



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

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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

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Key words:

Systematic review, arterial switch operation, dextro transposition of the great arteries, Jatene operation.

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ABSTRACT:**Introduction:**

Dextro-transposition of the great arteries (d-TGA) is a life threatening congenital health defect that requires rapid surgery. The most widely used approach is the arterial switch operation (ASO) developed by Jatene in the seventies. The first set of children who received this intervention are now adults. The objective of this scoping review of the literature are to document the short (less than one year), medium (one year to twenty years) and long term (more than twenty years) outcomes in children who underwent the ASO. Our primary outcome is survival, but we will explore other secondary surgical, cardio-vascular, reproductive and quality of life outcomes.

Methods and analyses:

Using a systematic scoping review approach, we will conduct a systematic search of the published literature for experimental and observational studies published on children who received the ASO intervention for classic d-TGA. We will search PubMed, Excerpta Medica Database (EMBASE), Cumulative Index to Nursing and Allied Health Literature (CINAHL) and LILACS (Literatura Latino Americana em Ciências da Saúde) from 1973 (date of the first successful ASO) to February 2014. Identified articles will be screened in duplicate and full text for selected articles will be retrieved. Data extraction will be done in duplicate. Discrepancies will be resolved by consensus or by consulting a third author. Where possible proportions will be pooled using the inverse variance method. Our findings will be reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) and Meta-analysis Of Observational studies in Epidemiology (MOOSE) guidelines.

Ethics and dissemination:

The results of this paper will be disseminated as peer reviewed publications, at conferences and at clinical rounds. Our findings may answer important questions for surgeons who perform the ASO intervention and clinicians who take care of patients after surgery and throughout their lifespans.

Registration: Prospero/CRD42014007590.

ARTICLE SUMMARY:**Article focus:**

To outline the plan for a scoping systematic review of the short, medium and long term outcomes in children who underwent the arterial switch operation for dextro transposition of the great arteries.

Key messages:

A scoping systematic review can provide insight to knowledge gaps in this field and provide guidance for clinical practice, policy and research.

Strengths and limitations of study:

A comprehensive and exhaustive search strategy.

It is unlikely that we will find experimental studies.

For peer review only

INTRODUCTION:

Dextro-transposition of the great arteries (d-TGA) is a rare but severe congenital heart defect. It affects 5 in 10,000 live births in the United States. If left untreated, it is the first cause of cardiac –related death in newborn babies and infants. 1

In this condition, the two main arteries (the pulmonary artery and the aorta) leaving the heart are switched or transposed. Under normal circumstances, systemic blood from the rest of the body enters the right part of the heart and is pumped to the lungs for oxygenation through the pulmonary artery. From the lungs, this oxygenated blood enters the left part of the heart and is pumped to the rest of the body through the aorta. In children born with TGA, the systemic (non-oxygenated) blood is pumped back to the rest of the body without oxygenation. Non-oxygenated blood is insufficient to support the body’s oxygen demands, making this condition rapidly fatal.

Infants born with d-TGA most often present with symptoms in the first few hours after birth, as the ductus arteriosus closes. Currently, the diagnosis of congenital heart disease is frequently done during fetal life, which facilitates arrangements for delivery closer to a pediatric cardiac care centre. Dextro-transposition of the great arteries seems to occur more often in Caucasian babies than others. 2 Definitive management of d-TGA is surgical. The procedures employed have evolved over the years, from “physiological” corrections to more stable “anatomical” corrections. In 1973 Dr. Adib Jatene conducted and reported the first case using the arterial switch technique or operation (ASO) which provided anatomical correction 3 It proved to be a superior alternative to the “physiological” corrective techniques employed in the previous years which were associated with risks of dysrhythmia, tricuspid insufficiency and right ventricular failure, along with pulmonary or systemic venous channel obstruction. Since then, this technique has become the standard management for d-TGA.4 The ASO is not without limitations. It can be technically challenging and even more so in children with complex TGA anatomic substrates, where this operation may not even be indicated.4 Despite the challenges, early and late post-operative outcomes for ASO are excellent. 4-7 Abnormal neurologic development has also been noted in some patients. 8

Over the years, as the first set of babies who received this intervention are in their mid-forties, a significant amount of literature has been published. There has also been significant improvement and refinement in the technique, which reflects in better outcomes as the specialists “learned” the new technique.9 It is necessary to summarise the short, mid- and long term outcomes for this widely used technique.

The purpose of this review is to inform surgeons, clinicians, policy makers and researchers on the outcomes associated with the arterial switch operation (ASO). The objectives of this review

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3 are to document the short (less than one year), medium (one year to twenty years) and long
4 term (more than twenty years) outcomes in children who underwent the ASO.
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7 **METHODS AND ANALYSES:**

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9 We will adopt a systematic scoping review approach. This differs from the standard systematic
10 review approach in that we do not seek to answer a specific research question, but rather to
11 appraise a broad body of evidence, identify gaps in knowledge and make recommendations for
12 practice and research.¹⁰
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15 **Criteria for including studies in this review:**

16 **Types of studies:**

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18 Experimental (randomized and non-randomized) and observational studies (longitudinal, cross-
19 sectional and systematic reviews) will be considered. For inclusion, the arterial switch operation
20 must be described either exclusively or in comparison with another intervention, at least one
21 short-term (less than one year), mid-term (one to twenty years), or long-term (twenty years to
22 end of life) outcome must be assessed at follow-up; and the follow-up period must be at least
23 one year.
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29 Studies that describe the arterial switch operation as corrective therapy for patients
30 experiencing complications of a prior atrial baffle operation will be excluded.
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33 **Types of participants:**

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35 We will include studies with children born with classic d- TGA (atrioventricular concordance and
36 ventriculoarterial discordance, with intact ventricular septum or a ventricular septal defect)
37 diagnosed before or at birth. By definition, we will include papers reporting the usual form of
38 heart with transposition of the great arteries, including the following descriptors: heart in the
39 left chest, usual atrial arrangement (situs solitus), morphologically right ventricle if on the right
40 side and the morphologically left ventricle is on the left side, with right hand topology or
41 ventricular d-loop, the aorta anterior and to the right of the pulmonary artery (atrioventricular
42 concordance and ventriculo-arterial discordance).
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48 We will exclude papers focusing on children with “corrected” transposition of the great arteries
49 (atrioventricular and ventriculoarterial discordance), double outlet right ventricle with
50 subpulmonary stenosis; visceral heterotaxy and ambiguous atrial situs, right or left atrial
51 isomerism, dextrocardia and situs inversus totalis and supero-inferior ventricles. The heart with
52 “corrected” transposition or l-TGA represents a completely different heart than the ones with
53 d-TGA, which are the focus of our study. L-TGA hearts have the morphologic right ventricle on
54 the left side pumping oxygenated blood to the aorta and the morphologic left ventricle on the
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right side pumping less oxygenated blood to the pulmonary artery. The main reasons for exclusion of reports on children with heterotaxy and ventriculo-arterial discordance are related to the more complex anatomical malformations and hemodynamic consequences for the patients, who require more complex type of surgical repairs or palliation.

Interventions/exposure:

The intervention/exposure of interest is ASO with or without Lecompte maneuver, with or without ventricular septal defect (VSD) closure, atrial septal defect (ASD) or patent foramen ovale (PFO) closure and ductus arteriosus ligation. Catheter balloon atrial septostomy (BAS) is usually performed in patients with poor mixing and significant desaturations after birth, to allow for weaning from prostaglandin and ventilator support. We will include patients who did or did not have the BAS procedure.

The following interventions will be excluded:

- The atrial switch operations (Mustard and Senning);11
- The Rastelli operation; 12
- Complex d-transposition or its repair operations (“réparation à l’étage ventriculaire” and Nikaidoh procedures); 13, 14
- Interventions for l-transposition, double outlet right ventricle with sub-pulmonary VSD.

Outcomes:

Our primary outcome is:

- Survival rate.

Our secondary outcomes are:

- Re-operations (cardiac surgery within first year)
- Early mortality (<30 days post operatively)
- Late mortality from cardiac cause (> 30days post operatively)
- Aortic insufficiency
- Pulmonary stenosis
- Coronary anomaly
- Perfusion defects
- Neuropsychiatric development
- Obesity or metabolic syndrome
- Other cardiovascular risk factors, such as obesity, smoking, alcohol, exercise capacity, substance addiction, diabetes etc.

- Employment/insurability
- Pregnancy outcomes in women
- Quality of life (as reported by authors).

Search strategy for identification of studies:

We will conduct an exhaustive search for published studies in all languages reporting the outcomes of children who underwent the ASO.

Electronic searches:

We will search PubMed, Excerpta Medica Database (EMBASE), Cumulative Index to Nursing and Allied Health Literature (CINAHL) and LILACS (Literatura Latino Americana em Ciências da Saúde) from 1975 (date of the first successful ASO) to February 2014. The following search terms and their MESH equivalents will be used in various combinations: arterial switch operation, arterial switch procedure, Jatene procedure, transposition of the great vessels, transposition of the great arteries, complete transposition, simple transposition, dextro-transposition, d-transposition ventriculo-arterial discordance, discordant ventriculo-arterial connection, intact ventricular septum, heart septal defects, outcomes.

Reference lists:

The reference lists of relevant citations will be searched for articles of interest.

Grey literature:

Authors, experts, research organization and foundations will be contacted for any relevant material.

Data collection and analyses:

Screening:

Two authors (LM and DK) will independently screen citations and abstracts for relevance. Duplicate citations will be removed. Full text for relevant articles will be downloaded for a second round of screening. If the study meets our inclusion criteria. Article eligibility will be evaluated using a pre-tested form. Arbitration for disagreements will be done by consulting a third author (RD or LT). In the event that the reports are unclear, the corresponding authors may be contacted for clarification or missing information.

Data extraction:

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Data extraction will be conducted independently in duplicate by LM and DK. Data such as study design, setting, participant characteristics, duration of follow, details of surgery and outcomes will be include on the data extraction form.

Assessment of methodological quality:

Two authors will independently appraise the methodological quality of the included studies. Randomized trials will be appraised using the Jadad scale,¹⁵ while non-randomized/observational studies will be appraised using the Newcastle- Ottawa scale,¹⁶ and systematic reviews will be appraised using the AMSTAR (Assessing the Quality of Systematic Reviews) criteria.¹⁷ Discrepancies will be resolved by consensus and by consulting a third author.

Agreement on screening, data abstraction and methodological quality will be measured using the Kappa statistic.¹⁸

Analyses and Reporting:

For randomized trials, only data from the intervention arm (ASO) will be used. If the RCT is comparing different technical aspects of the ASO procedure, outcomes from both arms will be used. For outcomes reported as rates or proportions, a pooled estimate of the proportion will be estimated by weighting the studies according to their sample sizes (inverse variance). When inconsistency is high ($I^2 > 75\%$) we will report a random effects meta-analyses of proportions. For similar continuous outcomes measured on the same scale the mean difference (MD) (standard deviation; SD) will be reported. If the scales are different on not readily convertible (e.g. length of time) we will report the standardized mean difference (SMD). Survival curves will be pooled by meta-analysis of failure-time data.¹⁹ Data will be analysed using Statistical Analysis Software (SAS) Version 9.3 (SAS Institute, Cary, North Carolina, USA, 2009). Our findings will be reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) and Meta-analysis Of Observational studies in Epidemiology (MOOSE) guidelines.^{20, 21} Narrative synthesis will be conducted when statistical data pooling is impossible.

ETHICS AND DISSEMINATION:

The results of this paper will be disseminated as peer reviewed publications, at national and international conferences and at clinical rounds.

DISCUSSION:

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4 A rich body of literature is developing on the outcomes in children who received ASO. 4-8 This
5 literature is going to continue growing as the first set of children who received this intervention
6 get older. In this review we will answer important questions related to their survival, quality of
7 life and other risk factors which arise as a result of their surgery. These findings will have
8 implications for surgeons who perform this intervention and clinicians who take care of patients
9 after surgery and throughout their lifespans. For the many interventions in pediatric cardiac
10 surgery in which it is inappropriate or unethical to conduct randomized trials,²² an objective
11 summary of reports may be the best available source of evidence.
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15 16 17 18 **LIST OF ABBREVIATIONS**

19	ASD	Atrial Septal Defect
20	ASO	Arterial Switch Operation
21	BAS	Balloon Atrial Septostomy
22	CINAHL	Cumulative Index to Nursing and Allied Health Literature
23	EMBASE	Excerpta Medica Database
24	LILACS	Literatura Latino Americana em Ciências da Saúde
25	MD	Mean Difference
26	MOOSE	Meta-analysis Of Observational studies in Epidemiology
27	PFO	Patent Foramen Ovale
28	PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
29	SMD	Standardized Mean Difference
30	VSD	ventricular septal defect

31 32 33 34 35 36 37 38 39 40 41 **ACKNOWLEDGMENTS:**

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43 None.

44 45 46 **COMPETING INTERESTS:**

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48 None declared.

49 50 51 **AUTHORS' CONTRIBUTIONS:**

52 RC, LT and RD conceived of the study. All authors revised the research question, and provided
53 content to the design. All authors read and approved the final version of the manuscript.
54

55 56 57 58 59 60 **FUNDING STATEMENT:**

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Complete List of Authors:	Mbuagbaw, Lawrence; Centre for Development of Best Practices in Health, Yaounde Central Hospital, Forlemu-Kamwa, Doris; McMaster University, Faculty of Health Sciences Chu, Angela Thabane, Lehana; McMaster University, Department of Clinical Epidemiology and Biostatistics Dillenburg, Rejane; McMaster University, Departments of Paediatrics and Anaesthesia
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One strength is our comprehensive and exhaustive search strategy.

One limitation is that it is unlikely that we will find experimental studies.

INTRODUCTION:

Dextro-transposition of the great arteries (d-TGA) is a rare but severe congenital heart defect. It affects 5 in 10,000 live births in the United States. If left untreated, it is the first cause of cardiac –related death in newborn babies and infants. [1]

In this condition, the two main arteries (the pulmonary artery and the aorta) leaving the heart are switched or transposed. Under normal circumstances, systemic blood from the rest of the body enters the right part of the heart and is pumped to the lungs for oxygenation through the pulmonary artery. From the lungs, this oxygenated blood enters the left part of the heart and is pumped to the rest of the body through the aorta. In children born with TGA, the systemic (non-oxygenated) blood is pumped back to the rest of the body without oxygenation. Non-oxygenated blood is insufficient to support the body's oxygen demands, making this condition rapidly fatal without intervention, unless there is enough intra-cardiac and extra-cardiac mixing and mild obstruction to pulmonary blood flow.

Infants born with d-TGA most often present with symptoms in the first few hours after birth, as the ductus arteriosus closes. Currently, the diagnosis of congenital heart disease is frequently done during fetal life, which facilitates arrangements for delivery closer to a pediatric cardiac care centre. Dextro-transposition of the great arteries seems to occur more often in Caucasian babies than others. [2] Definitive management of d-TGA is surgical. The procedures employed have evolved over the years, from “physiological” corrections to more stable “anatomical” corrections. In 1973 Dr. Adib Jatene conducted and reported the first case using the arterial switch technique or operation (ASO) which provided anatomical correction [3] It proved to be a superior alternative to the “physiological” corrective techniques employed in the previous years which were associated with risks of dysrhythmia, tricuspid insufficiency and right ventricular failure, along with pulmonary or systemic venous channel obstruction. Since then, this technique has become the standard management for d-TGA.[4]. The ASO is not without limitations. It can be technically challenging and even more so in children with complex TGA anatomic substrates, where this operation may not even be indicated.[4] Despite the challenges, early and late post-operative outcomes for ASO are excellent. [4-7] Abnormal neurologic development has also been noted in some patients. [8] Given the above, it is unlikely that the ASO will be compared to any of the older techniques in a trial, as it would be unethical to randomize children to sub-optimal care.

Over the years, as the first set of babies who received this intervention are in their mid-forties, a significant amount of literature has been published. There has also been significant improvement and refinement in the technique, which reflects in better outcomes as the specialists “learned” the new technique.[9] It is necessary to summarise the short, mid- and long term outcomes for this widely used technique.

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3 The purpose of this review is to inform surgeons, clinicians, policy makers and researchers on
4 the outcomes associated with the arterial switch operation (ASO). The objectives of this review
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6 term (more than twenty years) outcomes in children who underwent the ASO.
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10 We will adopt a systematic scoping review approach. This differs from the standard systematic
11 review approach in that we do not seek to answer a specific research question, but rather to
12 appraise a broad body of evidence, identify gaps in knowledge and make recommendations for
13 practice and research.[10]
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22 end of life) outcome must be assessed at follow-up; and the follow-up period must be at least
23 one year.
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32 ventriculoarterial discordance, with intact ventricular septum or a ventricular septal defect)
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36 side and the morphologically left ventricle is on the left side, with right hand topology or
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38 concordance and ventriculo-arterial discordance).
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d-TGA, which are the focus of our study. L-TGA hearts have the morphologic right ventricle on the left side pumping oxygenated blood to the aorta and the morphologic left ventricle on the right side pumping less oxygenated blood to the pulmonary artery. The main reasons for exclusion of reports on children with heterotaxy and ventriculo-arterial discordance are related to the more complex anatomical malformations and hemodynamic consequences for the patients, who require more complex type of surgical repairs or palliation.

Interventions/exposure:

The intervention/exposure of interest is ASO with or without Lecompte maneuver, with or without ventricular septal defect (VSD) closure, atrial septal defect (ASD) or patent foramen ovale (PFO) closure and ductus arteriosus ligation. Catheter balloon atrial septostomy (BAS) is usually performed in patients with poor mixing and significant desaturations after birth, to allow for weaning from prostaglandin and ventilator support. We will include patients who did or did not have the BAS procedure.

The following interventions will be excluded:

- The atrial switch operations (Mustard and Senning);[11]
- The Rastelli operation; [12]
- Complex d-transposition or its repair operations (“réparation à l'étage ventriculaire” and Nikaidoh procedures); [13 ,14]
- Interventions for l-transposition, double outlet right ventricle with sub-pulmonary VSD.

Outcomes:

Our primary outcome is:

- Survival rate.

Our secondary outcomes are:

- Re-operations (cardiac surgery within first year)
- Early mortality (<30 days post operatively)
- Late mortality from cardiac cause (> 30days post operatively)
- Aortic insufficiency
- Pulmonary stenosis
- Coronary anomaly
- Perfusion defects
- Neuropsychiatric development
- Obesity or metabolic syndrome

- Other cardiovascular risk factors, such as obesity, smoking, alcohol, exercise capacity, substance addiction, diabetes etc.
- Employment/insurability
- Pregnancy outcomes in women
- Quality of life (as reported by authors).

Search strategy for identification of studies:

We will conduct an exhaustive search for published studies in all languages reporting the outcomes of children who underwent the ASO.

Electronic searches:

We will search MEDLINE, Excerpta Medica Database (EMBASE), Cumulative Index to Nursing and Allied Health Literature (CINAHL) and LILACS (Literatura Latino Americana em Ciências da Saúde) from 1975 (date of the first successful ASO) to May 2014. The following search terms and their MESH equivalents will be used in various combinations: arterial switch operation, arterial switch procedure, Jatene procedure, transposition of the great vessels, transposition of the great arteries, complete transposition, simple transposition, dextro-transposition, d-transposition ventriculo-arterial discordance, discordant ventriculo-arterial connection, intact ventricular septum, heart septal defects, outcomes. Table 1 is a proposed search strategy for MEDLINE via Ovid.

Table 1: Proposed search strategy for Ovid

Database: Ovid MEDLINE(R)

Search Strategy:

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- 1 arterial switch operation.mp.
 - 2 arterial switch procedure.mp.
 - 3 jatene.mp.
 - 4 exp "Transposition of Great Vessels"/
 - 5 transposition of the great arteries.mp.
 - 6 complete transposition.mp.
 - 7 simple transposition.mp.
 - 8 dextro-transposition.mp.
 - 9 d-transposition.mp.
 - 10 ventriculoarterial discordance.mp.
 - 11 discordant ventriculoarterial connection.mp.
 - 12 intact ventricular septum.mp.
 - 13 exp Heart Septal Defects, Ventricular/
 - 14 lecompte.mp.

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4 15 outcomes.mp.
5 16 1 or 2 or 3
6 17 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15
7 18 16 and 17
8 19 18 and "Humans".sa_suba.
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Reference lists:

The reference lists of relevant citations will be searched for articles of interest.

Grey literature:

Authors, experts, research organization and foundations will be contacted for any relevant material.

Data collection and analyses:

Screening:

Two authors (LM and DK) will independently screen citations and abstracts for relevance. Duplicate citations will be removed. Full text for relevant articles will be downloaded for a second round of screening if the study meets our inclusion criteria. Article eligibility will be evaluated using a pre-tested form. Arbitration for disagreements will be done by consulting a third author (RD or LT). In the event that the reports are unclear, the corresponding authors may be contacted for clarification or missing information. Corresponding authors will be contacted in the following circumstances: 1) If the report doesn't permit us to decide if it should be included or excluded from our review; 2) If reports are ambiguous and may be subject to multiple interpretations or 3) If data relevant to our review was collected but not reported.

Data extraction:

Data extraction will be conducted independently in duplicate by LM and DK. Data such as study design, setting, participant characteristics, duration of follow-up, details of surgery and outcomes will be included in the data extraction form.

Assessment of methodological quality:

Two authors will independently appraise the methodological quality of the included studies. Randomized trials will be appraised using the Jadad scale,[15] while non-randomized/observational studies will be appraised using the Newcastle- Ottawa scale, [16]

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3 and systematic reviews will be appraised using the AMSTAR (Assessing the Quality of
4 Systematic Reviews) criteria. [17]Discrepancies will be resolved by consensus and by consulting
5 a third author (LT or RD) if no consensus is reached.
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8 Agreement on screening, data abstraction and methodological quality will be measured using
9 the Kappa statistic.[18]
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12 13 14 **Analyses and Reporting:**

15 For randomized trials, only data from the intervention arm (ASO) will be used. If the RCT is
16 comparing different technical aspects of the ASO procedure, outcomes from both arms will be
17 used. For outcomes reported as rates or proportions, a pooled estimate of the proportion will
18 be estimated by weighting the studies according to their sample sizes (inverse variance). When
19 inconsistency is high ($I^2 > 75\%$) we will report a random effects meta-analysis of proportions.
20 For similar continuous outcomes measured on the same scale the mean difference (MD)
21 (standard deviation; SD) will be reported. If the scales are different or not readily convertible
22 (e.g. length of time) we will report the standardized mean difference (SMD). Survival curves will
23 be pooled by meta-analysis of failure-time data. [19]Data will be analysed using Statistical
24 Analysis Software (SAS) Version 9.3 (SAS Institute, Cary, North Carolina, USA, 2009). Our
25 findings will be reported according to the Preferred Reporting Items for Systematic Reviews and
26 Meta-Analyses (PRISMA) and Meta-analysis Of Observational studies in Epidemiology (MOOSE)
27 guidelines.[20 ,21] Narrative synthesis will be conducted when statistical data pooling is would
28 not yield meaningful results for example, in the presence of considerable clinical heterogeneity
29 or irreconcilable outcome measures. .
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38 **ETHICS AND DISSEMINATION:**

39 The results of this paper will be disseminated as peer reviewed publications, at national and
40 international conferences and at clinical rounds.
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44 **DISCUSSION:**

45 A rich body of literature is developing on the outcomes in children who received ASO. [4-8] This
46 literature is going to continue growing as the first set of children who received this intervention
47 get older. In this review we will answer important questions related to their survival, quality of
48 life and other risk factors which arise as a result of their surgery. These findings will have
49 implications for surgeons who perform this intervention and clinicians who take care of patients
50 after surgery and throughout their lifespans. For the many interventions in pediatric cardiac
51 surgery in which it is inappropriate or unethical to conduct randomized trials,[22] an objective
52 summary of reports may be the best available source of evidence.
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LIST OF ABBREVIATIONS

ASD	Atrial Septal Defect
ASO	Arterial Switch Operation
BAS	Balloon Atrial Septostomy
CINAHL	Cumulative Index to Nursing and Allied Health Literature
EMBASE	Excerpta Medica Database
LILACS	Literatura Latino Americana em Ciências da Saúde
MD	Mean Difference
MOOSE	Meta-analysis Of Observational studies in Epidemiology
PFO	Patent Foramen Ovale
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
SMD	Standardized Mean Difference
VSD	ventricular septal defect

ACKNOWLEDGMENTS:

None.

COMPETING INTERESTS:

None declared.

AUTHORS' CONTRIBUTIONS:

RC, LT and RD conceived of the study. All authors revised the research question, and provided content to the design. All authors read and approved the final version of the manuscript.

FUNDING STATEMENT:

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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

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Rejane Dillenberg⁵.

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Dillenburg - dillenburg@mcmaster.ca.

Key words:

Systematic review, arterial switch operation, dextro transposition of the great arteries, Jatene operation.

Word count:

2007

ARTICLE SUMMARY:**Article focus:**

To outline the plan for a scoping systematic review of the short, medium and long term outcomes in children who underwent the arterial switch operation for dextro transposition of the great arteries.

Key messages:

A scoping systematic review can provide insight to knowledge gaps in this field and provide guidance for clinical practice, policy and research.

Strengths and limitations of study:

One strength is ourA comprehensive and exhaustive search strategy.

One limitation is that it is unlikely that we will find experimental studies.

ABSTRACT:**Introduction:**

Dextro-transposition of the great arteries (d-TGA) is a life threatening congenital health defect that requires rapid surgery. The most widely used approach^{ed} is the arterial switch operation (ASO) developed by Jatene in the seventies. The first set of children who received this intervention are now adults. The objective of this scoping review of the literature are to document the short (less than one year), medium (one year to twenty years) and long term (more than twenty years) outcomes in children who underwent the ASO. Our primary outcome is survival, but we will explore other secondary surgical, cardio-vascular, reproductive and quality of life outcomes.

Methods and analyses:

Using a systematic scoping review approach, we will conduct a systematic search of the published literature for experimental and observational studies published on children who received the ASO intervention for classic d-TGA. We will search MEDLINE, Excerpta Medica Database (EMBASE), Cumulative Index to Nursing and Allied Health Literature (CINAHL) and LILACS (Literatura Latino Americana em Ciências da Saúde) from 1973 (date of the first successful ASO) to February 2014. Identified articles will be screened in duplicate and full text for selected articles will be retrieved. Data extraction will be done in duplicate. Discrepancies will be resolved by consensus or by consulting a third author. Where possible proportions will be pooled using the inverse variance method. Our findings will be reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) and Meta-analysis Of Observational studies in Epidemiology (MOOSE) guidelines.

Ethics and dissemination:

The results of this paper will be disseminated as peer reviewed publications, at conferences and at clinical rounds. Our findings may answer important questions for surgeons who perform the ASO intervention and clinicians who take care of patients after surgery and throughout their lifespans.

Registration: Prospero/CRD42014007590.

INTRODUCTION:

Dextro-transposition of the great arteries (d-TGA) is a rare but severe congenital heart defect. It affects 5 in 10,000 live births in the United States. If left untreated, it is the first cause of cardiac-related death in newborn babies and infants. [1]

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Infants born with d-TGA most often present with symptoms in the first few hours after birth, as the ductus arteriosus closes. Currently, the diagnosis of congenital heart disease is frequently done during fetal life, which facilitates arrangements for delivery closer to a pediatric cardiac care centre. Dextro-transposition of the great arteries seems to occur more often in Caucasian babies than others. [2] Definitive management of d-TGA is surgical. The procedures employed have evolved over the years, from "physiological" corrections to more stable "anatomical" corrections. In 1973 Dr. Adib Jatene conducted and reported the first case using the arterial switch technique or operation (ASO) which provided anatomical correction [3] It proved to be a superior alternative to the "physiological" corrective techniques employed in the previous years which were associated with risks of dysrhythmia, tricuspid insufficiency and right ventricular failure, along with pulmonary or systemic venous channel obstruction. Since then, this technique has become the standard management for d-TGA.[4]. The ASO is not without limitations. It can be technically challenging and even more so in children with complex TGA anatomic substrates, where this operation may not even be indicated.[4] Despite the challenges, early and late post-operative outcomes for ASO are excellent. [4-7] Abnormal neurologic development has also been noted in some patients. [8] Given the above, it is unlikely that the ASO will be compared to any of the older techniques in a trial, as it would be unethical to randomize children to sub-optimal care.

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31 We will include studies with children born with classic d- TGA (atrioventricular concordance and
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34 heart with transposition of the great arteries, including the following descriptors: heart in the
35 left chest, usual atrial arrangement (situs solitus), morphologically right ventricle if on the right
36 side and the morphologically left ventricle is on the left side, with right hand topology or
37 ventricular d-loop, the aorta anterior and to the right of the pulmonary artery (atrioventricular
38 concordance and ventriculo-arterial discordance).
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42 (atrioventricular and ventriculoarterial discordance), double outlet right ventricle with
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44 isomerism, dextrocardia and situs inversus totalis and supero-inferior ventricles. The heart with
45 “corrected” transposition or l-TGA represents a completely different heart than the ones with
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d-TGA, which are the focus of our study. L-TGA hearts have the morphologic right ventricle on the left side pumping oxygenated blood to the aorta and the morphologic left ventricle on the right side pumping less oxygenated blood to the pulmonary artery. The main reasons for exclusion of reports on children with heterotaxy and ventriculo-arterial discordance are related to the more complex anatomical malformations and hemodynamic consequences for the patients, who require more complex type of surgical repairs or palliation.

Interventions/exposure:

The intervention/exposure of interest is ASO with or without Lecompte maneuver, with or without ventricular septal defect (VSD) closure, atrial septal defect (ASD) or patent foramen ovale (PFO) closure and ductus arteriosus ligation. Catheter balloon atrial septostomy (BAS) is usually performed in patients with poor mixing and significant desaturations after birth, to allow for weaning from prostaglandin and ventilator support. We will include patients who did or did not have the BAS procedure.

The following interventions will be excluded:

- The atrial switch operations (Mustard and Senning);[11]
- The Rastelli operation; [12]
- Complex d-transposition or its repair operations (“réparation à l'étage ventriculaire” and Nikaidoh procedures); [13 ,14]
- Interventions for l-transposition, double outlet right ventricle with sub-pulmonary VSD.

Outcomes:

Our primary outcome is:

- Survival rate.

Our secondary outcomes are:

- Re-operations (cardiac surgery within first year)
- Early mortality (<30 days post operatively)
- Late mortality from cardiac cause (> 30days post operatively)
- Aortic insufficiency
- Pulmonary stenosis
- Coronary anomaly
- Perfusion defects
- Neuropsychiatric development
- Obesity or metabolic syndrome

- Other cardiovascular risk factors, such as obesity, smoking, alcohol, exercise capacity, substance addiction, diabetes etc.
- Employment/insurability
- Pregnancy outcomes in women
- Quality of life (as reported by authors).

Search strategy for identification of studies:

We will conduct an exhaustive search for published studies in all languages reporting the outcomes of children who underwent the ASO.

Electronic searches:

We will search [MEDLINE PubMed](#), Excerpta Medica Database (EMBASE), Cumulative Index to Nursing and Allied Health Literature (CINAHL) and LILACS (Literatura Latino Americana em Ciências da Saúde) from 1975 (date of the first successful ASO) to [MayFebruary](#) 2014. The following search terms and their MESH equivalents will be used in various combinations: arterial switch operation, arterial switch procedure, Jatene procedure, transposition of the great vessels, transposition of the great arteries, complete transposition, simple transposition, dextro-transposition, d-transposition ventriculo-arterial discordance, discordant ventriculo-arterial connection, intact ventricular septum, heart septal defects, outcomes. [Table 1 is a proposed search strategy for MEDLINE via Ovid.](#)

[Table 1: Proposed search strategy for Ovid](#)

[Database: Ovid MEDLINE\(R\)](#)

[Search Strategy:](#)

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- [1 arterial switch operation.mp.](#)
 - [2 arterial switch procedure.mp.](#)
 - [3 jatene.mp.](#)
 - [4 exp "Transposition of Great Vessels"/](#)
 - [5 transposition of the great arteries.mp.](#)
 - [6 complete transposition.mp.](#)
 - [7 simple transposition.mp.](#)
 - [8 dextro-transposition.mp.](#)
 - [9 d-transposition.mp.](#)
 - [10 ventriculoarterial discordance.mp.](#)
 - [11 discordant ventriculoarterial connection.mp.](#)
 - [12 intact ventricular septum.mp.](#)
 - [13 exp Heart Septal Defects, Ventricular/](#)
 - [14 lecompte.mp.](#)

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4 15 outcomes.mp.

5 16 1 or 2 or 3

6 17 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15

7 18 16 and 17

8 19 18 and "Humans".sa suba.

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13 **Reference lists:**

14 The reference lists of relevant citations will be searched for articles of interest.

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17 **Grey literature:**

18 Authors, experts, research organization and foundations will be contacted for any relevant
19 material.

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25 **Data collection and analyses:**

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27 **Screening:**

28 Two authors (LM and DK) will independently screen citations and abstracts for relevance.
29 Duplicate citations will be removed. Full text for relevant articles will be downloaded for a
30 second round of screening ~~ifg-~~if the study meets our inclusion criteria. Article eligibility will be
31 evaluated using a pre-tested form. Arbitration for disagreements will be done by consulting a
32 third author (RD or LT). In the event that the reports are unclear, the corresponding authors
33 may be contacted for clarification or missing information. Corresponding authors will be
34 contacted in the following circumstances: 1) If the report doesn't permit us to decide if it
35 should be included or excluded from our review; 2) If reports are ambiguous and may be
36 subject to multiple interpretations or 3) If data relevant to our review was collected but not
37 reported.

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44 **Data extraction:**

45 Data extraction will be conducted independently in duplicate by LM and DK. Data such as study
46 design, setting, participant characteristics, duration of follow-up, details of surgery and
47 outcomes will be included in the data extraction form.

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51 **Assessment of methodological quality:**

52 Two authors will independently appraise the methodological quality of the included studies.
53 Randomized trials will be appraised using the Jadad scale,[15] while non-
54 randomized/observational studies will be appraised using the Newcastle- Ottawa scale, [16]
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3 and systematic reviews will be appraised using the AMSTAR (Assessing the Quality of
4 Systematic Reviews) criteria. [17]Discrepancies will be resolved by consensus and by consulting
5 a third author (LT or RD) if no consensus is reached.
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8 Agreement on screening, data abstraction and methodological quality will be measured using
9 the Kappa statistic.[18]
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12 13 14 **Analyses and Reporting:**

15 For randomized trials, only data from the intervention arm (ASO) will be used. If the RCT is
16 comparing different technical aspects of the ASO procedure, outcomes from both arms will be
17 used. For outcomes reported as rates or proportions, a pooled estimate of the proportion will
18 be estimated by weighting the studies according to their sample sizes (inverse variance). When
19 inconsistency is high ($I^2 > 75\%$) we will report a random effects meta-analyses of proportions.
20 For similar continuous outcomes measured on the same scale the mean difference (MD)
21 (standard deviation; SD) will be reported. If the scales are different on not readily convertible
22 (e.g. length of time) we will report the standardized mean difference (SMD). Survival curves will
23 be pooled by meta-analysis of failure-time data. [19]Data will be analysed using Statistical
24 Analysis Software (SAS) Version 9.3 (SAS Institute, Cary, North Carolina, USA, 2009). Our
25 findings will be reported according to the Preferred Reporting Items for Systematic Reviews and
26 Meta-Analyses (PRISMA) and Meta-analysis Of Observational studies in Epidemiology (MOOSE)
27 guidelines.[20 ,21] Narrative synthesis will be conducted when statistical data pooling is would
28 not yield meaningful results for example, in the presence of considerable clinical heterogeneity
29 or irreconcilable outcome measures. impossible.
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38 **ETHICS AND DISSEMINATION:**

39 The results of this paper will be disseminated as peer reviewed publications, at national and
40 international conferences and at clinical rounds.
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44 **DISCUSSION:**

45 A rich body of literature is developing on the outcomes in children who received ASO. [4-8] This
46 literature is going to continue growing as the first set of children who received this intervention
47 get older. In this review we will answer important questions related to their survival, quality of
48 life and other risk factors which arise as a result of their surgery. These findings will have
49 implications for surgeons who perform this intervention and clinicians who take care of patients
50 after surgery and throughout their lifespans. For the many interventions in pediatric cardiac
51 surgery in which it is inappropriate or unethical to conduct randomized trials,[22] an objective
52 summary of reports may be the best available source of evidence.
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LIST OF ABBREVIATIONS

ASD	Atrial Septal Defect
ASO	Arterial Switch Operation
BAS	Balloon Atrial Septostomy
CINAHL	Cumulative Index to Nursing and Allied Health Literature
EMBASE	Excerpta Medica Database
LILACS	Literatura Latino Americana em Ciências da Saúde
MD	Mean Difference
MOOSE	Meta-analysis Of Observational studies in Epidemiology
PFO	Patent Foramen Ovale
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
SMD	Standardized Mean Difference
VSD	ventricular septal defect

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COMPETING INTERESTS:

None declared.

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RC, LT and RD conceived of the study. All authors revised the research question, and provided content to the design. All authors read and approved the final version of the manuscript.

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Correction

Mbuagbaw L, Forlemu-Kamwa D, Chu A, *et al.* Outcomes after corrective surgery for congenital dextrotransposition of the great arteries using the arterial switch technique: a protocol for a scoping systematic review. *BMJ Open* 2014;4:e005123. The surname of the last author of this paper was misspelt; the correct spelling is 'Rejane Dillenburg.'



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BMJ Open 2014;4:e005123. doi:10.1136/bmjopen-2014-005123corr1