



Two-year Outcomes of Extremely Preterm Infants with Surgical Necrotizing Enterocolitis: Changes over Time

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Disclosures

- Speaker: Ravi M. Patel, MD, MSc
- Dr. Patel serves on the scientific advisory board for Noveome and on the data-safety monitoring committee for Infant Bacterial Therapeutics/Premier Research. Any real or apparent conflicts of interest related to the content of this presentation have been resolved.
- This presentation will not involve discussion of unapproved or off-label, experimental or investigational use of a drug.

Background

- Understanding NEC-related neurodevelopmental and other long-term outcomes is important to patients, families and clinicians

Canvasser et al. Semin Perinatol. 2023;47(1):151696.

- There has been limited characterization of functional outcomes among extremely preterm NEC survivors

- Rates of NEC, NEC-related death and surgical treatment for NEC have decreased over time in the US

Han et al. J Pediatr Surg. 2020 Jun;55(6):998-1001

Wolf et al. JAMA Netw Open. 2023 Mar 1;6(3):e231511

- It is unknown if outcomes among infants with surgery for NEC have improved

Objective

To understand changes over time in 2-year outcomes for extremely preterm infants with surgical NEC

Study Design

- Retrospective observational cohort study using prospectively collected data from the NICHD Neonatal Research Network
- Population:
 - Gestational age < 27 weeks
 - Surgery for NEC (excluding infants with spontaneous intestinal perforation)
 - Birth at study hospital from 7/1/12-12/31/19
- Primary Exposure: Birth epoch
 - Epoch 1: 7/1/12-12/31/16
 - Epoch 2: 1/1/17-12/31/19

Primary Outcome

- Death or moderate-to-severe neurodevelopmental impairment (NDI) at 2 years corrected age
- Defined as the presence of any of:
 - Gross Motor Function Classification System (GMFCS) level ≥ 2
 - BSID-III cognitive composite score of < 85
 - BSID-III motor composite score of < 85
 - Severe bilateral visual impairment consistent with 20/200
 - Severe bilateral functional hearing impairment

Secondary Outcomes

- Components of primary outcome
- Severe NDI, defined as one or more of the following:
 - GMFCS ≥ 4 (CP or non-CP)
 - Bilateral blindness
 - Bilateral hearing impairment with or without amplification
 - BSID-III cognitive composite score < 70
- Cerebral palsy, including severity
- Functional outcomes
- Growth

Sample Size and Power Estimates

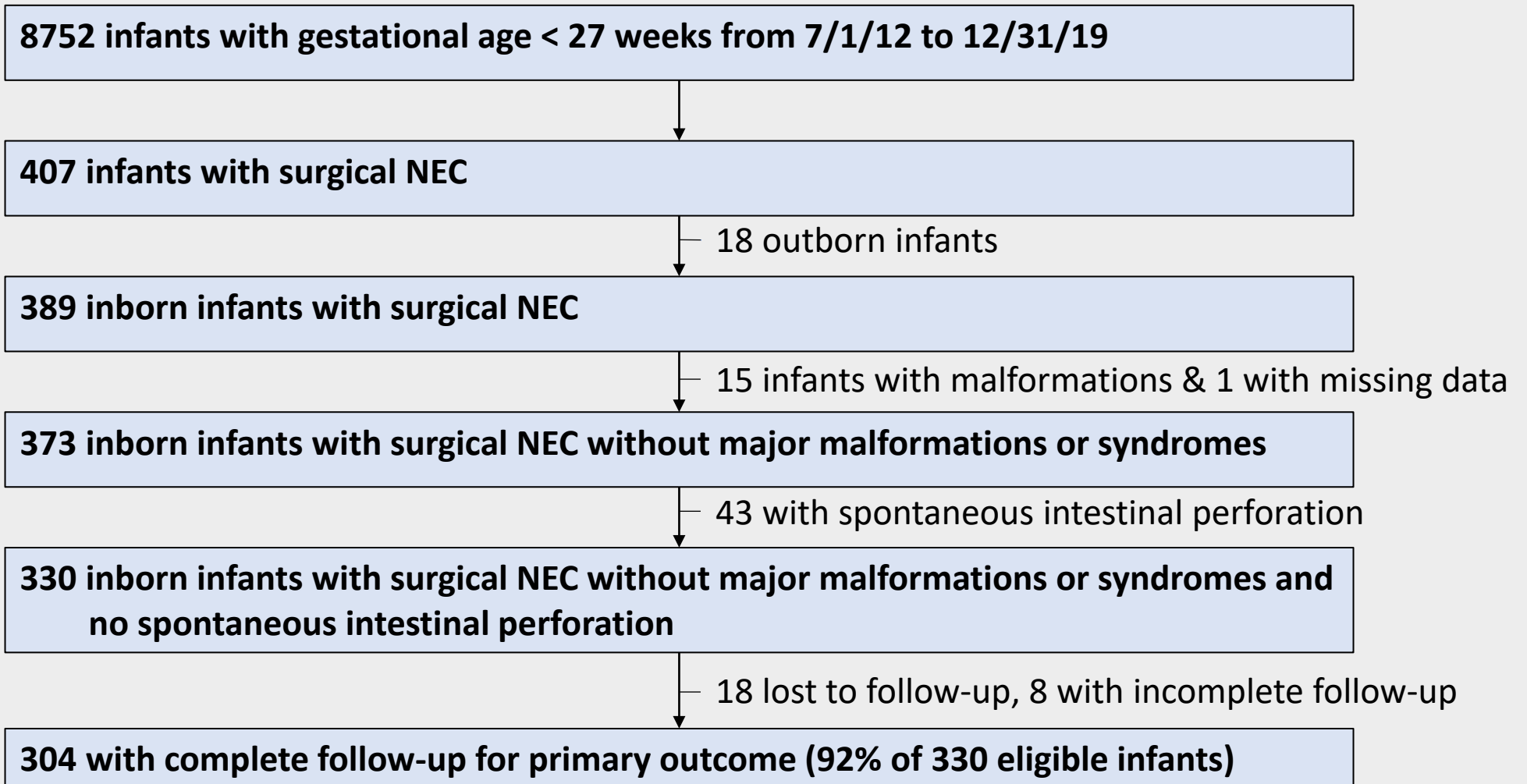
- We estimated a total available potential population of 373 infants with surgical NEC
- Estimated 84% follow-up rate
- Based on these assumptions and an alpha of 0.05, we had 80% power to detect an 18% relative risk reduction in death or moderate-severe NDI from 81% in epoch 1 to 67% in epoch 2 (14% absolute risk reduction)

Statistical Analysis

- Poisson regression with robust variance estimators for primary outcome
- Adjustment for the following a priori determined characteristics:
 - maternal race/ethnicity
 - maternal age
 - antenatal corticosteroids
 - multiple birth
 - sex
 - gestational age
 - birth weight
 - maternal education
- Center accounted for as a cluster effect

Results

Study Population



Baseline and Clinical Characteristics

Characteristic	2012-2016 N=173	2017-2019 N=131	P
Gestational age, median (IQR) weeks	24 (23-25)	24 (23-25)	0.38
Birth weight, median (IQR) grams	667 (590-780)	685 (580-810)	0.56
Any antenatal corticosteroids	92%	93%	0.69
Initial NEC surgery			
Laparotomy	68%	62%	0.30
Peritoneal drain	32%	38%	
Any human milk intake	92%	98%	0.02

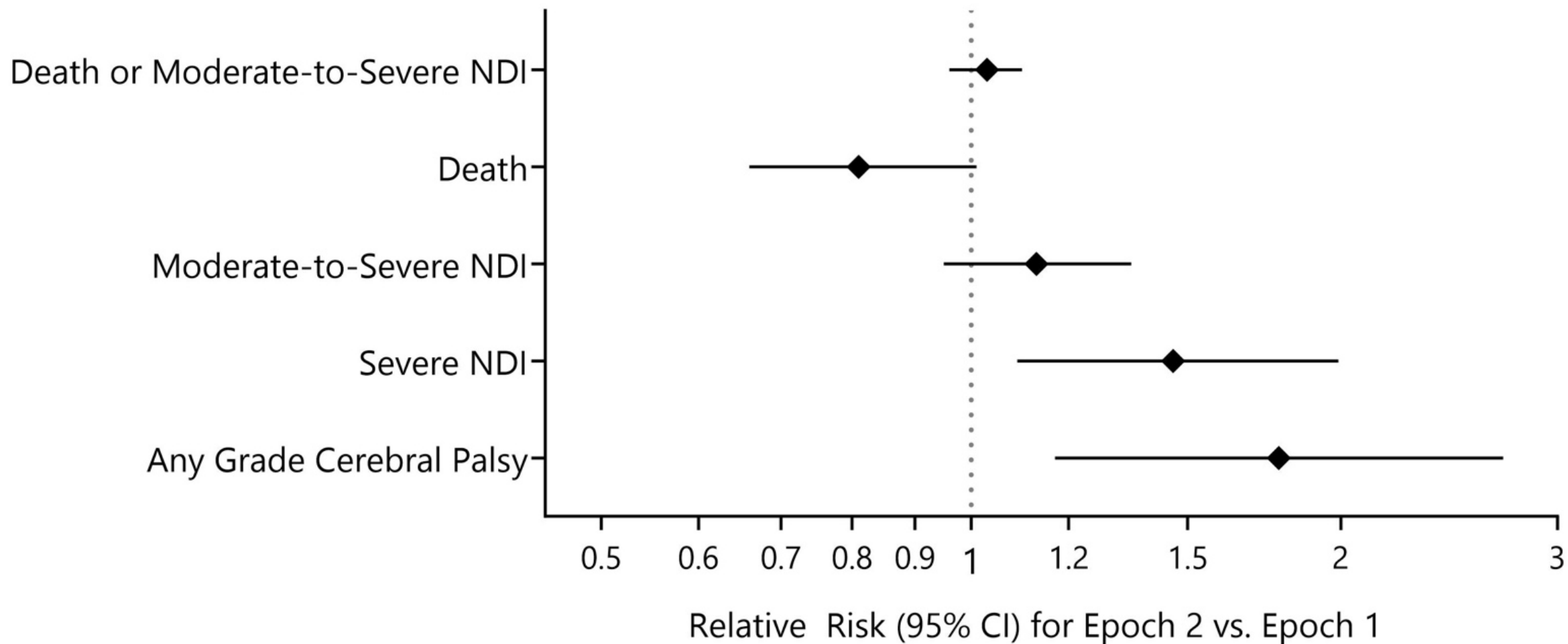
Changes Over Time

Outcome	2012-2016 N=173	2017-2019 N=131	Adjusted Relative Risk (95% CI)
Death or moderate-severe NDI (primary outcome)	89%	91%	1.03 (0.96-1.10)
Death	58%	47%	0.81 (0.66-1.01)
Moderate-severe NDI among survivors	54/73 (74%)	58/70 (83%)	1.13 (0.95-1.35)
No or mild	27%	17%	
Moderate	27%	23%	
Severe	46%	59%	1.46 (1.08-1.99)

Increases in Cerebral Palsy and Cognitive Impairment Over Time

Outcome	2012-2016	2017-2019	Adjusted Relative Risk (95% CI)
Any grade of cerebral palsy	27%	52%	1.78 (1.17-2.71)
Moderate or severe cerebral palsy	23%	32%	1.46 (0.87-2.45)
Bayley III cognitive score <85	59%	74%	1.33 (1.09-1.63)
Bayley III cognitive score <70	31%	45%	1.48 (1.07-2.04)

Changes Between 2012-2016 and 2017-2019

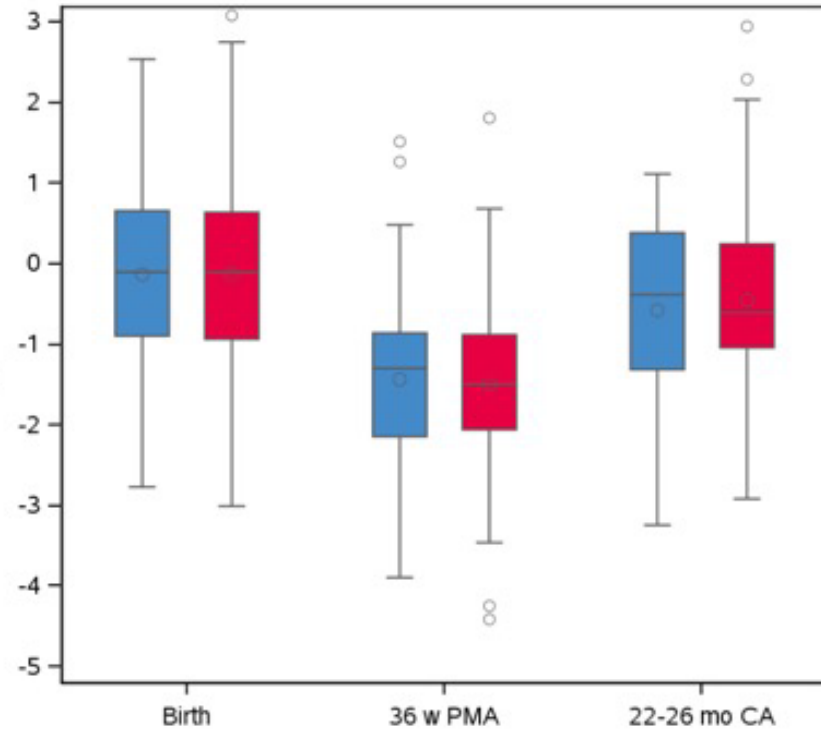


Additional Outcomes Among Surviving Children

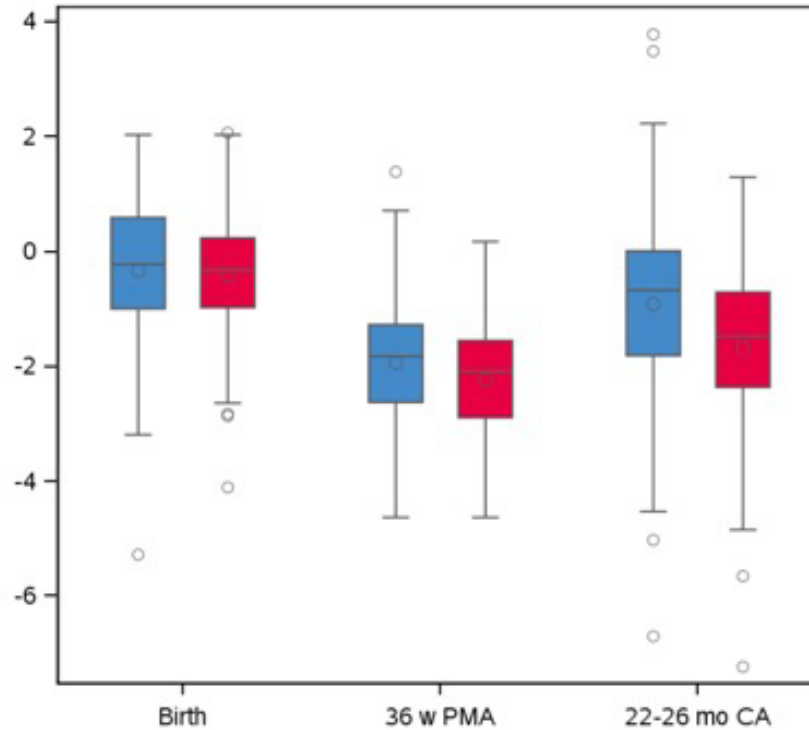
Outcome	2012-2016 N=73	2017-2019 N=70
Rehospitalization (including surgery)	62%	76%
Surgery after discharge (including ostomy closure)	60%	61%
Mobility aids/supportive equipment	22%	33%
No or limited oral feeding	30%	33%
-Total parenteral nutrition use	9%	26%
Gastrostomy or other tube feeding	29%	36%

Growth Outcomes

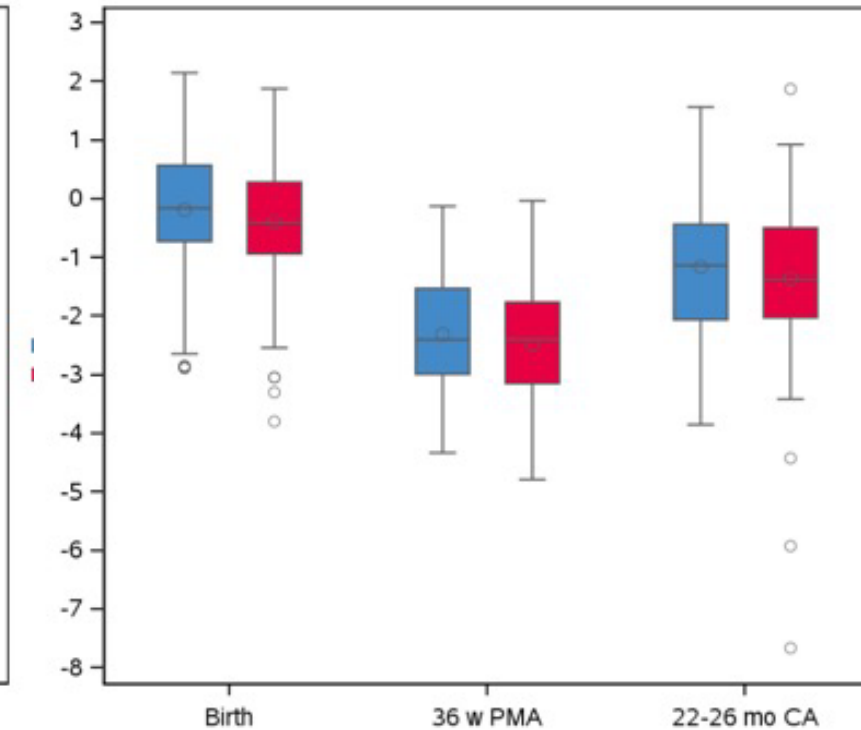
Weight



Head Circumference



Length



The mean difference (95% CI) in Z-score at follow-up comparing 2017-2019 vs. 2012-2016:

Weight = 0.12 (-0.33, 0.58); P=0.60

Head Circumference = -0.65 (-1.33, 0.02); P=0.06

Length = -0.09 (-0.70, 0.51); P=0.76

■ 2012-2016
■ 2017-2019

Conclusions

- We observed no change in the risk of death or NDI among extremely preterm infants with surgical NEC from 2012 through 2019.
- Increases in severe NDI over time, as well as cerebral palsy and cognitive impairment, may have been offset by decreases in mortality.
- Our findings highlight the continued high rates of adverse 2-year outcomes for children born extremely preterm with surgical NEC.

Neonatal Research Network Centers (Current: 2023-2030)

- Case Western Reserve University
- Cincinnati Children's Medical Center
- Duke University
- Emory University
- Lurie Children's/Northwestern U
- RTI International
- Sharp Memorial Hospital/UCSD
- Stanford University
- University of Alabama
- University of Iowa
- University of Mississippi
- University of New Mexico
- University of Pennsylvania
- University of Texas Southwestern
- University of Texas Health Science Center at Houston
- University of Utah

Neonatal Research Network Centers (2016-2023)

- Brown University
- Case Western Reserve University
- Cincinnati Children's Medical Center
- Duke University
- Emory University
- Nationwide Children's Hospital, Ohio State University
- RTI International
- Stanford University
- University of Alabama at Birmingham
- University of Iowa
- University of New Mexico
- University of Pennsylvania
- University of Rochester
- University of Texas Southwestern
- University of Texas Health Science Center at Houston
- University of Utah

Neonatal Research Network Centers (2011-2016)

- Brown University
- Case Western Reserve University
- Children's Mercy Hospitals and Clinics, University of Missouri-Kansas City
- Cincinnati Children's Medical Center
- Duke University
- Emory University
- Indiana University
- Nationwide Children's Hospital, Ohio State University
- RTI International
- Stanford University
- University of Alabama at Birmingham
- University of California – Los Angeles
- University of Iowa
- University of New Mexico
- University of Pennsylvania
- University of Rochester
- University of Texas Southwestern
- University of Texas Health Science Center at Houston
- Wayne State University

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Short-term Outcomes

Characteristic	2012-2016 N=173	2017-2019 N=131
Severe IVH (Grade 3 or 4)	24%	26%
PVL	12%	10%
BPD (physiologic definition)	72%	83%
Late-onset Sepsis	42%	42%
Short Bowel Syndrome	20%	21%
Length of Stay, median days (IQR)	89 (23-149)	114 (32-187)