

PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Innovative approaches to investigator-initiated, multi-centre pediatric clinical trials in Canada
AUTHORS	Kelly, Lauren; Richer, Lawrence; Ali, Samina; Plint, AMy; Poonai, Naveen; Freedman, Stephen; Knisley, Lisa; Shimmin, Carolyn; Hickes, Serena; 't Jong, Geert; Pechlivanoglou, Petros; Offringa, Martin; Lacaze, Thierry; Klassen, Terry

VERSION 1 - REVIEW

REVIEWER	Allison Tong The University of Sydney Australia
REVIEW RETURNED	05-Mar-2019

GENERAL COMMENTS	This manuscript describes key challenges and learnings in conducting trials enrolling children and highlights well the need for partnership and patient/family involvement. There is certainly a pressing need for further efforts (and evaluation of these efforts) in involving children (not only the parents) in research to inform best practice on how their priorities and views can be integrated across all stage of the research. I thank the authors for their contribution.
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REVIEWER	Brian Smith Duke University US
REVIEW RETURNED	11-Mar-2019

GENERAL COMMENTS	Overall Well written experience of multicenter pediatric clinical trials network established in Canada. Specific 1. Were there any unique challenges/lessons learned from establishing this network. 2. Why was use of this complex group of entities more/less efficient than engaging a single CRO?
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REVIEWER	Laura Folgori Paediatric Infectious Diseases Unit Department of Paediatrics, Luigi Sacco Hospital Milan, Italy
REVIEW RETURNED	20-Mar-2019

GENERAL COMMENTS	<p>Thank you for asking me to review this interesting Communication, which deals with a very important topic such the challenging in conducting clinical trials in children.</p> <p>This study represents an innovative approach to facilitate the conduction of drug investigational trials in the paediatric population.</p> <p>I really like the attempt to speed up the process and harmonise the trial design and conduction among different institutions, and I think that this shared use of the resources (research nurses, monitors) and the centralisation of the data collection/analysis can definitely overcome many of the problems frequently encountered in the conduction of these trials in children. Also, the involvement of patients/parents to gain suggestions on how to improve recruitment can really be very helpful.</p> <p>I look forward to seeing the results of this network's project and hope this design will be adopted also from other non-Canadian clinical trials network.</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer: 1: This manuscript describes key challenges and learnings in conducting trials enrolling children and highlights well the need for partnership and patient/family involvement. There is certainly a pressing need for further efforts (and evaluation of these efforts) in involving children (not only the parents) in research to inform best practice on how their priorities and views can be integrated across all stage of the research. I thank the authors for their contribution.

Response: We agree that this is pressing work and it was our pleasure.

Reviewer: 2: Overall Well written experience of multicenter pediatric clinical trials network established in Canada.

1. Were there any unique challenges/lessons learned from establishing this network.
2. Why was use of this complex group of entities more/less efficient than engaging a single CRO?

Response: We have added a statement on the comparable use of CRO's (which are cost prohibitive for academic led studies) which reads: There are financial challenges for investigators to engage a CRO and there are limited options with pediatric expertise in Canada. We have a section on challenges and solutions which highlights our obstacles and lessons learned.

Reviewer: 3: Thank you for asking me to review this interesting Communication, which deals with a very important topic such the challenging in conducting clinical trials in children.

This study represents an innovative approach to facilitate the conduction of drug investigational trials in the paediatric population. I really like the attempt to speed up the process and harmonise the trial

design and conduction among different institutions, and I think that this shared use of the resources (research nurses, monitors) and the centralisation of the data collection/analysis can definitely overcome many of the problems frequently encountered in the conduction of these trials in children. Also, the involvement of patients/parents to gain suggestions on how to improve recruitment can really be very helpful. I look forward to seeing the results of this network's project and hope this design will be adopted also from other non-Canadian clinical trials network.

Response: thank-you for your words of encouragement. We believe this is important work that will hopefully help move the pediatric clinical trial field forward.

VERSION 2 – REVIEW

REVIEWER	Brian Smith Duke University, USA
REVIEW RETURNED	24-Apr-2019
GENERAL COMMENTS	The reviewer completed the checklist but made no further comments.