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Title	Examining the incidence of DELIRIUM in Canadian Cardiac Surgery patients: a protocol for the DELIRIUM-CS Canada cross-sectional study
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Reviewer 1	Babar Khan
Institution	Indiana University System, Pulmonary/Critical Care Medicine, Bloomington, Indiana, USA
General comments (author response in bold)	The Delirium-CS study is a nice undertaking by a group of investigators well versed in conducting delirium and delirium related research. Overall the protocol is well written and will achieve the goals identified. I have some minor comments for the protocol. **Response: Thank you for the kind comments.** 1. I would presume all the sites are screening for delirium already. A plan for training the sites if they are not using RASS/SAS/CAM-ICU/ICDSC will be helpful to ensure the validity of the assessments. **Response: Each centre has undergoing formalized training of the ICU team in either the CAM-ICU or ICDSC screening tool using previously described processes (e.g. Devlin, J. W et al (2008). Combined didactic and scenario-based education improves the ability of intensive care unit staff to recognize delirium at the bedside. Critical Care (London, England), 12(1), R19.) prior to the initiation of data capture for this initiative. This has now been included in the manuscript.** 2. Extending the observation from 7 days to till they are discharged from the ICU will provide another variable of delirium duration that has it own prognostic significance. **Response: We full agree that would be a potential valuable addition. The focus of this initiative was delirium in the early phase (i.e. less than 7 days). The rationale for this restriction is based on the hypothesis that early postoperative delirium is likely to a different process (inflammation, anesthesia, low cardiac output, new AKI, pharmacologic agents) than delirium that occurs at later time points (i.e. wound infection, mediastinitis, sepsis, etc...) (see: Martin, B.-J et al. (2010). Delirium as a predictor of sepsis in post-coronary artery bypass grafting patients: a retrospective. To avoid complications of further heterogeneity due to other non-perioperative factors, we have limited the analysis to the earlier phase of the postoperative period.** 3. Delirium severity could be an adjunct measure for this specific population. 4. Drug exposure is not addressed that may affect delirium incidence. **Response for #3 and #4: We agree these would both be potentially useful adjuncts. Both delirium screening tools used in this protocol are 'binary' in identifying delirium; neither permits an evaluation of delirium severity. Indeed, delirium severity tools such as the Delirium Rating Scale (DRS) require verbal communication, which may be impractical requirement in mechanically ventilated patients or subjects having just undergone cardiac surgery. Moreover, no delirium severity tool has been adequately validated in the critically ill. Duration of delirium (using an accumulation of 'delirium positive' days with either scale, as opposed to an 'ever delirium' binary consideration) will be tallied in the context of this study to test whether it reflects a 'delirium burden'.** 5. Severity of illness is another factor that is essential to adjust for. **Response: We agree with the reviewer. As the majority of cardiac surgery patient do not have multisystem issues (i.e. an APACHE < 15 in the majority of cases), we have chosen to use a cardiac specific risk score, the EuroSCORE II (Nashef, S. a M., Roques, F., Sharples, L. D., Nilsson, J., Smith, C., Goldstone, A. R., & Lockowandt, U. (2012). EuroSCORE II. European Journal of Cardio-Thoracic Surgery : Official Journal of the European Association for Cardio-Thoracic Surgery, 41(4), 734–44; discussion 744–5). The elements that are collected within the CRF will permit the research team to risk-adjust for EuroSCORE II.**
Reviewer 2	Dr. Ruth Hall
Institution	Institute for Clinical Evaluative Sciences, Toronto, ON
General comments (author response in bold)	This is a very well described protocol for a relevant acute hospital quality of care issue. **Response: Thank you for the kind comments.** 1. I think it would be helpful to provide examples of cardiac procedures most likely to have ICU admissions and the proportion of cardiac procedures that go to ICU. An appendix could include procedures and volumes at the participating site to provide context. **Responses: This is an important point. In each of the centres that are participating (as for all cardiac surgery sites in Canada) all cardiac surgery patients (excluding. Pacemaker implants) or sternal debridement admitted to the ward) are admitted to an postoperative intensive care unit. This would include coronary artery bypass grafting (CABG), valve replacement, thoracic aortic procedures, cardiac transplant and other procedures requiring cardiopulmonary bypass. This has been added to the revised manuscript. All participating centres perform at least 700 cases/annum. The actual month volume will vary in each site from month to month. As such we will be able to provide actual numbers of patients included once the study is closed. As stated in the Section "Sample Size" "As the primary goal of this study is to determine the incidence of postoperative delirium, there is no required sample size that has been calculated for this study. However, based on our19 and other recent analyses13,22,23, the average surgical volumes of each of the centers involved, we expect approximately 150-400 patients per site to be enrolled for the three month evaluation period.** I have a few questions the authors may want to consider addressing: 2. How will perioperative delirium be defined? **Response: Delirium will be categorized by the use of Intensive Care Delirium Screen Checklist (ICDSC) or the Confusion Assessment Method – Intensive Care Unit (CAM-ICU) tool (Table 1) to detect delirium. We believe that that the use of two well validated tools will allow for comparison between rates using the ICDSC and CAM-ICU; we**

	anticipate the recruitment volume at each site will make comparisons between delirium rates using each tool possible, since the variability with each over multiple studies differs. This has notion has been added to the manuscript. 3. How does Accreditation Canada (AC) define delirium? 4. What tool does the AC use define delirium ? **Response: This is an interesting point. The Canadian Accreditation Standard 10.9 defines delirium as a "...heighten state of agitation, contributes to increased length of stay and may cause clients to self-extubate or remove catheters...". Furthermore, it does not specify a specific tool to detect delirium other than the team must "...consistently [apply] a delirium screening tool..." The difficult with this standard, however, is bias toward hyperactive symptoms. It is now well understood that the delirium presentation exist within a spectrum of hypo to hyperactive symptoms (see: Inouye, S. K., et al (2014). Delirium in elderly people. Lancet (London, England), 383(9920), 911–22, Bergeron, N et al (2001). Intensive Care Delirium Screening Checklist: evaluation of a new screening tool. Intensive Care Medicine, 27(5), 859–64 and Ely, E. W. et al. (2001). Evaluation of delirium in critically ill patients: Validation of the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU), JAMA 29(7). We therefore believe one of the key strengths of this protocol is the inclusion of validated screening tools (that are easily implemented in a clinical setting) that identify the full spectrum of delirium. With the use of a pair sedation and agitation scale, we will be able to determine the relative contribution of hypo and hyperactive delirium in studied patients.** 5. The team may want to consider including a knowledge user like AC on their project time or include presenting the findings of this study to AC as part of their KT strategy. This study would likely be of great interest to AC. **Response: Thank you for this excellent suggestion. One of the co-Authors of this initiative (Dr. Yoanna Skrobik) has been intimately involved with the establishment of Canadian standards and accreditation implementation (see: http://www.patientsafetyinstitute.ca/en/toolsResources/Hospital-Harm-Measure/Documents/Resource-Library/HHIR%20Delirium.pdf). Dr. Alison Fox-Robichaud is the current President of the Canadian Critical Care Society (http://www.canadiancriticalcare.org). The lead Author is a co-Founder and current President of the Canadian Cardiovascular Critical Care Society (www.cancaresociety.com), a member of the Society of Thoracic Surgery Critical Care Workforce, a Past President of the American Delirium Society (www.americandeliriumsociety.com), a co-founder of an international federation of delirium societies with the mandate of delirium awareness and advocacy (iDelirium; www.idelirium.org). We hope to be able to leverage these KT platforms to engage AC and other policy makers at multiple levels.** 6. Include a footnote below table of the psychometric properties of the delirium assessment tools selected in this study. **Response: Apologies, however we are not clear on what the Reviewer is requesting. Both the tools used in this initiative are based on the American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders. 4th edition. Washington, DC: 1994. If this is what is request, we have now included at the bottom of the associated table.** 7. I also suggest including ICU nursing education session(s) as another part of KT strategy. 8. No mention of when or how often staff will be trained in use of screening tools. I think more information is required given the next sentence (line 40, pg 11) says this is an important first step. **Response: As per the response # 1 to Reviewer #1, each centre has undergoing formalized training of the ICU team in either the CAM-ICU or ICDSC screening tool using previously described processes (e.g. Devlin, J. W et al (2008). Combined didactic and scenario-based education improves the ability of intensive care unit staff to recognize delirium at the bedside. Critical Care (London, England), 12(1), R19.) prior to the initiation of data capture for this initiative. This has now been included in the manuscript.** 9. Reg Reqmt section – Are Data Sharing Agreements with participating sites required? **Response: Yes this was completed for each participating site. This has now been clarified in the text.**