# Multiple Comorbid Conditions in Adults With Hyperkalemia: A Retrospective Cohort Study Using Association Rule Mining

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## BACKGROUND

- Hyperkalemia (HK) is a common electrolyte abnormality that can lead to life-threatening cardiac arrhythmia.[1]
- HK is one of the major reasons that clinical-guideline–directed medications such as renin-angiotensin-aldosterone system inhibitors (RAASi) doses are reduced or discontinued among patients with chronic kidney disease (CKD) and/or heart failure.[2]
- Limited information exists on the extent of multiple comorbid conditions (MCCs) in adult patients with HK.

## OBJECTIVE

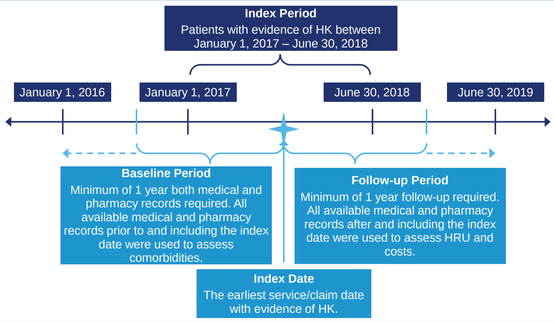
- Quantify the prevalence of individual chronic conditions and MCCs in patients with HK and examine the associations between MCCs, healthcare resource utilization (HRU), and costs.

## METHODS

### STUDY DESIGN

- A retrospective cohort study was conducted using a large administrative claims database from 1/1/2016 to 6/30/2019 (**Figure 1**).

### Figure 1. Study Design




### INCLUSION/EXCLUSION CRITERIA

**Inclusion**

- Patients with HK (ICD-10-CM: E87.5; serum potassium >5.0 mEq/L; or NDC codes for either patiromer or sodium polystyrene sulfonate) during the index period. The earliest service/claim date with evidence of HK was identified as the index date.
- Qualified patients had at least 12 months of enrollment before and after the index date.
- Age ≥18 years on the index date.

**Exclusion**

- Patients who enrolled in hospice care any time in study period.

**Outcomes**

- The prevalence of specific comorbid conditions (CCs) and MCCs among adult patients with HK.
- The proportion of HK patients with emergency department (ED) visits, length of hospital stay, and total healthcare costs during the follow-up period.

**Statistical Analysis**

- Association rule mining was applied to identify MCCs.
- Generalized linear models were used to examine the associations between MCCs, HRU, and costs.

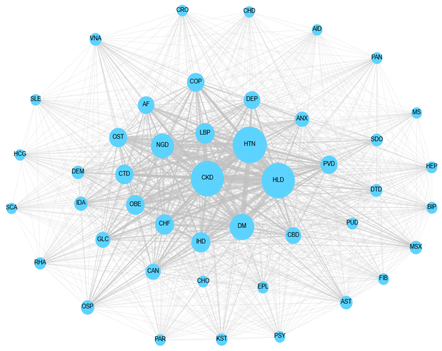
## RESULTS AND DISCUSSION

### Table 1. Baseline Demographics and Comorbidities of Patients With HK by Age Groups

| Characteristics | Overall N=22,154 | Age <65 Years n=5409, 24.42% | Age ≥65 years n=16,745, 75.58% |
|---|---|---|---|
| Mean age, years (SD) | 71.02 (12.49) | 53.92 (9.17) | 76.58 (7.28) |
| Male, n (%) | 11,490 (51.86) | 3,146 (58.16) | 8,344 (49.83) |
| **Geographic region, n (%)** | | | |
| Midwest | 4,729 (21.31) | 688 (12.35) | 4052 (24.20) |
| Northeast | 6,261 (28.26) | 1,171 (21.65) | 5,090 (30.5) |
| South | 9,933 (44.84) | 2,915 (53.89) | 7,018 (41.91) |
| West | 1,240 (5.60) | 655 (12.11) | 585 (3.49) |
| Urban-rural | | | |
| Urban | 6,962 (31.43) | 2,089 (28.62) | 4,873 (29.10) |
| Sub-urban | 6,564 (29.63) | 1,558 (28.80) | 5,006 (29.90) |
| Rural | 8,628 (38.95) | 1,762 (32.58) | 6,866 (41.00) |
| **Insurance type, n (%)** | | | |
| Commercial | 3,721 (16.80) | 3721 (68.79) | 0 (0) |
| Medicare Advantage | 18,433 (83.20) | 1688 (31.21) | 16,745 (100%) |
| **Comorbidities, n (%)** | | | |
| Chronic kidney disease | 18,883 (85.24) | 4,719 (87.24) | 14,164 (84.59) |
| Hypertension | 18,460 (83.33) | 3,539 (65.43) | 14,921 (89.11) |
| Hyperlipidemia | 17,851 (80.58) | 2,662 (67.70) | 14,189 (84.74) |
| Diabetes | 10,453 (47.18) | 2,300 (42.52) | 8,153 (48.69) |
| Congestive heart failure | 5,031 (22.71) | 701 (12.96) | 3,630 (21.68) |

SD, standard deviation.

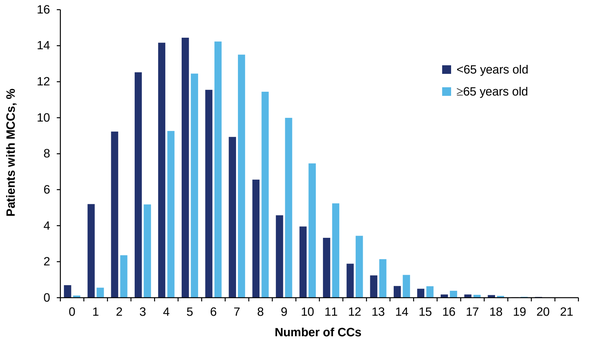
### Figure 2. Network Analyses of Multimorbidity in Patients With HK



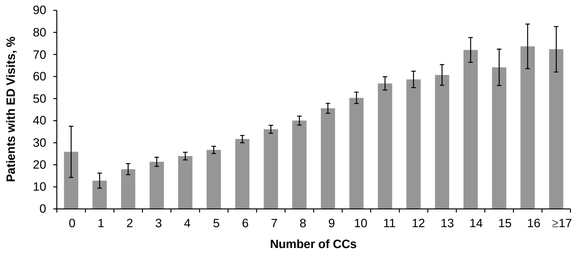

The nodes represent comorbidities; the lines linking the nodes represent the connection between two comorbidities. The size of node corresponds to the prevalence of the comorbidity. The thicker the line is, the more frequently the two comorbidities co-existed. The network is dominated by CKD, hypertension, and hyperlipidemia.

AF, atrial fibrillation; AID, acquired immunodeficiency syndrome; ANX, anxiety; AST, asthma; BIP, bipolar disorder; CAN, malignant cancer; CBD, cerebrovascular disease; CHD, congenital heart disease; CHF, congestive heart failure; CHO, cholelithiasis/cholecystitis; CKD, chronic kidney disease; COP, chronic obstructive pulmonary disease; CRO, Crohn's disease; CTD, chronic thyroid disorders; DEM, dementia; DEP, depression; DM, diabetes mellitus; DTD, diverticular disease; EPL, epilepsy; FIB, fibromyalgia; GLC, glaucoma; HCG, hypercoagulable syndrome; HEP, hepatitis; HLD, hyperlipidemia; HTN, hypertension; IDA, iron deficiency anemia; IHD, ischemic heart disease; KST, kidney stones; LBP, lower back pain; MSS, multiple sclerosis; MSX, metabolic syndrome; NGD, nonspecific gastritis/dyspepsia; OBE, obesity; OSP, osteoporosis; OST, osteoarthritis; PAN, pancreatitis; PAR, Parkinson's disease; PSY, psychosis; PUD, peptic ulcer disease; PVD, peripheral vascular disease; RHA, rheumatoid arthritis; SCA, sickle cell anemia; SDO, substance-related disorders; SLE, systemic lupus erythematosus; VNA, ventricular arrhythmia.

### Figure 3. Percent With MCCs by Age Group



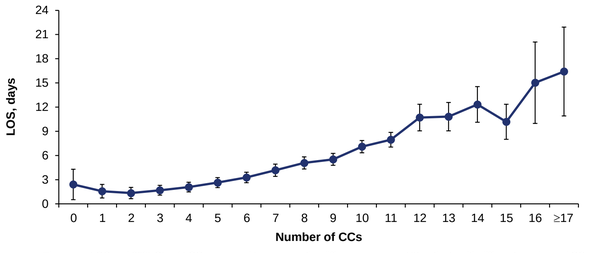

### Figure 4. Percent With ED Visits by Number of MCCs




The averages and 95% confidence intervals (CIs) of proportion of HK patients with ED visits were used to compare the differences among HK patients with different numbers of CC.
Data was adjusted for age, gender, region, rural or urban, household incomes, and type of health insurance.

- With each additional CC the odds of an ED visit increased by 20% (adjusted odds ratio [95% CI]: 1.20 [1.19–1.21], *P* <0.0001).

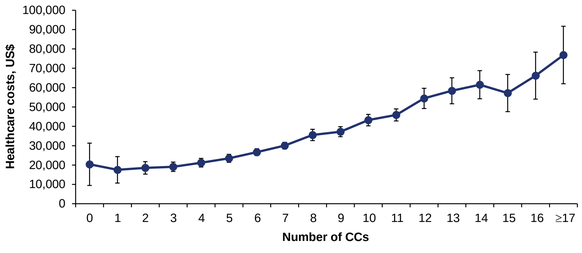
### Figure 5. Length of Hospital Stay (LOS) by Number of MCCs




The mean LOS and 95% CIs of LOS were used to compare the differences among HK patients with different numbers of CC.
Solid dots represent the mean LOS; high and low bar represent 95% CIs.
Data was adjusted for age, gender, region, rural or urban, household incomes, and type of health insurance.

- The length of hospital stays (LOS) increased with increased number of CCs.
- There was a 5.8% increase in LOS (in days) for HK patients each additional CC (*P* <0.0001).

### Figure 6. Total Healthcare Costs (Mean Annual) by Number of MCCs




The mean healthcare cost and 95% CIs of healthcare costs of healthcare costs were used to compare the differences among patients with HK with different numbers of CC.
Solid dots represent the mean total healthcare cost; high and low bar represent 95% CIs.
Data was adjusted for age, gender, region, rural or urban, household incomes, and type of health insurance.

- Healthcare costs increased with increased number of CC.
- There was a 7.8% increase in total healthcare costs for HK patients with each additional CC (*P* <0.0001).

## LIMITATIONS

- This is an administrative claims data analysis; therefore, we may have underestimated MCCs prevalence rates, HRU, and costs due to unavailable out-of-network service-utilization data.
- There are no standard operational definitions for diseases or chronic conditions that should be used in such studies. Classification of most conditions was based on ICD-10-CM codes alone; misclassification is likely.
- The purpose of association rule mining is to identify combinations of CCs that are interesting and worthy of further investigation, but without addressing statistical significance.

## CONCLUSIONS

- MCCs are highly prevalent among patients with HK.
- MCCs are strongly associated with HRU and costs.
- Understanding the patterns of MCCs is useful for decision-making to improve clinical outcomes and reduce medical costs.
- Association rule mining provides a useful new way to study patterns of MCCs.

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