Article details: 2018-0190	
Title	Repeat adverse drug events to outpatient medications: a descriptive analysis
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Reviewer 1	Balthasar Hug
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General comments (author response in bold)	Abstract Well done, except adaption the conclusion section as outlined below. **We have edited the conclusion statement.** Methods Very well done description of regression methods. **Thank you.** Patient recruitment on p. 6: the authors mention "three prospective multicenter studies" (line 96), then they mention three hospitals as source of their study patients. This is confusing: Is it a multicenter study with these three study centers or three multicenter studies as the authors write? The authors should be clear about this point and adapt their wording accordingly. **All three primary studies were multi-centre. We have clarified this in Appendix A.** Exclusion criteria, p. 7: The authors write on lines 115-117: "We excluded patients presenting to hospitals from which we were unable to access complete paper-based and electronic records, and patients with illegible records.(14-16)" It is not clear why the authors cite three of their own references here. If they would like to make a point about their selection procedure they should describe it and not leave the reader alone with references and no explanation. **We moved these references to a more logical place (line 132) to indicate the primary studies.** Results P. 10, lines 200-202: "Patients presenting with repeat events were more likely to have a mental health diagnosis (OR=201 1.39; 95%CI, 1.02-1.88) or renal failure (OR=2.01; 95%CI, 1.32-3.07) compared with patients experiencing adverse drug events for the first time (Table 5)." This is one of the main results of the study if not the main result. **No edits required.** Discussion P. 10, lines 200-202: The main patient classes affected by these repeat ADEs are patients with mental illnesses and renal failure. The latter association has been described in other studies. This is part of the main results of the study and should be expanded upon; one sentence in the results section is not enough. That's where clinicians can focus on when trying to reduce potential repeat ADEs. **While the risk was greater in these patient groups than in others, many repeat events occurred in other patient groups. We have emphasized this finding in our discussion (lines 237-239). However, the main finding is that repeat adverse drug events are common. We believe the main reason for these preventable re-exposures and repeat ADEs is lack of informational continuity about prior adverse drug events across the patient's circle of care. If care providers were aware of prior adverse drug events, we believe they would less likely re-expose the patient to medications that caused harm previously.** Conclusions The conclusions have to be re-written; they don't convey the results of the study. The conclusions now consist of two sentences: the first one is well done and focuses on the preventability of repeat ADEs. The second one does not convey any of the results and should be rewritten. The authors have important messages for the reader at this point: these events are 1) quite common 2) most are preventable and 3) the patients to focus on are a) those with mental illness and b) those with kidney failure (see discussion above). Then the authors might want to add a third sentence what the focus of future research might be. **We have edited our conclusion.** Tables Table 4: Since there are many long tables in this paper I would move table 4 to the appendix, also since the title suggests that ADEs are the focus of the paper and not ADRs. Third, the messages of the two tables overlap in large parts. **Done.** Minor The reference counting is successive and repeat references are counted twice: e.g. ref #22=#3, #30=13 and 31=11. Please check with the journal guidelines on this topic. Reference #19 needs an internet link: https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-information.html and when the authors have accessed it last. **We have addressed this.**
Reviewer 2	David G. Bailey
Institution	Lawson Health Research Institute, London, Ont.
General comments (author response in bold)	The authors have assessed the re-occurrence of adverse drug events in emergency departments of Vancouver hospitals with the purpose of identifying causative factors that could result in novel system-level interventions. **No edits required.** Methods: The authors used 'data from three prospective multi-centre observational studies' as the basis for determining which patients had repeat adverse drug interactions. However, they did not provide references for these three studies. If these studies have not had previous peer review and been published or accepted for publication, it raises and important concern about the quality of these studies. **The references for the primary studies are included.** Abstract: Results could provide greater impact by including the finding that 64.6% repeat events were due to re-exposures to previously-harmful medications and that the most common co-morbidities were hypertension (45.2%), diabetes (21.0%), and atrial fibrillation (20.6%). They might consider removing 'Medications most commonly implicated in repeat events were warfarin (12.4%), insulin (8.1%), hydrochlorothiazide (5.5%), furosemide (4.3%), hydromorphone (4.0%) and oxycodone (4.0%) and Patients with diabetes (odds ratio [OR] 1.5; 95% CI, 1.1 to 2.1) and renal failure (OR 1.9; 95% CI, 1.2 to 2.9) were more likely to experience repeat events' if the word count has been exceeded.

	This recommendation contradicts reviewer 1 recommendations to emphasize renal failure, renal failure and mental health diagnoses. Abstract: Conclusions could be made more meaningful. I thought it was important to note that 'repeat adverse drug events to outpatient medications were 100-fold more common than events resulting from medication transcribing, dispensing and administration errors, and 7-fold more common than drug interactions' and that ' We hypothesize that the high rate of repeat events in our study is due to lack of standardized documentation of adverse drug events in medical records, and suboptimal communication between care providers.' These are stated in the Discussion. What possible interventions and new metrics are needed? **We have edited the conclusions in the abstract and paper, and have edited the discussion.** Discussion: What specific recommendations could be made based on the likely cause? **We have edited the discussion and added a recommendation for developing interoperable health information technologies that will enable communication of adverse drug event information between health providers.** Conclusions: Same as for that in the Abstract. **We have edited the conclusion.** 1. Hohl CM, Kuramoto L, Yu E, Rogula B, Stausberg Jr, Sobolev B. Evaluating adverse drug event reporting in administrative data from emergency departments: a validation study. BMC Health Services Research. 2013;13:473-84.