Association of Comorbidities with Healthcare Resource Utilization and Cost for Post-discharge Heart Failure Patients with Chronic Kidney Disease

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Abstract

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BACKGROUND: Heart failure is a serious and incurable condition that often coexists with chronic kidney disease. Approximately 83% of patients were hospitalized after their HF diagnosis, accounting for the majority of their medical costs. Numerous studies have reported that comorbidities are associated with HF hospitalization and costs. However, no study has been found so far that investigates the incremental economic burden of commonly reported comorbidities, namely diabetes, hypertension and coronary heart disease of post-discharge HF patients with chronic kidney disease.

OBJECTIVE: To assess the incremental healthcare resource utilization and costs associated with additional comorbidities among post-discharge heart failure patients with chronic kidney disease, at 30-day and 1-year post discharge.

METHODS: This retrospective cohort analysis was conducted using the IBM® Watson MarketScan® Commercial Claims and Encounters and Medicare Supplemental databases. Our population of interest was adult patients discharged after a HF hospitalization from Jan 1, 2011 to Dec 31, 2018, with concurrent chronic kidney disease with and without additional comorbidities of diabetes and/or hypertension and/or coronary heart disease. Primary outcome measures were incremental differences in healthcare resource utilization and total costs between heart failure patients with chronic kidney disease and heart failure patients with chronic kidney disease plus one or more comorbidities of diabetes, hypertension and coronary heart disease. Healthcare resource utilization was defined as hospital all-cause readmission, emergency room visit days, outpatient service visit days and unique drug categories of outpatient prescription fills. We separately evaluated patient out-of-pocket costs and payer costs. Multivariable regressions were used to assess outcomes of interest at 30-day post-discharge and a regression-based Kaplan Meier sample average method was used to evaluate each outcome over 1-year post-discharge.

RESULTS: A total 71,612 patients were identified and included in the study. The mean age of patients ranged from 71.4 to 79.2. Additional comorbidities of diabetes with/without hypertension and/or coronary heart disease were associated with higher healthcare resource utilization at both 30-days and 1-year post discharge. Incremental differences found between groups in patient out-of-pocket cost 30-day post discharge are marginal. We found that individuals with co-occurring diabetes with/without hypertension and/or coronary heart disease incurred more out-of-pocket costs and

payer costs 1-year post discharge. Patients with co-occurring coronary heart disease have similar healthcare resource utilization and total costs. In contrast, patients with co-occurring hypertension with or without coronary heart disease had similar healthcare resource utilization, and similar out-of-pocket costs but lower payer total costs.

CONCLUSIONS: The number, as well as the type of comorbidities, impact the association between comorbidities and healthcare resource utilization and costs for post-discharge heart failure patients with chronic kidney disease. Diabetes is the comorbidity with the biggest impact in this study, which contributes to higher healthcare resource utilization and medical costs. Payers should focus on managing patients with diabetes to reduce medical costs for these patients.

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1. INTRODUCTION

Heart failure (HF) is a chronic and progressive condition characterized by substantial morbidity, mortality, and economic burden to the healthcare system. Approximately 6.9 million adults in the United States currently have HF.[1] Lifetime risk for HF is very high, ranging from 20% to 46% for people between 40 to 95 years old.[2] Even though the life expectancy of people with HF has improved with modern treatments, the mortality rate remains high. The 1-year and 5-year mortality rates are 20% - 30% and 40% - 60%, respectively.[3,4] Both prevalence and total cost are expected to continue to increase due to the aging population. Specifically, an increase of 24% is projected in the prevalence of HF from 2020 to 2030 (8.5 million)[1] and the total cost for HF patients is estimated to increase from $43.6 billion in 2020 to $69.7 billion in 2030 in the US.[1]

Approximately 83% of patients are hospitalized after their HF diagnosis.[5] Hospitalization is the major contributor to the total medical cost for HF care.[6,7,8] The mean estimated lifetime hospitalization cost is $83,980 per person, accounting for 77% of total lifetime costs for HF patients ($109,541 per person).[7] Previously hospitalized HF patients are also more likely to be rehospitalized or experience cardiovascular death, regardless of their ejection fraction, which leads to higher healthcare costs.[9]

Chronic kidney disease (CKD) often coexists with HF due to shared risk factors, bidirectional mechanisms of organ injury, and dysfunction. One study reported more than 50% of HF patients also had chronic kidney disease.[10] Among Medicare beneficiaries over 65 years old, HF is four times as common in people with CKD than those without CKD, and the prevalence of HF is positively correlated with worsening

renal function.[11] Comorbidities other than CKD are also reported to be strongly associated with HF hospitalization and increase the cost of general HF patients.[5,6] Hypertension (HTN), diabetes (DM), and coronary heart disease (CHD) are commonly reported comorbidities of people with both HF and CKD.[12-17]

Despite much evidence on the association of comorbidities with hospitalization and cost of general HF patients, no studies have been found so far that investigated the incremental economic burden of additional comorbidities of post-discharge HF patients with chronic kidney disease. The primary aim of this study was to quantify differences in healthcare resource utilization (HRU) and cost for post-discharge HF patients with CKD with and without co-occurring hypertension (HTN), diabetes (DM), and coronary heart disease (CHD) 30-days and 1 year after discharge from HF hospitalization. This study will help identify specific comorbidities with significant economic impact and guide clinicians on disease management to help their post-discharge HF patients reduce financial burden.

2. METHODS

2.1 Study Design and Data Source

Our study was a retrospective cohort study that utilized the IBM® Watson MarketScan® databases between January 1, 2010, through December 31, 2019. Specifically, we used *Commercial Claims and Encounters (CCAE)* and *Medicare Supplemental databases (MDCR)*. The MarketScan® databases are a national database that captures individual clinical utilization, expenditures, and enrollment. CCAE contains data from a representative sample of commercially insured individuals

while MDCR includes Medicare-eligible retirees with employer-sponsored Medicare Supplemental plans. All patient-level data are de-identified and compliant with the Health Insurance Portability and Accountability Act (HIPAA), and therefore this study was exempt from the Institutional Review Board (IRB) review by the University of Washington Human Subjects Division.

2.2 Sample Selection

Individuals were eligible if they were at least 18 years of age at the index date, discharged from HF hospitalization between Jan 1, 2011, and Dec 31, 2018, continuously enrolled in a health plan for 12 months prior to the index date, and had comorbidity of CKD. The index date was defined as the date on which individuals were discharged from the first captured HF hospitalization. Individuals who met all the eligibility criteria aforementioned and who did not have comorbidities of DM, HTN, or CHD served as our reference group. We determined that individuals had certain comorbidities if they had at least 1 inpatient service claim or at least 2 outpatient service claims within 6 months of each other during the 12-month pre-enrollment period prior to the index date. Subjects were grouped into one of 8 mutually exclusive pre-defined cohorts, namely HF+CKD, HF+CKD+DM, HF+CKD+HTN, HF+CKD+CHD, HF+CKD+DM+HTN, HF+CKD+DM+CHD, HF+CKD+HTN+CHD, and HF+CKD+HTN+CHD+DM. We followed individuals for up to 1-year post-discharge from their first captured HF hospitalization. Patients who were lost to follow-up due to discontinuation of continuous enrollment in insurance coverage were censored on their last date of insurance eligibility. The study timeline is shown in Figure 1.

2.3 Study Measures and Outcomes

Baseline characteristics including age, sex, geographic region, health insurance plan type, employment status, and length of stay of initial HF hospitalization were collected during the 12-month period preceding the index date. Charlson comorbidity index (CCI) scores were calculated and categorized by 0,1,2, and 3+. The CCI scores were modified by excluding diagnoses of HF, CKD, DM, HTN, and CHD to avoid double-counting and collinearity.

The primary outcomes of interest were incremental HRU and incremental cost. Both HRU and costs were captured at two-time points: 30-days post-discharge and 1-year post-discharge. We were interested in estimating both patient out-of-pocket (OOP) total costs and payer total costs. HRU was defined as the count of hospital all-cause readmission, outpatient visit days, emergency room visit days, and unique drug category prescription claims. Outcomes of interest were calculated as mean cost per patient and mean HRU per patient.

The secondary outcomes of interest were the incremental differences in patient out-of-pocket costs and payer costs separately from inpatient services, outpatient services, emergency room services, and outpatient prescription fills. The influence of age and sex on total patient out-of-pocket cost and total payer cost 1-year post-discharge were explored and compared between groups. Age was stratified into <65 years old, 65-74 years old, 75-84 years old, and ≥ 85 years old. Cost outcomes were reported in 2022 US dollars. We used the medical care component of the U.S. consumer price index to adjust cost values in all years prior to 2022.[18]

2.4 Statistical Analysis

Baseline characteristics were summarized descriptively. Continuous variables were presented using means and standard deviations (SD) and categorical variables were presented using counts and proportions. We used one-way ANOVA and chi-square tests to compare differences between cohorts for continuous and categorical variables, respectively.

We used the regression-based Kaplan-Meier sample average (KMSA) method to estimate differences between cohorts in the outcomes of interest 1-year post-discharge from the initial HF hospitalization. The 1-year follow-up period was divided into 12 one-month time intervals. The mean HRU or cost of each time interval was estimated using an appropriate regression model. Obtained mean HRUs or costs were then weighted by the probability of individuals remaining in the follow-up period at the beginning of the respective time interval. This probability was estimated using a Cox proportional hazards model. Average total HRUs or costs for the 1-year follow-up period were the sums of the 12 weighted means.[19] Multivariable adjustments were made using the same covariates for all the outcomes and Cox Proportional Hazards models. Multivariable regressions were used for estimation of outcomes of interest 30-day post-discharge. Covariates included in the regression models were age, sex, modified CCI, length of stay of initial HF hospitalization, and insurance plan (commercial or Medicare). These are included based on the literature review of factors associated with healthcare resource utilization and cost for HF patients.[20-22] 95% confidence intervals (CI) were generated via non-parametric bootstrapping methods to assess the

uncertainty in each outcome. For each outcome estimate, we sampled 1000 replicates with the same sample size as the cohort population with replacement allowed.

All statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC) and RStudio version 1.4.1106(Rstudio Inc., Boston, MA)

3. RESULTS

3.1 Baseline Characteristics

A total of 71,612 patients from the Marketscan® databases met the inclusion criteria, of which, 6.0%, 5.8%, 30.2%, 0.6%, 36.3%, 0.8%, 8.1%, and 12.1% are cohorts of HF+CKD, HF+CKD+DM, HF+CKD+HTN, HF+CKD+CHD, HF+CKD+DM+HTN, HF+CKD+DM+CHD, HF+CKD+HTN+CHD, and HF+CKD+HTN+CHD+DM, respectively (Figure 2). Baseline characteristics are presented in Table 1. The mean age for each cohort was over 71 years old. Compared to the reference group, cohorts with co-occurring HTN or CHD had similar mean ages. However, the cohort with additional comorbidities of HTN+CHD was older while cohorts with additional comorbidities DM, DM+HTN, DM+CHD, and HTN+CHD+DM were younger. More than a third of individuals in the reference group and cohorts of HF+CKD+HTN, HF+CKD+CHD, and HF+CKD+HTN+CHD were over 85 years old. The majority of individuals included in the study were male. HF+CKD+CHD cohort (27.68%) and HF+CKD+DM+CHD (28.86%) cohort had much lower proportions of females than the reference group (40.5%). The proportions of modified CCI scores were similar among the reference group and cohorts of HF+CKD+DM and HF+CKD+HTN. The other cohorts had higher proportions of CCI scores of 2 and 3 or greater than the reference group. The average length of stay for

initial HF hospitalization for the reference group was 6.7 ± 9.2 days. HF+CKD+CHD cohort and HF+CKD+DM+CHD cohort had similar lengths of stay. In comparison, the rest comparison groups had a shorter length of stay than that of the reference group. For all cohorts, the majority of individuals are Medicare enrollees, non-full-time status, with health insurance of preferred provider organization (PPO) plans and comprehensive (COMP) plans, and lived in the northeast and south region.

3.2 Incremental Healthcare Resource Utilization

3.2.1 30-days post-discharge outcomes

Incremental healthcare resource utilization 30-days post-discharge from initial HF hospitalization is shown in Table 2. Individuals with additional comorbidities of DM, DM+HTN, DM+CHD, and HTN+CHD+DM had significantly higher hospital readmissions (0.03, 0.03, 0.06, and 0.05 higher counts per patient, respectively), more days spent for outpatient services (0.39, 0.49, 1.09, and 1.03 more days per patient, respectively), and more unique drug categories of the outpatient prescription claim (0.93, 0.62, 1.09, and 1.11 more categories per patient, respectively). We also estimated 0.04 and 0.05 more days for ER visits among individuals with additional comorbidities of DM+HTN and HTN+CHD+DM, respectively. Although not statistically significant, cohorts with additional comorbidities of DM, and DM+CHD also had more days for ER visits. Individuals with additional comorbidities of HTN+CHD were estimated to have 0.03 higher hospital readmissions, 0.03 more days for ER visits, and 0.24 more unique drug categories for their outpatient prescription claims. However, the magnitude of the incremental difference is smaller than that of other cohorts. Individuals with additional

comorbidity of CHD had similar days for outpatient visits and ER visits, and similar unique drug categories of outpatient prescription claims as to the reference group, but 0.06 higher hospital readmissions. We estimated a small decrease in days for outpatient visits for individuals with additional comorbidities of HTN (0.22 fewer days per patient).

3.2.2 1-year post-discharge outcomes

Similar trends existed for incremental HRU 1-year post-discharge (Table 3). Individuals with additional comorbidities of DM, DM+HTN DM+CHD, and HTN+CHD+DM were estimated to have higher hospital readmissions (0.18, 0.22, 0.41, 0.27 higher counts per patient, respectively), more days for outpatient visit (7.83, 9.96, 8.61, 12.09 more days per patient, respectively), more days for ER visits (0.12, 0.19, 0.32, 0.30 more days per patient, respectively), and more unique drug categories for outpatient prescription claims (8.10, 6.08, 8.34, 8.58 more categories per patient, respectively). We estimated 0.07 more days for ER visits and 1.22 more unique drug categories for outpatient prescription claims among individuals with additional comorbidities of HTN+CHD, however, again, the magnitude of the incremental difference is smaller than that of other cohorts. No significant differences were found for individuals with additional comorbidities of CHD. We estimated a small increase in days for outpatient visits for individuals with additional comorbidities of HTN (1.44 more days per patient).

3.3 Incremental Direct Healthcare Cost

3.3.1 30-days post-discharge outcomes

Incremental patient out-of-pocket costs 30-days post-discharge are shown in Table 4. Overall, the magnitude of incremental differences between groups are small.

Compared to the reference group, individuals with additional comorbidities of HTN and HTN+CHD had significantly lower patient out-of-pocket total costs of $23.76 and $38.82, respectively. We estimated a $38.30 higher patient out-of-pocket total cost for the cohort with additional comorbidity of DM+HTN. No significant differences were found between the reference and comparison groups for inpatient service cost, outpatient service cost, and outpatient prescription cost, except for individuals with additional comorbidity of DM+CHD ($37.27 lower for outpatient service cost). Significant higher ER costs were also found for individuals with additional comorbidities of DM+HTN, HTN+CHD, and HTN+CHD+DM, however, the differences are negligible.

Incremental payer costs 30-days post-discharge are shown in Table 5. Approximately $1400 lower payer total cost was estimated for both cohorts with additional comorbidities of HTN and HTN+CHD. The lower costs were driven mainly by the lower inpatient cost for both cohorts. Significant higher payer costs in outpatient services and outpatient prescriptions occurred in individuals with additional comorbidities of DM, DM+HTN, DM+CHD, and HTN+CHD+DM. All cohorts had similar ER costs 30-day post-discharge from initial HF hospitalization. No significant differences were found for individuals with co-occurring CHD.

3.3.1 1-year post-discharge outcomes

Incremental patient out-of-pocket costs 1-year post-discharge are shown in Table 6. Individuals with additional comorbidities of DM, DM+HTN, HTN+CHD+DM paid approximately $400 more than the reference group ($473.93, $353.00, $411.56 higher per patient, respectively). These cohorts incurred higher costs in mainly inpatient

services and outpatient prescription fills. We estimated $127.13 higher per patient for outpatient prescription costs among individuals with additional comorbidity of DM+CHD. Individuals with additional comorbidity of CHD were estimated to have $245.55 lower in patient out-of-pocket total cost, which was driven mainly by lower outpatient services costs. A smaller magnitude of mean differences in the outpatient prescription costs was found in individuals with additional comorbidities of HTN and HTN+CHD ($44.61 and $66.81 lower per patient, respectively).

For the payer total costs 1-year post-discharge from the initial HF hospitalization (Table 7), individuals with additional comorbidities of DM, DM+HTN, HTN+CHD+DM incurred higher costs ($8269.11, $5835.36, and $9592.51 higher per patient, respectively). Outpatient services costs, followed by outpatient prescription costs, were the major contributors to such differences described above. In contrast, inpatient services costs, followed by outpatient services costs contributed the most to the higher estimates in payer total costs for individuals with additional comorbidities of DM+HTN ($5835.36 higher per patient). We estimated $4969.5 and $6963.79 lower in payer total costs for individuals with additional comorbidities of HTN and HTN & CHD. Significantly lower costs were found in inpatient services and outpatient prescription fills for these two cohorts. Individuals with additional comorbidities of HTN & CHD also incurred lower outpatient services costs, however, lower inpatient services costs were the main driver for the difference in total costs for both cohorts compared to the reference group. No significant differences were found for individuals with additional comorbidities of CHD.

We also performed subgroup analyses to investigate the influence of age and gender on the association of comorbidities with patient out-of-pocket total costs and payer total costs (Table 6 & Table 7). For cohorts with additional comorbidities of DM, DM+HTN, and HTN+CHD+DM, individuals who are younger than 65 years old and who are 85 years or older incurred significantly higher patient out-of-pocket total costs. The magnitude of the mean difference was almost double for individuals who are younger than 65 years old compared to those who are 85 years or older. For the cohort with additional comorbidity of HTN, only individuals who were 85 years or older were estimated to have significantly higher patient out-of-pocket total costs. Different trends were observed for individuals who are between 75 to 84 years old versus those who are 85 years or older, within the cohort with additional comorbidities of HTN+CHD ($411.84 lower and $79.54 higher, respectively). We estimated $569.73 significantly lower and $131.99 significantly higher patient out-of-pocket total cost for individuals between 65 to 74 years old with additional comorbidities of CHD and individuals who are 85 years or older with additional comorbidities of HTN, respectively. No significant differences were found among individuals in different age groups within the cohort with additional comorbidities of DM+CHD. In regard to the influence of age on the association of comorbidities with payer total costs, similar trends were observed among cohorts with additional comorbidities of HTN, DM+HTN, and HTN+CHD, in which individuals younger than 65 years old incurred fewer payer total costs and individuals who are between 75 and 84 years old or who are 85 years or older incurred higher payer total cost. The magnitude of mean differences is much larger for individuals younger than 65 years old

than those who are between 75 and 84 years old or who are 85 years or older. For cohorts with additional comorbidities of DM and HTN+CHD+DM, individuals who are between 75 and 84 years old or who are 85 years or older had higher payer total costs compared to the reference group. In addition, for individuals with additional comorbidities of DM+CHD, only individuals who are between 75 and 84 years old incurred significantly higher payer total costs. No significant differences were found among individuals in different age groups within the cohort with additional comorbidities of CHD. For out-of-pocket costs, females in the cohorts with additional comorbidities of DM, and HTN+CHD+DM had significantly higher estimates while males in the cohorts with additional comorbidities of CHD, and HTN+CHD had significantly lower estimates. For incremental payers costs, different significances were observed in cohorts with additional comorbidities of DM, HTN, and DM+CHD between females and males.

4. DISCUSSION

4.1 Result Summary

In this retrospective claim analysis, we investigated the association of comorbidities, specifically DM, HTN, and CHD, with healthcare resource utilization and cost for post-discharge heart failure patients with chronic kidney disease. Individuals with additional comorbidities of DM with or without HTN and/or CHD had more hospital readmissions, more days with outpatient services and ER visits, and more unique drug categories for their outpatient prescription claims at both 30-days and 1-year post-discharge. Only marginal differences were found among these individuals, compared to the reference group, for their out-of-pocket costs 30-day post-discharge.

Their payers, however, were estimated to pay a few hundred dollars more for outpatient services and outpatient prescription fills 30-day post-discharge. Additional comorbidities of DM, DM+HTN, and HTN+CHD+DM are associated with a higher patient out-of-pocket total cost, mainly driven by inpatient service and outpatient prescription fills, and higher payer total cost, mainly driven by outpatient service and outpatient prescription fills, 1-year post-discharge. Additional comorbidities of DM+CHD are associated with a small increase in out-of-pocket outpatient prescription cost, and higher payer total cost, for inpatient and outpatient services being the major contributors.

Yoon et al. reported that discordant conditions are associated with higher medical costs.[23] The higher costs can be explained by more challenges in medication compliance and more adverse drug interactions among patients with discordant conditions.[24-26] In our study, diabetes is a discordant condition, affecting different organ systems from HF or CKD conditions, leading to higher HRU and costs. It is hard to say if the higher HRU and costs are beneficial for patients or not as it is controversial to state that higher HRU or higher medical costs were the results of closer and / or better disease management.

Individuals with additional comorbidities of CHD are estimated to have similar healthcare resource utilization and costs 30-day and 1-year post-discharge, except for lower out-of-pocket costs, driven by lower outpatient service costs 1-year post-discharge. Our results indicate that not only the number of comorbidities, but also different combinations of comorbidities are responsible for the difference in medical costs. This finding is supported by previous papers.[23, 27]

For individuals with additional comorbidities HTN with or without CHD, estimated significant incremental differences in HRU are marginal. Certain medications such as angiotensin converting enzyme inhibitors or angiotensin II receptor blockers can be used and are recommended by clinical guidelines to treat concurrent conditions of HF, HTN and/or CHD. Therefore, comparable HRU for HF patients with or without HTN and/or CHD is not unexpected. These individuals paid a similar amount with the reference group out-of-pocket 30-day and 1-year post-discharge. However, their payers had fewer total cost 30-day and 1-year post-discharge. This finding may seem surprising at first glance, as one would not expect lower costs with additional comorbidities. In a meta-analysis study, Doughty et.al reported that patients with heart failure with preserved ejection fraction (HFpEF) more often have HTN, compared with heart failure patients with reduced ejection fraction (HFrEF).[28] Patients with HFrEF were reported to have a higher cost, a longer length of stay, and a shorter time to first readmission compared to patients with HFpEF during the 2-year post-discharge period after HF hospitalization.[29] Our finding of significantly lower payer costs, mainly due to lower inpatient services costs, estimated for cohorts with additional comorbidities of HTN with and without CHD could be due to a higher proportion of HFpEF in these cohort samples.

In a systematic review, Urbich et al reported that heart-failure-related costs are sensitive to patient characteristics including comorbidities and age.[30] Similarly, we found that associations of comorbidities with patient out-of-pocket costs and payer costs depend on age and gender. The magnitude of differences in costs for individuals

younger than 65 years old is much larger than that of individuals over 65 years old. This is expected because generally higher costs are associated with commercially insured patients compared to the Medicare enrollees.

4.2 Strengths and Limitations

In our study, approximately 50% of the population in each cohort discontinued enrollment from their insurance at the end of 1-year follow-up (Figure 2). The KMSA method we utilized allowed us to avoid potential survival bias and have more accurate estimates for the outcome of interest with the presence of the missing data. We are able to examine the source of differences found in HRU and costs by delineating our outcomes of interest into different categories. By examining the HRU and costs at two-time points of 30-day and 1-year post-discharge, our study was able to capture the time frame where the incremental differences in HRU and costs exist.

There are several limitations to our study. First, our population of interest is mostly Medicare enrollees due to their advanced age. However, the MarketScan® Medicare Supplement Database we used is not completely representative of the Medicare population. People with Medicaid insurance or those who were not insured are not captured in our study either. These factors could impact the generalizability of our study. Secondly, ICD-9 and ICD-10 codes solely did not allow us to collect reliable information about disease severity such as stages of chronic kidney diseases and functional classification of heart failure. If the proportion of patients with more severe heart failure and/or chronic kidney disease were not balanced between the comparison groups, bias may occur. Thirdly, we didn't study HFrEF and HFpEF patients separately,

who were reported to have different HRU and costs in previous literature.[29] One previous study found that more than 40% of HF-related claims were submitted as unspecified HF.[31] An algorithm developed by Mahesri et al was only able to identify 32% of HErEF correctly using the MarketScan® database as well.[32] Different results may be found if we are able to more accurately identify the population's HF status. Future studies using databases with patients' clinical outcomes are needed to investigate if there is a difference in the association of additional comorbidities with HRU and cost for HFrEF patients compared to HFpEF patients, with CKD. Last but not least, we focus on all-cause costs which may not provide as much preciseness for our outcomes of interest as if one would examine the HF and/or CKD-related costs instead.

4.3 Study Implications

To our knowledge, this is the first study that investigated the association between additional comorbidities and HRU and cost for post-discharge heart failure patients with concurrent chronic kidney disease. The findings of this study can provide useful information for payers in regard to which group of patients needs more attention for their disease management in order to decrease the medical costs. Our study also emphasizes the importance of the holistic approach to patient care. Healthcare providers who aim to manage all disease conditions of their patients simultaneously, instead of just focusing on disease conditions of their expertise, will be able to reduce the financial burden for their patients.

5. CONCLUSION

This retrospective claim analysis found that the association of additional comorbidities and HRU and costs for post-discharged patients with chronic kidney disease not only depends on the number of comorbidities but also on different combinations of the comorbidities. Individuals with additional comorbidities of DM with/without HTN and/or CHD tend to utilize more HRU and incur higher medical costs. Special attention should be given to managing this group of patients to reduce total healthcare expenditures.

6. TABLES

Table 1. Baseline Characteristics

Characteristics	HF & CKD (N= 4289)	HF, CKD & DM (N= 4194)	HF, CKD & HTN (N= 21709)	HF, CKD & CHD (N= 466)	HF, CKD, DM & HTN (N= 26073)	HF, CKD, DM & CHD (N= 589)	HF, CKD, HTN & CHD (N= 5799)	HF, CKD, DM, HTN & CHD (N= 8675)	P-value
Age at index year, mean (SD)	76.71(14.19)	71.93 (12.46)	76.82 (14.69)	77.47 (13.18)	71.80 (12.54)	71.42 (11.91)	79.19 (12.02)	72.95 (11.46)	<0.001
Age group, n (%)									<0.001
<65	939 (21.89%)	1294 (30.85%)	4741 (21.84%)	98 (21.03%)	8259 (31.68%)	192 (32.60%)	846 (14.59%)	2355 (27.15%)	
65-74	559 (13.03%)	962 (22.94%)	2648 (12.20%)	57 (12.23%)	5850 (22.44%)	148 (25.13%)	787 (13.57%)	2098 (24.18%)	
75-84	1247 (29.07%)	1223 (29.16%)	6084 (28.03%)	145 (31.12%)	7460 (28.61%)	164 (27.84%)	1856 (32.01%)	2753 (31.73%)	
>=85	1544 (36.00%)	715 (17.05%)	8236 (37.94%)	166 (35.62%)	4504 (17.27%)	85 (14.43%)	2310 (39.83%)	1469 (16.93%)	
Sex Female, n (%)	1738 (40.52%)	1653 (39.41%)	9749 (44.91%)	129 (27.68%)	11294 (43.32%)	170 (28.86%)	2089 (36.02%)	3192 (36.80%)	<0.001
Modified Charlson Comorbidity Index, n (%)									<0.001
0	1361 (31.73%)	1440 (34.33%)	6730 (31.00%)	113 (24.25%)	7366 (28.25%)	161 (27.33%)	1217 (20.99%)	1693 (19.52%)	
1	1447 (33.74%)	1471 (35.07%)	7047 (32.46%)	151 (32.40%)	8575 (32.89%)	183 (31.07%)	1736 (29.94%)	2652 (30.57%)	
2	815 (19.00%)	722 (17.22%)	4145 (19.09%)	95 (20.39%)	5356 (20.54%)	139 (23.60%)	1406 (24.25%)	2132 (24.58%)	
3+	666 (15.53%)	561 (13.38%)	3787 (17.44%)	107 (22.96%)	4776 (18.32%)	106 (18.00%)	1440 (24.83%)	2198 (25.34%)	
Length of stay of initial HF hospitalization, mean (SD)	6.72 (9.18)	6.09 (7.07)	5.53 (5.90)	6.81 (13.04)	5.74 (5.81)	6.54 (9.30)	5.42 (6.64)	5.63 (6.33)	<0.001
Commercial / Medicare, n (%)									<0.001
Commercial	896 (20.89%)	1218 (29.04%)	4599 (21.18%)	95 (20.39%)	7902 (30.31%)	184 (31.24%)	807 (13.92%)	2255 (25.99%)	
Medicare	3393 (79.11%)	2976 (70.96%)	17110 (78.82%)	371 (79.61%)	18171 (69.69%)	405 (68.76%)	4992 (86.08%)	6420 (74.01%)	

Table 1. Baseline Characteristics -Continuous

Characteristics	HF & CKD (N= 4289)	HF, CKD & DM (N= 4194)	HF, CKD & HTN (N= 21709)	HF, CKD & CHD (N= 466)	HF, CKD, DM & HTN (N= 26073)	HF, CKD, DM & CHD (N= 589)	HF, CKD, HTN & CHD (N= 5799)	HF, CKD, DM, HTN & CHD (N= 8675)	P-value
Geographic region, n (%)									<0.001
North central	907 (21.15%)	784 (18.69%)	4038 (18.60%)	102 (21.89%)	4733 (18.15%)	119 (20.20%)	1172 (20.21%)	1733 (19.98%)	
Northeast	1361 (31.73%)	1275 (30.40%)	7514 (34.61%)	136 (29.18%)	8968 (34.40%)	174 (29.54%)	2106 (36.32%)	3020 (34.81%)	
South	1351 (31.50%)	1341 (31.97%)	6878 (31.68%)	149 (31.97%)	8645 (33.16%)	184 (31.24%)	1798 (31.01%)	2884 (33.24%)	
West	610 (14.22%)	730 (17.41%)	2974 (13.70%)	72 (15.45%)	3282 (12.59%)	105 (17.83%)	683 (11.78%)	958 (11.04%)	
Unknown	60 (1.40%)	64 (1.53%)	305 (1.40%)	7 (1.505)	445 (1.71%)	7 (1.19%)	40 (0.69%)	80 (0.92%)	
Employment status, n (%)									<0.001
Full time	419 (9.77%)	528 (12.59%)	2101 (9.68%)	48 (10.30%)	2971 (11.39%)	70 (11.88%)	407 (7.02%)	1051 (12.12%)	
Non-Full time	3870 (90.23%)	3666 (87.41%)	19608 (90.32%)	418 (89.70%)	23102 (88.6%)	519 (88.12%)	5392 (92.98%)	7624 (87.88%)	
Health Insurance Plan Type, n (%)									<0.001
B/MM	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
COMP	1969 (45.91%)	1540 (36.72%)	8932 (41.14%)	182 (39.06%)	9018 (34.59%)	190 (32.26%)	2407 (41.51%)	3110 (35.85%)	
EPO	18 (0.42%)	33 (0.79%)	145 (0.67%)	2 (0.43%)	208 (0.80%)	3 (0.51%)	28 (0.48%)	65 (0.75%)	
HMO	329 (7.67%)	578 (13.78%)	2422 (11.16%)	43 (9.23%)	3463 (13.28%)	87 (14.77%)	651 (11.23%)	1029 (11.86%)	
Non-Cap POS	190 (4.43%)	222 (5.29%)	735 (3.39%)	16 (3.43%)	1101 (4.22%)	29 (4.92%)	148 (2.55%)	307 (3.54%)	
PPO	1547 (36.07%)	1560 (37.20%)	8157 (37.57%)	193 (41.42%)	10538 (40.4%)	240 (40.75%)	2200 (37.94%)	3525 (40.63%)	
Cap/ Part Cap POS	18 (0.42%)	22 (0.52%)	145 (0.67%)	3 (0.64%)	214 (0.82%)	9 (1.53%)	107 (1.85%)	134 (1.54%)	
CDHP	83 (1.94%)	91 (2.17%)	496 (2.28%)	8 (1.72%)	568 (2.18%)	10 (1.70%)	75 (1.29%)	200 (2.31%)	
HDHP	34 (0.79%)	29 (0.69%)	191 (0.88%)	8 (1.72%)	241 (0.92%)	6 (1.02%)	44 (0.76%)	95 (1.10%)	
NA	101 (2.35%)	119 (2.84%)	486 (2.24%)	11 (2.36%)	722 (2.77%)	15 (2.55%)	139 (2.40%)	210 2.42%)	

B/MM= basic/major medical; COMP=comprehensive; EPO=exclusive provider organization; HMO=health maintenance organization; Non-Cap POS= non-capitated point-of-service; PPO=preferred provider organization; Cap or Part Cap POS= capitation or partially capitation point-of-service; CDHP=consumer-driven health plan; HDHP=high deductible health plan

Table 2. 30-day Healthcare Resource Utilization (Mean (95%CI))

	Reference	Incremental Change Compared to Reference Group						
	HF & CKD	**HF, CKD & DM**	**HF, CKD & HTN**	**HF, CKD & CHD**	**HF, CKD, DM & HTN**	**HF, CKD, DM & CHD**	**HF, CKD, HTN & CHD**	**HF, CKD, DM, HTN & CHD**
Readmission counts	0.095 (0.084, 0.11)	0.031 (0.015, 0.047)*	0.00093 (-0.011, 0.013)	0.063 (0.011, 0.11)*	0.033 (0.021, 0.044)*	0.063 (0.029, 0.10)*	0.025 (0.010, 0.042)*	0.050 (0.036, 0.064)*
Outpatient visits days	6.57 (6.40, 6.75)	0.39 (0.12, 0.65)*	-0.22 (-0.42, -0.0090)**	0.071 (-0.47, 0.64)	0.49 (0.28, 0.70)*	1.09 (0.58, 1.61)*	0.028 (-0.20, 0.25)	1.03 (0.81, 1.26)*
ER visit days	0.049 (0.039, 0.061)	0.013 (-0.0043, 0.029)	0.0098 (-0.0026, 0.022)	0.015 (-0.025, 0.061)	0.035 (0.022, 0.047)*	0.052 (-0.000050, 0.11)	0.030 (0.012, 0.049)*	0.052 (0.035, 0.068)*
Unique drug category outpatient prescription claim	3.73 (3.62, 3.83)	0.93 (0.76, 1.09)*	-0.12 (-0.24, 0.0072)	0.30 (-0.090, 0.65)	0.62 (0.50, 0.74)*	1.09 (0.74, 1.43)*	0.24 (0.11, 0.39)*	1.11 (0.96, 1.26)*

*Significant higher
**Significant lower

Table 3. 1-year Healthcare Resource Utilization (Mean (95%CI))

	Reference	Incremental Change Compared to Reference Group						
	HF & CKD	HF, CKD & DM	HF, CKD & HTN	HF, CKD & CHD	HF, CKD, DM & HTN	HF, CKD, DM & CHD	HF, CKD, HTN & CHD	HF, CKD, DM, HTN & CHD
Readmission counts‡	0.75 (0.71, 0.79)	0.18 (0.12, 0.24)*	0.0090 (-0.030, 0.047)	0.085 (-0.041, 0.22)	0.22 (0.17, 0.26)*	0.41 (0.27, 0.57)*	0.024 (-0.026, 0.075)	0.27 (0.21, 0.32)*
Outpatient visits days‡‡	37.05 (35.89, 38.28)	7.83 (6.07, 9.56)*	1.44 (0.074, 2.74)*	0.36 (-2.98, 3.75)	9.96 (8.56, 11.30)*	8.61 (5.06, 12.13)*	0.91 (-0.62, 2.41)	12.09 (10.42, 13.69)*
ER visit days‡‡‡	0.50 (0.46, 0.55)	0.12 (0.054, 0.19)*	0.039 (-0.0091, 0.085)	0.065 (-0.055, 0.24)	0.19 (0.15, 0.24)*	0.32 (0.15, 0.53)*	0.074 (0.013, 0.14)*	0.30 (0.24, 0.38)*
Unique drug category outpatient prescription claim‡‡‡	29.61 (28.70, 30.55)	8.10 (6.73, 9.59)*	-0.23 (-1.21, 0.75)	2.19 (-0.78, 5.04)	6.08 (5.07, 7.06)*	8.34 (5.12, 11.35)*	1.22 (0.015, 2.42)*	8.58 (7.31, 9.83)*

*Significant higher

‡GLM, Zero-inflated poisson distribution

‡‡GLM, Negative binomial distribution

‡‡‡GLM, Zero-inflated negative binomial distribution

Table 4. 30-day Patient Out-of-Pocket Cost (Mean (95%CI))

	Reference	Incremental Change Compared to Reference Group						
	HF & CKD	**HF, CKD & DM**	**HF, CKD & HTN**	**HF, CKD & CHD**	**HF, CKD, DM & HTN**	**HF, CKD, DM & CHD**	**HF, CKD, HTN & CHD**	**HF, CKD, DM, HTN & CHD**
Patient out-of-pocket total cost	258.81 (238.45, 280.00)	1.88 (-26.31, 27.64)	-23.76 (-46.93, -1.02)**	-39.45 (-92.30, 32.13)	38.30 (11.74, 65.23)*	-19.99 (-56.77, 18.52)	-38.82 (-68.55, -6.01)**	32.93 (-9.31, 81.33)
Inpatient cost	37.93 (29.62, 46.87)	-6.25 (-18.87, 6.39)	-5.53 (-15.75, 4.17)	-5.38 (-30.47, 27.01)	5.22 (-6.00, 16.20)	1.58 (-17.76, 25.31)	-4.50 (-15.16, 7.04)	-1.31 (-12.70, 9.80)
Outpatient cost	159.77 (142.15, 178.35)	-15.25 (-37.43, 7.64)	-11.14 (-29.97, 8.33)	-43.69 (-76.38, 1.32)	22.51 (-0.70, 47.18)	-37.27 (-66.20, -9.55)**	-26.89 (-53.27, 2.92)	25.22 (-15.60, 71.51)
Emergency room cost	1.22 (0.59, 1.97)	0.46 (-0.66, 1.64)	0.61 (-0.24, 1.44)	-0.31 (-1.55, 1.20)	1.74 (0.48, 3.24)*	1.05 (-1.09, 3.86)	3.36 (0.25, 8.13)*	1.83 (0.51, 3.41)*
Outpatient prescription cost	61.11 (58.22, 64.47)	23.38 (18.23, 28.52)	-7.10 (-10.86, -3.74)	9.62 (-7.75, 35.86)	10.58 (6.74, 14.10)	15.70 (6.02, 26.26)	-7.43 (-11.70, -3.64)	9.03 (4.95, 12.89)

Costs are presented in 2022 USD
*Significant higher
**Significant lower

Table 5. 30-day Payer Cost (Mean (95%CI))

	Reference	Incremental Change Compared to Reference Group						
	HF & CKD	**HF, CKD & DM**	**HF, CKD & HTN**	**HF, CKD & CHD**	**HF, CKD, DM & HTN**	**HF, CKD, DM & CHD**	**HF, CKD, HTN & CHD**	**HF, CKD, DM, HTN & CHD**
Payer total cost	5965.60 (5018.23, 7020.05)	383.25 (-1120.93, 1727.62)	-1401.52 (-2531.76, -406.03)**	4077.62 (-1077.84, 10295.52)	-75.45 (-1217.32, 906.99)	-201.01 (-1970.20, 2129.65)	-1399.23 (-2647.81, -190.41)**	334.22 (-857.12, 1367.33)
Inpatient cost	4784.10 (3621.97, 6133.34)	70.38 (-1799.60, 1714.00)	-1805.26 (-3191.93, -576.90)**	4899.97 (-1328.03, 12585.04)	-934.23 (-2316.08, 284.98)	-1182.77 (-3066.46, 1397.74)	-1590.94 (-3043.23, -148.94)**	-713.46 (-2234.99, 473.63)
Outpatient cost	2153.15 (1963.85, 2352.56)	283.36 (4.46, 579.50)*	56.76 (-170.05, 280.12)	-22.75 (-558.06, 629.82)	629.93 (409.98, 844.45)*	540.52 (9.53, 1244.01)*	-319.36 (-569.19, -59.89)**	589.29 (330.33, 829.67)*
Emergency room cost	36.80 (24.78, 50.52)	21.16 (-3.58, 45.61)	29.93 (10.23, 52.19)	19.30 (-32.44, 96.07)	44.97 (25.87, 66.47)	45.26 (-16.18, 132.50)	22.82 (0.73, 47.37)	70.29 (44.72, 99.30)
Outpatient prescription cost	438.02 (380.02, 504.48)	129.31 (44.49, 207.05)*	-84.67 (-153.02, -26.02)**	-1.44 (-152.26, 160.18)	66.47 (1.24, 126.18)*	156.64 (20.73, 325.59)*	-68.59 (-146.88, 7.80)	150.75 (77.18, 222.24)*

Costs are presented in 2022 USD
*Significant higher
**Significant lower

Table 6. 1-year Patient Out-of-Pocket Cost (Mean (95%CI))

	Reference	Incremental Change Compared to Reference Group						
	HF & CKD	HF, CKD & DM	HF, CKD & HTN	HF, CKD & CHD	HF, CKD, DM & HTN	HF, CKD, DM & CHD	HF, CKD, HTN & CHD	HF, CKD, DM, HTN & CHD
Patient out-of-pocket total cost	1610.40 (1463.87, 1821.39)	473.93 (147.67, 842.73)*	-35.58 (-253.31, 131.60)	-245.55 (-496.51, -14.30)**	353.00 (113.50, 571.54)*	178.60 (-95.36, 437.19)	-151.44 (-403.00, 169.26)	411.56 (130.51, 688.28)*
Inpatient cost	213.25 (190.94, 235.65)	154.71 (7.25, 419.85)*	21.43 (-7.16, 54.46)	-25.33 (-91.57, 44.31)	59.29 (33.69, 90.10)*	28.89 (-31.19, 92.81)	-3.82 (-34.91, 30.54)	81.96 (30.79, 146.75)*
Outpatient cost	910.08 (775.05, 1110.28)	129.89 (-119.87, 363.69)	-12.40 (-225.68, 143.06)	-233.93 (-458.89, -40.62)**	231.29 (-0.28, 424.93)	22.58 (-219.98, 243.19)	-80.81 (-322.38, 235.65)	247.24 (-22.90, 509.62)
Emergency room cost	9.84 (7.67, 12.26)	2.23 (-1.60, 6.20)	0.65 (-2.14, 3.13)	-2.85 (-7.60, 2.10)	6.31 (3.23, 9.15)*	2.37 (-2.64, 8.09)	7.16 (0.44, 16.65)*	9.43 (5.95, 13.06)*
Outpatient prescription cost	487.08 (465.57, 509.51)	189.33 (154.92, 222.57)*	-44.61 (-69.72, -21.62)**	13.71 (-53.16, 88.00)	62.43 (28.42, 96.79)*	127.13 (62.62, 196.78)*	-66.81 (-94.28, -39.06)**	82.37 (50.61, 116.40)*
Sex								
Female	1492.21 (1379.61, 1598.47)	577.13 (158.78, 1304.60)	25.96 (-114.15, 197.78)	-154.10 (-463.23, 211.43)	451.40 (299.54, 630.30)	-27.20 (-301.82, 279.59)	20.89 (-351.61, 682.71)	417.87 (203.30, 688.34)
Male	1695.03 (1474.94, 2069.33)	399.76 (-3.97, 795.77)	-73.46 (-451.80, 166.12)	-317.73 (-721.36, -21.74)	464.30 (78.45, 764.23)	233.14 (-197.10, 584.71)	-264.59 (-627.59, -18.42)	394.06 (-40.41, 778.92)
Age Subgroups								
<65 yo	2690.78 (2473.36, 2914.11)	713.48 (0.19, 1749.07)*	138.10 (-172.87, 469.36)	-332.93 (-846.62, 254.63)	470.81 (162.64, 815.71)*	21.39 (-446.17, 533.31)	-203.70 (-493.94, 103.76)	623.22 (215.46, 1131.95)*
65-74 yo	1774.12 (1571.25, 2022.78)	216.72 (-202.21, 635.95)	-160.98 (-405.89, 56.13)	-569.73 (-957.17, -210.72)**	93.75 (-162.03, 348.06)	-164.99 (-501.96, 187.32)	386.66 (-539.72, 1970.05)	315.45 (-180.91, 1075.18)
75-84 yo	1693.48 (1315.55, 2361.33)	-217.17 (-909.06, 195.69)	-275.08 (-942.22, 134.83)	-375.86 (-1067.47, 155.12)	38.09 (-668.01, 502.56)	-203.90 (-933.48, 322.40)	-411.84 (-1073.72, -13.14)**	-219.03 (-881.48, 185.59)
85+yo	850.23 (813.25, 928.07)	290.57 (154.05, 421.59)*	131.99 (59.10, 201.26)*	-1.98 (-132.34, 202.73)	234.55 (189.12, 409.48)*	119.53 (-101.92, 407.47)	79.54 (0.94, 196.25)*	248.87 (179.68, 358.97)*

Costs are presented in 2022 USD
*Significant higher
**Significant lower

Table 7. 1-year Payer Cost (Mean (95%CI))

	Reference	Incremental Change Compared to Reference Group						
	HF & CKD	HF, CKD & DM	HF, CKD & HTN	HF, CKD & CHD	HF, CKD, DM & HTN	HF, CKD, DM & CHD	HF, CKD, HTN & CHD	HF, CKD, DM, HTN & CHD
Payer total cost	311107.91 (27664.45, 34488.41)	8269.11 (3657.57, 13384.08)*	-4969.5 (-8529.99, -1221.29)**	7458.58 (-5939.23, 23257.38)	5835.36 (1937.41, 9635.94)*	14976.44 (5487.34, 27648.35)*	-6963.79 (-11082.27, -2812.88)**	9592.51 (5611.01, 13837.66)*
Inpatient cost	20982.11 (17612.63, 24486.70)	$4489.62 (-$408.53, $8918.17)	-6355.28 (-9822.74, -2752.61)**	7183.50 (-7507.54, 24109.30)	-248.64 (-3846.74, 3439.66)	12884.60 (2539.11, 26906.81)*	-6530.94 (-10674.82, -2636.24)**	1980.59 (-1710.93, 5847.81)
Outpatient cost	13772.91 (12332.34, 15260.06)	4227.30 (2049.69, 6507.62)*	299.36 (-1281.74, 1838.82)	1353.30 (-3094.87, 6619.85)	5951.46 (4152.56, 7705.57)*	3655.54 (96.87, 8021.86)*	-2937.34 (-4562.61, -1227.22)**	5851.69 (3970.70, 7686.56)*
Emergency room cost	247.50 (177.82, 346.00)	167.24 (34.34, 307.62)*	43.76 (-54.80,124.98)	114.22 (-128.81, 414.57)	271.32 (160.12, 367.01)*	333.19 (36.20, 771.46)*	19.09 (-92.91,111.74)	356.38 (227.81, 478.51)*
Outpatient prescription cost	3704.56 (3360.73, 4070.76)	1439.43 (898.00, 1900.06)*	-641.06 (-1039.43, -276.77)**	-290.86 (-1237.49, 843.32)	698.69 (288.34, 1100.62)*	1316.58 (373.01, 2434.23)*	-671.61 (-1222.41, -122.36)**	1244.04 (803.60, 1669.07)*
Sex								
Female	28438.59 (24004.03, 33419.16)	6660.06 (-270.11, 12866.08)	-6246.05 (-11218.04, -1365.72)**	8508.95 (-11796.00, 37931.21)	8227.84 (3240.74, 13027.52)*	17907.95 (-1295.38, 43005.98)	-7883.59 (-13617.13, -2472.97)**	7624.44 (2384.47, 12897.45)*
Male	32884.29 (28620.69, 37306.48)	9296.55 (2602.66, 15319.74)*	-3526.86 (-8345.68, 797.21)	6244.36 (-8995.91, 28739.83)	7576.36 (2940.42, 12084.62)*	13219.90 (1534.44, 26452.69)*	-6581.21 (-12159.54, -1484.25)**	10707.99 (5381.23, 16056.97)*
Age Subgroups								
<65 yo	109738.5 (97225.65, 123260.18)	-9695.46 (-26732.93, 5970.82)	-28772.62 (-42306.57, -14664.36)**	24888.63 (-25953.25, 88748.12)	-20926.24 (-34742.01, -7698.03)**	-7973.64 (-38603.74, 30753.84)	-18702.28 (-35778.67, -538.50)**	-6197.47 (-21333.84, 8534.86)
65-74 yo	23278.24 (17989.89, 28434.34)	-1079.24 (-6981.69, 5377.80)	-671.80 (-6076.03, 4851.96)	9554.61 (-15678.95, 43353.72)	2867.94 (-2239.68, 7937.74)	8289.79 (-1343.27, 19216.52)	5116.72 (-2435.31, 12768.33)	4647.41 (-837.93, 10367.34)
75-84 yo	10462.82 (9270.95, 11794.2)	2116.11 (153.27, 3969.59)*	3134.93 (1707.90, 4671.06)*	3121.53 (-1201.32, 8881.83)	5444.52 (3898.84, 6893.81)*	11554.65 (4598.71, 18626.55)*	3061.69 (1124.37, 4954.17)*	6989.94 (5150.31, 8913.74)*
85+yo	6114.37 (5496.81, 6864.53)	2086.32 (1338.91, 3886.92)*	2020.63 (1525.68, 3114.98)*	827.66 (-911.92, 2982.43)	4507.31 (4192.29, 6015.06)*	853.43 (-499.67, 4744.26)	2314.22 (1425.20, 3560.39)*	4756.22 (3851.98, 6463.60)*

Costs are presented in 2022 USD *Significant higher **Significant lower

7. FIGURES

Figure 1. Study Timeline

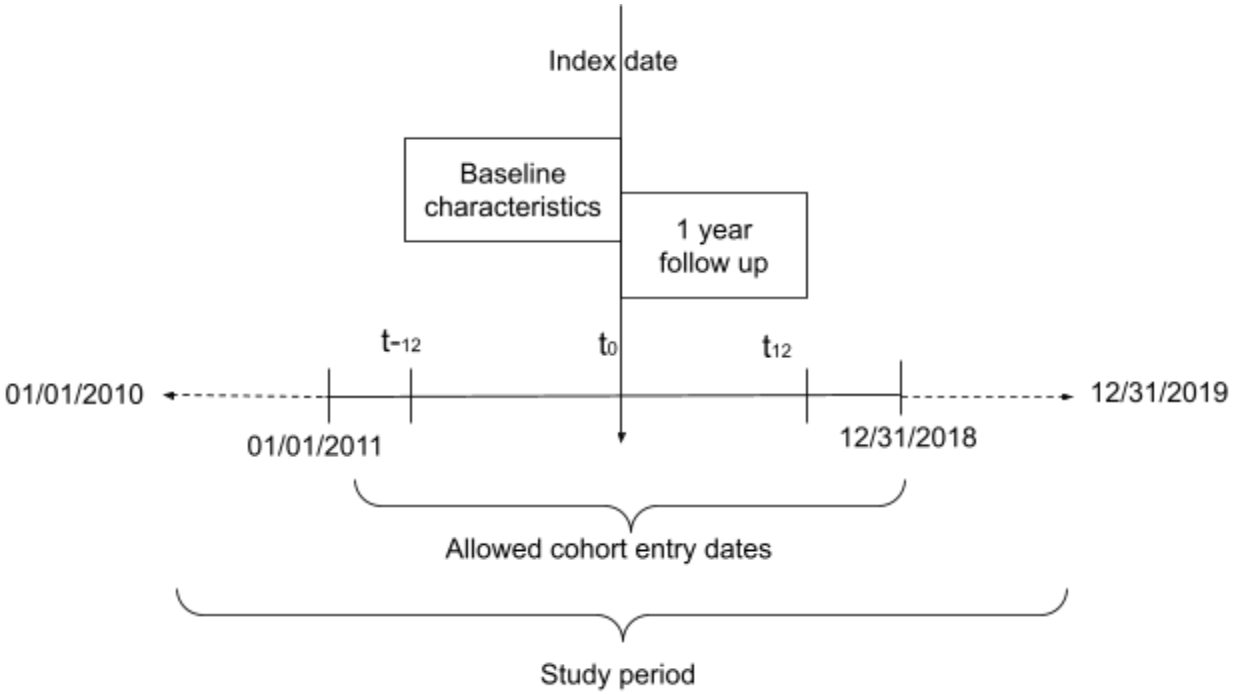
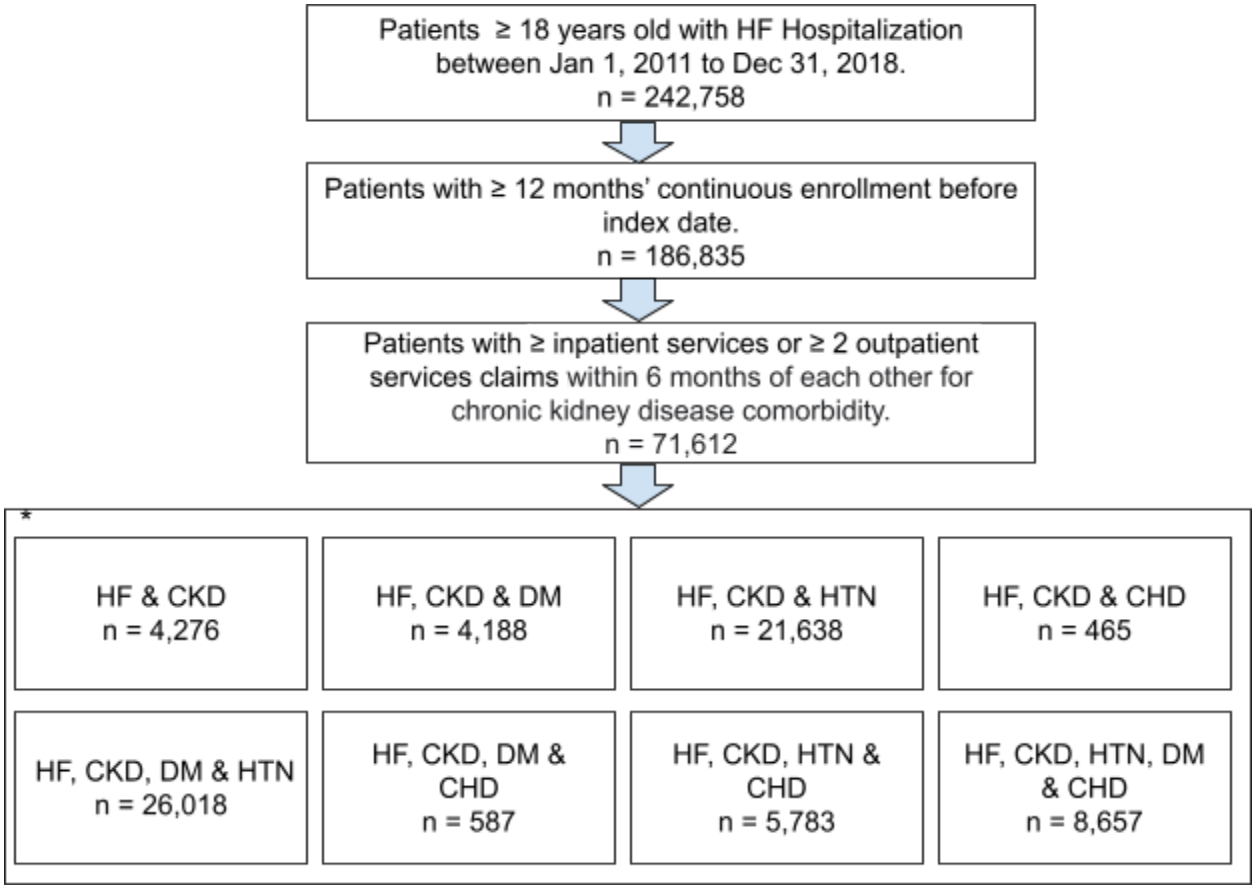
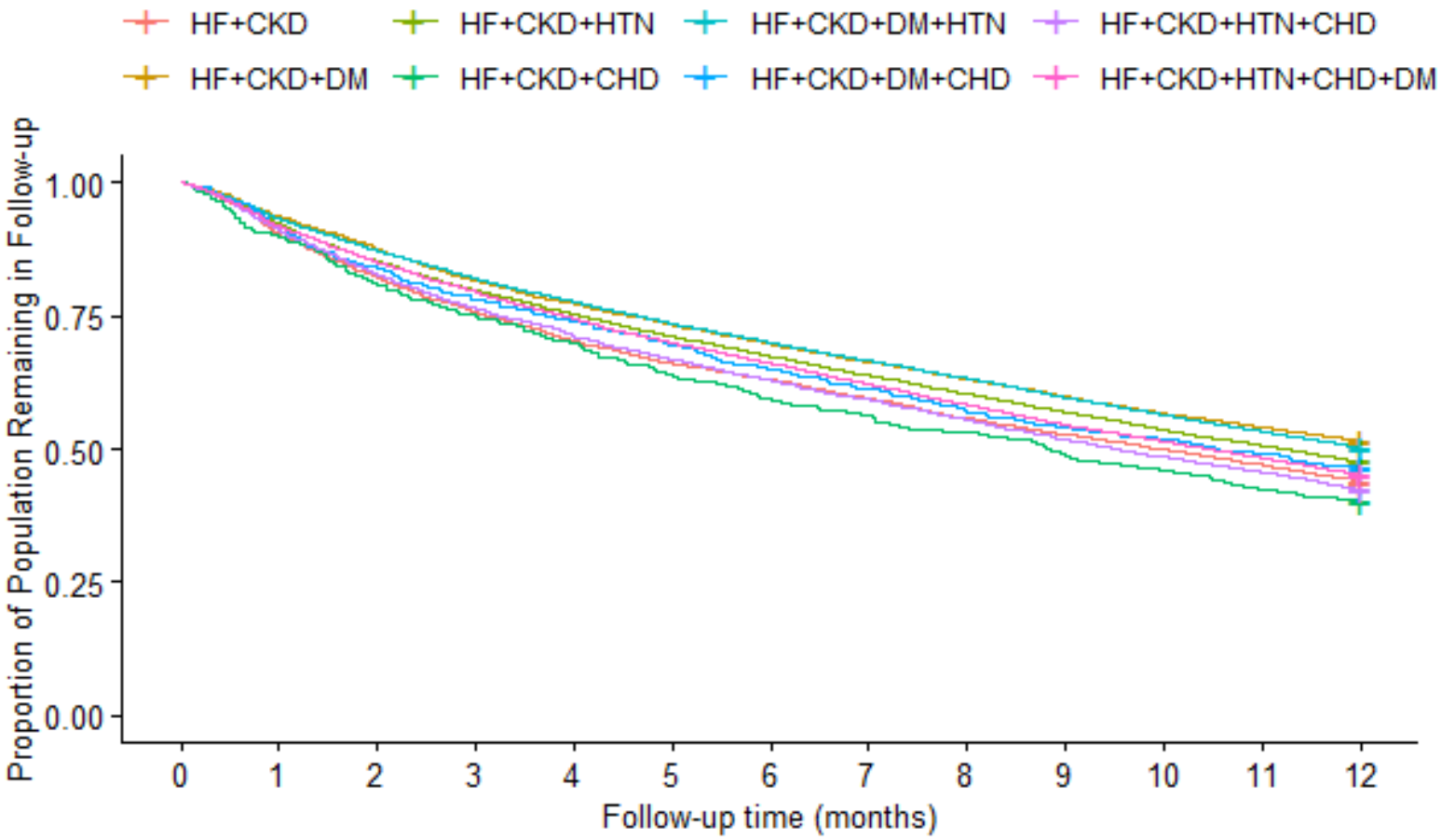


Figure 2. Sample Attrition Diagram



* Groups are mutually exclusive

Figure 3. Proportion of Population Remaining in Follow-up with Continuous Enrollment



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