Reviewers' comments and author responses 2019-0015		
Title: Impact of a multifaceted and multidisciplinary intervention on pain, agitation, and delirium management in a Canadian community intensive care unit: a quality improvement study protocol		
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	Responses	**Location**
Reviewer 1: Giulio DiDiodato		
Affiliation: Royal Victoria Regional Health Centre, Critical Care Medicine		
I applaud the authors and their ICU program for committing themselves so fully to ensuring the alleviation of patient suffering during critical illness. Many patients suffer both in the ICU and afterwards with PICS, and hopefully some of this suffering can be relieved using protocalized bundles such as the ABCDEF bundle. In addition, I realize how difficult it is to conduct research in community-based hospitals, and I applaud the researchers for their efforts in this regard.	Thank you!	
The background provided by the authors was comprehensive, highlighting both the reach and severity of these issues, along with the evidence to support both the efficacy and effectiveness of interventions highlighted in the PADIS guidelines. The authors have used a collaborative approach to developing the intervention tools to support the adoption, implementation and maintenance of this bundle. I think the researchers would be wise to submit their work for publication in a QI journal.	Thank you for the valuable comment. Yes, this is a quality improvement study. Because improving pain, agitation and delirium management in a community ICU is an important topic, I feel that CMAJ Open would be a good place to publish our protocol.	
Firstly, in my reading of this protocol, I interpret this study as a quality improvement study as it seeks to answer the question of adoption/implementation/maintenance equipoise. I am not sure why the authors have referred to this as a 'pilot' study as it's primary purpose does not appear to be determining the feasibility of conducting a larger study or conducting a larger study on a smaller scale. As for the design, this appears to be an uncontrolled before-after study.	Thank you for your suggestion. We have since changed our study into quality improvement uncontrolled before-after study.	P1L3, P2L8, P210, P219, P4L2, P2L11, P8L6, P8L11, P8L19, P8L34, P8L37
While the authors state they will collect demographic data, this remains undefined as there are no demographic variables included in the data collection instrument. In addition, the authors don't explain how this demographic and clinical data will be used to account for any confounding between the beforeafter periods.	Thank you. The only demographic data we would collect are date of ICU admission and medical record number. The main objective of this study is to determine whether the implementation of the multidisciplinary intervention would improve the management of pain, agitation and delirium. The metrics we are collecting are primarily process measure. As such, the minimal demographic data that we would collect would have no bearing on accounting confounding factors between before and after period. Instead, we will be using DVT prophylaxis and gastric ulcer prophylaxis rate as a control	P7L44, P8L1-2

	measure to account for potential secular trend.	
Another problematic issue is one of serial correlation between data. It appears the authors intend on collecting data daily for all enrolled patients. This will lead to serial correlations between the measured data and there is no mention as to how the	This quality improve study aims to study whether a multidisciplinary intervention targeting nurses, physicians and family would improve the management of pain, agitation and delirium on ICU	P7L24-26
authors will account for patient clustering of data in their analysis.	patients. We are interested in whether our nurses are assessing and managing pain, agitation and delirium according to PAD guidelines daily and whether physicians are ordering target RASS for ICU patients. There are all process measures rather than patient outcome measures. As such, our approach should not lead to issues related to serial correlations between measured data.	
The authors expect to enroll 240 patients in the 2 study periods, but it is not clear how this sample size was determined as there are no formal hypotheses defined in the protocol. The authors define the outcomes but not the expected intervention effect differences between the outcomes and so it is impossible to know if this sample size is adequate.	This is a pragmatic quality improvement study in a community ICU. We attempted to balance the feasibility of this quality improvement study in a community ICU setting with scientific rigor. Due to infrastructural restraints, we decided that a 6-week before and 6-week after data collection of all admitted ICU patients would be ideal from the feasibility point of view. As such, we did not perform a sample size calculation.	See P8L34-39 for further explanation
While I don't believe these methodologic and analytic issues cannot be revised, I do believe they require major revisions to ensure the considerable efforts already expended by these researchers is not wasted.	Thank you for your invaluable comments. I hope I have made relevant revisions and responded to your comments to your satisfaction.	
Reviewer 2: George Djaiani		
Affiliation: Toronto General Hospital		
This is very topical and important trial.	Thank you!	
It is not clear to me if any pharmacological prevention/treatment of delirium are incorporated in this trial?	Thank you for your question. This is a quality improvement study evaluating a multifaceted and multidisciplinary intervention on the assessment and management of pain, agitation and delirium. Pharmacological prevention/treatment of delirium	

	are not incorporated in this study.	
Reviewer 3: Charles Fancoeur		
Affiliation: CHU de Québec - Université Laval, Anesthesiology and Critical Care		
The authors present a protocol for a pilot study evaluating the effect of a multimodal intervention in a community ICU on successful implementation of recent PAD guidelines and its effect on analgesia, sedation and delirium management.	Thank you!	
In the introduction, they state the high prevalence of delirium, pain and agitation in ICU patients and present recent Society of Critical Care Medicine guidelines on the subject, before addressing the known barriers to implementation and adherence. They subsequently resume different successful interventions studied in trials that will be the basis for their own planned multimodal approach. They submit that the novelty of their study is the multifaceted/multidisciplinary approach and the community setting. Well written and complete.		
In the method section, they plan a pre-post prospective design, with interventions aimed at nurses, families and physicians in a single center that is well described. Their eligibility criteria include all patients admitted to the ICU for more than 24 hours. Although their ICU seems to be exclusively adult, I would mention 'All adult patients' in the eligibility criteria.	Thank you for your comment. We have amended our manuscript as suggested.	P4L35
I do not see any mention about consent from patients or proxies about data collection. Is the study under quality improvement rules? Did the ethic committee agreed to a waiver of consent? Please specify if consent is obtained, and why if not. If consent is needed, the enrollment prediction will have to incorporate consent rate estimation in the calculation, not only ICU volume. Same comment for post-intervention data collection.	This study was approved by local research ethics board as a quality improvement study. We fulfilled the confidentiality requirement set out by research ethics board and the board allowed for waiver of consent.	P7L6
The intervention includes introduction of CPOT as a pain evaluation measure, added to the existing NPRS scale already in place. I would mention when each will be used (CPOT in patients unable to self report and NPRS in others). Is the NPRS already in place in the unit a visual or verbal one?	Thank you for your advice. We have amended our manuscript accordingly. The NPRS in place in our unit is a verbal one. Of note, at the moment, CPOT is not being used at all in our unit. Therefore, we feel that this study is very important.	P7L29-30
In the methodology and interpretation sections, I did not find any mention of a future large-scale trial. It is not obvious from the manuscript that it is designed to inform a future trial and the authors actually state that 'The results of this study will inform improvement strategies of PAD management in Canadian community ICUs. This pilot study is the first step in promoting the	Thank you for the comments. This is a quality improvement study with an uncontrolled beforeafter design in one community ICU. This study is also to evaluate if the implementation of multidisciplinary PAD intervention in community ICU	P4L11, P8L19-26
adoption of and adherence to PAD guidelines to improve the PAD management in Canadian community ICUs.' If it is a pilot, the goal is to prepare for a larger, more definitive trial, not to change or inform practices. And to do the latter, sample size calculation and effect size analyses are essentil. My question is: Is this a feasibility study (to evaluate if the implementation of a multifaceted intervention based on PADIS guidelines in a community setting is feasible?) OR a pilot study (to inform the design of a larger trial and hence to evaluate the	setting is feasible. I have made the appropriate changes in the manuscript.	

intervention, the adequacy of outcome measures, the ease and accuracy of data collection, and to estimate the effect size in order to adequately power the next phase?) OR a pre-post intervention study aimed at changing PAD management across Canadian ICU units? I am under the impression that it was designed as a feasibility study, in which case the title and the both the knowledge translation and interpretation sections must be modified accordingly. However, if the goal is really to implement such an intervention across Canadian units, then these ambitions call for a different design, either a larger trial as the next step (which needs to be explicitly stated in the interpretation section) or for a hypothesis-testing design including sample size calculation and a quantitative effect size analysis. It is worth mentioning that a sample size of 120 in each arm is probably enough to detect a moderate effect size (although not a small one) of the intervention, for example on the proportion of patients with positive CAM-ICU screening.		
Reviewer 4: Kelsey Uminski		
Affiliation: Internal Medicine, University of Manitoba		
I note only that the present manuscript does not adhere to the 2500-word limitation for length excluding abstract, figure, tables and references	Thank you. I have made the relevant changes in the manuscript and now the total word count is 2493	P1L28
Introduction section limited to two paragraphs.	Thank you. I have made the relevant changes and now the number of paragraphs in the introduction section is now two.	P3 and P4
Background: The prevalence of delirium within the ICU setting is presented as a means of transition into the clinical practice guidelines; however, a reference to prevalence of pain and agitation are not included, nor their relation to delirium. Given that the aim of the study is to address each of these components, introducing each of these topics with some reference of commonality or potentiation would perhaps better set the stage for proposed study.	Thank you for your advice. I have added pain and agitation to our background in the abstract.	P2L3-4
Methods: I would recommend including a succinct description of the intervention to be completed. Given limitations in word length of the abstract, you could try to simplify the statistical analysis plan presented in the abstract.	Thank you. I have revised the manuscript accordingly.	P2L10-18
Interpretation: I would also highlight, that this study will provide information on adherence to PAD guidelines within a Canadian community ICU setting.	Thank you. I have revised the manuscript as such.	P2L19-20
Line “Delirium can affect up to 80% of critically ill patients” is slightly misleading, as based on the reference provided, this frequency was seen only in the SICU setting of one of the four papers cited. Perhaps providing a range, and also commenting on the variability dependent on patient location would be important.	Thank you. We have changed the incidence to 6087% based on the references we quoted.	P3L4
For line 2, in citing the multiple adverse outcomes eg. Mortality, hospital length of stay, I would suggest citing each of the references following the outcome measure as opposed to at the end of the sentence as “1-13”. I would apply this throughout the manuscript.	Thank you. I have made the relevant changes.	P3L4-6
What validated tools are currently recommended in the treatment and prevention of PAD per guidelines? How does this relate to the present interventions outlined and used?	The validated tools for the assessment of pain, agitation, and delirium are Critical Care Pain Observation Tool (CPOT),	P4L13-16

	Richmond AgitationSedation Scale (RASS), and Confusion Assessment Method for the ICU (CAM-ICU), respectively. These are the tools that are outlined and used in this study. I have amended the Background section accordingly.	
I would verify the in-text citation “9o9o9i 35”, to ensure that appropriate citation from reference list provided.	Thank you for picking up on the typo. I have corrected it.	P3L23
Noted in paragraph two, “2 months”, I would opt for writing out the number as opposed to use of a numeral for any number less than or equal to ten throughout the manuscript.	Based on your comment about making the Background more concise, I have removed that section.	
Overall impression is that the introduction is quite verbose. I like the order in which the authors present the project: 1) Introduction of delirium within the ICU, linking this to pain and agitation and its importance on patient morbidity and mortality 2) Highlighting the PADIS guidelines 3) Barriers to implementation and adherence to guidelines 4) Previous studies with aim to improve management of PAD 5) Gaps in prior studies leading to current intervention	I have attempted to make the introduction less verbose	P3 and P4
I would consider condensing paragraph 1, given the limitation in introduction length of two paragraphs. Would look at this as simply introducing the topic at hand as a common problem, with important patient implications.	Thank you. I have made the appropriate changes.	P3
Within paragraph 2, the addition of immobility and sleep disruption categories within the PADIS guidelines are introduced. Given that this is not an outcome within the present study, I am uncertain how important this is within the introduction and may be a distractor.	Thank you. I have removed the PADIS guidelines.	P3 and P4
What was the ABCDEF bundle employed by Barnes-Daly? Is there any way in which the studies cited looking at various interventions can be broken into general categories for intervention to be more concise? Eg. Telemonitoring, educational programming etc. This can then be used to inform justification for current multimodal intervention.	The ABCDE bundle includes Awakening and Breathing Coordination, Choice of drugs, Delirium monitoring and management, Early mobility and Family engagement. I have attempted to break down interventions into categories to make the introduction more concise.	P3L32-42
What is the study hypothesis? Would include this with stated study aim and objectives. Any anticipated differences from the community ICU setting compared to academic ICUs, where bulk of literature is coming from?	I have added the study hypothesis: We hypothesize that the implementation of multidisciplinary intervention co-developed by frontline healthcare staff would improve PAD	P4L4-6

	management in a community ICU.	
Within the “setting” paragraph, reference is made to the NPRS, RASS, and CAM-ICU without a citation. I would include a citation for each, and also comment on whether nursing staff received formal training on use at the same prior to intervention (latter in which training provided).	I have amended the manuscript accordingly.	P4L25-29
I would consider change to placement of the paragraph “preintervention data collection”. As it currently reads, I am left after reading this paragraph wondering what the process, outcome, balancing and control measures are, which are presented following a discussion of the intervention. Perhaps this doesn’t need to be introduced within this paragraph as currently written to the same level of detail, but provide some additional details of data capture.	Thank you. I have made the appropriate changes.	P4L39-43
Will the research assistant only be capturing data for specific hours of the day in which they are present, or will this be for the entire 24-hour time interval daily?	It would be for the entire 24-hour time interval daily.	
Any consideration of patient engagement on the PAD Advisory Committee?	This is a great idea. As we spread and scale up this QI program, we would likely include patient engagement.	
Both the nurse and physician focused interventions address pain, agitation and delirium; however, the family member-focused intervention for education is largely focused on delirium. Why not include pain and agitation in this intervention?	This is a great question. When we design our familyfocused components of the intervention, we wanted to stay focus in order not to overwhelm our patient family. I think adding pain and agitation education for our patient family members would be something we could consider doing in the future.	
Although a large participation of patient’s within the ICU are unable to actively participate in their care due to the nature of their illness and treatment, some may be able to do so. How can this be factored into the PAD intervention?	For patients who could actively participate in their care, we would provide the patients with familyfocused components of the intervention such as the education pamphlet and video. We could also interview the patients themselves rather than family members.	
How will patient admitting diagnosis and comorbidities be captured and factored into control measures such as time within target RASS, and pain control. Eg. In a patient with illness	This is a pragmatic quality improvement study in a community ICU. When we designed our study, we needed to balance feasibility with scientific rigor	
resulting in altered level of consciousness, target RASS may not be achievable.	given the limited research resources. As such, we decided not to conduct an	

	extensive data collection to include admitting diagnosis and comorbidities etc and not to conduct complex statistical analysis. That being said, we will collect patient medical record number. Should we have the resources, we could retrospectively collect admitting diagnosis and comorbidities and conduct retrospective data analysis for the above. This would be done with a separate REB approval.	
Data will be analyzed as % patient per day. How will multiple repeated measures within a single patient be factored into analysis, if at all? Any potential limitations in excluding this?	Our unit of analysis will be patient-day because we are interested in the assessment and management of pain, agitation and delirium by nurses and physicians per day. As such, we it would eliminate the concern of repeated measures. I have made the relevant changes in the manuscript.	P7L24-44, P8L1-2