Article details: 2014-0010	
Title	The effect of pharmacist-led medication review in high-risk emergency department patients: evaluation protocol of a quality improvement program
Authors	Corinne M. Hohl MD MHSc, Kimberlyn McGrail PhD, Boris Sobolev PhD
Reviewer 1	Lauren Bresee PhD
Institution	Alberta Health Services, Pharmacy Services
General comments	Thank you for the opportunity to review the study protocol entitled: "The effect of medication review in high-risk emergency department patients: a prospective controlled study". As the study authors mention, adverse events related to medications are a significant source of visits to emergency departments and hospitalizations. While I believe a strategy to effectively identify and manage medication-related adverse events is very important, I believe this study suffers from a number of flaws that will limit the conclusions that can be drawn from the results. Major Comments: 1) In terms of the exposure, a medication review pharmacist compared with usual care, defined as an emergency department pharmacist, I am concerned about the Hawthorne effect - the protocol, to me, seems that medication review pharmacists and emergency department pharmacists are located in the same emergency department. As a result, is it not feasible that the emergency pharmacists, knowing there is a study going on, could provide more in-depth care to patients in the emergency department? Also, the authors mention that medication review pharmacists only spend 20-30% of their time in emergency, with the rest of their time in other acute areas, whereas emergency pharmacists are noted as being "full time" in the study protocol. Also, how do the authors know that emergency pharmacists rarely complete medication reviews? **Author response:** Please see our response to Comment 5, and edits to the manuscript. 2) With regards to patient exclusion criteria, what is the definition of "social problems"? Why are individuals with social problems being excluded from the study? **Author response:** Please see our response to Comment 10. These patients are excluded from the study, as we do not think it likely that they will benefit from medication review. Their main reason for being in the emergency department is of a social and not a medical nature. 3) I disagree with the exclusion of post-operative patients, as this is a population at risk for medication-related adverse events. **Author response:** We are not excluding post-operative patients, but only those who are presenting with a post-surgical complication. Patients with post-surgical complications are usually seen directly by a surgical service in our centre, unlikely post-operative patients who may present with an adverse drug event, but not seen directly by a surgical service. 4) I was confused by the process for identifying patients who may be eligible for the study. Are patients noted as high-risk on the emergency department census? The explanation for not conducting a true RCT given by the authors was due to the risk of enrolling those who are sicker in the treatment group, and those who are less sick in the control group, confounding the relationship between exposure and the outcome of length of stay. I don't see how the proposed method for including patients avoids this, however. If someone deemed high-risk is sent home from the emergency department before the pharmacist can assess them for inclusion, are they then excluded from the study? Or do they enter the control group? If they enter the control group, having not seen the medication review pharmacist, the issue of confounding by indication still exists since the less sick individuals would be more likely to go home before the pharmacist could see them. **Author response:** The pharmacists will systematically allocate a patient to the intervention or control groups. Any "missed" patient is excluded from the study. We have edited this section extensively to clarify the enrolment algorithm. We discussed adding an Appendix to clarify this further during our telephone conversation, but we now believe that the text is clear. We would be happy to provide an example in an Appendix if you feel that this is still required. 5) Human bias is inherent, which is why it is recommended that those who are performing the intervention generally are not the individuals responsible for enrolling people into the study. What strategies have been put in place to ensure the medication review pharmacists are not preferentially enrolling patients they know they can impact by a medication review? **Author response:** Unfortunately, we do not have the resources to hire additional study personnel to enrolpatients as this is funded as a quality improvement project and not a research study. We have stipulated a systematic enrolment algorithm to ensure that pharmacists do not hand pick patients for medication review to limit the potential for bias in this regard.

	6) If the maximum follow up is 30 days for patients included in the study, it is necessary to complete a Cox analysis? Also, for the Cox analysis, how will time be defined? Does it start at hospital discharge? Or time of arriving at the emergency department? **Author response:** We have revised the analytic technique for the secondary outcomes, and have provided edits in the text. Minor Comments: 1) What does the two week training and pilot period entail for the medication review pharmacists? Does this education differ from education that would be received by a full-time emergency department pharmacist? **Author response:** This training period includes an orientation to the quality improvement project, specifically to the systematic selection algorithm for patient enrolment, and to the emergency department as a work area (*e.g.,* access and location of patient records, access to laboratory data, introduction to flow of patients through the emergency department). It does not include the standard evaluation and training period of our regular emergency department pharmacist who participates in resident education, has administrative tasks, reviews and participates in medication dispensing and stocking, and answers specific medication-related questions and consultations. 2) In terms of including the number of active medications a patient is taking as a proxy for health care access and comorbidity, would the accuracy of this information not be biased by the study exposure (full medication review or not)? **Author response:** This information will be obtained through linkage with PharmaNet, the provincial medication dispensing record on the date of the ED visit. All medication information will have been entered by the community pharmacist, and therefore is not biased by study exposure. 3) How are the authors able to tell if a patient has received an outpatient medication review? **Author response:** Outpatient medication review is noted in the patient's PharmaNet record. 4) Will the authors adjust for whether the patients in the control group received a medication review from the full-time emergency department pharmacist? **Author response:** We are unable to adjust for this, as the regular emergency department pharmacists do not document their consultations in the administrative data. Based on our pilot data, emergency department pharmacists see fewer than 5% of incoming patients per day. Therefore, we believe that the risk of bias from this will be minimal. 5) For patients who are admitted to hospital, will you capture if the patient received a medication review on the acute care unit? **Author response:** We are unable to capture this, as the ward pharmacists do not document their consultations in the administrative data. We have acknowledged this as a limitation in our Discussion.
Reviewer 2	Elan Paluck PhD
Institution	Regina Qu'Appelle Health Region, Research & Performance Support
General comments	Study Title: Should be revised to more accurately reflect the content of the paper. **Author response:** We have revised the title. Page 5, Line 8 Was REB approval obtained for the study? The REB waived the need for oral/written consent, but was the entire study exempted as a QI project? **Author response:** Please see our response to Comment 2. Page 6 - Participants The information contained within the Study Enrolment and Group Allocation section is important. In my opinion, the last sentence on page 6 is the rationale for writing this paper. and needs to be highlighted earlier in the paper. **Author response:** We have revised the introduction. Page 7 In general, I found this section onfusing as it did not clearly describe the proposed randomization process. A study enrollment algorithm may be useful. I have assumed, and perhaps incorrectly, that the Triage Nurse conducts the preliminary risk assessment using the tool in Figure 1. The patients identified as being High Risk, form the pool for the High Risk patient census that the Emergency Pharmacist reviews at the beginning of his/her shift. **Author response:** We have revised the methods section to clarify. Line 5-10 -Re: assumption that the presentation to the ER is random? Unclear what is meant by the "sequence of patients". Is it intended to mean that the

	presentation of High Risk and less than high-risk patients is random? If so, did the pilot study data support this assumption? **Author response:** The sequence of patient presentation (regardless of risk status) within any one hour is random. In other words, whether Patient A, Patient B or Patient C arrives first within a 60-minute time frame is likely to be random and unlikely to introduce bias. Line 11/12 - Which patient characteristics are the pharmacists blinded to? Without patient characteristics being consi dered, it wasn't clear how would the pharmacist would estimate the number of medication reviews that could be completed during a shift, and how the time required to work with High Risk patients would change significantly from one shift to the next. **Author response:** The pharmacist is blinded to age and gender, but is able to see the patient's high/low-risk status, the patient's name, location in the emergency department and the chief complaint. The pharmacist is blinded to the remainder of the patient information at the time of enrolment in order to minimize any selection bias that would occur if he/she chose to inappropriately include/exclude patients or violate the systematic selection algorithm based on pretreatment variables. The pharmacists base their judgment about the number of patients they can see based on data from pharmacist observations during the pilot period. Page 11 - Interpretation Lines 19-39 - it would be helpful to describe some of the limitations of the previous studies that have been done, as this supports the paper's rationale. **Author response:** This has been added to the discussion.