PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Retrospective chart review and survey to identify adverse safety events in the Emergency Medical Services care of children with out-of-hospital cardiac arrest in the United States: A study protocol
AUTHORS	Eriksson, Carl; Schoonover, Amanda; Harrod, Tabria; Meckler, Garth; Hansen, Matt; Yanez, David; Daya, Mo; Jui, Jonathan; Guise, Jeanne-Marie

VERSION 1 – REVIEW

REVIEWER	Maxim Ben-Yakov University of Toronto, Canada
REVIEW RETURNED	18-Apr-2020

GENERAL COMMENTS	Thank you for creating a database of such important magnitude. This is a protocol publication of a collection of data points that may predict outcomes in out-of hospital arrest for pediatric patients. My only suggestions would be to make the abstract more precise about the overall numbers of data sources, and primary outcomes of the project.

REVIEWER	Dr. Michael Rieder University of Western Ontario London, Ontario Canada
REVIEW RETURNED	13-May-2020

GENERAL COMMENTS	This proposal is to study out-of-hospital cardiac arrest (OHCA) in children across 5 jurisdictions in the United States with the goal of determining if serious adverse events (SAEs) during care and transport contribute to mortality, drawing on the experience of adult emergency medicine systems where addressing SAEs by training and policy has resulted in improved outcomes. Similar improvements have not been noted in childre and hence the rationale for the study to explore variables that may impact on outcome. The authors have assembled a robust team and have thoughtfully assembled a comprehensive and insightful list of variables that may impact outcome. The study will cover a range of years and jurisdictions, the latter important as policy and training differences across the centres provide a natural experiment to explore the role of key variables in outcome. This reviewer has three issues that the authors may wish to consider. First is the question of the time span (2013-18) of the study. Is it possible that there may have been training/policy

	changes in the organizations involved and if so how will this be accounted for? The second issue is numbers. The authors propose to study 1500 cases based on GEE logistic regression and a series of well considered assumptions. However this reviewer wonders if this is achievable, even over a several year study. The total all-causes mortality for people under age 18 in in the United States is approximately 10,000 per year (CDC, https://www.cdc.gov/nchs/fastats/child-health.htm). Given that many - in fact, for some age groups most - deaths occur in hospital on a reasonably expected basis, is the goal of 1500 out of hospital cardiac arrests feasible? Data from the involved systems as to annual number of deaths/ambulance calls involving children would be helpful to determine this. Finally there is the issue of biology. In the case of adults, many out of hospital cardiac arrests are electrical, i.e. due to cardiac arrythmias secondary to coronary artery disease. In contrast, this is much less common among children an death is more often the result of either trauma or the end result of multi-organ failure in the face of serious chronic disease. In both cases it is much less likely that intervention is likely to be successful notably in the case of the latter. Some consideration of the different causes of death may be useful when comparing adult to child outcomes.

REVIEWER	Kentaro Kajino Kansai Medical University Japan
REVIEW RETURNED	14-May-2020

GENERAL COMMENTS	None. I am looking forward to seeing next manuscript.

VERSION 1 – AUTHOR RESPONSE

Reviewer 1 comments and author responses (Page and line number where addressed in document with tracked changes)
Comment: My only suggestions would be to make the abstract more precise about the overall numbers of data sources, and primary outcomes of the project.
Response: Good points. We have modified the abstract as suggested. (Page 2, lines 9-10, line 13)

Reviewer 2 comments and author responses (Page and line number where addressed in document with tracked changes)
Comment: First is the question of the time span (2013-18) of the study. Is it possible that there may have been training/policy changes in the organizations involved and if so how will this be accounted for?
Response: Thank you for your comment. This has been an area of discussion among our team of investigators and our clinical reviewers. To account for changes in protocol (either in PALS or NRP), clinical reviewers will be using the PALS and NRP guidelines that were in place at the time of each individual encounter. Recognizing the limitations of agency responders' memories when reporting past policies and training, we are only capturing their current approaches.

Comment: The second issue is numbers. The authors propose to study 1500 cases based on GEE logistic regression and a series of well considered assumptions. However this reviewer wonders if this

is achievable, even over a several year study. The total all-causes mortality for people under age 18 in in the United States is approximately 10,000 per year (CDC, https://www.cdc.gov/nchs/fastats/child-health.htm). Given that many - in fact, for some age groups most - deaths occur in hospital on a reasonably expected basis, is the goal of 1500 out of hospital cardiac arrests feasible? Data from the involved systems as to annual number of deaths/ambulance calls involving children would be helpful to determine this.
Response: Thank you for this thoughtful comment. Previously reported incidence of pediatric OHCA in the U.S. is approximately 8 per 100,000 person-years (Fink et al., 2016). Our currently participating EMS agencies serve over 2.5 million children, resulting in approximately 1,400 expected pediatric OHCA cases over 7 years. We have already received over 1,300 eligible patient care reports from these participating agencies, and are currently recruiting additional agencies. We have updated Table 1 to more accurately reflect the pediatric population served by our participating agencies. (Table 1, Page 6, lines 10-12)

Comment: Finally there is the issue of biology. In the case of adults, many out of hospital cardiac arrests are electrical, i.e. due to cardiac arrythmias secondary to coronary artery disease. In contrast, this is much less common among children an death is more often the result of either trauma or the end result of multi-organ failure in the face of serious chronic disease. In both cases it is much less likely that intervention is likely to be successful notably in the case of the latter. Some consideration of the different causes of death may be useful when comparing adult to child outcomes.
Response: Thank you. We agree that the causes of pediatric and adult OHCA are often different. Respiratory failure is a major cause of OHCA in children, where superb BLS can make a difference. Seemingly dismal outcomes from various conditions have been improved through quality of care initiatives. Pediatric cancer and adult OHCA are great examples that were thought to be hopeless years ago but through ongoing research and quality improvement, many formerly unsalvageable patients are now saved. It is our belief that excellent EMS care will result in fewer adverse safety events (our primary outcome), and that fewer ASEs will maximize survival for children with OHCA. We have clarified in the Abstract that ASEs are our primary outcome.

We will exclude cases where there were obvious signs of death, but we acknowledge that even with perfect care, some of these children would still die. Our study focuses on ASEs rather than survival, and will provide valuable information about whether ASEs are more common in treatment of different types of OHCA. We hope that our findings will improve EMS care for children with OHCA, and maximize their likelihood of survival. (Page 2, lines 9-10)

VERSION 2 – REVIEW

REVIEWER	Dr. Michael Rieder University of Western Ontario London, Ontario Canada
REVIEW RETURNED	15-Jul-2020

GENERAL COMMENTS	The authors have addressed the concerns of this reviewer in this revised protocol