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Real-world management of hyperkalemia with patiromer among United States Veterans

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1. Introduction

Hyperkalemia (HK) is a common and life-threatening clinical problem that is most often a result of impaired urinary potassium (K\textsuperscript{+}) excretion due to reduced kidney function (acute or chronic kidney disease [CKD]) and/or disorders or drugs interfering with the renin-angiotensin-aldosterone system (RAAS) [1–10]. Guideline-recommended RAAS inhibitor (RAASi) utilization is critical to slow CKD progression [11–14], reduce morbidity and mortality [15–17], improve clinical outcomes, and reduce healthcare costs; however, RAASi use can be hindered by HK [17–19].

The chronic management of HK is aimed at reducing extra-cellular K\textsuperscript{+} concentration, yet little is known about the real-world management of HK and associated outcomes—especially among patients with heart disease, kidney disease, and/or type 2 diabetes mellitus. Patiromer was approved for the treatment of HK by the US Food and Drug Administration in October 2015 [20]. Patiromer is a sodium-free non-absorbed polymer that exchanges calcium for K\textsuperscript{+}, thus removing K\textsuperscript{+} from the body and lowering serum K\textsuperscript{+} [21].

The efficacy of patiromer for HK treatment in patients with CKD, diabetes, hypertension, and/or heart failure and receiving RAASi therapy was established in two prospective, randomized, clinical trials, which have been described previously [19,21,22]. In the AMETHYST-DN trial [19], treatment with patiromer resulted in a statistically significant reduction in serum K\textsuperscript{+} concentration after 4 weeks, which was maintained through 52 weeks in patients with mild (5.0 to <5.5) or moderate (>5.5 to <6.0) HK. Significant mean decreases in serum K\textsuperscript{+} concentration were observed at each monthly point with an average daily dose of 19.4 g/day (mild HK) and 27.2 g/day (moderate HK). The proportion of patients with a normal K\textsuperscript{+} concentration (3.8–5.0 mmol/L) ranged from 77%–95% following 1 year of patiromer therapy. In OPAL-HK [20], during the 4-week treatment phase, patients with mild HK (5.1 to <5.5 mmol/L) and moderate HK (5.5 to <6.5 mmol/L) received
patiromer 8.4 g and 16.8 g per day, respectively. At 4 weeks, the majority (76%) of patiromer recipients achieved normokalemia (K⁺ concentration 3.8 to <5.1 mmol/L).

There are no published real-world studies that evaluated K⁺ concentration changes over time in non-dialysis CKD patients with HK receiving patiromer. The present retrospective, observational study endeavored to address this evidence gap by: (1) describing real-world patiromer utilization, (2) describing and analyzing K⁺ concentrations pre- and post-patiromer initiation, and (3) describing RAASi therapy continuation post-patiromer initiation.

2. Methods

2.1. Study design and data source

A retrospective cohort study was conducted among US Veterans with HK using ‘real-world’ data from the Veterans Affairs (VA) Corporate Data Warehouse (VA-CDW). This data source includes data from inpatient and outpatient encounters as well as pharmacy dispensing data, laboratory data (including test results), and other data available in the VA electronic health record. The medication data used in this study originated from outpatient pharmacy dispensings (identified using VA Drug Class Codes). The Logical Observation Identifiers Names and Codes (LOINC) universal standard for identifying medical laboratory observations was used. Extensive laboratory data quality and cleaning were conducted to ensure correct specimen classification and validate LOINC mapping. The following LOINCs were used to classify K⁺ tests and results: 2823–3, 77142–8, 75940–7, and 6298–4.

2.2. Inclusion/exclusion criteria

During the study period (1 January 2016 to 31 August 2018), US Veterans with HK (K⁺ ≥5.1 mmol/L) were included on the date of the initial patiromer dispensing (index date). Patients were required to have baseline evidence (i.e. within 12 months pre-index) of heart failure, renal disease, or type 2 diabetes mellitus (Table S1 and S2). Patients were excluded who had baseline evidence of end-stage renal disease (ESRD) and who did not receive routine healthcare through the VA Health System (an encounter at least every 6 months in the baseline period). Medical conditions were identified using the International Classification of Diseases, 9th and 10th Revision, Clinical Modification (ICD-9/10-CM) coding system.

2.3. Follow-up

Follow-up began on the index date and continued until a censoring event; patiromer discontinuation, initiating a K⁺ binder other than patiromer (i.e. sodium polystyrene sulfonate [SPS]; sodium zirconium cyclosilicate was not available during the study period), death, or the study period end date (i.e. 31 August 2018), whichever occurred first.

2.4. Exposure classification during follow-up

Patiromer exposure was identified from outpatient pharmacy dispensing data using the following search logic: VA drug class code = AD400, and generic product name contained ‘patiromer.’ The dispensing date and days supplied associated with each dispensing were used to determine the duration of patiromer treatment episodes. Discontinuation of a patiromer treatment episode was defined by a >30-day gap in therapy between a subsequent patiromer dispensing (or no dispensing) and the date of exhausted supply from the previous dispensing. If this occurred, follow-up was censored on the date of exhausted supply for the previous patiromer dispensing. Follow-up was also censored on the dispensing date of a K⁺ binder other than patiromer.

2.5. Baseline patient characteristics

Baseline variables were ascertained in the VA-CDW 12 months prior to and including the index date (unless otherwise specified). Baseline demographic variables included age, sex, and race. Comorbidities were classified using ICD-9/10-CM codes. Medication dispensings (classified using VA drug class codes) and healthcare resource utilization (e.g. hospital admissions and ED visits) were classified within 6 months pre-index. Baseline K⁺ concentration was classified using the highest outpatient K⁺ concentration value within 3 months pre-index (including the index date). Using the last outpatient baseline serum creatinine assessment (LOINC 2160–0, 77140–2, 14682–9, 40248–7, and 4026–4) in addition to age, sex, and race, eGFR was determined using the CKD-Epidemiology Collaboration equation. If race was missing, white race was imputed.

2.6. Patiromer utilization outcomes

The duration of the first continuous patiromer episode (i.e. to the first censoring event) was described with a medication persistence curve (using Kaplan-Meier methodology). For comparison to patiromer persistence, we also present the medication persistence curve for SPS to contextualize use and adherence with an alternative K⁺ binder. The data for SPS persistence was collected using the exact same methodology as previously described for patiromer. In addition, we described the patiromer starting dose and (1) number of medication fills, (2) days supplied, and (3) proportion of days covered (PDC) in three analysis intervals post-index (i.e. 0–1, 0–3, and 0–6 month(s)). PDC was calculated as the quotient of the total number of days supplied (the numerator) divided by the total number of days in the analysis interval (the denominator). Patiromer days supplied was truncated on the dispensing date of a subsequent patiromer dispensing, if the subsequent dispensing date occurred before the exhausted supply date (i.e. early fills were not shifted to the end of the days supplied for the previous dispensing). Patients were included in the patiromer utilization analyses if they were followed continuously through the end of the follow-up interval being analyzed; however, in order to evaluate the real-world utilization of patiromer, for these analyses only, we did not stop follow-up upon patiromer discontinuation or initiation of a different K⁺ binder. All other censoring criteria were enforced.
2.7. $K^+$ concentration pre- and post-patiromer initiation

$K^+$ concentration was assessed in the baseline period (i.e. 3 months pre-index) and in three analysis intervals post-index (i.e. 0–1 month, 1–3 months, and 3–6 months). By design, all patients were required to have a pre-index $K^+$ concentration value $\geq 5.1$ mmol/L. In the baseline period, the highest $K^+$ concentration value was selected for each patient. In each follow-up interval, the last $K^+$ concentration value (furthest from the index date) was selected for each patient.

Mean $K^+$ concentration and 95% confidence interval (CI) were described in the baseline period and in each follow-up interval. The change in mean $K^+$ concentration (pre-index vs post-index) was analyzed for each follow-up analysis interval and compared to the mean baseline $K^+$ concentration. Patients were included in the $K^+$ analyses who (1) had a recorded $K^+$ value in the follow-up interval being analyzed and (2) were followed through the end of the analysis interval. We also described the proportion of patients (95% CI) with $K^+$ concentration $<5.1$ (i.e. normokalemia) and $<5.5$ mmol/L (i.e. normokalemia/mild hyperkalemia).

2.8. RAASI continuation outcome

RAASI continuation was assessed at 0–1, 0–3, and 0–6 month(s) post-index for patients who were continuously exposed to a RAASI for the last 6 months of the baseline period (including the index date; allowable ≥90-day RAASI therapy gap). RAASI continuation was classified using outpatient pharmacy dispensing claims data for: angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, mineralocorticoid receptor antagonists, and direct renin inhibitors. The percentage of patients (95% CI) who continued RAASI therapy was estimated. Patients were included in the RAASI continuation analyses if they were followed through the end of the interval being analyzed.

2.9. Statistical analysis

Baseline characteristics were summarized as means with standard deviations (SD) and medians for continuous variables and the number of patients and percentages for categorical variables. Medication persistence survival curves and risk tables were developed using the Kaplan-Meier method. Mean $K^+$ concentration change (95% CI), pre- vs post-patiromer initiation, was analyzed using the paired t-test. The percentage (95% CI) of patients continuing RAASI therapy was estimated in each analysis interval post-patiromer initiation. Exact binomial 95% CIs were calculated using the Clopper-Pearson method. All statistical analyses were conducted using R version 3.5.1.

3. Results

3.1. Patient disposition and attrition during follow-up

Details of patient inclusion/exclusion by each criterion (e.g. patient disposition) are presented in Table S3. A total of 918,206 US Veterans had a $K^+$ concentration $\geq 5.1$ mmol/L from 1 January 2016 to 31 August 2018. Among these patients, 501 had an outpatient patiromer dispensing during the study period. Of these, 397 patients also had the required $K^+$ assessment and concentration ($K^+ \geq 5.1$ mmol/L) 3 months before the first patiromer dispensing, and 288 patients met the final inclusion/exclusion criteria after excluding 109 patients who (1) did not receive routine care at the VA Health System ($n = 5$); (2) used concomitant patiromer and SPS on the index date ($n = 2$); (3) had no baseline evidence of heart failure, diabetes mellitus, or CKD ($n = 4$); or (4) had baseline evidence of ESRD ($n = 98$).

Details of patient attrition during follow-up are presented in Table S4. Among the 288 included patients, 241, 68, and 25 remained under follow-up at 1, 3, and 6 months post-index, respectively. Prior to reaching the 6-month follow-up date, patients were censored for the following reasons: 184 patients discontinued patiromer, 69 patients reached the end of the study period, 7 patients initiated a different $K^+$ binder, and 3 patients expired. Plausible reasons for patiromer discontinuation are numerous and include, but not limited to: tolerability, progression of disease, physician/pharmacist/patient decision, effectiveness and drug price. Table S4 also includes patient attrition data for patients with continuous baseline RAASI utilization ($n = 92$).

3.2. Baseline patient characteristics

Baseline demographic and clinical characteristics are presented in Table 1. In summary, baseline characteristics were: median age 70 years, African-American race 24%, diabetes 83%, heart failure 32%, and CKD 95%. Patients had a median of 3 $K^+$ assessments within 3 months pre-index (~1 $K^+$ assessment/month). Using the highest baseline $K^+$ value for each patient, the median $K^+$ concentration was 5.7 mmol/L. Nineteen percent (19%), 53%, and 28% of patients had mild HK ($K^+ \geq 5.1 <5.5$ mmol/L), moderate HK ($K^+ \geq 5.5 <6.0$ mmol/L), and severe HK ($K^+ \geq 6.0$ mmol/L), respectively. Sixty-two percent (62%) of patients had a baseline estimated glomerular filtration rate (eGFR) $<30$ mL/min/1.73 m$^2$. Forty-three percent (43%) of patiromer initiators had a SPS dispensing during the baseline period and 32% had continuous RAASI use in the last 6 months of the baseline period (including the index date). High baseline healthcare resource utilization was observed, as the median number of outpatient medical encounters was 28 within 6 months pre-index (~1 per/week). Thirty-six percent (36%) and 42% of patients had a baseline hospital admission or emergency department (ED) visit, respectively.

3.3. Real-world patiromer utilization results

Patiromer utilization results are presented in Table 2 and Figure 1. For 96% of Veterans the initial patiromer dosage was 8.4 g per day (see Table 2). Through 6 months post-index, patiromer dose increases were uncommon (<4%). Within the 0–1-, 0–3-, and 0–6 month analysis intervals post-index, the mean numbers of patiromer dispensings (SD) were 1.2 (0.4), 2.0 (1.0), and 2.7 (1.8), respectively. The median PDC for each analysis interval were 100%, 66%, and 44%, respectively. The mean days supplied per dispensing (SD) for all follow-up intervals was approximately...
Table 1. Baseline characteristics of patiromer initiators.

<table>
<thead>
<tr>
<th>Patients, N</th>
<th>288</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographic data (at index)</strong></td>
<td>Mean</td>
</tr>
<tr>
<td>Age</td>
<td>70</td>
</tr>
<tr>
<td>Age ≥75, n (%)</td>
<td>68 (23.6)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>283 (98.3)</td>
</tr>
<tr>
<td>Caucasian Non-Hispanic, n (%)</td>
<td>199 (69.1)</td>
</tr>
<tr>
<td>African American Non-Hispanic, n (%)</td>
<td>70 (24.3)</td>
</tr>
<tr>
<td><strong>Comorbidities – 12 months prior to index date, n (%)</strong></td>
<td></td>
</tr>
<tr>
<td>Cardiac dysrhythmias</td>
<td>80 (28)</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>51 (18)</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>273 (95)</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>92 (32)</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>113 (39)</td>
</tr>
<tr>
<td>Diabetes type II</td>
<td>238 (83)</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>21 (7)</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>79 (27)</td>
</tr>
<tr>
<td><strong>Medications – 12 months prior to index date, n (%)</strong></td>
<td></td>
</tr>
<tr>
<td>SPS</td>
<td>125 (43)</td>
</tr>
<tr>
<td>Beta blocker</td>
<td>198 (69)</td>
</tr>
<tr>
<td>Diuretic</td>
<td>206 (72)</td>
</tr>
<tr>
<td>Loop</td>
<td>170 (59)</td>
</tr>
<tr>
<td>Potassium-sparing</td>
<td>29 (10)</td>
</tr>
<tr>
<td>Thiazide</td>
<td>71 (25)</td>
</tr>
<tr>
<td>Insulin</td>
<td>159 (55)</td>
</tr>
<tr>
<td>RAASI (any use)</td>
<td>175 (61)</td>
</tr>
<tr>
<td>ACE inhibitor</td>
<td>125 (43)</td>
</tr>
<tr>
<td>ARB</td>
<td>57 (20)</td>
</tr>
<tr>
<td>RAASI (continuous exposure)</td>
<td>92 (32)</td>
</tr>
</tbody>
</table>

**Laboratory-3 months prior to or on index date**

<table>
<thead>
<tr>
<th>Number of K+ assessments</th>
<th>3.3</th>
<th>2.2</th>
<th>3.0</th>
</tr>
</thead>
<tbody>
<tr>
<td>K+ concentration a, mmol/L</td>
<td>5.8</td>
<td>0.4</td>
<td>5.7</td>
</tr>
<tr>
<td>K+ ≥5.1–5.4, n (%)</td>
<td>54 (19)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>K+ ≥5.5–5.9, n (%)</td>
<td>153 (53)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>K+ ≥6.0, n (%)</td>
<td>81 (28)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>eGFR value a, ml/min/1.73 m2</td>
<td>28.9</td>
<td>15.9</td>
<td>24.3</td>
</tr>
<tr>
<td>eGFR 60–89, ml/min/1.73 m2, n (%)</td>
<td>9 (3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>eGFR 30–59, ml/min/1.73 m2, n (%)</td>
<td>94 (33)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>eGFR 15–29, ml/min/1.73 m2, n (%)</td>
<td>132 (46)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>eGFR &lt;15, ml/min/1.73 m2, n (%)</td>
<td>46 (16)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**HRU – 6 months prior to index date**

<table>
<thead>
<tr>
<th>Number of outpatient visits</th>
<th>33</th>
<th>23</th>
<th>28</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with ≥1 hospitalization, n (%)</td>
<td>103 (36)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients with ≥1 emergency department visit, n (%)</td>
<td>122 (42)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

ACE, angiotensin-converting enzyme; ARB, angiotensin II receptor blocker; RAASI, renin-angiotensin-aldosterone system inhibitor; SD, standard deviation; SPS, sodium polystyrene sulfonate.

aHighest K+ value in the 3 months pre-index.

bLast serum creatinine assessment 3 months prior to index.

38 days (20 days). Figure 1 shows the Kaplan-Meier medication persistence curves for continuous exposure to patiromer and SPS. For patiromer patients, the percentages of patients continuously exposed at 1, 3, and 6 months post-index were approximately 97%, 40%, and 25%, respectively. For SPS patients, the percentages of patients continuously exposed were 25%, 5%, and 2%, respectively.

3.4. K+ concentrations pre- and post-patiromer initiation

Mean K+ concentrations and change (pre- vs post-patiromer initiation) are depicted in Figure 2. In the 0–1, 1–3, and 3–6 month analysis intervals post-index, 153, 55, and 21 patients, respectively, had a K+ concentration assessment in the follow-up analysis interval and remained under follow-up through the end of the interval. Compared to before patiromer initiation, statistically significant (P < 0.001) K+ concentration changes were observed after patiromer initiation. Across all analysis intervals, the mean K+ concentration change was −1.00 to −1.05 mmol/L for patients who remained continuously exposed to patiromer. Among the 153 patients included in the 0–1 month pre- vs post-index analyses, mean (SD) K+ concentrations were 5.8 (0.5) mmol/L pre-index and 4.8 (0.5) mmol/L post-index (mean K+ Δ: −1.01 mmol/L; 95% CI: −1.1, −0.9; P < 0.001). Additional descriptive K+ concentration data are provided in Table S5 (supplemental material).

Figure 3 shows the percentage of patiromer initiators with a K+ concentration <5.1 and <5.5 mmol/L in the baseline period and in each follow-up analysis interval. At 3–6 months post-index, in 71% of patients (95% CI: 47%–89%) the last K+ concentration was <5.1 mmol/L, whereas all patients entered the study with a baseline K+ concentration ≥5.1 mmol/L. In 95% of patients (95% CI: 76%–100%) the last K+ concentration was <5.5 mmol/L, compared to 19% before patiromer initiation.

3.5. RAASI continuation results

Baseline RAASI utilization was identified for 92 (32%) patiromer initiators. Baseline characteristics for this group are presented in Table S6. In the 0–1, 0–3, and 0–6 month analysis intervals, 75, 28, and 14 patients were included, respectively. Figure 4 shows the percentage (and 95% CI) of patients who remained continuously exposed to RAASI therapy post-index. Despite the small sample sizes and limited precision, approximately 80% (95% CI: 49%–95%) of baseline RAASI users continued RAASI therapy through 6 months post-index.

4. Discussion

This is the first study to provide an early report about patiromer utilization among US Veterans with HK. Recently, a real-world analysis of patiromer for the treatment of hyperkalemia in chronic hemodialysis patients was published [23]. However, to our knowledge, no other published studies have evaluated HK management with patiromer in a real-world setting of primarily CKD patients. Prior to the approval of patiromer, SPS was the
only oral HK therapy; however, SPS was neither studied nor commonly used for chronic HK management or prevention. The patiromer utilization results from the present study (Table 2 and Figure 1) depict utilization patterns consistent with chronic HK treatment (e.g. multiple refills, days supplied ≥30 days, PDC 47%–97%), rather than episodic or acute management strategies employed prior to patiromer availability. In prospective patiromer clinical trials, the protocols required upward titration of starting doses to achieve the desired K\(^{+}\) concentration. In this early report using real-world data, we observed that the initial patiromer dose is rarely titrated.

Comparing K\(^{+}\) concentration change observed in the present study with that seen in published clinical trials [22,24–27], mean K\(^{+}\) concentration reductions following patiromer initiation were similar at −1.00 to −1.05 mmol/L (Figure 2). In the OPAL-HK trial [21], the mean (± standard error) change in the serum K\(^{+}\) concentration was −1.01 ± 0.03 mmol/L (P < 0.001). At 1, 3, and 6 months following patiromer initiation in the present study, 63%–76% of patients’ last K\(^{+}\) concentration was <5.1 mmol/L and <5.5 mmol/L for 87%–95% of patients. This compares to 0% of patients with a K\(^{+}\) concentration <5.1 mmol/L and 19% with <5.5 mmol/L before initiating patiromer (Figure 3). A similar percentage of patients achieving normokalemia (K\(^{+}\) <5.1 mmol/L) was reported in two prospective, randomized trials (AMETHYST-DN [77%–95%] and OPAL-HK [76%]) [23,24].

Consistent with the recently published AMBER trial and previous clinical trial findings [24], the present study also reports RAASI continuation in approximately 80% of patients with continuous patiromer exposure (Figure 4). In the AMBER trial, patients with resistant hypertension and CKD were enabled to continue spironolactone therapy in 86% of patients...
receiving patiromer compared to 60% receiving placebo at 12 weeks \( (P < 0.0001) \) [28].

Like all observational studies, the present study has several limitations. The selection criteria were broadly inclusive of US Veterans with HK exposed to patiromer in routine clinical practice, yet 21% of patients were excluded by requiring a baseline \( \text{K}^+ \) concentration \( \geq 5.1 \text{ mmol/L} \) within 3 months prior to patiromer initiation. It is not evident how this may affect the generalizability of the study findings; however, including patients with \textit{bona fide} evidence of HK is critical to preserving internal validity and is required in order to analyze pre- vs post-patiromer \( \text{K}^+ \) concentrations. The single-arm, within-patient (i.e. pre-vs-post) \( \text{K}^+ \) concentration analyses do not provide causal conclusions regarding the effectiveness of patiromer. The observed results may be associated with continuous patiromer exposure, or perhaps related to other concomitantly employed HK management strategies. Further research with a suitable comparator group and comparative methodology is warranted to fully assess patiromer’s real-world effectiveness. Outpatient pharmacy dispensing data have been shown to reliably predict medication exposure in published validation studies [27,29–33]; however, exposure misclassification (i.e. classifying patients as treated when they were not treated) related to nonadherence or undocumented discontinuation may have occurred for a variety of reasons. The effect of patiromer misclassification would likely result in attenuated outcome estimates (e.g. no difference in pre- vs post-index \( \text{K}^+ \) concentration analyses); however, the observed \( \text{K}^+ \) concentration reductions – which are consistent with other prospective study findings – suggest that patiromer

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**Figure 3.** Percentage of patients (95% CI) with \( \text{K}^+ \) concentration <5.1 and <5.5 mmol/L pre- and post-patiromer initiation. *To be included in the study, all patients were required to have a baseline \( \text{K}^+ \) \( \geq 5.1 \text{ mmol/L} \) within 3 months prior to patiromer initiation. **N** is the number of patients who were followed through the end of each analysis interval and who had a \( \text{K}^+ \) measurement in the interval (i.e. the denominator for each analysis).

CI, confidence interval; \( \text{K}^+ \), potassium.

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**Figure 4.** Percentage of patients (95% CI) continuing RAASi therapy post-patiromer initiation. N is the number of patients who remained under follow-up through the end of each analysis interval AND who were continuously exposed to RAASi therapy (inhibition of the renin-angiotensin-aldosterone system) during the 6-month baseline period (i.e. the denominator for each analysis).

CI, confidence interval; RAASi, renin-angiotensin-aldosterone system inhibitor.
exposure may have been correctly classified, given the pharmacy dispensing data utilized and methodology employed. Limited precision is evident in the wide CIs for the RAASi continuation analyses – particularly at 6 months post-index. Further research in this subgroup is justified as patiromer use increases. Adverse events related to patiromer utilization was not an aim of this analysis and these data were not available to the authors. Furthermore, the effectiveness of patiromer in patients continuously exposed as opposed to those discontinued at each time interval was not an aim but would be of interest and warrants future research.

5. Conclusion
This study provides a novel assessment of real-world HK management among US Veterans with HK. The observed patiromer utilization results suggest a potential paradigm shift toward chronic HK management from acute or episodic treatment prior to the approval of patiromer. The observed statistically significant K⁺ concentration reductions were consistent with well-controlled prospective clinical trials. The successful management of HK may have contributed to the observed high rate of RAASi therapy continuation. Further research, with a suitable comparator group to control for confounding and a larger sample size, is warranted to corroborate and extend these findings as patiromer use increases.

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Data sharing
The data that support the findings of this study are available from the corresponding author, upon reasonable request.

Disclosures of interest

**CPK** reports consultant fees from AstraZeneca and Relypsa, Inc., a Vifor Pharma Group Company; **EOG** reports no relevant disclosures; **SDW** and **JJF** report employment by Relypsa, Inc., a Vifor Pharma Group Company and Vifor stock ownership; **CGR** reports consultant fees from Covidia, Keryx, Halozyme, Vifor, AbbVie and Relypsa, Inc., a Vifor Pharma Group Company, and founded COHRDATA; **JHL** and **BCS** report research support from COHRDATA.

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