

**Request for Applications
Data Analysis Core (DAC)
of the
Cardiac Neurodevelopmental Outcome Collaborative (CNOC)**

I. Introduction: Overview and Background

The purpose of this request for applications is to invite applications from a CNOC institutional member to develop and implement a Data Analysis Core (DAC) for the Cardiac Neurodevelopmental Outcome Collaborative (CNOC, www.cardiacneuro.org). CNOC was established as a collaborative multicenter, multinational, and multidisciplinary group of healthcare professionals who are committed to working together and partnering with families to optimize neurodevelopmental outcomes for individuals with pediatric and congenital heart disease through clinical, quality, and research initiatives, intending to maximize quality of life across the lifespan. The overall goals of CNOC include characterization of the pattern and variation of developmental functioning of individuals with pediatric heart disease from infancy through adolescence.

CNOC is collaborating with ArborMetrix and the Pediatric Cardiac Critical Care Consortium (PC4) to set up a robust and easily accessible central database to house neurodevelopmental outcome data, in addition to preexisting medical data, with the University of Michigan serving as the Data Coordinating Center (DCC) for CNOC and Children's National Health System as the Neurodevelopmental Core (NDC). The CNOC Data Analysis Core will coordinate with the DCC and the NDC to create clean datasets and specifically conduct data and statistical analyses. The DAC will begin with a focused set of research aims, characterizing the development of infants, toddlers, and preschoolers who have undergone neonatal cardiac surgery using a limited list of demographic, medical history, surgical, and neurodevelopmental outcome variables. In addition the DAC will be responsible for conducting the data analyses for a quality improvement project in our school age population. As initial aims are achieved, additional research questions will be generated and additional sources of support will be sought.

II. Roles and Responsibilities

The Data Analysis Core (DAC) will fulfill the following roles and responsibilities:

- While data auditing will be handled by the DCC (non-neurodevelopmental data) and NDC (neurodevelopmental outcome data), the DAC will consult and work closely with the DCC and NDC on any issues surrounding data cleaning or data quality.
- Development and generation of data reports for CNOC committees, including the Database Committee and the Research Committee, and participating sites. Reports would include information about data quality and completeness, benchmarking of neurodevelopmental outcomes across sites, and other data summaries as needed.
- Development of statistical analyses, including descriptive and inferential statistics, and formal quality improvement statistical techniques (run-charts, statistical process control) for the current study and quality improvement aims (specified below) and preparation of future manuscripts involving CNOC data.
- Provision of statistical and methodological input for future grant applications.

The initial responsibility of the DAC is to characterize the pattern of developmental delays in infants, toddlers, and preschoolers with heart disease who undergo neonatal surgery, as well as additional demographic, medical history, and surgical variables for these patients. Specific neurodevelopmental outcomes, study aims, and hypotheses for the 0-5 age group (infants, toddlers, and preschoolers) have been outlined. In addition, a quality improvement (QI) project targeting the school age cohort will be conducted with a limited set of variables. The details of all the initial projects are outlined in the appendices (see attached).

Statistical analyses to answer the study aims and hypotheses will be provided by the DAC. After successful implementation of these efforts, additional research questions will be generated. It is expected that the DAC would be involved in future grant submissions that would provide additional funding for biostatistical support and analyses.

III. Award Information

Total funds available are \$30,000/year for a period of five years, beginning June 1, 2018. It is possible that the funding may increase in subsequent years depending on CNOC funding and external grants obtained. Indirect costs should not exceed 10%. Due date for applications is March 15, 2018.

IV. Eligibility Information

Eligibility is limited to CNOC institutional members.

V. Application and Submission Information

Prospective applicants are asked to submit an application by March 15, 2018. The procedural plan is the most important component of the DAC application, and should be limited to 8 pages. This plan would include an overall description of aims and plans for data quality assurance, data summarization, and data analyses, including plans to address the roles and responsibilities of the DAC as mentioned in Section II.

Appendix materials should include the following components:

Personnel: A brief management plan describing staffing and roles and responsibilities of proposed DAC staff members should be provided. List of prior experience with multicenter research studies where the Principal Investigator held significant responsibility for statistical analyses should be noted. NIH biosketches of key personnel should be included as additional information.

Budget: A detailed budget including salary support for the Principal Investigator and research team members for effort on this project should be included. The total budget may not exceed \$30,000 per year including indirect costs.

Institutional Support/Environment: A description of the environment and available institutional support for the DCC should be provided.

Complete applications should be submitted to Jennifer Butcher, Ph.D. (CNOB Secretary), at jennbutc@med.umich.edu by March 15, 2018.

VI. Application Review Process

All submitted applications will initially be reviewed by the Database Committee, with final decisions regarding the choice of the DAC to be made by the CNOB Steering Committee. Selection is expected to be completed by May 1, 2018.

Appendix A: Specific Aims for 0-5 cohort

Specific Aim 1: Describe what patient and center level variables are associated with returning for recommended ND follow-up in infancy and the variation in service provided.

Hypothesis: Socioeconomic status will have a bigger impact on both rate of ND follow-up and services received than individual clinical and center-level variables.

Primary Outcome: Percent of recommended individuals evaluated in cardiac ND follow-up clinics in infancy.

Inclusion: All individuals at a participating CNO center undergoing cardiac surgery before 30 days of age and eligible for 6-9 month follow-up between October 2018 and September 2019.

Outcome Measures: Data fields from the IWG Neurodevelopment Subsection Worksheet

Covariates: Diagnosis/intervention specific; complication specific; center specific; ND program specific

Approach: Participating centers performing infant evaluations will submit ND follow-up data from the IWG ND worksheet for all individuals undergoing evaluation at 6-9 months of age. In addition, clinical and demographic data for all individuals undergoing cardiac surgery in the first month of life that are eligible for infant ND follow-up, regardless of participation in follow-up clinic will be obtained from the PC4 registry. Centers that do not submit to either registry will be required to independently enter a very limited matching dataset. Center-level practice variation will be determined by aggregating clinical/surgical data (age at surgery, LOS, intubation time) and results from the site survey.

Specific Aim 2: Describe what patient and center level variables are associated with returning for recommended ND follow-up at 18-24 months and their association with ND outcome.

Hypothesis: Cardiac diagnosis, surgical risk category, and hospital LOS will have the biggest impact on ND outcomes independent of the factors associated with rate of ND follow-up.

Primary Outcome: Deficiencies identified from indices of Bayley-III (cognitive, language, motor) and the ABAS-3 (conceptual, practical, social).

Inclusion: All individuals at a participating CNO center undergoing cardiac surgery before 30 days of age and eligible for 18-24 month ND follow-up between October 2018 and September 2019.

Outcome Measures: Bayley-III; ABAS-3

Covariates: Diagnosis/intervention specific; complication specific; center specific; ND program specific

Approach: Participating centers performing toddler evaluations will submit ND results for all individuals undergoing recommended testing at 18-24 months of age. In addition, clinical and demographic data for all individuals undergoing cardiac surgery in the first month of life that are eligible for toddler ND testing, regardless of follow-up, will be obtained from the PC4 registry. Centers that do not submit to PC4 will be required to independently enter a very limited matching dataset. Center-level practice variation will be

determined by aggregating clinical/surgical data (age at surgery, LOS, intubation time), and results from the site survey.

Specific Aim 3: Define the school readiness profile of children who are evaluated at cardiac ND follow-up programs and its association with clinical and regional variables.

Hypothesis: A comprehensive profile from a core battery of tests will identify more children with CHD at risk for difficulty in school than a single school readiness screener.

Primary Outcome: Deficiencies identified in four domains (cognitive skills, functional/adaptive skills, executive function and social/emotional function) from a core battery compared to the deficiency estimated from a single screener (Bracken School Readiness Assessment)

Inclusion: All individuals undergoing ND evaluation at a participating CNOCC center between 4-5 years of age from October 2018 and September 2019.

Outcome Measures: WPPSI-IV Core, BRIEF-2, BASC-3, ABAS-3, CELF Preschool 2 (selected subtests), BSRA-3

Covariates: Cardiac diagnosis, surgical procedure, age at surgery, neonatal length of stay, chromosomal abnormality, major non-cardiac abnormality, race, ethnicity, maternal education, patient zip code, surgical center, ND evaluation center

Approach: Participating centers performing pre-school evaluations will submit all ND testing and survey results from the core battery. The minimal clinical variable dataset for children undergoing ND evaluation will be required.

Appendix B: Quality Improvement project for School Aged Cohort

We hypothesize that many high-risk, school-age children with pediatric heart disease are not receiving formal neurodevelopmental evaluation and/or services outside of infancy. For example, we suspect that some cardiologists and families may believe the child is doing “fine” in school when in fact opportunities exist to enhance their academic performance and ultimately quality of life by identifying neurodevelopmental challenges commonly seen in these children and systematically working to improve them. Therefore, the aim of the CNOC school-age quality improvement initiative is:

AIM: To increase the proportion of high-risk, school-age children with pediatric heart disease who undergo dedicated neurodevelopmental evaluation and/or services.

MEASURES/METRICS (To be determined by QI Committee: sample measures given below):

- **Outcome measure (sample):** Proportion of high-risk, school-age children with pediatric heart disease receiving formal neurodevelopmental evaluation and/or services
- **Process measure (sample):** Proportion of high-risk, school-age children with pediatric heart disease whose outpatient cardiology clinic note documents the child’s neurodevelopmental status
- **Balancing measure (sample):** Proportion of patients with elevated BMI receiving weight/nutrition counseling

Anticipate manual data extraction/chart review of a random sample (TBD) of school-age patients seen in outpatient cardiology to be entered monthly into a registry by each participating site

INTERVENTIONS/CHANGE STRATEGIES

- TBD by QI Committee
- Examples might include Lurie EPIC/other EHR “SmartForm” screening tool, EPIC/other EHR “SmartPhrase” or template for outpatient cardiology ND documentation status

Patient Demographic Information

1. MRN
2. Age at time of outpatient cardiology encounter
3. DOB
4. Date of outpatient cardiology clinic visit
5. Gender
6. Race
7. Ethnicity
8. Insurance status

Risk Stratification and Neurodevelopmental Capture Information

1. Cardiologist
2. General or specialty cardiologist. If sub- specialty, list below
3. Is the patient high-risk by AHA criteria?
4. If yes, which criteria?
 - a. Open heart surgery with cardiopulmonary bypass in the first year of life
 - b. Cyanotic without open heart surgery in the first year of life
 - c. CHD with comorbidities

5. If risk criterion 3 is met, which comorbidities are present?
 - a. Prematurity (<37 weeks)
 - b. Developmental delay recognized in infancy
 - c. Suspected genetic abnormality or syndrome associated with developmental delay
 - d. History of mechanical circulatory support (ECMO or VAD use)
 - e. Heart transplantation
 - f. Cardiopulmonary resuscitation (CPR) at any point
 - g. Prolonged hospitalization (postoperative length of stay > 2 weeks in hospital)
 - h. Perioperative seizures related to CHD surgery
 - i. Significant abnormalities on neuroimaging or microcephaly
 - j. Details on comorbidities (if applicable)
6. Fundamental diagnosis (based on STS definition)
7. Other Non-Cardiac Major Diagnosis (based on STS definition)
8. Genetic condition (based on STS definition)
 - a. If yes, list.
9. Neurological condition (e.g., stroke, intracranial hemorrhage, seizure disorder, etc.)
 - a. If yes, list.
10. Were formal neurodevelopmental services previously **recommended** *in infancy*?
 - a. If yes, details on services that were recommended (services through “multidisciplinary neurodevelopmental clinic” or free text)
11. Did the child previously **receive** formal outpatient neurodevelopmental services *in infancy*?
 - a. If yes, details on services that were recommended (services through “multidisciplinary neurodevelopmental clinic” or free text)
12. Was there **documentation** of the child’s neurodevelopment status in the most recent (routine) outpatient Cardiology clinic note?
 - a. Documentation of child being seen in a multidisciplinary neurodevelopmental clinic
 - b. Neuropsychology/psychology
 - c. Developmental-behavioral pediatrics
 - d. PT
 - e. OT
 - f. Speech therapy
 - g. Specialized school services such as an IEP or 504
 - h. Social work
 - i. Other
 - i. If other, details
13. Has the child been **referred** for formal neurodevelopmental services?
 - a. Child has been referred to a multidisciplinary neurodevelopmental clinic
Neuropsychology/psychology
 - b. Developmental-behavioral pediatrics
 - c. PT
 - d. OT
 - e. Speech therapy
 - f. Specialized school services such as an IEP or 504
 - g. Social Work
 - h. Other
 - i. If other, details

14. Has the child been seen by neurodevelopmental specialists or are they currently **receiving** formal neurodevelopmental services *since turning school-age*?
 - a. Child has been seen or is being followed in a multidisciplinary neurodevelopmental clinic
 - b. Neuropsychology/psychology
 - c. Developmental-behavioral pediatrics
 - d. PT
 - e. OT
 - f. Speech therapy
 - g. Specialized school services such as an IEP or 504
 - h. Social work
 - i. Other
 - i. If other, details
15. Were any new or modified **recommendations** (e.g., modification to school IEP or other developmental services) made following neurodevelopmental evaluation?
 - a. New or modification recommendation details
16. Were any new specific **referrals** recommended as a result of neurodevelopmental evaluation?
 - a. New referral details

General Information about School/Education

1. What type of schooling is the patient receiving?
 - a. Public school
 - b. Private school
 - c. Homebound
 - d. Homeschooled
 - e. Not enrolled
 - f. Unknown
2. Highest grade level completed (Number 1-12 / Unknown)
3. Repeated grade (Yes/No/Unknown)