	
Classes of oral antidiabetic medications, mean (SD)	0.84 (±0.86)	1.02 (±0.86)	<.0001	0.89 (±0.92)	1.16 (±0.86)	<.0001
GLP-1 agonists, mean (SD)	0.03 (±0.43)	0.05 (±0.59)	<.0001	0.12 (±0.96)	0.24 (±1.34)	<.0001
Insulins, mean (SD)	1.17 (±3.21)	0.76 (±2.57)	<.0001	1.31 (±3.26)	0.80 (±2.65)	<.0001
Classes of cardiovascular medications, mean (SD)	3.85 (±2.19)	2.90 (±1.76)	<.0001	3.51 (±2.34)	2.25 (±1.61)	<.0001
Diabetes complications severity index, mean (SD)	3.77 (±2.21)	2.10 (±1.97)	<.0001	2.85 (±2.27)	0.88 (±1.36)	<.0001
Deyo Charlson comorbidity index, mean (SD)	3.81 (±2.69)	2.53 (±2.11)	<.0001	3.00 (±2.72)	1.41 (±1.51)	<.0001
Count of HbA1c tests, mean (SD)	1.83 (±1.42)	2.07 (±1.31)	<.0001	1.31 (±1.31)	1.72 (±1.21)	<.0001
Specialty of prescribing physician, n (%)						
Cardiology	160 (0.2%)	108 (0.2%)	<.0001	13 (0.5%)	20 (0.3%)	<.0001
Endocrinology	0	< 10		0	< 10	
Gastroenterology	38 (0.1%)	49 (0.1%)		< 10	18 (0.2%)	
Primary care	34525 (52.6%)	38611 (63.7%)		1301 (51.1%)	5307 (71.0%)	
Other	2901 (4.4%)	3005 (5.0%)		137 (5.4%)	487 (6.5%)	
Unknown	27958 (42.6%)	18881 (31.1%)		1092 (42.9%)	1635 (21.9%)	
Comorbid conditions, n (%)						
Acute heart failure	16203 (24.7%)	2253 (3.7%)	<.0001	476 (18.7%)	76 (1.0%)	<.0001
Acute myocardial infarction	4136 (6.3%)	637 (1.1%)	<.0001	199 (7.8%)	65 (0.9%)	<.0001
Alcohol use	1100 (1.7%)	505 (0.8%)	<.0001	59 (2.3%)	52 (0.7%)	<.0001
Amputations	633 (1.0%)	210 (0.3%)	<.0001	35 (1.4%)	13 (0.2%)	<.0001
Chronic kidney disease	21227 (32.4%)	11544 (19.0%)	<.0001	612 (24.1%)	457 (6.1%)	<.0001
Coronary artery disease	18754 (28.6%)	6752 (11.1%)	<.0001	625 (24.6%)	425 (5.7%)	<.0001
Erectile dysfunction or male impotence	1025 (1.6%)	1267 (2.1%)	<.0001	50 (2.0%)	107 (1.4%)	0.0616
Gastrointestinal autonomic dysfunction	876 (1.3%)	324 (0.5%)	<.0001	44 (1.7%)	24 (0.3%)	<.0001
Hyperlipidemia	38673 (59.0%)	36735 (60.6%)	<.0001	1325 (52.1%)	3896 (52.2%)	0.95

Hypertension	50139 (76.5%)	42016 (69.3%)	<.0001	1765 (69.4%)	4179 (55.9%)	<.0001
Ischemic heart disease	23331 (35.6%)	8829 (14.6%)	<.0001	687 (27.0%)	485 (6.5%)	<.0001
Ischemic stroke or transient ischemic attack	5404 (8.2%)	2272 (3.7%)	<.0001	173 (6.8%)	127 (1.7%)	<.0001
Lower limb abscess or ulcer	6528 (10.0%)	2060 (3.4%)	<.0001	261 (10.3%)	190 (2.5%)	<.0001
Neuropathy	11067 (16.9%)	8844 (14.6%)	<.0001	274 (10.8%)	462 (6.2%)	<.0001
Peripheral vascular arterial surgery	12279 (18.7%)	6488 (10.7%)	<.0001	300 (11.8%)	224 (3.0%)	<.0001
Diabetic retinopathy and other eye complications	8597 (13.1%)	8467 (14.0%)	<.0001	272 (10.7%)	444 (5.9%)	<.0001
Skin complications	2065 (3.1%)	995 (1.6%)	<.0001	91 (3.6%)	96 (1.3%)	<.0001

SD: standard deviation.

eAppendix Table 13. Baseline Clinical Characteristics of Renal and no Renal Cohorts

Measure	Medicare Cohorts			Commercial Cohorts		
	Renal	no Renal	<i>P</i> -value	Renal	no Renal	<i>P</i> -value
n	114136	105461		5969	14644	
Classes of oral antidiabetic medications, mean (SD)	0.88 (±0.87)	1.03 (±0.86)	<.0001	0.96 (±0.93)	1.17 (±0.87)	<.0001
GLP-1 agonists, mean (SD)	0.03 (±0.46)	0.05 (±0.59)	<.0001	0.15 (±1.07)	0.22 (±1.27)	0.0002
Insulins, mean (SD)	1.05 (±3.04)	0.71 (±2.48)	<.0001	1.21 (±3.22)	0.81 (±2.71)	<.0001
Classes of cardiovascular medications, mean (SD)	3.43 (±2.10)	2.89 (±1.77)	<.0001	2.89 (±2.11)	2.21 (±1.62)	<.0001
Diabetes complications severity index, mean (SD)	3.18 (±2.20)	1.91 (±1.84)	<.0001	2.01 (±2.03)	0.77 (±1.22)	<.0001
Deyo Charlson comorbidity index, mean (SD)	3.40 (±2.59)	2.30 (±1.94)	<.0001	2.49 (±2.46)	1.28 (±1.32)	<.0001
Count of HbA1c tests, mean (SD)	1.88 (±1.41)	2.06 (±1.28)	<.0001	1.37 (±1.29)	1.70 (±1.17)	<.0001
Specialty of prescribing physician, n (%)						
Cardiology	220 (0.2%)	188 (0.2%)	<.0001	< 10	31 (0.2%)	<.0001
Endocrinology	< 10	< 10		0	20 (0.1%)	
Gastroenterology	70 (0.1%)	84 (0.1%)		< 10	32 (0.2%)	
Primary care	62523 (54.8%)	68152 (64.6%)		3262 (54.6%)	10308 (70.4%)	
Other	5056 (4.4%)	5103 (4.8%)		375 (6.3%)	1020 (7.0%)	
Unknown	46265 (40.5%)	31933 (30.3%)		2318 (38.8%)	3233 (22.1%)	
Comorbid conditions, n (%)						
Acute heart failure	21422 (18.8%)	6390 (6.1%)	<.0001	617 (10.3%)	244 (1.7%)	<.0001
Acute myocardial infarction	3796 (3.3%)	1063 (1.0%)	<.0001	152 (2.5%)	113 (0.8%)	<.0001
Alcohol use	1663 (1.5%)	797 (0.8%)	<.0001	110 (1.8%)	77 (0.5%)	<.0001
Amputations	771 (0.7%)	207 (0.2%)	<.0001	41 (0.7%)	22 (0.2%)	<.0001
Chronic kidney disease	32518 (28.5%)	15120 (14.3%)	<.0001	1080 (18.1%)	578 (3.9%)	<.0001
Coronary artery disease	22784 (20.0%)	11535 (10.9%)	<.0001	718 (12.0%)	697 (4.8%)	<.0001
Erectile dysfunction or male impotence	1777 (1.6%)	1981 (1.9%)	<.0001	97 (1.6%)	185 (1.3%)	0.0426
Gastrointestinal autonomic dysfunction	1078 (0.9%)	389 (0.4%)	<.0001	61 (1.0%)	48 (0.3%)	<.0001
Hyperlipidemia	65684 (57.5%)	63679 (60.4%)	<.0001	2874 (48.1%)	7513 (51.3%)	<.0001

Hypertension	84600 (74.1%)	71850 (68.1%)	<.0001	3943 (66.1%)	8031 (54.8%)	<.0001
Ischemic heart disease	28596 (25.1%)	15545 (14.7%)	<.0001	852 (14.3%)	826 (5.6%)	<.0001
Ischemic stroke or transient ischemic attack	7912 (6.9%)	3096 (2.9%)	<.0001	290 (4.9%)	192 (1.3%)	<.0001
Lower limb abscess or ulcer	8598 (7.5%)	3096 (2.9%)	<.0001	457 (7.7%)	308 (2.1%)	<.0001
Neuropathy	18534 (16.2%)	14074 (13.3%)	<.0001	592 (9.9%)	852 (5.8%)	<.0001
Peripheral vascular arterial surgery	17850 (15.6%)	10216 (9.7%)	<.0001	488 (8.2%)	358 (2.4%)	<.0001
Diabetic retinopathy and other eye complications	14924 (13.1%)	13910 (13.2%)	0.429	520 (8.7%)	864 (5.9%)	<.0001
Skin complications	2699 (2.4%)	1364 (1.3%)	<.0001	193 (3.2%)	193 (1.3%)	<.0001

SD: standard deviation.

eAppendix Table 14. Baseline All-Cause Healthcare Resource Utilization Costs of CV and Cohorts

Measure	Medicare Cohorts			Commercial Cohorts		
	CV		<i>P</i> -value	CV		<i>P</i> -value
n	204398	184325		16831	36904	
Healthcare resource utilization, n (%)						
Inpatient	38125 (18.7%)	9392 (5.1%)	<.0001	3505 (20.8%)	2100 (5.7%)	<.0001
Outpatient	200606 (98.1%)	182899 (99.2%)	<.0001	16094 (95.6%)	36489 (98.9%)	<.0001
Emergency department	83639 (40.9%)	34740 (18.8%)	<.0001	6314 (37.5%)	6276 (17.0%)	<.0001
Healthcare cost PPPM, mean (SD)	936.70 (±685.20)	548.87 (±322.58)	<.0001	1,460.65 (±1,057.74)	788.90 (±513.76)	<.0001
Medical cost PPPM, mean (SD)	696.31 (±580.04)	343.81 (±268.70)	<.0001	1,134.87 (±1,008.11)	511.01 (±464.52)	<.0001
Inpatient cost PPPM, mean (SD)	171.78 (±407.25)	38.95 (±137.37)	<.0001	317.89 (±647.61)	81.59 (±252.91)	<.0001
Outpatient cost PPPM, mean (SD)	394.58 (±297.56)	244.36 (±181.03)	<.0001	673.74 (±618.60)	363.42 (±323.18)	<.0001
Emergency department cost PPPM, mean (SD)	42.83 (±37.86)	16.54 (±22.67)	<.0001	88.45 (±90.36)	36.99 (±47.81)	<.0001
Pharmacy cost PPPM, mean (SD)	240.39 (±332.73)	205.06 (±152.21)	<.0001	325.78 (±206.01)	277.89 (±168.57)	<.0001

PPPM: per patient per month, SD: standard deviation.

All cost measures were weighted based on the age distribution of BRFS T2DM population.

eAppendix Table 15. Baseline All-Cause Healthcare Resource Utilization Costs of HF and Cohorts

Measure	Medicare Cohorts			Commercial Cohorts		
	HF		<i>P</i> -value	HF		<i>P</i> -value
n	65582	60656		2544	7470	
Healthcare resource utilization, n (%)						
Inpatient	33430 (51.0%)	12314 (20.3%)	<.0001	1322 (52.0%)	1156 (15.5%)	<.0001
Outpatient	64510 (98.4%)	60403 (99.6%)	<.0001	2419 (95.1%)	7408 (99.2%)	<.0001
Emergency department	39811 (60.7%)	18567 (30.6%)	<.0001	1445 (56.8%)	1726 (23.1%)	<.0001
Healthcare cost PPPM, mean (SD)	2,046.32 (±1,254.47)	948.66 (±603.02)	<.0001	3,522.46 (±2,515.14)	1,324.70 (±993.51)	<.0001
Medical cost PPPM, mean (SD)	1,750.82 (±1,103.34)	714.13 (±560.20)	<.0001	3,110.06 (±2,487.75)	1,001.26 (±955.46)	<.0001
Inpatient cost PPPM, mean (SD)	935.26 (±888.45)	253.45 (±367.17)	<.0001	1,855.16 (±2,052.07)	384.23 (±620.61)	<.0001
Outpatient cost PPPM, mean (SD)	514.64 (±380.67)	335.66 (±260.06)	<.0001	982.31 (±932.33)	512.73 (±536.87)	<.0001
Emergency department cost PPPM, mean (SD)	72.93 (±55.43)	30.53 (±33.37)	<.0001	136.91 (±137.25)	57.76 (±69.58)	<.0001
Pharmacy cost PPPM, mean (SD)	295.50 (±565.74)	234.53 (±174.58)	<.0001	412.40 (±241.00)	323.44 (±219.43)	<.0001

PPPM: per patient per month, SD: standard deviation.

All cost measures were weighted based on the age distribution of BRFSS T2DM population.

eAppendix Table 16. Baseline All-Cause Healthcare Resource Utilization Costs of Renal and no Renal Cohorts

Measure	Medicare Cohorts			Commercial Cohorts		
	Renal	no Renal	<i>P</i> -value	Renal	no Renal	<i>P</i> -value
n	114136	105461		5969	14644	
Healthcare resource utilization, n (%)						
Inpatient	46339 (40.6%)	17337 (16.4%)	<.0001	2416 (40.5%)	1884 (12.9%)	<.0001
Outpatient	112284 (98.4%)	104932 (99.5%)	<.0001	5725 (95.9%)	14507 (99.1%)	<.0001
Emergency department	62557 (54.8%)	28824 (27.3%)	<.0001	2984 (50.0%)	3213 (21.9%)	<.0001
Healthcare cost PPPM, mean (SD)	1,582.14 (±1,012.76)	809.70 (±481.88)	<.0001	2,715.38 (±1,902.03)	1,108.22 (±702.83)	<.0001
Medical cost PPPM, mean (SD)	1,301.36 (±888.14)	586.73 (±433.96)	<.0001	2,321.92 (±1,855.27)	795.85 (±661.74)	<.0001
Inpatient cost PPPM, mean (SD)	588.14 (±680.30)	183.10 (±280.98)	<.0001	1,117.34 (±1,338.66)	248.15 (±410.60)	<.0001
Outpatient cost PPPM, mean (SD)	474.68 (±352.21)	306.65 (±233.63)	<.0001	967.48 (±880.28)	457.53 (±409.20)	<.0001
Emergency department cost PPPM, mean (SD)	63.12 (±49.50)	26.79 (±31.54)	<.0001	128.04 (±130.21)	50.68 (±70.42)	<.0001
Pharmacy cost PPPM, mean (SD)	280.78 (±449.76)	222.97 (±175.74)	<.0001	393.46 (±254.63)	312.37 (±174.82)	<.0001

PPPM: per patient per month, SD: standard deviation.

All cost measures were weighted based on the age distribution of BRFSS T2DM population.