Reviewer's report

Title: Using Novel Canadian Resources to Improve Medication Reconciliation at Discharge: A Cluster Randomized Trial

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Reviewer: Jeffrey K Aronson

Reviewer's report:

Major comments:

1. "Adverse drug events" is a term that is widely used but that poorly specifies the different things that it implies. Bates et al (JAMA 1995; 274: 29-34) originally defined an adverse drug event as "an injury resulting from medical intervention related to a drug", a definition that confusingly encompasses not only all adverse drug reactions, whether caused by medication errors or not, and harms other than adverse drug reactions caused by medication errors. However, the authors here use a different definition altogether: "Adverse drug events are defined as the occurrence of new signs and symptoms post-discharge that are judged to have a moderate to high probability of being drug-related." What they are therefore describing is not adverse drug events as originally defined, but suspected adverse drug reactions, which is the term that they should use, for the sake of clarity and avoidance of confusion. The FDA has defined a suspected adverse reaction as "any adverse event for which there is a reasonable possibility that the drug caused the adverse event"; in this definition "reasonable possibility" implies that there is "evidence to suggest a causal relationship between the drug and the adverse event" (http://edocket.access.gpo.gov/2010/pdf/2010-24296.pdf).

2a. The authors say that "Reconciliation ... is critical in reducing the risk of preventable ADEs", but they do not specifically cite the evidence that that is so. Instead they quote papers about the accreditation requirement for reconciliation and papers that detail the challenges to implementation.

2b. Nor do they refer to the possible downsides of reconciliation. For example, expense. There is some evidence of the cost-effectiveness of reconciliation (e.g. Karnon et al. J Eval Clin Pract 2009; 15(2): 299-306), but does that extend to the method that the authors propose? They quote the amount of money that might be saved, but do not mention the costs of the system. Adding value, as studied in the authors' pilot study, or rather the perceived value according to physicians and nurses (Fig 2), is not enough; the added value has to be worth the cost. Another possible downside is the risk of adverse drug reactions that are due to reconciliation rather than despite it. If, for example, the community drug list specifies a drug that the patient was not in fact taking, even though it had been prescribed and dispensed, then reconciliation might introduce a drug that the patient was thought to be taking but had not in fact previously taken, one that might subsequently (even after discharge, with appropriate reconciliation with the
hospital list) cause adverse reactions. One should not always assume that the community list must be replicated exactly. Thus, the term "current medicines" is inadequate; the authors need to distinguish between currently prescribed medicines and currently taken medicines and address the question of how accurately they can make that distinction.

3. The authors intend to use the Naranjo criteria for judging the probability of a suspected adverse drug reaction. This is fraught with difficulties, as indeed are all algorithms for assessing such reactions. They would do well to consider using more than one such method, as a cross-check, such as the UMC's method (http://www.who-umc.org/graphics/4409.pdf) and the method of Bégaud et al (Eur J Clin Pharmacol 2005; 61(3): 169-73), although other methods are possible (see the systematic review by Agbabiaka et al. Drug Saf 2008; 31(1): 21-37). The fact that the Naranjo method is the most widely used, as the authors point out, is no recommendation. Nor does achieving a consensus among three clinicians guarantee an accurate assessment of the probability that an adverse event is an adverse reaction, if they are all using the same faulty tool. Reproducibility is no guarantee of reliability.

Minor comments:

4. The data that the authors quote (numbers of admissions associated with suspected adverse drug reactions, etc) are largely drawn from the US literature. Although it is likely that they apply equally to Canadian practice, they should make that assumption clear. Are the dollar costs that they quote US or Canadian dollars?

5. For the sample size calculation, the authors would do better to use a worst case scenario and plan to randomize more than their current estimate (say 4000-4500 patients), particularly because of the risks of introducing bias that they discuss.

6. CPOE is better expanded as "computerized prescriber order entry", since in some places others besides physicians are empowered to prescribe.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I declare that I have no competing interests