Manuscript Title: Reducing prescribing errors through creatinine clearance alert redesign

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Running Title: Prescribing errors with creatinine clearance alerts

Number of References: **42**

Number of Tables: **3**

This is the author's manuscript of the article published in final edited form as:
Melton, B. L., Zillich, A. J., Russell, S. A., Weiner, M., McManus, M. S., Spina, J. R., & Russ, A. L. (2015). Reducing Prescribing Errors Through Creatinine Clearance Alert Redesign. The American Journal of Medicine, 128(10), 1117–1125. http://doi.org/10.1016/j.amjmed.2015.05.033

Number of Figures: **2**

Word Length for Article (max 3000): **2927 (includes abstract, text, and acknowledgements)**

Word Length for Abstract (max 250): **243**

Key Words: patient safety, health information technology, evaluation, renal disease, electronic health records

Abstract

Background: Literature has shown that computerized creatinine clearance alerts reduce errors during prescribing, and applying human factors principles may further reduce errors. Our objective was to apply human factors principles to creatinine clearance alert design and assess whether the redesigned alerts increase usability and reduce prescribing errors compared to the original alerts.

Methods: Twenty Veterans Affairs (VA) outpatient providers: 14 physicians, 2 nurse practitioners, and 4 clinical pharmacists completed two usability sessions in a counterbalanced study to evaluate original and redesigned alerts. Each session consisted of fictional patient scenarios with three medications that warranted prescribing changes due to renal impairment, each associated with creatinine clearance alerts. Quantitative and qualitative data were collected to assess alert usability and the occurrence of prescribing errors.

Results: There were 43% fewer prescribing errors with the redesigned alerts compared to the original alerts (p=0.001). Compared to the original alerts, redesigned alerts significantly reduced prescribing errors for allopurinol and ibuprofen (85% vs 40%, and 65% vs 25%, p= 0.012, 0.008 respectively), but not for spironolactone (85% vs 65%). Nine (45%) providers voiced confusion about why the alert was appearing when they encountered the original alert design. When laboratory links were presented on the redesigned alert, laboratory information was accessed 3.5 times more frequently.

Conclusion: Although prescribing errors were high with both alert designs, the redesigned alerts significantly improved prescribing outcomes. This investigation provides some of the first evidence on how alerts maybe designed to support safer prescribing for patients with renal impairment.

Introduction

Renal function can be assessed through multiple methods; one common approach is to estimate creatinine clearance. People with impaired renal function are 5.5 times more likely to die than those without. [1,2] Adverse drug events and inappropriate prescribing related to renal function are estimated to occur in 20% to 46% of patients with impaired renal function, 91% of which may be preventable.[3-7]

Computerized alerts can reduce prescribing errors associated with nephrotoxic medications, renally cleared medications, and renal impairment.[6, 8-12] However, the approach to presenting information to providers via alerts may affect how providers assess and use that information.[13-15] For example, if the alert information is unclear this can result in inappropriate prescribing and increased patient risks.[16] Alert effectiveness is related to its usability, defined as the 'extent to which a [alert] can be used by specified users to achieve specified goals with effectiveness, efficiency and satisfaction'.[17] Usability is influenced by the alert's interface display, which can be modified using human factors principles to improve safety.[18-20]

Previously, we conducted an investigation to assess the use of alerts in outpatient care, which identified 44 factors that influence the human-computer interaction between providers and alerts, along with several weaknesses of alert designs.[20] For instance, providers suggested that the timing of creatinine clearance alerts be modified so they appear in response to specific medication orders, such as allopurinol and non-steroidal anti-inflammatory drugs. Thus, the present work was undertaken to redesign and evaluate creatinine clearance alerts. We hypothesized that redesigned alerts, which incorporated human factors principles, would significantly reduce prescribing errors compared to the original alerts. This investigation was part of a larger study, published elsewhere,[21] that examined efficiency, mental workload, perceived satisfaction, and prescribing errors across several alert types, but did not assess findings by alert type. Herein, we present findings specific to creatinine clearance alerts

for the first time. Distinct contributions of this article also include prescribing errors for individual medications; an in-depth analysis of prescribing actions, including how prescribers responded to dose dependent versus contraindicated medications; and prescribers' utilization of laboratory results for resolving alerts.

Methods

Study design

Participants completed prescribing tasks for fictional patients.[22] Each participant completed two, 30-minute sessions (i.e., original and redesign) in a counterbalanced design, with a washout period of at least 2 weeks between sessions so participants would be less likely to remember the tasks in each session. They were informed that they could order, discontinue, or change any medications. All participants were able to choose a medical or pharmaceutical textbook worth up to $50 for each session as an acknowledgement of their time.

The study was approved by the Indiana University Institutional Review Board and Veterans Affairs (VA) Research and Development Committee, and was conducted at the VA Health Services Research and Development Human-Computer Interaction and Simulation Laboratory.[23] This manuscript was prepared using the STAtement on the Reporting of Evaluation studies in Health Informatics (STARE-HI) guidelines.[24]

Participants

Twenty VA providers (6 men, 14 women) participated, consisting of 14 physicians, 4 clinical pharmacists, and 2 nurse practitioners. Clinical pharmacists were included in this study because they have prescribing privileges in VA outpatient care and also receive alerts. None of the research team members were study participants. Additionally, none of the participants had any involvement in the development of study materials or data analysis. This sample size is within the acceptable range reported

by other human-computer interaction studies[25-28]. Participants had a mean age of 41 (range: 29-56) and an average of 7.5 years experience (range: 1-13.5 years) with VA computerized provider order entry.[21] Providers were recruited through e-mail and face-to-face communication and were eligible to participate if they were staff at the VA primary care clinics, and had at least one year of experience with VA computerized provider order entry. Students and residents were excluded from the study.

Apparatus

Prototypes

Two prototypes were developed within a mock electronic health record. The original alerts (Figure 1.A) represented those in use at the VA. These alerts appear before the medication list is displayed, warning providers "pre-emptively". Alert redesigns (Figure 1.B) were iteratively developed by a team that included human factors engineers and clinicians, and informed by our previous study, where we identified limitations of alert designs within outpatient care.[20] Redesigns were further informed by literature evidence and a VA advisory panel.[21, 29-31] Human factors principles incorporated in the redesigned alerts included presenting alerts in a tabular format[32], embedding links to additional laboratory information[30], adding information on medication risks[31], and changing the timing of the alert so that it appeared in association with specific medications. For both alert designs, participants could access the 'Labs' tab in the mock electronic health record, but this required exiting the ordering process.

Scenarios

A pharmacist and physician developed two fictional patient scenarios to evaluate the alerts and reviewed the scenarios for completeness. Predefined, objective criteria for errors were developed a-priori from Micromedex guidelines[33] (Table 1, column 5) and used as the standard for error determinations.

Scenarios included three medications that required adjustment or discontinuation due to renal impairment (Table 1). For the original design, two creatinine clearance alerts were produced, each near the beginning of the associated scenario. These alerts presented a general warning about estimated creatinine clearance and other lab results when the prescriber first enters the computerized provider order entry system (see Figure 1A). In contrast, redesigned alerts appeared immediately after order details for each medication were entered; thus, three alerts could appear. Additional prescribing tasks were interspersed between alerts to mimic workflow that occurs during patient care. Scenarios were identical between the two sessions, aside from the patient's name. Scenarios were pilot tested by three clinicians, not included as study participants, prior to data collection to ensure scenarios were clear, clinically appropriate, and followed standards of care.

Data Collection

Participants were recorded using Morae® (Okemos, MI) software which captures video of the computer screen actions. We collected qualitative data using the Think-aloud technique, where participants are asked to verbalize their thoughts as they use the alerts.[34-36] Debrief interviews were conducted if time permitted. All verbalized statements were recorded and transcribed for later analysis.

Data Analysis

Video data were evaluated to assess usability. These data were analyzed by one individual with previous usability evaluation experience who was not part of the alert redesign team. This individual reviewed the videos, examined computer screen actions, and transcribed Think-aloud statements to assess the usability of the alerts. A pharmacist who was involved in neither the scenario development nor the redesign effort reviewed the videos and used the predefined criteria to evaluate prescribing errors. Another pharmacist double-checked each categorization to ensure accuracy.[37] Prescribing errors and accessing laboratory results were compared across the two alert designs using Wilcoxon signed-rank

test for all three medications and McNemar tests for individual medications. All statistical tests were conducted with SPSS version 20.0.

Results

Prescribing errors related to renal impairment

Across the scenarios, participants made significantly fewer prescribing errors (n=26) when using the redesigned versus original creatinine clearance alerts (n=47, p=0.001; Figure 2A). There were 43% fewer prescribing errors with the redesigned alerts. Results for individual medications are shown in Figure 2B.

Prescribing Actions for dose-dependent verses contraindicated medications

As shown in Table 1, allopurinol required at least a dose reduction, while spironolactone and ibuprofen were contraindicated for the scenarios. Table 2 outlines prescribing actions taken for each. Providers appropriately decreased the dose of allopurinol three times more often when they encountered the redesigned alerts. Several prescribers incorrectly reduced the dose of spironolactone rather than canceling the order, although more prescribers cancelled spironolactone with the redesigned alert.

Usability of Creatinine Clearance Alerts

Usability findings are shown in Table 3.

Accessing laboratory results

With the original alerts, additional laboratory information could only be accessed through the 'Labs' tab, but when providers used the redesigned alerts, laboratory information was accessed 3.5 times more frequently using the 'more labs' hyperlink than the 'Labs' tab. Overall, there was a modest improvement in appropriately discontinuing the spironolactone with the redesigned alerts (Figure 2B), but this was not due to the ease of viewing laboratory results: 2 of 5 providers who viewed labs with the original alerts

proceeded with the order, while 7 of 11 providers who viewed labs with the redesigned alerts proceeded with the order for spironolactone (Table 2).

Discussion

To our knowledge, this scenario-based study is the first to systematically compare two different designs for creatinine clearance alerts. Other studies noted a 16% reduction in prescribing errors when renal dosing alerts occurred during medication dispensing, and as much as a 42% reduction in prescribing errors during medication ordering compared to no alert, but neither study compared different alert designs nor examined the application of human factors principles on prescribing safety.[6, 11,12] Our result of 43% fewer prescribing errors with the redesigns, supported the hypothesis that applying human factors alert design would reduce prescribing errors. Approximately 26 million Americans have chronic kidney disease.[1] Preventable medication errors occur in this population about 7 million times and cost about $18 million annually.[38] If the alerts reduce medication errors by 43%, as in our study, this could prevent harm to approximately 3 million patients and save nearly $8 million dollars annually.[38]

Four features of the redesigned alerts likely contributed to safer prescribing. First, the redesigned alerts occur closer to the time of medication decision-making, whereas the original alerts may have appeared too *early* in prescribing workflow, thereby increasing errors. The original alerts appeared before the provider attempted to order or select a medication. Recent literature advocates for preemptive alerts that appear before prescribing decisions which may minimize workflow interruptions.[39] However, when the original alerts were presented prior to medication selection, providers vocalized confusion about the alert's purpose and prescribing errors were significantly greater. This early timing for alerts requires the provider to remember that the patient has renal impairment and assumes providers will know which medications are contraindicated or require a dosage adjustment later in the workflow of the session when specific medications are ordered. Our findings provide evidence that safer prescribing

occurs when alerts are provided closer to the point of decision-making – in this case, *later* in prescribing workflow - when the provider is attempting to prescribe a potentially harmful medication. The redesigned alerts are 'smarter' than the original alerts in that the redesigns are specific to renally dosed medications, whereas the original alerts appear regardless of what is being ordered. In cases where providers are not ordering any renal dosing medications, the redesign could also reduce inappropriate alerts as well as the number of alerts presented. Similarly, the later presentation of the alert indicated that providers may need some type of action, as indicated by the increased number of providers who adjusted doses when presented with the redesigned alerts.

Second, safer prescribing may have occurred in some cases because participants accessed laboratory results more frequently with the redesign, which included embedded links to lab results. This may facilitate clinical workflow by providing better data access, and allowing providers to more rapidly view information for clinical decision-making. Literature suggests that patient specific information, should be summarized and readily accessible within the alert, if solicited.[40]

Third, the redesigned alerts displayed information in a tabular format, instead of one string of laboratory information. This format likely allowed providers to readily identify pertinent information when responding to alerts. Providers indicated the original design was difficult to read, and in one case, incorrectly interpreted the patient's renal function as acceptable; the original design assumes that the provider will recognize an abnormal creatinine clearance, whereas the redesigned alerts specify the creatinine clearance is 'low'.

Fourth, providing information regarding medication risk may promote safer prescribing. According to warning design literature, risk information is key to help individuals recognize the level of danger.[19,29] With the redesigned alerts, safer prescribing occurred for two medications with risks of hepatotoxicity

and renal failure, which providers may perceive as more serious than the risk of hyperkalemia with spironolactone.

Despite improved safety for allopurinol and ibuprofen, errors still occurred. This may be because estimated creatinine clearance was slightly below the accepted threshold of 30 mL/min, and providers may be inclined to renew these medications as this simulated patient had no previous problems. Errors were unlikely due to providers completely overlooking the alerts, since participants were asked to think aloud as they encountered alerts.[21]

Other factors may explain why errors remained high with spironolactone. Providers might have determined that hyperkalemia could be monitored and managed with other interventions like dietary restrictions rather than changing spironolactone. In the scenario, spironolactone needed to be cancelled because potassium was trending upward and above normal limits on the day of prescribing (Table 1). Neither alert design provided potassium results on the initial alert interface; this may have promoted some types of prescribing errors. Providers might not have been aware of the associated risk of hyperkalemia with renal impairment with the original design. Redesigned alerts occurred in association with spironolactone and stated a risk of hyperkalemia, but even with these changes, 65% of providers still proceeded with the order (Figure 2). With the redesign, seven providers who viewed lab results, presumably noting the elevated potassium level, continued with the spironolactone order. This indicates that easy access to lab results from the alert is not sufficient to promote safer decisions, but may improve workflow. One implication of these findings is that alerts may be improved by specifying whether a medication is ‘contraindicated’ or requires a ‘dose reduction’, since prescribers demonstrated confusion about what actions were warranted. This could be explicitly stated as part of the alert warning. Our findings for spironolactone are consistent with results from a clinical trial, which reported that over 80%

of outpatient physicians overrode drug-drug interactions alerts where the risk was hyperkalemia, even when the alert showed a potassium value above 5 mEq/L.[41]

Future Work

The overall error rate in our study, 60%, was still relatively high, but lower than reported in other studies of inappropriate renal prescribing, which found error rates of approximately 75%.[4] Future research should focus on elucidating providers' decision-making process. Additionally, differences between provider types should also be explored. With the redesign, some providers wanted information on dosing guidelines to inform their decisions. Providing dosing guidance may further reduce errors. Results provide evidence that presenting alerts too early in the prescribing process may weaken safety, but the optimum timing for creatinine clearance alerts is unknown. Similarly, adding laboratory results to the initial ordering screen should be evaluated. The redesigned alerts should also be piloted and evaluated in live clinical environments. Finally, because the Think-Aloud technique may confound time measurement[42], time to address the alerts was not analyzed in this study, and future work should examine time required in both laboratory and clinical settings.

Limitations

Providers were aware that patients were simulated; potentially reducing the precision of their clinical decision-making compared to clinical practice. Only three medications were used to evaluate creatinine clearance alerts and a larger number of medications may produce different results. Furthermore, our predefined criteria for errors may be more conservative than actual practice. Providers' responses might differ for inpatient scenarios, although we do not have data to support this. Finally, providers were recruited from one VA medical center and other providers may have responded differently.

Conclusions

Overall, alerts redesigned according to human factors principles led to safer prescribing for scenarios involving renal impairment. This study provides some of the first evidence on how to design creatinine clearance alerts to promote safety. Results indicate that creatinine clearance alerts should appear in association with specific medications, rather than as a general, 'preemptive' alert. Alerts should also present information regarding risks. Easy access to laboratory results may aid workflow and increase viewing of labs. Redesigned alerts significantly reduced errors for ibuprofen and allopurinol. Study findings may be used to improve medication safety for patients with renal impairment.

Acknowledgements

Thanks to Jason Hawsey and Anthony Puleo for input on VA alerts. Elizabette Johnson, and Drs. Amanda Kobylinski, Bradley Doebbeling, Jason Saleem, and Siying Chen assisted with study design and/or analysis. Bryce Melton assisted with graphics. This work was supported by VA HSR&D grant #PPO 09-298 (PI: Russ). Drs. Russ, and Zillich were supported by VA HSR&D Research Career Development Awards (CDA 11-214, and RCD 06-304-1, respectively). Views expressed in this article are those of the authors and do not necessarily represent the views of the Department of Veterans Affairs or the U.S. government.

Conflict of Interest

Conflicts of interest: none.

References:

1. National Kidney Foundation. About chronic kidney disease. Available at: http://www.kidney.org/kidneydisease/aboutckd.cfm. Accessed June 10, 2014.

2. Levy EM, Vicoli CM, Horwitz RI. The effect of acute renal failure on mortality. A cohort analysis. *JAMA* 1996; 275: 1489-1494.

3. Hug BL, Witkowski DJ, Sox CM, et al. Occurrence of adverse, often preventable, events in community hospitals involving nephrotoxic drugs or those excreted by the kidney. *Kidney Int* 2009; 76:1192-1198.

4. Salomon L, Deray G, Jaudon MC, et al. Medication misuse in hospitalized patient with renal impairment. *Int J Qual Health Care* 2003; 15:235– 40.

5. A van Dijk E, Drabbe NRG, Kruijtbosch M, De Smet P AGM. Drug dosage adjustments according to renal function at hospital discharge. *Ann Pharmacother* 2006; 40:1254–60.

6. Chertow GM, Lee J, Kuperman GJ et al. Guided medication dosing for inpatients with renal insufficiency. *JAMA* 2001; 286:2839-2844.

7. Sellier E, Colombet I, Sabatier B, et al. Effect of alerts for drug dosage adjustments in inpatients with renal insufficiency. *J Am Med Inform Assoc* 2009; 16:203-210.

8. Schiff GD, Klass D, Peterson J, Shah G, Bates DW. Linking laboratory and pharmacy. *Arch Intern Med* 2003; 163:893-900.

9. TawardrousD, Shariff SZ, Haynes RB, Iansavichus AV, Jain AK, Garg AX. Use of clinical decision support systems for kidney-related drug prescribing: a systematic review. *Am J Kidney Dis* 2011; 58:903-14.

10. Oppenheim MI, Vidal C, Velasco FT, et al. Impact of a computerized alert during physician order entry on medication dosing in patients with renal impairment. *Am Med Inform Assoc Annual Symposium Proceedings* 2002; 577-581.

11. Galanter WL, Didomenico RJ, Polikaitis A. A trial of automated decision support alerts for contraindicated medications using computerized physician order entry. *J Am Med Inform Assoc* 2005; 12:269-274.

12. Bhardwaja B, Carroll NM, Raebel MA, et al. Improving prescribing safety in patients with renal insufficiency in the ambulatory setting: The Drug Renal Alert Pharmacy (DRAP) Program. *Pharmacotherapy* 2011; 11:346-356.

13. Schedlbauer A, Prasad V, Mulvaney C, et al. What evidence supports the use of computerized alerts and prompts to improve clinicians' prescribing behavior? *J Am Med Inform Assoc* 2009; 16:531-8.

14. Khajouei R, Jaspers MW. The impact of CPOE medication systems' design aspects on usability, workflow and medication orders: a systematic review. *Methods Inf Med* 2010; 49:3-19.

15. Torsvik T, Lillebo B, Mikkelsen G. Presentation of clinical laboratory results: an experimental comparison of four visualization techniques. *J Am Med Inform Assoc* 2012; 0:1-7.

16. van der Sijs H, Aarts J, Vulto A, Berg M. Overriding of drug safety alerts in computerized physician order entry. *J Am Med Inform Assoc* 2006; 13:138-47.

17. International Organization for Standardization (ISO). *Ergonomic requirements for office work with visual display terminals (VDTs). Part 11: Guidance on usability.* 9241-11. Geneva: ISO, 1998.

18. Seidling HM, Phansalkar S, Seger DL, et al. Factors influencing alert acceptance: a novel approach for predicting the success of clinical decision support. *J Am Med Inform Assoc.* 2011 Jul-Aug;18(4):479-84.

19. Phansalkar S, Edworthy J, Hellier E, et al. A review of human factors principles for the

design and implementation of medication safety alerts in clinical information systems. J Am Med Inform Assoc. 2010 Sep-Oct;17(5):493-501.

20. Russ AL, Zillich AJ, McManus MS, et al. Prescribers' interactions with medication alerts at the point of prescribing: A multi-method, in situ investigation of the human-computer interaction. *Int J Med Inform* 2012 Apr; 81:232-43.

21. Russ AL, Zillich AJ, Melton BL, Russell SA, Chen S, Spina J, Weiner M, Johnson E, Daggy JK, McManus MS, Hawsey J, Puleo A, Doebbeling BN, Saleem JJ. "Applying Human Factors Principles to Alert Design Increases Efficiency and Reduces Prescribing Errors in a Scenario-Based Simulation". *J Am Med Inform Assoc* Published Online First: March 25, 2014. doi:10.1136/amiajnl-2013-002045.

22. Melton BL, Spina JR, Zillich AJ, et al. Development of standardized patient scenarios for usability testing of medication alerts. *American Medical Informatics Association Symposium November 15-20 2013, Washington D.C.* p.995.

23. Russ AL, Weiner M, Russell SA, et al. Design and implementation of a hospital-based usability laboratory: insights from a department of Veterans Affairs laboratory for health information technology. *The Joint Commission Journal on Quality and Patient Safety* 2012; 38:531-40.

24. Talmon J, Ammenwerth E, Brender J, et al. STARE-HI--Statement on reporting of evaluation studies in Health Informatics. *Int J Med Inform* 2009 Jan; 78:1-9.

25. Bauer DT, Guerlain S, Brown PJ. The design and evaluation of a graphical display for laboratory data. J Am Med Inform Assoc. 2010; 17(4):416-24.

26. Saleem JJ, Patterson ES, Militello L, et al. Impact of clinical reminder redesign on learnability, efficiency, usability, and workload for ambulatory clinical nurses. J Am Med Inform Assoc. 2007; 14(5):632-40.

27. Thyvalikakath TP, Monaco V, Thambuganipalle HB, et al. A usability evaluation of four commercial dental computer-based patient record systems. J Am Dent Assoc. 2008; 139(12):1632-42.

28. Scott GP, Shah P, Wyatt JC, et al. Making electronic prescribing alerts more effective: scenario-based experimental study in junior doctors. J Am Med Inform Assoc. 2011; 18(6):789-98.

29. Wogalter MS. Ch 5: Communication-Human Information Processing (C-HIP) model. In: Wogalter MS, editor. Handbook of Warnings. Mahwah, NJ: Lawrence Erlbaum Associates; 2006. p. 51-61.

30. Marino CJ, Mahan RR. Configural displays can improve nutrition-related decisions: an application of the proximity compatibility principle. Hum Factors. 2005 Spring;**47**(1):121-30.

31. Wickens CD, Lee JD, Liu Y, et al. An Introduction to Human Factors Engineering. 2nd ed. Upper Saddle River, NJ: Pearson Prentice Hall; 2004.

32. Russ AL, Zillich AJ, Melton B, Spina J, Weiner M, Russell SA, McManus MS, Kobylinski A, Doebbeling BN, Hawsey J, Puleo A, Johnson E, Saleem JJ. "Applying Human Factors Principles to Improve Medication Alerts" podium presentation for the American Medical Informatics Association (AMIA) Chicago, IL, pg 1651, Nov 3-7, 2012.

33. Micromedex 2.0. Drug Monographs. Available at: http://www.micromedexsolutions.com/micromedex2/librarian/. Accessed June 10, 2014.

34. Jaspers MWM. A comparison of usability methods for testing interactive health technologies: Methodological aspects and empirical evidence. *Int J Med Inform* 2009; 78:340-53.

35. Jaspers MWM, Steen T, van den Bos C, et al. The think aloud method: a guide to user interface design. *Int J Med Inform*. 2004: 73:781-95.

36. Ericsson KA, Simon HA. Protocol Analysis: verbal reports as data. Cambridge, MA: The MIT Press; 1993.

37. Miller AM, Boro MS, Korman NE, et al. Provider and pharmacist responses to warfarin drug-drug interaction alerts: a study of healthcare downstream of CPOE alerts. J Am Med Inform Assoc 2011;18(Suppl 1):i45–50.

38. Liles AM. Medication pitfalls in the CKD clinic: Case presentations. *Adv Chronic Kidney Dis*. 2014;21(4):349-54.

39. Hayward J, Thomson F, Milne H, et al. 'Too much, too late': mixed methods multichannel video recording study of computerized decision support systems and GP prescribing. *J Am Med Inform Assoc*. 2013 Mar 7.

40. Sittig DF, Wright A, Osheroff JA, et al. Grand challenges in clinical decision support. *J Biomed Inform*. 2008; 41:387-92.

41. Duke JD, Li X, Dexter P. Adherence to drug-drug interaction alerts in high-risk patients: a trial of context-enhanced alerting. *J Am Med Inform Assoc*. 2013; **20**(3):494-8.

42. Lewis JR. Section 8: Human-computer interaction, Chapter 46: Usability testing. In: Salvendy G. ed Handbook of human factors and ergonomics. 4th edn. Hoboken, NJ: John Wiley and Sons, 2012:1267.

Figure 1: Screen shots of the original and redesigned creatinine clearance alerts. A) Original alert design. This alert appears when the provider starts the prescribing process but before a specific medication is selected. The provider must proceed past this alert before s/he is able to access the list of medications that can be ordered in the computerized provider order entry system. This screen shot is nearly identical to the alerts currently used in the VA system. Providers can also access laboratory results through the electronic health record, but not while the creatinine clearance alert is displayed on the screen. B) Redesigned alert. This alert appears only when a renally dependent drug is being ordered for a patient with a reduced creatinine clearance. The alert provides the provider with risks associated with medication use, estimated creatinine clearance, and a link to more laboratory results. Providers are also able to either cancel or accept the order within the alert. C) More labs. This screen shot presents the information displayed to providers when the 'more labs' link in the redesigned alerts is selected. It shows laboratory results relevant to renal function along with reference ranges and the date the test was conducted. Providers can close this window to return to the redesigned alert.

Figure 2: Percentage of prescribing errors (N=20 providers). A) Distribution of errors across all scenarios between the original and redesigned creatinine clearance alerts. (Maximum number of errors per provider for each alert design = 3). B) Percentage of prescribing errors for individual medications.

Table 1: Description of patient scenarios related to creatinine clearance alerts and predefined criteria for errors.

1. Medication	2. Fictitious Patient Description	3. Relevant Laboratory Information†	4. Prescribing Task	5. Correct/ Incorrect Actions	6. Prescribing Guidelines[33]
Spironolactone	This patient came in today for follow-up. He is a 62-year-old black male veteran that presented 2 months ago with congestive heart failure and lower extremity edema. He has also been recently diagnosed with panic disorder and depression.	**Today:** Est CrCL: 29.5 SCr: 2.4 BUN: 40 K+: 5.7 **2 weeks ago:** K+: 5 **4 weeks ago:** K+: 3.6 **6 weeks ago:** K+: 3.7	The patient has been taking spironolactone for heart failure. Spironolactone was prescribed about a month ago and he only has a few tablets left. **Begin renewing spironolactone.**	Correct: Order cancelled‡ *Incorrect: medication renewed (any dose)*	Contraindicated in hyperkalemia (K+>5.5)
Allopurinol	Patient is an 89-year-old black male veteran who presented today for follow-up of hypertension. He had a myocardial infarction 6 months ago as a result of uncontrolled hypertension and dyslipidemia, and now has ventricular arrhythmias. He has diet-controlled Type II diabetes mellitus, is also being treated for depression successfully with nefazodone, which he has taken for the past year without any problems. The patient indicated he had just finished his treatment with ketoconazole, which was prescribed for oral candidiasis.	**Yesterday:** Est CrCL: 28.3 SCr: 1.4 BUN: 18 K+: 4.2 **1 Year ago:** SCr: 1 BUN: 10 K+: 4.1	The patient has been taking allopurinol for gout since 1983 but has run out of refills on his prescription and needs it renewed. **Begin renewing allopurinol for gout**.	Correct: Medication dose decreased to ≤200mg or order cancelled‡ *Incorrect: medication renewed, dose increased*	Reduced CrCL: dose ≤ 200 mg/daily
Ibuprofen			He has chronic pain due to osteoarthritis and has been managing it with ibuprofen since 2006. He asks you for a new prescription for his ibuprofen since he is about out and has no more refills. **Begin renewing ibuprofen.**	Correct: Order cancelled‡ *Incorrect: medication renewed (any dose)*	Ibuprofen use not recommended in advanced renal disease

*Information in columns 2-4 was provided to the providers as part of the scenario introduction and tasks or was available within the mock EHR system for the fictitious patient. Information in column 5 (Correct/Incorrect Actions) was for researcher use only and was not provided to participants. Figure 1 shows the information presented for each alert design.

†Abbreviations: Est CrCL: estimated creatinine clearance SCr: serum creatinine; BUN: blood urea nitrogen; K+: Potassium

‡Cancelling the medication was correct whether or not an alternative medication was ordered. Any alternative medication could be ordered and no assessment was made concerning the correct or incorrect prescribing of the alternative medication.

Table 2: Providers' responses to alerts (N=20 providers)

	Spironolactone			Allopurinol			Ibuprofen		
	Original	Redesign	p-value	Original	Redesign	p-value	Original	Redesign	p-value
ACTION TAKEN									
Ordered as is	15	8		16	8		12	4	
Decreased Dose†	2	5		3	9		1	1	
Increased Dose	0	0		1	0		0	0	
Did not order	3	7		0	3		7	15	
Correct Action†	3	7	0.289	3	12	0.012*	7	15	0.008*
Physicians (n=14)	1	4		3	8		6	10	
Pharmacists (n=4)	2	2		0	2		0	3	
Nurse Practitioner (n=2)	0	1		0	2		1	2	
LAB RESULTS									
Accessed additional laboratory information	5	11	0.109	5	13	0.021*	1	6	0.063
Via 'Labs' tab	5	3‡		5	4‡		1	2	
Via alert link	N/A	10‡		N/A	10‡		N/A	4	

*Significant McNemar test

†Dose reduced to ≤200mg for allopurinol was considered correct. Dose reductions of any size for spironolactone and ibuprofen were considered incorrect. Cancelling any of these three medications was correct whether or not an alternative was ordered. See Table 1 for pre-defined correct and incorrect actions.

‡2 participants used both the Labs tab and the alert link for spironolactone, and 1 participant used both for allopurinol.

Table 3: Summary of usability findings for original and redesigned alerts for creatinine clearance

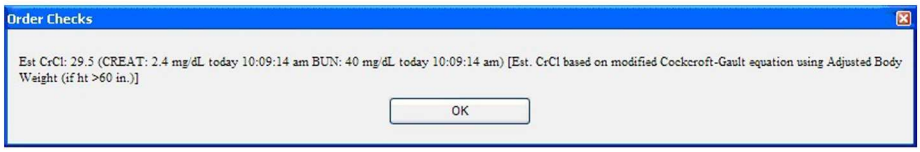
ORIGINAL ALERTS		**REDESIGNED ALERTS**		
Design Feature	**Usability Findings**	**Redesign Feature**	**Usability Findings**	**Potential Design or Safety Implications**
Timing: alert appears before the provider selects any specific medication	9 (45%) participants voiced frustration or confusion about the timing of the alert. Example quotes from two participants: *"Why is this popping up now?"* *"…I only want to see if it it's a drug I have to renally adjust."* 2 (10%) stated they would ignore the alert because it was not relevant for the medication they needed to order. *"I got the usual creatinine alert and I ignored it because it doesn't really matter for simvastatin."*	Timing: alert appears only when the provider has selected a renally dependent drug	No participants voiced frustration or confusion about CrCL alerts being triggered by specific medications	Presenting the alert in association with specific medications reduces confusion.
Text and layout: prose format (e.g, Figure 1A)	3 (15%) participants expressed that the CrCL alerts were difficult to read. *"It's kind of written like all in one line which doesn't make it as easy to read."*	Text and layout: tabular format and half the number of words used (e.g., Figure 1B)	No participants voiced concerns about readability, but two (10%) provided positive comments. E.g., *"…[it's] easier to read because it's less wordy…"*	Text and layout influences perceptions of CrCL alerts; brief statements are viewed positively and may increase providers' attention to alerts.
Navigation: 'OK' button is only option	No usability issues occurred related to alert navigation.	Navigation: 'Accept Order' or 'Cancel Order' buttons are options	5 (25%) participants saw the alert and then decided to adjust the dose, but had difficulty figuring out how to do this from the alert. To modify the dose, navigation requires provider to 'Accept	Alerts should facilitate actions to adjust medication dose. With the redesign (Figure 1.B), there is a risk the provider may inadvertently

			Order' but then go back and change the order, or 'Cancel Order' and start again with order entry	order or cancel a medication when attempting to adjust the dose.
Results provided for Est CrCL, SCr, and BUN.	A critical usability issue occurred with one participant who viewed the alert and then stated *"His kidney function is fine."* Another participant stated: *"[the creatinine of] 2.4 is the number I zoomed in on….I didn't really read the rest."*	Alert displays Est CrCL. Link on alert can be used to access information on SCr and BUN. Link also provides K^+ results, which were added. For displayed lab results reference ranges were also provided.	- 6 (30%) participants indicated they liked the ability to access some other lab results from the alert - 5 (25%) vocalized a desire for more information on labs, but did not use the link - Two participants wanted to know the K^+, when the risk was hyperkalemia with spironolactone, but only one accessed the 'more labs' link - Two participants expected to see liver function tests for the alert related to allopurinol, but this was not provided	For a given alert, the lab results a provider would like to see may vary widely. It is likely that the lab value(s) presented on the alert interface are most salient for decision-making, and reference ranges should be provided or abnormals clearly indicated. Ideally, alerts should also provide easy access to all available labs.
Only lab results are displayed on the alert	3 (15%) participants indicated it is helpful to have labs in the alert. *"Having the estimated creatinine clearance and creatinine's nice when ordering something. But that'd be nice to just simplify that a little bit."*	Alert states that creatinine clearance is low, and states medication name and risk	3 (15%) participants (2 physicians, 1 pharmacist) asked for additional references/assistance or dosing guidelines for allopurinol in addition to the labs. *"I'm not sure how allopurinol causes hepatotoxicity. So I would probably go to the pharmacist and double check and make sure that creatinine is okay without renal adjustment which is a big issue."*	Providing risk information on the alert may help providers identify what additional labs to review. However, labs may not be sufficient for decision-making. Alerts should provide dosing recommendations or easy access to dosing guidelines.

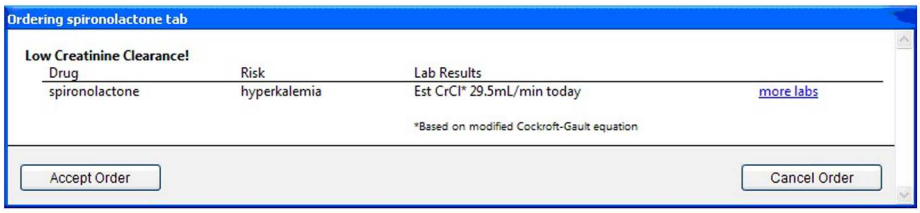
*Abbreviations: Est CrCL: estimated creatinine clearance SCr: serum creatinine; BUN: blood urea nitrogen; K+: Potassium

Figure 1:

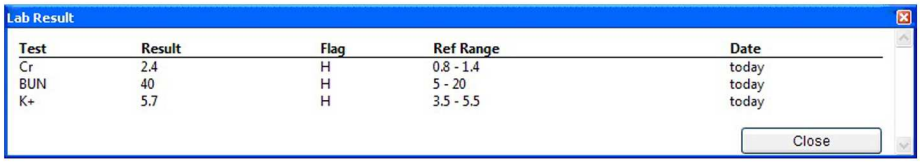
A:



B:



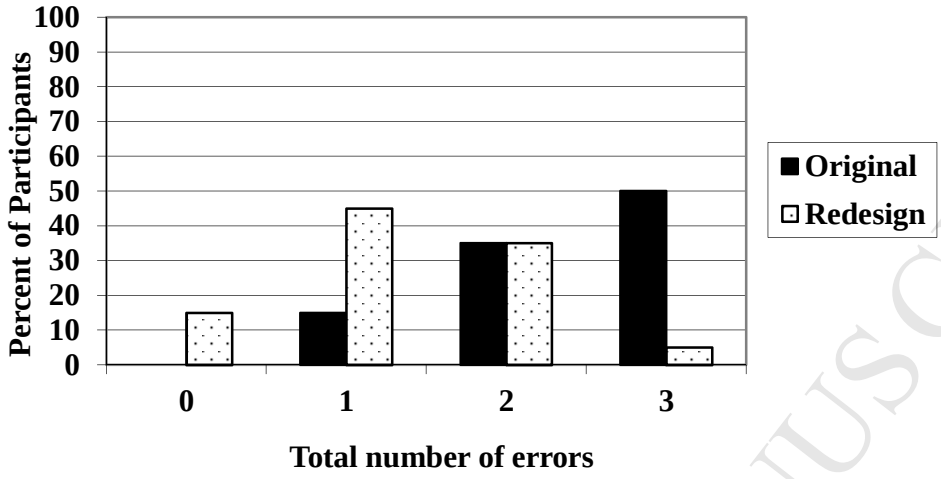
C:



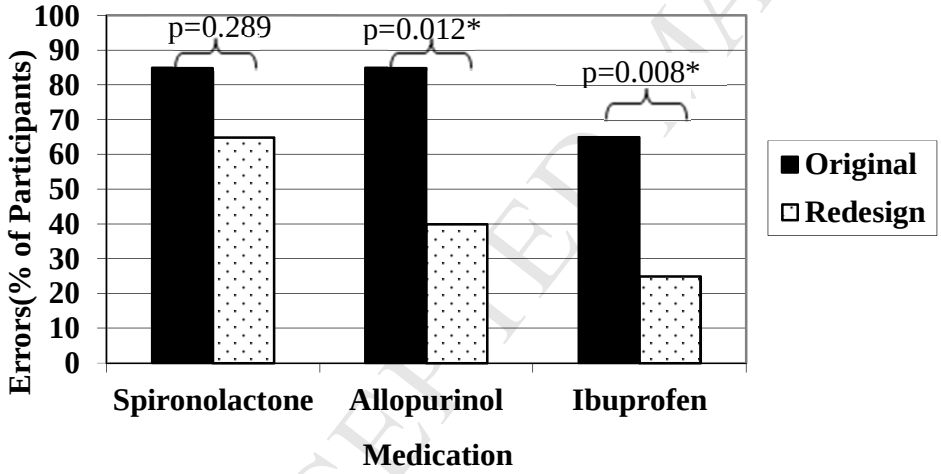
Reducing prescribing errors through creatinine clearance alert redesign

Figure 2:

A



B



*Significant difference in prescribing errors between original and redesigned alerts.

Clinical Significance

- This study provides some of the first evidence on how to design creatinine clearance alerts to promote safety for patients with renal impairment.
- Links to more information within alerts allow providers to more easily view relevant lab results related to renal function.
- Alerts that describe potential adverse events associated with a medication may promote safer prescribing decisions for patients with renal impairment.