Neonatal Neurobehavior, Medical Risk & 2 year Developmental Outcomes

Elisabeth C. McGowan, MD

Associate Professor of Pediatrics, Warren Alpert Medical School

Women & Infant's Hospital, Providence, RI

emcgowan@wihri.org

PAS 2021 VIRTUAL

BROWN Alpert Medical School

Women & Infants
New England's premier hospital for women and newborns

NOVI

Neonatal Neurobehavior, Medical Risk & 2 year Developmental Outcomes

Co-authors:

M Camerota, PhD; J Hofheimer PhD; M O'Shea, MD; Brian Carter, MD; H Kilbride, MD; S Pastyrnak PhD; C Neal, MD, PhD; L Smith MD; J Helderman MD, MS; J Check MD; L Dansereau MSPH; S DellaGrotta MPH; B Lester PhD

PAS 2021 VIRTUAL

Dr. McGowan has no financial relationships to disclose or Conflicts of Interest (COIs) to resolve

BROWN Alpert Medical School

Women & Infants
New England's premier hospital for women and newborns

NOVI

Background

- Infants born preterm (PT) are at increased risk for neurodevelopmental and behavioral delays
- Medical morbidities ↑↑ this risk
- Socio-economic factors are linked to poor outcomes
  - Post-NICU home environment is a critical mediator of development & behavior
- NICU is a non-optimal environment for PT infant growth & development
- Infant neurobehavioral assessments can be completed while in the NICU
- Provide an early window into understanding the infant's ability to respond to multisensory environment, ***prior to the influences of the home environment.***

Women & Infants
New England's premier hospital for women and newborns

PAS
Pediatric Academic Societies

Neonatal Neurobehavior & Outcomes in Very PT Infants (NOVI) Study

AIMS: To determine among infants born < 30wks gestation

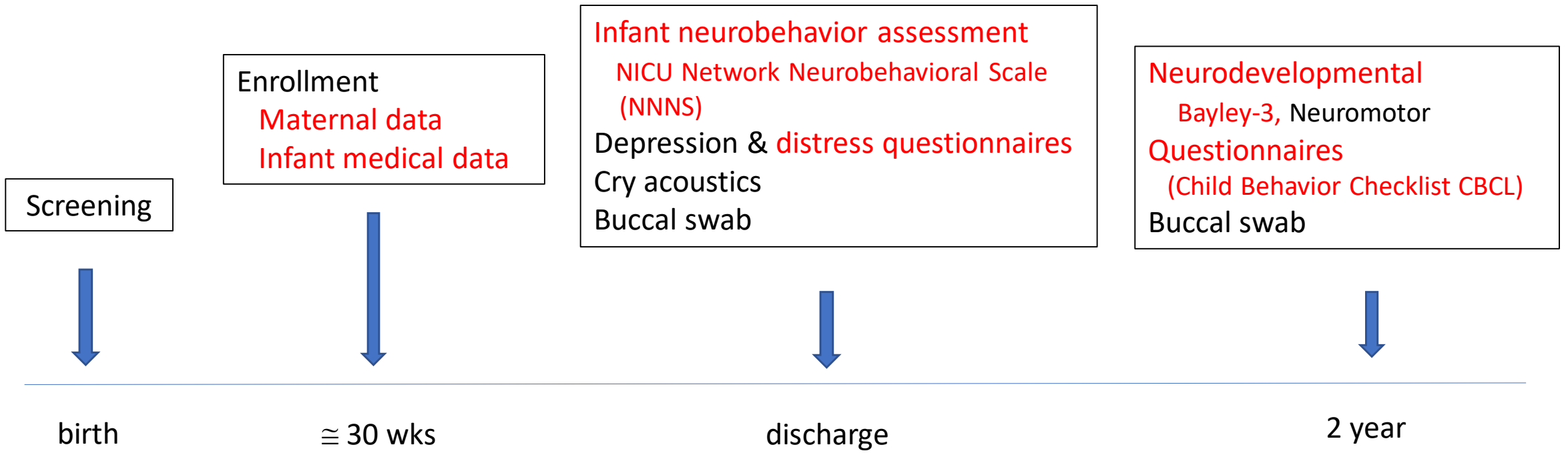
1. Associations between medical risk, neurobehavior (at NICU discharge) & 2 year development
2. Relations between medical risk & neurobehavior
3. Role of the post-discharge environment in explaining associations between medical conditions, neurobehavior & 2 yr outcomes

Multi-center, prospective, observational cohort study (9 U.S. NICUs enrolled pts between 2014-2016)

Women & Infants
New England's premier hospital for women and newborns

PAS
Pediatric Academic Societies

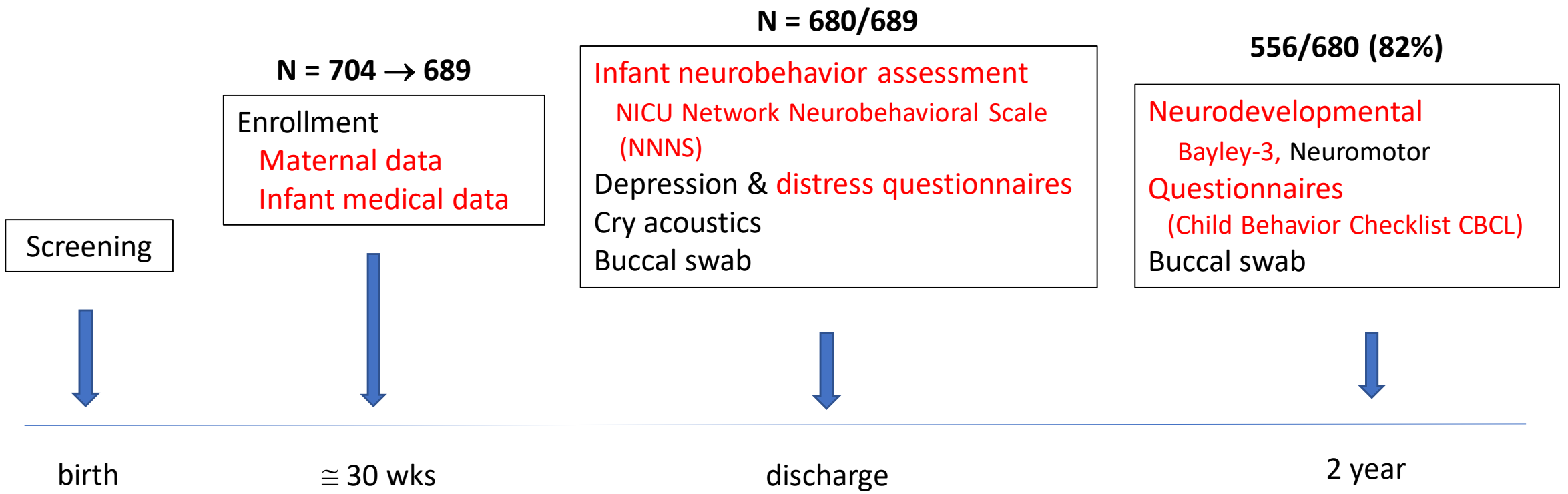
NOVI Study Flow



- *Inclusion: PMA <30wk, likely to survive to d/c, inborn + outborn, live w/in 3 hrs NICU & FU Clinic, Maternal Lang (English, Spanish, Japanese, Chinese)*
- *Exclusion: maternal death, age < 18y, cognitive impairment; infant congenital anomaly*

PAS
Pediatric Academic Societies

NOVI Study Flow



- *Inclusion: PMA <30wk, likely to survive to d/c, inborn + outborn, live w/in 3 hrs NICU & FU Clinic, Maternal Lang (English, Spanish, Japanese, Chinese)*
- *Exclusion: maternal death, age < 18y, cognitive impairment; infant congenital anomaly*

PAS
Pediatric Academic Societies

Statistics

- **NNNS Profiles** (Latent Profile Analysis, LPA)

  Group infants in mutually exclusive, clinically unique subgroups→ 12 NNNS summary scores

  6 distinct profiles were calculated

  Profiles 1-4 (most “typical”) vs profiles 5-6 (most “atypical”) were compared

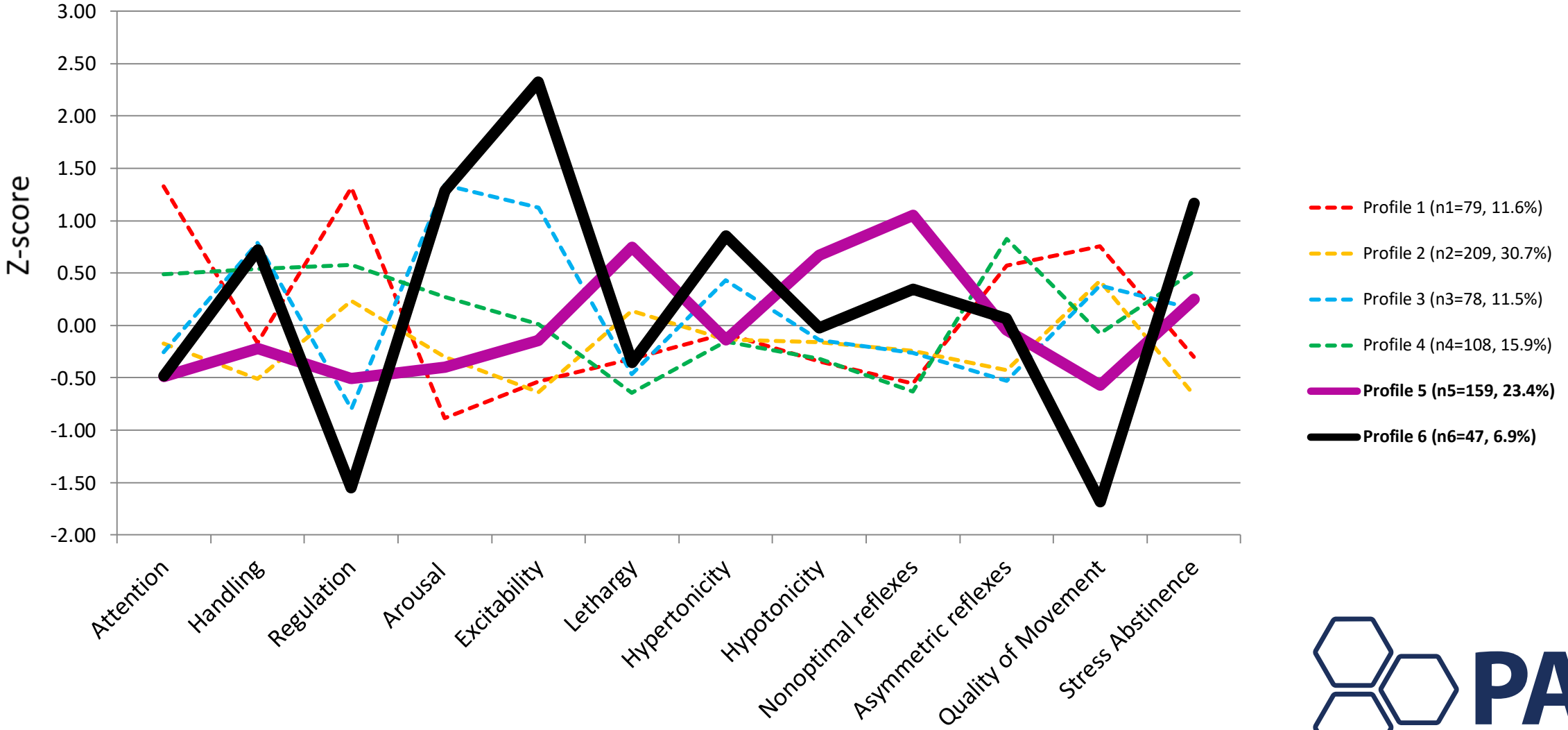
- **Primary outcomes**: 2 year Bayley-3 composite scores & Child Behavior Checklist (CBCL) T-scores
- Generalized estimating equation (GEE) models* tested association between NNNS profiles 5-6, neonatal medical risk (≥ 2 major medical morbidities) & 2 year developmental & behavioral outcomes.
- Covariates included site, maternal SES**, race/ethnicity, maternal primary language, partner status, maternal distress, infant sex, PMA at birth

Women & Infants
New England's premier hospital for women and newborns

** Accounted for multiple births*
*** Hollingshead criteria*

PAS
Pediatric Academic Societies

Total NOVI Cohort - 6 Behavioral Profiles



PAS
Pediatric Academic Societies

Results – Maternal characteristics by NNNS Profiles

N (%), mean (SD)	Profile 5-6 *N = 135*	Profile 1-4 *N = 331*	P-value
Non-English Primary Language	27 %	17 %	< .01
Low SES *	17 %	7 %	<.01
Minority race/ethnicity	56 %	54 %	0.4
Single	27 %	27 %	0.9
Maternal Distress Screening ** *Brief Symptom Inventory (BSI)*	0.3 (.4)	0.27 (.3)	0.5

Women & Infants
New England's premier hospital for women and newborns

* *Hollingshead category 5*

** *average total from discharge and 2 yrs*

PAS
Pediatric Academic Societies

Results –Infant characteristics by NNNS Profiles

N (%), mean (SD)	Profile 5-6 *N = 157*	Profile 1-4 *N = 389*	P-value
PMA at birth	26 .8 (2)	27.0 (2)	.2
Female	42 %	46 %	.4
Brain Injury *	17 %	10 %	.03
NEC/Sepsis	23 %	16 %	.05
CLD	51 %	51 %	.9
Severe ROP	6 %	6 %	.9

Women & Infants
New England's premier hospital for women and newborns

** (by ultrasound) parenchymal echodensity, cPVL, ventricular dilation (+/- hemorrhage)*

PAS
Pediatric Academic Societies

Results – 2y Neurodevelopmental outcomes by Medical Risk & NNNS Profiles

Bayley-3	Medical Risk aOR (95% CI)	NNNS Profiles 5-6 aOR (95% CI)
Cognitive comp < 85	1.6 (1.2, 2.2)	1.8 (1.1, 3.1)
Motor comp < 85	2.4 (1.7, 3.3)	2.3 (1.4, 4.0)
Language comp < 85	1.4 (1.1, 1.8)	1.1 (0.7, 1.7)
Cognitive comp < 70	3.0 (1.9, 4.5)	3.9 (1.7, 9.0)
Motor comp < 70	4.4 (2.7, 7.1)	4.1 (1.7, 9.8)
Language comp < 70	1.4 (0.9, 2.1)	1.7 (0.9, 3.2)

Adjusted for low SES, minority race/ethnicity, maternal primary language, single, BSI average, PMA, sex, study site

Women & Infants
New England's premier hospital for women and newborns

PAS
Pediatric Academic Societies

Results – 2y Behavior outcomes by Medical Risk & NNNS Profiles

Child Behavior Checklist (CBCL)	Medical Risk aOR (95% CI)	NNNS Profiles 5-6 aOR (95% CI)
Internalizing T-score > 63	1.0 (0.6, 1.7)	2.7 (1.2, 5.8)
Externalizing T-score > 63	0.7 (0.4, 1.0)	1.4 (0.7, 2.8)
Total Problem Score T-score > 63	0.9 (0.6, 1.4)	2.6 (1.3, 5.5)

Women & Infants
New England's premier hospital for women and newborns

Adjusted for low SES, minority race/ethnicity, maternal primary language, single, BSI average, PMA, sex, study site

PAS
Pediatric Academic Societies

Summary

- Among infants born < 30 weeks, clinically valid neurobehavioral patterns or “profiles” can be quantified with precision.
- Neonatal medical risk remains a consistent concern for poor cognitive, language and motor performance.
- After controlling for medical risks, atypical neonatal neurobehavioral patterns were significant predictors adverse cognitive and motor outcomes.
- Atypical neurobehavior *at NICU discharge* was associated with behavioral problems (clinical range for internalizing & total behavioral scores) *at 2 years*.
- **NNNS assessment at NICU discharge suggests that the profiles are an early predictive clinical tool that can inform targeted interventions *prior to discharge to the home environment.***

Women & Infants
New England's premier hospital for women and newborns

PAS
Pediatric Academic Societies

Acknowledgements

PI's

- **Barry Lester, PhD** *(Women & Infants Hospital, RI)*
- **Michael O'Shea, MD, MPH** *(UNC Chapel Hill, NC)*

- Julie Hofheimer PhD *(UNC Chapel Hill, NC)*
- Brian Carter, MD *(Children's Mercy, MO*)
- Jennifer Helderman, MD, MS *(Wake Forest Univ, NC)*
- Jennifer Check, MD *(Wake Forest Univ, NC)*
- Charles Neal, MD, PhD *(Univ Hawaii, Honolulu, HI)*
- Steve Pastyrnak PhD *(Helen DeVos Hospital, MI)*
- Lynne Smith MD *(Harbor UCLA, CA)*
- Antoine Soliman MD (*Miller UCLA, CA*)

Brown Center/NOVI Data Center

- Lynne Danserau, MSPH
- Sheri DellaGrotta, MPH
- Linda LaGasse, PhD

- **Study Site Co-Investigators**
- **NNNS examiners**
- **Study coordinators**
- **Ultrasound Consultants**

- **NICU Staff**
- **Family participants**

Funding

- NIH NICHD R01HD072267

Women & Infants
New England's premier hospital for women and newborns

BROWN
Alpert Medical School

NOVI

PAS
Pediatric Academic Societies