Reliability of Charting the Clinical Course of Chronic Hyperkalemia Treatment through an Ontology-Based Protocol Applied to Prior Authorization Drug Review Notes

Qualls, J [1,2], Patel S [1,2], Sauer B [1,2]

1. George E Wahlen VAMC, Department of Veterans Affairs
2. University of Utah School of Medicine Department of Epidemiology

Background

Traditional therapy to treat hyperkalemia consists of: introducing a low potassium diet, reducing or discontinuing medications that can increase potassium (e.g., RAASi), and trialing Sodium polystyrene Sulfonate (SPS), loop diuretics, or thiazide diuretics[1,2,3].

Historically SPS has been associated with increased incidence of severe adverse events[4,5]. This has led to newer agents, such as patiromer (Veltassa®) to be preferred for treatment of chronic hyperkalemia.

Patiromer is currently available in the Veterans Health Administration (VHA) as a restricted formulary agent. Explicit criteria for use guidelines have been put in place by the VHA to ensure other pharmacotherapy strategies are attempted before dispensation of patiromer[6]. These attempts are documented in VHA clinical records as Prior Authorization Drug Review Notes.

Patiromer Critiera for Use

- Review for discontinuation of medications that may contribute to hyperkalemia
- Initiation or escalation of a loop or thiazide diuretic
- Instruction on a low potassium diet
- Consider reducing or discontinuing RAASi medications
- A trial of SPS as appropriate

Patient and Note Selection

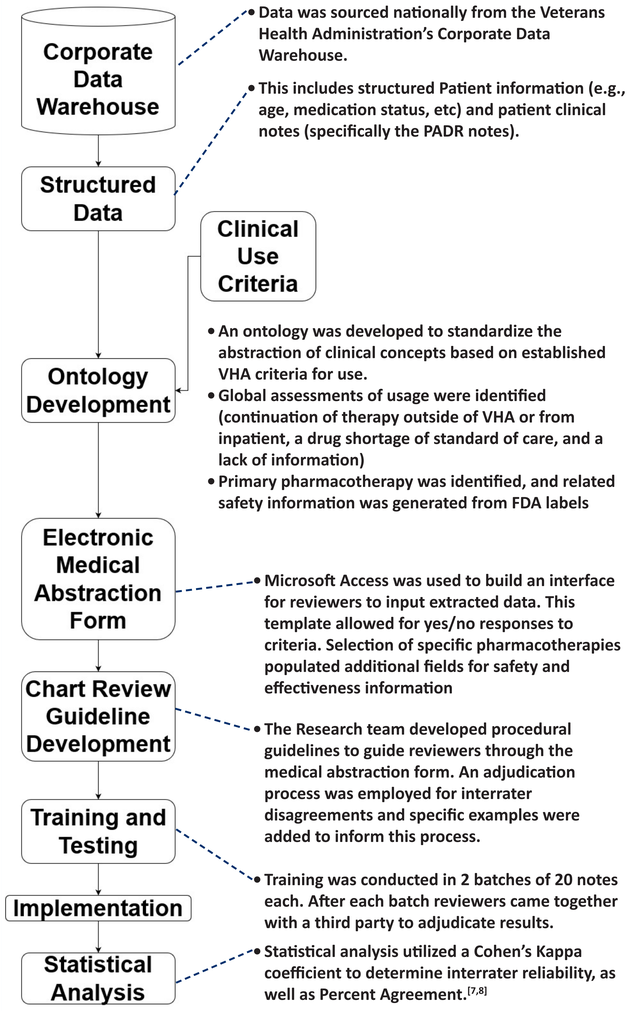
Patient Selection

This was a national study of Veterans who received an outpatient dispensing of patiromer between January 2016 and February 2021. Veterans were required to have an outpatient diagnosis of Chronic Kidney Disease at least 1 year before initiating patiromer and a dispensation of SPS within the 3 months prior to patiromer initiation.

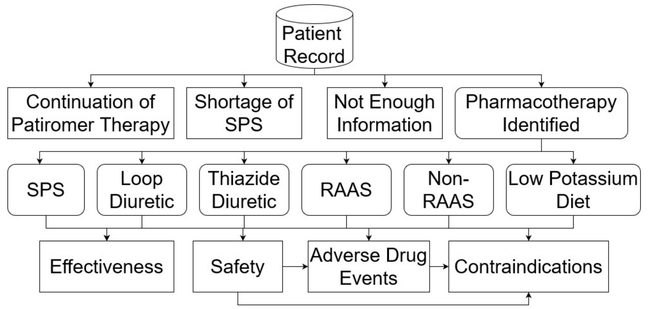
Clinical Notes

Prior Authorization Drug Review (PADR) Notes were selected for concept extraction. PADR notes are clinical notes written by pharmacists within the VHA which document treatment strategies providers have attempted to treat the diagnosed conditions. To be approved for dispensation of patiromer, a provider must have attempted, or had reason to avoid VHA criteria for use of non-formulary agents.

Methods



- Data was sourced nationally from the Veterans Health Administration's Corporate Data Warehouse.
- This includes structured Patient information (e.g., age, medication status, etc) and patient clinical notes (specifically the PADR notes).
- An ontology was developed to standardize the abstraction of clinical concepts based on established VHA criteria for use.
- Global assessments of usage were identified (continuation of therapy outside of VHA or from inpatient, a drug shortage of standard of care, and a lack of information)
- Primary pharmacotherapy was identified, and related safety information was generated from FDA labels
- Microsoft Access was used to build an interface for reviewers to input extracted data. This template allowed for yes/no responses to criteria. Selection of specific pharmacotherapies populated additional fields for safety and effectiveness information
- The Research team developed procedural guidelines to guide reviewers through the medical abstraction form. An adjudication process was employed for interrater disagreements and specific examples were added to inform this process.
- Training was conducted in 2 batches of 20 notes each. After each batch reviewers came together with a third party to adjudicate results.
- Statistical analysis utilized a Cohen's Kappa coefficient to determine interrater reliability, as well as Percent Agreement.[7,8]



Results

$$kappa(\kappa) = \frac{P_o - P_e}{1 - P_e}$$

P_o is the observed agreement among graders. P_e is the hypothetical chance of the graders arriving at the same

Kappa Value	Level of Agreement[7]
<0	Less than chance agreement
0.01-0.20	Slight Agreement
0.21-0.40	Fair Agreement
0.41-0.60	Moderate Agreement
0.61-0.80	Substantial Agreement
0.81-0.99	Almost Perfect Agreement

Sodium Polystyrene Sulfonate Pharmacotherapy Identification		Reviewer 1		
		Yes	No	Total
Reviewer 2	Yes	204	18	222
	No	8	142	150
	Total	212	160	372

P_o=(204+142)/372=**0.93**
P_{yes}=(222/372)*(212/372)=0.34
P_{no}=(160/372)*(150/372)=0.17
P_e=0.34+0.17=**0.51**
K=(0.93-0.51)/(1-0.51)
K=0.856 - Almost Perfect Agreement
95% CI = 0.803-0.909

Interrater Agreement of Primary Pharmacotherapy Identification

Treatment	Shared Opinion	Divergent Opinion	Patients on Pharmacotherapy	Percent Agreement	Kappa	95 CI
SPS	346	26	204	93.01	0.856	0.803-0.909
Loop	342	30	63	91.94	0.757	0.674-0.839
Thiazide	363	9	4	97.58	0.459	0.163-0.756
RAAS	348	24	35	93.55	0.708	0.598-0.818
Non-RAAS	362	10	3	97.31	0.361	0.055-0.668
LPD	323	49	63	86.83	0.634	0.540-0.727

Interrater Agreement of Global Assessments

Record	Shared Opinion	Divergent Opinion	Percent Agreement	Kappa	95% CI
Patiromer Therapy Cont.	364	8	97.85	0.815	0.689-0.940
Shortage of SPS	360	12	96.77	0.911	0.861-0.960
Not Enough Information	364	8	97.85	0.903	0.836-0.969

Conclusions

High interrater agreement was shown utilizing this approach with the majority of concepts extracted having a substantial agreement. Identification of global, document level, concepts all maintain almost perfect agreement.

This approach also demonstrates the viability of the clinical Prior Authorization Drug Review (PADR) note as a source of understanding for provider treatment strategies. Further studies will be need to see if PADR notes offer similar levels of insight into provider prescribing habits outside of patiromer for the treatment of hyperkalemia.

Interpretation of Global Assessment Agreement	
Patiromer Therapy Cont.	Almost Perfect Agreement
Shortage of SPS	Almost Perfect Agreement
No Information Available	Almost Perfect Agreement

Interpretation of Pharmacotherapy Agreement	
SPS	Almost Perfect Agreement
Loop Diuretic	Substantial Agreement
Thiazide Diuretic	Moderate Agreement
RAAS	Substantial Agreement
non-RAAS	Fair Agreement
LPD	Substantial Agreement

The use of a Cohen's Kappa assessment to determine interrater reliability may not present the full picture, by itself. For instance, between "Patiromer Therapy Cont" and "Shortage of SPS" the percent agreement is decreased, but interrater agreement increases. This is likely due to an imbalance in rater concepts extracted, with the former being very heavily skewed towards an agreed yes.

Likewise, non-RAAS pharmacotherapy had the lowest interrater agreement, but still had 97% agreement. This is likely due to 10 disagreements occurring, but only having 3 instances of shared identification. This may represent a pitfall of using Kappa alone to measure the reliability of chart review methods.

Acknowledgement

Joshua Qualls, PharmD, is supported by VA Office of Academic Affiliations Advanced Fellowship Program in Medical Informatics. This work was supported by the VA HSR&D Informatics, Decision-Enhancement, and Analytic Sciences (IDEAS) Center of Innovation

References

1. Clase CM, Carrero JJ, Ellison DH, et al. Potassium homeostasis and management of dyskalemia in kidney diseases: conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference. Kidney Int. 01 2020;97(1):42-61. doi:10.1016/j.kint.2019.09.018
2. Palmer BF, Carrero JJ, Clegg DJ, et al. Clinical Management of Hyperkalemia. Mayo Clin Proc. 03 2021;96(3):744-762. doi:10.1016/j.mayocp.2020.06.014
3. Fried L, Kovesdy CP, Palmer BF. New options for the management of chronic hyperkalemia. Kidney Int Suppl (2011). Dec 2017;7(3):164-170. doi:10.1016/j.kisu.2017.09.001
4. Noel JA, Bota SE, Petrcich W, et al. Risk of Hospitalization for Serious Adverse Gastrointestinal Events Associated With Sodium Polystyrene Sulfonate Use in Patients of Advanced Age. JAMA Intern Med. 08 01 2019;179(8):1025-1033. doi:10.1001/jamainternmed.2019.0631
5. Laureati P, Xu Y, Trevisan M, et al. Initiation of sodium polystyrene sulphonate and the risk of gastrointestinal adverse events in advanced chronic kidney disease: a nationwide study. Nephrol Dial Transplant. 09 01 2020;35(9):1518-1526. doi:10.1093/ndt/gfz150
6. Patiromer Criteria for Use (VA Pharmacy Benefits Management Services) (March 2021).
7. Viera AJ, Garrett JM. Understanding interobserver agreement: the kappa statistic. Fam Med. May 2005;37(5):360-3
8. McHugh ML. Interrater reliability: the kappa statistic. Biochem Med (Zagreb). 2012;22(3):276-82.

Contact information: Joshua.Qualls@utah.edu