PI: [redacted]	Title: [redacted]	
Received: 10/01/2015	FOA: PA15-200	Council: 05/2016
Competition ID: FORMS-C	FOA Title: Studies at Periviable Gestation (R01)	
[redacted]	Dual:	Accession Number: 3861613
IPF: [redacted]	Organization: [redacted]	
Former Number:	Department: Pediatrics	
IRG/SRG: ZRG1 NRCS-V (08)F	AIDS: N	Expedited: N
Subtotal Direct Costs (excludes consortium F&A) Year 1: 499,901 Year 2: 499,913 Year 3: 499,901 Year 4: 499,901 Year 5: 499,900	Animals: N Humans: Y Clinical Trial: Y Current HS Code: 44 HESC: N	New Investigator: N Early Stage Investigator: N

Senior/Key Personnel:	*Organization:*	*Role Category:*
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

OMB Number [redacted]
Expiration Date 06/30/2016

APPLICATION FOR FEDERAL ASSISTANCE
SF 424 (R&R)

3. DATE RECEIVED BY STATE	**State Application Identifier**

1. TYPE OF SUBMISSION*

○ Pre-application ○ Application ● Changed/Corrected Application

4.a. Federal Identifier

b. Agency Routing Number

2. DATE SUBMITTED | **Application Identifier**

c. Previous Grants.gov Tracking Number [redacted]

5. APPLICANT INFORMATION **Organizational DUNS*:** [redacted]

Legal Name*: [redacted]
Department: [redacted]
Division:
Street1*: [redacted]
Street2:
City*: [redacted]
County:
State*: [redacted]
Province:
Country*: [redacted]
ZIP / Postal Code*: [redacted]

Person to be contacted on matters involving this application

Prefix: First Name*: [redacted] Middle Name: Last Name*: [redacted] Suffix:

Position/Title: [redacted]
Street1*:
Street2:
City*:
County:
State*:
Province:
Country*:
ZIP / Postal Code*:

Phone Number*: [redacted] Fax Number: [redacted] [redacted]

6. EMPLOYER IDENTIFICATION NUMBER *(EIN) or (TIN)** [redacted]

7. TYPE OF APPLICANT* H: Public/State Controlled Institution of Higher Education

Other (Specify):
Small Business Organization Type ○ Women Owned ○ Socially and Economically Disadvantaged

8. TYPE OF APPLICATION*

● New ○ Resubmission
○ Renewal ○ Continuation ○ Revision

If Revision, mark appropriate box(es).

○ A. Increase Award ○ B. Decrease Award ○ C. Increase Duration
○ D. Decrease Duration ○ E. Other *(specify)* :

Is this application being submitted to other agencies?* ○Yes ●No What other Agencies?

9. NAME OF FEDERAL AGENCY* [redacted]

10. CATALOG OF FEDERAL DOMESTIC ASSISTANCE NUMBER
TITLE:

11. DESCRIPTIVE TITLE OF APPLICANT'S PROJECT*
Periviable Perinatal Research Network (PPRN)

12. PROPOSED PROJECT
Start Date* 07/01/2016
Ending Date* 06/30/2021

13. CONGRESSIONAL DISTRICTS OF APPLICANT [redacted]

Tracking Number: [redacted]

Funding Opportunity Number: [redacted] Received Date: [redacted]

SF 424 (R&R) APPLICATION FOR FEDERAL ASSISTANCE

14. PROJECT DIRECTOR/PRINCIPAL INVESTIGATOR CONTACT INFORMATION

Prefix: First Name*: [redacted] Middle Name: Last Name*: [redacted] Suffix:

Position/Title: [redacted]
Organization Name*: [redacted]
Department: [redacted]
Division: [redacted]
Street1*: [redacted]
Street2: [redacted]
City*: [redacted]
County:
State*: [redacted]
Province:
Country*: [redacted]
ZIP / Postal Code*: [redacted]
Phone Number*: [redacted] Fax Number: [redacted]

15. ESTIMATED PROJECT FUNDING

a. Total Federal Funds Requested*	$4,006,670.00
b. Total Non-Federal Funds*	$0.00
c. Total Federal & Non-Federal Funds*	$4,006,670.00
d. Estimated Program Income*	$0.00

16.IS APPLICATION SUBJECT TO REVIEW BY STATE EXECUTIVE ORDER 12372 PROCESS?*

a. YES ○ THIS PREAPPLICATION/APPLICATION WAS MADE AVAILABLE TO THE STATE EXECUTIVE ORDER 12372 PROCESS FOR REVIEW ON:

DATE:

b. NO ● PROGRAM IS NOT COVERED BY E.O. 12372; OR

○ PROGRAM HAS NOT BEEN SELECTED BY STATE FOR REVIEW

17. By signing this application, I certify (1) to the statements contained in the list of certifications* and (2) that the statements herein are true, complete and accurate to the best of my knowledge. I also provide the required assurances * and agree to comply with any resulting terms if I accept an award. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties. (U.S. Code, Title 18, Section 1001)

● I agree*

** The list of certifications and assurances, or an Internet site where you may obtain this list, is contained in the announcement or agency specific instructions.*

18. SFLLL or OTHER EXPLANATORY DOCUMENTATION File Name:

19. AUTHORIZED REPRESENTATIVE

Prefix: First Name*: [redacted] Middle Name: Last Name*: [redacted] Suffix:

Position/Title*: [redacted]
Organization Name*: [redacted]
Department: [redacted]
Division:
Street1*: [redacted]
Street2:
City*: [redacted]
County:
State*: [redacted]
Province:
Country*: [redacted]
ZIP / Postal Code*: [redacted]
Phone Number*: [redacted] Fax Number: [redacted]

Signature of Authorized Representative*

[redacted]

Date Signed*

10/01/2015

20. PRE-APPLICATION File Name:

21. COVER LETTER ATTACHMENT [redacted]

424 R&R and PHS-398 Specific Table Of Contents

Project/Performance Site Location(s)

Project/Performance Site Primary Location

❍ I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name: [redacted]
Duns Number: [redacted]
Street1*: [redacted]
Street2: [redacted]
City*: [redacted]
County:
State*: [redacted]
Province:
Country*: [redacted]
Zip / Postal Code*: [redacted]
Project/Performance Site Congressional District*: [redacted]

Project/Performance Site Location 1

❍ I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name: [redacted]
DUNS Number: [redacted]
Street1*: [redacted]
Street2:
City*: [redacted]
County:
State*: [redacted]
Province:
Country*: [redacted]
Zip / Postal Code*: [redacted]
Project/Performance Site Congressional District*: [redacted]

Project/Performance Site Location 2

❍ I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name: [redacted]
DUNS Number: [redacted]
Street1*: [redacted]
Street2:
City*: [redacted]
County:
State*: [redacted]
Province:
Country*: [redacted]
Zip / Postal Code*: [redacted]
Project/Performance Site Congressional District*: [redacted]

Project/Performance Site Location 3

❍ I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name: [redacted]
DUNS Number: [redacted]
Street1*: [redacted]
Street2:
City*: [redacted]
County:
State*: [redacted]
Province:
Country*: [redacted]
Zip / Postal Code*: [redacted]
Project/Performance Site Congressional District*: [redacted]

Project/Performance Site Location 4

❍ I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name: [redacted]
DUNS Number: [redacted]
Street1*: [redacted]
Street2:
City*: [redacted]
County:
State*: [redacted]
Province:
Country*: [redacted]
Zip / Postal Code*: [redacted]
Project/Performance Site Congressional District*: [redacted]

File Name

Additional Location(s)

[redacted]

RESEARCH & RELATED Other Project Information

1. Are Human Subjects Involved?* ● **Yes** ○ **No**

1.a. If YES to Human Subjects

Is the Project Exempt from Federal regulations? ○ Yes ● No

If YES, check appropriate exemption number: _ 1 _ 2 _ 3 _ 4 _ 5 _ 6

If NO, is the IRB review Pending? ● **Yes** ○ **No**

IRB Approval Date:

Human Subject Assurance Number 00005960

2. Are Vertebrate Animals Used?* ○ **Yes** ● **No**

2.a. If YES to Vertebrate Animals

Is the IACUC review Pending? ○ Yes ○ No

IACUC Approval Date:

Animal Welfare Assurance Number

3. Is proprietary/privileged information included in the application?* ○ **Yes** ● **No**

4.a. Does this project have an actual or potential impact - positive or negative - on the environment?* ○ **Yes** ● **No**

4.b. If yes, please explain:

4.c. If this project has an actual or potential impact on the environment, has an exemption been authorized or an environmental assessment (EA) or environmental impact statement (EIS) been performed? ○ Yes ○ No

4.d. If yes, please explain:

5. Is the research performance site designated, or eligible to be designated, as a historic place?* ○ **Yes** ● **No**

5.a. If yes, please explain:

6. Does this project involve activities outside the United States or partnership with international collaborators?* ○ **Yes** ● **No**

6.a. If yes, identify countries:

6.b. Optional Explanation:

	Filename
7. Project Summary/Abstract*	1251-ProjectSummary.pdf
8. Project Narrative*	1252-ProjectNarrative.pdf
9. Bibliography & References Cited	1253-Bibliography_PPRN_Sept25_2015.pdf
10.Facilities & Other Resources	1254-Facilities[redacted]2015.pdf
11.Equipment	

Project Summary

This "Periviable Perinatal Research Network (PPRN)" application represents the development of a collaborative effort among four high volume regional perinatal centers [redacted]. A unique research team brings together well established investigators with complementary expertise in neonatal intensive care, maternal fetal medicine, health behavior, and applied developmental psychology. This proposal will develop a Research Network that is distinct from either the NICHD Maternal-Fetal Medicine Units Network (MFMU) or the Neonatal Research Network (NRN) as it integrates the expertise of both maternal-fetal medicine investigators and neonatologists and extends the period of gestation being evaluated to 20 weeks and earlier.

Very premature infants at the threshold of viability contribute disproportionately to infant mortality and morbidity. The development of a periviable pregnancy database is essential to provide the necessary information to develop hypotheses and design studies in this population, in addition to serving as a resource to understand the characteristics of periviable pregnancy and its outcomes. In order to optimize shared decision-making in the periviable period, the outcomes important to parents and underlying motivations need to be determined, the utility of quantitative estimates of outcome determined, and Decision Aids developed.

The Specific Aims of the PPRN are:

Specific Aim (1) To develop a Periviable Pregnancy Database (PeriPD) to determine the incidence, characteristics, and outcomes of periviable pregnancies

Specific Aim (2) Determine whether the use of the NICHD NRN Outcome Estimator, Outcome Trajectory Estimator, and BPD Estimator for parental counseling leads to increased parental satisfaction, increased clinician satisfaction, changes in therapies, and improved clinical outcomes of periviable infants

Specific Aim (3) To define the neonatal outcomes in which parents are most interested, develop a better means of framing and communicating clinical evidence, and develop Decision Aids for enabling parents of periviable infants to make better informed decisions

The successful completion of the studies in this project may lead to a better understanding of the epidemiology of periviable pregnancy, help decision-making by parents and clinicians, lead to the establishment of new standards of care, and improve the management of extremely premature infants worldwide.

Project Narrative:

Periviable births at the threshold of viability between 20 weeks and 25 weeks 6 days of gestation are at high risk for early death and handicaps. In this study, maternal-fetal medicine specialists and neonatologists from four medical centers will develop a database of periviable pregnancy, determine outcomes important to parents of periviable pregnancies and their underlying motivations, find out if quantitative estimates of outcome are useful, and develop decision aids.

Facilities and Other Resources

[redacted]

POPULATION AVAILABLE FOR CLINICAL STUDIES

The [redacted] is a Level IV neonatal intensive care unit that admits inborn and outborn infants. On average, 1394 neonates per year were admitted to the NICU at [redacted] during the designated two-year (2013-2014) period. Outborn infants accounted for 14% of the NICU admissions. The [redacted] has a high rate of enrollment in RCTs and studies. The patient population is similar to that of most large academic health centers and includes a broad representation of birthweights, gestational ages, racial/ethnic groups, admitting diagnoses, obstetrical parameters, and socioeconomic/payment classes. The number of admissions to the NICU at [redacted] has been over 1,000 per year since 20 years ago. In addition, there are over 300 surgical admissions per year to the NICU at [redacted] at the [redacted]. [redacted] program is the only Level IV NICU and perinatal service in the [redacted]. Strategies to maintain access to a large number of obstetrical and neonatal patient admissions include a state-wide referral network, a large community hospital NICUs network managed by [redacted], and dedicated telephone numbers and operators to facilitate referrals.

Patient Population

Patient Population Available for Clinical Trials for 2013 and 2014

	2013	**2014**
Number of births	3958	4022
Number of NICU admissions	1383	1406
NICU inborn admissions < 34 weeks	500	522
NICU inborn admissions < 29 weeks	201	195
NICU inborn admissions < 1500 grams birth weight	336	295
NICU inborn admissions < 1000 grams birth weight	194	160
NICU outborn admissions < 34 weeks	61	58
NICU outborn admissions < 29 weeks	40	29
NICU outborn admissions < 1500 grams birth weight	53	40
NICU outborn admissions < 1000 grams birth weight	34	20
NICU transport admissions	179	194
Number of patients receiving CPAP only	155	125
Number of patients receiving ventilator care	296	280
Number of patients ≤ 34 weeks receiving ventilator care	243	173
Number of ECMO cases	10	20
Number of surgical cases overall and specific subcategories including:	313	353
Number of patients with congenital diaphragmatic hernia (CDH)	6	13
Number of infants with congenital gastrointestinal malformations	47	42
Number of patients with NEC with surgical intervention	21	16
Number of cardiac surgery excluding patent ductus arteriosus	147	157
Number of patients with any retinopathy of prematurity (ROP)	84	71
Number of patients with threshold ROP	14	14
Number of patients with BPD	95	88
Number of patients with NEC using Bell's classification of ≥ stage 2	36	36
Number of patients ≥ 36 weeks with hypoxic ischemic encephalopathy (HIE)	18	8
Number of patients ≥ 36 weeks with HIE treated at ≤ 6 hours of age	15	8
Number of patients 33-35 weeks with HIE	1	3

It is anticipated that the number of NICU admissions and other numbers for the above subgroups will remain stable during the upcoming five years (2016-2021).

MATERNAL FETAL MEDICINE UNIT

The Division of Maternal-Fetal Medicine (MFM) in the Department of Obstetrics and Gynecology at [redacted] has a large service for delivery of high-risk pregnancies and is nationally recognized as a leader in perinatal research, patient care, and education. There is a strong history of and ongoing research collaborations toward excellent clinical care, database accessibility, and research productivity. The Division is one of the top performing sites of the *Eunice Kennedy Shriver* NICHD MFM Units Network clinical centers and a leader during the last five 5-year cycles. [redacted] staff the high-risk perinatal service. The Perinatal Center at [redacted] provides high-risk and comprehensive prenatal care through a [redacted] antepartum public health clinics and the Health Department clinics in surrounding counties. The Division of MFM maintains the [redacted] system, which provides up-to-date computer-based prenatal, labor and delivery, and postnatal data online wherever obstetrical patients are seen in the system and provides a means of tracking, analyzing, and reporting the data collected. The electronic medical record for patients on both services is integrated and mother-infant data are linked, facilitating access for maternal and infant information. Collaborative research, one of the foremost goals for the two divisions, has led to extensive cooperation and close interaction in numerous randomized clinical trials and other clinical studies during the past years, including 8 major NIH-funded grants [redacted] Close communication is maintained by daily informal patient care-oriented activities and a formal monthly meeting. Meetings of clinical investigators from both divisions are held as needed to assure close interaction and prevent conflict in research endeavors, particularly as both divisions are current members of their respective Eunice Kennedy Shriver NICHD research networks. The scholarly MFM faculty and large high-risk delivery service provide a unique environment and opportunity for a clinical center of the PPRN.

Maternal Population from 2013 and 2014 at [redacted]

	2013	**2014**
Number of deliveries	3958	4022
Number of C-sections	1304	1213
Number of multiple pregnancies delivered	134	155
Number of patients with diabetes (including gestational and prior)	271	285
Number of women with PIH and chronic hypertension	810	877
Number of deliveries that are low birth weight (<2500 grams)	995	1027
Number of very low birth weight (<1500 grams)	470	410
Number of extremely low birth weight (<1000 grams)	187	137
Number of antenatal consults performed by neonatology	84	130

Maternal Fetal Medicine Investigator and other MFM Subspecialists

Primary Investigator: [redacted] is Professor of OBGYN (tenured), the [redacted] Network site PI since [redacted], and the designated MFM attending on this application. [redacted] is both a practicing MFM subspecialist and perinatal epidemiologist (PhD). [redacted] has in-depth skills in the conduct of clinical research, particularly multicenter randomized trials, having had formal training in advanced clinical trial methods. [redacted] has been extremely active within the MFMU Network since joining [redacted] in 2005. [redacted] has [redacted] MFMU Ne [redacted] of Medicine which helped shape national and international recommendations [redacted] is the PI/PD of 2 [redacted] of [redacted] time is protected for research initiatives, with MFMU Network participation as top priority. [redacted] peer-reviews major obstetric and general journals and is a consultant editor (Journal Club) for Obstetrics and Gynecology, the official journal of the American College

of Obstetricians and Gynecologists. [redacted] also currently serves on NIH/NICHD scientific review committees and as a consultant for the World Health Organization.

[redacted] is Professor of Obstetrics & Gynecology, board-certified in MFM, Chairman of the Department of Obstetrics and Gynecology at [redacted], [redacted] of the OBGYN Research and Diagnosis Laboratory. [redacted] served as consultant and the only obstetrician co-author [redacted] e [redacted].

[redacted]

SUBSPECIALTY INFORMATION

The [redacted] upport from pediatric and surgical subspecialists at each site. The clinical center is participating in these trials with [redacted] several [redacted], and a pediatric [redacted] actively involved with the research team. The pediatric surgeons and cardiologists are available 24 hours a day. [redacted]

CLINICAL CAPABILITIES

Subspecialists

The Department of Pediatrics at [redacted] has a full complement of pediatric and pediatric surgical subspecialists who fully support the ongoing and future research as documented by high enrollment rates and performance in all trials which require subspecialist involvement.

Neonatal Clinical Capabilities

The NICU has a [redacted] that opened in February 2010. Support for research is strong, including an institutional research pharmacy with three full-time research pharmacists with experience in randomization, blinding, etc. The clinical nursing and respiratory therapy staff fully support research as this is a core mission of the hospital. The Division of Neonatology has five full-time clinical research coordinators who recruit patients 24 hours a day, 7 days a week [redacted] studies.

Full clinical capabilities are available for neonates at the [redacted], including extracorporeal membrane oxygenation; high-frequency jet ventilation; high-frequency oscillatory ventilation; inhaled nitric oxide; transplant of heart, liver, kidney, and bone marrow; pediatric cardiac surgery; neonatal endoscopic surgery; and most other innovative medical and surgical therapies. The Department of Pediatrics has over [redacted] e MD faculty members including a full range of pediatric and pediatric surgical subspecialists who are currently collaborating on ongoing [redacted] research [redacted] a perinatal pathologist and Professor of Pathology and Obstetrics and Gynecology, is board certified in Anato[redacted] subspecialty boarded in [redacted] has received advanced training in embryo-fetal and placental pathology. [redacted] conducts all autopsies and oversees all other pathology services related to the [redacted].

The staff of the NICU consists of the following personnel: a nurse manager, one clinical nurse specialist, one discharge planning nurse, [redacted] lactation consultants, [redacted], certified audiologists, 24 hour pharmacists, and 12 clerical support members. A pharmacist, a nutritionist, a biomedical engineer, a chaplain, a physical and occupational therapist, and two medical social workers are assigned to NICU. There is a research pharmacy and staff capable of supporting clinical research as demonstrated by full

participation in ongoing [redacted]). Medical care is provided by a team that consists daily of pediatric resident team (4 PL III or PL II residents, 5 PL I interns), a pediatric hospitalist, and four certified neonatal nurse practitioners, a neonatology fellow, a physician, and three neonatology attendings. In addition, two board-certified pediatric ophthalmologists perform eye examinations for ROP and other evaluations.
Facilities located a block away from the NICU are utilized for comprehensive multi-disciplinary follow-up of NICU graduates with capacity to follow children past school age.

Obstetrical Clinical Capabilities
[redacted] has a full range of perinatal subspecialists, clinic capabilities, and support staff housed in the state-of-the art 400,000 square feet [redacted]r at [redacted] that includes the obstetrics, gynecology, NICU, and well-baby nursery. The labor and delivery service including the operating room as immediately contiguous to the NICU. The MFM group has several full-time dedicated research coordinators [redacted] here is capability for full antenatal (including ultrasound, amniocentesis, and genetic evaluation) and intra-partum testing. There are facilities for prenatal and postpartum care and an emergency department/medical evaluation unit exclusively dedicated to pregnant women.

[redacted] maintain agreements for performance of perinatal research given the unique integration of the services including enrollment of patients [redacted]y and co-enrollment in trials. The effective integration of the services has resulted in both MFMU and NRN [redacted] centers being among the most productive centers of both networks. There is ample and effective collaboration between all physicians and staff in clinical care and research as documented during the [redacted] of the NRN and MFMU grants at [redacted].

NEWBORN FOLLOW-UP PROGRAM
An established neonatal follow-up program with tracking and retaining of over 95% of patients at 22-26 months has been well established at [redacted] for over 35 years. There have been [redacted] those enrolled in trials requiring follow-up, and those with abnormal neurodevelopmental screens prior to hospital discharge are followed. Other selected high-risk neonates are followed depending on research and clinical needs. The follow-up protocol involves pre-discharge neurodevelopmental evaluation and a minimum of four follow-up visits (corrected ages of 4-6 months, 10-12 months, and 22-26 months; at 3 years of chronological age) during the first three years and longer for specific protocols. The follow-up clinics are held twice a week in designated space. Clinical capabilities within the Follow-Up Program include neurological examination, developmental assessment, nutritional assessment, hearing and vision assessment, psychological evaluations such as the Bayley Scales of Infant Development and Differential Ability Scale, and other services frequently needed by the former high risk neonates. Longer term follow-up is done, and children of 6-7.5 years of age are currently being followed for a research protocol. The follow-up program is funded by the Department of Pediatrics and the Division of Neonatology in addition to patient revenues.

	Year 2013	**Year 2014**
Cardiac	73	100
ECMO	14	19
HIE	27	28
<1000 gram	481	522
1000-1500 gram	131	156
>1500 gram	17	16
Total	743	841

Professional Staff
The follow-up program is directed by [redacted], Professor of Pediatrics, who is board certified in [redacted] Pediatrics and is the [redacted] Follow-Up PI. The

multidisciplinary evaluation team includes two additional developmental pediatricians, two PhD clinical psychologists (including [redacted], consultant for the development of the Bayley), audiologist, optometrist, nutritionist, physical therapist, occupational therapist, pediatric nurse practitioner, and a clinic coordinator. In addition, pediatric neurologists, pediatric surgeons, and other consultants are available for specific protocols. Most of the professional staff has been associated with the Follow-Up Program for more than twenty years. These professionals hold faculty appointments within various schools at [redacted].

Neonatal Intensive Care Follow-Up Database

The Neonatal Intensive Care Follow-Up Program maintains a complete database that includes pregnancy, perinatal, neonatal, and follow-up information. The Follow-Up Program and database have been used in single center innovative outcomes research [redacted].

Policies and Procedures for Conducting Clinical Research in the Follow-Up Program

Clinical research is an essential component of the Follow-Up Program. Any project that requires follow-up is discussed with the Director of the Follow-Up Program. The follow-up protocol is modified to meet the needs of specific studies.

Mechanism in Place to Insure Compliance and Assistance with Follow-Up

A follow-up rate higher than the highly desirable 90% (actual at [redacted] is 95%) at 22-26 months corrected age has been maintained during the current five-year NRN cycle. This high follow-up rate has been accomplished through dedicated research personnel for tracking and intensive personal contact with families. Prior to discharge, a conference is held between the follow-up staff and family to provide in-depth information on the importance of follow-up of these high risk infants and the availability of early intervention programs. Contact information is updated with several names and telephone numbers of extended family and friends. The first appointment to the clinic is also given. Telephone contact is maintained once or twice between scheduled visits to strengthen the relationship between the follow-up staff and the family. Frequent contacts alert the follow-up staff to any family relocation and prompt them to start tracking through alternative contacts immediately. The parents are contacted immediately after a missed appointment. Other tracking mechanisms include use of greeting cards, contact with the child's primary care providers, certified letters, and internet search. Appointment reminder letters are sent one month ahead of scheduled appointments and confirmation by telephone is made 1-2 weeks before the appointment date. In response to missed appointments, the follow-up coordinators attempt to contact the family on the day of the scheduled visit and continue until the appointment is rescheduled. Evaluations through home visits are arranged for those families unable or unwilling to come to the clinic. Fourteen follow-up visits, which include the Bayley and neurological exam, have been conducted at home during 2013-2014.

PERINATAL DATA SYSTEM

The Perinatal Data System consists of several large data resources that are readily available to the Division of Neonatology. The data resources include the integrated MFM and neonatology Cerner electronic medical record, the Neonatology database, the [redacted] database, and the Neonatal Intensive Care Follow-Up database. Biostatistical consultation and data management resources are provided by the Department of Biostatistics [redacted]

Neonatology Database

The Division of Neonatology's computerized database was established in 1984. The purpose of this database is to collect, tabulate, and monitor bio-demographic, survival, and morbidity data in order to permit rapid identification of trends in certain neonatal problems and morbidities. The data information coordinator uses standardized protocols for extracting data from the medical record onto the data sheets upon a patient's discharge. The data processing specialist is responsible for data entry, quality control, data analysis, and generation of reports. Precision and accuracy are insured by chart review and procedures internal to the computer program, as well as by downloading and external analysis by other computer programs. Quarterly audits of entered forms are compared with hard copy logs to ensure that each infant is represented in the database. Over 160 variables are collected on each patient. The database fields and

variables are reviewed and can be updated as necessary to ensure that data are relevant and up-to-date while maintaining compatibility with previous formats.

The database is routinely used for research, clinical care, and administrative purposes. The neonatal database has been used in conjunction with the [redacted] system and Hospital Information System database for recent studies that reported the association of [redacted], the effect of month of birth on neonatal outcomes ([redacted]) and the high incidence of late referrals of infants with selected serious congenital heart disease ([redacted]). In-office reports can be generated upon request. The Division will be transitioning this database to the [redacted] in 2015.

Transmission of Data
A dedicated database administrative support staff is available to transmit data once a week. Edits and queries can be resolved on a weekly basis

SPECIAL STRENGTHS
High Level of Enrollment in Trials and Studies
A major strength of the [redacted] site is the research organization which leads to [redacted] High enrollment is due to enrollment 24-hours and day and 7-days a week, daily in-house research coordinators, priority given to the NRN studies, and a large high risk population.

Weekly Division-wide and Research Coordinators Meeting
One hour weekly meetings allow discussion of on-going and planned trials, updates on enrollment, problems with enrollment or conduct of trials, adverse events, etc.

Expertise in the Conduct of Innovative Trials
The [redacted] team has expertise in the design and conduct of innovative randomized clinical trial designs for therapies to treat respiratory disorders and prevent their morbidities. [redacted] data analysis techniques. He has published extensively on neural network, [redacted] analyses, and other innovative approaches in the NRN.

Translational Program in Normal and Disordered Development
[redacted] is the Director of the [redacted] and the [redacted]. The [redacted] program is an interdisciplinary program for evaluation of structure, function, and injury in developing (fetal and neonatal) organ systems with existing core facilities [redacted] robotic systems for high-throughput RNA, DNA, and protein isolation and analysis; flexiVent; flow cytometry; image analysis software), dedicated personnel, and expertise. Ongoing projects in [redacted] where [redacted] and sophisticated bioinformatics analyses for personalized genomics can be performed. [redacted] With

[redacted]

[redacted] the Microbiome/Bioinformatics core facility at [redacted] directed by [redacted], which provides state-of-the-art microbiome analysis. [redacted] that are associated with subsequent development of BPD ([redacted]

Advanced radiologic and pediatric cardiology imaging facilities are also available at [redacted], including a Philips Brilliance iCT 256 slice CT scanner and Philips Ingenia 1.5T and 3T MRI scanners. For 3D reconstruction, 3D reconstruction software packages are available from both TerraRecon and Philips Intellispace.

Collaborations with research pharmacology are established. [redacted], Professor of Clinical Pharmacology has expertise in pharmacokinetic and pharmacodynamics studies in neonates and infants.

A major strength of the clinical center at [redacted] is the strong emphasis on multidisciplinary research that fosters collaboration between various departments, schools, and research units within [redacted] which have led to [redacted]). [redacted] has a [redacted]. [redacted] has established collaboration with the Obstetrics/MFM Division at [redacted]. Both groups are leaders in their respective Eunice Kennedy Shriver NICHD Networks as detailed earlier. Finally, the [redacted] clinical center has had exceptional performance including being the number one enroller in clinical trials and studies and among the top in first author publications.

[redacted]

Population Available for Clinical Trials

	2013	2014
Number of livebirths	414	734
NICU admissions	169	331
Inborn NICU admissions	383	1004
NICU admissions < 34 wks (inborn)	324	317
NICU admissions < 29 wks (inborn)	29	124
NICU admissions < 1500g BW (inborn)	84	176
NICU admissions < 1000g BW (inborn)	95	95
NICU admissions < 34 wks (outborn)	7	7
NICU admissions < 29 wks (outborn)	8	7
NICU admissions < 1500g BW (outborn)	60	59
NICU admissions < 1000g BW (outborn)	0	3
NICU transport admissions	286	327
Average daily census for the NICU	96	00
Patients receiving continuous positive airway pressure **(CPAP)** only	76	182
Patients receiving ventilation	69	499
Patients ≥ 34 wks receiving ventilation	244	294
Neonatal ECMO cases	5	13

Surgical cases (overall, including infants in subcategories below, not including ROP)	255	275
Congenital diaphragmatic hernia	2	13
Congenital gastrointestinal malformation	68	69
Surgical NEC cases (includes spontaneous intestinal perforation and surgery for possible NEC)	33	24
Cardiac surgical cases [excluding patent ductus arteriosus (PDA)]	58	59
Number of patients with any ROP	5	47
Number of patients with treated (threshold) ROP	4	13
Number of patients with bronchopulmonary dysplasia **(BPD)** (O_2 at 36 wks if < 32 wks GA; O_2 at 28 d if ≥ 32 wks GA)	96	95
Number of patients with NEC ≥ stage 2	31	18
Number of patients ≥ 36 weeks with hypoxic-ischemic encephalopathy **(HIE)**	30	21
Number of patients ≥ 36 wks with HIE at ≤ 6 hrs and hypothermia treatment	22	16
Number of patients 33-35 wks with HIE	2	4

Clinical Capabilities

[redacted] **NICU (Level IV)**

The [redacted] NICU is a state-of-the-art [redacted]-bed unit that opened in [redacted] and added a private room expansion in [redacted]. The [redacted] sq ft unit on the [redacted] floor is mixed Level 2-4 acuity arranged in seven 8-12 patient pods that surround physician work areas, call rooms, and ancillary staff offices. In addition to private rooms with sleeping facilities for parents of critically ill infants, there is a family area for parents that includes washers, dryers, and kitchen facilities. The [redacted] sq ft unit on the [redacted] acuity arranged in five pods of 6-8 single-patient rooms each. The NICU has two large conference rooms and several smaller conference areas that can be used for private discussions with parents. There is a research area where locked files, equipment, and other research supplies are kept. There is also a table-top centrifuge and a –20°C freezer.

[redacted] is a women's and children's hospital with its own administration [redacted] are immediately above the NICU floors). The labor, delivery, and high-risk MFM services [redacted] and there are medical and surgical ICUs for critically ill peri-partum mothers within the hospital. [redacted] the pediatric subspecialists.

Physician coverage in the [redacted] NICU is organized into [redacted]. Daytime coverage includes [redacted] (PL2s-PL4s), and [redacted] NNPs. Night coverage includes an in-house neonatologist, 2 fellows or NNPs, and a resident (PL2-4).

The [redacted] NICU staff includes [redacted] FTEs, [redacted] FTEs for respiratory therapy, [redacted] neonatal dieticians, [redacted] PharmDs, [redacted] lactation consultants, and [redacted] social workers. These personnel provide strong bedside support for NRN studies and have been valuable assets in study planning and implementation. Our senior dietician was instrumental in setting up the procedures that our [redacted] One of our PharmDs was extremely helpful in developing a plan for the drug and placebo preparations that were included in the [redacted] Our respiratory therapy supervisors were heavily involved in the implementation and masking for the Premie Nitric Oxide NRN trial.

Follow-up Clinic

The clinic is located across the street from [redacted] and the Medical School. There are 6 exam rooms in the same area as the subspecialty pediatric clinics. See additional information on Follow-up Program below.

Clinical Research Office

The neonatal research team is housed within the Neonatal Division at the Medical School. Their 548 sq ft dedicated neonatal clinical research space was renovated in 2010 to optimize efficient use of the space as a clinical research office. The office is immediately adjacent to the medical school entrance to the hospital and provides a secure space for record storage, data transmission (the NRN computer is located here), and fax communication. We also have dedicated space in the NICU for storage of non-secured research documents (blank consent forms, blank exam forms) and study information that is readily accessible to the clinical staff in the NICU.

Maternal Fetal Medicine Unit

The Neonatology and Maternal Fetal Medicine **(MFM)** Divisions at [redacted] have a long history of successful collaboration in clinical care, education, and research. We have a weekly conference to discuss complex upcoming deliveries and a monthly conference where MFM and Neonatology fellows jointly present interesting cases for discussion. Our Fetal Center at [redacted] includes faculty in Maternal-Fetal Medicine, Pediatric Surgery, Neonatology, Genetics, Pediatric Neurosurgery, Pediatric Cardiology, Pediatric Cardiovascular Surgery and other subspecialties. The center is a regional referral center for prenatal intervention of twin-twin transfusion, fetal myelomeningocele, and other fetal anomalies. This expansion has been partially responsible for the increase in high-risk deliveries at [redacted].

Our institution has been participating in both the Neonatal and Maternal Fetal Medicine Unit (MFMU) Research Networks [redacted] The clinical research infrastructure includes 1) well-trained and stable staff (2 study research coordinators, 4 full-time research nurses, 1 data quality and entry specialist, and several part time research assistants), 2) research space in inpatient and outpatient clinical locations, and 3) laboratory, office, and administration space within the medical school. A computerized perinatal database provides additional resources for single center observational studies as well as planning for larger multicenter clinical trials. Our MFMU and NRN PIs and coordinators assist each other with data definitions, consent procedures, and data collection procedures. Follow-up **(FU)** of neonates enrolled in studies is performed in the Neonatology Division's Follow-up clinic. In addition to [redacted], our site has two other senior investigators ([redacted]) with extensive experience as clinical researchers in maternal-fetal medicine; both are former PIs of MFMU Network sites. [redacted] is the [redacted] of our Maternal-Fetal Medicine Fellowship training program.

In addition to NRN and MFMU activities, our Divisions ([redacted]) participated in the NICHD-[redacted] a project that required extensive cooperation between the Divisions and with [redacted] to retrieve and transmit the necessary data. [redacted] mentored [redacted] ([redacted] for Obstetrics/Gynecology) on [redacted] – a randomized clinical trial **(RCT)** of [redacted] (2) One of our Center [redacted] ([redacted]) has recently collaborated with obstetricians from our site on a secondary analysis of data from the [redacted] MFMU trial. (3) [redacted] and [redacted] have worked with [redacted] (MFMU PI) and other obstetricians from our site on another analysis of the MFMU Network [redacted] data that showed that [redacted] Our analysis provides external [redacted], and [redacted] have collaborated in mentoring [redacted] (resident in Obstetrics/Gynecology) on a quality improvement **(QI)** study (in progress) to evaluate the effect of the timing of physician rounds on the obstetrics service on patient satisfaction.

Obstetrics Population:

	2013	2014
Number of deliveries	4461	4790
Number of C-sections	1847	2015
Number of multiple pregnancies delivered	138	144
Patients with diabetes (incl gestational)	571	657
Patients with hypertension	592	657

Deliveries that are		
Low-birth-weight **(LBW)** (<2500g)	746	745
Very low-birth-weight **(VLBW)** (<1500g)	184	176
Extremely low-birth-weight **(ELBW)** (>1000g)	95	95
Number of antenatal consults	309	332

* includes only NICU admissions at [redacted]

Obstetric Clinical Services

[redacted] has an academically oriented [redacted] division of [redacted] faculty. Since 2011, the [redacted] Division has published 255 peer-reviewed articles, of which 70 were multicenter studies. They see patients for prenatal diagnosis and MFM consultation at [redacted] and 9 other [redacted]) system sites. [redacted] services provide first trimester screening, chorionic villous sampling, genetic counseling, amniocentesis, Level II targeted and 3-D ultrasound, Doppler examination of fetal vessels, and antenatal surveillance tests. Specialized clinics care for women with medical complications (diabetes, vascular disease, HIV, connective tissue disorders), increased risk for preterm birth (multiple gestation, cervical insufficiency), and fetal conditions (structural abnormality, chromosomal anomaly, and genetic syndrome). Placental and perinatal pathology examinations are performed by a board certified pediatric/perinatal pathologist, [redacted]. The [redacted] inpatient transfer service accepts maternal referrals from other hospitals within and outside the [redacted] system. In 2013 and 2014, we had 814 maternal transports.

[redacted] Investigational Drug Service

Our research pharmacy offers services including implementation of randomization and preparation of masked active and placebo study medications. Research pharmacists are onsite during regular business hours and otherwise available by pager. These services have been successfully used in many obstetric and neonatal studies. The [redacted] investigational pharmacy oversees research pharmacy activities for the [redacted] hospital with dispensing done by the onsite pharmacists at [redacted].

Follow-up Program

To improve patient outcomes and FU compliance, we provide comprehensive pediatric care for infants who require NRN FU and for selected other infants (eg, BPD, NEC surgery, severe intraventricular hemorrhage, hypothermia). In addition to primary preventive care, we provide care for acute and chronic illnesses and case management; our patients have direct cell phone access 24/7 to our clinic medical providers. Since [redacted] joined our NRN site in 2011, we have been offering comprehensive care in our clinic to GDB and other study patients from [redacted]. Our FU population is 43% Black/non-Hispanic, 29% White Hispanic, 17% White non-Hispanic, 6% Asian, 1% Native American and 2% combined or unknown. Our FU clinic is located in the [redacted] Professional Building, across the street from [redacted]. The clinic is staffed by 2 pediatricians who work full-time in NICU follow-up and the Level 2 NICU and by a full-time clinic pediatric nurse practitioner **(PNP)**. There are 6 examination rooms in our clinic; other pediatric subspecialty clinics are located in the same building.

Services. As part of the [redacted] pediatric outpatient facility, we work closely with subspecialists in Neurology, Neurosurgery, Ophthalmology, Pediatric Surgery, Pulmonology, Gastroenterology, Cardiology, and other subspecialties as needed. We operate clinics Monday through Friday. Most patients are seen within 2 weeks of discharge and then as medically indicated. Patients are seen for regular well-child visits at 3 days-2 weeks post-discharge, 2 months, 6 months, 9 months, 12 months, 15 months, and 2 years of age; additional sick visits and follow-up visits are scheduled as needed. Most patients are transitioned to general pediatric care at 2 years of age. In 2013 and 2014, there were 3888 visits in 443 patients. Over half of the patients were being followed for research; the others were attending the clinic for clinical care only. If a family is unable to come to the clinic for a required research study visit, we schedule a home visit or an appointment for the weekend or after hours.

Personnel. Our current FU-PI, [redacted] has been working in NRN FU since [redacted] Our FU [redacted] had 11 years experience as an NICU nurse before taking the research coordinator position in February 2014. [redacted] is certified annually to perform the neurodevelopmental evaluations. [redacted] has also certified [redacted], a full-time PNP in the FU clinic and [redacted] our research coordinator, to perform the neurodevelopmental assessments. [redacted], is a board-certified clinical psychologist, and is our site's gold-standard examiner for all

NRN neuropsychological assessments, including the Bayley-III and WISC. [redacted] has trained and certified [redacted] and [redacted] as additional Bayley examiners. [redacted] is a psychologist and statistician who served as a gold standard examiner for the maternal IQ assessment for the 6 year follow-up of the hypothermia trial and with [redacted] has proposed inclusion of term reference infants in generic NRN follow-up. [redacted] our clinic coordinator, schedules appointments and maintains tracking along with [redacted] has been working in the follow-up clinic since 2000. [redacted] and [redacted] are both fluent in Spanish. Pediatric Ophthalmology and Audiology clinics are available in the same building for infants who need follow-up of vision and hearing problems or concerns.

Measures to Maximize Follow-up. We offer comprehensive pediatric care for infants who require FU as a strategy to improve FU compliance as well as patient outcomes. This program is modeled after the one shown to reduce loss to follow-up as well as serious illness in a large randomized trial. (4) Our comprehensive FU program is supported by [redacted] and [redacted] and is our most effective mechanism for maintaining high compliance with FU. Additional support for research tracking and visits is provided by the NRN and other research grants. The provision of comprehensive care for the infants enrolled in our FU program affords easy tracking of infants through their 22-26 month visit. The first FU visit is scheduled before hospital discharge. In addition, we obtain the mailing address, email address and phone numbers for the parents, relatives, and close friends prior to hospital discharge. These contacts are verified at each visit. Our FU clinic pediatricians also work in the Level 2 NICU, so some of our FU patients have established a relationship with the FU provider before hospital discharge. Our long-term in-depth relationships with the families engender trust that facilitates tracking through early school age. This 22-26 month NRN assessment is scheduled with the 2-year well child check whenever possible for the ease of the families. The day before each visit, our clinic coordinator contacts the family to remind them of their appointment. Parents are given parking reimbursement and a $50 Walmart gift card at the 22 month visit. If needed for the 22 month visit, transportation and lodging arrangements are provided. For any patient who misses an appointment, a clinic visit is promptly rescheduled. Whenever a parent cannot be quickly contacted using our contact information, an intensive and systematic effort is initiated to locate the family. Some of our tracking methods include phone calls to friends and family, letters asking the parents to call to schedule an appointment, and hospital databases. Online networking sites (eg, Facebook) have been extremely effective in helping us locate patients we had not been able to find. When other measures fail, we use peoplefind.com. If a family is unable to come to clinic for a required research study visit, we schedule a home visit or an appointment for the weekend or after hours.

Compliance. From the April 30, 2015 NRN Monthly Report, our FU rates are as follows for the ongoing NRN RCTs: Optimizing Cooling 91%, Laparotomy vs Drainage for NEC 94%, Late Hypothermia 92%, Hydrocortisone for BPD 100%. The FU rate for the SUPPORT School-age Cohort (internal center data as of May 15, 2015) is 25 completed evaluations/32 enrolled survivors with closed windows = 78%. Our follow-up rate for the GDB FU Cohort infants for 2011- 2014 (from NRN Monthly Reports) is 173/202 = 86%.

Data Collection. Definitions for all data items are kept in the research office. Our research nurse enters the data to ensure that all data are entered within a week, if not on the day of the visit, using an database login from computers in the clinic or our research office. All research conducted in the FU setting requires approval from the Institutional Review Board and parental consent. Consent is obtained at the time of trial enrollment for RCTs and at the time of hospital discharge for patients in the GDB cohort. This consent includes permission for the contact methods described under “Measures to Maximize Follow-up” above.

[redacted]

MFM Facilities and Other Resources

Abbreviations for MFMU Studies

ALPS- Antenatal Late Preterm Steroids: A Randomized Placebo-Controlled Trial

APPS- A Randomized Trial of Arabin Pessary and Progesterone in Singletons with a Short Cervix

ARRIVE- Induction in Nulliparous Women at 39 Weeks to Prevent Adverse Outcomes: A Randomized Controlled Trial

CMV- A Randomized Trial to Prevent Congenital Cytomegalovirus Infection

GDM-FU- Mild GDM Management and Long Term Maternal and Child Health: Follow-Up of the Mild GDM Trial

HCV- An Observational Study of Hepatitis C Virus in Pregnancy
PROSPECT- A Randomized Trial of Pessary and Progesterone for Preterm Prevention in Twin Gestation with a Short Cervix
STAN- A Randomized Trial of Fetal ECG ST Segment and T Wave Analysis as an Adjunct to Electronic Fetal Heart Rate Monitoring
TSH- A Randomized Trial of Thyroxine Therapy for Subclinical Hypothyroidism or Hypothyroxinemia Diagnosed During Pregnancy

Population Available for Clinical Trials

The [redacted]s an academically-oriented center composed of two sites: the primary site, [redacted], and the satellite site, [redacted]. In 2014, [redacted] performed 2912 deliveries and [redacted] performed 4204 deliveries (Table 1). These numbers have been stable over the past two years. Both sites are tertiary

Table 1- Obstetric Data	[redacted]			[redacted]	
OBSTETRIC	**2013**	**2014**		**2013**	**2014**
Total number of deliveries	2889	2912		3963	4266
Total Babies Delivered	2918	2934		4015	4342
Cesarean deliveries – total	760	698		1091	1282
Cesarean deliveries – primary	382	318		608	749
Cesarean delivery rate	26.3%	24.0%		27.5%	30.1%
VBAC rate	74.8%	75.9%		71.1%	72.8%
Total number of obstetrical admissions	3735	3699		8862	9472
Antepartum admissions	852	783		1303	1340
Maternal transports	88	66		530	585
Obstetric outpatient visits	29715	29649		59261	61144
High-risk obstetric patient clinic visits	4280	6562		2463	3924

	[redacted]			[redacted]	
RACE/ETHNICITY	**2013**	**2014**		**2013**	**2014**
Caucasian	39.10%	37.30%		42.30%	40.30%
African American	46.70%	46.90%		53.60%	52.50%
Asian	2.60%	2.60%		0.80%	1.10%
American Indian/Alaskan Native	0.20%	0.20%		0.08%	0.11%
Hawaiian/ Pacific Islander	0.20%	0.30%		0%	0%
Multiracial	0.30%	0.00%		0.58%	0.02%
Declined	10.40%	12.90%		1.10%	2.20%
Unknown	0.90%	0.20%		1.40%	3.70%
Hispanic	11.30%	11.50%		3%	3%
	[redacted]			[redacted]	
OBSTETRIC IMAGING AND TESTING	**2013**	**2014**		**2013**	**2014**
Total Ultrasounds	12418	13524		23668	29472
First Trimester Screens	1315	1685		1860	2046
Routine Anatomy	2601	2706		4108	5070
Targeted Level II	716	837		1778	2523
Antenatal Testing NST/BPP/Doppler	2076	2185		2995	4945

referral centers with Level III NICU services and academic MFM Divisions. The faculty at both centers are employed physicians for their respective institutions. As tertiary referral centers both institutions accepted maternal and neonatal transfers from outlying or affiliated institutions. Both systems have a closed medical

staff model limiting admitting privileges to faculty physicians and mid-level providers. Therefore, all patients are potential participants for MFMU research studies. The vast majority of patients receive their obstetric care primarily from employed physicians, nurse practitioners, and nurse midwives of their respective institutions.

Referrals from outside each system are a minority of total deliveries (Table 1).

Each institution is a tertiary referral center, serving an urban population. The obstetric high risk rate is approximately 22% when using low birth weight, congenital malformations, aneuploidies, placenta previa, multiple gestations, and preterm premature rupture of the membranes to define obstetrical high risk (Table 2). The medical complications of pregnancy rate is also significant (Table 2). If we define this population by the following characteristic: obesity, hypertensive disease, diabetes mellitus in pregnancy, and cardiac disease, well over 50% of patients have one or more of these diagnoses. We can reliably state that over 50% of all deliveries have a high risk diagnosis.

Table 2	[redacted]			[redacted]	
PRENATAL CARE CHARACTERISTICS	**2013**	**2014**		**2013**	**2014**
Number and/or percentage of obstetrical patients who receive prenatal care at the institution	2871	2893		3369	3626
Care Initiated First Trimester (Denominator Babies)	1788	1823		2021	2176
Care Initiated 2nd Trimester (Denominator Babies)	663 (22.7%)	646 (22.0%)		1011	1088
Care Initiated 3rd Trimester (Denominator Babies)	340 (11.7%)	240 (8.2%)		337 (8.50%)	363 (8.51%)
Care Outside of System (Denominator Babies)	109 (3.7%)	206 (7.0%)		396 (9.99%)	427
No Prenatal Care (Denominator Babies)	18 (0.6%)	19 (0.6%)		198 (5.00%)	213 (4.99%)
Nulliparity	44.30%	39.90%		39.30%	40%
Pregnant diabetics (admitted/discharged) Type I, II and gestational	5.60%	6.10%		804	1174
Multiple gestations	56 (1.9%)	52 (1.8%)		92 (2.3%)	124 (2.9%)
Cardiac disease in pregnancy	7	8		100 (2.5%)	65 (1.5%)
Hypertensive disease in pregnancy	15.90%	8.00%		12.30%	12.90%
Overweight BMI 25-30	26.90%	25.10%		26%	26%
Obesity BMI >30	45.60%	39.90%		50%	51%
Placenta previa	7	5		19	34
Preterm premature rupture of membranes <34	50	78		28	45
Antenatal Chorioamnionitis	26	23	*	254	274
Major fetal malformation or genetic disease	60	91		117	242
nfants < 1,500 grams	121	107		146	180
nfants 1,501-2,499 grams	358	331		459	502
Perinatal mortality rate (per 1,000 births)	13.8	13		15	17
Stillbirths (per 1000 births)	6.2	6.5		7	9
Neonatal Deaths (per 1000 births)	7.6	6.5		8	8

Prior MFMU studies have recruited participants during the first trimester. Approximately 50-60% of our obstetric populations initiate prenatal care during the first trimester within our institutions based on first visit and [redacted]. [redacted] has a slightly lower proportion secondary to a higher number of maternal transports. Over 20% initiate prenatal care during the second trimester and approximately 10% during the third trimester. Many of the individuals initiating care during the second or third trimester have received care at other institutions and are presenting to our systems as referrals. All of these individuals would be candidates for MFMU trials. [redacted]

Multi-site Collaboration for [redacted]

Recruitment Performance

[redacted] was approved to join [redacted] as a satellite institution i[redacted] and began actively recruiting i[redacted] Since acceptance into the network [redacted] has participated in each study [redacted] participated in

ALPS and is actively enrolling in CMV, HCV, and ARRIVE. [redacted] was not part of the network [redacted] They are gearing up to enroll for PROSPECT and APPS. Recruitment for our two sites is provided in study enrollment tables. A greater number of participants have been recruited at [redacted] than at [redacted] for a variety of reasons. We have used our technological advances in our EMR to identify potential candidates. The [redacted] system only recently adopted an outpatient EMR. [redacted] completed implementation of [redacted] 014. Our use of the EMR to efficiently identify potential candidates can be seen in our enrolled to screened ratio for ARRIVE. We have the lowest total number of patients screened but rank in the upper half of clinical centers. Recruitment differences can also be explained by some unique features of the two institutions. [redacted] is the defacto center for opiate dependent pregnant women. This is the likely reason for high recruitment for the [redacted] at [redacted] compared to [redacted].

Multi-site Management

Managerial oversight is coordinated through monthly meetings between the P.I.'s of each site ([redacted]). Meetings consist of P.I.s and study coordinators ([redacted]) and other relevant personnel. [redacted] is responsible for ensuring adequate staffing at each site and communicates with [redacted]. [redacted] identifies specific staff members to be responsible for each on-going study. This individual is responsible for assisting and organizing start up and training. This organizational structure provides greater redundancy when questions arise.

General research training and in-servicing is organized through [redacted] at [redacted]. [redacted] provides regular programs on the conduct of research. [redacted] specific in-servicing and training is organized by [redacted]. [redacted] assists [redacted] with IRB submission along with the [redacted] IRB specialist when needed. The IRB monitors human subjects training and sends out reminders to staff when certifications are about to expire. The [redacted] Grants Administration office requires and monitors CITI (Collaborative Institutional Training Initiative) certification for human subjects training. [redacted] IRB tracks training and does not permit submission or participation in studies if research staff have not maintained their certification. The staff member assigned to be the principal for each new study attends training sessions that are conducted during and prior to steering committee meetings along with [redacted]. This ensures that two individuals are familiar with each new study.

Data management is monitored and managed by our [redacted], [redacted]. [redacted] became our [redacted] in 2012. [redacted] and [redacted] review edit and audit requests on a regular basis to identify common patterns that are amenable to rapid process improvement. [redacted] assigns each query received from the DCC to the appropriate individual and ensures timely response. [redacted] communicates with our satellite site by fax and phone keeping [redacted] up to date on active queries. Staff assigned to be at [redacted] assist in reviewing information to answer queries. Information sheets are carried back or faxed back to [redacted] to update the [redacted] data base. [redacted] and [redacted] review performance on a regular basis to develop interventions for regularly occurring problems.

We have developed a cost effective system for study management and staffing. By using both per diem and full time staff we have significant flexibility to ensure adequate staffing. Our staffing model allows us to deploy personnel at two different institutions without duplicating services. We have used the EMR of each institution to assist in screening and personnel deployment. We have one of the highest rates of enrollment to screens for the ARRIVE study using these cost effective strategies. The [redacted] ([redacted]) provides us with additional resources such as nursing staff for low frequency events such as study drug infusions for CMV. We developed other cost cutting strategies. For example, we were given approval to store some study drugs in our research area to give us 24/7 access by the research pharmacy. This satellite storage was approved at [redacted] and [redacted] for ALPS. We have been given approval to store the study drug for PROSPECT in a similar manner. We have acquired the required monitoring equipment to ensure that appropriate storage temperature is maintained.

Neonatal Intensive Care Unit

[redacted] *NICU*

The division of Neonatology is directed by [redacted] who holds a joint appointment in the Department [redacted] also directs the [redacted] fellowship training program, a joint program with the [redacted] Clinic. Fellows spend 50% of their time at [redacted] and 50% of their clinical

time at [redacted]. The fellowship program accepts 3 fellows annually for 3 years of fellowship training. The NICU at [redacted] is a 49- bed level III Neonatal ICU with over 500 annual admissions (Table 3). The NICU at [redacted] provides both ICU and step down level services in a single unit. The neonatology division consists of 6 full-time board certified neonatologists with two attending's assigned each month. The Divisions of Neonatology and MFM work closely together providing joint educational programs for both fellowships, collaborate on research, and develop joint guidelines around areas of controversy such as the management of periviable gestations (22 and 23 week estimated gestational age).

[redacted] NICU at [redacted] is the Division Director of Neonatology and the [redacted] The NICU at [redacted] is [redacted] member of the Neonatal Research Network (NRN) of the NICHD. [redacted] is the current director of the NRN grant at [redacted]. The current NICU opened in [redacted] and is located adjacent to labor and delivery and is connected by a bridge spanning the two buildings. [redacted] also supports a Neonatal Fellowship Program that is directed by [redacted]. The program recruits 3 fellows annually for 3 years of training. The NICU facility is a 38-bed level III Neonatal ICU with ECMO services. There are more than 1200 annual admissions to the NICU annually. In addition, [redacted] provides a 40 bed transitional care nursery/step down unit to support chronically ill neonates and those being discharged to home.

Table 3	[redacted]			[redacted]	
NEONATAL	**2013**	**2014**		**2013**	**2014**
Number of NICU admissions	490	520		1240	1400
NICU inborn admissions < 34 weeks	149	172		264	289
NICU inborn admissions < 29 weeks	70	46		111	110
NICU inborn admissions < 1,500 grams birth weight	94	72		146	180
NICU inborn admissions < 1,000 grams birth weight	50	28		86	84
NICU transport admissions	7	3		222	285
Average daily census for the NICU	42	31.22		30.15	34.56
Average daily census for intermediate care/special care nursery	N/A	N/A		26.71	28.48
Average NICU length of stay	28.8	23.3		14.9	14.1
Follow Up Clinic Appointments	769	659		526	516
Attendance Rate of Scheduled Appt	71.10%	72.10%		76.60%	73%
F/U Compliance	97%	98%		97%	97%

CLINICAL INFRASTRUCTURE

Inpatient Facilities

[redacted]: The Perinatal Unit at [redacted] is located in a secure area on the [redacted] of the [redacted] Building. The unit consists of 9 LDR (Labor, Delivery, and Recovery) rooms, 5 high risk rooms, 8 antepartum rooms, 6 triage rooms, 3 operating rooms, a 4 bed post-anesthesia care unit, and an ultrasound exam room. The perinatal unit is designed around high risk pregnancies. The 5 high risk rooms are immediately adjacent to the Labor and Delivery unit ensuring ready access to physicians and staff. The rooms are utilized for intensive monitoring of women during the antenatal and postpartum period. This typically occurs in patients with underlying medical or obstetric complications. The antenatal unit is used for stable patients such as those with arrested preterm labor, preterm premature rupture of the membranes, non-hemorrhagic placenta previa, glucose management of diabetes mellitus, and stabilization of opiate withdrawal. The perinatal center is [redacted] the Emergency Department and Level 1 Trauma center. [redacted] currently has the only level 1 Trauma center in the city. The 3 room operating room facility is dedicated to obstetric procedures and separate from the main operating room located one floor below labor and delivery. The close proximity provides support for more complicated procedures.

All rooms in the perinatal unit are equipped for central fetal heart rate monitoring. The entire area is covered by a secure wireless network to allow ambulatory fetal heart rate monitoring through [redacted]. Two portable monitors are available for use in the hospital such as Trauma/Emergency Department, Main

Operating Rooms, and the Intensive Care Units. These are connected to [redacted] through the institutional WiFi Network.

Labor and delivery is supervised by two attending's from 7 am to 5 pm during the week. One attending is a MFM faculty member and the second attending is a generalist obstetrician-gynecologist. MFM consultation is available 24/7. Night and weekend in-house coverage is divided between the full-time faculty.

Two 12 single bed postpartum units are located on the second floor of the [redacted] Building on the far side of the NICU. Each postpartum unit has a normal newborn nursery. The NICU is separated into [redacted] for the 49 bassinets. The unit is located between postpartum and the perinatal unit.

Patients needing prolonged intensive care (e.g. chronic ventilation, major trauma, cardiac care, cardiac telemetry) are transferred to one of 6 Intensive Care Units based on the primary system or service involved (Trauma, Surgical, Medical, Cardiac, Pediatric, Burn). Patients are co-managed with MFM and the surgical/medical subspecialty services. The perinatal unit is staffed by nurses, operating room technicians, and patient care coordinators. The perinatal unit is also staffed with a dedicated Anesthesia attending on a 24/7 basis. [redacted] is the director of obstetric anesthesia. Anesthesia is also supported by Certified Nurse Anesthetists and anesthesia residents.

[redacted] is also a tertiary perinatal center on the east side of [redacted]. They are organized into an [redacted] bed Labor, Delivery, and Recovery unit on the [redacted] of [redacted]. The unit has a biological specimen processing lab and provides on-site testing for blood gas measurement, blood glucose levels, and hematocrit and hemoglobin levels. Twenty-four hour anesthesia coverage is available in labor and delivery. The Division of Obstetric Anesthesia is under the co-directorship of [redacted]. and [redacted]. The department supports fellowship training in obstetric anesthesia. The labor and delivery unit has 4 dedicated operating rooms, and a 3 bed neonatal resuscitation unit immediately adjacent to the operating rooms. They participate in the [redacted] Blood Bank. Labor and delivery is supervised by primarily the generalist faculty with 24/7 availability of MFM consultation.

The [redacted] floor of [redacted] houses the newly renovated 21-bed / 20 room antepartum unit which is supervised by the [redacted] faculty. The [redacted] floors serve as the postpartum units with a total of 39 single patient rooms.

[redacted] provides specialized intensive care unit services including medical, surgical, cardiac, neurosurgery and pediatric that are available to support obstetric patients. The neonatal intensive care unit contains a 38 bed NICU, a 31 bed step-down unit, and a convalescent unit. [redacted] provides this regions only ECMO program. The regions level 1 pediatric trauma unit is located at [redacted].

Outpatient Facilities

[redacted]***:*** The Ob/Gyn department occupies the [redacted] of the [redacted] on the main campus. The [redacted] clinic space is divided into three sections. One waiting area for faculty patients and a second waiting area for resident continuity clinic, and high risk MFM clinics. The 3rd area is reserved for fetal imaging and antenatal testing, our [redacted] All obstetrical imaging within the [redacted] beyond the first trimester is performed by the Department of Obstetrics and Gynecology. First trimester ultrasounds for dating, bleeding, or confirmation of viability are done in either radiology or the [redacted] based on provider preference and level of urgency. All first trimester nuchal translucency exams are performed in the [redacted] The MFMU research staff have two offices located within the clinic, one located in the center of the [redacted] and one office between the two outpatient clinic areas. These offices are used for counseling and consenting study patients. It affords patients privacy away from the high volume clinical traffic. MFMU study staff are able to talk with patients in exam rooms as they wait for their physicians as well as in the nurse intake rooms. The clinic staff are enlisted to help identify potential participants. Lists of potentially eligible participants that were identified from appointment lists are given to intake staff so that study staff can be informed of their arrival. This way they can be approached during waiting periods to optimize the time spent in the outpatient clinic.

The [redacted] System has many ultrasound units that are committed to subspecialty care such as cardiology, emergency/trauma which are not used for any type of obstetrical imaging. The MFM division operates imaging services at the FDC and at our outpatient office in the [redacted] located south west of the main campus. Service expansion is planned for this coming year to our [redacted] clinic located in south eastern [redacted] and in [redacted] locate at the southern end of

[redacted]. The imaging facilities run by MFM are staffed by 7 [redacted] sonologists who are credentialed for nuchal translucency examinations. We operate 7 ultrasound systems, 3 [redacted] imaging systems. The [redacted] systems are being replaced in June by [redacted]. The [redacted] is being used primarily in our antenatal testing unit for BioPhysical Profile's, and amniotic fluid assessments. Five units are located at the [redacted] and 2 units are located at the [redacted] office. These systems provide 3D & 4D imaging as well as pulse and color Doppler capabilities. The [redacted] has 3 fetal heart rate monitors for performing NST's. Radiology maintains a total of 10 ultrasound units primarily [redacted] systems. Five units are located on main campus for general imaging. One unit is located at the following off-site locations [redacted]. The MFM division has been working with radiology at [redacted] and [redacted] for expanding our capabilities in these regional offices. We expect to provide some limited imaging at these locations which will be supervised by MFM faculty. Genetic counseling services are provided only on the main campus by [redacted] genetic counselors and is supervised by our medical geneticist, [redacted]. The [redacted] main campus clinic provides the largest volume of obstetrical visits although prenatal care is also available at [redacted] of [redacted] System locations that span all of [redacted]. The volume of obstetric visits at eastside locations are significantly lower than the west side locations of [redacted] and [redacted]. **MFM** services are provided at [redacted] offsite locations including [redacted] and the [redacted] clinic. Planned expansion to [redacted] is expected in the fall of 2015. Low and high risk obstetrical visits are available 5 days a week at our [redacted]. Specialty high risk clinics occur throughout the week. Currently our diabetes in pregnancy program is held on Mondays. Our prematurity and fetal anomalies clinics occur on Tuesdays. Our medical complications of pregnancy clinic and our addiction clinic occur on Wednesday. General MFM clinics occur on Thursday and Fridays. Our nurse practitioners offer a special teen clinic focusing on 1st pregnancies in teenagers. Our generalist staff see patients with the residents in their continuity clinic as well as having their own clinic sessions throughout the week. The faculty clinic contains 4 bays each bay containing 4 exam rooms. Within this area is our video colposcopy exam room and urogynecology exam rooms with the appropriate equipment. The continuity and high risk clinic areas have 3 bays with 4 exam rooms each. An additional wound care room is available for minor procedures within the MFM clinic area.

[redacted]: The Ob/Gyn department provides ambulatory services on the [redacted] of [redacted] and on the [redacted] of [redacted] and operate multiple off site facilities.

The generalist and CNM division provide obstetrical services on the main campus and at 4 off site locations, [redacted] and [redacted] all on the [redacted] side of [redacted] and in [redacted] on the west side of [redacted]. The MFM Division provides services on [redacted] as well as 4 additional off site locations, two operated by [redacted] ([redacted] and [redacted]) and 2 under contract [redacted] and [redacted]).

MFM outpatient services at main campus is located in [redacted]. The division has 4 dedicated ultrasound rooms, 2 consultation rooms and 3 patient exam rooms. The unit is equipped with 4 [redacted] systems and uses [redacted] and report management. Antenatal Non-stress testing is provided in the fetal monitoring room. The [redacted] office operates 4 [redacted] ultrasound units with 2 consultation rooms. The [redacted] office located in [redacted] operates 3 [redacted] ultrasound units with 2 consultation rooms and 3 patient exam rooms. Limited services are available at the 2 contract locations. The ultrasound units are operated by 12 ARDMS certified technicians. All are working toward CLEAR certification for transvaginal cervical length measurements in preparation for the PROSPECT trial if prior certification was not obtained during prior studies. The offsite offices have portable fetal monitoring units available when needed.

The MFM division provides consultation and antenatal care throughout the week at main campus in [redacted]. They also supervise two high risk resident clinics during the week with one committed to Diabetes in Pregnancy and the other a general high risk clinic. Genetic counseling services at [redacted] are supervised by two Ob/Gyn Geneticists [redacted] also supported by genetic counselors and medical geneticists.

The [redacted] is the primary clinical space for ambulatory obstetrics and gynecology.

The generalist division is direct by [redacted] and consists of [redacted] board certified/eligible physicians in obstetrics and gynecology. Clinical services are provided 5 days a week on the main campus and various days at the four other offsite locations. The nurse-midwifery division is managed by [redacted] who oversees [redacted] other [redacted] who provide care in the [redacted] and the [redacted] other offsite clinic locations.

Research Pharmacy Facilities

The research pharmacy at [redacted] is located in the outpatient cancer pavilion which is connected and adjacent to the [redacted] The research pharmacy is managed by [redacted] P[redacted]. The research pharmacy has successfully supported MFMU studies for the past [redacted] The pharmacy currently prepares study infusions for the CMV trial and past trials including BEAM, Progesterone, BEARS, CAPPS, STTARS, OMEGA-3, and ALPS. The research pharmacy monitors, stores and dispenses study medications to our research staff. The research pharmacy has worked with MFMU coordinators over the three cycles to develop offsite controlled locked storage for some select study medications. This has provided us with 24/7 access to medications for administration and participant convenience. The research pharmacy assists with management of randomization codes, and study drug administration.

The research pharmacy at [redacted] is located on the [redacted] of [redacted]. It is a 1500 square foot facility directed by [redacted]. The research pharmacy provides the staff for monitoring storage, dispensing and documentation for study trials. This facility has provided support for the MFMU as well as for all other approved research programs at [redacted]. [redacted] has worked with the [redacted] to approve offsite storage, monitoring and dispensing of study medications similar to [redacted] on select studies such as ALPS. All CMV infusions are being performed at [redacted] in the [redacted] and are dispensed by the staff of [redacted]. Because of the low total numbers of individuals in the randomized portion of the [redacted] trial we found this to be cost effective and efficient for training and staffing.

Follow-Up Program

[redacted] ***Neonatal Follow Up Program***

The neonatal follow up program at [redacted] is led by [redacted]. The follow up clinic serves all high-risk infants discharged from [redacted] NICU. [redacted] Neonatal follow up clinic has approximately 700 annual visits (Table 3). The clinic emphasizes infants with the following problems for long term follow up: VLBW infants (<1500 grams birth weight), Grades 2-4 intracranial hemorrhage (IVH), periventricular leukomalacia (PVL), hypoxic-ischemic encephalopathy (HIE), meningitis, TORCH infections, small for gestational age infants (SGA), chronic lung disease (CLD), apnea of prematurity. Infants with these types of complications are seen regularly through the first 2-years of life (corrected age) typically on the following schedule: 1 week post discharge, then at 1, 4, 7, 12, 18, and 24 months corrected age. Additional visits are scheduled as needed for specific problems that require closer follow up. Neonatal follow up coordination is provided by [redacted]. [redacted] meets the family members prior to discharge and contacts them prior to their first clinic visit to facilitate the transition from inpatient to outpatient care. [redacted] tracks follow-up compliance and coordinates home nursing along with the other members of the team. Many of our discharged neonates have a visiting nurse visit within 24-48 hours after discharge. The NICU follow up clinic is located on the first floor of the [redacted]. [redacted] has [redacted] years of experience in NICU follow-up and leads a multi-disciplinary team of neonatologists, fellows, clinic coordinators, social workers, nurse practitioners, physical and occupational therapists, respiratory therapists, and neonatal nutritionist ([redacted]), all of whom are present for each clinic session (see [redacted]). NICU infants and normal newborns undergo hearing screening with the Audiology/ENT service who arrange follow-up as needed. VLBW infants with retinopathy of prematurity (ROP) are followed by the pediatric ophthalmology team led by [redacted]. Pediatric neurology follow up is provided by [redacted], and [redacted]. Developmental follow up is led by [redacted] in Behavioral Health. A team of 4 psychologists perform developmental assessments on NICU graduates. Evaluations for MFMU network studies is provided by [redacted] (TSH) and [redacted] (CMV).

[redacted] ***Neonatal Follow Up Program @*** [redacted]

The NICU follow up clinic is locate in [redacted]. Neonates graduating from the NICU at [redacted] have similar follow up arrangements to neonates graduating from the NICU at [redacted]. NICU infants at [redacted] are

[redacted]

onduct clinical research, in the provision of data required for grant submission n this grant submission, and to determine research feasibility. The data base has rs and is currently stored in the Microsoft Access format. [redacted] and [redacted] perform data entry. The data abstraction form contains demographic information, obstetrical and medical history, and delivery information. The information is recorded for every delivery and entered into the perinatal database. The database is used to generate reports on a monthly and annual basis to evaluate quality and clinical volumes. Quality control of this data is performed by cross checking with other administrative data systems, including billing, hospital administration, and specialized reports generated from the EMR. IRB approval has been obtained to search the database to determine research feasibility. This approval is reviewed on an annual basis by the IRB.

In addition to providing demographic information for this grant application the database has been used to provide information on prevalence of various obstetric characteristics for MFMU studies and other grant applications. Recently the Perinatal Database was queried to determine the obesity rate in our obstetric population for a grant titled [redacted] submitted by [redacted]. Patients admitted to labor and delivery have height and weight recorded on admission. This information was then used to calculate BMI. The information is provided in our demographic details table for 2013 and 2014 (Table 2 above). We used the database to determine frequency of preterm labor and delivery prior to 32 weeks estimated gestational age for a planned placebo controlled tocolytic trial.

NICU newborn data is collected by [redacted] (NICU [redacted]) and [redacted] (NICU [redacted]) and entered into a separate neonatal data base. Other resources that are used for research queries include the [redacted] computerized EMR (EPIC, Verona, WI), R4 Ultrasound Reporting System (Hyland, Westlake, OH), and [redacted]-Fetal Monitoring System (Elgin, IL). Our prior fetal monitoring system (OB-Tracevue) was replaced by [redacted] in 2013 because of improved integration with EPIC. [redacted] FHR tracings were converted and stored using open source software to insure retrievability of the 163k episodes.

EPIC has been our EMR vendor since its acceptance for outpatient management in 2001 and inpatient management in 2009. [redacted] has been a national leader in EMR and was recognized as the first hospital system to achieve [redacted] We expect to adopt the [redacted] in 2016. EPIC provides a data search tool to create queries for quality, research, and administrative report generation called [redacted] access to all clinical data stored in EPIC since its introduction in 2001.

[redacted] using the EPIC EMR. Queries can be generated to compare our institution to this large database of health information. EXPLORYS is used for quality evaluation as well as for research with IRB approval. We have used EPIC to our advantage as an innovative tool for efficient staffing and human resource management.

[redacted]
The perinatal database at [redacted] was established in 1985 and is currently in a Microsoft Access format. The database has been managed by the [redacted] since [redacted]. The [redacted] manages data entry, quality control, report generation, and responds to data queries. The data for our satellite site was generated through a request to the [redacted] The NICU at [redacted] was a founding member of the Neonatal Research Network and has a well-established database used to track neonatal outcomes for birth weights less than 1500 grams. The NICU database collects over 200 different elements related to maternal and neonatal outcomes. All told, specific perinatal related information is stored in 5 independent but overlapping database systems that can be queried for maternal and neonatal outcomes. This permits cross-checking to evaluate data reliability.

The [redacted] uses [redacted] both inpatient and outpatient EMR management. Eclipsys EMR was adopted by [redacted] in 2010 for inpatient management. The outpatient EMR was introduced into the obstetric practice in March 2014 with a planned phase in for all new obstetric patients. This phase in was completed in December 2014. [redacted] uses [redacted] Viewpoint for image archive and report generation. [redacted] is also connected to [redacted] and is available for queries of [redacted] specific information.

[redacted] and [redacted] and [redacted] belong to the [redacted] data is abstracted onto standardized forms and submitted electronically using VON specific software. Reports are provided to each institution for comparison with other [redacted] member institutions. Query reports can be made for additional analyses if needed.

Because of the redundancy of the information that is collected by many of these data systems it is possible to cross-check databases against one another. We have provided a description of our processes that are used to address data edit and audit requests previously in this application. These requests are managed by [redacted] our data management expert.

Neonatal Facilities

The [redacted] at [redacted] has been designated as a Level III C Unit by the [redacted]. **It includes the High Risk Pregnancy and Maternity Unit at [redacted] the Neonatal Program at [redacted], and a network of level 2 hospitals.** The Neonatal Program includes the 38 bed NICU, 44 step-down beds, Follow-up Program, ECMO Program, Outreach and Transport and the full array of 135 pediatric medical, and 20 surgical subspecialists. Newborns are transferred from surrounding counties and states for specialized care.

The **NICU** contains a 38 intensive care bed in a single room configuration opened in 2009. An operating room is located in [redacted] unit permitting major surgical procedures with minimal movement of critically ill infants. Facilities for residents, fellows and teaching are incorporated into the unit to facilitate medical teaching and research. There are extensive family support areas that encourage family participation in care- and lead to few reverse transports. Staff support areas include flexible office work areas for data collection and secure study equipment storage. Each bed is equipped with cardiorespiratory monitors and stand-alone pulse oximeters with artifact detection software equipped for data capture. Adjacent to the Intensive Care Unit is the Respiratory Therapy Laboratory that provides around the clock support and service for the unit. The entire fleet of mechanical ventilators are in the process of an upgrade. There are point-of-care analytic modules in the NICU for microscopic blood analysis. Bedside in-line blood gas monitors (VIA Medical Systems) are used for those neonates with <1.0 kg birthweight to minimize losses from phlebotomy. All patient care orders are entered on wireless computers and laboratory data are available at bedside. Digital radiographs are viewed on in unit monitors. Both inpatient and outpatient sites have an integrated electronic medical record which further facilitate data retrieval and streamline research.

The 44 bed **Convalescent Unit** is located on the contiguous [redacted] of the uniquely designed bed tower. There is a central monitoring system. The unit is staffed by the neonatal division attendings and fellows together with neonatal nurse practitioners and residents. Our neonatal team cares for all patients in

both units ensuring continuity not only of clinical care but also for clinical trials. Once admitted to our center, the families of most of our patients choose to complete their entire hospitalization here in part because of a unique environment on the [redacted] that provides a homelike space that includes living space for the parent at the bedside of every patient. **Thus, fewer than 5% of our patients are transferred back to the referral hospital prior to discharge to home ensuring that neonates enrolled in studies are not lost through transfer.**

2. Laboratory Facilities

A. Clinical Laboratories:

[redacted], which incorporates [redacted], is the primary affiliate of [redacted], and has a complete complement of laboratory facilities which are provide prompt service throughout the day and night, with microtechniques that require minimal blood from infants. Laboratories include Hematology, Chemistry, Endocrinology and Microbiology, with complete facilities for identification and characterization of bacteria, fungi, and viruses. Radioimmunoassays are routinely performed in a number of laboratories including the Special Pediatric Endocrinology and Immunology Laboratory. The Genetic Laboratory processes all amniotic fluid samples, measures the alpha-fetoprotein, and determines the karyotypes from blood, amniotic fluid, or chorionic villus samples. Molecular techniques, such as fluorescence in situ hybridization (FISH) to detect specific abnormalities and better delineate complex karyotypes, are available. The [redacted] offers direct DNA analysis using PCR methodologies, DNA hybridization, methylation analysis, sequence analysis and Microarray analyses.

B. Research Laboratories:

The Neonatal Division has a number of **specialized laboratories** including those within the [redacted] Center for [redacted] wo neonatal pulmonary laboratories; one for basic science research and the other for clinical research; a dedicated pulmonary center with infant pulmonary function capability, and additional research laboratories in metabolism, biochemistry, drug metabolism, and developmental neurophysiology.

B1. [redacted] Center f[redacted] The [redacted] was first funded in 2007 and has accelerated the pace of discovery and translation from the bench to the bedside. Within the [redacted] there are numerous resources which serve to support the work of the NRN including: Central IRB, a web based Research match program to link interested parents to ongoing research studies including NRN studies. The [redacted] incorporates laboratories to apply cutting edge Bayesian statistical analyses to gene expression and uncover patterns of gene expression in various disease states- these innovative methods have accelerated discovery and promise to bring new tools to bear in neonatal disease. The [redacted] houses the genome wide association center and microarray processing, as well as the nationally recognized [redacted] led by [redacted]. [redacted] refers to the large-scale study of proteins, particularly their structures and functions, to detect protein trafficking associated with a disease. Such information may ultimately inform both disease mechanisms and therapeutic development.

B2.The [redacted] Laboratory (3000 sq. ft.) contains a full range of equipment for measuring cardiorespiratory physiologic parameters in newborn and mature animals (e.g., rodents and piglets). This is complemented by equipment for performing neuroanatomical studies, immunohistochemistry, brightfield, fluorescent and confocal microscopy. We can perform microdialysis to detect neurotransmitter release and can perform microinjections. Equipment for molecular biology studies is available for Western and Northern blotting, PCR and RT-PCR. Collaboration with basic science specialists allows the recording of intracellular pH and analysis of metabolites in subregions of the brainstem, patch clamp techniques, and molecular tools to define expression of early genes.

B3. The [redacted] Laboratory: (1500 sq. ft) is integrated into the Step Down Unit at [redacted]. Under the direction of [redacted] and [redacted], it is staffed by a research engineer [redacted] and neonatal research nurse. Studies in this laboratory are performed on hospitalized preterm infants. State of the art equipment is available for measuring

ventilation, pulmonary function, respiratory muscle EMGs, and frequency of central and obstructive apnea as well as gastro-esophageal reflux. The studies performed serve both clinical and research protocols. There is close collaboration between [redacted] and the Dept. of Biomedical Engineering at [redacted] to develop novel non-invasive monitoring techniques.

B4. The [redacted] Laboratory under the direction of [redacted] conducts clinical research on brain organization and maturation, and better characterization of brain disorders. A combination of video, EEG, and polygraphic data are used to create algorithms that describe functional brain organization. Collaboration with biomedical engineers have led to the development of novel signal processing strategies that more clearly delineate deviations from expected brain patterns. Using these algorithms, together with clinical and epidemiologic data, prenatal and postnatal influences on brain function are being investigated.

B5. [redacted] Clinical Research Core: Two dedicated suites in the [redacted] provide office space for the NICHD NRN Coordinators and research nurses, Follow-up coordinator and data manager. The space includes secure data/computer room for data storage, input and analysis. Additional office space is provided onsite at [redacted] to facilitate efficient patient enrollment and data capture.

C. The Radiology Department has an extremely competent staff, wide range of equipment and the necessary expertise to interpret all films. In addition to the standard X-ray techniques, there are an adequate number of the latest generation of ultrasound machines with color flow doppler for both antenatal and post delivery use. The latest models of CT scanners, PET scanners, and MRI scanners are available. A dedicated MRI compatible transport incubator and ventilator permit imaging of even the tiniest babies. The Radiology Department has been very cooperative with performing our required studies in a timely manner. Software permits data transfer to DVDs or flash drive for transmission to the central data center or to independent study readers.

[redacted]

1. Division of Neonatal-Perinatal Medicine:

The Division of Neonatal-Perinatal Medicine is part of the Department of Pediatrics located in the adjacent [redacted]. [redacted] and [redacted] are the major teaching affiliates of the [redacted] for Newborn Care and Pediatrics. The Division of Neonatal-Perinatal Medicine is composed of [redacted] Neonatologists based at [redacted], [redacted] Neonatologists based at our 3 level II facilities who rotate into [redacted] for tertiary care experience, [redacted] Fellows in Neonatal-Perinatal Medicine, a Pediatrician based in the Follow-up Clinic, [redacted] PhD Scientists, [redacted] part time Neonatologists, [redacted] full-time and [redacted] part-time Pediatricians to oversee the Mother-Baby Unit at [redacted] and [redacted] Psychologists who staff the Study of Children at Risk[redacted].

The Division of Neonatal-Perinatal Medicine is academically oriented and has a long-standing and deep commitment to maintain a robust perinatal research program in addition to high quality teaching and clinical care. All faculty are expected to have a research focus whether it be clinical or laboratory based. The Program in Neonatal-Perinatal Medicine is led by [redacted], who has provided the protected time, environment and research support to create a vibrant and productive research enterprise. In addition to Divisional funds, the [redacted] in Pediatrics is held by [redacted] and funds from this endowment are used to support research initiatives of young investigators in perinatal research. A sampling of current laboratory based investigations includes [redacted]

[redacted]). WIH has been in the top tier of research funding among members of the National Association of Children's Hospitals and Related Institutions (NACHRI) since the rankings were initiated in 2011.

The milieu created by the research enterprise at [redacted] has permeated the NICU and created a top down dissemination of the importance and appreciation of research for attaining the best possible outcomes. This approach has created a NICU culture where there is an expectation that research is part of clinical care. Our Nurses, Respiratory Therapists, Pharmacists, Nurse Practitioners and House-staff have come to expect research initiatives and consider it one of the perks of working in an academic institution. Staff turnover is an important issue for health care institutions and has an important effect regarding the environment to conduct research in critically ill patients. Whether it is the geography or the limited number of level III/IV NICUs in proximity to [redacted], there are an increasing number of Nurses and Respiratory Therapists who have been at [redacted] for more than 10 years. These front line providers have experienced changes in our approach to sick neonates as a direct result of clinical translational research conducted in the NRN; examples include use of therapeutic hypothermia for newborn encephalopathy, use of inhaled nitric oxide for persistent pulmonary hypertension in the late preterm and term infant, and outcomes associated with different targets for oxygen saturation. This exposure facilitates maintenance of the research milieu by personnel other than the Investigators and research staff.

2. NICU at [redacted]:

High-risk infants are cared for in the Neonatal Intensive Care Unit located on the [redacted] floors [redacted] opened in 2009. It functions as a level III/IV NICU and [redacted] is the Medical Director. The NICU is a state of the art facility that has 70 rooms (61 singleton, 8 twin and 1 evaluation area) and can house 80 infants. The average daily census is 65 infants. [redacted] twin rooms are approximately 180ft^2 and 240ft^2, respectively, and have family (couch/bed, closet), infant (warmer/incubator, monitor) and nursing sections. Within the NICU is a satellite pharmacy which operates from 7am until 11pm and is responsible for filling all NICU medication orders and has sterile facilities for mixing parenteral nutrition. A Pharmacist with expertise in neonatal pharmacology directs the satellite pharmacy and participates on daily rounds. Each NICU floor has a satellite laboratory where blood gases are processed. Dedicated devices for sonography, X-rays and echocardiography are available on each NICU floor. Three teams care for infants in the NICU and a family centered approach has been adopted whereby parents are part of the team and can be present for rounds. Rounds are multi-disciplinary and involve Medicine (Attending, Fellow, House-staff, Nurse Practitioners), Nursing, Nutritionists, Case Managers, Respiratory Therapy and Social Work.

We have systematically studied the impact of a single family room NICU on neuro-behavior and medical outcomes of preterm infants. Multiple outcomes were improved in the single family room environment compared to our prior open bay configuration. Structural equation modeling provided insight into the mediators of the observed improvement. The results support that the improved outcomes associated with a single family room NICU are attributable to more developmental intervention and maternal involvement for which there is more opportunity in a single family room NICU. Since 2009, we have hosted visits from 35 national and international programs considering creation of a single-family room NICU. Characteristics of infants cared for in the NICU are:

	2013	2014
Number of births	8,605	8,587
Number of NICU admissions	1,199	1,207

Number of neonatal transports	167	180
NICU inborn admissions < 34 wks	311	316
NICU inborn admissions < 29 wks	95	92
NICU inborn admissions < 1500 gm BW	178	169
NICU inborn admissions < 1000 gm BW	84	70
NICU out-born admissions < 34 wks	36	42
NICU out-born admissions < 29 wks	8	10
NICU out-born admissions < 1500 gm BW	20	20
NICU out-born admissions < 1000 gm BW	4	6
Number of infants 1500 -2499 gm BW	596	634
Number receiving ventilator care	328	297
Number ≥ 34 wks receiving ventilator care	152	119
Number receiving CPAP only	155	211
Number ≥ 34 wks receiving CPAP only	52	104
Number of surgical cases[1]	86	69
ECMO	5	1
Congenital diaphragmatic hernia	3	1
Congenital gastrointestinal malformations[2]	30	21
NEC ≥ stage 2	17	13
NEC requiring surgery	7	7
Spontaneous intestinal perforation	5	2
Other surgical conditions[3]	31	38
Number with any ROP	54	62
Number with ≥ stage 3 ROP	11	14
Number receiving laser[4]	5	6
Number receiving Avastin[5]	3	5
Number with BPD< 1500gm[6]	48	42
Number ≥ 36 wks with HIE	13	10
Number ≥ 36 wks with HIE-cooling at < 6hrs	10	8
Number 33-35 wks with HIE	1	1

[1]Patients that require cardiac surgery are transferred to [redacted]

GI malformations include atresias, abdominal wall defects, Hirschprung's disease, webs and stenoses

[3] Other surgical conditions include meconium ileus and peritonitis, volvulus, choanal atresia, intussusception, small bowel obstruction, hernia repair, tracheostomy, testicular torsion

[4] In each year, 2 infants received laser therapy twice

[5] In each year 2 infants received both laser and Avastin

[6] BPD is based on O_2 use at 36 weeks post-menstrual age

For infants < 34 weeks born during 2013 and 2014, 88 and 90% were in-born, respectively; for infants < 29 weeks born during 2013 and 2014, a slightly higher percent were in-born (90 and 92%, respectively). This reflects an active regional maternal transport program which is closely adhered to by obstetric providers in the community. These statistics speak strongly to recognition among Obstetricians and Pediatricians of the importance of regionalized care for both high-risk mothers and infants.

The cohort of infants cared for in the [redacted] NICU demonstrates that there are a constant number of high-risk infants available for participation in clinical trials. It is difficult to predict changes in the health care delivery system in [redacted] given the uncertain impact of government and third party payer initiatives to improve health, quality of service and efficiency of care. However, we are optimistic that our well

regionalized perinatal care system will remain intact since multiple studies have reported that outcomes of high-risk pregnancies (mothers and babies) are improved with regionalization of care.

3. Follow-up Program for High-Risk Neonates:

Critical to the study of periviable pregnancies and to conduct studies in the PPRN is a well-developed and effective Follow-up Program. The Follow-up Clinic is located in an outpatient facility 1 mile from [redacted], is family friendly, handicap accessible and has free parking. [redacted] was established in 1974 and has been continuously led by [redacted], who is recognized as a leader in the field of follow-up of high-risk neonates. The Follow-up Program consists of a multi-disciplinary team experienced in tracking, retaining patients for long term studies and comprehensive assessments. The team includes a Director, [redacted] (gold standard examiner for the Movement ABC II and certified center exam(PI and gold standard for 2 year neuro-motor exam and SUPPORT school age neurologic examiner for 2 year neuro-motor exam), [redacted] (board certified in Neonatal-Perinatal Medicine and a certified examiner for the Movement ABC II), 2 Psychologists ([redacted], gold standard for Bayley III, and [redacted], gold standard for NEPSYII and the Woodcock Johnson III assessments), 1 Pulmonologist ([redacted]), 2 Social Workers, a Parent Resource Specialist, a Nutritionist, a Clinic Manager, a Clinic Coordinator, Receptionist, Data Entry Personnel and Data Analyst. This team has expertise in performing Bayley Scales of Infant Development Assessments II and III, a variety of additional psychometric tests for older ages, neurological examinations, behavioral assessments, growth parameters including skin fold thickness, medical assessments and hearing and vision assessments. The program has been successfully integrated into the Rhode Island Pediatric community since it complements the care provided by Primary Care Practitioners.

All infants < 32 weeks gestation are scheduled at 3, 6, 12, 24 and 30 months corrected age and at 5 years. The eligibility criteria apply to infants discharged from [redacted] and those retro-transferred to level II NICUs in the catchment area of [redacted]. Additional criteria, regardless of gestational age, include ECMO, neurologic complications, supplemental O_2 at discharge, use of home monitors, feeding problems and social environmental risk. Currently, children from birth to 7 years of age are enrolled in prospective longitudinal studies for the NRN. The clinic has 6 sessions per week with designated times for home visits. There were 1563 & 1863 assessments in 2013 and 2014 respectively. Our well defined catchment area with minimal overlap from other level III/IV NICUs is highly conducive to retention of eligible infants in the Follow-up Program.

[redacted], the program's [redacted], oversees our efforts to maintain compliance and multiple strategies are used to stress the importance of attendance at the Follow-up Program as follows: family conferences with the medical team prior to discharge explain the importance of the Follow-up Program, a formal discharge class further reinforces the need to attend the Follow-up Program, appointments for the Follow-up Program are made by the NICU Case Manager as part of preparation for discharge and a welcome home packet with a clinic brochure is provided at discharge. Families are accommodated by providing transportation, travel reimbursement or home visits if unable to attend clinic. All staff are trained to provide comprehensive family-centered visits in the clinic or at home; 2 staff members attend home visits for safety and to aid in execution of testing. Each month an average of 2 home visits are performed. The staff send birthday and holiday cards to all children who were <1000 grams for the first 5 years. [redacted] has traveled to multiple sites to complete school age assessments for infants enrolled from other NRN centers. She has also traveled to other states and countries to test infants for the MFMU Network.

Stepwise tracking is typically performed in a sequential fashion and uses the following algorithm: family or friend contacts (General Information Form); Pediatrician's office; Early Intervention center; Hospital database; State database [redacted] Internet search using a number of web sites (e.g., www.searchsystems.net). Compliance rates for follow-up visits are listed in the Research Strategy/Approach/Section 2. As evident from our follow-up rates, school age follow-up is extremely challenging. As part of a [redacted] ated higher completion of short term study related outcomes (demographics, health information, ER visits, hospitalizations and depression assessments) compared to traditional

Research Assistants and Social Workers (see Research Plan/Approach/Section 2). We are eager to pilot use of FRS to determine if they can favorably impact long term follow-up retention.

Extra-mural Support for the Follow-up Clinic Includes the Following:

- Neonatal Research Network:
- Maternal Fetal Medicine Unit Network:

Intramural Support for the Follow-up Clinic: The Division of Neonatal-Perinatal Medicine has a long standing history of recognizing the importance of a high caliber follow-up program, especially for a regional program. The Division provides salary support to complement revenues derived from patient visits and extramural funding of the Follow-up Clinic. Unfortunately, similar to other states, reimbursement for patient visits is poor in spite of the complex and highly sophisticated testing required for the evaluation of high-risk infants. In fiscal year 2014, the Division provided almost $120,000 to support salaries of Follow-up personnel.

4. Clinical Capabilities at [redacted]:

The [redacted] has the full range of clinical services to care for complex pregnancies and critically ill neonates. The infrastructure for conducting multi-center clinical trials and prospective observational studies is also in place. The details are as follows:

a. *The Program in Fetal Medicine:* The Program in Fetal Medicine has been recognized as one of the designated Programs of [redacted] since 2000. It is under the direction of [redacted] and [redacted]. [redacted] serves as the Neonatal liaison. The program consists of a consultative component via the [redacted] initiative, and a therapeutic component via the Fetal Treatment Program of [redacted]. The Program in Fetal Medicine is a joint effort of [redacted] and [redacted]. It utilizes specialists from more than 15 divisions and departments at both hospitals (including Maternal-Fetal Medicine, Neonatology, Pediatric Surgery, Fetal and Neonatal Cardiology, Pediatric Urology, Pediatric Neurosurgery, Pediatric and Fetal Imaging, Genetics and Metabolic Disorders, Pediatric and Perinatal Pathology, Nephrology, Neurology, Pediatric Hematology, Medical Ethics, Pediatric Plastic Surgery, Pediatric Orthopedics and Molecular Cytogenetics). Referred cases are discussed at the [redacted] conference to create and share care plans among clinical services who will be involved with the mother and newborn. The Fetal Treatment Program of [redacted] offers endoscopic laser ablation of placental vessels for severe Twin-to-Twin Transfusion Syndrome (15-20 patients/year), acardiac twin gestations, amniotic band syndrome and tracheal occlusion for severe congenital diaphragmatic hernia (CDH). Ex Utero-Intra-partum (EXIT) procedures are offered for congenital high airway obstruction, and open fetal surgery repair for fetal myelomeningocele. The Program coordinates care for approximately 200 complex fetal patients each year.

b. *Perinatal Pathology:* There is a strong Department of Pathology at [redacted] which is made up of 5 full time Pathologists all of whom have extensive expertise in placental pathology. All placentas from pregnancies where the birth weight is < 1500gms along with selected conditions among other pregnancies are routinely sent for pathological examination. The Department of Pathology has an active perinatal research program.

c. *Institutional Pharmacy*: The NICU is exceptionally well supported by the hospital pharmacy and a full-time [redacted]. [redacted] rounds with the clinical teams daily and coordinates all research projects requiring pharmacological interventions. Our center is currently participating in the Inositol trial and the Hydrocortisone to Prevent BPD trial, both requiring Pharmacy support. There have been as many as [redacted]

d. *Respiratory Therapy:* [redacted] is the Director of Respiratory Therapy which is made up of 21.6 FTEs, 1 Manager and 1 Educator. The NICU is equipped to provide mechanical ventilation using either conventional or high frequency modes of ventilation, and has all necessary equipment for the care of critically ill neonates with respiratory morbidities. Respiratory Therapists attend high-risk deliveries and perform a key role in airway management in all resuscitations. Satellite laboratories, including blood gas machines, are located on each NICU floor and are staffed by certified Lab Technicians. Our Respiratory Therapists have been involved in multiple NRN studies in the past (SAVE, Early iNO, iNO for preterm infants, SUPPORT, inhaled PGE). ECMO is available in the PICU of [redacted].

e. *Nutrition:* The NICU has outstanding Nutritional support provided by 4.1 FTE Nutritionists. Our Nutritionists are an integral component of the medical team and are part of daily rounds. They are responsible for optimizing parenteral and/or enteral nutrition based on fluid intake, associated morbidities and any specific patient concerns. They order all parenteral nutrition after review with the medical staff. They participate in our Follow-up Program and provide recommendations for optimizing nutrition for high-risk infants. Our Nutritionists participate in the divisional academic mission and have been Co-Investigators in a single site randomized trial of [redacted] protein intake of parenteral nutrition for ELBW infants [redacted].

f. [redacted]*:* Clinical care of critically ill and convalescing neonates is supported by a full complement of medical sub-specialists from [redacted] with 80 full-time Faculty. The 2 hospitals are connected by a tunnel facilitating movement of personnel and patients between the two facilities. The NICU is also supported by excellent pediatric surgical services including General Pediatric Surgery, Ophthalmology, Neurosurgery, Urology, Otolaryngology, Maxillo-Facial Plastic Surgery and Orthopedics. Surgical cases are performed in the operating rooms of [redacted] and infants are transported and recover in the NICU. Unstable infants are operated on at the bedside in our single family room NICU.

5. Perinatal Database:

The Division of Neonatology maintains 4 data bases focusing on different aspects of neonatal care. All databases are Access based and protected health information is kept secure on a hospital based SQL server. The databases are in addition to being a member of the [redacted] Network and include the following:

a. *Divisional Database:* This database collects core information on every admission to the NICU including maternal and delivery history, infant demographics and characteristics, out-born status, major morbidities and disposition at discharge. It is used to track utilization of our NICU resources and to follow trends in the medical conditions cared for. The database is maintained by our Transport Coordinator, who also serves as a Liaison with the community. The database is checked for accuracy by comparison with the hospital NICU admission records, comparing admissions (inborn, out-born, transfers within the hospital and readmissions) to discharges (disposition to home, Mother-Baby unit, community hospital, other tertiary centers and death), and insuring that the sum of birth weight categories equal the sum of gestational age categories. Upper and lower limits are used to identify outliers and prompt review.

b. *Follow-up Database:* Data for the Follow-up Program includes anthropometrics, clinical information, neurological examination, developmental scores and limited socio-demographic items for infants with a gestational age < 32 weeks. The database is maintained by a Research Statistician Analyst.

c. *ROP Database:* The ROP database was established in collaboration with our Ophthalmology colleagues to i) track and demonstrate comprehensive screening for ROP for inpatient and outpatients to insure timely intervention if indicated, ii) correlate assessment of ROP rates over time with changes in clinical practice such as altered oxygen saturation targets, and iii) monitor use of therapies such as laser and new interventions such as Avastin. The database is checked for accuracy by comparison of the number of first ROP screening exams with NICU admissions, deaths and transfers to other hospitals prior to the first ROP examination. Exam results of infants transferred to other hospitals are retrieved by the ROP Coordinator to reconcile all infants who should be initially screened. A similar process occurs for follow-up screening examinations. The ROP Coordinator accounts for all scheduled out-patient visits and follows up with families who missed an appointment. The database is maintained by the ROP Coordinator.

d. *Nutrition Database:* Our Nutritionists maintain a database of nutritional support provided to infants with a birth weight < 1000gms which is used to review our practices, identify practices that should be altered or discussed and provide data for relevant research within the Division. Data are collected by our Nutritionist group and consists of parenteral and enteral macro-nutrient and caloric intake on day 0, 1, 4 and weeks 1, 2, 3, 4, 5, 6, 8, 10, 12 and at 36 weeks, and growth parameters at selected ages.

We plan on integrating the Divisional Database and the Follow-up Database in the coming years. We have used the latter 2 data-bases to develop a joint Obstetrics, Maternal-Fetal Medicine and Neonatology guideline for the approach to extreme prematurity at [redacted] As part of this initiative, a summary document

and a convenient reference card was created for all providers so that the same local data are used in discussions and counseling of families prior to delivery.

Maternal-Fetal Medicine at [redacted]:

Antenatal Fetal Testing

The [redacted] diagnostic and therapeutic services. The [redacted] PDC employs 5 full time masters-level genetic counselors, 2 nurses, 1 phlebotomist, 5 full-time equivalent sonographers, and clerical support staff. The [redacted] PDC is a [redacted]-owned and [redacted] MFM Division-operated 4,500 square foot sister unit which employs 5 full time equivalent sonographers, 1 phlebotomist, a 0.6 FTE masters-level genetic counselor, and clerical support staff. In 2014, these two sites performed 13,559 Level 2 fetal sonographic studies, 732 fetal echocardiograms, 13,442 fetal growth studies, and provided 1,478 genetic counseling sessions. Additionally, 1,384 non-stress tests and 4,244 biophysical profiles were performed in these sites in 2014. The MFM Division provides fetal interventions for diagnosis and therapy as part of the Program in Fetal Medicine, a cooperative venture of [redacted], [redacted] and [redacted]. During 2014, 56 amniocenteses, 21 chorionic villus samplings, 14 fetal blood samplings, 11 fetal blood transfusions, and 11 placental vascular laser ablations for twin-twin transfusion syndrome were performed.

Intra-partum Diagnosis

The LDR Suite is composed of 20 private rooms, each equipped with electronic monitoring recording. Fetal heart rate data and alpha-numeric notations entered into this record are stored on laser disc (QMI System, Marquette Electronics, Milwaukee, WI). Blood gas testing of maternal, fetal and neonatal blood samples is performed in the NICU blood gas laboratory lying 120 feet from the center of the LDR Suite. Each labor/delivery room is immediately adjacent to a fully equipped neonatal resuscitation room. Invasive neonatal monitoring, intubation, and other respiratory support can be initiated on site, prior to transport to the NICU. Fetal ultrasonography and maternal ventilation and Swan-Ganz invasive and Doppler cardiovascular monitoring can be provided in the LDR Suite, in the operating rooms and in the post-anesthesia care unit.

Laboratory Testing

Clinical activities at [redacted] are fully supported by a round-the-clock state of the art, high throughput, on-site multi-specialty laboratory. Additionally, the [redacted] perform approximately 10,000 prenatal screening tests per year, serving local and national physicians. The laboratory also supports reproductive and medical endocrinology, and oncology, with more than 35,000 samples processed and 50,000 tests run per year.

The Division of Laboratory Genetics [redacted] offers both conventional and high resolution karyotype analysis, interphase rapid fluorescence in situ hybridization (FISH) for amniocytes and blood samples to detect common trisomies, and FISH analysis for micro-deletion syndromes and telomere rearrangements and Her-2 gene amplification for breast cancer. The Laboratory performs molecular testing for single gene disorders such as Fragile X syndrome, Prader-Willi-Angelman syndromes, Cystic Fibrosis, Coagulation disorders and others, using polymerase chain reaction (PCR), Southern blot analysis, linkage analysis, methylation analysis and micro-satellite marker analysis. In addition, the laboratory also performs Microarray analysis to detect genome wide genetic imbalances in individuals with congenital anomalies and mental retardation. The Genetics laboratory performs approximately1, 500 karyotype analyses, 600 FISH analyses, 200 DNA diagnostic tests and 3,000 CF screening tests and 400 microarray analyses annually.

Division of Perinatal and Pediatric Pathology

The Division is composed of five perinatal pathologists [redacted] and two specialty-trained Perinatal Pathologists Assistants. The Division's clinical and academic activities are focused on pathologic examination of the placenta, fetus and newborn. The Pathologists are board-certified in Pathology and Laboratory Medicine and in the Subspecialty Board of Developmental and Pediatric Pathology. Annually, the Division performs over 100 postmortem examinations on perinates over 20 weeks' gestation, and more than 110 complex perinatal examinations on fetuses of less than 20 weeks. In addition, 5000 placentas, mostly from high-risk pregnancies, and 3,000 products of conceptions from early losses are examined annually. Eight hospitals in two neighboring states regularly refer perinatal specimens to the Division to be evaluated. The Division has been the main center for Placental and Fetal Pathology in the Stillbirth

Collaborative Research Network (SCRN). The protocols for detailed and standardized placental and post mortem examination were established and published by the [redacted], [redacted].

Members of the Division are involved with externally funded research activities [redacted], stem cell related techniques and *in vivo* tissue implantation models. Clinical material including post mortem, products of conception and placenta reports, tissue blocks and slides have been retained since 1958. The reports and images of archival post mortem cases and their associated placentas are digitized and are accessible by a searchable database. Since 2001, the macroscopic images have been digitized and arguably the Division has the most comprehensive digital image collection of perinatal specimens available. A recent addition to the facility is a large capacity glass slide scanner where entire histologic sections can be scanned and utilized for diagnostic or investigative purposes. This system has advanced image analysis and quantification capabilities. In addition telepathology is also possible. Routine postmortem techniques include digital photography, digital radiography, microbiological cultures, microscopic examination and molecular and classical cytogenetics. In addition to routine histological methods, an immunohistochemical staining facility using a wide variety of antibodies is available, as are transmission and scanning electron microscopy for metabolic/neuromuscular diseases. Molecular investigative techniques such as RT PCR, FISH, CISH and SNP analysis are routinely utilized. Cytogenetics is available, but microarray analysis is used even for routine post mortem and other clinical cases.

Follow-up Program

NICU Based: The Neonatal Follow-up Program at [redacted] was established in 1974 and consists of a team experienced in neonatal follow-up tracking, retaining patients for long term studies and comprehensive multidisciplinary assessments. Team members include [redacted] (internationally-recognized for pediatric follow-up research), 3 additional physicians including a pulmonologist 1 nutritionist, 2 psychologists, 2 social workers, parent consultant, clinic manager, data entry personnel, and data analyst. This team has expertise in performing Bayley Scales of Infant Development Assessments, neurological examinations, growth parameters including skin fold thickness, medical assessments and hearing and vision assessments. All infants having birth weights of <1500 grams or < 34 weeks gestation are scheduled for follow-up exams at 3, 6, 12, 24 months corrected age, 30 months and at 5 years. Additional criteria for entry into the Follow-up Program regardless of birth weight include ECMO, HIE, neurologic complications, oxygen, feeding problems, social environmental risk, and sepsis. [redacted] The Clinic is family friendly, handicapped-accessible and has free parking. Home visits are made for study patients who are unable to come to clinic. There were 1563 and 1863 assessments completed in 2013 and 2014 respectively.

Compliance rates for study patients

Study	Age of Assessment	Dates	Follow-up Rate
NICHD NRN Generic	24 months CA	2013	89%
NICHD NRN Generic	24 months CA	2014	86%
Support Trial	3-4 years	2014	98%
Support Trial	7 years	2014	87%
Late Hypothermia	24 months	2014	92%

The program's clinic coordinator implements the following strategy to maintain compliance:

- NICU staff and discharge class inform families of the follow-up program.
- A welcome home packet with clinic brochure is provided.
- Families are accommodated by providing transportation if needed, or offering a travel reimbursement.
- The staff sends birthday cards to all children who were < 1000 grams for the first 5 years.

All staff is trained to provide comprehensive family centered visits both in the clinic and at home. The number of home visits performed each month averages 2.5. Stepwise tracking is usually performed in a sequential fashion: Family or friend contacts (General Information Form); Pediatrician's office; Hospital database; State database [redacted]; Internet search.

Specific to the MFMU Network

Currently, the MFMU Network TSH study requires infant follow-up (through age 5 with yearly developmental screening). This screening is conducted in the [redacted] Follow-Up Clinic under the direction of the MFMU Follow-Up Coordinator [redacted]. [redacted] maintains contact with the child's mother through telephone calls, e-mails and mailings. When the appointment time approaches, [redacted] arranges the appointment and sends reminder letters. MFMU personnel are available to assist with transportation and child care. During the yearly visit, during which [redacted] performs the required developmental testing, an MFMU nurse is present to complete study paperwork as well as reinforce a relationship with the child's mother and update any demographic changes. To date, this approach has resulted in a follow-up rate of 100%.

The CMV study also has follow up. Infants in this protocol have a hearing screen at the [redacted] with Audiologist [redacted] and [redacted] staff. This visit is facilitated by the MFMU study coordinator [redacted]. [redacted]t and [redacted] RA [redacted] have established great rapport with the mothers during their monthly infusions. The infants are also seen at 1 year of age and then again at 2 years of age for their final visit, hearing test and Bayley. Our first child in the study has a scheduled 2 year follow up and one year visits are ongoing with no loss to follow up at this point.

The HCV study requires follow [redacted]or labs at 4 months and again at 18 months. [redacted] and [redacted] follow these women and children as well. Women come to the triage area of the main hospital for the 4 month visit and are met by our study personnel at the [redacted]or the 18 month visit. We have obtained 100% of samples on all children who have made it to the 18 month window.

The ALPS and Arrive studies both have telephone/email follow up. We have established a research hotline for calls and have available staff M-F 7a-11p. Any patient who is unavailable for calls during these hours is reported to the coordinator for weekend contact. Our 3 and 6 month follow up is on-going and our follow up rate is 97% at 3 months and 95% at 6 months.

Perinatal Data System

[redacted] has used [redacted] since 2006 as its electronic medical and perinatal data system. An extensive array of perinatal data is captured by this system on all pregnant and puerperal women (and their neonates) admitted to the hospital, from the antepartum through the post-partum period. Several hundred data elements are recorded, including demographics, payer status, and clinical descriptors. These data can be accessed by authorized users at any computer terminal throughout [redacted] The system is maintained by the [redacted] Information Technology group. On a regular basis, core perinatal variables are subjected to audit for accuracy and consistency of recording and reporting. One illustration of the use of the system for MFMU research is for the ALPS study. We worked with [redacted] IT personnel to design an automatic paging system so that any time any pregnant patient presented to our busy triage unit in the eligible gestational age window (34 -36 weeks) an automatic page went to a dedicated pager carried 24/7 by an MFMU research nurse. This required a workflow modification in triage: gestational age became a required field in the triage intake evaluation form (a Cerner-based form). As triage was the main portal of entry for ALPS-eligible patients, this paging system proved invaluable.

[redacted]: The [redacted] Research Institute of [redacted] is a 30,000 square foot facility with extensive multi-user laboratory facilities. [redacted] houses the laboratories of 14 investigators in Pediatrics, Obstetrics and Gynecology and Pathology. Core facilities include shared cell culture facilities, a Bioinformatics Core, an *Affymetrix* microarray facility, and a Microscopy and Imaging Core. The facility also houses a Luminex® multiplex bead array laser and a Becton Dickinson FACS Canto flow cytometer. [redacted] and [redacted] work closely with a number of scientists at the Kilguss facility. A[redacted], many other technologies are available to researchers, including a Molecular Pathology Core which provides biomedical and engineering researchers with the technical expertise and scientific equipment needed to apply histopathological, immunohistochemical, and immunocytological methods to evaluate pathological alterations from the nano to the organismal level. There is also a Proteomics Core, a Genomics Core, a

Transgenic Mouse Core, and an Imaging Core with fluorescence, confocal and electron microscopy supported by awards from the National Institutes of Health and the National Science Foundation.

[redacted]: [redacted] is a private non-profit specialty hospital dedicated to women's health. Established in [redacted], it is the major provider of obstetric and gynecologic services in the [redacted] and southeastern [redacted]. It is the only teaching hospital for obstetrics and gynecology at the [redacted]. The Labor, Delivery, and Recovery (LDR) Suite is composed of 20 private rooms, each equipped with electronic monitoring recording. Fetal heart rate data and alpha-numeric notations entered into this record are stored on laser disc (QMI System, Marquette Electronics, in Milwaukee, WI). Blood gas testing of maternal, fetal and neonatal blood samples is performed in the NICU blood gas laboratory lying 120 feet from the center of the LDR Suite. Each labor/delivery room is immediately adjacent to a fully equipped neonatal resuscitation room. Invasive neonatal monitoring, intubation, and other respiratory support can be initiated on site, prior to transport to the NICU. Fetal ultrasonography and maternal ventilation and Swan-Ganz invasive and Doppler cardiovascular monitoring can be provided in the LDR Suite, in the operating rooms and in the post-anesthesia care unit. [redacted] has 80 neonatal intensive care beds and 60 newborn bassinettes.

Clinical: In 2014, 8,425 women gave birth at [redacted] -- over [redacted]% of hospital-based births in [redacted]. The population served by [redacted] is ethnically and racially diverse and representative of [redacted] general population. As for all of our clinical trials, we will recruit from among all women (irrespective of insurance, provider, etc.) who deliver at [redacted]. There is historically strong and ongoing institutional support (including financial) commitment to our research team. There is intellectual rapport with both the university faculty and the private physician groups and established, proven procedures for recruitment and follow-up from both hospital practice and private-practice physician offices. These private-practice groups enjoy the prestige of displaying manuscripts resulting from the participation of their patients in our research.

[redacted]: The [redacted] is a [redacted]-owned and [redacted] MFM Division-operated 12,500 square foot unit dedicated to integrated prenatal diagnostic and therapeutic services. The [redacted] PDC employs 5 full time masters-level genetic counselors, 2 nurses, 1 phlebotomist, 5 full-time equivalent sonographers, and clerical support staff. The [redacted] PDC is a [redacted]-owned and [redacted] MFM Division-operated 4,500 square foot sister unit which employs 5 full time equivalent sonographers, 1 phlebotomist, a 0.6 FTE masters-level genetic counselor, and clerical support staff. In 2014, these two sites performed 13,559 Level 2 fetal sonographic studies, 732 fetal echocardiograms, 13,442 fetal growth studies, and provided 1,478 genetic counseling sessions. Additionally, 1,384 non-stress tests and 4,244 biophysical profiles were performed in these sites in 2014. The MFM Division provides fetal interventions for diagnosis and therapy as part of the Program in Fetal Medicine, a cooperative venture of [redacted], [redacted] and [redacted]. During 2014, 56 amniocenteses, 21 chorionic villus samplings, 14 fetal blood samplings, 11 fetal blood transfusions, and 11 placental vascular laser ablations for twin-twin transfusion syndrome were performed.

[redacted] In 2014, the [redacted] had approximately 30,000 patient visits. Among the women who present for care, more than 70% have income levels that make them eligible for state assistance. Approximately 35% self-identify as Hispanic, 17% as African American and 3% as Pacific Islanders. The ethnic diversity of the patients is reflected in the diversity of the clinical staff. The facilities of the [redacted] include 18 general examination rooms, 4 special procedure rooms equipped with colposcopy and video capabilities, 8 consultation rooms, a conference room, and offices for administration, faculty, nurse practitioners, social workers and family planning counselors. Nutrition services, a satellite lab, an ultrasound unit and a fetal evaluation unit are all on the same floor. The Department of Behavioral Medicine is located across the hall from the [redacted] and the [redacted], specializing in the treatment of women suffering from depression, is on the first floor of the same building. Emergency services for the [redacted] patients are provided through the [redacted] emergency department/triage unit and the information from these visits are available to the [redacted] providers through the hospital's linked information management system.

Laboratory Services: The [redacted] lab is certified by the Clinical Laboratory Improvement Act and participates in routine external proficiency programs. The lab computers are linked to the hospital server and password protected.

Computer: [redacted] provides server-based personal computers to all professional staff. Research staff have a desktop computer. All staff has access to complete word processing, data management and analytical software. Our research staff is experienced in extracting, auditing and downloading research data while observing all applicable institutional, local, state, and federal confidentiality regulations.

Office: Faculty each has a private office within the Division of Maternal Fetal Medicine. They have a desktop computer, telephone, access to multiple printers, a facsimile machine, and a color copy machine. Research staff has access to computers, printers, facsimile machines, and copy machines. [redacted] has a media production department which produces color brochures for investigators.

[redacted]

[redacted] is one of the world's leading independent not-for-profit research institutes with the extensive institutional support, facilities, and resources necessary to successfully operate a data coordinating center (DCC) for a complex, multicenter clinical research network. Our staff of more than 2,800 provide research expertise to governments, foundations and businesses in more than 40 countries in the areas of health and pharmaceuticals, education and training, surveys and statistics, advanced technology, international development, economic and social policy, energy and the environment, and laboratory and chemistry services.

Three [redacted] universities—[redacted], the [redacted] and [redacted] in 1958 as the first scientific research organization based in the newly created [redacted] is a separately operated affiliate of these schools though scientists from [redacted] and these universities often work together on research programs and projects and maintain such relationships as adjunct faculty appointments, cooperative research programs, and other professional contacts. For example, the [redacted] sponsored by the Agency for Healthcare Research and Quality produces systematic reviews and analyses of the scientific evidence on a variety of health care and health policy topics, including maternal and child health.

[redacted] to Support Data Coordinating Centers

[redacted] structure encourages collaboration across multiple disciplines. Our staff encompass a diverse set of research expertise, including the following areas potentially relevant to the proposed Periviable Perinatal Research Network (PPRN):

Health Research—We conduct basic and applied research in public health, health economics, health behaviors, epidemiology, HIV/AIDS and other infectious diseases, and genetics and biotechnical sciences. We conduct numerous multicenter studies, including registries, clinical trials, and behavioral studies. We have active programs in comparative effectiveness research and health communications and marketing.

Laboratory and Chemistry Services—We maintain state-of-the-art capabilities in analytical chemistry, toxicology, materials testing, and methods development. We have substantial expertise in collection, storage, and processing of biospecimens from epidemiological studies and clinical trials.

Statistical Research—Our statisticians specialize in sampling design and selection, environmental and clinical trials, research data analysis, and all other facets of quantitative and statistical analysis.

Computing services and data management systems—[redacted] computer and data management professionals specialize in developing systems for research data acquisition and transfer, data management, study monitoring, and communications among participating institutions in both domestic and international research studies.

R.1 Resources Available from [redacted] Prior Experience as a DCC for Multicenter Clinical Studies

Since 1975, [redacted] has served as the DCC for more than 40 complex multicenter research studies. We have around 120 statisticians, 50 epidemiologists, 130 programmers, and other research professionals providing a breadth and depth of expertise that helps enhance scientific productivity by allowing flexibility in responding to the needs of collaborative research.

Exhibit R-1 lists many of the pertinent resources that have evolved and continue to evolve through our DCC projects. These resources are based on [redacted] extensive experience conducting and coordinating all phases of multicenter clinical studies, such as developing protocols, manuals of operations, and related study materials; developing and coordinating data collection activities; establishing data management systems; and assuring the data quality received from clinical centers. [redacted] professionals provide daily operational support and technical expertise to facilitate and oversee these efforts.

Exhibit R-1. Major Resources Available from [redacted] Past Data Coordinating Centers, which Facilitated Collaboration on Programs with Multiple Protocols

- **Data acquisition systems**, including distributed, real-time, and web-based electronic data capture (EDC) systems for acquisition of medical and specialized research data; each system includes real-time quality assurance and quality control procedures to reduce data errors and study management tools to enhance the protocol implementation and operational efficiency at the clinical sites
- **Website templates and tools** for developing, implementing, and managing a secure website to facilitate communication and study activities and public websites to facilitate network data sharing
- **Distributed patient tracking systems** that reside locally at the site to protect patient confidentiality but that can interact with the study data management system (DMS) to facilitate site operations
- **Web-based biospecimen tracking system** to support collection, inventory management, and transport of specimens and to facilitate the analysis and reporting of results
- **Site patient capitation reporting and invoicing system** to facilitate the tracking, monitoring, and payment of capitation expenses efficiently for both DCC processing and research unit reconciliation
- **Standard processes and templates for developing study materials**, including clinical protocols, manuals of operation, data management plans, site monitoring plans, checklists for site monitoring visits, site monitoring visit reports, statistical analysis plans, and monthly study status and data monitoring reports
- **Standard Operating Procedures (SOPs)** to promote quality assurance and support uniform conduct of regulated activities for studies conducted under an IND or IDE from the FDA.
- **Established procedures for tracking and implementation of statistical analysis** to support efficient and scientifically rigorous collaboration with clinical investigators in high volume settings

[redacted] current role as **DCC for the** [redacted] resources that are most relevant for this application. The DCC for the [redacted] was transitioned to [redacted] in 1998 and enrolls premature babies from [redacted] nical centers into multiple clinical trials and observational studies to rigorously investigate the safety and efficacy of treatment and management strategies for newborn infants. [redacted] collaborates with the [redacted] clinical investigators in identifying high-priority research topics, developing and implementing research protocols (including distribution of capitation payments), disseminating study results, and providing leadership in statistical design and analysis. Generally, four to seven clinical trials and observational studies are active in the network at any given time. Resources available from our [redacted] experience affording in-depth knowledge of current NRN studies such as the Generic Database registry of periviable NICU admissions and long standing working relationships with NRN investigators that are part of the proposed PPRN; (2) proven track record of exceptional scientific productivity, with [redacted] support for over 200 publications and around 300 presentations at scientific meetings from the [redacted] and other studies in neonatal/perinatal settings; (3) multidisciplinary expertise in biostatistics, bioinformatics, and health economics; (4) a robust data management system customized for the [redacted], incorporating automated data transmission, intra- and cross-form edits and reporting, that can be adapted for PPRN use; and (5) a flexible staffing structure that optimizes personnel resources to respond quickly to changing study needs. Other examples of [redacted] current experience as a DCC for active studies that provide resources relevant to this application are described in ***Exhibit R-2***.

R.2 Adequacy of [redacted] Facilities, Equipment, and Systems

[redacted] offers the secured facilities, equipment, and other resources necessary to support smooth functioning of the PPRN across multiple clinical sites.

R.2.1 Physical Facilities

In addition to [redacted] campus in [redacted] is of particular importance to this project because the proposed Principal Investigator is stationed in this [redacted] office, which currently occupies 22,000 square feet of well-equipped office space and is home to approximately 55 staff

who specialize in chronic and infectious disease epidemiology, genomics and statistical genetics, survey research, and the design, coordination, and analysis of multicenter studies. This office routinely hosts Steering Committee and other meetings for our NIH-funded DCC projects. It has four available conference rooms, two of which have video conferencing capabilities. The largest conference room, which can accommodate up to 58 people, provides a flexible seating configuration (meeting, training, conference styles) and includes video streaming and webinar capabilities with a built in projector. All conference rooms are available for Network meetings, training sessions, or conferences. WiFi access is available throughout the office for all visitors and on-site IT personnel are available to assist with technical support.

Exhibit R-2 [redacted] Current Experience as a DCC for Multicenter Clinical Research

Project Title/ Sponsor/ Time Period	Description	Relevant Resources available to the NRN DCC
[redacted] NICHD 2011 to present	This network studies clinical and health aspects of pelvic floor disorders in women. Areas of investigation include urinary incontinence, fecal incontinence, pelvic organ prolapse, surgical and nonsurgical treatments, social and behavioral contributions, pharmacologic therapies, and prevention efforts. The network consists of nine clinic locations throughout the United States.	• Study website with Integrated user management, project calendar, and email distribution system • Computer-assisted quality of life (QOL) call center case management and data collection • Automated electronic capitation system linked to EDC and QOL call management systems • Web-based EDC using Medidata RAVE and integrated randomization system
[redacted] 2010 to present	This is a multicenter prospective cohort study of 10,000 nulliparous women with singleton gestations to study the mechanisms for and prediction of adverse pregnancy outcomes in women in their first pregnancy. [redacted] coordinates 19 sites, including protocol development and implementation, common hypothesis templates, and web-based collaboration tools. [redacted] develops study materials, acquires validated instruments and assessments, and implements a biospecimen tracking system.	• Standard templates and policies for Steering Committee review of substudies and ancillary studies • Web-based data management system • Web-based procedures for tracking multiple study certification procedures • Comprehensive website with online gestational age (GA) calculator and study visit scheduling tool driven by GA • Web-based biospecimen tracking system
[redacted] NICHD 2008 to 2014	The [redacted] carries out pharmacological research to enhance understanding of obstetrical pharmacokinetics (PK) and pharmacodynamics (PD) and improve appropriate therapeutics during pregnancy. Currently, four clinical research sites and the DCC are funded to develop coordinated research on basic questions in pharmacology for women during pregnancy.	• Processes for transition from paper to web-based electronic data collection (EDC) • SOPs for developing and validating study-specific systems using the web-based EDC • Standard operating procedures for obtaining FDA IND approval and conducting study under IND
[redacted] NICHD 2003 to 2013	Multicenter network, with [redacted] as DCC, to study the extent and causes of stillbirth in the United States. The study is a population-based cohort and nested control study, with prospective enrollment of stillbirths and live births at the time of delivery.	• Study website with tools for sub-study development and biospecimen collection and tracking • Established SOPs for biospecimen sampling, transport, and storage • Detailed monitoring templates for conducting site visits

Project Title/ Sponsor/ Time Period	Description	Relevant Resources available to the NRN DCC
[redacted] NICHD 2001 to present	[redacted] is the DCC for this Network aimed at reducing morbidity and mortality among women and children globally. Initially, each of 10 research units (RU) conducted individual protocols. The seven RUs in Phase 2 of the Network conduct collaborative protocols aimed at addressing common problems.	• Sustainability and data quality assurance through comprehensive central monitoring • Study materials and communication in multiple languages. • Assistance with procurement and installation of hardware for data management and transmission systems.

R.2.2 Computing Facilities, Network, and Security

[redacted] Information Technology Service (ITS) supports our voice, video, and information systems. Systems are available and monitored 24 hours a day/7 days a week/365 days a year (24/7/365). Significant investments have been made to ensure the systems maintain an extremely high level of availability and reliability in support of the campus and global networks. This includes, but is not limited to, redundant power systems, virtual private network (VPN) and redundant networking technologies, load-balancing devices, clustering, and multiple data centers.

R.2.2.1 Server Infrastructure. ITS supports over 500 Windows, Linux, and high-performance cluster computing servers. Data storage capacity is in excess of 125 terabytes. RAID disk arrays and Storage Area Network technologies are used for performance and redundancy in the event of a disk failure. Microsoft Exchange servers are used for electronic messaging and scheduling. Microsoft SQL and Oracle servers are provided for database applications.

Web delivery is provided using multiple Federal Information Processing Standards (FIPS) 140-2 compliant hardware load-balancers. Web server farms running Microsoft Internet Information Server, Oracle Application Server, Adobe ColdFusion, and Apache Tomcat are currently supported and in use. Significant levels of redundancy are achieved through the geographical separation of redundant servers and services. Additionally, third-party applications, such as NSI's Double-Take, are used to minimize service disruption.

R.2.2.2 [redacted] Workstations. The workstation of the typical [redacted] professional is an Intel Pentium or Centrino computer running Microsoft XP or Windows 7 Professional with the latest patches and updates. Hard drives of all portable workstations are encrypted using Pointsec. Workstations are connected to the [redacted] data network, giving access to all the facilities and software described in this section. A wide variety of software is available including MS Word, Excel, PowerPoint, Visio, Project, and Outlook; and utilities, such as Adobe Acrobat, ZipCentral, CupertinoFTP, and McAfee antivirus software. Available statistical software includes SAS statistical packages (all modules); R; SUDAAN 10.0; STATA; and other popular statistical packages. Power and sample size software includes N-Query, PASS, and SAS and R modules.

R.2.2.3 Security. Microsoft's Windows Server operating system family supports several security features, including local desktop security (i.e., user identification and password is required for access), lockout of account upon repeated entry of an invalid password, NT File System (NTFS) per file and per directory security, and administrator-defined user groups. Password management is critical to maintain computer and network security. [redacted] are established for each project, and access to each share is restricted to ITS management and staff assigned to the project who need access to those particular files. Within the share, access to specific folders may be further limited to a relevant subset of staff.

Under normal operating conditions, a complete backup of all files on every disk is written to tape weekly. Every business day, a differential backup is performed of all files created or modified since the last complete backup. In the event of a hardware or software failure, files can be restored to their status as of the time of the last differential backup, usually the evening of the previous business day. Tapes from complete backups are kept for approximately three months. [redacted]

R.2.2.4 Physical Facilities Housing Computing Infrastructure. [redacted] ITS maintains two data centers in Research Triangle Park to support both administrative and project systems. Entrance into the computer rooms is controlled by automatically locking doors that are locked and monitored by [redacted] Corporate Security at all times. Fire protection, cooling temperature, humidity, and water levels are monitored and alarmed.

Both [redacted] data centers are protected by uninterruptible power supplies capable of sustaining data center operations until emergency backup generators come online. Nonauthorized personnel needing to access either data center are logged in and escorted in accordance with established ITS SOPs.

R.3 Data Management Systems

As summarized previously, [redacted] has a long history of providing data collection and management support to multicenter clinical research studies. We have established a reputation for developing and implementing innovative distributed or web-based data collection and management systems that are designed to meet the unique needs of each NIH-funded research network that we support. [redacted] web-based EDC systems were developed internally, to meet specific network needs. Our goal is to adapt the available systems, whether licensed from commercial developers or developed internally, to meet the needs of the [redacted] and its specific studies. In this section, we highlight a selection of DMS that [redacted] has employed on recent clinical studies.

[redacted] Resources. On the [redacted] medical records or other sources into a quality-oriented DMS. Known as [redacted], this is a table-driven system that can be quickly deployed for additional studies and was later adapted to support the [redacted]. [redacted] is in the process of transitioning the [redacted] quickly implemented, provides a user-friendly data entry interface, enables medical record storage, generates various data reports, supports biospecimen tracking, and ensures data quality by incorporating point-of-entry data consistency checks and an audit trail of data modifications

Other Resources. [redacted] developed the [redacted] a distributed data entry system with patient enrollment and randomization components, data entry, study biospecimen label creation, reporting and data editing, data transmission, a tool to enter general notes, and an e-mail feature used for such items as adverse event (AE) reporting. The [redacted] is also a table-driven, easily customizable system that has been adapted for use on over 16 studies used in over 12 countries in 4 different languages.

R.4 Project Management and Financial Systems

Crucial to the management of any project is the ability to complete all aspects of the project within the specified time period and within budget. Key members of the [redacted] management team have all been formally trained and gained substantial experience in project management at [redacted].

Financial Systems. [redacted] uses [redacted] the most widely used cost accounting system among Federal government contractors, to detail project costs on a semi-monthly basis. Monthly cost reports are reviewed and approved by the PI and task leaders. [redacted] produces a variety of cost reports including:

- A Project Status Report, which summarizes "booked" cost data (i.e., costs processed by [redacted] Accounting Department) by cost category, including prior years, current period, year-to-date, and contract to date. This report also documents budget variance and commitments.
- A Project Labor Report, which shows labor hours and labor costs for the current period, year-to-date, and contract inception to date.
- A Project ODC Report, which shows details for other direct costs (ODCs). This report provides support and detail for ODC charges that appear on the Project Status Report.
- Contract Task Summary Report, which provides a summary of booked costs, budgeted costs, and the remaining funds for all tasks within the project.

In addition to reporting on booked costs, [redacted] utilizes its fiscal management system [redacted] to develop cost-to-complete analyses. PRESTO allows the Principal Investigator and task leaders to forecast labor hours for each member of the project team and other direct costs across the duration of the project. Each month, the project staff analyzes any variance between the forecasted costs in [redacted] This analysis pinpoints any financial, technical, or schedule issues that may need to be addressed.

Internal Reviews. To ensure that we are performing at the level expected by our funding agencies, [redacted] employs an internal project review system that monitors the quality of work and technical performance on projects. Project reviews involve 2-3 meetings per year with the project director, task leaders and a review committee comprised of the [redacted] Status of the project, technical schedule and deliverables, and financial information are reviewed. This is another means of early identification of potential financial, technical, or schedule issues that may need to be addressed.

RESEARCH & RELATED Senior/Key Person Profile (Expanded)

PROFILE - Project Director/Principal Investigator			
Prefix:	First Name*: [redacted]	Middle Name	Last Name*: [redacted] Suffix:
Position/Title*: [redacted]r			
Organization Name*: [redacted]			
Department: [redacted]			
Division: [redacted]			
Street1*: [redacted]			
Street2: [redacted]			
City*: [redacted]			
County:			
State*: [redacted]			
Province:			
Country*: [redacted]			
Zip / Postal Code*: [redacted]			
Phone Number*: [redacted]	Fax Number: [redacted]		
Credential, e.g., agency login: [redacted]			
Project Role*: [redacted]	Other Project Role Category:		
Degree Type: [redacted]	Degree Year: [redacted]		
Attach Biographical Sketch*:	File Name: [redacted]		
Attach Current & Pending Support:			

PROFILE - Senior/Key Person

Prefix: First Name*: [redacted] Middle Name [redacted] Last Name*: [redacted] Suffix:

Position/Title*: [redacted]
Organization Name*:
Department:
Division:
Street1*:
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Zip / Postal Code*:

Phone Number*: [redacted] Fax Number [redacted] E-Mail*: [redacted]

Credential, e.g., agency login: [redacted] A

Project Role*: [redacted] Other Project Role Category:

Degree Type: [redacted] Degree Year: [redacted]

File Name

Attach Biographical Sketch*: [redacted]

Attach Current & Pending Support:

PROFILE - Senior/Key Person

Prefix: First Name*: [redacted] Middle Name [redacted] Last Name*: [redacted] Suffix:

Position/Title*: [redacted]
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Phone Number*: [redacted] Fax Number: E-Mail* [redacted]

Credential, e.g., agency login: [redacted]

Project Role*: [redacted] Other Project Role Category:

Degree Type: [redacted] Degree Year: [redacted]

File Name

Attach Biographical Sketch*: [redacted]

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Degree Type: [redacted] Degree Year: [redacted]

File Name

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File Name

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Zip / Postal Code*: [redacted]

Phone Number*: [redacted] Fax Number: E-Mail*: [redacted]

Credential, e.g., [redacted]

Project Role*: [redacted] Other Project Role Category:

Degree Type [redacted] Degree Year: [redacted]

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Degree Type [redacted] Degree Year: [redacted]

File Name

Attach Biographical Sketch*: [redacted]

Attach Current & Pending Support:

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contr butors.

Follow this format for each person. DO NOT EXCEED FIVE PAGES.

NAME: [redacted]

eRA COMMONS USER NAME (agency login): [redacted]

POSITION TITLE: [redacted]

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
[redacted]	[redacted]	[redacted]	[redacted]

A. Personal Statement

As [redacted] I lead a basic science laboratory in addition to managing and directing single center and multicenter observational and interventional clinical studies. The [redacted] is a regional perinatal center with approximately 350 VLBW infant births per year (200+ ELBW infants/year), and our center is a member of the NICHD Neonatal Research Network (I am [redacted]), the [redacted] and the MFMU Network. I have > [redacted] publications to date, of which 70 are as first or senior author. In the [redacted], I am [redacted] of the [redacted] subcommittee and the [redacted] and serve on the Late Hypothermia, Diuretics, MoCHA, and high dose caffeine subcommittees. I have > [redacted] publications to date, of which 70 are as first or senior author. The focus of my research is on biomarkers and prediction of outcomes in premature infants. I have recently published on genomic analyses in [redacted], intercenter variations in outcome, and prediction models of extremely premature outcomes. I also lead one of the four research centers in the [redacted] project funded by the NIH. In brief, I have a demonstrated record of successful and productive multicenter clinical, translational, and basic science research projects in the field of research on extreme prematurity, and am uniquely suited to be the [redacted] of the [redacted].

[redacted]

B. Positions and Honors

Positions and Employment

[redacted]

Other Experience and Professional Memberships

[redacted]

Honors

[redacted]

C. Contribution to Science

1. Prediction of outcomes in critically ill infants: [redacted] including classification and regression tree (C[redacted]s were developed using data from large multice[redacted]n outcome trajectories in neonatal intensive ca[redacted] low birth weight infants by using prognostic factors available over the course of NICU hospitalization.Data on infants with birth weight ≤ 1.0 kg admitted to 18 large academic tertiary NICUs during [redacted] were used to develop multivariable regression models following stepwise variable selection. Models were developed by using all survivors at specific times during hospitalization (in delivery room [n = 8713], 7-day [n = 6996], 28-day [n = 6241], and 36-week postmenstrual age [n = 5118]) to predict death or death/neurodevelopmental impairment at 18 to 22 months. We found that prediction of death or neurodevelopmental impairment in extremely premature infants is improved by using information available later during the clinical course. The importance of birth weight declines, whereas the importance of respiratory illness severity increases with advancing postnatal age. Dynamic models of the changing probability of individual outcome can improve outcome predictions in preterm infants. Various current and future scenarios can be modeled by input of different clinical possibilities to develop individual "outcome trajectories" and evaluate impact of possible morbidities on outcome.

[redacted]

[redacted]

2. Pulmonary hypertension in extremely preterm infants:Pulmonary hypertension is associated with bronchopulmonary dysplasia in extremely low birth weight (ELBW) infants and contributes to morbidity and mortality. We prospectively determined the prevalence of pulmonary hypertension among ELBW infants by screening echocardiography and evaluate subsequent outcomes. We found that pulmonary hypertension is noted in a fifth of extremely low birth weight infants, primarily those with moderate or severe bronchopulmonary dysplasia, and persists to discharge in many infants. Routine screening of ELBW infants by echocardiography at 4 weeks of age identifies only one-third of the infants diagnosed with pulmonary hypertension.

[redacted]

3. Genomics of BPD: Bronchopulmonary dysplasia (BPD) has a strong genetic component, but conventional single-marker approaches have not successfully explained more than a small fraction of the heritability of BPD. In recent study [redacted]), we identified biological pathways that contribute to the heritability of BPD using gene set analysis. Our analysis suggests involvement of known pathways (e.g. phosphorus oxygen lyase activity) and molecules (e.g. CD44) involved in lung development and repair. In addition, we identified novel pathways (e.g. targets of miR-219) and molecules (e.g. ADARB2, CD44) that may be involved in genetic predisposition to BPD or death. We validated this survey of gene sets associated with BPD in extremely preterm infants using a gene expression dataset from an independent population and evaluated selected molecules in a newborn mouse model and by gene expression in autopsy lung samples of BPD lung compared to normal preterm and term lung. Our results also indicate that severe BPD or death are associated with pathways distinct from mild/moderate BPD, suggesting that they have a different pathophysiologic basis, and that much variation is present in genetic predisposition to BPD by race/ethnicity.

   In another study, we identified that genetic polymorphisms of HO-1 are associated with BPD as well as death in preterm infants ([redacted]).

   We also identified genes regulated by methylation during normal septation in mice and during disordered septation in bronchopulmonary dysplasia. Twenty genes and three pathways methylated during mouse lung development also demonstrated changes in methylation between preterm and term human lung. In humans, 23 genes were differentially methylated with reciprocal changes in expression in bronchopulmonary dysplasia compared with preterm or term lung.

[redacted]

[redacted]

4. Evaluation of lung development and injury: We have recently shown that a combination of vitamin A (VA) and retinoic acid (RA) in a 10: 1 molar ratio (VARA) synergistically increases lung retinoid content in newborn rodents, more than either VA or RA alone in equimolar amounts.We observed that VARA increased lung retinol stores, and attenuated hyperoxia-induced alveolar simplification while increasing lung compliance and lowering resistance. VARA attenuated hyperoxia-induced increases in DNA damage and protein oxidation accompanied with a reduction in nuclear factor (erythroid-derived 2)-like 2 protein (Nrf2) but did not alter malondialdehyde adducts, nitrotyrosine, or myeloperoxidase concentrations. IFN-γ and MIP-2α mRNA and protein increased with hyperoxia and this increase was attenuated by VARA. Our study suggests that the VARA combination may be a potential therapeutic strategy in conditions characterized by vitamin A deficiency and hyperoxia-induced lung injury during lung development, such as bronchopulmonary dysplasia in preterm infants.

   To determine the mechanisms of lung alveolar septation, we measured miRNA and mRNA expression for postnatal lung development in mice and used mirDREM (MIRna Dynamic Regulatory Events Miner, a probabilistic modeling method that uses input–output hidden Markov models to reconstruct dynamic regulatory networks that explain how temporal gene expression is jointly regulated by miRNAs and transcription factors) to study the regulation of this process.The reconstructed dynamic network correctly identified known miRNAs and transcription factors. The method has also provided predictions about additional miRNAs regulating this process and the specific developmental phases they regulate, several of which were experimentally validated. Our analysis uncovered links between miRNAs involved in lung development and differentially expressed miRNAs in idiopathic pulmonary fibrosis patients, some of which we have experimentally validated using proliferation assays.

   We also determined the long-term effects of hypoxia or hyperoxia on cardiopulmonary development and function in an immature animal model. Newborn C57BL/6 mice were exposed to either air, hypoxia (12% oxygen), or hyperoxia (85% oxygen) from postnatal day 2 to 14 and then returned to air for 10 weeks.The major findings of this study were that both neonatal hypoxia and hyperoxia exposure resulted in an emphysema phenotype in adult mice, and neonatal hyperoxia (but not hypoxia) exposure increased adult airway reactivity and was associated with left ventricular dysfunction. Increase in adult airway reactivity with neonatal hyperoxia exposure was also accompanied by a decrease in the size of small caliber airways, increase in the quantity of bronchial smooth muscle, and a decrease in thickness and number of septa attached per bronchi.

[redacted]

D. Research Support

Ongoing Research Support

[redacted]

[redacted]

Completed Research Support

[redacted]

OMB No. [redacted] (Rev. 08/12 Approved Through 8/31/2015)

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contr butors.

Follow this format for each person. DO NOT EXCEED FIVE PAGES.

NAME: [redacted]

eRA COMMONS USER NAME (agency login): [redacted]

POSITION TITLE: PROFESSOR (with Tenure)

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
[redacted]			

A. Personal Statement

I am a practicing [redacted] and current PI of [redacted] clinical site of the NICHD Maternal Fetal Medicine Units (MFMU) network. I participate in the design and oversee the conduct of several ongoing multicenter collaborative perinatal trials and observational studies within and outside the framework of the MFMU network. I have been extremely active in the MFMU steering and publications committees and protocol sub-committees for various studies including some focusing on preterm birth. I was lead author of the well-received MFMU report on optimal timing of cesarean delivery that has helped shaped national and international recommendations. With NICHD R-01 funding as PI/PD, I [redacted] My major focus research areas are in preterm birth, medical and obstetric complications of pregnancy, perinatal infections, perinatal epidemiology including obstetric trials and global health. I received advanced training in the design and implementation of complex trials as an NICHD [redacted]. In addition to the MFMU network trials and other ongoing studies, I have designed and overseen the successful implementation of other large perinatal randomized clinical trials and observational studies. Given my background, experience, well-protected time, and departmental support, and our center's exceptional contribution to the evidence-base for perinatal care, I believe I am well-positioned to serve as co-PI in the proposed periviable preterm birth project.

B. Positions and Honors

Positions and Employment

[redacted]

[redacted]

Other Experience and Professional Memberships

-

[redacted]

Honors

[redacted]

C. Contribution to Science

1. My contributions involve the use of epidemiological and clinical trial methods to address medical and obstetric complications of pregnancy in order to improve maternal and perinatal survival globally. My collaborators and I have investigated the safe management of labor and delivery, including the optimal timing of delivery. The body of work provides evidence that early term delivery is associated with increased risks of neonatal morbidity and clarifies the role of fetal lung maturity testing. Our findings contributed to national guidelines recommending the optimal timing for non-medically indicated births as well as medically indicated preterm and early term births (references a & b). Additionally, we have studied methods of preventing post-partum hemorrhage, another significant contributor to maternal morbidity and mortality. The randomized controlled trial provides evidence for oxytocin dosing after vaginal delivery (reference c). I have recently served on [redacted] management of preterm [redacted]

[redacted]

2. In addition to the above work, I have a strong interest in perinatal infections and preterm birth. Although perinatal infections are strongly associated with preterm birth, there is a paucity of effective strategies to prevent preterm birth associated with perinatal infection. Our group continues to investigate mechanisms that may help advance the knowledge in this area.

[redacted]

3. I have a strong interest in the medical complications of pregnancy, including chronic hypertension, diabetes, and obesity. The majority of evidence used to guide management of these diseases comes from non-pregnant patients; therefore, my team of co-investigators and I study the management of these diseases during pregnancy. Additionally, I served as an expert panelist for the [redacted].

[redacted]

4. My recent and ongoing work has focused on preventing maternal infectious morbidity at the time of cesarean delivery. Infection is one of the top 5 causes of pregnancy-related death and morbidity in the US and throughout the world. Cesarean delivery, which accounts for over 30% of deliveries, is associated with a 5-10 times increased risk of infection compared with vaginal delivery. Our work provides evidence for methods to reduce the incidence of post-cesarean wound infection, endometritis and wound breakdown. I served as the principal investigator or senior investigator in these studies and recently completed enrollment into a large trial (N=2013) to evaluate azithromycin-based extended-spectrum antibiotic prophylaxis for cesarean delivery.

[redacted]

[redacted]

D. Research Support

Ongoing Research Support

[redacted]

Completed Research Support

[redacted]

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contr butors.

Follow this format for each person. DO NOT EXCEED FIVE PAGES.

NAME: [redacted]

eRA COMMONS USER NAME (agency login): [redacted]

POSITION TITLE: [redacted]

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
[redacted]	[redacted]	[redacted]	[redacted]

A. Personal Statement

I have extensive experience in clinical research including the design, implementation, data analysis, and reporting of neonatal and childhood research performed in developing countries and in the US including the [redacted], the [redacted], and the [redacted]. I lead clinical sites of two NIH-funded networks including the [redacted] for [redacted] and the [redacted]. I have successfully implemented two large scale multicenter studies in 6 developing countries that enrolled over 190,000 babies and resulted in large and significant reduction in neonatal and perinatal mortality. I have developed a high frequency ventilator, a flow interrupter to perform pulmonary function testing, and a low-cost oxygen air blender. I am focused on reducing mortality and major morbidities during early childhood in the US and developing countries funded by the NIH. I have been the [redacted] for the [redacted] site of the [redacted] since [redacted]. I am highly qualified to be a co-investigator on this exciting new project on periviable pregnancy and its outcomes.

[redacted]

B. Positions and Honors

Positions and Employment

[redacted]

Other Experience and Professional Memberships

[redacted]

Honors

[redacted]

C. Contribution to Science

1. [redacted] compared target ranges of oxygen saturation of 85 to 89% or 91 to 95% among 1316 extremely preterm infants. We found that a lower target range of oxygenation (85 to 89%), as compared with a higher range (91 to 95%), did not significantly decrease the composite outcome of severe retinopathy or death, but it resulted in an increase in mortality and a substantial decrease in severe retinopathy among survivors. The increase in mortality is a major concern, since a lower target range of oxygen saturation is increasingly being advocated to prevent retinopathy of prematurity.

   [redacted]

2. Current guidelines, initially published in 1995, recommend antenatal corticosteroids for mothers with preterm labor from 24 to 34 weeks' gestational age, but not before 24 weeks due to lack of data. However, many infants born before 24 weeks' gestation are provided intensive care. We determined if use of antenatal corticosteroids is associated with improvement in major outcomes for infants born at 22 and 23 weeks' gestation. We analyzed data collected prospectively on inborn infants with a birth weight between 401 g and 1000 g (N = 10,541) born at 22 to 25 weeks' gestation between January 1, 1993, and December 31, 2009, at 23 academic perinatal centers in the United States. It was observed that among infants born at

23 to 25 weeks' gestation, antenatal exposure to corticosteroids compared with nonexposure was associated with a lower rate of death or neurodevelopmental impairment at 18 to 22 months.

[redacted]

3. Cerebral palsy (CP) has been considered to result from exposure to proinflammatory cytokines during development. We wished to determine if selected pro-inflammatory and anti-inflammatory cytokines and/or mediators of inflammation reported to be related to the development of CP were predictors of neurodevelopmental outcome in extremely low birth weight infants. We analyzed 5 cytokines (interleukin [IL] 1β; IL-8; tumor necrosis factor-α; regulated upon activation, normal T-cell expressed, and secreted (RANTES); and IL-2) in infants with birth weights ≤1000 g (n = 1067) who had blood samples collected at birth and on days 3 ± 1, 7 ± 1, 14 ± 3, and 21 ± 3. IT was observed that IL-8 was higher on days 0-4 and subsequently in infants who developed CP compared with infants who did not develop CP in both unadjusted and adjusted analyses. Other cytokines (IL-12, IL-17, tumor necrosis factor-β, soluble IL rα, macrophage inflammatory protein 1β) were found to be altered on days 0-4 in infants who developed CP. These results suggest that CP in preterm infants may, in part, have a early neonatal inflammatory origin.

[redacted]

4. Of the 3.7 million neonatal deaths and 3.3 million stillbirths each year, 98% occur in developing countries. We evaluated community-based interventions designed to reduce the number of these deaths. [redacted] was assessed among 57,643 infants with the use of a before-and-after design. The Neonatal Resuscitation Program intervention was assessed as a cluster-randomized, controlled trial involving 62,366 infants. The primary outcome was neonatal death in the first 7 days after birth.The rate of neonatal death in the 7 days after birth did not decrease after the introduction of Essential Newborn Care training of community-based birth attendants, although the rate of stillbirths was reduced significantly relative risk with training, 0.69; 95% CI, 0.54 to 0.88; P=0.003). These results indicate that training in Essential Newborn Care results in better recognition of depressed infants and improved resuscitation, permitting survival of infants who would have been previously considered stillbirths.

[redacted]

[redacted]

[redacted]

D. Research Support

Ongoing Research Support

[redacted]

[redacted]

[redacted]

Completed Research Support

[redacted]

[redacted]

[redacted]

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contr butors.

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NAME: [redacted]

eRA COMMONS USER NAME (agency login): [redacted]

POSITION TITLE: [redacted]

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
[redacted]	[redacted]	[redacted]	[redacted]

A. Personal Statement

[redacted] is a [redacted] with a specific interest in health behavior. [redacted] developed the S[redacted], the first and only measure of smokers' abstinence-related expectancies [redacted], and has published manuscripts showing that these expectancies are meaningful predictors of overnight abstinence-induced withdrawal symptoms [redacted], mediate the associations of race and gender with motivation to quit and abstinence self-efficacy [redacted]. [redacted] also published the first and to date only manuscript characterizing the early time course of tobacco cigarette withdrawal effects [redacted], and just completed a NIDA-funded project [redacted] designed to pilot a smoking cessation intervention. Finally, [redacted] has a keen interest in statistics, having received his doctoral minor in the subject, and has broad experience in longitudinal analyses, including Generalized Estimating Equations (GEEs). [redacted] is very well acquainted with the methodology and logistics involved in the proposed project, and in defining the neonatal outcomes in which parents are most interested, develop a better means of framing and communicating clinical evidence, and developing Decision Aids for enabling parents of periviable infants to make better informed decisions. In summary, [redacted] experiences have thus prepared him well to successfully contribute to the proposed [redacted].

[redacted]

B. Positions and Honors

Positions and Employment

[redacted]

Other Experience and Professional Memberships

[redacted]

Honors

[redacted]

C. Contribution to Science

1. Development of questionnaire and measurement of expectancies: [redacted] has been involved in several projects investigating smoking-related expectancies. Recently [redacted] has focused on smokers' expectancies for the process of cessation (i.e., abstinence-related expectancies) via the development and application of the [redacted]. No prior work had directly examined smokers' expectancies for the cessation process, nor did an instrument exist that assessed these expectancies. [redacted] work in this area indicates that abstinence-related expectancies as measured by the SAQ demonstrate robust correlations with a number of smoking-related constructs including dependence, mediate the relations of race and gender with motivation to quit and abstinence self-efficacy [redacted], mediate the relations of substance use with motivation to quit [redacted] and prospectively predict abstinence-induced withdrawal symptoms and smoking cessation treatment outcome [redacted]. Ultimately novel tobacco dependence interventions aimed at modifying these expectancies may be designed. For this periviable pregnancy project, similar questionnaires will be developed, and expectancies evaluated.

[redacted]

[redacted]

2. Prediction of outcome, development of health behavior modification techniques: [redacted] dissertation project focused on the early time course of smoking withdrawal effects and found that symptoms of smoking withdrawal begin to emerge as early as 30 minutes postcessation [redacted]. This study remains widely cited. A pilot study [redacted] completed as a postdoctoral fellow extended this line of research and demonstrated that early smoking withdrawal symptoms predict a number of indices of treatment outcome, including smoking status [redacted]. Taken together, these results suggest that early abstinence may be meaningful to the treatment of tobacco dependence and interventions that focus on this time period may demonstrate efficacy. [redacted] recently completed piloting such an intervention with funding from [redacted] ([redacted] award). In this three-year study, [redacted] tested the feasibility and evaluated the potential efficacy of a smoking cessation intervention designed to help smokers develop and refine withdrawal regulation techniques during exposure to early smoking withdrawal. Results from this developmental project will inform an R01 application to conduct a larger clinical trial (anticipated submission: Fall 2015). In addition, in December of [redacted] received R01 funding from the [redacted] to characterize the early time course of e-cigarette withdrawal effects and evaluate their clinical significance. This R01 study will facilitate FDA regulation of e-cigarettes by informing the addictive nature of these increasingly popular products.

[redacted]

Complete list of published works
http://www.ncbi.nlm.nih.gov/pubmed/?term=hendricks+ps

D. Research Support

Ongoing Research Support

[redacted]

Completed Research Support

[redacted]

[redacted]

[redacted]

BIOGRAPHICAL SKETCH

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INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
[redacted]	[redacted]	[redacted]	[redacted]

A. Personal Statement

I have been the [redacted] Newborn Follow-up Program and have been a [redacted] for the Neonatal Research Network. I have participated in the experimental design and staff training for the BRAIN-HIT, an early neurodevelopmental intervention trial of infants/toddlers who had experienced birth asphyxia in developing countries. In addition, I have assisted in the design of several neuropsychological studies related to exposure of children to toxic substances in utero, prematurity, and maternal hypothyroidism. I have worked in the field of Neurodevelopmental Disabilities for over 30 years and for the past 5 years as Director of the [redacted] and [redacted]. In addition, I have a long history of service and research related to Early Intervention with at risk populations. I am a member of the state [redacted] serve on the [redacted] and conduct research on computer interventions with children who have an Autism Spectrum Disorder. In addition, I participate in the training of developmental, child and pediatric psychologists. I am a member of the [redacted] and [redacted] at the [redacted]. I also have expertise in the field of parenting skills, self-efficacy and parental views relevant to the proposed project. In summary, I have a demonstrated record of successful and productive research projects in psychology and health behavior related to extreme prematurity, and I am uniquely suited to contribute as an investigator to the Periviable Pregnancy Research Network (PPRN).

[redacted]

B. Positions and Honors

Positions and Employment

[redacted]

Other Experience and Professional Memberships

- Member, JCCEO Head Start Health Advisory Committee

1986 - 1995 [redacted]

Honors

[redacted]

C. Contribution to Science

1. Assessment of outcomes in preterm infants: I have participated in several MFMU and NRN studies including the Magnesium Sulfate study, the Hypothyroid study in which I helped design the Neuropsych battery of tests used in that longitudinal study, and a study assessing the impact of intrauterine infections of a child's development.

[redacted]

[redacted]

2. Early developmental intervention: [redacted]-HIT) Project, a multicenter trial of the [redacted]This home-based parent-implemented early developmental intervention (EI) involved both in infants with mild to moderate birth asphyxia and in infants without perinatal complications as a healthy comparison group in a randomized controlled trial. The trial evaluated the impact of a resource-intensive early intervention (EI) program on the outcomes in infants born in rural communities in [redacted] It involved twice a month home visits between parents and the parent trainers for 3 years. The control group received the same frequency of home visits with enhanced health counseling (HC). The overall goal was to implement and evaluate an EI program for infants following birth asphyxia, which is sustainable in developing countries. A group of infants without perinatal complications was also randomized to the same conditions in order to provide a comparison of what may be achieved from the intervention in healthy infants in developing countries. A final aim was to address individual variation in EI effects that could be due to child and/or family characteristics. Children were evaluated by masked examiners at three time points (12, 24, and 36 month's assessments). We found that the EI children made substantial gains in all areas of development compared to the control group. The gains increased over the three years. We also developed a 12 month infant development screener that can be used in low and middle income countries. I am also participating in two new studies in [redacted]studying prenatal/infant exposure to methylmercury [redacted]and smoke inhalation [redacted]n the development of infants and toddlers. I was a primary investigator or co-investigator on these publications:

[redacted]

3. Parenting skills, self-efficacy and parental views, and research on autism: We assessed the effectiveness of infant massage in improving the parenting skills, feelings of self-efficacy and parental views of several at risk maternal populations and a computer avatar to teach emotion recognition to children with an Autism Spectrum Disorder (ASD). We found that the impact of infant massage was quite effective in improving parental feelings of self-efficacy and parental knowledge and the FaceSay game improved social skills in children with an ASD. In addition, we have recently studied the impact of social skills training on the peer interactions and social status of children with ASD following this training. Children in the social skills intervention did have improved social status following training. We are currently conducting studies investigating the effectiveness of using a computerized robot to teach children with ASD to spend more time looking at the face of someone they are speaking with and to improve their social skills. In addition,

we are beginning a study to assess the impact of a motor skills group intervention on the social skills of children with ASD and their peer social status

[redacted]

D. Research Support

Ongoing Research Support

[redacted]

OMB No. [redacted] (Rev. 08/12 Approved Through 8/31/2015)

BIOGRAPHICAL SKETCH

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POSITION TITLE: [redacted]

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]

A. Personal Statement

With [redacted] experience focused on prediction and prevention of preterm birth and other adverse pregnancy outcomes, I have developed clinical expertise in the care of high-risk pregnancies and obstetric ultrasound, particularly pregnancies complicated by multiple gestations, fetal abnormalities and at risk for preterm birth (PTB) and premature rupture of the membranes (PROM). I have developed expertise in clinical research, particularly in the design, conduct, and analysis of single and multicenter studies, including randomized controlled trials, and studies requiring detail phenotypic evaluation of pregnant women in relation to their risk for adverse pregnancy outcomes and biologic specimen collection for analysis. [redacted] have participated in protocol development, recruitment and analysis of successful prospective observational and interventional studies, and have participated in major prematurity related trials and other research resulting in over 260 peer reviewed publications. [redacted] from the first pregnancy of cardiovascular disease and metabolic syndrome, and secondarily focused on prediction of recurrent adverse pregnancy outcomes in the original cohort [redacted]). Additionally I serve as center [redacted]) for [redacted] within the [redacted]. Locally, I have served as an integral part of unique multidisciplinary team, led by [redacted] studying the factors associated with fetal membrane integrity and the mechanisms of physiologic membrane rupture at term. Our team has made significant strides in the understanding of fetal membranes, their component parts, and the impact of inflammation and antioxidants on their biomechanical and biochemical properties.

I have participated in MFMU Network research for over [redacted] years, since completing my Fellowship in Maternal-Fetal, serving as [redacted]. As a [redacted] for [redacted] in the NICHD-funded Maternal-Fetal Medicine Units research network from [redacted], I served on protocol subcommittees for prediction of prematurity [redacted], obstetric determinants of outcome [redacted] conservative management of [redacted]. These studies have changed clinical management for women at risk for [redacted]. I have actively participated on key administrative NICHD-MFMU committees, including the [redacted],

[redacted] and recruitment committee [redacted], and [redacted]. My participation in these committees provided valuable experiences that with allow me to provide mentorship in administrative issues related to multicenter research. [redacted]
Fetal Med [redacted]
women, a [redacted]
administration of multicenter research groups, prioritization of research and analyses, and coordination of manuscript preparation and the publication process. This experience will enable me to contribute to the Periviable Pregnancy Research Network (PPRN).

[redacted]

B. Positions and Honors

Positions and Employment

[redacted]

Other Experience and Professional Memberships

[redacted]

[redacted]

Honors

[redacted]

C. Contribution to Science

1. Preterm Premature Rupture of the Membranes (pPROM): Throughout my research career, my efforts have focus on prediction and prevention of preterm birth and its complications, with a particular focus on premature rupture of the membranes and very early birth near the limit of viability (periviable birth).pPROM is responsible for approximately 1/3 of preterm births, is associated with short latency, increased perinatal infection and gestational age dependent morbidities, and is a major cause of perinatal and infant mortality. My efforts in this area have expanded the understanding of the causes and predictive factors for PROM and its complications (a,b), resulted in routine introduction of antibiotic therapy to reduce infant morbidities through pregnancy prolongation after early pPROM (c), as well as the general practice of expeditious delivery after pPROM near term (d).

[redacted]

2. Prediction of Preterm birth: I have collaborated in research that has been seminal in our understanding of the causes and prediction of preterm birth, including recurrent preterm birth. These efforts have resulted in incorporation of predictive tools into clinical practice, and had guided clinical studies for preventative efforts.

[redacted]

[redacted]

3. Periviable birth: Periviable birth, occurring near the limit of viability is particularly morbid, requiring clear understanding of the potential maternal/fetal/newborn outcomes associated with various interventions to prevent imminent periviable birth and its complications, as well as the ability to engage the healthcare team in effective family counselling in what often becomes a evolving circumstances with rapidly changing maternal/fetal/neonatal conditions. I have collaborated in research and that has increased our understanding of these issues, and ultimately co-led the multidisciplinary NICHD-SMFM Workshop that resulted in recommendations for care and counseling regarding periviable birth.

[redacted]

4. Prevention of Preterm Birth: Incorporation of research ideas into clinical practice typically requires successful completion of Randomized Clinical Trials that address the safety and efficacy of intended interventions. Within the NICHD-funded MFMU Network and CPEP study, I have had the opportunity to participate in studies that have directly impacted care regarding prevention of preterm birth (Progesterone to prevent recurrent preterm birth (a), Progesterone in Twin (b) and Triplet [Caritis, 2009], progesterone in nulliparas with a short cervical length (c), Omega-3 supplementation (d). Each of these studies has directly impacted the practice of obstetrics in the USA and abroad.

[redacted]

[redacted]

5. Prevention of Preterm Birth: In addition to the RCTs listed in the above sections, I have collaborated in research aimed at Reduction of Newborn Complications related to preterm birth and at term within the NICHD MFMU Network[redacted], Weekly antenatal steroids [redacted], Fetal Pulse Oximetry [redacted], Implications of early term birth [redacted], and locally (a-d). Each of these studies has either changed practice directly or influenced our understanding of the impact of interventions on perinatal outcomes.

[redacted]

D. Research Support

Ongoing Research Support

[redacted]

[redacted] (Rev. 08/12 Approved Through 8/31/2015)

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contr butors.

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NAME: [redacted]

eRA COMMONS USER NAME (agency login): [redacted]

POSITION TITLE: [redacted]

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
[redacted]			

A. PERSONAL STATEMENT

I am well trained, experienced and motivated to contribute as lead neonatologist at the [redacted] site for the Periviable Pregnancy Research Network (PPRN). My research career is focused at the nexus of generation of new evidence through clinical trials, translation of these finding into practice through rigorous quality improvement science, and evaluation of the effectiveness of interventions when incorporated in practice. [redacted] and outcomes of persistent pulmonary hypertension of the newborn. Since [redacted] Investigator for the [redacted] site of the NICHD [redacted] and have been privileged to conduct pivotal trials that have generated the new evidence that has substantially improved the care of preterm and term neonates. I became [redacted] in [redacted] and have expanded our faculty in clinical research and clinical trials to include five Masters prepared researchers, a biomedical research engineer, and an integrated team of research nurses.

[redacted]

[redacted]

B. POSITIONS AND HONORS

Positions and Employment

[redacted]

Other Experience and Professional Memberships

- [redacted]
-
-

Honors

[redacted]

C. Contribution to Science

1. Pulmonary Hypertension and Hypoxic Respiratory Failure in Term Newborns. I have focused my career on lung disease in term and preterm newborns. Early in my career I grappled with the epidemiology of pulmonary hypertension of the newborn (PPHN), treatments and outcomes. This led to my involvement in several studies evaluating inhaled nitric oxide. It has been gratifying to participate in the evolution of treatments for PPHN which led to improved survival. Now a disease that had an 80% mortality rate has

been converted to one with over 90% survival with excellent neurodevelopmental and pulmonary outcomes.

[redacted]

2. Bronchopulmonary Dysplasia (BPD).The most common morbidity of preterm birth is BPD which may lead to life-long pulmonary compromise. My work has involved improving the definition of BPD through the use of a standard room air challenge. This definition has become the standard in neonatal trials as it minimizes the impact of different oxygen saturation targets. I have contributed to several trials designed to prevent BPD including inhaled nitric oxide, postnatal corticosteroids and a CPAP-based strategy (SUPPORT Trial referenced above). [redacted]o test the utility of quality improvement strategies to reduce BPD.

[redacted]

3. Research to Improve the Conduct of Clinical Trials. I have actively contributed to research to improve the conduct of clinical trials including the complex issues around informed consent, standardizing definitions within a trial, and the emerging field of comparative effectiveness research.

[redacted]

[redacted]

D. RESEARCH SUPPORT

Ongoing Research Support

[redacted]

Role: CPI

Completed Research Support

[redacted]

[redacted]

[redacted]

[redacted]

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contr butors.

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NAME: [redacted]

eRA COMMONS USER NAME (agency login): [redacted]

POSITION TITLE: [redacted]y

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
[redacted]	[redacted]	[redacted]	[redacted]

A. Personal Statement

The most challenging and dispiriting aspect of the clinical practice of maternal-fetal medicine is periviable birth. Its antecedents are often obscure, and usually its severe consequences can only be mitigated but not prevented. Thus I am excited about the prospect of participating in our proposed “Periviable Pregnancy Research Network” (PPRN). Our proposal pulls together strong, proven and productive researchers, all known to one another, with an interest in, and a commitment to beginning to understand and unravel the problem of periviable birth, with the ultimate goal of preventing it when possible and minimizing its adverse consequences when it occurs.

[redacted]

B. Positions and Honors

Positions and Employment

[redacted]

[redacted]

[redacted]

Other Experience and Professional Memberships

[redacted]

C. Contribution to Science

1. The following two decision analyses that I have conceived and led have influenced obstetric care delivery on a population level and informed National guidelines

   [redacted]

2. The following two studies, both analyses of prospectively instituted protocols, have influenced labor management in the United States and around the world. Both have been used as the basis for ACOG's labor management guidelines

   [redacted]

3. The following MFMU Network randomized trial demonstrated that 17-alpha hydroxyprogesterone caproate is not effective in preventing preterm birth in twins

[redacted]

4. The following MFMU Network randomized trial demonstrated that magnesium sulfate, when administered to women at imminent risk of early preterm birth, lowers the risk of disabling cerebral palsy in their surviving children. It is the largest trial of four on this topic, and collectively these four trials have resulted in National guidelines in the United States, Canada, Great Britain, Australia, and New Zealand (among others) for the use of magnesium sulfate to prevent cerebral palsy.

[redacted]

[redacted]

[redacted]

D. Research Support

Ongoing Research Support

[redacted]

Completed Research Support

[redacted]

[redacted]

BIOGRAPHICAL SKETCH

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NAME: [redacted]

eRA COMMONS USER NAME (credential, e.g., agency login): [redacted]

POSITION TITLE: [redacted]

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]

A. Personal Statement

I am an academic Neonatologist [redacted]at [redacted]. [redacted] is the primary teaching affiliate for [redacted]. My primary research interest is hypoxic-ischemic brain injury of late preterm and term infants. Most of my investigations are focused through the NICHD Neonatal Research Network (NRN) where I serve as the [redacted] for the [redacted]. I have successfully performed this function since [redacted]until present and in two different NRN centers. My first 17 years of research experience was laboratory based at [redacted]. In the laboratory, I developed my expertise in neuroprotection, specifically hypothermia. After the departure of the NRN Principal Investigator at [redacted], I split my research time between the laboratory and serving as the site PI for the combined [redacted] and [redacted] center [redacted]. Based on the initiation of specific neuroprotection trials with hypothermia in the NRN, I transitioned to purely clinical research and have focused on maintaining our center, first at [redacted], and now at the [redacted] as an efficient, high functioning and productive NRN center. I have had a long standing interest in hypoxic-ischemic brain injury and modification by temperature, substrate availability and magnesium concentration. Other research interests include neuroprotection for both preterm and term infants, thermal regulation and medical issues of the late preterm infant. Like all Neonatologists, I have a strong interest in improving the care of infants born at the edge of viability. As the Medical Director of the NICU, I have taken on building strong collaborations with our Obstetric and Maternal Fetal Medicine colleagues to find the best way of meeting the needs of families confronted with pregnancies at the extremes of prematurity.

[redacted]

[redacted]

B. Positions and Honors

Positions and Employment

[redacted]

Other Experience and Professional Memberships

[redacted]

Honors

[redacted]

C. Contribution to Science

1. My major contribution to the area of perinatal research early in my career has been to provide laboratory data that demonstrate the robustness of neuroprotection attributable to modest hypothermia. Chronically instrumented newborn swine were used to examine neuroprotection associated with 3°C reductions in core body temperature for hypoxic-ischemic brain injury. The latter was determined using histological assessment of neuronal injury and clinical scores of neuro-behavior of each animal up to 72 hours following the interval of hypoxia-ischemia. Whole body hypothermia initiated prior to or immediately after a hypoxic-ischemic interval was associated with less brain injury compared to animals maintained normothermic. Hypothermia was not beneficial when initiated at an interval after the insult (delayed resuscitation) and reflected the short duration of hypothermia studied (1 hour). These publications informed other investigators of changes needed in the intervention (longer duration of hypothermia following hypoxia-ischemia) and was used by others in subsequent studies to demonstrate neuroprotection. Our results represent some of the earliest observations in neonatal animals demonstrating less hypoxic-ischemic brain injury associated with relatively small changes in temperature. These studies are part of the foundation that justified moving hypothermia from the laboratory to the Neonatal Intensive Care Unit for clinical testing.

[redacted]

[redacted]

2. After transitioning to clinical research, my major contributions to perinatal research have been in conjunction with the randomized trials of hypothermia performed by the NRN. Three trials have been conducted and I have been either the [redacted] I made important contributions to the design, implementation, performance and dissemination of each of these trials. The first Hypothermia trial established cooling as the only treatment that can provide neuroprotection based on a randomized clinical trial; this study and others similar to it have changed clinical practice with the dissemination of therapeutic hypothermia throughout the neonatal community. [redacted] generated a large number of important secondary studies, some of which I served as the lead investigator. An important observation from one of these secondary studies (citation "a" below) determined that many infants in the usual care group of the first hypothermia trial had elevated esophageal temperature; furthermore, there was a strong association between death or disability at 18 months and increased esophageal temperature. This publication raised an awareness of the importance of avoiding ambient conditions which may exacerbate elevated temperatures. In addition, steps were added to the Late Hypothermia trial to minimize elevated esophageal temperatures among infants of the non-cooled control group. Data from the first hypothermia trial provided systematic data to examine the outcome of infants with a low Apgar score at 10 minutes (citation "b" below). Analyses indicated that the risk of death or disability at 18 months of age increases with progressively lower Apgar scores at 10 minutes. However a larger number of infants than expected with an Apgar score of 0 at 10 minutes (25%) did not die or have a severe/moderate disability. These observations have impacted recommendations of the 2010 International Liaison Committee on Resuscitation and Neonatal Resuscitation Program [redacted] regarding the duration of resuscitation.

[redacted]

3. Use of the NRN Generic Database allowed me to examine [redacted] infants upon admission to Neonatal Intensive Care Units of [redacted]

recognized that premature infants can quickly drop their temperature following birth and avoidance of cold stress has been part of the Neonatal Resuscitation Program steps for newborn stabilization. Our survey of NRN centers reported unexpectedly very high rates of low admission temperatures which were affected by center, gestational age and extent of stabilization needed in the delivery room. Lower admission temperature was also associated with an increase in mortality and late onset sepsis. Whether the latter observations are simply markers of acuity or in the causal pathway is not clear. This paper triggered a large number of other investigations examining how well delivery services can prevent cold stress as a quality marker. I am currently reviewing data of admission temperatures from [redacted] centers to assess performance in a more contemporary cohort when practices have evolved with multiple interventions implemented to avoid cold stress at birth.

[redacted]

4. Based on my participation in the NRN Benchmarking trial (citation "a"), I have continued to study different aspects of BPD in our NICU. As part of an intervention in conjunction with the Benchmarking trial, we changed our pulse oximeter alarm limits and oxygen saturation goal range at [redacted] to reduce high values. We prospectively collected down loads of oxygen saturation for infants in oxygen to determine changes in the distribution of oxygen saturation. The altered goal range and alarm limits reduced the time with oxygen saturation values above the upper alarm limit, but was associated with an unexpected increase in the time with lower oxygen saturations (< 80%). This finding has implications for centers that may change their oxygen saturation goals and alarms in response to the recent oxygen saturation target trials. We recently published (citation "d") a prospective cohort of infants < 28 weeks gestation to determine the incidence of early pulmonary hypertension (at 10-14 days, diagnosed by echocardiography) and the association with BPD at 36 weeks post-menstrual age. These observations are important in view of concerns raised in the literature about whether all premature infants should be screened for pulmonary hypertension at different time points of their hospitalization.

[redacted]

Complete List of Published Work in MyBibliography:

[redacted]

D. Research Support

Ongoing Research Support

[redacted]

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contr butors.

Follow this format for each person. DO NOT EXCEED FIVE PAGES.

NAME: [redacted]

eRA COMMONS USER NAME (agency login): [redacted]

POSITION TITLE: [redacted]

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]

A. Personal Statement

I am personally committed to supporting the development of the [redacted]. When I returned to academic medicine in [redacted], I joined the [redacted] because of the commitment to clinical research as reflected in membership in the NRN. Continued participation in neonatal clinical studies is our division's first priority. I believe that my background and experience have prepared me to contribute to neonatal research projects. I have formal training in research methods with a degree in [redacted] from [redacted]. I completed a certificate degree in [redacted] with [redacted] graduate hours in [redacted] at the [redacted]. I have discussed clinical research projects with many parents and have personally obtained consent for participation many times. I have a long-standing interest in periviable birth, as seen in the following publications.

[redacted]

B. Positions and Honors

Positions and Employment

[redacted]

[redacted]

Other Experience and Professional Memberships

[redacted]

Honors

[redacted]

C. Contribution to Science

1. I published an important conceptual paper in [redacted]. This was the first publication articulating the problem of [redacted] – specifically over representation of small for dates newborns and under representation of well grown newborns. The paper continues to be cited regularly. Although the co-authors contributed to the paper in a number of ways, the idea for paper originated entirely with the first author.

   [redacted]

2. Since joining the [redacted] at [redacted] in [redacted], I have had the opportunity to contribute to scholarly discussions regarding treatment of newborns delivered near the limits of viability.

   [redacted]

3. More recently I have become very involved in the question of the possibility of unrecognized harm secondary to phototherapy among the most premature newborns. I am currently overseeing the day to day details of a multicenter pilot study testing the effectiveness of cycled phototherapy.

.

[redacted]

D. Research Support

[redacted]

Completed Research Support

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contr butors.

Follow this format for each person. DO NOT EXCEED FIVE PAGES.

NAME: [redacted]

eRA COMMONS USER NAME (agency login): [redacted]

POSITION TITLE: [redacted]

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
[redacted]	[redacted]	[redacted]	[redacted]

A. Personal Statement

I have the experience, expertise, and objective evidence to be the MFM investigator at [redacted] for the [redacted]. To this job I bring clinical experience of over [redacted] years of working in the [redacted], [redacted] years in private practice, and the [redacted] years spent in academics. In my first [redacted] years of being in [redacted], we successfully started the only [redacted] in [redacted]; I was its director from 2[redacted], and published [redacted] peer reviewed articles during that time. But to collaborate with other clinical researchers and contribute to the best clinical trials in obstetrics, I moved to [redacted] in [redacted] to actively participate in the MFMU Network.

Though new to the Network, it should be noted that in the last [redacted] years I have [redacted] reviewed publications, [redacted] of which were randomized clinical trials (RCT). Matter of fact, [redacted] as a resident [redacted] and as a fellow were RCTs [redacted]. Congruent with [redacted] major aims, we have published [redacted] articles on preterm, including a recent RCT on the use of 17-hydroxyprogeserone with arrest of preterm labor [redacted]. [redacted] and [redacted] publications on fetal growth abnormalities.

While in private practice, we published multi-centered studies (Ref 1, 2). To enable obstetric residents and MFM fellows to do multi-centered investigations, I successfully proposed FAR (Fellows And Residents) [redacted], which has consistently published their findings. In [redacted] and [redacted], I have published secondary analyses of MFMU data [redacted]. In the first year as an [redacted], we had two proposals [redacted] and collaboratively published with two centers in the MFMU Network [redacted].

Lastly, understanding the commitments for this project, my Chairperson has ensured that I have no other major [redacted], except being a member of IRB and being a [redacted], both of which enhance my capabilities as one of the investigators of the [redacted].

[redacted]

[redacted]

B. Positions and Honors

Positions and Employment

[redacted]

Other Experience and Professional Memberships

[redacted]

Honors

[redacted]

C. Contribution to Science

1. My contribution to obstetric literature is exemplified by the following: 1) publications being cited in over [redacted] instances; 2) H-index of [redacted] 3) being co-author of [redacted] publications that were categorized in the [redacted]; 4) participation in publication of [redacted] national guidelines, [redacted] for [redacted] and [redacted] for [redacted] 5) being a member of [redacted] for neonatal brachial plexus palsy and contributing to the publication on neonatal encephalopathy and neurologic outcomes; and [redacted] pregnancy [redacted]. The diversity of my scholarly activities is demonstrated by multiple peer-reviewed publications on a specific topic: [redacted] on cesarean delivery, [redacted] on amniotic fluid, [redacted] on fetal growth restriction, [redacted] on macrosomia, [redacted] on estimated fetal weight, and [redacted] on shoulder dystocia and its complications. A suggestion that one's publication has influenced clinical practice in the US is that it is referenced in Practice Bulletins published by American College of Obstetricians and Gynecologists (ACOG). Our work has been cited in [redacted] different bulletins on obstetric topics. The current ACOG recommendations that clinical and sonographic estimate have similar accuracy in the detection of macrosomic newborn and that maximum vertical pocket, not amniotic fluid index, should be used to assess amniotic fluid are linked to our publications.

[redacted]

[redacted]

D. Research Support

Ongoing Research Support

[redacted]

Completed Research Support

[redacted]

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contr butors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: [redacted]

eRA COMMONS USER NAME (credential, e.g., agency login): [redacted]

POSITION TITLE: [redacted]

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]

A. Personal Statement

This project seeks to set up a periviable pregnancy database, which will provide the necessary information to develop hypotheses and design studies in this population (20-25w GA), in addition to serving as a resource to understand the characteristics of periviable pregnancy and its outcomes. I have provided biostatistical leadership for clinical trials and studies on a similar population of newborn infants for 16 years as a senior [redacted] for the [redacted] and helped design all the recently conducted and currently ongoing NRN studies from their inception. Aside from biostatistical leadership, as PI for the DCC, I lead our efforts in data management and operational support. The team under my direction provides crucial biostatistical input from study conception, design, implementation, to final analysis, and publication; data management support; and facilitates communication across collaborating institutions. I have several publications examining the intricacies and correlates of clinical care and outcomes in neonates. I specialize in the design of intervention studies, including randomized clinical trials (RCTs), and modeling, analysis and interpretation of public health data. I have helped conduct research on neonatal and neurodevelopmental morbidities in premature babies, fetal alcohol effects, longitudinal effects of prenatal substance use on child developmental trajectories, cluster-randomized trials to reduce adolescent pregnancies, and intervention studies of maternal-infant nutrition in developing countries. I have extensive experience in leading DCCs that provide statistical, data management and logistical support to collaborative multicenter clinical research networks. In summary, I have helped conceptualize, design, develop, implement, monitor, analyze, and publish the results from more than a dozen studies in periviable birth settings over the last [redacted] years. I have a demonstrated record of successful and productive collaborative clinical research in this area that is ideally suited for my role in leading the Data Coordinating Center for the proposed Periviable Perinatal Research Network.

[redacted]

[redacted]

B. Positions and Honors

Positions and Employment

[redacted]

Professional Memberships

[redacted]

Honors

[redacted]

C. Contributions to Science

1. Design and analysis of observational studies in [redacted] As a biostatistician, my contributions to science have been primarily through collaborations with public health researchers on the statistical design and analyses of epidemiologic studies and randomized clinical trials. Developing the evidence base for neonatal medicine often requires conducting rigorous observational studies both in situations where randomized trials are impossible (because of lack of preliminary data, ethical concerns or lack of equipoise among neonatologists) and for Phase 4 effectiveness studies. I have been instrumental in the selection, review, design, analyses, and reporting of numerous such studies conducted by the [redacted], many of them seminal studies whose influence on clinical practice is demonstrated by their citations in American Academy of Pediatrics (AAP) and American Congress of Obstetricians and Gynecologists (ACOG) policy

statements, practice guidelines, and clinical reports on a variety of topics, including management of neonates at the threshold of viability, neonatal sepsis, developmental follow-up, use of surfactants and steroids (ante and postnatal), and breast feeding.

[redacted]

2. Design and analysis of RCTs in neonatology. Modern neonatology has introduced a number of principles of management and innovative methodologies for patient care without rigorous evaluation of efficacy and safety through randomized controlled trials (RCTs). Because of the urgent demands of sick infants, care is often based on limited knowledge of new treatment modalities. Dramatic advances in survival of extremely premature babies in the past have led to more incremental improvements in recent years, with in-hospital morbidities such as BPD and long-term neurodevelopmental outcomes still leaving much room for improvement. As the principal [redacted] for the [redacted] over the last [redacted] years, I have led the statistical design for at least 14 multicenter [redacted] from inception through implementation, interim/final analyses, and publication. Trials I have helped design and analyze in neonatal/perinatal settings have spanned a variety of designs (factorial, Bayesian, comprehensive cohort, cluster randomized, phase II dosing, and PK) and settings (comparative effectiveness, drug development, investigational therapies, and behavioral interventions), and have often changed clinical practice.

[redacted]

[redacted]

3. Design and analysis of international studies in maternal and child health. Sub-optimal nutrition among women of childbearing age and pregnant women in developing countries has been implicated as a principal reason for poor birth outcomes (such as low birth weight, length and IUGR), and continued poor growth and stunting into childhood. Optimal intervention studies that can effectively and sustainably isolate and target this problem in a consistent manner across the developing world are thus needed. I have been the principal statistician on a number of such studies in the international setting, leading their conceptualization, statistical design, formulation and execution of interim and final data analyses, study implementation and dissemination of results. Collectively, these studies have significantly increased our knowledge of the issues, opportunities and workable solutions in this important area of research.

[redacted]

Complete list of published work in MyBibliography:

[redacted]

D. Research Support

Ongoing Research Support

[redacted]

[redacted]

[redacted]

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 1

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: [redacted]

Start Date*: 07-01-2016 **End Date*:** 06-30-2017 **Budget Period: 1**

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1 .		[redacted]		[redacted]		[redacted]	[redacted]	1.20			16,535.00	4,977.00	21,512.00
2 .		[redacted]	[redacted]	[redacted]		[redacted]	[redacted]	0.60			9,165.00	2,759.00	11,924.00
3 .		[redacted]		[redacted]		[redacted]	[redacted]	0.60			9,165.00	2,759.00	11,924.00
4 .		[redacted]		[redacted]		[redacted]	[redacted]	0.60			6,603.00	1,988.00	8,591.00
5 .		[redacted]		[redacted]		[redacted]	[redacted]	0.60			5,749.00	1,731.00	7,480.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name:

Total Senior/Key Person **61,431.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Research Coordinator	7.20			39,120.00	13,575.00	52,695.00
1	**Total Number Other Personnel**					**Total Other Personnel**	**52,695.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**114,126.00**

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 1

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ● Project ❍ Subaward/Consortium

Organization: [redacted]

Start Date*: 07-01-2016 **End Date*:** 06-30-2017 **Budget Period: 1**

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	
Total Equipment	

Additional Equipment: File Name:

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	4,868.00
2. Foreign Travel Costs	
Total Travel Cost	**4,868.00**

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 1

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ● Project ❍ Subaward/Consortium

Organization: [redacted]

Start Date*: 07-01-2016 **End Date*:** 06-30-2017 **Budget Period: 1**

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	
2. Publication Costs	
3. Consultant Services	
4. ADP/Computer Services	
5. Subawards/Consortium/Contractual Costs	624,012.00
6. Equipment or Facility Rental/User Fees	
7. Alterations and Renovations	
Total Other Direct Costs	**624,012.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**743,006.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . MTDC	47.00	118,994.00	55,927.00
2 . MTDC	47.00	100,000.00	47,000.00
		Total Indirect Costs	**102,927.00**

Cognizant Federal Agency [redacted]

(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**845,933.00**

J. Fee	Funds Requested ($)*

K. Budget Justification* File Name: 1234-Budget [redacted]

(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

Tracking Number: [redacted] [redacted] Received Date: 2015-10-01T15:46:46.000-04:00

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 2

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: [redacted]

Start Date*: 07-01-2017 **End Date*:** 06-30-2018 **Budget Period: 2**

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1 .		[redacted]		[redacted]		[redacted]	[redacted]	1.20			16,535.00	4,977.00	21,512.00
2 .		[redacted]	[redacted]	[redacted]		[redacted]	[redacted]	0.60			9,165.00	2,759.00	11,924.00
3 .		[redacted]		[redacted]		[redacted]	[redacted]	0.60			9,165.00	2,759.00	11,924.00
4 .		[redacted]		[redacted]		[redacted]	[redacted]	1.20			13,207.00	3,975.00	17,182.00
5 .		[redacted]		[redacted]		[redacted]	[redacted]	0.60			5,750.00	1,731.00	7,481.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name:

Total Senior/Key Person **70,023.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Research Coordinator	12.00			65,200.00	22,624.00	87,824.00
1	**Total Number Other Personnel**					**Total Other Personnel**	**87,824.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**157,847.00**

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 2

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ● Project ❍ Subaward/Consortium

Organization: [redacted]

Start Date*: 07-01-2017 **End Date*:** 06-30-2018 **Budget Period: 2**

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	
Total Equipment	

Additional Equipment: File Name:

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	0.00
2. Foreign Travel Costs	
Total Travel Cost	**0.00**

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 2

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ● Project ❍ Subaward/Consortium

Organization: [redacted]

Start Date*: 07-01-2017 **End Date*:** 06-30-2018 **Budget Period: 2**

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	
2. Publication Costs	
3. Consultant Services	
4. ADP/Computer Services	
5. Subawards/Consortium/Contractual Costs	554,452.00
6. Equipment or Facility Rental/User Fees	
7. Alterations and Renovations	
Total Other Direct Costs	**554,452.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**712,299.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . MTDC	47.00	157,847.00	74,188.00
		Total Indirect Costs	**74,188.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number): DHHS, Steven Zurf, 301-492-4855

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**786,487.00**

J. Fee	Funds Requested ($)*

K. Budget Justification* File Name: 1234-Budget [redacted]

(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

[redacted]

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 3

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: [redacted]

Start Date*: 07-01-2018 **End Date*:** 06-30-2019 **Budget Period:** 3

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1.		[redacted]		[redacted]		[redacted]	[redacted]	1.20			16,535.00	4,977.00	21,512.00
2.		[redacted]	[redacted]	[redacted]		[redacted]	[redacted]	0.60			9,165.00	2,759.00	11,924.00
3.		[redacted]		[redacted]		[redacted]	[redacted]	0.60			9,165.00	2,759.00	11,924.00
4.		[redacted]		[redacted]		[redacted]	[redacted]	1.20			13,207.00	3,975.00	17,182.00
5.		[redacted]		[redacted]		[redacted]	[redacted]	0.60			5,750.00	1,731.00	7,481.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name:

Total Senior/Key Person **70,023.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Research Coordinator	12.00			65,200.00	22,624.00	87,824.00
1	**Total Number Other Personnel**					**Total Other Personnel**	**87,824.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**157,847.00**

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 3

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ● Project ❍ Subaward/Consortium

Organization: [redacted]

Start Date*: 07-01-2018 **End Date*:** 06-30-2019 **Budget Period: 3**

C. Equipment Description

List items and dollar amount for each item exceeding $5,000

Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	
Total Equipment	

Additional Equipment: File Name:

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	2,034.00
2. Foreign Travel Costs	
Total Travel Cost	**2,034.00**

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 3

ORGANIZATIONAL DUNS*: [redacted]
Budget Type*: ● Project ○ Subaward/Consortium
Organization: [redacted]

Start Date*: 07-01-2018 **End Date*:** 06-30-2019 **Budget Period:** 3

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	2,000.00
2. Publication Costs	
3. Consultant Services	
4. ADP/Computer Services	
5. Subawards/Consortium/Contractual Costs	547,207.00
6. Equipment or Facility Rental/User Fees	
7. Alterations and Renovations	
Total Other Direct Costs	**549,207.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**709,088.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . MTDC	47.00	161,881.00	76,084.00
		Total Indirect Costs	**76,084.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number): DHHS, Steven Zurf, 301-492-4855

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**785,172.00**

J. Fee	Funds Requested ($)*

K. Budget Justification* File Name: 1234-Budget
[redacted]
(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 4

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: [redacted]

Start Date*: 07-01-2019 **End Date*:** 06-30-2020 **Budget Period: 4**

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1 .		[redacted]		[redacted]		[redacted]	[redacted]	1.20			16,535.00	4,977.00	21,512.00
2 .		[redacted]	[redacted]	[redacted]		[redacted]	[redacted]	0.60			9,165.00	2,759.00	11,924.00
3 .		[redacted]		[redacted]		[redacted]	[redacted]	0.60			9,165.00	2,759.00	11,924.00
4 .		[redacted]		[redacted]		[redacted]	[redacted]	1.20			13,207.00	3,975.00	17,182.00
5 .		[redacted]		[redacted]		[redacted]	[redacted]	0.60			5,750.00	1,731.00	7,481.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name:

Total Senior/Key Person **70,023.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Research Coordinator	12.00			65,200.00	22,624.00	87,824.00
1	**Total Number Other Personnel**					**Total Other Personnel**	**87,824.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**157,847.00**

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 4

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ● Project ❍ Subaward/Consortium

Organization: [redacted]

Start Date*: 07-01-2019 **End Date*:** 06-30-2020 **Budget Period: 4**

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	
Total Equipment	
Additional Equipment: File Name:	

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	2,387.00
2. Foreign Travel Costs	
Total Travel Cost	**2,387.00**

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 5

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: [redacted]

Start Date*: 07-01-2020 **End Date*:** 06-30-2021 **Budget Period: 5**

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1 .		[redacted]		[redacted]		[redacted]	[redacted]	0.60			8,267.00	2,489.00	10,756.00
2 .		[redacted]	[redacted]	[redacted]		[redacted]	[redacted]	0.60			9,165.00	2,759.00	11,924.00
3 .		[redacted]		[redacted]		[redacted]	[redacted]	0.60			9,165.00	2,759.00	11,924.00
4 .		[redacted]		[redacted]		[redacted]	[redacted]	0.60			6,603.00	1,988.00	8,591.00
5 .		[redacted]		[redacted]		[redacted]	[redacted]	0.60			5,749.00	1,731.00	7,480.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name:

Total Senior/Key Person **50,675.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Research Coordinator	6.48			35,208.00	12,217.00	47,425.00
1	**Total Number Other Personnel**					**Total Other Personnel**	**47,425.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**98,100.00**

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 5

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ● Project ❍ Subaward/Consortium

Organization: [redacted]

Start Date*: 07-01-2020 **End Date*:** 06-30-2021 **Budget Period: 5**

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	
Total Equipment	
Additional Equipment: File Name:	

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	1,035.00
2. Foreign Travel Costs	
Total Travel Cost	**1,035.00**

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 5

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ● Project ❍ Subaward/Consortium

Organization: [redacted]

Start Date*: 07-01-2020 **End Date*:** 06-30-2021 **Budget Period: 5**

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	
2. Publication Costs	
3. Consultant Services	
4. ADP/Computer Services	
5. Subawards/Consortium/Contractual Costs	659,574.00
6. Equipment or Facility Rental/User Fees	
7. Alterations and Renovations	
Total Other Direct Costs	**659,574.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**758,709.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . MTDC	47.00	99,135.00	46,593.00
		Total Indirect Costs	**46,593.00**

Cognizant Federal Agency [redacted]
(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**805,302.00**

J. Fee	Funds Requested ($)*

K. Budget Justification* File Name: 1234-Budget
[redacted]
(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

TITLE

Periviable Pregnancy Research Network (PPRN)

DETAILED BUDGET

The following IDC and fringe rates were used: [redacted] Indirect cost recovery rate is 47%, fringe benefits are 30.10% faculty and 34.7% staff.

PERSONNEL [redacted]

[redacted] 1.2 calendar months

[redacted] 0.6 calendar months

[redacted] 0.6 calendar months

[redacted] 0.6 calendar months

[redacted] 0.6 calendar months

Technical personnel:

Research Coordinator (TBD) 7.2 calendar months

PERSONNEL [redacted]

[redacted] 1.2 calendar months

[redacted] 0.6 calendar months

[redacted] 0.6 calendar months

[redacted] 1.2 calendar months

[redacted] 0.6 calendar months

Technical personnel:

Research Coordinator (TBD) 12 calendar months

PERSONNEL [redacted]

[redacted] 1.2 calendar months

[redacted] 0.6 calendar months

[redacted] 0.6 calendar months

[redacted] 0.6 calendar months

[redacted] 0.6 calendar months

Technical personnel:

Research Coordinator (TBD) 6.48 calendar months

[redacted] will devote 1.2 calendar months of [redacted] effort to this project. [redacted] will be responsible for the design of all experiments and the overall planning, coordination and conduct of the program. [redacted] will take responsibility coordinating among the investigators and research coordinators at the research centers, and the data coordinating center. [redacted] will oversee preparation of experimental results for publication. [redacted] will supervise the Research Coordinator, and closely work with [redacted] and [redacted] on patient enrollment, data collection, and other aspects of the study. [redacted] has been working in the Regional NICU as an Attending Physician since [redacted], and has led several single-center randomized trials and observational studies, in addition to multicenter projects within the NICHD Neonatal Research Network (for which he is the [redacted]). [redacted] will be responsible for submitting all necessary documents to NIH including annual progress reports.

[redacted] will devote 0.6 calendar months of his time to the project. [redacted] is the [redacted] at [redacted], and is the center PI for the NICHD Neonatal Research Network. [redacted] has designed and led multiple single-center and multicenter randomized clinical trials and observational studies. [redacted] will provide the PI with assistance on patient enrollment, and with development of the decision support systems and their validation.

[redacted] will devote 0.6 calendar months of [redacted] time to the project. [redacted] is a Maternal-Fetal Medicine Specialist at [redacted], and is the center PI for the [redacted]. [redacted] has designed and led multiple single-center and multicenter randomized clinical trials and observational studies. [redacted] will provide the PI with assistance on patient enrollment, and with experimental design, and coordination of the studies among the centers.

[redacted], will devote 0.6 calendar months of [redacted] time to the project in Yr 1 (and Yr 5) and 1.2 cal mo/yr in Years 2-4. He is an [redacted] in the [redacted], and will develop the models and analyses for Aims 2 and 3.

[redacted], will devote 0.6 calendar months of [redacted] time to the project [redacted] is Associate Professor in the [redacted], [redacted], and [redacted]. [redacted] will assist with the psychological surveys in Aims 2 and 3, and with analyses of the resulting data.

Research Coordinator (TBD), will devote 7.2 calendar months of his/her time to the project in Year 1 (increasing to 12 calendar months in Years 2-4, and decreasing to 6.48 months in Yr 5). The research coordinator will be in charge of patient enrollment, data collection, and assist with regulatory paperwork (IRB) and other record-keeping.

TRAVEL $4868 in Year 1, $2034 in Yr 3, $2387 in Yr 4, $1035 in Yr 5
One trip for PI and co-investigators for face-to-face discussion with other PIs (in addition to meeting at SMFM, PAS, weekly teleconferencing).

SUPPLIES
Supplies needed for study for processing of samples: $2000 in Yr 3, $6000 in Yr 4

OTHER DIRECT COSTS IN YEAR 1

Subawards/Consortium/Contractual Costs to [redacted] $ 138,600 (includes direct cost of $90,000 + IDC of $48,600)
Subawards/Consortium/Contractual Costs to [redacted] $144,180 (includes direct cost of $90,000 + IDC of $54,180)
Subawards/Consortium/Contractual Costs to [redacted] $142,579 (includes direct cost of $89,955 + IDC of 52,264)
Subawards/Consortium/Contractual Costs to [redacted] $ 198,653 (includes direct cost of $110,952+ IDC of $87,701)

OTHER DIRECT COSTS IN YEAR 2

Subawards/Consortium/Contractual Costs to [redacted]n $ 138,600 (includes direct cost of $90,000 + IDC of $48,600)
Subawards/Consortium/Contractual Costs to [redacted] $144,180 (includes direct cost of $90,000 + IDC of $54,180)
Subawards/Consortium/Contractual Costs to [redacted] $142,579 (includes direct cost of $89,955 + IDC of 52,264)
Subawards/Consortium/Contractual Costs to [redacted]$ 129,093 (includes direct cost of $72,111+ IDC of $56,982)

OTHER DIRECT COSTS IN YEAR 3

Subawards/Consortium/Contractual Costs to [redacted] $ 138,600 (includes direct cost of $90,000 + IDC of $48,600)
Subawards/Consortium/Contractual Costs to [redacted] $144,180 (includes direct cost of $90,000 + IDC of $54,180)
Subawards/Consortium/Contractual Costs to [redacted] $142,579 (includes direct cost of $89,955 + IDC of 52,264)
Subawards/Consortium/Contractual Costs to [redacted] $ 121,848 (includes direct cost of $68,065+ IDC of $53,783)

OTHER DIRECT COSTS IN YEAR 4

Subawards/Consortium/Contractual Costs to [redacted]$ 138,600 (includes direct cost of $90,000 + IDC of $48,600)
Subawards/Consortium/Contractual Costs to [redacted] $144,180 (includes direct cost of $90,000 + IDC of $54,180)
Subawards/Consortium/Contractual Costs to [redacted] $142,579 (includes direct cost of $89,955 + IDC of 52,264)
Subawards/Consortium/Contractual Costs to [redacted]$ 114,053 (includes direct cost of $63,712+ IDC of $50,341)

OTHER DIRECT COSTS IN YEAR 5

Subawards/Consortium/Contractual Costs to [redacted] $ 138,600 (includes direct cost of $90,000 + IDC of $48,600)
Subawards/Consortium/Contractual Costs to [redacted] $144,180 (includes direct cost of $90,000 + IDC of $54,180)
Subawards/Consortium/Contractual Costs to [redacted] $142,579 (includes direct cost of $89,955 + IDC of 52,264)
Subawards/Consortium/Contractual Costs to [redacted] $ 234,215 (includes direct cost of $130,810+IDC of $103,405)

RESEARCH & RELATED BUDGET - Cumulative Budget

	Totals ($)	
Section A, Senior/Key Person		322,175.00
Section B, Other Personnel		363,592.00
Total Number Other Personnel	5	
Total Salary, Wages and Fringe Benefits (A+B)		685,767.00
Section C, Equipment		
Section D, Travel		10,324.00
1. Domestic	10,324.00	
2. Foreign		
Section E, Participant/Trainee Support Costs		
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other		
6. Number of Participants/Trainees		
Section F, Other Direct Costs		2,932,657.00
1. Materials and Supplies	8,000.00	
2. Publication Costs		
3. Consultant Services		
4. ADP/Computer Services		
5. Subawards/Consortium/Contractual Costs	2,924,657.00	
6. Equipment or Facility Rental/User Fees		
7. Alterations and Renovations		
8. Other 1		
9. Other 2		
10. Other 3		
Section G, Direct Costs (A thru F)		3,628,748.00
Section H, Indirect Costs		377,922.00
Section I, Total Direct and Indirect Costs (G + H)		4,006,670.00
Section J, Fee		

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 1

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ❍ Project ● Subaward/Consortium

Enter name of Organization: [redacted]

Start Date*: 07-01-2016 **End Date*:** 06-30-2017 **Budget Period: 1**

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1 .		[redacted]		[redacted]	[redacted]	[redacted]		0.60			9,165.00	3,034.00	12,199.00
2 .		[redacted]		[redacted]	[redacted]	[redacted]		0.60			9,165.00	3,034.00	12,199.00
3 .		TBA		TBA		[redacted]		12.00			49,288.00	16,314.00	65,602.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name:

Total Senior/Key Person **90,000.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Total Number Other Personnel					**Total Other Personnel**	
						Total Salary, Wages and Fringe Benefits (A+B)	**90,000.00**

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 1

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ❍ Project ● Subaward/Consortium

Organization: [redacted]

Start Date*: 07-01-2016 **End Date*:** 06-30-2017 **Budget Period: 1**

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	
Total Equipment	
Additional Equipment: File Name:	

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	
2. Foreign Travel Costs	
Total Travel Cost	

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 1

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ❍ Project ● Subaward/Consortium

Organization: Brown University

Start Date*: 07-01-2016 **End Date*:** 06-30-2017 **Budget Period: 1**

F. Other Direct Costs	Funds Requested ($)*
Total Other Direct Costs	

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	90,000.00

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . Modified Total Direct Cost	60.20	90,000.00	54,180.00
		Total Indirect Costs	54,180.00

Cognizant Federal Agency [redacted]
(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	144,180.00

J. Fee	Funds Requested ($)*

K. Budget Justification* File Name: 1235-[redacted]BudgetJustif091815.pdf
(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 2

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ❍ Project ● Subaward/Consortium

Enter name of Organization: [redacted]

Start Date*: 07-01-2017 **End Date*:** 06-30-2018 **Budget Period: 2**

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1 .		[redacted]		[redacted]	MD	[redacted]		0.60			9,165.00	3,034.00	12,199.00
2 .		[redacted]t		[redacted]	MD	[redacted]		0.60			9,165.00	3,034.00	12,199.00
3 .		TBA		TBA		[redacted]		12.00			49,288.00	16,314.00	65,602.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name:

Total Senior/Key Person **90,000.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Total Number Other Personnel					**Total Other Personnel**	
						Total Salary, Wages and Fringe Benefits (A+B)	**90,000.00**

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 2

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ❍ Project ● Subaward/Consortium

Organization: [redacted]

Start Date*: 07-01-2017 **End Date*:** 06-30-2018 **Budget Period: 2**

C. Equipment Description

List items and dollar amount for each item exceeding $5,000

Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	
Total Equipment	

Additional Equipment: File Name:

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	
2. Foreign Travel Costs	
Total Travel Cost	

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 2

ORGANIZATIONAL DUNS*: [redacted]
Budget Type*: ○ Project ● Subaward/Consortium
Organization: [redacted]

Start Date*: 07-01-2017 **End Date*:** 06-30-2018 **Budget Period:** 2

F. Other Direct Costs	Funds Requested ($)*
Total Other Direct Costs	

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	90,000.00

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . Modified Total Direct Cost	60.20	90,000.00	54,180.00
		Total Indirect Costs	54,180.00

Cognizant Federal Agency [redacted]
(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	144,180.00

J. Fee	Funds Requested ($)*

K. Budget Justification* File Name: 1235-[redacted]BudgetJustif091815.pdf
(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 3

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ❍ Project ● Subaward/Consortium

Enter name of Organization: [redacted]

Start Date*: 07-01-2018 **End Date*:** 06-30-2019 **Budget Period: 3**

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1 .		[redacted]		[redacted]	[redacted]	[redacted]		0.60			9,165.00	3,034.00	12,199.00
2 .		[redacted]		[redacted]	MD	[redacted]		0.60			9,165.00	3,034.00	12,199.00
3 .		TBA		TBA		Research Coordinator		12.00			49,288.00	16,314.00	65,602.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name:

Total Senior/Key Person **90,000.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Total Number Other Personnel					**Total Other Personnel**	
						Total Salary, Wages and Fringe Benefits (A+B)	**90,000.00**

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 3

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ❍ Project ● Subaward/Consortium

Organization: [redacted]

Start Date*: 07-01-2018 **End Date*:** 06-30-2019 **Budget Period: 3**

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	
Total Equipment	
Additional Equipment: File Name:	

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	
2. Foreign Travel Costs	
Total Travel Cost	

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 3

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ❍ Project ● Subaward/Consortium

Organization [redacted]

Start Date*: 07-01-2018 **End Date*:** 06-30-2019 **Budget Period: 3**

F. Other Direct Costs	Funds Requested ($)*
Total Other Direct Costs	

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	90,000.00

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . Modified Total Direct Cost	60.20	90,000.00	54,180.00
		Total Indirect Costs	54,180.00

Cognizant Federal Agency [redacted]
(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	144,180.00

J. Fee	Funds Requested ($)*

K. Budget Justification* File Name: 1235-[redacted]BudgetJustif091815.pdf
(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 4

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ○ Project ● Subaward/Consortium

Enter name of Organization: [redacted]

Start Date*: 07-01-2019 **End Date*:** 06-30-2020 **Budget Period:** 4

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1.		[redacted]		[redacted]		[redacted]		0.60			9,165.00	3,034.00	12,199.00
2.		[redacted]		[redacted]e		[redacted]		0.60			9,165.00	3,034.00	12,199.00
3.		TBA		TBA		[redacted]		12.00			49,288.00	16,314.00	65,602.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name:

Total Senior/Key Person **90,000.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*

Total Number Other Personnel **Total Other Personnel**

Total Salary, Wages and Fringe Benefits (A+B) **90,000.00**

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 4

ORGANIZATIONAL DUNS*: 0698519130000
Budget Type*: ❍ Project ● Subaward/Consortium
Organization: [redacted]

Start Date*: 07-01-2019 **End Date*:** 06-30-2020 **Budget Period: 4**

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	
Total Equipment	
Additional Equipment: File Name:	

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	
2. Foreign Travel Costs	
Total Travel Cost	

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 4

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ❍ Project ● Subaward/Consortium

Organization: [redacted]

Start Date*: 07-01-2019 **End Date*:** 06-30-2020 **Budget Period: 4**

F. Other Direct Costs	Funds Requested ($)*
Total Other Direct Costs	

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**90,000.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . Modified Total Direct Cost	60.20	90,000.00	54,180.00
		Total Indirect Costs	**54,180.00**

Cognizant Federal Agency [redacted]
(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**144,180.00**

J. Fee	Funds Requested ($)*

K. Budget Justification* File Name: 1235-[redacted]BudgetJustif091815.pdf
(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 5

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ❍ Project ● Subaward/Consortium

Enter name of Organization: [redacted]

Start Date*: 07-01-2020 **End Date*:** 06-30-2021 **Budget Period: 5**

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1 .		[redacted]		[redacted]	[redacted]	[redacted]		0.60			9,165.00	3,034.00	12,199.00
2 .		[redacted]		[redacted]	[redacted]	[redacted]		0.60			9,165.00	3,034.00	12,199.00
3 .		TBA		TBA		Research Coordinator		12.00			49,288.00	16,314.00	65,602.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name:

Total Senior/Key Person **90,000.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Total Number Other Personnel					**Total Other Personnel**	
						Total Salary, Wages and Fringe Benefits (A+B)	**90,000.00**

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 5

ORGANIZATIONAL DUNS*: [redacted]
Budget Type*: ○ Project ● Subaward/Consortium
Organization: [redacted]

Start Date*: 07-01-2020 **End Date*:** 06-30-2021 **Budget Period:** 5

C. Equipment Description

List items and dollar amount for each item exceeding $5,000

Equipment Item **Funds Requested ($)***

Total funds requested for all equipment listed in the attached file

Total Equipment

Additional Equipment: File Name:

D. Travel **Funds Requested ($)***

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)
2. Foreign Travel Costs

Total Travel Cost

E. Participant/Trainee Support Costs **Funds Requested ($)***

1. Tuition/Fees/Health Insurance
2. Stipends
3. Travel
4. Subsistence
5. Other:

Number of Participants/Trainees **Total Participant Trainee Support Costs**

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 5

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ❍ Project ● Subaward/Consortium

Organization: [redacted]

Start Date*: 07-01-2020 **End Date*:** 06-30-2021 **Budget Period: 5**

F. Other Direct Costs	Funds Requested ($)*
Total Other Direct Costs	

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**90,000.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . Modified Total Direct Cost	60.20	90,000.00	54,180.00
		Total Indirect Costs	**54,180.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number) DHHS Robert I. Aaronson 1-212-264-1823

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**144,180.00**

J. Fee	Funds Requested ($)*

K. Budget Justification* File Name: 1235-[redacted]BudgetJustif091815.pdf

(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

Budget Justification

[redacted]

RESEARCH & RELATED BUDGET - Cumulative Budget

	Totals ($)
Section A, Senior/Key Person	450,000.00
Section B, Other Personnel	
Total Number Other Personnel	
Total Salary, Wages and Fringe Benefits (A+B)	450,000.00
Section C, Equipment	
Section D, Travel	
1. Domestic	
2. Foreign	
Section E, Participant/Trainee Support Costs	
1. Tuition/Fees/Health Insurance	
2. Stipends	
3. Travel	
4. Subsistence	
5. Other	
6. Number of Participants/Trainees	
Section F, Other Direct Costs	
1. Materials and Supplies	
2. Publication Costs	
3. Consultant Services	
4. ADP/Computer Services	
5. Subawards/Consortium/Contractual Costs	
6. Equipment or Facility Rental/User Fees	
7. Alterations and Renovations	
8. Other 1	
9. Other 2	
10. Other 3	
Section G, Direct Costs (A thru F)	450,000.00
Section H, Indirect Costs	270,900.00
Section I, Total Direct and Indirect Costs (G + H)	720,900.00
Section J, Fee	

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 1

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ❍ Project ● Subaward/Consortium

Enter name of Organization: [redacted]

Start Date*: 07-01-2016 **End Date*:** 06-30-2017 **Budget Period: 1**

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1 .		[redacted]	C	[redacted]	[redacted]	[redacted]	[redacted]	0.60			9,165.00	2,475.00	11,640.00
2 .		[redacted]		[redacted]	[redacted]	[redacted]	[redacted]	0.60			9,165.00	2,475.00	11,640.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name:

Total Senior/Key Person **23,280.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Research Coordinator	12.00			52,500.00	14,175.00	66,675.00
1	**Total Number Other Personnel**					**Total Other Personnel**	**66,675.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**89,955.00**

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 1

ORGANIZATIONAL DUNS*: [redacted]
Budget Type*: ○ Project ● Subaward/Consortium
Organization: [redacted]

Start Date*: 07-01-2016 **End Date*:** 06-30-2017 **Budget Period:** 1

C. Equipment Description

List items and dollar amount for each item exceeding $5,000

Equipment Item **Funds Requested ($)***

Total funds requested for all equipment listed in the attached file

Total Equipment

Additional Equipment: File Name:

D. Travel **Funds Requested ($)***

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)
2. Foreign Travel Costs

Total Travel Cost

E. Participant/Trainee Support Costs **Funds Requested ($)***

1. Tuition/Fees/Health Insurance
2. Stipends
3. Travel
4. Subsistence
5. Other:

Number of Participants/Trainees **Total Participant Trainee Support Costs**

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 1

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ❍ Project ● Subaward/Consortium

Organization: [redacted]

Start Date*: 07-01-2016 **End Date*:** 06-30-2017 **Budget Period: 1**

F. Other Direct Costs	Funds Requested ($)*
Total Other Direct Costs	

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	89,955.00

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . MTDC	58.50	89,955.00	52,624.00
		Total Indirect Costs	52,624.00

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number): Uyen Tran, DHHS 214-767-3261

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	142,579.00

J. Fee	Funds Requested ($)*

K. Budget Justification* File Name: [redacted] PPRN_Budget_Justification.pdf (Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 2

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ○ Project ● Subaward/Consortium

Enter name of Organization: [redacted]

Start Date*: 07-01-2017 **End Date*:** 06-30-2018 **Budget Period:** 2

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1.		[redacted]	C	[redacted]		[redacted]	[redacted]	0.60			9,165.00	2,475.00	11,640.00
2.		[redacted]		[redacted]		[redacted]	[redacted]	0.60			9,165.00	2,475.00	11,640.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name:

Total Senior/Key Person **23,280.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Research Coordinator	12.00			52,500.00	14,175.00	66,675.00
1	**Total Number Other Personnel**					**Total Other Personnel**	**66,675.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**89,955.00**

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 2

ORGANIZATIONAL DUNS*: [redacted]
Budget Type*: ○ Project ● Subaward/Consortium
Organization [redacted]

Start Date*: 07-01-2017 **End Date*:** 06-30-2018 **Budget Period:** 2

C. Equipment Description

List items and dollar amount for each item exceeding $5,000

Equipment Item **Funds Requested ($)***

Total funds requested for all equipment listed in the attached file

Total Equipment

Additional Equipment: File Name:

D. Travel **Funds Requested ($)***

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)
2. Foreign Travel Costs

Total Travel Cost

E. Participant/Trainee Support Costs **Funds Requested ($)***

1. Tuition/Fees/Health Insurance
2. Stipends
3. Travel
4. Subsistence
5. Other:

Number of Participants/Trainees **Total Participant Trainee Support Costs**

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 2

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ❍ Project ● Subaward/Consortium

Organization: [redacted]

Start Date*: 07-01-2017 **End Date*:** 06-30-2018 **Budget Period: 2**

F. Other Direct Costs	Funds Requested ($)*
Total Other Direct Costs	

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	89,955.00

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . MTDC	58.50	89,955.00	52,624.00
		Total Indirect Costs	52,624.00

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number): Uyen Tran, DHHS 214-767-3261

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	142,579.00

J. Fee	Funds Requested ($)*

K. Budget Justification* File Name: [redacted] PPRN_Budget_Justification.pdf

(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 3

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ○ Project ● Subaward/Consortium

Enter name of Organization: [redacted]

Start Date*: 07-01-2018 **End Date*:** 06-30-2019 **Budget Period:** 3

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1.		[redacted]	C	[redacted]		[redacted]	[redacted]	0.60			9,165.00	2,475.00	11,640.00
2.		[redacted]		[redacted]		[redacted]	[redacted]	0.60			9,165.00	2,475.00	11,640.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name:

Total Senior/Key Person **23,280.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Research Coordinator	12.00			52,500.00	14,175.00	66,675.00
1	**Total Number Other Personnel**					**Total Other Personnel**	**66,675.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**89,955.00**

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 3

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ❍ Project ● Subaward/Consortium

Organization: [redacted]

Start Date*: 07-01-2018 **End Date*:** 06-30-2019 **Budget Period: 3**

C. Equipment Description

List items and dollar amount for each item exceeding $5,000

Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	
Total Equipment	

Additional Equipment: File Name:

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	
2. Foreign Travel Costs	
Total Travel Cost	

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 3

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ❍ Project ● Subaward/Consortium

Organization: [redacted]

Start Date*: 07-01-2018 **End Date*:** 06-30-2019 **Budget Period: 3**

F. Other Direct Costs	Funds Requested ($)*
Total Other Direct Costs	

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	89,955.00

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . MTDC	58.50	89,955.00	52,624.00
		Total Indirect Costs	52,624.00

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number): Uyen Tran, DHHS 214-767-3261

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	142,579.00

J. Fee	Funds Requested ($)*

K. Budget Justification* File Name: [redacted] PPRN_Budget_Justification.pdf

(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 4

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ○ Project ● Subaward/Consortium

Enter name of Organization: [redacted]

Start Date*: 07-01-2019 **End Date*:** 06-30-2020 **Budget Period:** 4

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1.		[redacted]		[redacted]		[redacted]	[redacted]	0.60			9,165.00	2,475.00	11,640.00
2.		[redacted]		[redacted]		[redacted]	[redacted]	0.60			9,165.00	2,475.00	11,640.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name:

Total Senior/Key Person **23,280.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Research Coordinator	12.00			52,500.00	14,175.00	66,675.00
1	**Total Number Other Personnel**					**Total Other Personnel**	**66,675.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**89,955.00**

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 4

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ❍ Project ● Subaward/Consortium

Organization: [redacted]

Start Date*: 07-01-2019 **End Date*:** 06-30-2020 **Budget Period: 4**

C. Equipment Description

List items and dollar amount for each item exceeding $5,000

Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	
Total Equipment	

Additional Equipment: File Name:

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	
2. Foreign Travel Costs	
Total Travel Cost	

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 4

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ❍ Project ● Subaward/Consortium

Organization: [redacted]

Start Date*: 07-01-2019 **End Date*:** 06-30-2020 **Budget Period: 4**

F. Other Direct Costs	Funds Requested ($)*
Total Other Direct Costs	

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	89,955.00

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . MTDC	58.50	89,955.00	52,624.00
		Total Indirect Costs	52,624.00

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number): Uyen Tran, DHHS 214-767-3261

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	142,579.00

J. Fee	Funds Requested ($)*

K. Budget Justification* File Name: [redacted] PPRN_Budget_Justification.pdf (Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 5

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ❍ Project ● Subaward/Consortium

Enter name of Organization: [redacted]

Start Date*: 07-01-2020 **End Date*:** 06-30-2021 **Budget Period: 5**

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1 .		[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	0.60			9,165.00	2,475.00	11,640.00
2 .		[redacted]		[redacted]	[redacted]	[redacted]	[redacted]	0.60			9,165.00	2,475.00	11,640.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name:

Total Senior/Key Person **23,280.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Research Coordinator	12.00			52,500.00	14,175.00	66,675.00
1	**Total Number Other Personnel**					**Total Other Personnel**	**66,675.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**89,955.00**

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 5

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ❍ Project ● Subaward/Consortium

Organization: [redacted]

Start Date*: 07-01-2020 **End Date*:** 06-30-2021 **Budget Period: 5**

C. Equipment Description

List items and dollar amount for each item exceeding $5,000

Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	
Total Equipment	

Additional Equipment: File Name:

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	
2. Foreign Travel Costs	
Total Travel Cost	

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 5

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ❍ Project ● Subaward/Consortium

Organization: [redacted]

Start Date*: 07-01-2020 **End Date*:** 06-30-2021 **Budget Period: 5**

F. Other Direct Costs	Funds Requested ($)*
Total Other Direct Costs	

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	89,955.00

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . MTDC	58.50	89,955.00	52,624.00
		Total Indirect Costs	52,624.00

Cognizant Federal Agency [redacted]
(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	142,579.00

J. Fee	Funds Requested ($)*

K. Budget Justification* File Name: [redacted]
PPRN_Budget_Justification.pdf
(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

Budget Justification

[redacted]

[redacted]

[redacted]

Other Personnel:

Research Coordinator (TBD) 12 months, 100% effort) will submit IRB documents, oversee CRF and data collection.

RESEARCH & RELATED BUDGET - Cumulative Budget

	Totals ($)	
Section A, Senior/Key Person		116,400.00
Section B, Other Personnel		333,375.00
Total Number Other Personnel	5	
Total Salary, Wages and Fringe Benefits (A+B)		449,775.00
Section C, Equipment		
Section D, Travel		
1. Domestic		
2. Foreign		
Section E, Participant/Trainee Support Costs		
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other		
6. Number of Participants/Trainees		
Section F, Other Direct Costs		
1. Materials and Supplies		
2. Publication Costs		
3. Consultant Services		
4. ADP/Computer Services		
5. Subawards/Consortium/Contractual Costs		
6. Equipment or Facility Rental/User Fees		
7. Alterations and Renovations		
8. Other 1		
9. Other 2		
10. Other 3		
Section G, Direct Costs (A thru F)		449,775.00
Section H, Indirect Costs		263,120.00
Section I, Total Direct and Indirect Costs (G + H)		712,895.00
Section J, Fee		

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 1

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ❍ Project ● Subaward/Consortium

Enter name of Organization: [redacted]

Start Date*: 07-01-2016 **End Date*:** 06-30-2017 **Budget Period: 1**

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1 .		[redacted]		[redacted]		[redacted]		0.60			9,284.00	3,528.00	12,812.00
2 .		[redacted]		[redacted]		[redacted]		1.20			10,722.00	4,074.00	14,796.00
3 .		[redacted]		[redacted]		[redacted]		0.60			4,972.00	1,889.00	6,861.00
4 .		[redacted]		[redacted]		[redacted]		4.50			31,794.00	12,082.00	43,876.00
5 .		[redacted]		[redacted]		[redacted]		2.40			23,572.00	8,957.00	32,529.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name:

Total Senior/Key Person **110,874.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Total Number Other Personnel					**Total Other Personnel**	
						Total Salary, Wages and Fringe Benefits (A+B)	**110,874.00**

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 1

ORGANIZATIONAL DUNS*: [redacted]
Budget Type*: ○ Project ● Subaward/Consortium
Organization: [redacted]

Start Date*: 07-01-2016 **End Date*:** 06-30-2017 **Budget Period:** 1

C. Equipment Description

List items and dollar amount for each item exceeding $5,000

Equipment Item **Funds Requested ($)***

Total funds requested for all equipment listed in the attached file

Total Equipment

Additional Equipment: File Name:

D. Travel **Funds Requested ($)***

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)
2. Foreign Travel Costs

Total Travel Cost

E. Participant/Trainee Support Costs **Funds Requested ($)***

1. Tuition/Fees/Health Insurance
2. Stipends
3. Travel
4. Subsistence
5. Other:

Number of Participants/Trainees **Total Participant Trainee Support Costs**

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 1

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ❍ Project ● Subaward/Consortium

Organization: [redacted]

Start Date*: 07-01-2016 **End Date*:** 06-30-2017 **Budget Period: 1**

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	
2. Publication Costs	
3. Consultant Services	
4. ADP/Computer Services	78.00
5. Subawards/Consortium/Contractual Costs	
6. Equipment or Facility Rental/User Fees	
7. Alterations and Renovations	
Total Other Direct Costs	**78.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**110,952.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . Multiple Confidential Indirect Rates			87,701.00
		Total Indirect Costs	**87,701.00**

Cognizant Federal Agency
(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**198,653.00**

J. Fee	Funds Requested ($)*

K. Budget Justification*	File Name: 1[redacted]BudgetJustification.pdf (Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 2

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ❍ Project ● Subaward/Consortium

Enter name of Organization: [redacted]

Start Date*: 07-01-2017 **End Date*:** 06-30-2018 **Budget Period: 2**

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1 .		Abhik		Das		PD/PI		0.12			1,913.00	727.00	2,640.00
2 .		[redacted]		[redacted]r		[redacted]		1.20			11,044.00	4,197.00	15,241.00
3 .		[redacted]		[redacted]		[redacted]		0.24			2,049.00	778.00	2,827.00
4 .		[redacted]		[redacted]		[redacted]		2.40			17,465.00	6,637.00	24,102.00
5 .		[redacted]		[redacted]		[redacted]		1.95			19,727.00	7,496.00	27,223.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name: **Total Senior/Key Person** **72,033.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Total Number Other Personnel					**Total Other Personnel**	
						Total Salary, Wages and Fringe Benefits (A+B)	**72,033.00**

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 2

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ❍ Project ● Subaward/Consortium

Organization: [redacted]

Start Date*: 07-01-2017 **End Date*:** 06-30-2018 **Budget Period: 2**

C. Equipment Description

List items and dollar amount for each item exceeding $5,000

Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	
Total Equipment	

Additional Equipment: File Name:

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	
2. Foreign Travel Costs	
Total Travel Cost	

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 2

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ❍ Project ● Subaward/Consortium

Organization: [redacted]

Start Date*: 07-01-2017 **End Date*:** 06-30-2018 **Budget Period: 2**

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	
2. Publication Costs	
3. Consultant Services	
4. ADP/Computer Services	78.00
5. Subawards/Consortium/Contractual Costs	
6. Equipment or Facility Rental/User Fees	
7. Alterations and Renovations	
Total Other Direct Costs	**78.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**72,111.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . Multiple Confidential Indirect Rates			56,982.00
		Total Indirect Costs	**56,982.00**

Cognizant Federal Agency
(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**129,093.00**

J. Fee	Funds Requested ($)*

K. Budget Justification*	File Name: [redacted]BudgetJustification.pdf (Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 3

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ○ Project ● Subaward/Consortium

Enter name of Organization: [redacted]

Start Date*: 07-01-2018 **End Date*:** 06-30-2019 **Budget Period:** 3

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1.		[redacted]		[redacted]		[redacted]		0.12			1,970.00	749.00	2,719.00
2.		[redacted]		[redacted]		[redacted]		1.20			11,375.00	4,323.00	15,698.00
3.		[redacted]		[redacted]		[redacted]		0.24			2,110.00	802.00	2,912.00
4.		[redacted]		[redacted]		[redacted]		1.80			13,492.00	5,127.00	18,619.00
5.		[redacted]		[redacted]		[redacted]		1.95			20,318.00	7,721.00	28,039.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name:

Total Senior/Key Person **67,987.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Total Number Other Personnel					**Total Other Personnel**	
						Total Salary, Wages and Fringe Benefits (A+B)	**67,987.00**

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 3

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ❍ Project ● Subaward/Consortium

Organization: [redacted]

Start Date*: 07-01-2018 **End Date*:** 06-30-2019 **Budget Period: 3**

C. Equipment Description

List items and dollar amount for each item exceeding $5,000

Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	
Total Equipment	

Additional Equipment: File Name:

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	
2. Foreign Travel Costs	
Total Travel Cost	

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 3

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ❍ Project ● Subaward/Consortium

Organization: [redacted]

Start Date*: 07-01-2018 **End Date*:** 06-30-2019 **Budget Period: 3**

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	
2. Publication Costs	
3. Consultant Services	
4. ADP/Computer Services	78.00
5. Subawards/Consortium/Contractual Costs	
6. Equipment or Facility Rental/User Fees	
7. Alterations and Renovations	
Total Other Direct Costs	**78.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**68,065.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . Multiple Confidential Indirect Rates			53,783.00
		Total Indirect Costs	**53,783.00**

Cognizant Federal Agency
(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**121,848.00**

J. Fee	Funds Requested ($)*

K. Budget Justification*	File Name: 1[redacted] BudgetJustification.pdf (Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 4

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ○ Project ● Subaward/Consortium

Enter name of Organization: [redacted]

Start Date*: 07-01-2019 **End Date*:** 06-30-2020 **Budget Period:** 4

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1.		[redacted]		[redacted]		[redacted]		0.12			2,029.00	771.00	2,800.00
2.		[redacted]		[redacted]		[redacted]		1.20			11,717.00	4,452.00	16,169.00
3.		[redacted]		[redacted]		[redacted]		0.24			2,173.00	826.00	2,999.00
4.		[redacted]		[redacted]		[redacted]		1.20			9,264.00	3,521.00	12,785.00
5.		[redacted]		[redacted]		[redacted]		1.95			20,928.00	7,953.00	28,881.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name:

Total Senior/Key Person **63,634.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Total Number Other Personnel					**Total Other Personnel**	
						Total Salary, Wages and Fringe Benefits (A+B)	**63,634.00**

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 4

ORGANIZATIONAL DUNS*: [redacted]
Budget Type*: ○ Project ● Subaward/Consortium
Organization: [redacted]

Start Date*: 07-01-2019 **End Date*:** 06-30-2020 **Budget Period:** 4

C. Equipment Description

List items and dollar amount for each item exceeding $5,000

Equipment Item **Funds Requested ($)***

Total funds requested for all equipment listed in the attached file

Total Equipment

Additional Equipment: File Name:

D. Travel **Funds Requested ($)***

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)
2. Foreign Travel Costs

Total Travel Cost

E. Participant/Trainee Support Costs **Funds Requested ($)***

1. Tuition/Fees/Health Insurance
2. Stipends
3. Travel
4. Subsistence
5. Other:

Number of Participants/Trainees **Total Participant Trainee Support Costs**

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 4

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ❍ Project ● Subaward/Consortium

Organization: [redacted]

Start Date*: 07-01-2019 **End Date*:** 06-30-2020 **Budget Period: 4**

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	
2. Publication Costs	
3. Consultant Services	
4. ADP/Computer Services	78.00
5. Subawards/Consortium/Contractual Costs	
6. Equipment or Facility Rental/User Fees	
7. Alterations and Renovations	
Total Other Direct Costs	**78.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**63,712.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . Multiple Confidential Indirect Rates			50,341.00
		Total Indirect Costs	**50,341.00**

Cognizant Federal Agency
(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**114,053.00**

J. Fee	Funds Requested ($)*

K. Budget Justification*	File Name [redacted] BudgetJustification.pdf (Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 5

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ❍ Project ● Subaward/Consortium

Enter name of Organization: [redacted]

Start Date*: 07-01-2020 **End Date*:** 06-30-2021 **Budget Period: 5**

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1 .		[redacted]		[redacted]		[redacted]		0.60			10,450.00	3,971.00	14,421.00
2 .		[redacted]		[redacted]r		[redacted]		1.20			12,068.00	4,586.00	16,654.00
3 .		[redacted]		[redacted]		[redacted]		0.12			1,119.00	425.00	1,544.00
4 .		[redacted]		[redacted]		[redacted]		0.60			4,771.00	1,813.00	6,584.00
5 .		[redacted]		[redacted]		[redacted]		6.00			66,325.00	25,204.00	91,529.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name:

Total Senior/Key Person **130,732.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Total Number Other Personnel					**Total Other Personnel**	
						Total Salary, Wages and Fringe Benefits (A+B)	**130,732.00**

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 5

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ❍ Project ● Subaward/Consortium

Organization: [redacted]

Start Date*: 07-01-2020 **End Date*:** 06-30-2021 **Budget Period: 5**

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	
Total Equipment	
Additional Equipment: File Name:	

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	
2. Foreign Travel Costs	
Total Travel Cost	

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 5

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ❍ Project ● Subaward/Consortium

Organization: [redacted]

Start Date*: 07-01-2020 **End Date*:** 06-30-2021 **Budget Period: 5**

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	
2. Publication Costs	
3. Consultant Services	
4. ADP/Computer Services	78.00
5. Subawards/Consortium/Contractual Costs	
6. Equipment or Facility Rental/User Fees	
7. Alterations and Renovations	
Total Other Direct Costs	**78.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**130,810.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . Multiple Confidential Indirect Rates			103,405.00
		Total Indirect Costs	**103,405.00**

Cognizant Federal Agency
(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**234,215.00**

J. Fee	Funds Requested ($)*

K. Budget Justification* File Name: [redacted] BudgetJustification.pdf
(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

Budget Justification

The proposed budget below is based on our understanding of the goals and objectives of the Periviable Perinatal Research Network (PPRN) as set out in the Research Strategy. It pre-supposes that we will receive the necessary permissions to access and reuse any relevant data coordination, management and/or analyses related templates and resources that we have developed in our role as the longtime Data Coordinating Center (DCC) for the [redacted]

Personnel

[redacted] *Staff*

Note that all key personnel are prepared and would be happy to commit additional time to the study if requested by NICHD. [redacted] staff charge by the hour and their commitments to this effort can be varied across time, as required by project activities.

Percent Effort: [redacted] pays staff monthly, on the basis of 166.67 hours/month, which equals 2,000 hours/year. [redacted] billable salaries are not computed on 2,080 hours, because 80 hours are paid holidays, which cannot be worked or charged by staff. To recoup the holiday pay, [redacted] salaries are therefore computed on the basis of 2,000 billable hours/year. [redacted] holidays are not included in our Fringe Benefit pool. The Full-time Equivalent for [redacted] staff is budgeted at 1,833 hours/year. This amount is based on the 2,000 billable hours, less the average paid time off (PTO) of 167 hours. PTO hours are included in [redacted] Fringe Benefit rate and applied to direct labor salaries.

Key Staff

[redacted]

[redacted]

Other Direct Costs

Computer costs - Computer storage costs - $390

RESEARCH & RELATED BUDGET - Cumulative Budget

	Totals ($)	
Section A, Senior/Key Person		445,260.00
Section B, Other Personnel		
Total Number Other Personnel		
Total Salary, Wages and Fringe Benefits (A+B)		445,260.00
Section C, Equipment		
Section D, Travel		
1. Domestic		
2. Foreign		
Section E, Participant/Trainee Support Costs		
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other		
6. Number of Participants/Trainees		
Section F, Other Direct Costs		390.00
1. Materials and Supplies		
2. Publication Costs		
3. Consultant Services		
4. ADP/Computer Services	390.00	
5. Subawards/Consortium/Contractual Costs		
6. Equipment or Facility Rental/User Fees		
7. Alterations and Renovations		
8. Other 1		
9. Other 2		
10. Other 3		
Section G, Direct Costs (A thru F)		445,650.00
Section H, Indirect Costs		352,212.00
Section I, Total Direct and Indirect Costs (G + H)		797,862.00
Section J, Fee		

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 1

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ○ Project ● Subaward/Consortium

Enter name of Organization: [redacted]

Start Date*: 07-01-2016 **End Date*:** 06-30-2017 **Budget Period:** 1

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1	[redacted]							0.60			9,165.00	1,466.00	10,631.00
2.	[redacted]							0.60			9,165.00	1,466.00	10,631.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name:

Total Senior/Key Person **21,262.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Research Coordinator	9.60			52,000.00	13,520.00	65,520.00
1	**Total Number Other Personnel**					**Total Other Personnel**	**65,520.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**86,782.00**

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 1

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ❍ Project ● Subaward/Consortium

Organization: [redacted]

Start Date*: 07-01-2016 **End Date*:** 06-30-2017 **Budget Period: 1**

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	
Total Equipment	
Additional Equipment: File Name:	

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	3,218.00
2. Foreign Travel Costs	
Total Travel Cost	**3,218.00**

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 1

ORGANIZATIONAL DUNS*: [redacted]
Budget Type*: ○ Project ● Subaward/Consortium
Organization: [redacted]

Start Date*: 07-01-2016 **End Date*:** 06-30-2017 **Budget Period:** 1

F. Other Direct Costs	Funds Requested ($)*
Total Other Direct Costs	

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	90,000.00

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . MTDC	54.00	48,600.00	48,600.00
		Total Indirect Costs	48,600.00

Cognizant Federal Agency [redacted]
(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	138,600.00

J. Fee	Funds Requested ($)*

K. Budget Justification* File Name: [redacted] Budget Justification.pdf
(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

Tracking Number: [redacted]

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 2

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ❍ Project ● Subaward/Consortium

Enter name of Organization: [redacted]

Start Date*: 07-01-2017 **End Date*:** 06-30-2018 **Budget Period: 2**

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1.	[redacted]	[redacted]		[redacted]		[redacted]	[redacted]	0.60			9,165.00	1,466.00	10,631.00
2.	[redacted]	[redacted]	[redacted]	[redacted]		[redacted]	[redacted]	0.60			9,165.00	1,466.00	10,631.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name:

Total Senior/Key Person **21,262.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Research Coordinator	9.60			52,000.00	13,520.00	65,520.00
1	**Total Number Other Personnel**					**Total Other Personnel**	**65,520.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**86,782.00**

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 2

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ❍ Project ● Subaward/Consortium

Organization: [redacted]

Start Date*: 07-01-2017 **End Date*:** 06-30-2018 **Budget Period: 2**

C. Equipment Description

List items and dollar amount for each item exceeding $5,000

Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	
Total Equipment	

Additional Equipment: File Name:

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	3,218.00
2. Foreign Travel Costs	
Total Travel Cost	**3,218.00**

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 2

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ❍ Project ● Subaward/Consortium

Organization: [redacted]

Start Date*: 07-01-2017 **End Date*:** 06-30-2018 **Budget Period: 2**

F. Other Direct Costs	Funds Requested ($)*
Total Other Direct Costs	

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	90,000.00

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . MTDC	54.00	48,600.00	48,600.00
		Total Indirect Costs	**48,600.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number) DHHS, Arif Karim, (214) 767-3261

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	138,600.00

J. Fee	Funds Requested ($)*

K. Budget Justification* File Name: [redacted] Budget Justification.pdf
(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 3

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ❍ Project ● Subaward/Consortium

Enter name of Organization: [redacted]

Start Date*: 07-01-2018 **End Date*:** 06-30-2019 **Budget Period: 3**

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1.	[redacted]							0.60			9,165.00	1,466.00	10,631.00
2.	[redacted]							0.60			9,165.00	1,466.00	10,631.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name:

Total Senior/Key Person **21,262.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Research Coordinator	9.60			52,000.00	13,520.00	65,520.00
1	**Total Number Other Personnel**					**Total Other Personnel**	**65,520.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**86,782.00**

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 3

ORGANIZATIONAL DUNS*: [redacted]
Budget Type*: ○ Project ● Subaward/Consortium
Organization: [redacted]

Start Date*: 07-01-2018 **End Date*:** 06-30-2019 **Budget Period:** 3

C. Equipment Description

List items and dollar amount for each item exceeding $5,000

Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	
Total Equipment	

Additional Equipment: File Name:

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	3,218.00
2. Foreign Travel Costs	
Total Travel Cost	**3,218.00**

E. Participant/Trainee Support Costs	**Funds Requested ($)***
1. Tuition/Fees/Health Insurance	
2. Stipends	
3. Travel	
4. Subsistence	
5. Other:	
Number of Participants/Trainees **Total Participant Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 3

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ❍ Project ● Subaward/Consortium

Organization: [redacted]

Start Date*: 07-01-2018 **End Date*:** 06-30-2019 **Budget Period: 3**

F. Other Direct Costs	Funds Requested ($)*
Total Other Direct Costs	

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	90,000.00

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . MTDC	54.00	48,600.00	48,600.00
		Total Indirect Costs	48,600.00

Cognizant Federal Agency [redacted]
(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	138,600.00

J. Fee	Funds Requested ($)*

K. Budget Justification* File Name: [redacted] Budget Justification.pdf
(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 4

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ❍ Project ● Subaward/Consortium

Enter name of Organization: [redacted]

Start Date*: 07-01-2019 **End Date*:** 06-30-2020 **Budget Period: 4**

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1	[redacted]							0.60			9,165.00	1,466.00	10,631.00
2 .	[redacted]		[redacted].			t		0.60			9,165.00	1,466.00	10,631.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name:

Total Senior/Key Person **21,262.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Research Coordinator	9.60			52,000.00	13,520.00	65,520.00
1	**Total Number Other Personnel**					**Total Other Personnel**	**65,520.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**86,782.00**

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 4

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ❍ Project ● Subaward/Consortium

Organization: [redacted]

Start Date*: 07-01-2019 **End Date*:** 06-30-2020 **Budget Period: 4**

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	
Total Equipment	
Additional Equipment: File Name:	

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	3,218.00
2. Foreign Travel Costs	
Total Travel Cost	**3,218.00**

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 4

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ❍ Project ● Subaward/Consortium

Organization: [redacted]

Start Date*: 07-01-2019 **End Date*:** 06-30-2020 **Budget Period: 4**

F. Other Direct Costs	Funds Requested ($)*
Total Other Direct Costs	

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	90,000.00

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . MTDC	54.00	48,600.00	48,600.00
		Total Indirect Costs	48,600.00

Cognizant Federal Agency [redacted]
(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	138,600.00

J. Fee	Funds Requested ($)*

K. Budget Justification*	File Name: [redacted] Budget Justification.pdf (Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 5

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ○ Project ● Subaward/Consortium

Enter name of Organization: [redacted]

Start Date*: 07-01-2020 **End Date*:** 06-30-2021 **Budget Period:** 5

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1.	[redacted]							0.60			9,165.00	1,466.00	10,631.00
2	[redacted]							0.60			9,165.00	1,466.00	10,631.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name:

Total Senior/Key Person **21,262.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Research Coordinator	9.60			52,000.00	13,520.00	65,520.00
1	**Total Number Other Personnel**					**Total Other Personnel**	**65,520.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**86,782.00**

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 5

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ❍ Project ● Subaward/Consortium

Organization: [redacted]

Start Date*: 07-01-2020 **End Date*:** 06-30-2021 **Budget Period: 5**

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	
Total Equipment	
Additional Equipment: File Name:	

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	3,218.00
2. Foreign Travel Costs	
Total Travel Cost	**3,218.00**

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 5

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ❍ Project ● Subaward/Consortium

Organization: [redacted]

Start Date*: 07-01-2020 **End Date*:** 06-30-2021 **Budget Period: 5**

F. Other Direct Costs	Funds Requested ($)*
Total Other Direct Costs	

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**90,000.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . MTDC	54.00	48,600.00	48,600.00
		Total Indirect Costs	**48,600.00**

Cognizant Federal Agency [redacted]
(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**138,600.00**

J. Fee	Funds Requested ($)*

K. Budget Justification* File Name: [redacted] Budget Justification.pdf
(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

BUDGET JUSTIFICATION

PERSONNEL

[redacted]

(TBN) – Research Coordinator. The Research Coordinator will provide necessary support services to oversee IRB related correspondence and monitor coordination, submission approval and quality review of documents required for study, as per project assignment. They will have extensive experience in IRB submission and regulatory affairs for multicenter trial. They will assist the with the entry and retrieval of specific information pertaining to the project using database and/or spreadsheet software on a computer. They will transcribe data form source documents, and query and generate reports as required to support Principal Investigator. They will handle multiple projects at one time and provide results. The Research Nurse will devote 9.60 calendar months to the project each year.

Salary support requested for all personnel is equal to the level of effort contributed to the project. Fringe benefits are based on a fixed benefit tier.

Travel – Domestic ($3,218) per year

Travel funds are requested to support PI to attend annual meetings and site visits to present data and consult with other center PIs.

RESEARCH & RELATED BUDGET - Cumulative Budget

	Totals ($)	
Section A, Senior/Key Person		106,310.00
Section B, Other Personnel		327,600.00
Total Number Other Personnel	5	
Total Salary, Wages and Fringe Benefits (A+B)		433,910.00
Section C, Equipment		
Section D, Travel		16,090.00
1. Domestic	16,090.00	
2. Foreign		
Section E, Participant/Trainee Support Costs		
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other		
6. Number of Participants/Trainees		
Section F, Other Direct Costs		
1. Materials and Supplies		
2. Publication Costs		
3. Consultant Services		
4. ADP/Computer Services		
5. Subawards/Consortium/Contractual Costs		
6. Equipment or Facility Rental/User Fees		
7. Alterations and Renovations		
8. Other 1		
9. Other 2		
10. Other 3		
Section G, Direct Costs (A thru F)		450,000.00
Section H, Indirect Costs		243,000.00
Section I, Total Direct and Indirect Costs (G + H)		693,000.00
Section J, Fee		

Total Direct Costs less Consortium F&A

NIH policy (NOT-OD-05-004) allows applicants to exclude consortium/contractual F&A costs when determining if an application falls at or beneath any applicable direct cost limit. When a direct cost limit is specified in an FOA, the following table can be used to determine if your application falls within that limit.

Category	Budget Period 1	Budget Period 2	Budget Period 3	Budget Period 4	Budget Period 5	TOTALS
Total Direct Costs less Consortium F&A	499,901	499,913	499,901	499,901	499,900	**2,499,516**

PHS 398 Cover Page Supplement

[redacted]

1. Project Director / Principal Investigator (PD/PI)

Prefix:
First Name*: [redacted]
Middle Name:
Last Name*: [redacted]
Suffix:

2. Human Subjects

Clinical Trial? ○ No ● Yes
Agency-Defined Phase III Clinical Trial?* ○ No ● Yes

3. Permission Statement*

If this application does not result in an award, is the Government permitted to disclose the title of your proposed project, and the name, address, telephone number and e-mail address of the official signing for the applicant organization, to organizations that may be interested in contacting you for further information (e.g., possible collaborations, investment)?

● Yes ○ No

4. Program Income*

Is program income anticipated during the periods for which the grant support is requested? ○ Yes ● No

If you checked "yes" above (indicating that program income is anticipated), then use the format below to reflect the amount and source(s). Otherwise, leave this section blank.

Budget Period*	Anticipated Amount ($)*	Source(s)*

PHS 398 Cover Page Supplement

5. Human Embryonic Stem Cells

Does the proposed project involve human embryonic stem cells?* ● No ❍ Yes

If the proposed project involves human embryonic stem cells, list below the registration number of the specific cell line(s) from the following list: http://grants.nih.gov/stem_cells/registry/current.htm. Or, if a specific stem cell line cannot be referenced at this time, please check the box indicating that one from the registry will be used:

Cell Line(s): Specific stem cell line cannot be referenced at this time. One from the registry will be used.

6. Inventions and Patents (For renewal applications only)

Inventions and Patents*: ❍ Yes ❍ No

If the answer is "Yes" then please answer the following:

Previously Reported*: ❍ Yes ❍ No

7. Change of Investigator / Change of Institution Questions

❑ Change of principal investigator / program director

Name of former principal investigator / program director:

Prefix:

First Name*:

Middle Name:

Last Name*:

Suffix:

❑ Change of Grantee Institution

Name of former institution*:

PHS 398 Research Plan

Please attach applicable sections of the research plan, below. [redacted]

1. Introduction to Application (for RESUBMISSION or REVISION only)	
2. Specific Aims	1256-SpAims_PPRN_Sept25_2015.pdf
3. Research Strategy*	1257-ResStrategy_PPRN_Sept25_2015.pdf
4. Progress Report Publication List	
Human Subjects Sections	
5. Protection of Human Subjects	1258-Protection of Human Subjects_Sept2015.pdf
6. Inclusion of Women and Minorities	1259-Inclusion of Women and Minorities_Sept2015.pdf
7. Inclusion of Children	1260-Inclusion of Children_Sept2015.pdf
Other Research Plan Sections	
8. Vertebrate Animals	
9. Select Agent Research	
10. Multiple PD/PI Leadership Plan	1261-Multiple PI Leadership Plan_Sept2015.pdf
11. Consortium/Contractual Arrangements	1262-ConsortiumContractualArrangements_Sept2015.pdf
12. Letters of Support	
13. Resource Sharing Plan(s)	1263-Resource Sharing_Sept2015v2.pdf
Appendix (if applicable)	
14. Appendix	

Specific Aims

This "**Periviable Perinatal Research Network (PPRN)**" application is in response to [redacted]. This application represents the development of a collaborative effort among four high volume regional perinatal centers [redacted]. This unique research team brings together well established investigators with complementary expertise in neonatal intensive care [redacted] health behavior [redacted] applied developmental psychology [redacted] and perinatal biostatistics [redacted]. These four centers participate in both the Eunice Kennedy Shriver NICHD Neonatal Research Network (NRN, for which [redacted] is also the [redacted]) as well as the Maternal-Fetal Medicine Units Network (MFMU). So far, there has not been a focused development of an integrated infrastructure to specifically evaluate characteristics of periviable pregnancy (20-25w GA) or its outcomes. This proposal is designed to develop a research network (PPRN) that is focused on periviable gestation, is distinct from either the MFMU or the NRN, and builds upon the available infrastructure as it integrates the expertise of both maternal-fetal medicine investigators and neonatologists, extending the period of gestation being evaluated as early as 20 weeks.

Very premature infants at the threshold of viability contribute disproportionately to infant mortality and morbidity. However, there is a lack of standardized data collection of characteristics and maternal and neonatal outcomes (both short- and long-term) of women who present for medical care with problems in the periviable period. The development of a periviable pregnancy database is essential as a resource to understand in-depth the characteristics of periviable pregnancy and its outcomes, and provide the necessary information to develop hypotheses and design trials in this population.

The factors that parents and clinicians weigh during decision making relevant to periviable birth are poorly understood. The NRN has developed three prognostication/risk-stratification tools (available at https://neonatal.rti.org under "tools"): (1) Assessment of outcome of infants born at 22 to 25 weeks of gestation (Outcome Estimator), (2) Determination of the probability of bronchopulmonary dysplasia (BPD) at six postnatal ages using readily available clinical data (BPD estimator), and (3) Dynamic models of the changing probability of death or neurodevelopmental impairment in extremely low birth weight ($\leq$ 1000 g) infants based on information available at birth and later during the clinical course (Outcome Trajectory Estimator). In order to optimize shared decision-making in the periviable period, the outcomes important to parents and underlying motivations need to be determined, the utility of quantitative estimates of outcome determined, and Decision Aids developed. We hypothesize that the use of quantitative prognostic estimators and Decision Aids will improve parental and clinician satisfaction with the decision-making process, develop concordance between maternal fetal medicine specialists and neonatologists, change clinical processes, and improve neonatal outcomes.

The Specific Aims of the PPRN are:

Specific Aim (1) Develop a Periviable Pregnancy Database (PeriPD) to determine the incidence, characteristics, and outcomes of periviable pregnancies

Specific Aim (2) Determine whether the use of the NICHD NRN Outcome Estimator, Outcome Trajectory Estimator, and BPD Estimator for parental counseling leads to increased parental satisfaction, increased clinician satisfaction, changes in therapies, and improved clinical outcomes of periviable infants

Specific Aim (3) Determine the neonatal outcomes in which parents are most interested, develop a better means of framing and communicating clinical evidence, and develop Decision Aids to enable parents of periviable infants to make better informed decisions

The successful completion of the studies in this project will determine if quantitative estimates of outcome help improve decision-making by patients and clinicians. The Decision Aids may improve parental and clinician satisfaction with the decision-making process and possibly improve clinical processes and outcomes. Importantly, the integrated database on periviable pregnancies developed by this multicenter consortium of regional perinatal centers may lead to a better understanding of the epidemiology of periviable pregnancy, improvements in the management of extremely premature infants worldwide, and inform future discussions about standards of care.

Research Strategy

Background and Significance

Prematurity is a major public health problem

Preterm birth is one of the leading causes of neonatal death worldwide (0.97 million, ~35% of all neonatal deaths) (1, 2). Approximately 1 in 8 births in the United States are preterm (3). Preterm infants are at greater risk for mortality and morbidity. There are increased emotional and economic costs to families and implications for public-sector services such as educational, health insurance, and social support systems (3). The annual societal economic burden associated with preterm birth in the US was conservatively estimated at >$26.2 billion in 2005 (3).

Extremely preterm infants contribute disproportionately to morbidity and health care costs

Infants < 28 weeks of gestation represent just 6% of all preterm births (1.5% of all live births) but account for >33% of medical costs associated with preterm births (3). Extremely preterm infants are at very high risk of mortality and morbidity. Rates of survival to discharge decrease with decreasing GA (94% at 28 weeks to 7% at 22 weeks)(4). Overall, of extremely preterm (22-28 weeks and 401-1500g) infants, 93% have respiratory distress syndrome, 68% bronchopulmonary dysplasia, 16% severe intraventricular hemorrhage, and 36% late-onset sepsis (5). Special outpatient services (social work, visiting nurse, medical specialty, early intervention, speech and language services, occupational and physical therapy, and neurodevelopmental and behavioral services) use in extremely preterm infants is common (6). At 18-22 months' corrected age, 55% used more than 3 special outpatient services (6). While many former extremely preterm infants become functional young adults, a higher proportion compared to normal infants were neither employed nor in school at 22-25 years of age (7). Very preterm infants have poorer educational achievement compared to normal birth weight controls, and fewer go to college (8).

Periviable birth

While extremely preterm infants < 29 weeks of gestation contribute most to mortality, morbidity, and costs of prematurity, most infants in the 26-28 weeks range have better outcomes (80% or better survival free from handicap), and it is the infants <26 weeks' gestation at the limit of viability ("periviable") who are at highest risk. A recent study in the NICHD NRN found that although overall survival increased between 2009 and 2012 for infants at 23 and 24 weeks' gestation, there were no changes in survival without major morbidity for infants at 22-24 weeks' gestation (4). Periviable pregnancies are higher risk not just for the fetus but also for the mother. There is an increase in cesarean delivery risk, a high proportion being classical cesarean sections with a greater potential for immediate and future maternal morbidity that is not well defined. The Society for Maternal-Fetal Medicine, the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, the Section on Perinatal Pediatrics of the American Academy of Pediatrics, and the American College of Obstetricians and Gynecologists convened a joint workshop in 2013 on the management and counseling issues of women anticipated to deliver at a **periviable gestation (defined as 20w 0d through 25w 6d of gestation)** and the treatment options for the newborn period. The executive summary of this Periviable Pregnancy workshop was published concurrently in Obstetrics & Gynecology (9), Am J Obstet Gynecol (10), and the Journal of Perinatology (11). Major points raised included: (1) the marked variability in outcomes among studies, which relate to non-modifiable factors (eg. fetal weight and sex), modifiable factors (e.g. intent to intervene, antenatal steroid therapy), and study design and reporting features (e.g. single center vs. national data, definition of mortality; all live births vs. resuscitated infants vs. infants admitted to a NICU), (2) the limited evidence-based data regarding obstetric interventions at 20-25 weeks of gestation, since these gestational ages were considered non-viable until recently and the small number of women actually delivering at ≤25 weeks of gestation reduces statistical power to assess interventions (11). Therefore, the guidance for obstetric interventions in the workshop summary is based on limited data, leading to a "Not recommended" status for aggressive newborn resuscitation or magnesium sulfate for neuroprotection at 22w0d-22w6d and antenatal steroids at <22w0d, although these interventions are "Recommended" at more advanced gestations (11).

Potential for improvement

The first Specific Aim of our study has the goal of developing a Periviable Pregnancy Database to determine the incidence, characteristics, interventions, and outcomes of periviable pregnancies. A major recommendation for research from the Periviable Pregnancy workshop (11) was obstetric and newborn infant cohort studies regarding the epidemiology, antecedent causes, and outcomes of periviable births. A comprehensive registry over the continuum of periviable pregnancies and outcomes does not currently exist (the MFMU collects limited short-term data on neonatal outcome only for pregnancies included in trials and the NRN collects limited maternal data only if the infant is born alive at 22-28 weeks). There are very little

data on the frequency and causes for admission before periviable birth and the outcomes of periviable birth. Such data are essential to develop an understanding of the epidemiology of periviable birth and gain insights into the underlying biology. The obstetric and neonatal data will also be valuable for comparative effectiveness evaluations, in generating hypotheses that can be tested in multicenter trials, and in development of policy decisions based on the epidemiology. A prospectively collected database is needed to guide counseling and management of the pregnancy at risk for periviable birth and the periviable newborn, including development of understanding of the impact of specific factors (e.g. race/ethnicity, prenatal interventions such as antenatal steroid and magnesium sulfate administration, route of delivery, newborn interventions) using a comparative effectiveness research approach to develop effective interventions for counseling and treatment to prevent and mitigate periviable birth and its complications.

The second Specific Aim of our study is to evaluate the utility of the prognostic/risk-stratification web-based tools. It is well known that statistical prognostic models are more accurate than clinical intuition. Grove & Meehl showed that of 136 studies comparing predictions made by humans and statistical prediction rules (SPRs), 64 favored the SPR, 64 were roughly equal, and only 8 favored human judgment (12, 13). However, it is not clear how useful these prognostic models are in periviable pregnancy. Clinicians often use their past experience, judgment, and local data for counseling and prognosis, but caretaker intuitions of outcome in the neonatal intensive care unit are not very accurate (14). Significant between-hospital variation exists in the rates of initiating potentially life-threatening treatments after birth among periviable infants, which accounts for 78% of the between-hospital variation in survival at 22 or 23 weeks of gestation (15). Obstetricians and neonatologists continue to struggle with ethical questions and judging when intensive care is ethically mandatory, unwarranted, or optional and may differ on how parents can be best informed and counseled (16, 17). We have shown that physicians' willingness to provide care to more immature infants is associated with improved outcomes for more mature preterm infants (18). Both obstetricians and pediatricians consistently underestimate survival and freedom from serious handicap in preterm infants, and those who underestimate survival are less likely to provide interventions such as antenatal steroids and mechanical ventilation (19).

Evidence-based ethics may lead to better informed and more acceptable treatment decisions by parents and caregivers (17). For example, we have demonstrated that prediction of mortality is improved by using data from the first five minutes after birth (which includes the response to resuscitation) as compared to antenatal data alone when many decisions about provision of care at birth are made (20). While most parents appreciate a shared decision making process as compared to clinician decisions or informed decision making (21), many cultural influences modify this process (22). Communication with parents is important (23) but it is not clear if quantitative data such as from prognostic models improves the ability of parents to understand the issues involved and to make better decisions ("better" being defined as those with which parents and clinicians are more satisfied with at a later time point). Rational consensus periviability guidelines are well accepted by clinicians and are perceived by pregnant women as highly understandable, useful, consistent, and respectful (24). However, disconnects often exist between what clinicians believe parents have been informed about and what parents believe they have been told. Keenan et al.(25) interviewed mothers who delivered between 22 and 27 weeks of gestation and their counselors. While 67% of the mothers stated they had received a treatment recommendation, only 27% of the counselors stated they had made a recommendation, saying instead they had described the treatment plan or offered options (25). Therefore, counseling is often perceived as directive even when not intended to be directive. Use of quantitative estimates (e.g. 80% probability of death, with 70% probability of handicap if survival) may bring more objectivity to counseling, and it needs to be determined how these help decision-making.

Our third Specific Aim is to identify outcomes that are most important to parents and develop estimators and Decision Aids for these outcomes. Decision Aids are decision support systems that clarify decision and needs, provide facts and probabilities, clarify values, and guide deliberation and communication. Major recommendations from the Periviable Pregnancy Workshop (11) included increased family participation in research regarding counseling, understanding, and preferences, and studies to improve understanding of parental coping mechanisms, attitudes, and perceptions regarding death and long-term disabilities. The factors that parents and clinicians weigh during decision-making are likely to be different. To date, it has been assumed that parents are primarily interested in the same outcomes that neonatologists are interested in improving – mortality and neurodevelopmental impairment. This assumption has not been rigorously tested. Payot et al.(26) interviewed twelve parents and attending neonatologists immediately following consultation for risk of preterm delivery at 23-25 weeks gestation, followed by a subsequent interview 4-6 months later. It was found that clinicians and parents engage in decision making

from different standpoints; while neonatologists focus on management of the unborn baby, parents have yet to conceptualize their infant as a distinct entity as they are grieving their pregnancy and parenthood (26). Parents expressed the need to receive more than just factual information from neonatologists, bringing into question the traditional concept of neutral informed consent and suggesting the necessity of a shared decision-making model (26). It is not known when and how this decision making changes after birth and how the importance of different outcomes changes with the clinical situation such as illness severity. It is also not known how MFM specialists differ from neonatologists in their perspectives. Identification of outcomes important to parents at different points along the clinical course will enable identification of variables that contribute to these outcomes and enable the development of prediction models to determine probability of these outcomes and Decision Aids to help parents and clinicians.

Various prophylactic and therapeutic interventions are possible in the MFM and NICU setting. The effect of each intervention often depends on various patient characteristics (e.g. gestational age, postnatal age, illness severity, other co-morbidities or medications). Some interventions (e.g. higher oxygen saturation thresholds) may reduce an undesirable outcome (e.g. retinopathy of prematurity) by a great deal, but increase a more serious outcome (e.g. mortality) by a modest amount (27). Effectiveness may be defined not only on the basis of objective clinical outcomes such as mortality but also on less well-defined outcomes such as quality of life in later childhood and adolescence (28) that need to be weighed along with the risks, invasiveness, costs, legal considerations (29, 30), and parental preferences (31). A decision-support system for periviable pregnancy and the periviable infant that lists the current evidence base for possible interventions at that point in time based upon known clinical variables and risk factors and provides the anticipated benefits and risks would be valuable. Harmful, wasteful, or ineffective care may be reduced with the use of Decision Aids targeted to a pregnant woman's or neonate's risk factors. For example, an infant with respiratory distress syndrome soon after birth may benefit from caffeine (32, 33), maintenance of oxygen saturation in the 91-95% range rather than 85-89% (27), and avoidance of prolonged empirical antimicrobial therapy (34). Identification of outcomes that are most important to individual families may also enable the clinicians and the parents to work together on shared decision-making regarding processes of care and interventions that will optimize the probability of the desired outcome while reducing time or resource requirements. For example, the parents of a 8 day old 23 week infant with a bilateral large grade IV intracranial hemorrhage (IVH) who are most concerned about their ability to care for a severely handicapped infant and the adverse impact on their ability to provide adequate care and education to normal siblings may be best counseled about withdrawal of care as the probability of death or severe handicap is in excess of 95%. The parents of a newly born 23 week infant may be very concerned about the possibility of a severe IVH, and indomethacin prophylaxis may be considered to reduce severe IVH even though it does not have a statistically significant effect on overall neurodevelopmental outcome (35). This will lead to a paradigm shift of using a "personalized" approach based on the "Outcome Trajectories" concept of changing prognosis at different time points in the clinical course (36) overlaid on the protocol-driven management that is currently common in periviable pregnancy in MFM and NICU care.

Innovation

Innovative aspects of our proposal include:

(a) The development of a periviable pregnancy database covering the entire spectrum of pregnancy and neonatal events, which will provide the necessary detailed obstetric and neonatal information to develop hypotheses and design studies in this population, in addition to serving as a resource to understand the characteristics of periviable pregnancy.

(b) The evaluation of quantitative prognostic estimators in counseling, which may be important not just in sick newborn infants but in other patient populations as well.

(c) The identification of outcomes most important to parents of premature infants and development of Decision Aids specific for these outcomes.

(d) Online and offline accessibility of the Decision Aids to enable point of care usage and expanded availability.

Approach

This project will use appropriate and rigorous research methods to generate patient-centered evidence. One of the main strengths of this project is that it builds upon the research expertise available at the research centers even though this project is distinct from the NRN and MFMU.

Study Design:

This will be a prospective cohort study of periviable pregnancies at [redacted] which are high performing centers in the MFMU and NRN. Study Aims 2 and 3 will be in collaboration with the Department of Health Behavior [redacted] and Medical Clinical Psychology Division [redacted].

Specific Aim (1) Develop a Periviable Pregnancy Database (PeriPD) to determine the incidence, characteristics, and outcomes of periviable pregnancies

Rationale: The epidemiology of periviable pregnancy is characterized by limited and mostly retrospective data subject to multiple biases. Until recently, infants <24w gestation were considered below the threshold of viability and were generally not resuscitated and sometimes not even evaluated by neonatologists (some infants labeled as stillbirths may in fact have been livebirths). It is important to know the frequency and causes for admission before periviable birth and the outcomes of periviable birth to develop an understanding of the epidemiology of periviable birth, gain insights into the underlying biology, create information for counseling, and generate hypotheses that can be tested in multicenter trials.

Preliminary Data: Most studies to date have evaluated extreme prematurity, and not the higher-risk subset of periviable births. [redacted] (37) in a retrospective cohort study evaluated all pregnancies from 1974 to 2004 at their center that delivered a live- or stillborn infants at >20 w of gestation. In this study, periviable births were defined as between 20w 0 d and 26w 6d (not 25w 6d as in this proposal) with birth weight between 150 and 1499g. It was observed that 1981 deliveries (1.9%) of 104,921 pregnancies resulted in periviable births. One third of these (33.1%) occurred between 20w and 22w6d. Causes of admission before periviable birth were labor (36.3%), PROM (34.1%), vaginal bleeding (10.4%), fetal death (6.2%), preeclampsia (4.0%), fetal abnormalities (2.4%), incompetent cervix (0.5%), fetal growth restriction (0.2%), and other complications (2.0%)(37). In this cohort, just 4% were twin/multifetal gestations. Women with periviable births were more likely to have had >2 previous spontaneous or induced abortions (23.8% vs. 7.1%, p<0.0001) and to have had a previous preterm birth (21.1% vs. 15.6%, p<0.0001) versus those without such a history, although the history of a previous preterm birth by itself was not very sensitive (79% of women with periviable birth have either no previous delivery or have had only term deliveries). Except for women with pre-eclampsia with early cervical dilation who remained undelivered for almost 30h on average, most women with periviable births were in the hospital for only 13 to 15 hours before delivery (**Table**). While this study provides important information, there are limitations due to shifting practices over the last decade, need for prospective data collection to capture intended interventions, and lack of data on chorioamnionitis (either clinical or histological) or fetal distress. An important knowledge gap is women who are admitted in the periviable period but move through to deliver at a later gestational age.

Indication for admission	Time to delivery (h)	Cervix (cm)
Preterm labor	13.7 (21.5)	4.4 (2.8)
Premature rupture of the membranes	15.4 (35.5)	3.4 (2.8)
Twins/multifetal gestations	14.1 (24.4)	4.6 (3.3)
Vaginal bleeding	13.2 (17.6)	4.1 (3.3)
Preeclampsia	29.5 (31.6)	0.7 (0.9)

Data are given as mean (SD).

Table: Time from admission to delivery and cervical dilation at admission for 919 women who were delivered at 20-26w GA between 1994-2004 (Mercer et al. AJOG 2005).

Design:

1. We plan to develop a Periviable Pregnancy Database (PeriPD) which will be a prospective registry of periviable pregnancies (defined as 20w 0d through 25w 6d of gestation) admitted to the four research centers of the PPRN. The PeriPD will collect observational baseline data in a uniform manner on both mothers and infants including the therapies used. The information collected will be comprehensive and patient-focused rather than limited to a disease or treatment.
2. Data will be analyzed to detect associations and trends between baseline information, treatments, maternal outcome, and infant outcome to facilitate design of future PPRN trials.
3. The data collection instruments will be based on those used in the Generic Database (GDB) of the NRN for extremely preterm infants (https://www.clinicaltrials.gov/ct2/show/NCT00063063) except that the forms used in this study will include data on periviable pregnancies independent of live birth and detailed maternal data including data on previous pregnancies. The MFMU does not currently have such a registry of periviable births, and the NRN collects limited information on the mother if the infant is alive at birth and born between 22 and 28 weeks. [redacted] (DCC) for this proposal,

also manages the GDB for the NRN and has expertise with the development of registries, data collection instruments, validation, and analysis.

4. Informed consent will be as required by local IRBs at individual centers. All centers have trained research coordinators with many years of experience in patient enrollment and data collection.
5. The data collected will include information on:

a. Mother's detailed pregnancy history and complications, dating criteria for estimated date of delivery, including data on proximate causes of and antecedents, and measurements from ultrasound scans in first and second trimesters if available; medical conditions (including diet, obesity, mental disorders etc) preceding the pregnancy, and maternal medications.
b. Counseling provided by obstetrician and neonatologist
c. Details of labor and delivery characteristics and interventions (e.g. time of rupture of membranes, antenatal steroids, magnesium sulfate, tocolysis, antimicrobial therapy, mode of delivery)
d. Details of timing of events (from symptoms to presentation to physician, from symptoms to arrival at hospital, from admission at hospital to delivery, etc) will be critical. Hospital length of stay of mother and infant as well as duration of various periods (e.g. from antenatal steroid administration to delivery) will be calculable. Women will be tracked from their initial visit (to ER or Obstetric admissions) and admission (to hospital floor or Labor and Delivery) during the periviable period to birth of their infant and their discharge from hospital. Some women who present at 20-26w gestation may deliver much later (at term), and these outcomes will be recorded as well. Maternal outcomes after birth of a periviable infant (endometritis or other infections, lactation success) will also be tracked until her discharge.
e. Infant characteristics (e.g. liveborn or stillborn; if liveborn, Apgar scores, birth weight and other measurements, need for and nature of resuscitation, clinical course in NICU including complications and medical outcomes until discharge). These medical outcomes will include respiratory outcomes such as severity of RDS, diagnosis of BPD (physiologic and traditional definitions (38, 39), duration of mechanical ventilation, duration of parenteral nutrition, proven medical or surgical necrotizing enterocolitis (40), sepsis, intraventricular hemorrhage and grade/laterality (41), periventricular leukomalacia, retinopathy of prematurity and its severity (42) and need for therapy).
f. Placental pathology will also be evaluated, as placental histology using established criteria is done routinely in this population at all participating centers.
g. Early childhood outcome: inborn extremely preterm infants are followed-up at 22-26 months corrected age in all four centers using a complete standardized neurologic examination and BSID-III (cognitive, language, and motor outcomes) by certified examiners (43).
h. Descriptive and hypothesis-generating analyses will be performed by [redacted] to determine the risk factors, characteristics, and outcomes of periviable pregnancy and periviable infants similar to that done for extremely preterm infants in the GDB (4, 5, 43, 44).

Sample size and Statistical Analysis

We anticipate that we will have about 320 periviable pregnancies available for enrollment annually (a conservative estimate based on data in 2013 and 2014: the anticipated numbers of periviable admissions are 40-45/yr at [redacted], 70-80/yr at [redacted], 100-110/yr at [redacted], and 110-120/yr at [redacted]. As an example, at [redacted] in 2013, there were 128 women admitted between 20-25 weeks gestation who delivered 148 infants (18 infants with 0 NICU admissions at 20w, 12 with 1 NICU admission at 21w, 30 with 18 NICU admissions at 22w, 29 with 25 NICU admissions at 23w, 36 with 29 NICU admissions at 24w, and 23 with 21 NICU admissions at 25w).

The first 6 months of the grant period will be devoted to development of the Manual of Operations, data collection forms, training of coordinators, getting IRB approval, and other logistics. We anticipate enrolling for four years. If patient numbers remain steady (as they have in recent years), we should have 320 x 4 = 1280 periviable pregnancies of whom we plan to enroll ~1000 (assuming 80% consent rate, which is conservative compared to our 85-90% consent rate in MFMU/NRN observational studies). It is anticipated that there will be attrition as some women who are admitted at 20-26w gestation may not deliver, but may be discharged and lost to follow-up. Based on recent data, this number is <5%. Hence, we estimate we will have complete data on 1000 periviable pregnancies in 4 years of data collection.

The [redacted] will perform data cleaning, data lock, and statistical analysis using standard methods. Continuous variables are generally analyzed by t-test or rank sum test while categorical variables are analyzed by Chi-square test. Adjustment for covariates will be done using multivariable logistic regression. [redacted]

The available sample size (1000) is sufficient to detect relatively small effects (10% difference in relative risk for moderately prevalent outcomes) at 80% power, α=0.05 by the Chi-square test. For example, one can determine if antenatal magnesium sulfate, indomethacin tocolysis, or cesarean section delivery are associated with any reduction in severe IVH in periviable infants, after adjustment for other variables.

This will be the largest prospectively collected dataset of periviable pregnancy to date from large perinatal centers and sampling a very diverse population across the United States (e.g. 38% Hispanic/Latino at [redacted] vs. 2-3% at Case and [redacted]; 52% Black at [redacted] vs. 21% at [redacted]).

Anticipated Results, Potential Problems, and Alternative Strategies

No major problems are anticipated with development of the Periviable Pregnancy Database. Women with periviable pregnancies are being routinely evaluated and admitted to the four centers of our consortium. The PIs have the necessary expertise in large multicenter trials and have a track record of collaboration among themselves. The research coordinators have many years of enrolling patients and collecting data. The [redacted] has an excellent track record of serving as a data coordinating center and has worked with many of the investigators on this proposal on pioneering studies in the literature.

It is possible that enrollment may be slow, especially if there is competition for patients from the nearby perinatal centers. We will be able to enroll more patients if necessary by adding additional sub-sites (e.g. The [redacted] Division of Neonatology also provides neonatal care at 4 other level III NICUs in the same metropolitan area). Some patients who are admitted with periviable pregnancy may not deliver early but may deliver much later (after 26w gestation or perhaps even at term). We will collect data on these pregnancies for such data is important not only for counseling, but also to help identify characteristics of the women who are lower risk.

It is important to realize that the field is changing rapidly, and the research centers are a select group of regional perinatal centers. Data collected during this time period and from these centers may not be fully extrapolatable to data from subsequent time epochs or from other sites/regions. Hence, detailed characterization of our population in terms of race/ethnicity/socio-economic status and maternal/infant characteristics will be performed.

A biorepository of maternal samples (vaginal swabs, urine, plasma and cell pellet from 2 ml blood obtained at time of routine sampling from periviable admission) and neonatal samples (cord blood, urine in first 3 days, tracheal aspirate if intubated and tracheal suctioning is perfomed) will be collected and frozen following opt-in consent. Due to budgetary constraints, these samples will not be analyzed in this project, but will be stored for microbiomic, proteomic, and other –omic profiling if additional funding is obtained.

Specific Aim (2) Determine whether the use of the NICHD NRN Outcome Estimator, Outcome Trajectory Estimator, and BPD Estimator for parental counseling leads to increased parental satisfaction, increased clinician satisfaction, changes in therapies, and improved clinical outcomes of periviable infants

Rationale: Multiple prediction models have been developed in recent years to determine the probability of death or adverse outcome, using readily available clinical data. However, it needs to be determined if such quantitative data help counseling, improve satisfaction, or change processes of care and subsequent clinical outcomes of periviable pregnancy or periviable infants.

Preliminary Data: Three prognostication/risk-stratification tools are available for general public use at https://neonatal.rti.org under “tools”:

(1) Assessment of outcome of infants born at 22 to 25 weeks of gestation(46)
(2) Determination of the probability of BPD at six postnatal ages using readily available clinical data in infants 23-30 weeks gestation and 501-1250g birth weight (47)
(3) Dynamic models of the changing probability of individual outcome (death or neurodevelopmental impairment) in extremely preterm (22-32 w GA and 401-1000g birth weight) infants, based on information available at birth and later during the clinical course (36)

Current techniques of counseling parents on the risks of mortality or specific morbidity are qualitative rather than quantitative. The evidence base for decisions on initiating or forgoing intensive care for periviable infants is limited (48). Most clinicians use gestational age to determine the likelihood of a favorable outcome with intensive care in very preterm infants but a more accurate estimate can be obtained by consideration of sex, exposure to antenatal corticosteroids, whether single or multiple birth, and birth weight in addition to gestational age (46).

The NRN has made such an estimator available for public use (https://neonatal.rti.org under “tools”), where entry of data of these variables enables the viewer to observe the estimated outcomes of survival,

survival without profound neurodevelopmental impairment (NDI at 18-22 months' corrected age), survival without moderate/severe NDI, death, death or profound NDI, and death or moderate/severe NDI (46).

The NRN has developed a similar estimator to accurately determine the probability of BPD using a limited amount of readily available clinical information (47). Similar to the mortality estimator, the web-based BPD estimator is available for public use at https://neonatal.rti.org (**Figure 1**).

More recently, we have developed the innovative "Outcome Trajectory Estimator" for the NRN to predict prognosis with changes in the clinical course (36). Our objective was to develop serial predictions of outcome (death, death or NDI, or NDI in survivors) rather than prediction of outcomes based on inception variables alone. Models were developed for specific times during hospitalization (in delivery room, 7-day, 28-day, and 36-week postmenstrual age) to predict death or death/NDI at 18 to 22 months. We found that for death or NDI, the importance of birth weight declined over time, whereas the importance of respiratory illness severity increased with advancing postnatal age (36). Therefore, these dynamic models of the changing probability of individual outcome improved outcome predictions. Various current and future scenarios can be modeled on the interactive web-based model by input of different clinical possibilities to develop individual "outcome trajectories" and evaluate impact of possible morbidities on outcome (**Figures 2, 3**) (36). The benefits of these novel interactive tools include individualized prognostic information specific to postnatal age, identifying infants likely to benefit from preventive strategies, and stratifying infants for clinical trial enrollment (47).

The advantages of these prognostic/risk-stratification models are that (a) they provide a quantitative estimate, which help to more precisely define the magnitude of risk as most clinical factors only contribute a small fraction of the total risk, (b) statistical prognostic models are more accurate than clinical intuition (12, 13), (c) the web-based nature of the models enables their use anywhere – at the patients' bedside, during counseling sessions with parents, or at other locations, (d) the web-based models can be rapidly updated as new data become available, (e) the implementation of new evidence-based therapies can be accelerated by linking new evidence, and (f) the recommendations can be targeted to results of searches. A limitation of these models is that they use data from more than a decade ago and do not include infants <22w GA.

Neonatal BPD Outcome Estimator
Infants with GA 23-30 weeks & Birth Weight 501-1249g

Gestational Age (Weeks)	25
Birth Weight (Grams)	600
Sex	Male
Race / Ethnicity	White

Probability of Outcome (expressed as a percent)

Time Period	Ventilator Type	FiO2	Death	Severe BPD	Moderate BPD	Mild BPD	No BPD
Day 7	IMV/SIMV	40	13.2	33.3	34.7	18.1	0.8

Figure 1: BPD estimator: Output shown for a hypothetical 25 week 600g white male infant, who is on mechanical ventilation with 40% oxygen on postnatal day 7.

Probability of Outcome (expressed as a percent)

Time Period	Death or NDI	Death	NDI
Birth	78	46	57
Day 7	75	37	57

Figure 2: Outcome trajectory estimator: Output shown for a hypothetical 25 week 600g inborn male infant on postnatal day 7, with 5 min Apgar score of 6, exposed to antenatal steroids, who has been on a conventional ventilator from birth to day 7, and was diagnosed with a grade II IVH.

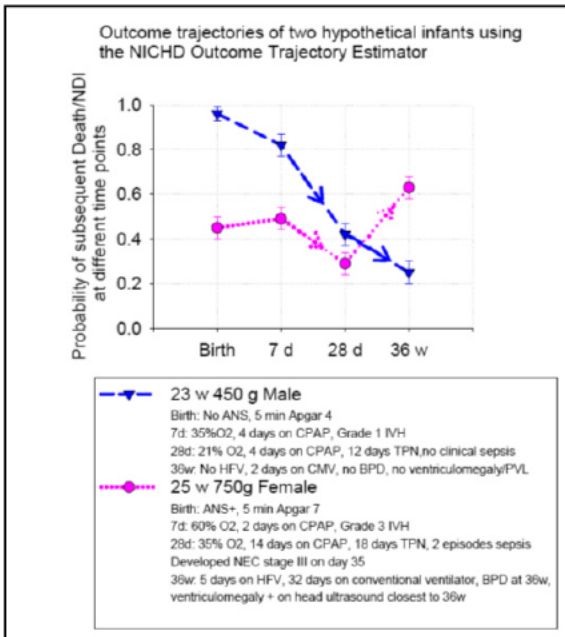

Figure 3: Outcome trajectory of two hypothetical infants using the outcome estimator. The trajectories are shown for a 23w 450 g male infant (blue triangle) and a 25w 750g female infant (pink circle), using data developed using the online estimator.

Overview of Process:

- Design: Prospective multi-center controlled before-and-after study (non-randomized) design
- "**PICOTS**":
  - **P**opulation: Parents of periviable infants and their clinicians
  - **I**ntervention: Counseling using Quantitative Estimators
  - **C**omparator: Counseling using standard qualitative estimates, specific for gestational age and illness severity

- **O**utcomes: Parental and clinician satisfaction with counseling process, changes in processes of care, and neonatal outcomes
- **T**iming of outcomes and length of follow-up: Outcomes in hospital by 36 weeks' post-menstrual age
- **S**ettings and providers: NICUs of participating research centers

Details of Process:

In association with the Department of Health Behavior at [redacted] and research coordinators will develop and pilot semi-structured interviews to evaluate parental and clinical satisfaction over the first year of the project period at [redacted]. This instrument will also collect information on which outcomes are perceived to be important to parents (for Aim 3). Data on clinical processes of care, therapies, and outcomes (mortality and short-term morbidity such as severe IVH, BPD, necrotizing enterocolitis, and late-onset septicemia) will be collected as in Aim 1.

Instrument development (Years 1-2) at [redacted]: Reliable and valid parent and clinician satisfaction instruments are essential for evaluating satisfaction from the use of these prognostic tools. Therefore, the first stage of this study is the development of reliable and valid instruments for both parents (Prognostic tool satisfaction: Parent measure) and clinicians (Prognostic tool satisfaction: Clinician measure).

We will develop these two satisfaction instruments in compliance with theoretical (49), and methodological (50) frameworks through several steps (51): 1) item generation, 2) item selection and content validation, 3) pretesting and item reduction, and 4) reliability and validity testing.

1. Item generation. The first step in item generation is to define the construct and specify its underlying dimensions (52), i.e., to determine the boundaries of the domains of parent and clinician satisfaction related to NICU activities in general and specifically, with the counseling process. Initially, areas of satisfaction to be included in the measures will be identified by reviewing the literature, examining measures previously developed for similar purposes, and conducting focus groups with parents and clinicians to learn what factors they feel contribute to satisfaction related to decision making. This will produce a pool of items assumed to have content validity. Several parent satisfaction instruments have been developed for use with NICU parents (49, 51, 53). For example, Mitchell-DiCenso et al.(53) developed a 27-item instrument for distinguishing parents who are satisfied with NICU care services from those who are not. Items in the published literature which reflect the important areas of parental satisfaction that may be related to use of prognostic tools, will be included in the *initial list of potential items*. Based on a review of existing published NICU satisfaction measures and related literature (54), we identified the following domains as being representative of parent and clinician satisfaction with NICU care: (a) decision making/involvement in care (49, 53), (b) communication,(49, 51, 54, 55) (c) processes of care (51), (d) outcomes of care (51), (e) knowledge acquisition/need for information/uncertainty (51) understanding information (53), (f) anxiety/worry (51), (g) hope (54), (h) assurance/trust (49, 53, 54), (i) pain management (49, 54), (j) support (49), understanding/ empathy (55). Based on our review we feel that decision making processes (communication, including conveying information in an understandable manner) and decision making outcomes will have the most application to satisfaction with prognostic tools. Thus, items will be developed with reference to these two domains. *Sample* items include: How satisfied are you with the information and explanations you received from the doctors and nurses?; How satisfied are you with the amount of time doctors and nurses devoted to talking to you?; How satisfied are you with the decisions made about your infant's treatment?; How satisfied are you with what happened because of those decisions?; How satisfied are you with your role in the decisions made? We will word these items at the fifth to sixth grade reading level (using Microsoft Word's Flesch-Kincaid Grade Level readability analysis). For clinician item generation, we were unable to identify specific measures in the literature. Therefore, we will develop parallel items regarding decision making satisfaction.

Focus groups among convenience samples will be conducted for parents and clinicians separately to identify their perspectives and needs with respect to prognostic tools. Following methods used by Butt et al. (51), our goal is to recruit 30 parents of extremely preterm (all inborn periviable infants) and 30 of their clinicians from MFM and Neonatology (attending physicians, fellows, and nurse practitioners who routinely counsel parents; selected using random assignment) over the first year of the study at [redacted]. This is feasible, as we have 100-120 periviable pregnancies per year, and our consent rate for clinical studies is well over 50%. Depending upon the clinical service load, some clinicians may be assessed more than once. Researchers will review the transcripts to collapse related topics into themes/domains (51) and compare the categorized domains with constructs identified in the literature for inclusion in the item list. We will also do qualitative analysis of the focus group data to identify themes and write items based on the themes.

2. Item selection and content validation. To select most appropriate items, a representative sample of at least 20 parents (not the same as in item 1) and 20 clinicians will be identified and asked to rate the importance of each item on a scale of 1-5 (5=very important). Researchers will browse selected items to eliminate redundant items (51), and re-classify the remaining items into pre-determined (above) domains of satisfaction (53). Cognitive interviews will be done to ensure that new items function as expected.

3. Pretesting and item reduction. The remaining items will be refined through pretesting with 20 parents and 20 clinicians at [redacted] (may overlap with parents/clinicians in item 2). The pretest is to minimize any bias attributable to vague wording. The implementation of the pilot instrument will then be done over the next six months. The instruments will then be assessed within a group of parents and their clinician respondents (n=30 each) for item reduction analysis according to statistical criterion (e.g. item-total correlation < 0.3). Coefficients alpha and omega will be computed and items with floor and ceiling effects will be identified (which would be candidates for removal from the scale). The factor structure will be verified for assessing structural validity.

4. Reliability and validity testing. Reliability of the instruments will be evaluated by computing Cronbach's coefficient α to assess internal consistency. This computation will be based on the same sample that is used for the item reduction analysis. Construct validity will be tested by analyzing the correlation between the instrument and an overall global rating of satisfaction using a single item rating "satisfaction" on a five-point scale (51) and confirmatory factor analysis for assessing the existence of factor/domain structure. The same sample of patients and clinicians will be used for factor analysis.

Evaluating satisfaction, changes in process of care, and outcomes (Years 3-4) in all 4 centers:

The evaluation study will be a two group posttest only design, in which the satisfaction of respondents in a "before" usual care versus "after" prognostic tool group will be assessed after parent's / clinician's decision making.

We will enroll 100 patients (parents or legal guardian of infant will be enrolled) and their corresponding 100 clinicians (MFM/OB or neonatologists) for the "before" group and the other 200 (100 patients and 100 clinicians) in the "after" group from all 4 centers. Informed consent will be obtained from both parents and clinicians, using IRB-approved consent forms. The inclusion criteria will be the same as during the instrument development phase: all patients eligible for the Periviable Pregnancy Database (PeriPD) will be eligible for this study.

Usual care and Prognostic tool Groups. Parents and clinicians from whom data are collected in the first year of this evaluation study (Year 3 of project) will comprise the "before" usual care group. During this time period, the current (intuitive) approaches to decision making will continue and satisfaction will be assessed at the specified time points (prior to birth, first 3 days, 7-10d, 28-35d, and 36w post-menstrual age). During the following year (Year 4), the prognostic tools will be used in decision making with a new cohort of parents (the "after" group) and satisfaction again will be assessed in parents and clinicians.

Measures: In addition to the satisfaction measure, we will also include demographic items, other NICU satisfaction measures and the global satisfaction item. Clinical factors (major outcomes and clinical processes associated with these outcomes) to be used in the analysis will be from data collected for Aim 1.

Sample size and Statistical Analysis

Following development of the instrument and its validation, we will enroll 100 parents and their corresponding 100 clinicians for the "before" group and the other 200 (100 patients and 100 clinicians) in the "after" group in all 4 centers. This sample size is feasible as [redacted] and [redacted] each have approximately >100 periviable pregnancies per year, and our average consent rate in NRN studies is 80-85%. The other 2 centers have lower patient volumes but more than adequate for this study. At α=0.05 with 80% power, a 50% change in outcome/processes (e.g. from 30 to 15, of 100) can be detected.

As the measures of satisfaction are primarily ordinal measures, we will use parametric evaluations (t-test, ANOVA, and Cohen's d) as well as non-parametric evaluations (Cliff's delta) in addition to multilevel/hierarchical modeling for modeling hierarchically structured data to separately estimate the predictive effects of an individual variable and its group level mean. The available sample size is adequate to detect a one point difference in a five point satisfaction scale (e.g. a change from 3 to 4, of 5) assuming the standard deviation in scores in each group is not more than 2. In addition to analysis as an ordinal measure, we will also analyze as categorical measures (fully or mostly satisfied vs. other responses). Evaluation of processes of care and outcomes will be categorical (either present or absent). Categorical measures will be analyzed by chi-square analysis.

Anticipated Results, Potential Problems, and Alternative Strategies

We anticipate that we will have reliable and valid measures of parent and clinician satisfaction based on processes and outcomes most important to these groups. These measures will be used in evaluating the utility of the Decision Aids based on the same outcomes (in Aim 3). Potential problems include omission of important satisfaction domains or factors and failure to confirm the anticipated factor. Alternative strategies will include pulling in more items from general NICU satisfaction measures for parents and clinicians to react to or using exploratory factor analysis which may require more cases.

We anticipate that different components of the prognostic tools will be considered more valuable by parents as compared to clinicians. Specifically, clinicians may consider the risk of subsequent mortality as more important than parents, who may rank survival with profound neurodevelopmental impairment as more relevant. Parents may also be more concerned about severe BPD rather than mild or moderate BPD, due to the higher likelihood of discharge home on oxygen, long-term impairment in lung function, and need for frequent rehospitalizations. It is likely that MFM/OB physicians may view certain outcomes (e.g. NDI or cerebral palsy) as more important than neonatologists, for whom mortality may be more significant.

One potential problem is that parents who do not consent to be interviewed may be different from those who are enrolled. We will evaluate patient characteristics (e.g. race, socio-economic status, maternal age) to determine how enrolled parents are different from eligible non-enrolled parents, and determine the impact of such factors. A small proportion of our patients (5-10%) are not English-speaking. We have access to interpreters, and interviews will be in the language in which parents are proficient.

Confounding issues may arise because the data will be collected on different clinicians. For instance, some clinicians may prefer conventional qualitative estimates over prognostic tools at certain time points. This issue will be addressed by multilevel /hierarchical model, taking into consideration the intraclass correlation among patients seen by the same provider at the same clinical location at different time points and to adjust for center effects. This can be applied to determine the direct effect of the diagnostic tools (the lowest level) on satisfaction by offsetting the moderating effect of higher level factors (i.e. Clinicians).

A limitation is that we do not have any quantitative estimators for periviable pregnancy (only for the neonate after birth), unless we use the outcome estimators for the time of birth with an estimated fetal weight (which is not very accurate). If quantitative estimators are proven useful, we will develop such estimators using data from Aim 1. Other limitations of our study are that it has a limited sample size, as periviable pregnancies are not very common even in a multicenter study, which limits our ability to evaluate race/ethnicity, socioeconomic status, and other variables as determinants of parental preferences.

Specific Aim (3) Determine the neonatal outcomes in which parents are most interested, develop a better means of framing and communicating clinical evidence, and develop Decision Aids to enable parents of periviable infants to make better informed decisions

Rationale/Background: Identification of outcomes important to parents at different points along the clinical course will enable identification of variables that contribute to these outcomes, and will also enable the development of prediction models to determine probabilities of these outcomes. Recent decades have witnessed a shift in medical ethics from physician paternalism to patient autonomy (56) indicating a need to have better informed parents, with a corresponding need to find out what they need to know. “Decision Aids” are necessary in order to optimize shared decision-making in the periviable period, determine outcomes important to parents and find their underlying motivations, clarify their values, and guide deliberation and communication.

In 1993, Helen Harrison stated “The Principles of Family Centered Neonatal Care”(57) of which the first four principles were:

1. Family-centered neonatal care should be based on open and honest communication between parents and professionals on medical and ethical issues.
2. To work with professionals in making informed treatment choices, parents must have available to them the same facts and interpretation of those facts as the professionals including medical information in meaningful formats, information about uncertainties surrounding treatments, information from parents whose children have been in similar medical situations, and access to the chart and rounds discussions.
3. In medical situations involving very high mortality and morbidity, great suffering, and/or significant medical controversy, fully informed parents should have the right to make decisions regarding aggressive treatment for their infants.
4. Expectant parents should be offered information about adverse pregnancy outcomes and be given the opportunity to state in advance their treatment preferences if their baby is born extremely prematurely and/or critically ill.

These principles were developed in 1992 by a consensus conference of 10 parents, who had a total of 32 children, 20 of whom were born prematurely, 4 of whom died in the NICU, and 7 of whom have handicap. These principles have strongly influenced current counseling practices. However, this group of parents, all of whom were articulate, with a high degree of participation in support organizations, disability rights groups, and hospital ethics committees, may not be fully representative of the population of parents of infants in most current NICUs due to cultural and socio-economic differences.

For example, in the NRN in 2010 (unpublished data), 53% of mothers were single, 83% were on Medicaid, and only 17% had a college or graduate degree. 38% of the mothers were black, 16% were Hispanic/Latino. Keenan et al. (25) interviewed parents to clarify what factors were important in decisions regarding resuscitation, and found disconnects between health care provider and parental needs. Most mothers responded with personal values, beliefs, or experiences, rather than the medical information that was presented during their counseling. Many mothers said that they simply wanted everything done ("Never a question not to do everything", "Wanted everything done for him"). Others relied on their faith, and only 2 mothers specifically mentioned the infant's prognosis, whether their infant would suffer, or the infant's future quality of life. Streiner et al.(58) found that 64% of parents who had a premature infant survive into their teens (some with handicaps) believed that all ELBW infants should be resuscitated regardless of prognosis, compared with only 6% of neonatologists and NICU nurses. Brinchmann et al.(59) found that parents wished to be consulted and wanted information but did not want the burden of making the final decision about withdrawal of support in the NICU.

It may appear to be a simple solution to just ask parents what they want to know and the level of information they want, but one needs to know the relevant issues well enough to know what questions to ask and what information to pursue. In addition, various cognitive biases are present in decision-making, regardless of level of education or intelligence. A cognitive bias is a tendency to make systematic errors in certain circumstances based on cognitive factors rather than evidence (60). As an example, the sunk-cost bias is the tendency to pursue a course of action, even after it has proved to be suboptimal, because resources have been invested in that course of action (60). An infant born at 28 weeks' gestation predicted at birth to have a good (>80% probability of normal outcome) may be found to have a bilateral large grade IV IVH at a week of age and the probability of a good outcome decreases to < 5%. However, clinicians and parents have already invested much effort and emotion into care in the first week which may influence their decisions. Unexamined biases in decision-making can contribute to health care disparities as they are complex but systematic, differing by racial-ethnic group (61). Common approaches such as stereotype suppression are ineffective for reducing non-conscious bias, and alternative approaches are needed (62).

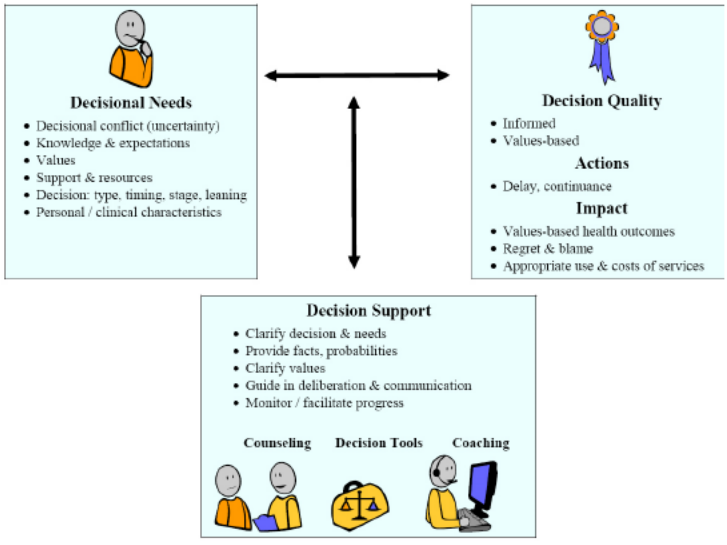

Figure 4. Ottawa Decision Support Framework from http://decisionaid.ohri.ca/docs/develop/ODSF.pdf

Design:

"**PICOTS**":

- **P**opulation: Parents of periviable infants
- **I**ntervention: Counseling using Decision Aids
- **C**omparator: Counseling without using Decision Aids
- **O**utcomes: Parental satisfaction with Decision Aids, changes in decisions
- **T**iming of outcomes and length of follow-up: Outcomes in hospital by 36 weeks' post-menstrual age
- **S**ettings and providers: NICUs of the 4 participating research centers.

1. The interviews conducted by the research coordinators in Aim 2 will be analyzed to determine the outcomes important to parents, and to evaluate the psychological and cultural factors involved in the decision-making process by the parents and the clinicians.
2. Prediction models will be developed (similar to models evaluated in Aims 2) for outcomes most important to the parents. This process will rely on the approaches developed by Gorini & Pravettoni (63), in which decision aids facilitate and support the shared decision-making and by Epstein et al.(64) which

details methods for communicating evidence that improve understanding, involvement in decisions, and outcomes. In general, these approaches include (a) presenting options with equipoise before asking parents about preferred decision-making roles, (b) presenting absolute risk reductions rather than relative risk which is often misleading, (c) presenting vertical bar graphs or cartoons for comparative information, and proportions rather than percentages (without confidence intervals), and (d) use of decision aids to limit impact of cognitive biases (63, 64).

3. The Decision Aids will be based on the Ottawa Decision Support Framework (ODSF) (www.ohri.ca/decisionaid). The ODSF uses concepts and theories from general and social psychology, decision analysis, decisional conflict, values, social support, and self-efficacy to arrive at a decision support system. (**Figure 4**). In particular, we will modify the tools (available at: http://decisionaid.ohri.ca/eval.html) for Decision Regret Scale, Decision Self-Efficacy Scale, Decision Support Analysis Tool (DSAT-10), and Decisional Conflict Scale for use in our population. Moro et al.(54) have successfully used the ODSF in a small single-center study to evaluate parent decision making for life support decisions for extremely premature infants.
4. These Decision Aids at the different time points (prior to birth, first 3 days, 7d, 28d, 36w PMA) will be evaluated in Year 3 in a similar manner to that done in Aim 2 (initial development in a small sample [n=50] followed by testing and item reduction [n=20] followed by validation [n=30] at [redacted]). The outcomes evaluated will be parental satisfaction with the Decision Aids and the nature of decisions made after using the Decision Aids (as determined in the interview).
5. Final testing and validation will be in 200 parents (mothers, or both parents if available) in all 4 centers - the initial 100 in Yr 4 without Decision Aids, and subsequent 100 in Yr 5 using Decision Aids.

Once validated, the Decision Aids will be made available on a publicly accessible website maintained by the PPRN.

Anticipated Results, Potential Problems, and Alternative Strategies

We anticipate determining the neonatal outcomes in which parents are most interested and associating these desired outcomes to their cultural and social environment. We also expect to develop a better means of framing and communicating clinical evidence (as described by Epstein et al.(64)): understanding the family's experience and expectations, building partnership, providing evidence including discussion of uncertainties, presenting recommendations informed by clinical judgment and parental preferences, and checking for understanding and agreement. Importantly, we expect to develop Decision Aids for enabling parents of very premature infants to make better informed decisions. While this Aim is primarily focused on neonatal outcomes, we will also develop Decision Aids for important maternal outcomes (e.g. avoidance of classical cesarean section) that are identified during the interview process.

Potential problems are that there may be marked lack of concordance in what different parents consider as important outcomes or between what the parent decides and what clinicians consider as decisions in the best interest of the child. Even within the same family, we sometimes observe different values and decision-making matrices. The father and the mother may have different expectations and arrive at different decisions. Such issues are inevitable and will arise despite the maximum amount of information, as perceptions are unique and may vary even within a single individual over time. We will include conflict-resolution tools within the Decision Aids, and provide additional counseling in such situations.

We anticipate finding that the Decision Aids will be used by many clinicians and will increase the proportion of evidence-based interventions in the neonatal intensive care. We expect that both clinicians and parents will be more satisfied with decisions made using this decision-support tool.

The study population is drawn from multiple academic large centers. The population is at higher risk than that at many private institutions with a smaller daily census and a higher socio-economic status. In the [redacted] NICU in 2010, 67% of mothers were single, 78% on Medicaid, with a mean age of 25 years (range 14-39), with only 7% known to have a college or graduate degree. 65% of the mothers were black, and 7% were Hispanic/Latino. Therefore, this population is one with more possible barriers than the average preterm birth in the United States, and hence an intervention successful in this population is likely to be generalizable.

Our statistical modeling will take into account the parent's cultural, educational, and social background in addition to ethnicity and center effect to enable a more personalized approach to decision-making. Our sample size calculations are appropriate to ensure suitable prognostic tool development and decision-support models, followed by model testing and validation. Our sample size is capable of detecting a 1-point difference (a change of sufficient magnitude to assure relevance) on a 5 point scale of patient or clinician satisfaction, with 80% power at α=0.05.

Protection of Human Subjects
1. Risks to the Subjects
Human Subjects Involvement and Characteristics

Periviable pregnancies (defined as 20w 0d through 25w 6d of gestation) have a very high risk of stillbirth or neonatal death (almost 100% mortality for 20-22 weeks, very limited survival at 23 weeks gestation, and a high risk of handicap even if the infant survives at 23-25 weeks gestation).

This proposal is designed to develop a Periviable Perinatal Research Network involving four large academic centers to develop a database of periviable pregnancy, identify the outcomes that clinicians and parents are most interested in, and develop decision aids to help counseling.

This proposal is observational (Aim 1) and interview-based (Aims 2 and 3). Although the population being studied is high-risk and highly vulnerable, participation in this study does not add any significant risk.

There are three separate Aims to this study:

In Aim 1, we plan to develop a Periviable Pregnancy Database (PeriPD) to determine the incidence, characteristics, and outcomes of periviable pregnancies.

The Periviable Pregnancy Database (PeriPD) will be a registry of periviable pregnancies (20w 0d through 25w 6d of gestation) admitted to the four research centers of the PPRN [redacted]. The PeriPD will collect observational baseline data in a uniform manner on both mothers and infants, and the therapies used and outcomes of the infants. The information collected will not be specific to a disease or treatment. All centers have trained research coordinators with many years of experience in patient enrollment and data collection.

Informed consent will be as required by local IRBs at individual centers.

Inclusion:

- Women with periviable pregnancies (20w 0d through 25w 6d of gestation) admitted to one of the participating centers for a pregnancy-related issue,
- Informed consent, if required by the IRB at the participating center

Exclusion

- Refusal or withdrawal of consent, if informed consent was required at the participating center
- Admission is brief (<24h) and just for observation

The data collected will be detailed information on the mother as well as on the infant.

Women will be tracked from their initial visit (to ER or Obstetric admissions) and admission (to hospital floor or Labor and Delivery) during the periviable period to birth of their infant and their discharge from hospital. Some women who present at 20-26w gestation may deliver much later (at term), and these outcomes will be recorded as well. Maternal outcomes after birth of a periviable infant (endometritis or other infections, lactation success) will also be tracked until her discharge. Infant characteristics (e.g. liveborn or stillborn; if liveborn, Apgar scores, birth weight and other measurements, need for and nature of resuscitation, clinical course in NICU including complications and medical outcomes until discharge). Data from routine newborn follow-up until 22-26 month corrected age will also be recorded.

In Aim 2, we will evaluate the utility of quantitative prediction models in parents and clinicians of periviable infants.

Initially, we will use focus groups for parents and clinicians separately to identify their specific perspectives and needs with respect to those prognostic tools. our goal is to recruit 30 parents of extremely preterm (all inborn periviable infants) and 30 of their corresponding clinicians from Obstetrics/MFM and Neonatology (Attending Physicians, Fellows, and Nurse Practitioners who routinely counsel parents; selected using random assignment) over the first year of the study period at [redacted].

Next, item selection and content validation will be done in a representative sample of at least 20 parents and 20 clinicians.

Pretesting and item reduction will be done with 20 parents and clinicians at [redacted]. The instruments will then be assessed with a group of parents and clinician respondents (n=30 each).

The evaluation study will be a two group posttest only design. We will enroll 100 patients (parents or legal guardian of infant will be enrolled) and their corresponding 100 clinicians (MFM/OB or Neonatologists) for the "before" group and the other 200 (100 patients and 100 clinicians) in the "after" group from all 4 centers.

Inclusion:

- Parents with periviable infants (20w 0d through 25w 6d of gestation) admitted to one of the participating centers (AND) the clinician (Attending Physician, Fellow, or Nurse Practitioner, selected using random assignment from those caring for the patient)
- Informed consent

Exclusion

- Refusal or withdrawal of consent

Informed consent will be obtained from both parents and clinicians, using IRB-approved consent forms.

In Aim 3, we plan to define the neonatal outcomes in which parents are most interested, develop a better means of framing and communicating clinical evidence, and develop Decision Aids for enabling parents of periviable infants to make better informed decisions

The interviews conducted by the research coordinators in Aim 2 will be analyzed to determine the outcomes important to parents, and to evaluate the psychological and cultural factors involved in the decision-making process by the parents and the clinicians. We will develop prediction models for outcomes most important to parents, and decision aids. Decision aids will be based on the Ottawa Decision Support Framework (ODSF) (www.ohri.ca/decisionaid). The ODSF uses concepts and theories from general and social psychology, decision analysis, decisional conflict, values, social support, and self-efficacy to arrive at a decision support system.

These Decision Aids at the different time points (prior to birth, first 3 days, 7d, 28d, 36w PMA) will be evaluated in Year 3, in a similar manner to that done in Aim 2 (initial development in a small sample [n=50] followed by testing and item reduction [n=20] followed by validation [n=30] at [redacted]). Final testing and validation will be in 200 parents (mothers, or both parents if available) in all 4 centers - the initial 100 in Yr 4 without Decision Aids, and subsequent 100 in Yr 5 using Decision Aids.

Inclusion:

- Parents with periviable infants (20w 0d through 25w 6d of gestation) admitted to one of the participating centers
- Informed consent

Exclusion

- Refusal or withdrawal of consent

Informed consent will be obtained from parents using IRB-approved consent forms.

A biorepository of remnant maternal samples (vaginal swabs, urine, plasma and cell pellet from 2 ml blood obtained at time of routine sampling from periviable admission) and remnant neonatal samples (cord blood, urine in first 3 days, tracheal aspirate if intubated and tracheal suctioning is perfomed) will be collected and frozen. Due to budgetary constraints, these samples will not be analyzed as part of this project, but samples will be stored for microbiomic, proteomic, and other –omic profiling if additional funding is obtained.

Clinical management: Medical interventions and all management will be conventional and based upon the clinical discretion during the hospital course. No changes in management are required for this observational cohort study. Periviable pregnancies are at high risk of stillbirth, and periviable infants are at extremely high risk of death or multiple complications of extreme prematurity (intraventricular hemorrhage, necrotizing enterocolitis, septicemia, bronchopulmonary dysplasia, long-term complications such as cerebral palsy, cognitive dysfunction etc), but enrollment in this study which is strictly observational and survey-based poses no additional risk or changes in clinical management.

There are many reasons why we propose studying periviable pregnancy (between 20w 0d and 25w 6d of gestation):

(i) Periviable pregnancies are at highest risk for adverse outcome, such as stillbirth (especially if before 23 completed weeks of gestation) and early neonatal death (especially if before 25 weeks of gestation)

or severe morbidity even if the infant survives. Studies in pregnancy that are more advanced are not being considered as they are not at high risk for poor outcome.

(ii) Very little is known about the epidemiology of periviable pregnancy, and this information is needed to establish new standards of care, and improve the management of periviable pregnancy and extremely premature infants worldwide.

(iii) Current approaches to counseling parents with periviable pregnancy at risk of preterm delivery are variable, varying by clinician and between centers. Decision aids are required to improve parental and clinician satisfaction with the decision making process, and potentially improve processes and outcomes.

Sources of materials

We will prospectively collect clinical data on patient characteristics, illness severity, and outcomes from the medical records of the enrolled women and their infants using electronic templates.

We will also collect information from parents and their clinicians using interviews, for determining if the use of quantitative estimators provides additional value, and to define outcomes of most interest to parents, and to help develop decision aids.

A biorepository of remnant maternal samples (vaginal swabs, urine, plasma and cell pellet from 2 ml blood obtained at time of routine sampling from periviable admission) and remnant neonatal samples (cord blood, urine in first 3 days, tracheal aspirate if intubated and tracheal suctioning is perfomed) will be collected and frozen. No invasive sampling will be done specifically for the purpose of this study.

Potential risks

This study is primarily an observational study (Aim 1), and interview-based (Aims 2 and 3), and is hence of minimal risk. The primary risks are those of loss of confidentiality and privacy.

For the Periviable Pregnancy Database (PeriPD), we will collect clinical data on patient characteristics, illness severity, and outcomes from the medical records of the enrolled patients and their infants. Results and their linked clinical data will then be assigned an unique identifying code and anonymized to minimize risks to confidentiality. Only the PI and research coordinator will have access to patient data before anonymization. No patient identifiers will therefore remain in the final data set that will be transmitted to the Data Coordinating Center.

We will also collect information using interviews, for evaluating quantitative estimators, and for defining outcomes of interest and for developing decision aids. These interviews will be with both parents and their clinicians in private settings, and the results of the interview will also be anonymized before transmission to the Data Coordinating Center.

We also plan to develop a biorepository using remnant samples (no invasive sampling will be done specifically for this study).

There is no financial risk from participation in this study.

A potential risk is of psychological harm to parents during the counseling process, as they become aware of the high risk of death or handicap to their child in periviable pregnancies. However, this risk is the same, whether or not the parents are in the study, as they all receive counseling regardless of being in this or other studies. The aim of this study is to improve the counseling process.

2. Adequacy of protection against risks

Recruitment and Informed Consent

We plan to prospectively study 1000 periviable pregnancies at [redacted] research centers [redacted] over approximately a 4-year period (total duration of study is five years) to develop the Periviable Pregnancy Database (PeriPD). Some of the women may be enrolled in the interviews for Aims 2 and 3, along with their clinicians. Institutional Review Board (IRB) approval will be obtained before initiation of the study. Informed consent will be obtained from all participants.

Protection against risk

This study is primarily an observational study (Aim 1), and interview-based (Aims 2 and 3), and is hence of minimal risk. The primary risks are those of loss of confidentiality and privacy. For the Periviable Pregnancy Database (PeriPD), we will collect clinical data on patient characteristics, illness severity, and

outcomes from the medical records of the enrolled patients and their infants. Results and their linked clinical data will then be assigned an unique identifying code and anonymized to minimize risks to confidentiality. Only the PI and research coordinator will have access to patient data before anonymization. No patient identifiers will therefore remain in the final data set that will be transmitted to the Data Coordinating Center.

We will also collect information using interviews, for evaluating quantitative estimators, and for defining outcomes of interest and for developing decision aids. These interviews will be with both parents and their clinicians in private settings, and the results of the interview will also be anonymized before transmission to the Data Coordinating Center.

3. Potential benefits of the proposed research to the subjects and others

There is no direct benefit to study participants from participating in Aim 1 as this Aim is development of the Periviable Pregnancy Database (PeriPD). Aim 2 (evaluation of quantitative estimators) and Aim 3 (Identification of outcomes most important to parents, and development of Decision Aids) may help both parents and their clinicians. The use of quantitative estimators may help parents develop a more realistic understanding of prognosis, and help in decision making. The interviews in Aim 3 may help parents clarify their thinking and identify which outcomes matter most to them, and what are their top priorities. The results of this study will be published in the peer-reviewed literature and then deposited in PubMed Central to make the manuscript freely available, which may benefit other investigators in the field as well as interested parents and family.

4. Importance of the knowledge to be gained

The successful completion of the studies in this project will indicate if quantitative estimates of outcome help improve decision-making by patients and clinicians. The Decision Aids may improve parental and clinician satisfaction with the decision-making process, and possibly improve clinical processes and neonatal outcomes. Most importantly, the data on periviable pregnancies developed by this multicenter consortium of regional perinatal centers may lead to a better understanding of the epidemiology of periviable pregnancy, the establishment of new standards of care, and improve the management of extremely premature infants worldwide.

Inclusion of Women

Women with periviable pregnancy are the primary population being studied. In addition, we will collect data for the periviable pregnancy database from their infants (either liveborn or stillborn). The proportion of female to male infants is expected to be approximately 1:1 in the population of infants to be studied. We will also perform interviews for Aims 2 and 3, which will include not only the mother, but also the father (if available), and the clinician. Clinicians may be either men or women.

Inclusion of Minorities

Women with periviable pregnancy will be recruited independent of ethnicity or race because periviable pregnancy occurs in all races. In addition, we will be interviewing their clinicians. Our study composition will reflect the epidemiology of periviable pregnancy and their clinicians in the state of [redacted] with approximately 37% being Black, 50% White, and the remaining Hispanic/Other.

Inclusion of Women and Minorities

Inclusion of Women

This proposal will study periviable pregnancies. In addition to women with periviable pregnancies, we will study their infants. The proportion of female to male infants is expected to be approximately 1:1 in the population of periviable infants to be studied.

We will interview the clinicians (both men and women) caring for the pregnant women with periviable pregnancies. Based on the sex ratio of women in faculty, fellows, and nurse practitioners in MFM and Neonatology in the participating centers, it is likely that the majority of the clinicians (50-60%) will be women.

Inclusion of Minorities

Women with periviable pregnancies will be recruited independent of ethnicity or race because periviable pregnancy occurs in all races. Our study composition will reflect the epidemiology of periviable pregnancy in the states of the participating research centers [redacted] with approximately 37% being Black (African-American), 50% White (Non-Hispanic Caucasian), and the remaining Hispanic/Other.

In addition, we will interview clinicians (of all race/ethnicities) caring for the pregnant women with periviable pregnancies. Our study composition will reflect the faculty/fellow/nurse practitioner composition in the participating research centers [redacted] with approximately 10% being Black (African-American), 50% White (Non-Hispanic Caucasian), and the remaining Asian, Hispanic/Other.

Planned Enrollment Report

Study Title: Periviable Pregnancy Database (PeriPD)

Domestic/Foreign: Domestic

Comments: Aim 1: To develop a Periviable Pregnancy Database (PeriPD) to determine the incidence, characteristics, and outcomes of periviable pregnancies. We anticipate enrolling 1000 periviable pregnancies from the four research centers of the Periviable Pregnancy Research Network (PPRN) over a period of four years.

Racial Categories	Ethnic Categories				Total
	Not Hispanic or Latino		Hispanic or Latino		
	Female	Male	Female	Male	
American Indian/Alaska Native	5	5	0	0	**10**
Asian	10	10	0	0	**20**
Native Hawaiian or Other Pacific Islander	0	0	0	0	**0**
Black or African American	160	160	25	25	**370**
White	180	180	70	70	**500**
More than One Race	50	50	0	0	**100**
Total	**405**	**405**	**95**	**95**	**1000**

Study 1 of 3

Planned Enrollment Report

Study Title: Evaluation of Quantitative Estimators in Periviable Pregnancy

Domestic/Foreign: Domestic

Comments: Specific Aim (2) Determine whether the use of the NICHD NRN Outcome Estimator, Outcome Trajectory Estimator, and BPD Estimator for parental counseling leads to increased parental satisfaction, increased clinician satisfaction, changes in therapies, and improved clinical outcomes of periviable infants. Instrument development: 200 parents and their 100 clinicians at UAB. Evaluation of instruments: 200 parents and their 200 clinicians. Total sample size: 600 individuals

Racial Categories	Ethnic Categories				Total
	Not Hispanic or Latino		Hispanic or Latino		
	Female	Male	Female	Male	
American Indian/Alaska Native	3	3	0	0	**6**
Asian	12	12	0	0	**24**
Native Hawaiian or Other Pacific Islander	0	0	0	0	**0**
Black or African American	110	110	10	10	**240**
White	100	100	30	30	**260**
More than One Race	35	35	0	0	**70**
Total	**260**	**260**	**40**	**40**	**600**

Study 2 of 3

Planned Enrollment Report

Study Title: Defining Neonatal Outcomes in Which Parents are Most Interested and Development of Decision Aids

Domestic/Foreign: Domestic

Comments: Specific Aim (3) To define the neonatal outcomes in which parents are most interested, develop a better means of framing and communicating clinical evidence, and develop Decision Aids for enabling parents of periviable infants to make better informed decisions. Initial development: 50 + testing and item reduction: 20 + validation: 30 =100 parents for initial stage at UAB. Final testing and validation in a sample size of 200 parents from all 4 centers. Total sample size = 300.

Racial Categories	Ethnic Categories				Total
	Not Hispanic or Latino		Hispanic or Latino		
	Female	Male	Female	Male	
American Indian/Alaska Native	1	1	0	0	**2**
Asian	3	3	0	0	**6**
Native Hawaiian or Other Pacific Islander	0	0	0	0	**0**
Black or African American	44	44	10	10	**108**
White	60	60	22	22	**164**
More than One Race	10	10	0	0	**20**
Total	**118**	**118**	**32**	**32**	**300**

Study 3 of 3

Inclusion of Children

We are investigating the epidemiology of periviable pregnancy, evaluating the use of quantitative estimators of prognosis, defining important outcomes and parental preferences related to these outcomes, and developing decision aids.

As the focus of this project is on periviable pregnancy (20w 0d to 25w 6d gestaional age), we will include the children born to women with periviable pregnancy, and perform detailed data collection on their characteristics, the clinical care provided to these infants, and their outcomes (mortality and morbidity). Infant born at later gestational ages are more mature and with better outcomes, and those at lower gestational ages (<20w) do not survive, and the focus of [redacted] (Studies at Periviable Gestation [redacted]) is therefore is only on pregnancy during this high risk period.

The PI and other investigators at all centers are board-certified in either Obstetrics/MFM or Neonatal-Perinatal medicine, and have been on the faculty for many years, and have performed numerous involving high risk pregnancies (MFM) or critically ill neonates and children (neonatologists).

The involvement of children as subjects in research will be in compliance with all applicable subparts of 45 CFR Part 46 as well as with other pertinent Federal laws and regulations.

Multiple PI Leadership Plan:

This grant application will use the Multiple PI option as defined in [redacted].

As defined by the NIH,

- **Principal Investigators**
  - All PIs are designated by the applicant institution
  - All PIs share the responsibility and authority for leading and directing the project
  - All listed PIs must be registered in eRA Commons with a PI role type.
  - All listed PIs will have access to Status on the eRA Commons at [redacted]
  - The first PI listed must be affiliated with the institution submitting the application and will serve as the contact PI.
  - The contact PI will be responsible for communication between the NIH and the rest of the leadership team.
  - Being named contact PI does not imply any particular role within the leadership team.
  - When requested by the grantee institution at the time of a non-competing application, another member of the leadership team may assume the role of contact PI.
  - All PIs will be listed on summary statements
  - All PIs will be listed on the Notice of Grant Award (NOGA)
  - All PIs will be listed in [redacted]
  - Any requested allocation of funds to components of the project or the associated PIs must be included in the Leadership Plan (see below). If an award is made, the requested allocation will be acknowledged in the NOGA. Unless limited by a specific term of award, the acknowledgment of the requested allocation will not limit institutional authority to manage the funds nor will it impose additional prior approval requirements.
  - The role type, "Co-PI" will not be used by the NIH

The Multiple PI Leadership Plan addresses the following administrative processes and PI responsibilities:

- Roles/areas of responsibility of the PIs
- Fiscal and management coordination
- Process for making decisions on scientific direction and allocation of resources
- Data sharing and communication among investigators
- Publication and intellectual property (if needed) policies
- Procedures for resolving conflicts

[redacted]

For the PI at each center, there is an alternate PI (co-investigator) with complementary expertise: [redacted]

The rationale for the multiple PIs is two-fold. First, the large multicenter clinical study involves the recruitment of many patients, extensive data collection, and management of several investigators across 4 centers. The large scale and complex nature of this study is best accomplished if led and shared by multiple PIs assisted by Clinical Coordinators and Data Coordinating Center. Secondly, the PIs have complementary and successful scientific backgrounds in MFM and Neonatology research.

PI#1 will be responsible for enrollment of patients in Aim 1 at [redacted], and in supervision of research coordinator. [redacted] will work closely with [redacted], and co-investigators [redacted] for enrollment in Aims 2 and 3, and for the initial analyses that will be done for Aims 2 and 3 at [redacted]. [redacted] will also oversee the multi-center evaluation components of Aims 2 and 3, and supervise the enrollment for these components at [redacted].

PI #2-4 will be responsible for the enrollment of patients in Aims 1-3 at their research centers. They will work closely with the alternate PI and research coordinator at their center to optimize enrollment, data collection, and transmission of data to the Data Coordinating Center.

The PIs will form a Steering Committee (membership will include the four PIs, alternate PIs, and [redacted] from the [redacted]) that will manage the oversight and coordination of project management, research administration, publications and data sharing, and integration of all resources needed for the project. The Institution will subdivide the award funds and each PI will be responsible for his own budget. The Steering Committee will oversee decisions on minor changes in research direction and have the authority to reallocate funds and resources between PIs. Scientific direction is well described in the research proposal. However, if unanticipated findings were to arise, such as those from interim analyses, study direction would be discussed and decided on by the Steering Committee.

PI#1 will serve as the initial Chair of the Steering Committee and be responsible for communication among PIs, including meeting schedules and agendas. The position of Chair will rotate among the PIs on an annual basis.

PI#1 will be designated the contact PI and be responsible for submitting all necessary documents to NIH, including IRB approvals, and annual progress reports.

The PIs routinely communicate with each other frequently. **Formal communication for this grant will include weekly email updates, twice-monthly conference calls over GoTo Meeting (with High-Definition video conferencing), and personal face-to-face meetings at least twice annually (once during the SMFM, and once during the PAS). Additionally, there will be travel of PIs between institutions at least once a year to discuss with other research personnel.** These meetings will cover, but not be limited to, review of screening and recruitment numbers, ongoing status with conduct and challenges, enrollment, and IRB and report needs.

For publications, it is estimated that at least 6-10 publications will result from this grant in high-impact journals. The PIs will divide up the first author and senior author spot depending upon the research expertise of the PI and the topic of the paper, and junior personnel at a PIs institution may be first author on papers for which they have made significant effort. For certain publications, a statement may be added that all four PIs contributed equally.

Coordinating Study Site, [redacted] will be responsible for:

- Maintaining the study protocol and making revisions
- Updating the site operations manual as needed
- Performing overall management and coordination of the trial
- Ensuring Institutional Review Board requirements are up to date at all sites
- Overseeing and assisting with recruitment, monitored by the data management and analysis team at [redacted]
- Providing training and support for data collection instruments and quality assurance and control
- Coordinating progress reports to the data management center at [redacted]

The [redacted] at [redacted] will be responsible for:

- Creation of the database and extraction tools
- Data cleaning, outlier detection, and preparation for analysis
- Primary analysis of interim data
- Additional analyses as requested by the DSMB
- Primary intention-to-treat analyses per protocol
- *A priori* planned secondary analyses per protocol

Participating Clinical Sites [redacted] *will be responsible for:*

- Screening and recruiting participants
- Managing and operating the site
- Determining participant eligibility
- Data entry
- Developing site-internal procedures and training/certifying staff members as appropriate
- Assuring compliance with Institutional Review Board requirements
- Responding to Quality Assurance visit reports
- Maintaining a good recruitment rate
- Reviewing and reconciling study data
- Entering participant data into study database and responding to data cleaning requests
- Submitting inquiries on procedural issues to the Coordinating Center
- Responding to all requests for data regarding interim and final analyses and safety

Data Safety and Monitoring Board (DSMB)

A DSMB will be established to ensure objective oversight of this study's safety and conduct. Although observational (Aim 1) and interview-based (Aims 2 and 3), the population being evaluated is highly vulnerable, and some oversight is required. The members of the DSMB will have complementary expertise in clinical trials, maternal-child health, obstetric and pediatric outcomes-based research, and epidemiology. Members are not involved in any aspect of the study operation. The DSMB will meet annually to review study progress and monitor adverse events. The DSMB will be confidentially briefed by the Data Coordinating Center regarding study progress and outcomes. None of that information will be available to study investigators unless disclosed by the DSMB. The DSMB will issue a written report to the investigators after each meeting outlining any study problems or necessary actions.

Intellectual Property

The PIs will grant necessary access rights to the pre-existing patents and or the patents potentially generated within the frame of this project for the purpose of this research project to all the other PIs and key personnel on a non-exclusive royalty-free basis. Each PI shall take appropriate measures to ensure that he/she can grant these access rights. Right in any pre-existing intellectual property will remain the property of the party that created and/or controls it.

Conflict Resolution

If a potential conflict develops, the PIs shall meet and attempt to resolve the dispute. If they fail to resolve the dispute, the disagreement shall be referred to an arbitration committee consisting of one impartial senior executive from each PI's institution and an impartial senior executive mutually agreed upon by both PIs. No members of the arbitration committee will be directly involved in the research grant or disagreement.

Change in PI Location

If one of the PIs moves to a new institution, a new PI will be recruited as a replacement, subject to the approval of the Steering Committee and the Institution.

Budget

Subcontracts for all participating institutions have been developed by the office of grants and contracts at the participating institutions, with the guidance of the PIs.

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64. Epstein RM, Alper BS, Quill TE. Communicating evidence for participatory decision making. JAMA. 2004;291(19):2359-66. PubMed PMID: 15150208.

Consortium/contractual arrangements:

The appropriate programmatic and administrative personnel of each institution involved in this grant application are aware of the pertinent Federal and/or non-Federal regulations and policies and are prepared to establish written subaward agreements that will ensure compliance with all such policies.

For this application, the PIs and the corresponding institutions are:

[redacted]

Name, address, and telephone number of the PD(s)/PI(s).

[redacted]

Roles of PIs

PI#1, PI#2, PI#3, and PI#4 will serve as PIs for the project. PI #1 and PI#4 are [redacted], while PI#2 and PI#3 are [redacted] specialists.

For the PI at each center, there is an alternate PI (co-investigator) with complementary expertise: [redacted]

The rationale for the multiple PIs is two-fold. First, the large multicenter clinical study involves the recruitment of many patients, extensive data collection, and management of several investigators across 4 centers. The large scale and complex nature of this study is best accomplished if led and shared by multiple PIs assisted by Clinical Coordinators and Data Coordinating Center. Secondly, the PIs have complementary and successful scientific backgrounds in MFM and Neonatology research.

PI#1 will be responsible for enrollment of patients in Aim 1 at [redacted] and in supervision of research coordinator. [redacted] will work closely with [redacted] and co-investigators [redacted] for enrollment in Aims 2 and 3, and for the initial analyses that will be done for Aims 2 and 3 at [redacted] [redacted] will also oversee the multi-center evaluation components of Aims 2 and 3, and supervise the enrollment for these components at [redacted].

PI #2-4 will be responsible for the enrollment of patients in Aims 1-3 at their research centers. They will work closely with the alternate PI and research coordinator at their center to optimize enrollment, data collection, and transmission of data to the Data Coordinating Center.

The PIs will form a Steering Committee (membership will include the four PIs, alternate PIs, and [redacted] from the [redacted] that will manage the oversight and coordination of project management, research administration, publications and data sharing, and integration of all resources needed for the project. The Institution will subdivide the award funds and each PI will be responsible for his own budget. The Steering Committee will oversee decisions on minor changes in research direction and have the authority to reallocate funds and resources between PIs. Scientific direction is well described in the research proposal. However, if unanticipated findings were to arise, such as those from interim analyses, study direction would be discussed and decided on by the Steering Committee.

PI#1 will serve as the initial Chair of the Steering Committee and be responsible for communication among PIs, including meeting schedules and agendas. The position of Chair will rotate among the PIs on an annual basis.

PI#1 will be designated the contact PI and be responsible for submitting all necessary documents to NIH, including IRB approvals, and annual progress reports.

The PIs routinely communicate with each other frequently. **Formal communication for this grant will include weekly email updates, twice-monthly conference calls over GoTo Meeting (with High-Definition video conferencing), and personal face-to-face meetings at least twice annually (once during the SMFM, and once during the PAS). Additionally, there will be travel of PIs between institutions at least once a year to discuss with other research personnel.** These meetings will cover, but not be limited to, review of screening and recruitment numbers, ongoing status with conduct and challenges, enrollment, and IRB and report needs.

For publications, it is estimated that at least 6-10 publications will result from this grant in high-impact journals. The PIs will divide up the first author and senior author spot depending upon the research expertise of the PI and the topic of the paper, and junior personnel at a PIs institution may be first author on papers for which they have made significant effort. For certain publications, a statement may be added that all four PIs contributed equally.

Coordinating Study Site, [redacted] will be responsible for:

- Maintaining the study protocol and making revisions
- Updating the site operations manual as needed
- Performing overall management and coordination of the trial

- Ensuring Institutional Review Board requirements are up to date at all sites
- Overseeing and assisting with recruitment, monitored by the data management and analysis team at [redacted]
- Providing training and support for data collection instruments and [redacted]

The Data Coordinating Center at [redacted] r:

- Creation of the database and extraction tools
- Data cleaning, outlier detection, and preparation for analysis
- Primary analysis of interim data
- Additional analyses as requested by the DSMB
- Primary intention-to-treat analyses per protocol
- *A priori* planned secondary analyses per protocol

Participating Clinical Sites [redacted] will be responsible for:

- Screening and recruiting participants
- Managing and operating the site
- Determining participant eligibility
- Data entry
- Developing site-internal procedures and training/certifying staff members as appropriate
- Assuring compliance with Institutional Review Board requirements
- Responding to Quality Assurance visit reports
- Maintaining a good recruitment rate
- Reviewing and reconciling study data
- Entering participant data into study database and responding to data cleaning requests
- Submitting inquiries on procedural issues to the Coordinating Center
- Responding to all requests for data regarding interim and final analyses and safety

Resource Sharing Plan

A. Tools (Devices, Monitors, Probes, Research tools, Reagents, Model Organisms)
Tools will be made available, in accordance with the NIH Data Sharing Policy (http://grants.nih.gov/grants/policy/data_sharing), to all researchers in both the private and public sector free or for a nominal charge and with minimal restriction.

B. Data Sharing (Results, Tables, Graphs, Raw Data, Analyses)
In accordance with NIH Data Sharing Policy, we will look to share data at the earliest opportunities throughout this research project, subject to intellectual property aspects and funding constraints. Results will be made available to the community at large.

C. Knowledge and Results (Abstracts, Papers, Publications, Patent Applications)
As a means of sharing knowledge, NIH encourages grantees to arrange for publication of NIH-supported original research in primary scientific journals. The awardees therefore will strive to publish their findings in a timely manner and acknowledge that the research was supported by the NIH. The investigators have published their data and results in numerous publications and worldwide scientific meetings over the last ten years and they intend to continue to share data at the earliest opportunities throughout this research project. In particular:

- Results will be written up and sent for publication in relevant journals such as The Journal of the American Medical Association (JAMA), The New England Journal of Medicine (NEJM), Lancet, Obstetrics & Gynecology, American Journal of Obstetrics and Gynecology, Pediatrics, or Journal of Pediatrics.
- The PIs will seek to present publishable results at scientific conferences such as the annual conference of the The Society for Maternal-Fetal Medicine, Pediatric Academic Societies' etc.