

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. Some articles will have been accepted based in part or entirely on reviews undertaken for other BMJ Group journals. These will be reproduced where possible.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Outcomes after corrective surgery for congenital dextro-transposition of the great arteries (d-TGA) using the arterial switch technique: a protocol for a scoping systematic review
AUTHORS	Mbuagbaw, Lawrence; Forlemu-Kamwa, Doris; Chu, Angela; Thabane, Lehana; Dillenburg, Rejane

VERSION 1 - REVIEW

REVIEWER	Charles Shey Wiysonge Centre for Evidence-based Health Care, Stellenbosch University, South Africa
REVIEW RETURNED	10-Apr-2014

GENERAL COMMENTS	<p>Major comments</p> <p>Mbuagbaw and colleagues describe the protocol for a scoping review of the literature to document survival and other outcomes in children who underwent the arterial switch operation. I read the manuscript with great interest and only have minor comments.</p> <p>Minor Comments</p> <p>Abstract:</p> <p>In the introduction and methods sections the authors have used "... approached..." instead of "... approach..."? </p> <p>In the "Strengths and limitations of study" section the authors have listed "A comprehensive and exhaustive search strategy" and "It is unlikely that we will find experimental studies." Which of these two is a strength and which is a limitation?</p> <p>Why is it unlikely that experimental studies will be found? I am not a content expert this topic, but why would the possibility of a (non)randomised trial of "physiological" and "anatomical" corrections of d-TGA, or a (non)randomised trial of different ASO techniques, be unlikely?</p> <p>Methods</p> <p>The search date needs to be moved forward from February 2014, as we are already in April 2014 and the protocol is not yet published.</p> <p>The authors should provide the proposed search strategy of at least one electronic database.</p>
-------------------------	---

	<p>The third sentence under screening is incomplete i.e. “If the study meets our inclusion criteria.”</p> <p>The authors indicate under screening that “In the event that the reports are unclear, the corresponding authors may be contacted for clarification or missing information.” Does this mean that the authors of publications with missing information will only be contacted in certain circumstances, and what are those circumstances?</p> <p>The following sentence under data extraction needs revision i.e. “Data such as study design, setting, participant characteristics, duration of follow, details of surgery and outcomes will be include on the data extraction form.”</p> <p>The authors write “Discrepancies will be resolved by consensus and by consulting a third author.” Does this mean that the third author will be consulted only when the two authors do not reach a consensus, or irrespective of whether the two authors reach consensus or not the third author will still be consulted?</p> <p>The authors state that a “Narrative synthesis will be conducted when statistical data pooling is impossible.” Such situations that would render a meta-analysis impossible should be stated.</p>
--	--

REVIEWER	Victor Bautista-Hernandez Victor Bautista-Hernandez, MD, PhD Department of Cardiovascular Surgery. Área de Gestión Integrada de A Coruña.
REVIEW RETURNED	19-Apr-2014

GENERAL COMMENTS	<p>The proposed protocol is interesting and could answer some relevant questions about the outcomes and management of patients borned with D-TGA. However, the study shows some controversial issues which need to be addressed;</p> <p>1) STUDY OF SHORT TERM OUTCOMES (less than one year). This is not a relevant issue. The early outcomes of patients with D-TGA and no associated anomalies is excellent with survival rates reaching 100% in selected centers.</p> <p>2) REVIEW OF STUDIES PUBLISHED ON CHILDREN WHO RECEIVED ASO INTERVENTION FOR CLASSIC D-TGA. What do the authors understand for "classic D-TGA? If they are considering D-TGA with two good sized ventricles and no associated anomalies, the surgery is very standard and the results are comparable between groups. Nevertheless, if they include patients with atypical coronary artery anatomy (specially intranural coronary arteries), some types of VSD, Taussig-Bing anomaly, borderline right or left ventricles... the surgery is not that standard and thus, the early and late results. Excluding patients who had atrial switch, Rastelli, REV, Nikaidoh and L-TGA is not going to fully avoid the groups we commented on.</p> <p>The authors need to define very well which groups are they considering and (if they decide to include these later groups) how are they going to specifically analyze those, since published series for those populations are scarce in the literature.</p>
-------------------------	---

	<p>One minor comment. L-TGA is a complete different disease (from anatomy, pathophysiology and surgical approach) and should not be even mentioned in the text.</p> <p>It has been consistently reported that surgical results of D-TGA with no associated anomalies are excellent. Moreover, since these patients do not usually have associated extracardiac anomalies, the ASO was initially reported as the paradigm of a surgical curative procedure for a complex heart disease. With increasing experience and follow-up, mid and long-term complications such as coronary problems, aortic root dilation and aortic regurgitation have come up.</p> <p>In my opinion, the interest of the proposed study would be to check for long-term outcomes in patients with D-TGA and no associated anomalies who had an ASO with the Lecompte maneuver and disregard about the other groups.</p> <p>Some other minor points</p> <p>1) although rare in this population, are you considering somewhere patients with a genetic disorder? This is very well-known to worsen outcomes.</p> <p>2) Regarding neuropsychiatric development; BAS has been reported to produce some morbidity such as brain bleeding? I think you should check for brain eco dopplers. Moreover, different intraoperative factors have been reported to produce cognitive deficits (anesthetics, cardiopulmonary by-pass, hematocrit on cardiopulmonary by-pass, deep hypothermia and circulatory arrest) and thus, should be checked.</p> <p>3) INTRODUCTION end of 2nd paragraph "... rapidly fatal, unless a large septal defect and/or PDA exists".</p> <p>4) SECONDARY OUTCOMES. What do you mean with coronary anomalies? Most of these patients have coronary anomalies at birth???? How are you going to check for perfusion defects??</p> <p>5) Refernces are not properly included throughout the text.</p> <p>6) REFERENCES. Number 8 is written twice.</p> <p>Conratulations on a very interesting protocol!</p>
--	--

VERSION 1 – AUTHOR RESPONSE

Reviewer comments	Responses
<p>Major comments</p> <p>Mbuagbaw and colleagues describe the protocol for a scoping review of the literature to document survival and other outcomes in children who underwent the arterial switch operation. I read the manuscript with great interest and only have minor comments.</p>	<p>We thank the author for his comments.</p>
<p>Minor Comments</p> <p>Abstract:</p> <p>In the introduction and methods sections the authors have used "... approached..." instead of "... approach..."?</p>	<p>We have corrected this error</p>

<p>In the “Strengths and limitations of study” section the authors have listed “A comprehensive and exhaustive search strategy” and “It is unlikely that we will find experimental studies.” Which of these two is a strength and which is a limitation?</p>	<p>The first is a strength and the second is a limitation. We have revised the statements to make them clearer.</p>
<p>Why is it unlikely that experimental studies will be found? I am not a content expert this topic, but why would the possibility of a (non)randomised trial of “physiological” and “anatomical” corrections of d-TGA, or a (non)randomised trial of different ASO techniques, be unlikely?</p>	<p>The answer to these two questions are summarized next. Historical technical development of cardiac surgery for d-TGA can be used as a framework to justify why experimental studies are not indicated and would not be ethical. As cardio-surgical outcomes evolved since 1970's to 1990's, with excellent outcomes obtained with the arterial switch operation, while looking at the long term complications of the atrial switch, it is intuitive that cardiologists and surgeons would not want to "go back" and compare outcomes between the two techniques. With regards to different ASO techniques, which is a different question than the "trial of physiological (atrial switch) and anatomical (arterial switch) corrections". Different arterial switch techniques do exist, such as using Lecompte maneuver or not, different techniques for translocating the coronary arteries (i.e, if the child has a single coronary or intramural coronary), but these details are not amenable to a trial, because they have to be a decision made in light of the specific anatomical defect in each child. We have clarified why it is unlikely to find trials in the introduction. See page 4, end of paragraph 4.</p>
<p>Methods</p> <p>The search date needs to be moved forward from February 2014, as we are already in April 2014 and the protocol is not yet published.</p>	<p>We have moved the search date to May 2014. See page 7, electronic searches line 3.</p>
<p>The authors should provide the proposed search strategy of at least one electronic database.</p>	<p>We have added the search strategy for MEDLINE via ovid as a table. See table 1 page 7.</p>
<p>The third sentence under screening is incomplete i.e. “If the study meets our inclusion criteria.”</p>	<p>This sentence has been revised.</p>
<p>The authors indicate under screening that “In the event that the reports are unclear, the corresponding authors may be contacted for clarification or missing information.” Does this mean that the authors of publications with missing information will only be contacted in certain circumstances, and what are those circumstances?</p>	<p>Authors of publications will only be contacted in the following circumstances:</p> <ol style="list-style-type: none"> 1. If the report doesn't permit us to decide if it should be included or excluded from our analysis. 2. If reports are ambiguous and may be subject to multiple interpretations. 3. If data relevant to our review is missing despite having been included in the objectives of the study. <p>We have added this clarification to the screening section. See page 8, screening.</p>

<p>The following sentence under data extraction needs revision i.e. "Data such as study design, setting, participant characteristics, duration of follow, details of surgery and outcomes will be include on the data extraction form."</p>	<p>The sentence has been revised. See page 8, data extraction.</p>
<p>The authors write "Discrepancies will be resolved by consensus and by consulting a third author." Does this mean that the third author will be consulted only when the two authors do not reach a consensus, or irrespective of whether the two authors reach consensus or not the third author will still be consulted?</p>	<p>The third author will be contacted only when the two authors do not reach a consensus. We have amended the statement.</p>
<p>The authors state that a "Narrative synthesis will be conducted when statistical data pooling is impossible." Such situations that would render a meta-analysis impossible should be stated.</p>	<p>Some instances when statistical data pooling would not produce meaningful results include: considerable clinical heterogeneity and irreconcilable outcome measures. We have modified the text to reflect this. See page 9, analysis and reporting.</p>

Reviewer 2

<p>The proposed protocol is interesting and could answer some relevant questions about the outcomes and management of patients borned with D-TGA. However, the study shows some controversial issues which need to be addressed;</p>	
<p>1) STUDY OF SHORT TERM OUTCOMES (less than one year). This is not a relevant issue. The early outcomes of patients with D-TGA and no associated anomalies is excellent with survival rates reaching 100% in selected centers.</p>	<p>We agree with the reviewer on this point but feel we can get a more accurate estimate and make a stronger argument for early excellent survival if we provide a joint report from multiple studies.</p>
<p>2) REVIEW OF STUDIES PUBLISHED ON CHILDREN WHO RECEIVED ASO INTERVENTION FOR CLASSIC D-TGA. What do the authors understand for "classic D-TGA? If they are considering D-TGA with two good sized ventricles and no associated anomalies, the surgery is very standard and the results are comparable between groups. Nevertheless, if they include patients with atypical coronary artery anatomy (specially intranural coronary arteries), some types of VSD, Taussig-Bing anomaly, borderline right or left ventricles... the surgery is not that standard and thus, the early and late results. Excluding patients who had atrial switch, Rastelli, REV, Nikaidoh and L-TGA is not going to fully avoid the groups we commented on.</p>	<p>We have provided a detailed description of classic d-TGA. See page 5, types of participants. We are only considering only d-TGA with two good sized ventricles and no associated anomalies. We agree that the outcomes are generally favorable, but this information has not been documented in a systematic way and the long term outcome are unknown, given that many of the children who underwent surgery are entering late adulthood.</p>
<p>The authors need to define very well which groups are they considering and (if they decide to include these later groups) how are they going to specifically analyze those, since published series for those populations are scarce in the literature.</p>	<p>This scoping review will also serve to identify gaps in the literature. Please see page 5,6,7 for details on the types of participants (inclusion/exclusion) and outcomes of interest.</p>
<p>One minor comment. L-TGA is a complete</p>	<p>We agree with this comment and mention L-TGA</p>

different disease (from anatomy, pathophysiology and surgical approach) and should not be even mentioned in the text.	to specify that we will exclude papers reporting on this.
It has been consistently reported that surgical results of D-TGA with no associated anomalies are excellent. Moreover, since these patients do not usually have associated extracardiac anomalies, the ASO was initially reported as the paradigm of a surgical curative procedure for a complex heart disease. With increasing experience and follow-up, mid and long-term complications such as coronary problems, aortic root dilation and aortic regurgitation have come up.	We agree with this comment and seek to document this evidence in a formal and comprehensive way.
In my opinion, the interest of the proposed study would be to check for long-term outcomes in patients with D-TGA and no associated anomalies who had an ASO with the Lecompte maneuver and disregard about the other groups.	This is indeed our goal. Even though we are primarily interested in the long term outcomes, we are still going to report on the short and mid term outcomes.
Some other minor points 1) although rare in this population, are you considering somewhere patients with a genetic disorder? This is very well-known to worsen outcomes.	If genetic outcomes are reported we will extract this data as participant characteristics. See page 8, data extraction.
2) Regarding neuropsychiatric development; BAS has been reported to produce some morbidity such as brain bleeding? I think you should check for brain eco dopplers. Moreover, different intraoperative factors have been reported to produce cognitive deficits (anesthetics, cardiopulmonary by-pass, hematocrit on cardiopulmonary by-pass, deep hypothermia and circulatory arrest) and thus, should be checked.	We thank the reviewer for bringing this up. We will consider any participant and surgical characteristics that may influence outcomes.
3) INTRODUCTION end of 2nd paragraph "... rapidly fatal, unless a large septal defect and/or PDA exists".	We have rephrased this: "... rapidly fatal without intervention, unless there is enough intracardiac and extracardiac mixing and mild obstruction to pulmonary blood flow
4) SECONDARY OUTCOMES. What do you mean with coronary anomalies? Most of these patients have coronary anomalies at birth????	We will be looking at the exact percentages of coronary artery variations and the different types.
How are you going to check for perfusion defects??	We will extract data on perfusion defects reported by the authors.
5) Refernces are not properly included throughout the text.	Our referencing is as per journal requirements. All automatic formatting is removed.
6) REFERENCES. Number 8 is written twice.	Number 8 is not written twice. What the reviewer sees is the last part of the page numbers of the reference.
Conratulations on a very interesting protocol!	We thank the reviewer for these constructive comments.

VERSION 2 – REVIEW

REVIEWER	Charles Shey Wiysonge Stellenbosch University, South Africa
REVIEW RETURNED	19-May-2014

GENERAL COMMENTS	In the abstract (methods and analyses), the authors could consider using "approach" instead of "approached" in the sentence: "Using a systematic scoping review approach, we will conduct a systematic search of the published literature for experimental..."
-------------------------	--

REVIEWER	Victor Bautista-Hernandez, MD, PhD Victor Bautista-Hernandez, MD, PhD Department of Cardiovascular Surgery. Área de Gestión Integrada de A Coruña.
REVIEW RETURNED	23-May-2014

GENERAL COMMENTS	The authors have responded to all my questions. They have answered and added all my comments and suggestions. In my opinion, the paper can be accepted for publication.
-------------------------	---