PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Medication Decision-Making for Patients with Renal Insufficiency in Inpatient and Outpatient Care at a U.S. Veterans Affairs Medical Center: A Qualitative, Cognitive Task Analysis
AUTHORS	Elkhadragy, Nervana; Ifeachor, Amanda; DiIulio, Julie; Arthur, Karen; Weiner, Michael; Militello, Laura; Glassman, Peter; Zillich, Alan; Russ, Alissa

VERSION 1 – REVIEW

REVIEWER	Talya Porat Imperial College London, UK
REVIEW RETURNED	29-Nov-2018

GENERAL COMMENTS	This paper describes a study where the authors conducted cognitive task analysis interviews to examine cognitive strategies that healthcare professionals use to identify and manage medication-related problems for patients with renal insufficiency. The paper is well written with clear motivation. The study is well defined, using an appropriate method for answering the research question. CTA is an appropriate method to understand way of thinking and decision making. The Critical Decision Method is a well-known method to elicit information and knowledge from experienced users in relation to their decision making usually during non-routine, critical incidents. The authors made good use of recall strategies to help HCPs remember the incident. Saying that, my main concern with this paper is its focus on a very specific aspect (how HCPs manage medication-related problems) of a specialised population (patients with renal insufficiency), as opposed to considering the higher-level problem. Very specific findings and solutions could be limiting and not so practical to implement in a complex environment with competing needs such as in healthcare. Qualitative research studies do study a specific phenomenon and generalizability might not be an expected attribute, however, it would be valuable to understand and discuss the larger problem context. For example, while the study's findings may be novel and unique to the renal-drug problems (e.g., the cyclical nature of the decision-making process), the proposed solutions could perhaps be more generalized. For example, could the proposed directions and solutions such as longitudinal tracking mechanisms and improved EHR visualisations and information trends support other

	health conditions which perhaps were not defined as having a cyclical nature but do require constant monitoring and medications adjustments over time (e.g., diabetes, cardiovascular diseases). Could they address prescription errors more generally caused by cognitive factors such as attention, memory, perception? Another interesting aspect to discuss would be the empowerment of patients in their self-management of treatments. What is the role of the patient in detecting renal-drug related problems. Patients involvement could reduce the need of the HCP to be in constant vigilance. Supplemental Materials – these include example quotes and a template of the Decision Requirements Table used. Would have been helpful to know who said the quote (provider vs pharmacist). It would also have been useful to display the Decision Requirements Table itself, not just the template.

REVIEWER	Guido Schmiemann, MD PhD,MPH Institute for Public Health and Nursing Science, Department for Health Services Research, Universität Bremen, Germany
REVIEW RETURNED	27-Jan-2019

GENERAL COMMENTS	Thanks for the opportunity to review this interesting paper on incident analysis in medication errors. I have some questions/ suggestions regarding details of the study and one major concern. Major concern: When reading the paper and the abstract of a paper cited (19) it seems as if the cited paper is dealing with the same topic. I could not get a full text, but according to the abstract it is possible that the analysis presented here is part of a larger project in which “3 categories of medication-related incidents: adverse drug reactions, drug-drug interactions, and drug-disease interactions” have been analyzed. The authors should clearly state the background of their study and to what extent the data have been published before. Minor aspects: P4 L 47 Please elaborate on the information given by the CPOE system for Health Care Professionals (HPC). When laboratory results are available will this include only a creatinine or is there any automatic calculation of an estimated GFR (like Cockroft, CKDEpi). P5 L14 “Who” invited the participants. Was the management of the clinic involved, were any precautions taken that participants avoided participation because of fearing some kind of “self-blaming”? P5 L21 A predefined goal of a sample size in a qualitative study is unusual. The main issue of a sample size should be the content saturation. Could the authors give some information on this? P5 L38 How was eligibility for an interview reached? Did those involved consent together or were there discrepancies in their ratings? If yes, how was a consent reached? P 5 L 44

	Please clarify what approximately “1 month” means (What was the range between incident and interview) P15 If available, do you have any information if participants differ from other hospital employees regarding age, sex, work experience? Discussion: Are there any more types of medication errors known from the literature that have not been mentioned/addressed in the interviews? The aspect of alert fatigue or over alert seems not to be mentioned in the interview but is usually one of the highest ranked reasons when discussing medication errors. Could you explain why this problem did not arise and how it would fit in your model? Another frequent encountered problem is the validity of the reference standard. I am not sure about the situation in the US, but many countries face problems regarding the reference standard (when is a dose reduction necessary/ appropriate). Additionally these recommendations are changing over time (for example regarding metformin or nitrofurantoin).

VERSION 1 – AUTHOR RESPONSE

Responses to reviewers’ comments

Manuscript ID #: bmjopen-2018-027439

Medication Decision-Making for Patients with Renal Insufficiency: A Cognitive Task Analysis

Reviewers’ Comments	Responses
Please ensure that you have fully responded to the comments from the Editor of BMJ Quality & Safety which were as follows:	
Note: most of the below edits were already incorporated in the manuscript before submitting to BMJ Open, as these comments were from BMJ Quality & Safety, therefore are not shown in a ‘track-change’ format.	
1. It is not clear why addressing the stated objective, to examine the cognitive strategies used in identifying and managing safety issues in patients with renal impairment, is helpful in preventing prescribing errors from happening in the first place (which seems to be the wider aim being outlined in the introduction)	Explained the rational more clearly in the Abstract (page 2) and in the Introduction (page 4): “Many research studies have adequately assessed prevalence and factors contributing to medication errors, but very few examined how healthcare professionals detect and manage safety concerns. Such knowledge would inform more effective error detection systems and decision support tools which can aid error prevention.”

2. There is no information in the paper about how long after the relevant incidents the interviews were conducted, which may affect recall bias.	Added this detail under “Interview process” section (page 6): “Interviews were conducted within 2 – 4 weeks after incidence occurrence.”
3. The section on the action taken following identification of a safety issue does not seem to differentiate actions on the part of prescribers vs non-prescribers, and yet it seems likely that their actions would be different.	We Explained our findings at the end of the paragraph “Model of Decision-Making Processes” (page 7): “Within our sample, we examined findings from prescribers versus non-prescribers, but did not find evidence that they relied on substantially different cognitive strategies to detect and manage renal-drug problems; instead, interview data indicated that their strategies were similar.”
4. The discussion section is disproportionately long relative to the results, and introduces new data.	We significantly shortened the discussion section and eliminated new data.
Reviewer #1	
R1.1 My main concern with this paper is its focus on a very specific aspect (how HCPs manage medication-related problems) of a specialized population (patients with renal insufficiency), as opposed to considering the higher-level problem. Very specific findings and solutions could be limiting and not so practical to implement in a complex environment with competing needs such as in healthcare. Qualitative research studies do study a specific phenomenon and generalizability might not be an expected attribute, however, it would be valuable to understand and discuss the larger problem context.	We agree that our study focused on a specific problem, i.e. renal-drug problems, although we expect that our findings may be applicable to many other diseases in which long-term follow-up is key to preventing complications (e.g. diabetes, cardiovascular diseases, COPD). We added a statement to the discussion section clarifying this point (page 9). See also next response below.
R1.2. While the study’s findings may be novel and unique to the renal-drug problems (e.g., the cyclical nature of the decision-making process), the proposed solutions could perhaps be more generalized. For example, could the proposed directions and solutions such as longitudinal tracking mechanisms and improved EHR visualizations and information trends support other health conditions which perhaps were not defined as having a cyclical nature but do require constant monitoring and medications adjustments over time (e.g., diabetes,	Thank you for this comment! We added more text in the discussion section (page 9-10), end of first paragraph: “Although we examined a specific problem, renal-drug safety applies to a large patient population. More than 15 % of all adults in the United States (30 million people) have chronic kidney disease.[1] Additionally, we expect that our findings can inform other chronic diseases (e.g. diabetes, cardiovascular diseases, COPD) that

cardiovascular diseases). Could they address prescription errors more generally caused by cognitive factors such as attention, memory, perception?	do not necessarily have a cyclical nature but often worsen with patient age and require regular monitoring and medication adjustments over time. Our findings may also inform more effective software solutions to aid attention, memory, and perception, and thus provide cognitive support to help prevent prescription errors more generally."
R1.3. Another interesting aspect to discuss would be the empowerment of patients in their self-management of treatments. What is the role of the patient in detecting renal-drug related problems? Patients' involvement could reduce the need of the HCP to be in constant vigilance.	Because renal disease is largely asymptomatic and not readily detected by patients, our study focused on HCP's strategies to detect the problem. Providing patient education to empower them to detect potential renal-drug problems could be a valuable future research that could build upon our findings. To convey this idea, we have added text in the discussion section, end of second paragraph (page 10): "Future studies could also build upon our findings and implement patient education programs to empower patients with knowledge on how to detect potential renal-drug problems and the importance of regular follow-up."
R1.4. Supplemental Materials – these include example quotes and a template of the Decision Requirements Table used. Would have been helpful to know who said the quote (provider vs pharmacist).	We added detail to the supplemental tables to indicate whether the quote was from a physician, nurse practitioner, or pharmacist.
R1.5. It would also have been useful to display the Decision Requirements Table itself, not just the template.	An individual, Decision Requirements Table was generated for each incident and we added an explanation to the text (page 6): "(The table template is found in the supplemental Table D, but individual completed tables are not shown in order to maintain participant confidentiality)."
Reviewer #2	
R2.1 When reading the paper and the abstract of a paper cited (19) it seems as if the cited paper is dealing with the same topic. I could not get a full text, but according to the abstract it is possible that the analysis presented here is part of a larger project in which "3 categories of medication-related incidents: adverse drug	We uploaded the cited paper as a supplemental file for reference. We also clarified how this study fits into the larger project by adding the following statement in the Introduction section (page 4): "This research is part of a larger study that examined decision-making for two other types of medication incidents: adverse drug reactions and

reactions, drug-drug interactions, and drug-disease interactions" have been analyzed. The authors should clearly state the background of their study and to what extent the data have been published before.	drug-drug interactions. Previously, we published a methods paper that describes how we adapted CTA for this research.[2] The present article presents results for HCPs' decision-making regarding renal-drug problems."
R2.2 P4 L 47 Please elaborate on the information given by the CPOE system for Health Care Professionals (HPC). When laboratory results are available will this include only a creatinine or is there any automatic calculation of an estimated GFR (like Cockroft, CKDEpi).	We clarified on page 4-5 in the Methods section under "Setting": "When patient laboratory results are available in VA's EHR, serum creatinine and estimated GFR are displayed automatically on a "labs tab" and the latter is based on standardized body surface area with units of ml/min/1.73m^2. The eGFR reported to prescribers is based on the Modification of Diet in Renal Disease (MDRD) equation and is adjusted for isotope dilution mass spectrometry (IDMS) traceable assays."
R2.3 P5 L14 "Who" invited the participants. Was the management of the clinic involved, were any precautions taken that participants avoided participation because of fearing some kind of "self-blaming"?	We added clarification in the Methods, (page 5): "A research team member, who had no clinical or managerial roles, was responsible for recruitment." We also added details to the limitations on (page 11): "Third, HCPs submitted renal-drug incidents voluntarily and since the study focused on medication problems, some individuals might have avoided participation even though we examined cases where participants intervened. Thus, the voluntary nature of this study might have influenced the sample of participants and type of incidents we captured. For instance, HCPs might have submitted incidents for which they felt the most confident that they had taken the best course of action for the patient."
R2.4 P5 L21 A predefined goal of a sample size in a qualitative study is unusual. The main issue of a sample size should be the content saturation. Could the authors give some information on this?	We added the following statement in the "Participant Recruitment and Sampling" section (page 5): "A study by Fusch and Ness found that qualitative data saturation is often reached within 12 participants,[3] but we intentionally sampled more because we expected a variety of renal-drug incidents.[2]"

	We also added the following statement under "Data analysis" (page 6): "No new codes were identified after analyzing 13 cases, which indicates adequate data saturation."
R2.5 P5 L38 How was eligibility for an interview reached? Did those involved consent together or were there discrepancies in their ratings? If yes, how was a consent reached?	We added the following statement under "Problem selection" to clarify how eligibility was determined (page 6): "Further details about interview eligibility and case selection is provided in the methods article by Russ et al.[2]"
R2.6 P 5 L 44 Please clarify what approximately "1 month" means (What was the range between incident and interview)	We edited the text to clarify the duration of time, under the "interview process" paragraph under "Data Collection section(page 6): "Interviews were conducted within 2 – 4 weeks after incidence occurrence."
R2.7 P15 If available, do you have any information if participants differ from other hospital employees regarding age, sex, work experience?	We have not found published studies that compare employees at the VA to other settings.
R2.8 Discussion: Are there any more types of medication errors known from the literature that have not been mentioned/addressed in the interviews? The aspect of alert fatigue or over alert seems not to be mentioned in the interview but is usually one of the highest ranked reasons when discussing medication errors. Could you explain why this problem did not arise and how it would fit in your model?	We added text on pg 10: "We did not find alert fatigue to be a notable factor for renal-drug problems, most likely because VA's CPOE system provides only limited renal alerts.[4] Additionally, our study examined decision-making for renal-drug problems broadly, regardless of whether or not CPOE alerts were involved in the incident. In the incidents we collected, HCPs detected problems not just during prescribing, but at other points of the medication use process, which typical CPOE alerts cannot detect. Our findings are important because they provide evidence that can inform future enhancements of alerts."

R2.9 Another frequent encountered problem is the validity of the reference standard. I am not sure about the situation in the US, but many countries face problems regarding the reference standard (when is a dose reduction necessary/ appropriate). Additionally these recommendations are changing over time (for example regarding metformin or nitrofurantoin).	Our interview data agree with these comments and we added detail to the Results, under “Stage 2: Gathering information” (page 8): “An important challenge that HCPs encountered while gathering information was the lack of consistency in drug resources. For example, a pharmacist participant found two different recommendations for dosing colchicine in dialysis patients, one reference recommended 0.3 mg twice a week, and the other recommended 0.6 mg and not repeating for 2 weeks.”
Editorial Requests	
E.1 Along with your revised manuscript, please include a copy of the SRQR checklist for reporting of qualitative research, indicating the page/line numbers of your manuscript where the relevant information can be found	We have included the SRQR checklist
E.2 Please provide details about the ethics approval obtained in the methods section. Please also include details about consent sought from the participants.	We have included the IRB approval letters
Formatting Amendments	
1. Please re-upload your supplementary files in PDF format.	PDF format is provided
2. Please provide a more detailed contributorship statement.	Contributorship details provided in the manuscript on page 12.
3. Patient and Public Involvement: We have implemented an additional requirement to all articles to include 'Patient and Public Involvement' statement within the main text of your main document. Please refer below for more information regarding this new instruction: Authors must include a statement in the methods section of the manuscript under the sub-heading 'Patient and Public Involvement'. This should provide a brief response to the	Added the paragraph on page 7: Patient and Public Involvement This study was conducted to assess renal-medication problems, specifically, to understand the decision-making processes that healthcare professionals use to detect and respond to these

following questions: How was the development of the research question and outcome measures informed by patients' priorities, experience, and preferences? How did you involve patients in the design of this study? Were patients involved in the recruitment to and conduct of the study? How will the results be disseminated to study participants? For randomised controlled trials, was the burden of the intervention assessed by patients themselves? Patient advisers should also be thanked in the contributorship statement/acknowledgements. If patients and or public were not involved please state this.	patient safety concerns. These types of medication problems are mostly preventable and often serious, which makes finding solutions a priority to improve patient care. Patients were not directly involved in this study nor were they recruited; instead, our participants were HCPs who addressed a renal-drug problem for one of their patients. Our results can inform future enhancements of healthcare systems to provide safer care for patients.

References:

1. Centers for Disease Prevention and Control. National Chronic Kidney Disease Fact Sheet, 2017. 2017. https://www.cdc.gov/diabetes/pubs/pdf/kidney_factsheet.pdf.
2. Russ AL, Militello LG, Glassman PA, Arthur KJ, Zillich AJ, Weiner M. Adapting Cognitive Task Analysis to Investigate Clinical Decision Making and Medication Safety Incidents. *Journal of Patient Safety.* 2017.
3. Fusch PI, Ness LR. Are we there yet? Data saturation in qualitative research. *The qualitative report.* 2015;20:1408.
4. Melton BL, Zillich AJ, Russell SA, et al. Reducing prescribing errors through creatinine clearance alert redesign. *The American journal of medicine.* 2015;128(10):1117-1125.

VERSION 2 – REVIEW

REVIEWER	Guido Schmiemann Institute for Public Health and Nursing Science Department for Health Services Research, Universität Bremen Grazer Str. 4, 28359 Bremen, Deutschland, Mail: schmiemann@uni-bremen.de
REVIEW RETURNED	12-Mar-2019

GENERAL COMMENTS	Thanks for resubmitting the paper. My comments have been answered sufficiently and I would recommend publication of the paper

VERSION 2 – AUTHOR RESPONSE

We made all the revisions as requested. Here are a description of the edits:

1. We changed the title, as shown above, to include the study setting and qualitative approach.

2. We added an “Ethics Approval” paragraph to the Methods with description of approving committees and participant consent (page 5):

“This study was approved by the Indiana University Institutional Review Board and the Richard L. Roudebush VA Research and Development Committee (IRB study #1301010433). Participants completed a voluntary, written consent prior to any study data collection: consent occurred before participants submitted any incidents.”

3. We moved the “Data Availability Statement” to page 12 (was under Methods in the prior submission).

4. We separated the “Conflicts of Interest and Funding” paragraph into two separate paragraphs: “Competing Interests”, and “Funding”. Page 12.

In addition to these changes, we added units to the rows in Table 1. (Table 1 data remained the same).