

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)	Development of a research platform for children with arthrogyposis multiplex congenita: Study protocol for a pilot registry.
AUTHORS	Dahan-Oliel, Noémi; Bedard, Tanya; Darsaklis, Vasiliki Betty; Hall, Judith; van Bosse, Harold; Hamdy, Reggie

VERSION 1 – REVIEW

REVIEWER	Bjarne Møller-Madsen Dept of Childrens Orthopaedics, Aarhus University Hospital, Denmark
REVIEW RETURNED	05-Feb-2018

GENERAL COMMENTS	Dear Authors, Please accept my complements for doing this study; it will be for the benefit of children without any doubt. Registries change the way physicians think and act. My reference is Nordic countries registries. A few questions: have you considered facial ++ photos of the participants to be helpful; do the contractures imply goniometry measurement; concerning sociocultural background /lifestyle habits – how and why to include these questions With my best wishes
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REVIEWER	Moez Trigui Department Of Orthopedic Surgery, Habib Bourguiba Hospital ans sfax Faculty of Medicine, University of Sfax, Tunisia
REVIEW RETURNED	09-Feb-2018

GENERAL COMMENTS	The development of this research platform should be encouraged to better understand this rare and heterogenous disorder.
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REVIEWER	B. Kerem AYDIN Selcuk University, Turkey
REVIEW RETURNED	04-Mar-2018

GENERAL COMMENTS	AMC is really an important topic for all branches of pediatrics including plastic surgeons, pediatric orthopedic surgeons etc. My only criticism is the exact diagnosis of AMC in multiple centers. As I understand there will be two consortiums including 12 experts. This may be a limitation for this study.
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REVIEWER	Cylie Williams Monash University/Peninsula Health, Australia
REVIEW RETURNED	19-Mar-2018

GENERAL COMMENTS	<p>Thank you for such a clearly defined and well written protocol. I had a few minor concerns that are mainly administrative. Could the authors please complete a spirit checklist. While there are components not relevant to this particular protocol, it allows the reader to determine the thoroughness of the protocol. It also acts as a reference guide (and helps review).</p> <p>Things identified as missing should be inserted including:</p> <ol style="list-style-type: none"> 1. Any registration. Also, the approval numbers from the relevant sites for ethics. 2. Table with protocol version identified with date (this should incorporate any changes made through review) 3. Participant eligibility: is there any criteria as to who and how the diagnosis has been made and the type. Please ensure this is clear within the Participants Eligibility section. 4. Design: while you are using some retrospective data, I disagree this is a retrospective study. Would recommend that the design remain as prospective registry with retrospective data used for comparison with current data. 5. Timeline only has the set number of items but no time associated with progression. 6. Recruitment - while the location is mentions, how will families actually be recruited. Will they be know, how will they be contacted, who will decide on who to contact, what happens if more than 20 respond etc? More detail is needed on recruitment. 7. Plan for data entry, coding, security and storage is needed. 8. Data monitoring committee details and if not needed, why, 9. Consenting procedures for parents and assenting for children of appropriate ages. 10. Dissemination policy - what are the reporting processes to sponsors and families who have participated? 11. Is there any intended publications and if so is there an authorship guideline that will apply.
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VERSION 1 – AUTHOR RESPONSE

Reviewers' Comments to Author:

Reviewer: 1

Reviewer Name: bjarne møller-madsen

Institution and Country: dept of childrens orthopaedics, aarhus university hospital, denmark

Competing Interests: none declared

Dear Authors,

Please accept my complements for doing this study; it will be for the benefit of children without any doubt.

Registries change the way physicians think and act. My reference is Nordic countries registries.

A few questions: have you considered facial ++ photos of the participants to be helpful; do the contractures imply goniometry measurement; concerning sociocultural background /lifestyle habits – how and why to include these questions

With my best wishes

B Moeller-Madsen

Response: Thank you for your comments. Yes, facial features are important for phenotyping/diagnostic purposes. We have included medical pictures as standard care now at our site but not included in the pilot registry due to confidentiality concerns. Sociocultural background/lifestyle habits are collected as part of the registry to identify potential risk factors for AMC. To address your comments, we have added medical pictures of the upper extremities, lower extremities and spine (all with patient consents uploaded). As for goniometric measurements, we have not included them in this pilot version of the registry as we are

conducting the interviews with family members who may not be aware of such precise measurements. However, this is definitely a variable we will consider when we implement the full international AMC registry, depending on the feasibility of ascertaining such measurements.

Reviewer: 2

Reviewer Name: Moez Trigui

Institution and Country: Department Of Orthopedic Surgery, Habib Bourguiba Hospital ans sfax Faculty of Medicine, University of Sfax, Tunisia

Competing Interests: None declared

The development of this research platform should be encouraged to better understand this rare and heterogenous disorder.

Response: Thank you for your positive comments! We look forward to sharing our findings once we have completed the pilot.

Reviewer: 3

Reviewer Name: B. Kerem AYDIN

Institution and Country: Selcuk University, Turkey

Competing Interests: None

AMC is really an important topic for all branches of pediatrics including plastic surgeons, pediatric orthopedic surgeons etc. My only criticism is the exact diagnosis of AMC in multiple centers. As I understand there will be two consortiums including 12 experts. This may be a limitation for this study.

Response: We apologize for any confusion in the manuscript. There was only in fact 1 consortium of experts that was initially established through federal funding. It is this panel of experts that determined the need to establish a registry. As such, only one consortium or panel of experts is referenced in this study. Indeed, content validation for the registry was done with a much broader spectrum of professionals however this will be discussed in another manuscript. To avoid confusion, we have changed the term consortium to panel of experts within the manuscript. Subsection "Case definition" and the section on "Eligibility Criteria" have been modified to further clarify this point. Thank you for your time in reviewing.

Reviewer: 4

Reviewer Name: Cylie Williams

Institution and Country: Monash University/Peninsula Health, Australia

Competing Interests: None declared.

Thank you for such a clearly defined and well written protocol. I had a few minor concerns that are mainly administrative. Could the authors please complete a spirit checklist. While there are components not relevant to this particular protocol, it allows the reader to determine the thoroughness of the protocol. It also acts as a reference guide (and helps review).

Response: Thank you for this recommendation. As the Spirit Checklist seems to apply to clinical trials we have taken the 22/33 points that could apply to this registry and have incorporated them into the revised manuscript. We have also changed the order of certain elements as well as headings so that revisions can be facilitated in the future. Please find the responses to your specific concerns below.

Things identified as missing should be inserted including:

1. Any registration. Also, the approval numbers from the relevant sites for ethics. Response: The protocol was not registered. We have added the approval numbers for ethics for both participating sites.
2. Table with protocol version identified with date (this should incorporate any changes made through review) Response: This has been added in text form to the "Research Ethics Approval and Protocol Amendments" section.
3. Participant eligibility: is there any criteria as to who and how the diagnosis has been made and the type. Please ensure this is clear within the Participants Eligibility section. Response: This has been clarified in the "Eligibility Criteria, Sample Size and Recruitment Procedures" section.
4. Design: while you are using some retrospective data, I disagree this is a retrospective study.

Would recommend that the design remain as prospective registry with retrospective data used for comparison with current data. Response: Study design has been rectified and more detail is provided in the “Study Design” section.

5. Timeline only has the set number of items but no time associated with progression. Response: We have added the appropriate time points to the timeline.

6. Recruitment - while the location is mentions, how will families actually be recruited. Will they be know, how will they be contacted, who will decide on who to contact, what happens if more than 20 respond etc? More detail is needed on recruitment. Response: This has now been addressed in the “Eligibility Criteria, Sample Size and Recruitment Procedures” section.

7. Plan for data entry, coding, security and storage is needed. Response: This has been added in the “Data management” section as well as “Confidentiality” section.

8. Data monitoring committee details and if not needed, why. Response: This concern has been addressed in the “Data Management” section.

9. Consenting procedures for parents and assenting for children of appropriate ages. Response: Please refer to the “Consent/Assent” section.

10. Dissemination policy - what are the reporting processes to sponsors and families who have participated? Response: Please refer to the “Dissemination Policy” section.

11. Is there any intended publications and if so is there an authorship guideline that will apply. Response: Please refer to the “Dissemination Policy” section.

VERSION 2 – REVIEW

REVIEWER	Cylie Williams Peninsula Health/Monash University
REVIEW RETURNED	08-May-2018
GENERAL COMMENTS	Thank you for so thoroughly addressing the concerns. I wish the team well in this research and have no doubt it will be of great benefit to both families and health care professionals.