AWARD NUMBER: W81XWH-22-1-0301

TITLE: TITRE: Trial of Indication-Based Transfusion of Red Blood Cells in ECMO

PRINCIPAL INVESTIGATOR: Dr Lynn Sleeper, ScD

CONTRACTING ORGANIZATION: Boston Children's Hospital, Boston, MA

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Fort Detrick, Maryland 21702-5012

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TITRE: Trial of Indication-Based Transfusion of Red Blood Cells in ECMO

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5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)

Lynn A. Sleeper, ScD

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

Children's Hospital Corporation, The
Office of Sponsored Programs
300 Longwood Ave
Boston, MA 02115-5724

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13. SUPPLEMENTARY NOTES

14. ABSTRACT

Background: Extracorporeal membrane oxygenation (ECMO) can provide life-saving mechanical cardiac and respiratory support to critically ill children. Survival to hospital discharge is approximately 50% in most populations, but adverse events are common and long-term function including quality of life (QOL) is compromised in many ECMO survivors. Children supported with ECMO undergo red blood cell (RBC) transfusions to maintain a threshold hematocrit (HCT) or hemoglobin (Hb) for tissue oxygen delivery (DO_2). However, observational studies of children on ECMO have shown an association between large-volume RBC transfusion and mortality. Further, the HCT (or Hb) level at which optimal DO_2 occurs is unknown. To address this crucial knowledge gap, we propose *TITRE - Trial of Indication-based Transfusion of Red Blood Cells in ECMO,* a multicenter, prospective, randomized clinical trial (RCT). **The overarching goal of TITRE is to determine whether restricting RBC transfusion according to an indication-based strategy for those with bleeding and/or deficit of tissue oxygen delivery, compared with transfusion based on center-specific Hb or HCT thresholds, can reduce organ dysfunction, and improve later neurodevelopment** in critically ill children receiving ECMO support.

Relevance to Topic Areas: The proposed research has relevance to the following Topic Areas: **Congenital Heart Disease (CHD); Cardiomyopathy; Emerging Viral Pathogens; Pathogen-Inactivated Blood Products; and Hemorrhage Control.** CHD is a common birth defect affecting approximately 8 per 1000 live births, many of whom require surgical correction or palliation. Many of the ECMO patients to be enrolled in the proposed RCT will have CHD. Cardiomyopathy is a rare disease, and ECMO can help rescue these patients from life threatening heart failure and serve as a bridge to transplantation. Similarly, ECMO can provide an invaluable support for critically ill adults and children with emerging viral pathogens as evidenced by its use in the H1N1 Influenza and COVID19 pandemics. The intervention to be tested is the optimal strategy for RBC transfusion, i.e., a rigorous evaluation of pathogen-inactivated blood products to reduce the incidence of end-organ dysfunction and mortality. Furthermore, the proposed RCT has relevance to the topic area of Hemorrhage Control, i.e., the proposed study is responsive to the DoD focus on the effects of transfusion guidelines on clinical outcomes.

Hypotheses: 1) Compared with threshold-based RBC transfusion during ECMO, improvement in organ dysfunction will be greater using an indication-based RBC transfusion protocol.

2) One-year neurodevelopmental outcomes in ECMO patients will be better in those assigned to an indication-based RBC transfusion protocol compared with a center-specific threshold-based RBC transfusion strategy.

Specific Aims*:* Aim 1**:** To test whether children < 6 years of age on ECMO support who are randomized to a strategy of indication-based *versus* center-specific threshold-based RBC transfusion will have greater improvement in organ function. Our primary trial outcome will be the baseline-adjusted change in Pediatric Sequential Organ Failure Score (pSOFA) from randomization (pre-ECMO cannulation) to the earliest of post-ECMO decannulation or 30 days post-randomization. Aim 2: To test whether survivors among children age < 6 years on ECMO support who are randomized to indication-based compared to center-specific threshold-based RBC transfusion will have better neurodevelopmental outcomes and health-related QOL at one year post-randomization.

Study Design: The *TITRE* Trial will be conducted in 18 large-volume pediatric ECMO centers, led by an experienced, multidisciplinary clinical trial leadership group. Dr. Lynn Sleeper (PI for this application and current DoD PI #W81XWH-17-1-0532) leads the Data Coordinating Center and Drs. Ravi Thiagarajan and Peta Alexander Co-Chair the Trial and lead the Clinical Coordinating Center. Importantly, the trial design has been affirmed by multiple stakeholders, i.e., across the disciplines that comprise pediatric ECMO programs and by leaders of both pediatric and adult professional societies. Key design features include: Randomization stratified by patient age (neonate, <28d vs. non-neonate) and by diagnosis (CHD vs. other diagnosis); and a target sample size of 228 patients. Endpoints will be evaluated during ECMO, at hospital discharge, and at 3, 6, 9, and 12 months. To ensure trial integrity, the primary outcome (pSOFA) will be adjudicated by an independent committee and neurodevelopmental assessments will be blinded and. The Aim 1 primary outcome is baseline-adjusted change in pSOFA score and secondary outcomes include mortality, days on ECMO and mechanical ventilation, renal function, donor exposures/total blood volume received during ECMO, and resource utilization. The Aim 2 outcomes include the Bayley Scales of Infant and Toddler Development-4th edition, or (depending on age and functioning) the Wechsler Preschool and Primary Scale of Intelligence-4th edition, behavioral assessments, and the PedsQL instrument.

Clinical Impact: Results from *TITRE* have the potential to shape the practice of blood management in critically ill children supported with ECMO world-wide. The results will also have implications for optimal transfusion strategies for the over 8,000 adults who receive ECMO annually.

Relevance to Military Health: Military children undergoing cardiac surgery may require post-operative ECMO and optimizing RBC transfusion in these children can improve outcomes. The trial results are also generalizable to adults and to ECMO use for other indications, including trauma. Thus the proposed RCT is especially relevant to the well-being of military personnel, who are at higher risk for traumatic injury. Decreasing exposure to RBC transfusion during ECMO in these patients can improve survival, as well as help conserve a scarce resource.

The significant experience in critical care, ECMO, transfusion medicine, DoD research, and the execution of complex pediatric trials by the Clinical and Data Coordinating Center teams at Boston Children's Hospital/Harvard Medical School and the *TITRE* network of study sites will ensure success of this important study, which will fill a knowledge gap with respect to optimal transfusion strategies in a critically ill patient population to improve survival and clinical outcomes.

15. SUBJECT TERMS					
Heart transplantation; children; immunosuppression; randomized clinical trial					
16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
					USAMRDC
a. REPORT	b. ABSTRACT	c. THIS PAGE	UU	23	19b. TELEPHONE NUMBER *(include area code)*
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TITRE - Trial of Indication-based Transfusion of Red Blood Cells in ECMO, a multicenter, prospective, randomized clinical trial (RCT). The overarching goal of TITRE is to determine whether restricting RBC transfusion according to an indication-based strategy for those with bleeding and/or deficit of tissue oxygen delivery, compared with transfusion based on center-specific Hb or HCT thresholds, can reduce organ dysfunction, and improve later neurodevelopment in critically ill children receiving ECMO support. The trial is being conducted at 20 centers, with leadership at Boston Children's Hospital (Data and Clinical Coordinating Centers). In this first year, all required trial infrastructure was developed and Screening and Recruitment began in April 2023, 9.5 months after grant award, in concordance with the original SOW. At the time of this annual report, 5 patients have been randomized. We have expanded from 18 to 20 study sites, and 15 have IRB/HRPO approval (with a smaller number fully activated and screening). We have made a small leadership change, with our ECMO experts Drs. Thiagarajan and Alexander now the Trial co-chairs and Dr. Newburger serving as Co-Investigator for her trials and neurodevelopment expertise. The data management system was moved to Production (go-live) mode. Our biobank infrastructure is established and blood/urine specimens are being collected. We have completed translation activities for the informed consent and study brochure. We held an Adjudication Committee webinar to standardize primary endpoint scoring procedures. Four research presentations on the TITRE trial design, transfusion strategies and the primary endpoint were presented at the EuroELSO Conference in April 2023.

TABLE OF CONTENTS

1. **INTRODUCTION:** *Narrative that briefly (one paragraph) describes the subject, purpose and scope of the research.*

Extracorporeal membrane oxygenation (ECMO) can provide life-saving mechanical cardiac and respiratory support to critically ill children. Survival to hospital discharge is approximately 50% in most populations, but adverse events are common and long-term function including quality of life (QOL) is compromised in many ECMO survivors. Children supported with ECMO undergo red blood cell (RBC) transfusions to maintain a threshold hematocrit (HCT) or hemoglobin (Hb) for tissue oxygen delivery (DO_2). However, observational studies of children on ECMO have shown an association between large-volume RBC transfusion and mortality. Further, the HCT (or Hb) level at which optimal DO_2 occurs is unknown. To address this crucial knowledge gap, we are executing *TITRE - Trial of Indication-based Transfusion of Red Blood Cells in ECMO,* a multicenter, prospective, randomized clinical trial (RCT). **The overarching goal of TITRE is to determine whether restricting RBC transfusion according to an indication-based strategy for those with bleeding and/or deficit of tissue oxygen delivery, compared with transfusion based on center-specific Hb or HCT thresholds, can 1) reduce organ dysfunction, and 2) improve later neurodevelopment** in critically ill children receiving ECMO support. Biospecimens will also be collected from each participant. The trial will be executed at 20 hospitals in North America and will enroll 228 participants, who will each be followed for one year. The significant experience in critical care, ECMO, transfusion medicine, DoD research, and the execution of complex pediatric trials by the Clinical and Data Coordinating Center teams at Boston Children's Hospital/Harvard Medical School and the *TITRE* network of study sites will ensure success of this important study, which will fill a knowledge gap with respect to optimal transfusion strategies in a critically ill patient population to improve survival and clinical outcomes.

2. **KEYWORDS:** *Provide a brief list of keywords (limit to 20 words).*

Children, red blood cells, transfusion, ECMO, randomized clinical trial, extracorporeal membrane oxygenation

ACCOMPLISHMENTS:

What were the major goals of the project?

The OVERALL AIM *of the research is to* conduct a multicenter randomized clinical trial enrolling 228 children at 20 study sites to determine if indication-based red blood cell (RBC) transfusion based on reduced tissue oxygen delivery, compared with RBC transfusion based on an institutional-specific approach, can reduce organ dysfunction and failure in critically ill infants and children receiving extracorporeal membrane oxygenation (ECMO) support, and improve their later neurodevelopmental, functional, and health-related quality of life outcomes.

Major Tasks per SOW include:

1. *Regulatory & Contractual Activities required for Study Launch* — *Months -6 to 6*
2. *Prepare Study Staff and Systems to Execute Trial* — *Months 1 to 9*
3. *Participant Recruitment* — *Months 10-27*
4. *Participant Follow-up and Evaluation* — *Months 10-39*
5. *Study Closeout and Analysis* — *Months 37 to 48*

Table 1. Statement of Work Tasks and Completion Status

Table 1. Progress Report based on Statement of Work for Major Tasks 1 to 5. Shaded rows indicate fully completed tasks.

TASK	Timeline (mo)	Status
Major Task 1: Regulatory & Contractual Activities required for Study Launch		
Subtask 1: Obtain regulatory approvals for study protocol		
Finalize trial protocol, approved by Trial Executive Committee	-6 to -2	✓
Obtain Boston Children's IRB approval of trial protocol and informed consent	-2 to 0	✓ 4/2022
Execute single IRB Reliance Agreements with study sites	-3 to 3	Ongoing
Submit final protocol for Military IRB (ORP/HRPO) review and approval of Boston Children's Hospital documents	0 to 3	✓ 06/16/22
Subtask 2: Execute financial agreements / subawards		
Coordinate with Sites for local IRB approval of informed consent forms	1-4	Ongoing

Obtain ORP/HRPO approval of protocol and consent form for each study site	1-6	15 of 20 complete
DSMB organizational and protocol review meeting, arranged by DCC	2	✓ 01/3/23
Submit amendments, adverse events and protocol deviations as needed	As Needed	
Prepare annual IRB report for continuing review	Annually	
Milestone Achieved: IRB approval for all Study Sites	4	
Milestone Achieved: Approval by Military HRPO for all Study Sites	6	
Coordinate with Sites to execute Subcontracts/ CTAs	1-6	12 of 19 complete
Execute Consultant Agreements with Adjudication Committee members and Medical Monitor	1-3	3 of 4 complete
Milestone Achieved: All Subcontracts and Consultant Agreements executed	1-6	
Major Task 2: Prepare Study Staff and Systems to Execute Trial		
Subtask 1: Training of Research Staff		
DCC/CCC to conduct in-person or webinar training session for certification on study protocol	6-9	✓ 12/15/22, 1/13/23
Adjudication Committee webinar to standardize primary endpoint scoring procedures	6-9	✓ 6/30/23
DCC/CCC/Medical Monitor webinar to standardize AE review procedures	6-9	✓ 5/17/23
Retrain site study coordinators/Train new coordinators as needed via Webinar	As Needed	Ongoing
Milestone Achieved: Research staff trained	9	
Subtask 2: Build Trial materials and communications and database system		
Finalize case report forms, including pilot testing with core site SCs	1-3	✓
Create Trial Manual of Operation (MOO)	3-9	✓

Develop Administrative website to post trial materials and secure documents	1-3	✓
Develop and test database management and randomization systems	3-9	✓
Neurodevelopment Core reviews videos of deidentified practice Bayley administration from study sites	6-9	
Harmonize with ELSO ECMO Registry- augment the ELSO infrastructure by adding data fields related to RBC transfusion	1-9	
Milestone Achieved: Study systems developed and functional for trial launch	9	
Major Task 3: Participant Recruitment		
Site Study Coordinators screen records for eligibility and randomize consented patients; CCC on call for eligibility questions from sites	10-27	24 screened 5 randomized of 228 target
Teleconference with SCs every other week and site PIs monthly	10-27	Ongoing
Milestone Achieved: Recruitment and randomization of 228 participants	27	
Major Task 4: Participant Follow-up and Evaluation (0,3,6,9,12 mo post-randomization)		
Subtask 1: Data collection - Complete participant study visits		
Complete required study visits, including neurodevelopment assessments	10-39	Ongoing
Submit participant clinical data to DCC database management system	10-39	Ongoing
Collect blood/urine samples and perform batch shipment to BCH Biobank	10-39	Ongoing
Submit adverse event reports to DCC and local IRB per required time frames	As needed	Ongoing
Milestone Achieved: Data collection complete	39	
Subtask 2: Event Reporting and Monitoring, Quality Assurance and Centralized Assessments		
DCC securely posts SAEs and Medical Monitor submits adjudications	10-39	Ongoing
DCC securely posts pSOFA case files and Committee submits adjudications	10-39	
DCC submits SAEs to IRB, HRPO and DSMB per required time frames	10-39	Ongoing

Site visits and data audits performed in person, 1 per site and for-cause	18-36	
Ongoing monitoring of data quality and completeness by DCC	As needed	Ongoing
Write and publish trial design manuscript prior to interim look	10-18	
DSMB meeting for one interim look at efficacy outcome (estimated timing)	20-22	
DCC coordinates DSMB meetings, prepares and securely post reports	16-36	Ongoing – next meeting 9/1/23
Milestone Achieved: Standardized assessments and QA/QC measures executed	39	
Major Task 5: Study Closeout and Analysis		
Subtask 1: Study closeout		
DCC collects all outstanding data & queries from Sites	37-42	
DCC distributes final site payments	40-42	
DCC collects all outstanding pSOFA endpoint assignments from Adjudic. Committee	40-42	
Neurodevelopment Core reviews all Scoring of assessments	40-42	
Form Trial Writing Committees for results manuscripts	37-42	
Milestone Achieved: Complete high quality trial data from all sources	42	
Subtask 2: Analysis and Dissemination		
Statistical analysis for final DoD report, Investig & DSMB meetings	43-48	
Statistical analysis programs developed for final results manuscript using dummy randomization and pre-specified table/figure shells from SAP	40-48	
Hold Writing Committee meetings to plan secondary analyses and interpret/discuss findings	36-48	
Identify targets for dissemination of results (presentations, publications, web)	40-45	
Submit main trial results abstract to national meeting	46	
DCC/CCC to hold Investigator meeting to discuss/share final results	48	

Present main trial results at national meeting	48	
Submit main trial results manuscript to journal	48	
Submit secondary manuscripts to journals	48	
Milestone Achieved: Analyses performed and dissemination targets identified	48	

What was accomplished under these goals?

In this Reporting Period (Year 1), trial launch was achieved, due to strong teamwork and establishment of processes for onboarding study sites and creating trial infrastructure.

Study Sites: Business agreements are complete for 12 of 19 sites. ORP/HRPO approval is complete for 15 of 20 sites.

Communications: Weekly Operations Committee and monthly Investigator and Study Coordinator webinars are held. A TITRE Trial newsletter is also disseminated twice a month.

Protocol Execution and Monitoring: The OpenClinica database management system, randomization system, and event monitoring systems are in full use.

Protocol/Safety Monitoring: One organizational DSMB meeting was held in Year 01 and the second meeting is scheduled (01Sep2023). Qualifying SAEs reviewed by the independent Medical Monitor are sent to the DSMB Chair in real time as needed.

Trial Tools:

a) www.ecmotitretrial.org – includes real-time screening and enrollment counts

b) Translation of informed consent forms and study brochure into Spanish, Portuguese, and Arabic.

Enrollment: Enrollment is active at a subset of sites and as of 6/30/23, a total of 5 patients have been randomized.

Trial Completion: Not applicable. Follow-up is at 1 year post-randomization (first completed participant will be spring 2024).

What opportunities for training and professional development has the project provided?

The EuroELSO Conference in April 2023 was a Continuing Medical Education (CME) event – See Bibliography of TITRE-related presentations.

How were the results disseminated to communities of interest?

Not applicable (trial not complete).

What do you plan to do during the next reporting period to accomplish the goals?

1. Continue screening and recruitment to meet target N=228.
2. Collect biospecimens.
3. Activate remaining study sites (complete DUAs, contracts and IRB).
4. Develop data quality/data monitoring reports
5. Hold a DSMB meeting for first data/safety review.
6. Initiate Adjudication Committee case reviews and submission of scores.

4. **IMPACT:**

What was the impact on the development of the principal discipline(s) of the project?

TITRE is the first randomized trial in pediatric ECMO in 40 years. TITRE has made an impact on the field by demonstrating for the first time that a collaborative clinical research network specific to pediatric ECMO can be successfully formed to efficiently execute multicenter research to improve the management and outcomes of children who have received ECMO support.

What was the impact on other disciplines?

The TITRE Trial has gained high visibility, and has demonstrated to the adult ECMO research community that collaborative multicenter research involving a rare patient population across multiple subspecialties (CICU, MSICU, NICU) is feasible.

What was the impact on technology transfer?

Nothing to report.

What was the impact on society beyond science and technology?

Nothing to report.

5. CHANGES/PROBLEMS:

Changes in approach and reasons for change

We have changed the trial design to have participant families be unblinded, because the families have access to the medical records and blinding is not possible. As a conservative measure, we have created a required telephone script for interaction with the family during virtual follow-ups in order to minimize bias (rather than free-form interaction), where the parent provides an assessment of their child's health and functional status.

Actual or anticipated problems or delays and actions or plans to resolve them

Describe problems or delays encountered during the reporting period and actions or plans to resolve them.

There is a newly funded NHLBI randomized trial for a subset of ECMO patients (ECPR patients) that will be executed under EFIC (Exception from informed consent) at Boston Children's and Texas Children's, called the Hydrogen FAST Trial. This trial overlaps with the TITRE target population for about 25% of patients. TITRE leadership has met with the FAST Trial team and has arranged a plan for the Control patients in FAST (target N=21 of all ages) to still be approached for participation in TITRE, if under age 6 years. The overlapping recruitment period will be approximately late 2023 and 2024.

ECSTATIC is a new randomized trial of platelet transfusion thresholds in pediatric ECMO that has overlap with one TITRE site (Emory/Atlanta). Coenrollment is contraindicated. A process for sharing eligible patients between ECSTATIC and TITRE is under discussion.

Changes that had a significant impact on expenditures

None.

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

Significant changes in use or care of human subjects

- The trial protocol has had 10 amendments approved. Amendment #10 was approved by the single IRB at Boston Children's Hospital on 06/05/23.
- IRB approval for Hospital Sick Children, Toronto, Canada (not a relying site) is still in process.
- The continuing review for the main protocol was approved by the Central IRB (Boston Children's Hospital) on 04/14/23.
- The continuing review for the main protocol approved by the Central IRB (Boston Children's Hospital) was approved by the DoD HRPO on 06/21/23

Significant changes in use or care of vertebrate animals

Not applicable.

Significant changes in use of biohazards and/or select agents

Not applicable.

6. PRODUCTS: *List any products resulting from the project during the reporting period. If there is nothing to report under a particular item, state "Nothing to Report."*

Publications, conference papers, and presentations

Accepted for Presentation:

1. Sleeper, LA et al. Ready, Set, Go: Efficient Launch of the Multicenter TITRE Trial of Indication-based Transfusion of Red Blood Cells in Pediatric ECMO. 8th World Congress of Pediatric Cardiology and Cardiac Surgery, August 2023, Washington, DC.

EuroELSO Conference: Invited Presentations and Published Abstracts, April 2023, Lisbon, Portugal:

2. Thiagarajan, R. TITRE: Trial of Indication-based Transfusion of Red blood cells in ECMO, April 29, 2023.

3. Thiagarajan, R. Decision algorithms for Blood and Blood Products, April 26, 2023.

4. Sleeper, LA et al. Chasing the Dream (of Equipoise): Design and Execution Challenges of the Multicenter TITRE Trial of Indication-Based Red Blood Cell Transfusion in Pediatric ECMO, April 28, 2023. *Perfusion* 2023; Vol. 38(1S) 82–212, #516.

5. Alexander, A. et al. Change in pSOFA Score as a Novel Outcome for Pediatric ECMO Research, April 27, 2023. *Perfusion* 2023; Vol. 38(1S) 82–212, #5

Other Published Abstracts:

6. Sleeper, LA et al. Chasing the Dream (of Equipoise): Design and Execution Challenges of the Multicenter TITRE Trial of Indication-Based Red Blood Cell Transfusion in Pediatric ECMO. *J Heart Lung Transpl* 2023, 42:4, Supplement, S481.

Books or other non-periodical, one-time publications.

See next page

ELSO (Extracorporeal Life Support Organization) Newsletter June 2023:

JUNE 2023 | ELSO NEWSLETTER

Trial of Indication-based Transfusion of Red Blood Cells in ECMO

TITRE

www.ecmotitretrial.org

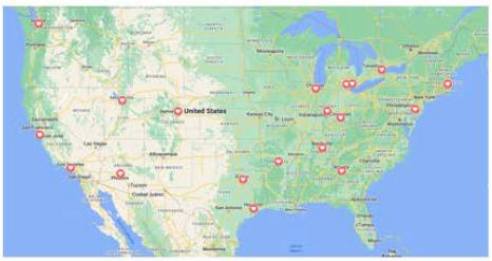
TITRE

Multicenter Randomized Trial comparing Threshold-based with Indication-based Red Blood Cell Transfusion on Organ Dysfunction and Neurodevelopment in Children on ECMO

SCAN ME

Funded by U.S. Department of Defense

Now enrolling



Current U.S. and Canada Trial Sites

For information about trial design or participation, please contact: peta.alexander@cardio.chboston.org; lynn.sleeper@cardio.chboston.org; ravi.thiagarajan@cardio.chboston.org

Boston Children's Hospital

TITRE: Trial of Indication-Based Transfusion of Red Blood Cells in ECMO

SCAN ME

TITRE

Compares Impact of **Center-Specific Threshold-Based** with **Indication-Based** RBC Transfusion on Organ Function and Long-Term Neurodevelopment in Pediatric ECMO

For information about trial design or participation, please contact: peta.alexander@cardio.chboston.org; lynn.sleeper@cardio.chboston.org; ravi.thiagarajan@cardio.chboston.org

Texas Children's Hospital · Baylor College of Medicine · children'shealth · Children's Medical Center · Seattle Children's · Arkansas Children's · Boston Children's Hospital · Cincinnati Children's · C.S. Mott Children's Hospital, University of Michigan Health · SickKids · Children's Hospital of Michigan · Phoenix Children's · Children's Hospital Los Angeles · Ann & Robert H. Lurie Children's Hospital of Chicago · Monroe Carell Jr. Children's Hospital at Vanderbilt · Stanford Children's Health · Intermountain Primary Children's Hospital · Children's Healthcare of Atlanta · Riley Children's Health, Indiana University Health · Children's Hospital of Philadelphia · Children's Hospital Colorado

U.S. DoD PRMRP Clinical Trial Award #W81XWH2210301

ecmotitretrial.org

Lynn Sleeper, PI of the study, with Ravi Thiagarajan and Peta Alexander Trial Co-Chairs

Other publications, conference papers and presentations.

Nothing to report.

Website(s) or other Internet site(s)

See: http://www.ecmotitretrial.org - 200 hits as of 6/30/23.

- **Technologies or techniques**

Nothing to report.

- **Inventions, patent applications, and/or licenses**

Nothing to report.

- **Other Products (presented in past Annual Reports)**

Not applicable.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

Name: Lynn Sleeper, ScD
Project Role: PD/PI, PI of DCC
Researcher Identifier (e.g. ORCID ID): 0000-0002-8055-768X
Nearest person month worked: 3
Contribution to Project: No change.

Name: Ravi Thiagarajan, MBBBS, MPH
Project Role: CCC PI/Study Co-Chair
Research Identifier (e.g. ORCID ID): 0000-0002-4154-1693
Nearest person month worked: 2.4
Contribution to Project: No change.

Name: Peta Alexander, MBBS
Project Role: Co-Investigator/CICU
Research Identifier (e.g. ORCID ID): 0000-0003-4837-7598
Nearest person month worked: 1.2
Contribution to Project: No change.

Name: Jane Newburger, MD, MPH
Project Role: Co-Investigator/Study Co-Chair
Research Identifier (e.g. ORCID ID): 0000-0002-7794-9017
Nearest person month worked: 1.2
Contribution to Project: No change.

Name: David Bellinger, PhD
Project Role: Co-Investigator/ Neurodevelopment
Research Identifier (e.g. ORCID ID): 0000-0003-3393-0119
Nearest person month worked: 1.2
Contribution to Project: No change.

Name: Daniel Kelly, MD
Project Role: Co-Investigator/Transf.
Research Identifier (e.g. ORCID ID): 0000-0002-4809-5139
Nearest person month worked: 1.2
Contribution to Project: No change.

Name: Anjali Sadhwani, PhD
Project Role: Collaborator/ Neurodevelopment
Research Identifier (e.g. ORCID ID): 0000-0003-0938-0591
Nearest person month worked: 1.2
Contribution to Project: No change.

Name: Lamia Sun
Project Role: DCC Project Director
Research Identifier (e.g. ORCID ID): N/A
Nearest person month worked: 12

Contribution to Project: No change.

Name: Thivya Thayananthan
Project Role: Data Manager
Research Identifier (e.g. ORCID ID): N/A
Nearest person month worked: 12
Contribution to Project: No change.

Name: Megha Shrivastava
Project Role: Research Assistant/IRB
Researcher Identifier (e.g. ORCID ID): n/a
Nearest person month worked: 12
Contribution to Project: No change

Name: Christine Tran
Project Role: Administrative Coordinator
Researcher Identifier (e.g. ORCID ID): n/a
Nearest person month worked: 6
Contribution to Project: Joined the project in December 2022

Name: Krislyn Boggs
Project Role: Project Manager
Research Identifier (e.g. ORCID ID): N/A
Nearest person month worked: 2
Contribution to Project: Joined the project in May 2023

Name: Minmin Lu, MS
Project Role: Statistical Programmer
Researcher Identifier (e.g. ORCID ID): n/a
Nearest person month worked: 0
Contribution to Project: No change – effort begins in Y2

Name: Jane Messere, RN
Project Role: Clinical Research Associate
Researcher Identifier (e.g. ORCID ID): n/a
Nearest person month worked: 1.2
Contribution to Project: No change – effort begins in Y2.

8.

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

We have made a small leadership change. Drs. Thiagarajan and Newburger were originally the Trial co-chairs. Our ECMO experts Drs. Thiagarajan and Alexander are now the Trial co-chairs and Dr. Newburger is serving as Co-Investigator for her trials and neurodevelopment expertise. Starting in Year 2, Dr. Alexander's effort will be 20% annually (2.4 calendar months) Dr. Newburger's effort will be 7.5% annually (0.9 calendar months).

What other organizations were involved as partners?

Nothing to Report.

9. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS: ***N/A***

QUAD CHARTS: ***N/A***

10. APPENDICES:

Previously published/listed in past Annual Reports:

Not applicable.