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The Environment and Experiences Influence on Neurological Outcomes in the Preterm Infant

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Professor of Pediatrics, University of California, Irvine



Objectives

1. Describe the key forms of brain injury in the preterm infant
2. Understand the impact of the environment and experiences in the NICU on brain development and outcomes
3. Describe the potential role of modification of the environment on neurodevelopment outcomes in the preterm infant

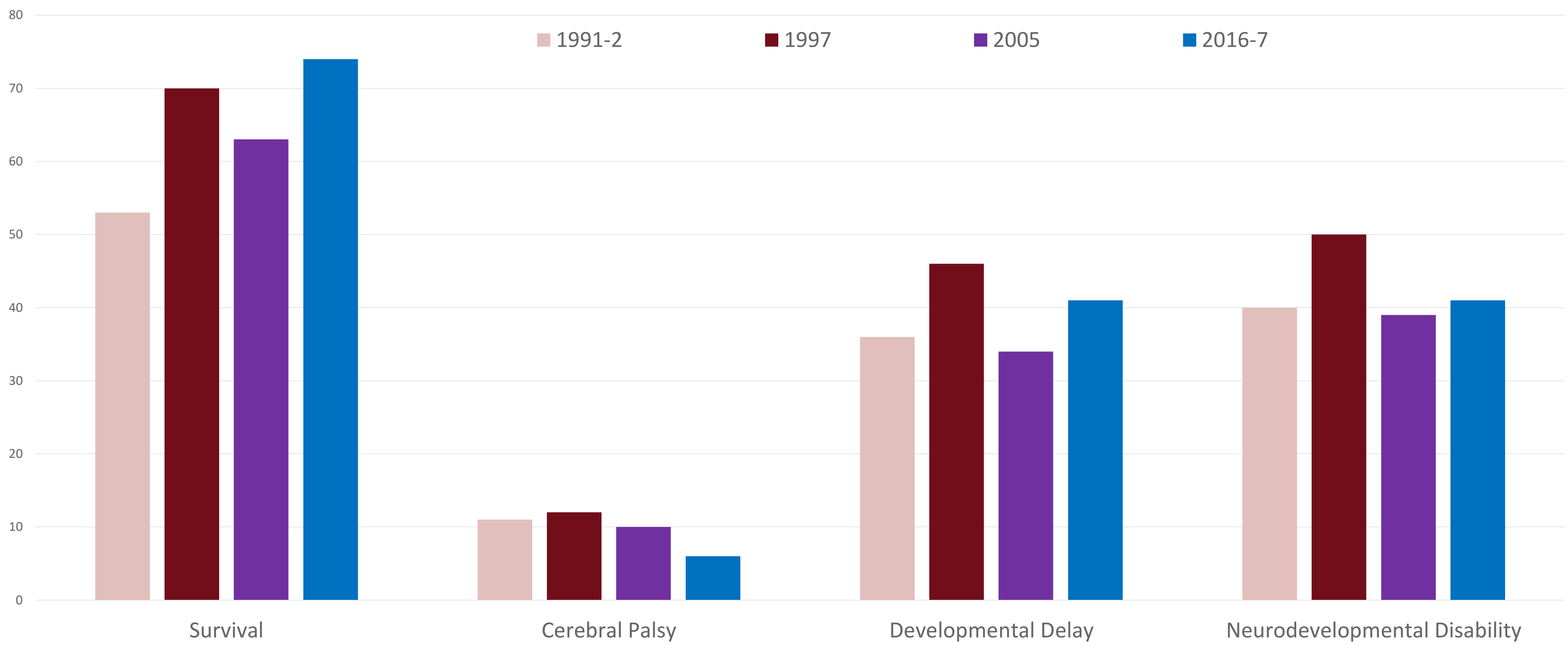
JAMA Pediatrics | Original Investigation

Temporal Trends in Neurodevelopmental Outcomes to 2 Years After Extremely Preterm Birth

Jeanie L. Y. Cheong, MD; Joy E. Olsen, PhD; Katherine J. Lee, PhD; Alicia J. Spittle, PhD; Gillian F. Opie, MBBS; Marissa Clark, MBBS; Rosemarie A. Boland, PhD; Gehan Roberts, PhD; Elisha K. Josev, PhD; Noni Davis, MBBS; Leah M. Hickey, MD; Peter J. Anderson, PhD; Lex W. Doyle, MD; for the Victorian Infant Collaborative Study Group

Cheong et al, JAMA Pediatrics, 2021

Victorian Infant Collaborative Study Group (VICS) – 2 years of age

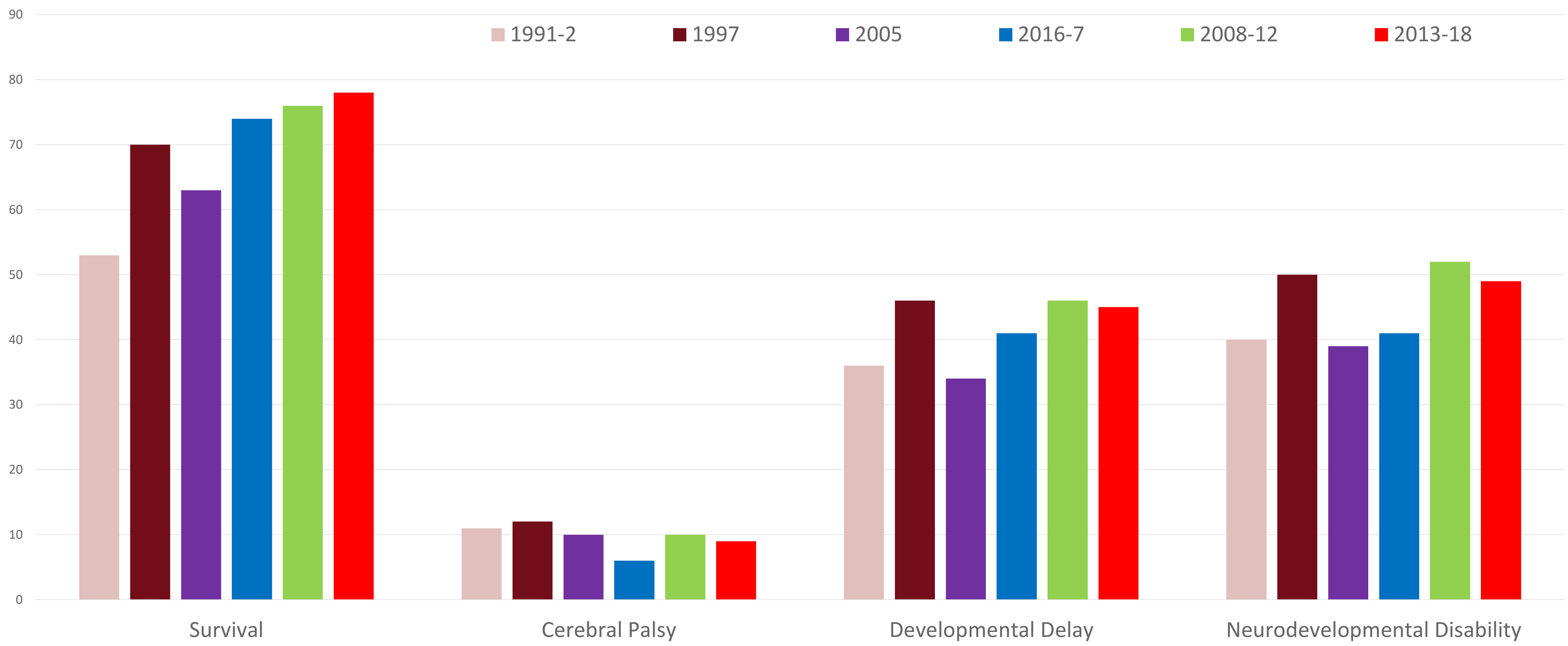


JAMA | Original Investigation

Mortality, In-Hospital Morbidity, Care Practices, and 2-Year Outcomes for Extremely Preterm Infants in the US, 2013-2018

Edward F. Bell, MD; Susan R. Hintz, MD, MS Epi; Nellie I. Hansen, MPH; Carla M. Bann, PhD; Myra H. Wyckoff, MD; Sara B. DeMauro, MD, MSCE; Michele C. Walsh, MD, MS; Betty R. Vohr, MD; Barbara J. Stoll, MD; Waldemar A. Carlo, MD; Krisa P. Van Meurs, MD; Matthew A. Rysavy, MD, PhD; Ravi M. Patel, MD, MS; Stephanie L. Merhar, MD, MS; Pablo J. Sánchez, MD; Abbot R. Laptook, MD; Anna Maria Hibbs, MD, MSCE; C. Michael Cotten, MD, MHS; Carl T. D'Angio, MD; Sarah Winter, MD; Janell Fuller, MD; Abhik Das, PhD; for the Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network

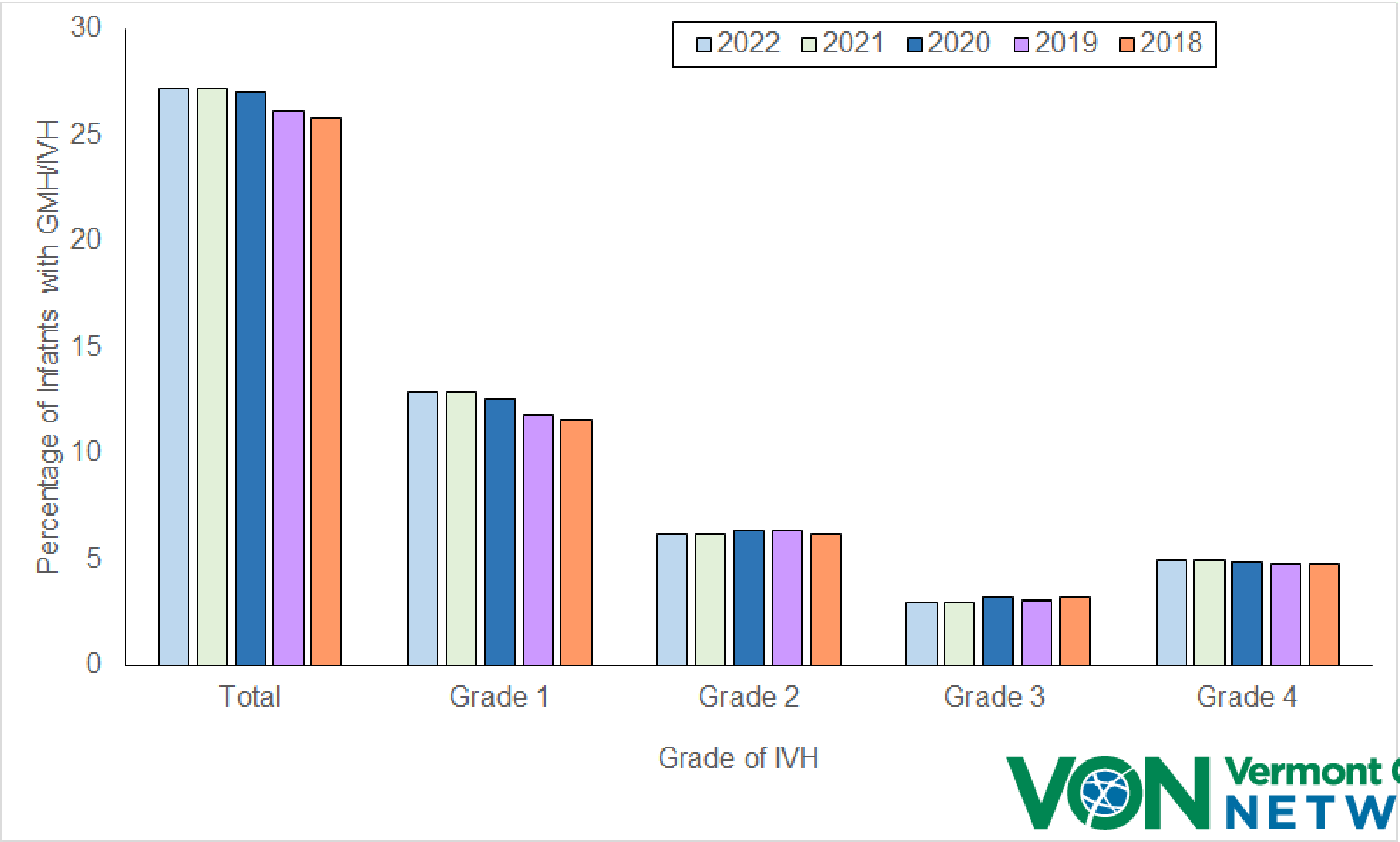
JAMA January 18, 2022 Volume 327, Number 3



Reinforcing the old - causes for adverse neurodevelopmental outcomes?

- **Brain Injury**
  - Intraventricular Hemorrhage
  - Cerebellar Hemorrhage
  - White Matter Injury

Data 2018-2022



Vermont Oxford NETWORK

Intraventricular Hemorrhage

Cerebral Immaturity

- Vascular immaturity
- Pressure Passive System

Delivery History

- Need for resuscitation
- Low Apgar scores

Metablic/Electrolytes

- Hypoglycemia
- Hypernatremia
- Metabolic Acidosis

Cardiac –

- **Hypotension (dopamine)**
- **Low cardiac output**
- **Volume expansion (cord clamping)**
- **PDA (prophylatic indocid)**

Inflammatory

- Chorioamnionitis
- Sepsis

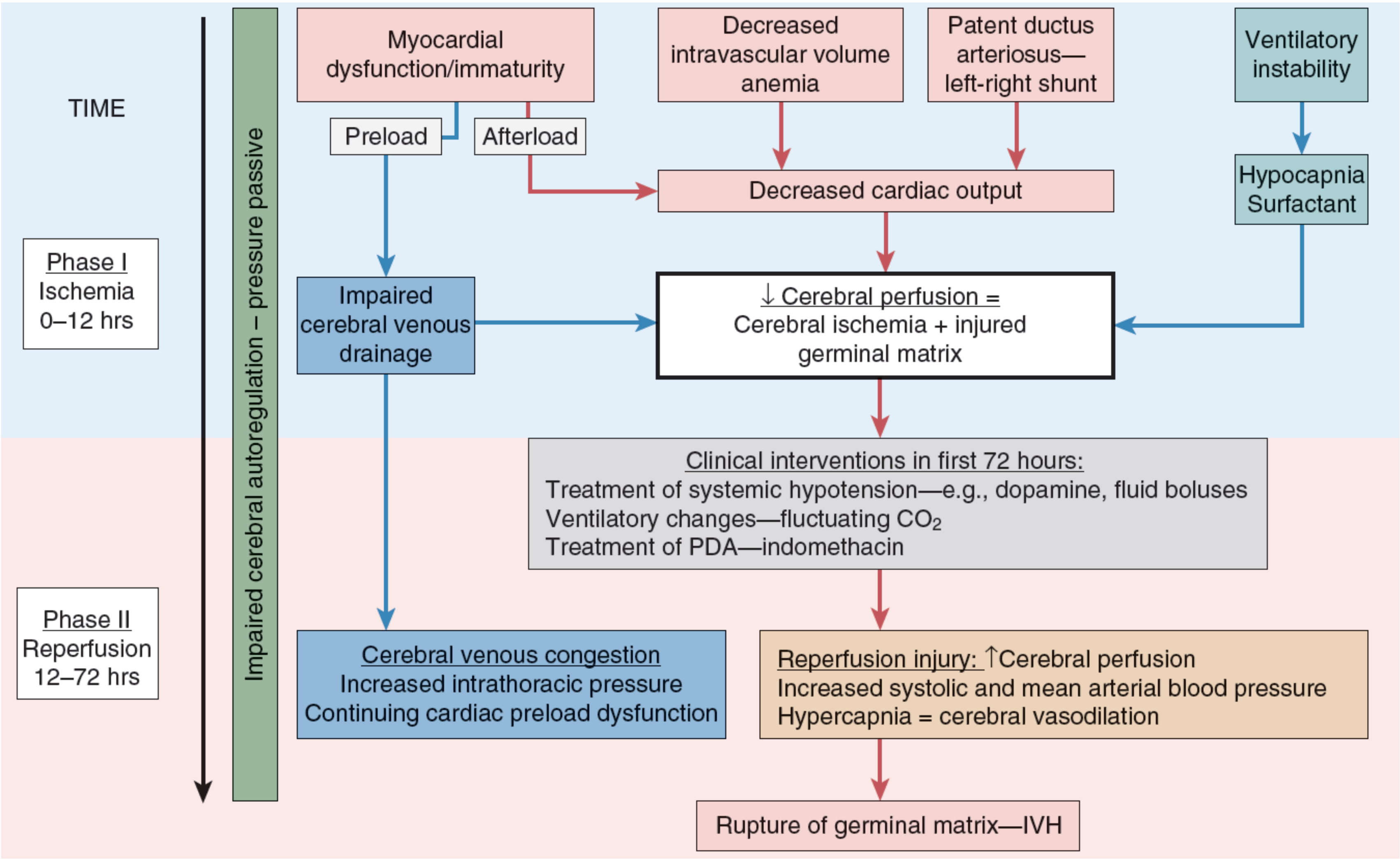
Respiratory

- **Hypercarbia/Hypocarbia**
- **Hypoxia**
- **Increased Central Venous Pressure**
    - **PPV and pneumothorax**

Hematologic

- Anemia
- Thrombocytopenia
- Coagulation disorders

Informed Vascular Physiological Care

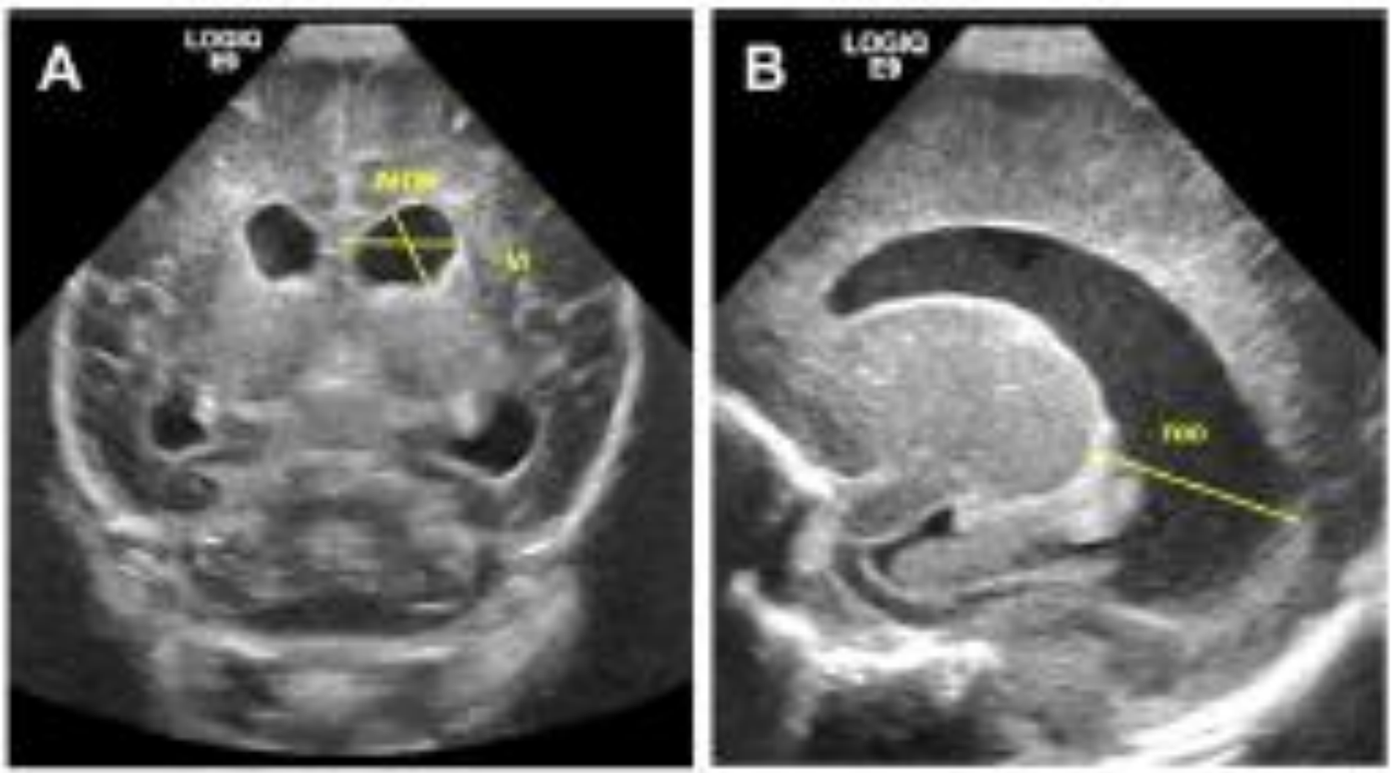


PHVD

[Management of Post-hemorrhagic Ventricular Dilatation in the Infant Born Preterm.]

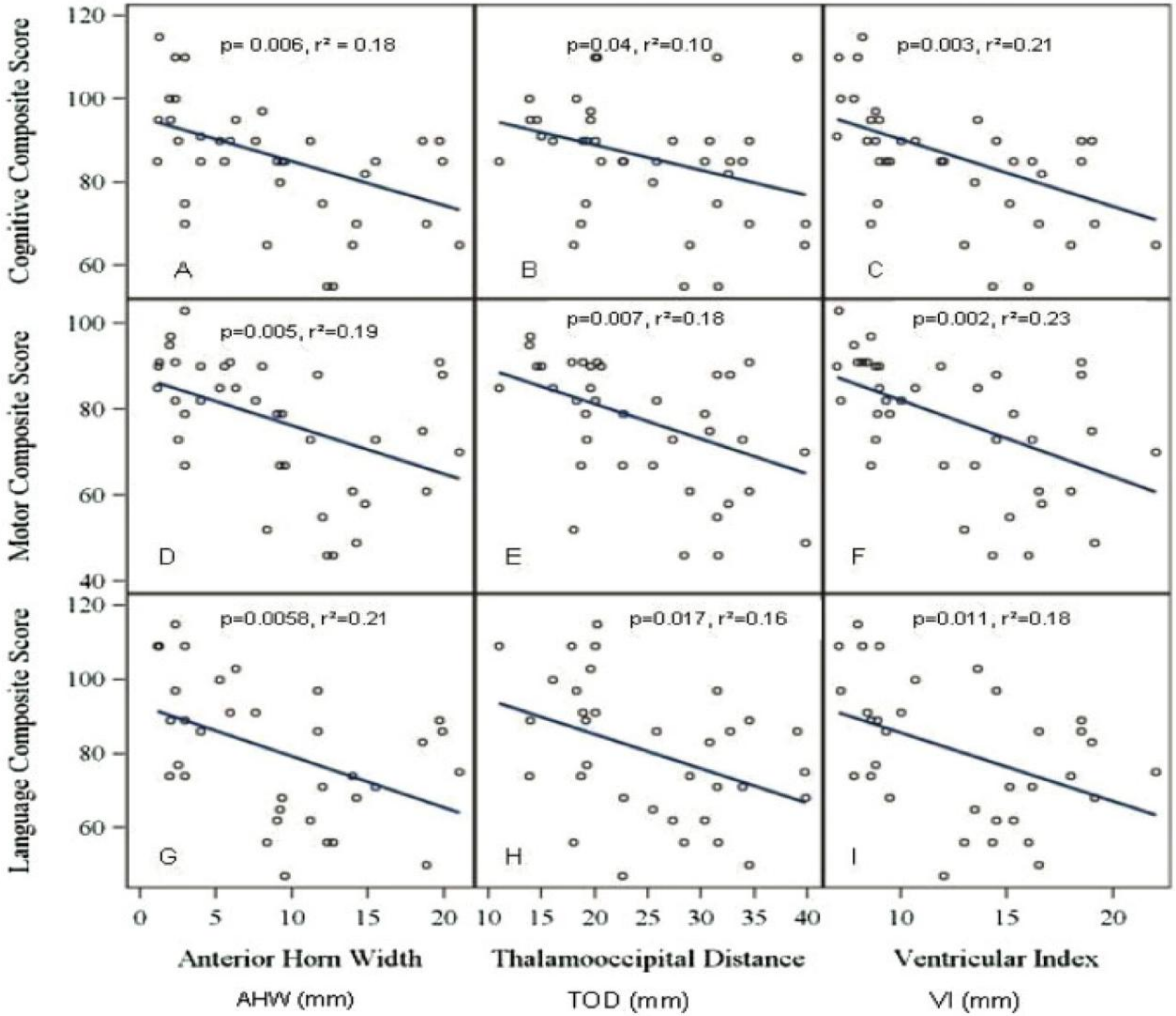
El-Dib M, Limbrick DD Jr, Inder T, Whitelaw A, Kulkarni AV, Warf B, Volpe JJ, de Vries LS.

J *Pediatr. 2020 Jul 30:S0022-3476(20)30978-1.*



When to Intervene?

[Posthemorrhagic ventricular dilatation-impact on early neurodevelopmental outcome.](#)
Srinivasakumar P, Limbrick D, Munro R, Mercer D, Rao R, Inder T, Mathur A.
Am J Perinatol. 2013 Mar;30(3):207-14.



Relationship between head ultrasound measures of ventricular dilatation and neurodevelopmental outcome at 18 to 24 months.

Randomized Controlled Early versus Late Ventricular Intervention Study in Posthemorrhagic Ventricular Dilatation: Outcome at 2 Years

Mehmet N. Cizmeci, MD[1,2,3], Floris Groenendaal, MD, PhD[1,2], Kian D. Liem, MD, PhD[4], Ingrid C. van Haastert, MA, PhD[1,2], Isabel Benavente-Fernández, MD, PhD[5], Henrica L. M. van Straaten, MD, PhD[6], Sylke Steggerda, MD, PhD[7], Bert J. Smit, MD, PhD[8], Andrew Whitelaw, MD, FRCPCH[9], Peter Woerdeman, MD, PhD[10], Axel Heep, MD[9,*], Linda S. de Vries, MD, PhD[1,2], and the ELVIS study group[†]

J Pediatr. 2020 Nov;226:28-35.

- This multicenter randomized controlled trial reviewed lumbar punctures initiated after either a low threshold (ventricular index of >p97 and anterior horn width of >6 mm) or high threshold (ventricular index of >p97 + 4 mm and anterior horn width of >10 mm).

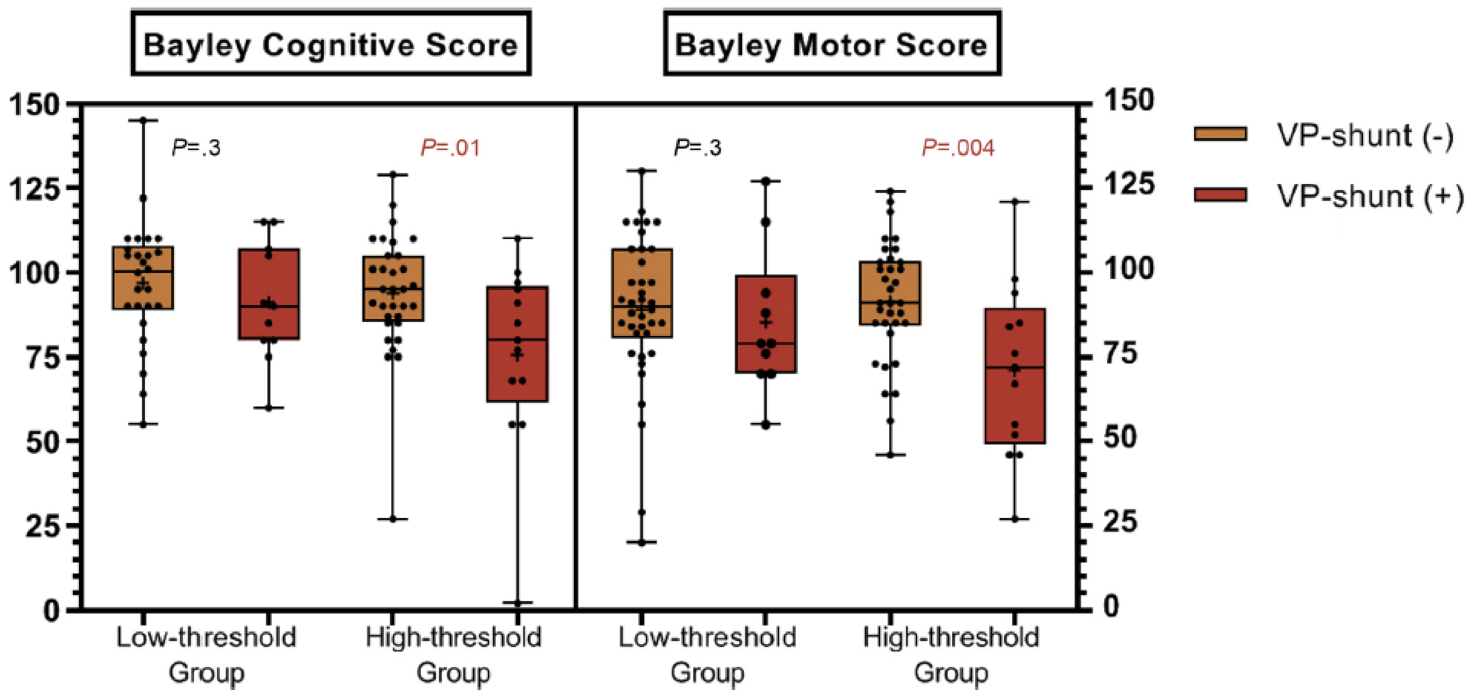


Figure 2. Box plot graphs showing the distribution of the Bayley cognitive and motor scores in relation to the timing of intervention and presence of ventriculoperitoneal shunt.

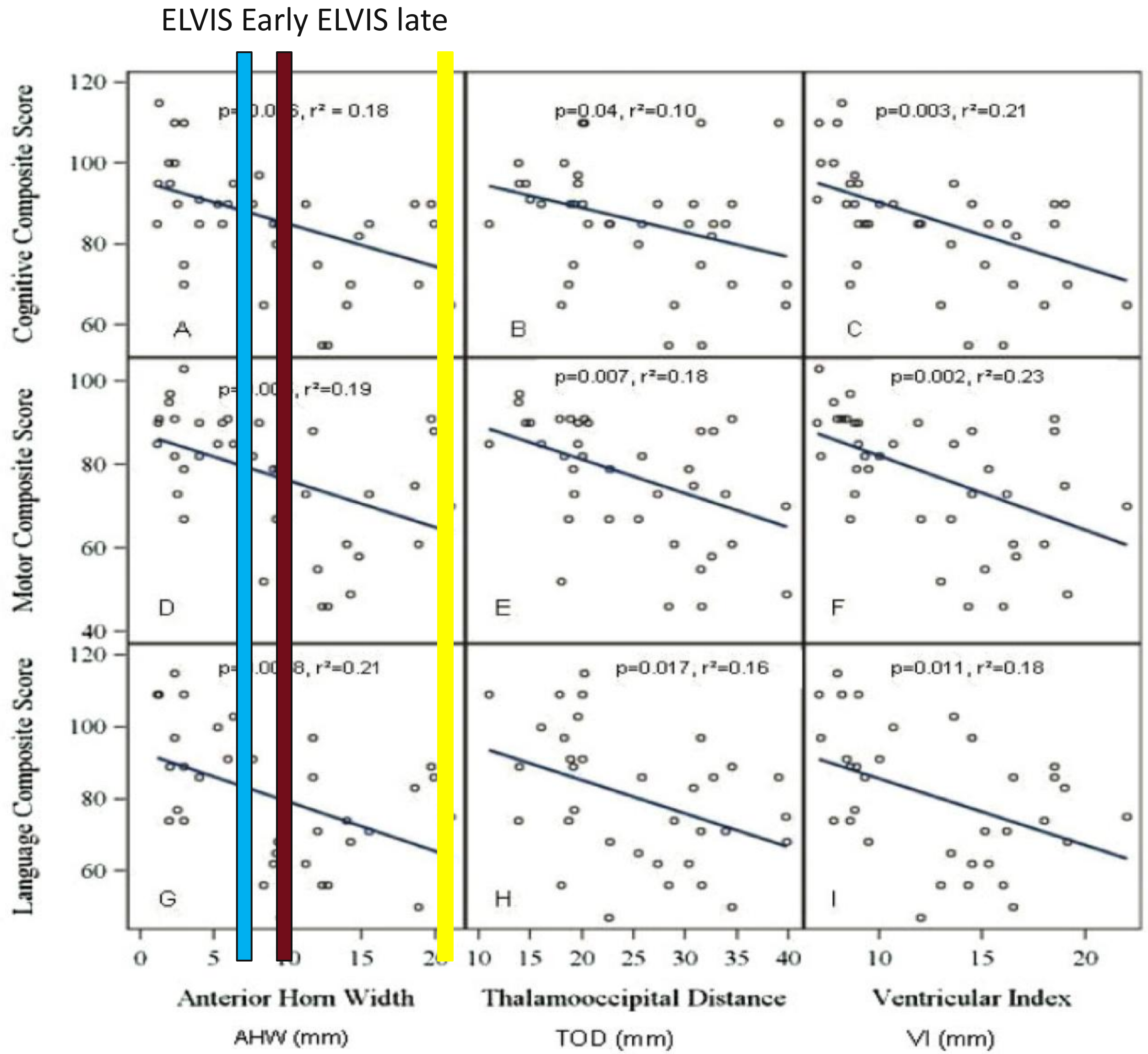
2 Year Outcome

-126 enrolled (64+62)
-109 Survivors
- 99 Had BSID
- 71% of infants tested cognitive composite score ≥ 85

	Early Intervention	Late Intervention	Stat
Poor Outcome (Death, CP or BSID <-2SD)	25/60 (42%)	32/56 (57%)	OR= 1.9 [0.9-3.6]
Mean Cognitive Score	98	95	NS
Cognitive Score < 70	8%	18%	aOR= 2.4[0.7-8.7]

J Pediatr. 2020 Nov;226:28-35.

When to Intervene?



Relationship between head ultrasound measures of ventricular dilatation and neurodevelopmental outcome at 18 to 24 months.

When to Intervene?

J Pediatr. 2020 Jul 30:S0022-3476(20)30978-1.

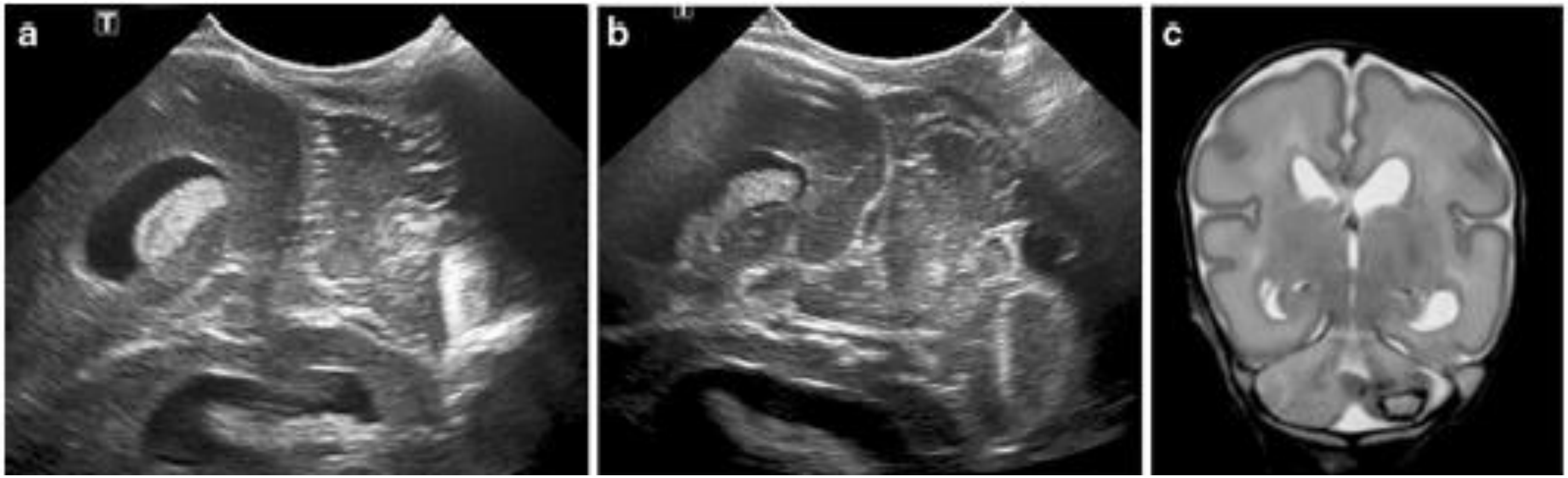
When to intervene in PHVD?

Green Zone	Yellow Zone	Red Zone
Key Criteria: Ventricular size with the following • VI ≤97^{th} percentile & • AHW ≤6 mm	**Key Criteria:** Ventricular size with the following • VI >97^{th} percentile & • AHW >6 mm &/or TOD >25 mm	**Key Criteria:** Ventricular size with the following • VI >97^{th} percentile + 4mm & • AHW >10 mm &/or TOD >25 mm
And Absence of the following clinical criteria: • HC growth >2 cm per week • Separated sutures • Bulging fontanelles	**And** Absence of the following clinical criteria: • HC growth >2cm per week • Separated sutures • Bulging fontanelles	**Or** Any of the following clinical criteria • HC growth >2 cm per week • Separated sutures • Bulging fontanelles
Management: • Observation in NICU • cUS twice a week until stable for 2 weeks then every 1-2 weeks till 34 weeks PMA • MRI at Term Equivalent	**Management:** • Referral to a regional center for neurosurgical review • Consider LP 2-3 times • cUS 2-3X a week until stable for 2 weeks then every 1-2 weeks till 34 weeks PMA • Neurosurgical intervention when no stabilization occurs • MRI at Term Equivalent	**Management:** • Consider LP 2-3 times • Neurosurgical intervention including either temporizing measures or VP shunt • MRI at Term Equivalent

Consider alterations in NIRS (ie decrease cerebral oxygenation) or Doppler US (ie Increase in Resistive Index) as additional information that may suggest impairment in cerebral perfusion and more urgent need for intervention.

Figure 5. Proposed risk stratification and management of infants with PHVD. *HC*, head circumference; *NIRS*, near-infrared spectroscopy; *PMA*, postmenstrual age.

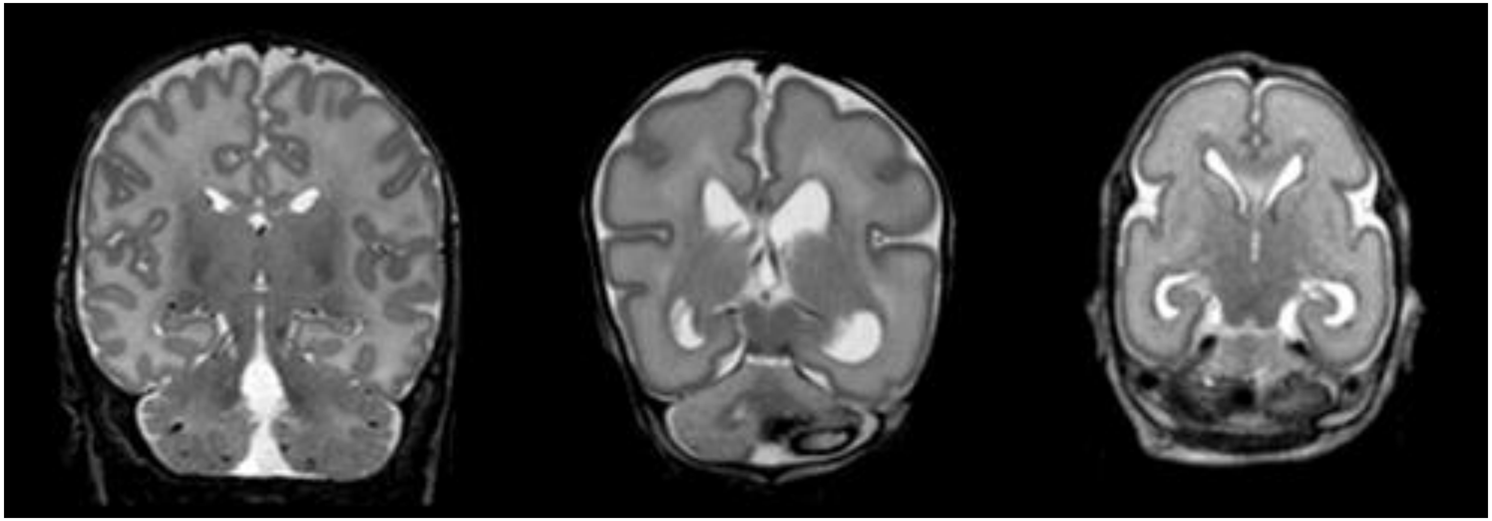
Cerebellar hemorrhage



Cerebellar hemorrhage recognized in 2-8% on CUS of preterm infants and 15-20% on routine MRI studies. Smaller CBH (<4mm) are only detectable on MRI.

Courtesy of Linda De Vries

Cerebellar Hemorrhage



- More common in most immature infants/sickest infants
- Association with opiate use ?vascular autoregulation impaired
- Larger hemorrhage associated with cognitive, language and behavioral abnormalities

Cerebellar Hemorrhage in Preterm Infants: A Meta-Analysis on Risk Factors and Neurodevelopmental Outcome

Frontiers in Physiology
June 2019:vol 10:800

Eduardo Villamor-Martinez[1†], *Monica Fumagalli*[2,3†], *Yaser Ibrahim Alomar*[1], *Sofia Passera*[2], *Giacomo Cavallaro*[2], *Fabio Mosca*[2,3] *and Eduardo Villamor*[1*]

CBH and mental developmental delay (k = 6)

Study name	Delayed / Total CBH-Yes	Delayed / Total CBH-No	Odds ratio	Lower limit	Upper limit	p-Value
Kidokoro 2014 cohort 2	3 / 15	10 / 34	0.64	0.15	2.80	0.556
Kidokoro 2014 cohort 1	2 / 12	21 / 168	1.40	0.29	6.83	0.677
Biran 2011	3 / 10	5 / 20	1.48	0.27	8.18	0.656
O'Shea 2008	8 / 14	87 / 396	4.74	1.60	14.01	0.005
Zayek 2012	16 / 32	88 / 588	5.68	2.74	11.78	0.000
Limperopoulos 2007	14 / 35	0 / 35	47.88	2.72	844.21	0.008
OVERALL			**2.95**	**1.21**	**7.20**	**0.017**

Heterogeneity: $I^2 = 60\%$; $p = 0.028$

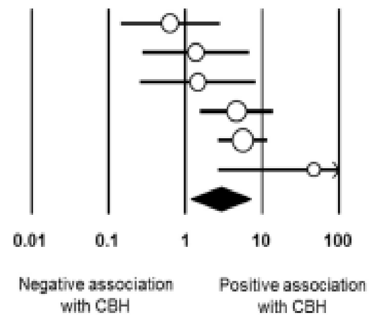


FIGURE 5 | Meta-analysis of the association between cerebellar hemorrhage (CBH) and risk of delayed mental development. CI, confidence interval.

CBH and psychomotor developmental delay (k = 6)

Study name	Delayed / Total CBH-Yes	Delayed / Total CBH-No	Odds ratio	Lower limit	Upper limit	p-Value
Kidokoro 2014 cohort 2	1 / 15	4 / 34	0.54	0.05	5.24	0.592
Kidokoro 2014 cohort 1	1 / 12	16 / 168	0.86	0.10	7.13	0.892
Biran 2011	2 / 10	2 / 20	1.59	0.16	15.35	0.689
Zayek 2012	18 / 32	123 / 588	4.86	2.35	10.05	0.000
O'Shea 2008	10 / 14	95 / 396	7.92	2.43	25.84	0.001
Limperopoulos 2007	17 / 35	0 / 35	67.16	3.82	1180.70	0.004
OVERALL			**3.62**	**1.34**	**9.76**	**0.011**

Heterogeneity: $I^2 = 54\%$; $p = 0.055$

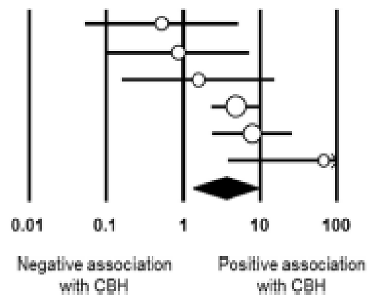
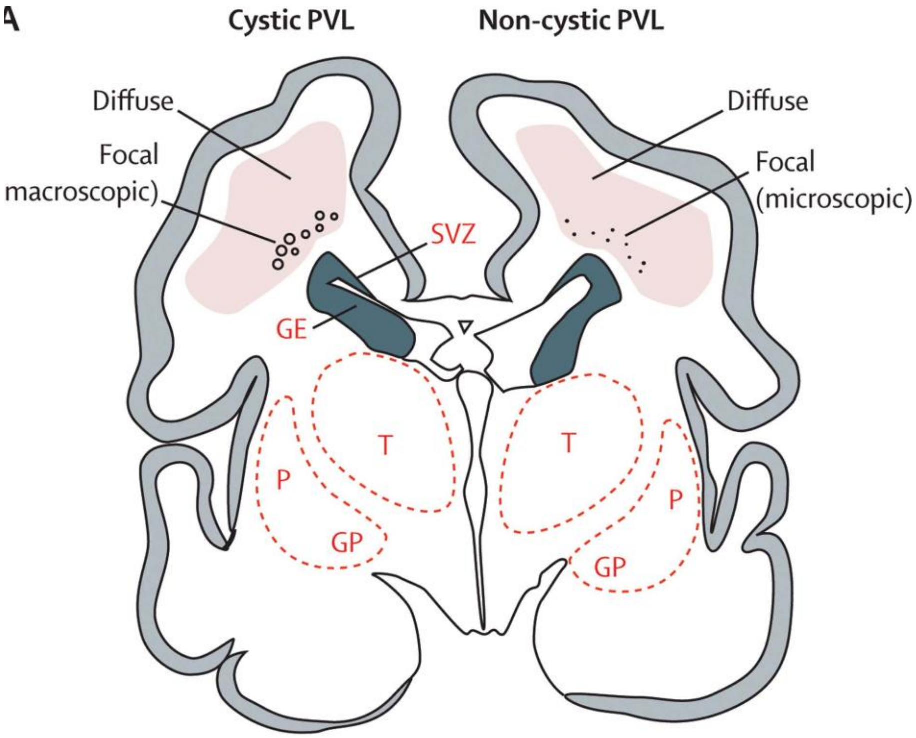


FIGURE 6 | Meta-analysis of the association between cerebellar hemorrhage (CBH) and risk of delayed psychomotor development. CI, confidence interval.

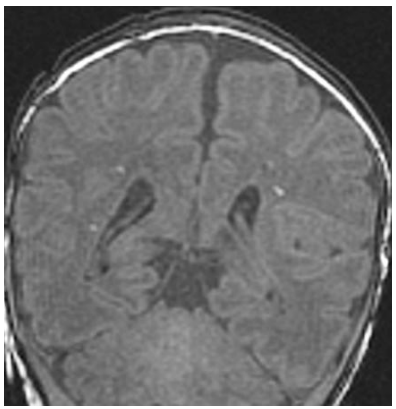
White matter Abnormalities



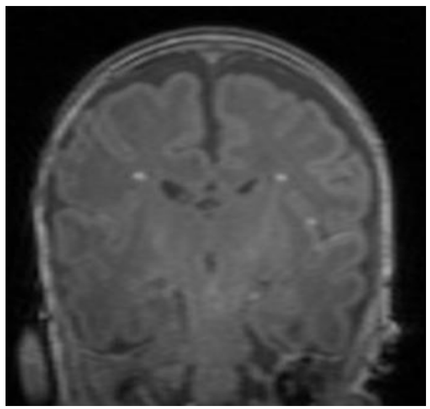
- Terminology
  - White matter cysts
  - White matter punctate lesions
  - Loss of white matter volume
  - Diffuse high signal changes throughout white matter

Volpe JJ Lancet Neurology 2009;8:110-24

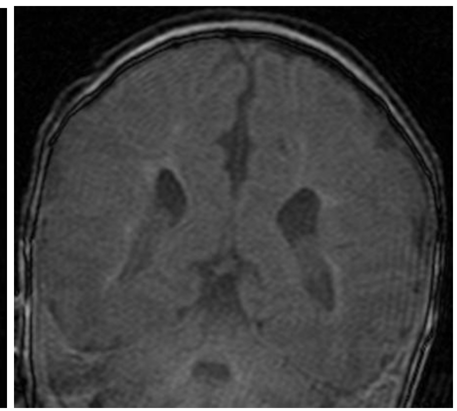
White Matter Injury – visible on MRI



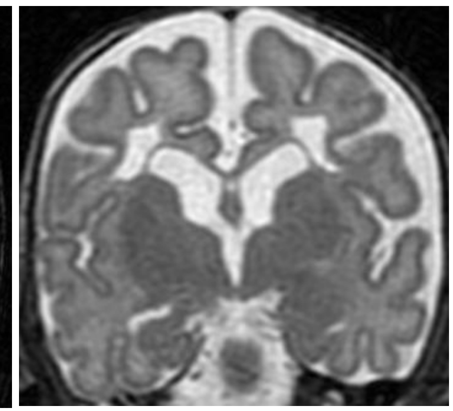
GRADE 1
Mild
25-50%



GRADE 2
Moderate
15%



GRADE 3
Severe linear scaring
2-5%



GRADE 4
Severe cystic
2%

White Matter Injury

- Ischemia and Reperfusion Injury
  - Similar vulnerability to IVH (common concurrent)
- Inflammatory mediated Injury
  - Perinatal sepsis
  - Postnatal sepsis
  - Necrotizing Enterocolitis

Nursing Intervention Bundle

561 infants <30 weeks gestation – two cohorts pre- and post-intervention

The Nursing Intervention Bundle consisted of:

1. Posture:

- a. Maintaining midline head position.
- b. Incubator tilted 15–30 degrees.
- c. Avoidance of head down position and sudden elevation of the legs.

2. **Avoiding rapid intravenous/arterial flushes and rapid arterial blood withdrawal (<30 s).**

The NIB was applied directly after birth starting in the delivery room and was continued during the first 72 postnatal hours. After 72 hours, all aspects of the NIB were still carried out with the exception that a prone position was allowed. The head was maintained in the midline when the infants were positioned in a supine position.

To cite: de Bijl-Marcus K, Brouwer AJ, De Vries LS, *et al*. *Arch Dis Child Fetal Neonatal Ed* 2020;**105**:F419–F424.

Blood volumes and draws

- **Preterm 500g**
- Blood volume 50 mls
- Draw 2.5 mls

(5% blood volume)

- Limited autoregulation

- **Adult 70 kg**
- 5000mls
- Equivalent 250 mls (blood donor pack in 60s)
- Intact autoregulation

Combined outcome

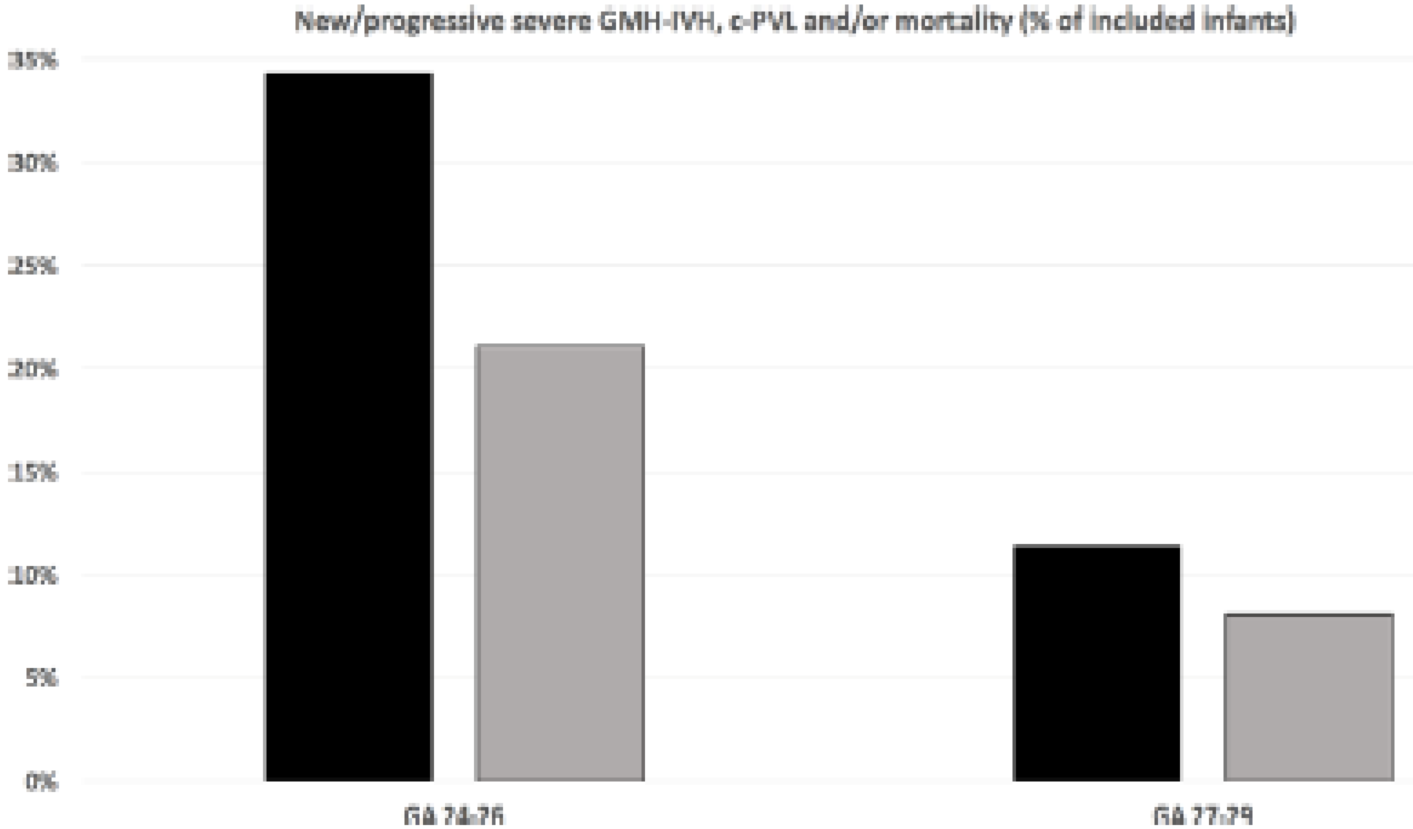


Figure 2 Percentage of infants who died or developed a new/ progressive severe germinal matrix-intraventricular haemorrhage (GMH-IVH) or cystic periventricular leukomalacia (c-PVL) (control group vs nursing intervention bundle group) stratified by gestational age (GA).

Interventions in the NICU and beyond

Early developmental intervention programmes provided post hospital discharge to prevent motor and cognitive impairment in preterm infants (Review)

Orton J, Doyle LW, Tripathi T, Boyd R, Anderson PJ, Spittle A

Orton J, Doyle LW, Tripathi T, Boyd R, Anderson PJ, Spittle A.
Early developmental intervention programmes provided post hospital discharge to prevent motor and cognitive impairment in preterm infants.
Cochrane Database of Systematic Reviews 2024, Issue 2. Art. No.: CD005495.
DOI: 10.1002/14651858.CD005495.pub5.

Early developmental intervention programmes for preterm infants:

- probably improve cognitive and motor outcomes during infancy (low- certainty evidence)
- at preschool age, intervention is shown to improve cognitive outcomes (high-certainty evidence) but not motor outcomes
- lack of good-quality evidence for cognitive and motor outcomes at school age (five to less than 18 years)

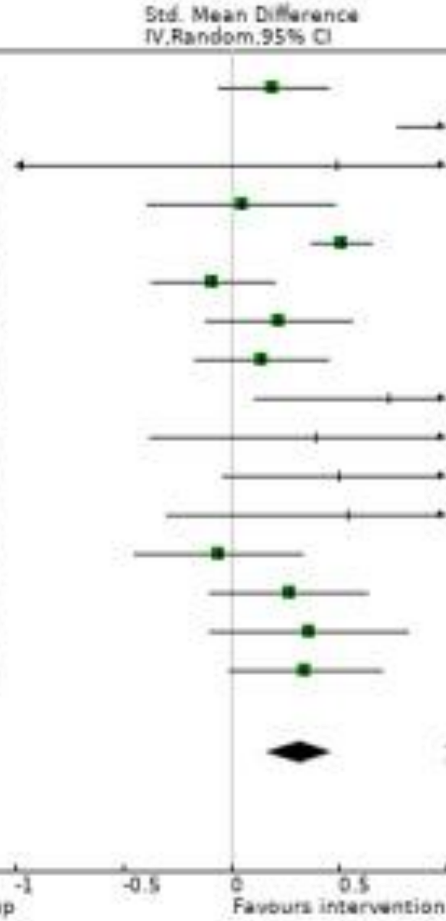
Considerable heterogeneity exists between studies due to variations in aspects of the intervention programmes, the population and outcome measures utilised.

Cognitive Outcomes at School Age

Review: Early developmental intervention programmes provided post hospital discharge to prevent motor and cognitive impairment in preterm infants
Comparison: 1 Early developmental intervention versus standard follow-up (all studies)
Outcome: 1 Cognitive outcome at infancy - DQ (Bayley and Griffiths)

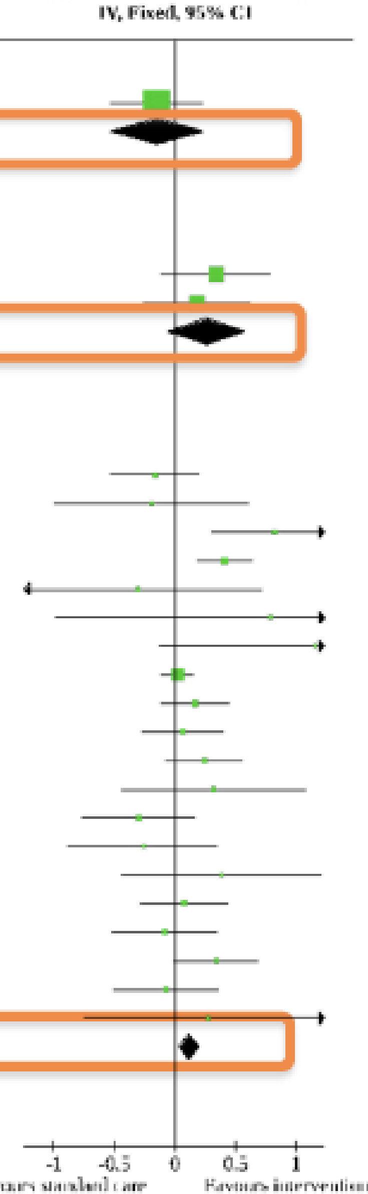
Study or subgroup	Treatment N	Mean(SD)	Follow-up N	Mean(SD)	Weight	Std. Mean Difference IV,Random,95% CI
APIP 1998	179	96.3 (17.1)	88	92.9 (18.7)	9.2 %	0.19 [-0.06, 0.45]
Bao 1999	36	104.5 (10.8)	41	89.9 (12)	5.5 %	1.26 [0.77, 1.75]
Dusing 2015	3	106.67 (12.58)	4	97.5 (17.56)	0.9 %	0.49 [-1.06, 2.04]
Goodman 1985	40	101.5 (10.5)	40	101 (11)	6.2 %	0.05 [-0.39, 0.48]
I.H.D.P. 1990	343	102.6 (19.37)	532	92.84 (19.08)	11.1 %	0.51 [0.37, 0.65]
Johnson 2009	91	91.3 (18.6)	103	92.9 (18.2)	8.7 %	-0.09 [-0.37, 0.20]
Kaaresen 2006	69	94.7 (17.3)	67	90.5 (20.7)	7.8 %	0.22 [-0.12, 0.56]
Koldewijn 2009	81	92.5 (18)	77	90 (17.5)	8.2 %	0.14 [-0.17, 0.45]
Melnyk 2001	20	102.5 (6.1)	22	88.9 (24.4)	4.1 %	0.73 [0.11, 1.36]
Nelson 2001	15	82.67 (21.65)	12	74.67 (17.26)	3.1 %	0.39 [-0.38, 1.16]
Nurcombe 1984	25	115.6 (12.4)	28	109.6 (11.1)	4.9 %	0.50 [-0.04, 1.05]
Ohgi 2004	12	76.4 (15.4)	11	67.9 (15.1)	2.7 %	0.54 [-0.30, 1.37]
Sajaniemi 2001	49	92.61 (17.41)	51	93.67 (16.26)	6.9 %	-0.06 [-0.45, 0.33]
Spittle 2009	58	99 (12.8)	57	95.6 (12.6)	7.3 %	0.27 [-0.10, 0.63]
Teti 2009	33	96.59 (11.8)	42	92.63 (9.9)	5.9 %	0.36 [-0.10, 0.82]
Wu 2014	98	99.17 (9.08)	45	96 (9.4)	7.5 %	0.34 [-0.01, 0.70]
Total (95% CI)	**1152**		**1220**		**100.0 %**	**0.32 [0.16, 0.47]**

Heterogeneity: Tau² = 0.05; Chi² = 39.38, df = 15 (P = 0.00056); I² =62%
Test for overall effect: Z = 3.95 (P = 0.000079)
Test for subgroup differences: Not applicable



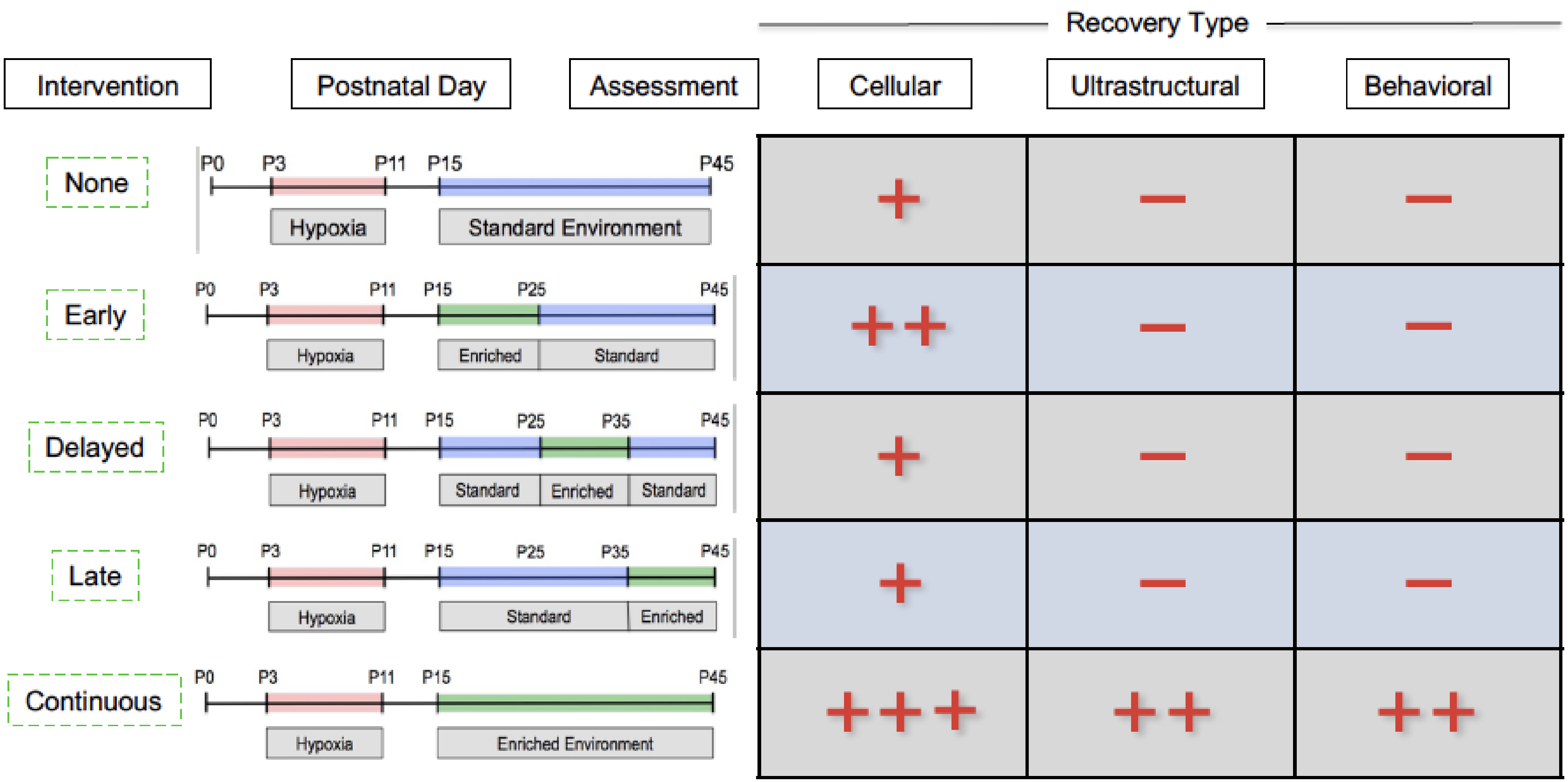
Pre-discharge appears more effective

Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
6.4.1 Parent-infant relationship								
Milgrom 2019	103.25	17.16	52	106.08	20.13	52	100.0%	-0.15 [-0.54 , 0.23]
Subtotal (95% CI)			**52**			**52**	**100.0%**	**-0.15 [-0.54 , 0.23]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.76 (P = 0.44)								
6.4.2 Infant development								
Bao 1999	98.3	13.9	36	93.6	13.1	41	48.7%	0.35 [-0.11 , 0.80]
Goodman 1985	108	18.5	40	105	13.5	40	51.3%	0.18 [-0.26 , 0.62]
Subtotal (95% CI)			**76**			**81**	**100.0%**	**0.26 [-0.05 , 0.58]**
Heterogeneity: Chi² = 0.25, df = 1 (P = 0.61); I² = 0%								
Test for overall effect: Z = 1.63 (P = 0.10)								
6.4.3 Parent-infant relationship and infant development								
Alberge 2023	91.8	9.1	57	93.3	9.8	57	4.7%	-0.16 [-0.53 , 0.21]
Apaydin 2023	104.66	9.59	12	106.5	9.12	12	1.0%	-0.19 [-0.99 , 0.61]
Cassel 2016	113.8	13	37	102.4	14.5	28	2.4%	0.82 [0.31 , 1.34]
Colditz 2019	99.6	13.01	150	94.1	13.54	148	12.2%	0.41 [0.18 , 0.64]
Dusing 2015	93.6	13.1	41	98	24.6	4	0.6%	-0.30 [-1.33 , 0.72]
Dusing 2018	86	7.6	3	70	21.63	3	0.2%	0.79 [-0.98 , 2.56]
Finlayson 2020	95.28	5.96	7	83.8	12.47	5	0.4%	1.16 [-0.12 , 2.44]
I.H.D.P. 1990	95.03	16.34	342	94.6	16.26	530	34.7%	0.03 [-0.11 , 0.16]
Johnson 2009	94.8	15.9	91	92	16.8	103	8.0%	0.17 [-0.11 , 0.45]
Kaaresen 2006	94.3	16.3	69	93.1	17.2	67	5.7%	0.07 [-0.27 , 0.41]
Koldewijn 2009	87.5	16	76	83.8	14	75	6.2%	0.24 [-0.08 , 0.57]
Nelson 2001	72.27	19.61	15	66.17	16.33	12	1.1%	0.32 [-0.44 , 1.09]
Nurcombe 1984	99.4	11.39	32	103	12.48	38	2.9%	-0.30 [-0.77 , 0.17]
Ochandorena-Acha 2022	30.25	7.15	20	32.1	6.83	21	1.7%	-0.26 [-0.87 , 0.36]
Ohgi 2004	69.8	19.2	12	63.1	13.6	11	0.9%	0.39 [-0.44 , 1.21]
Spittle 2009	99.9	14.8	58	98.6	16.9	57	4.8%	0.08 [-0.28 , 0.45]
Treyvaud 2022	100.6	16.4	42	101.9	14.9	39	3.4%	-0.08 [-0.52 , 0.35]
Wu 2014	99.17	9.08	98	96	9.4	45	5.1%	0.34 [-0.01 , 0.70]
Yoon 2021	95	16.9	43	96.3	19.1	39	3.4%	-0.07 [-0.51 , 0.36]
Ziegler 2021	100.14	3.86	7	96.75	15.47	8	0.6%	0.27 [-0.75 , 1.29]
Subtotal (95% CI)			**1212**			**1302**	**100.0%**	**0.12 [0.04 , 0.20]**
Heterogeneity: Chi² = 31.00, df = 19 (P = 0.04); I² = 39%								
Test for overall effect: Z = 2.93 (P = 0.003)								
Test for subgroup differences: Chi² = 2.67, df = 2 (P = 0.26), I² = 25.1%								



Environmental enrichment ameliorates perinatal brain injury and promotes functional white matter recovery

Thomas A. Forbes[1,2,5], Evan Z. Goldstein[1,5], Jeffrey L. Dupree[3], Beata Jablonska[1,2], Joseph Scafidi[1,2], Katrina L. Adams[1], Yuka Imamura[4], Kazue Hashimoto-Torii[1] & Vittorio Gallo[1,2]



Serial neuroimaging of brain growth and development in very preterm infants receiving tailored neuropromotive support in the NICU. Protocol for a prospective cohort study

Carmina Erdei[1,2*], Sara Cherkerzian[1,2], Roberta Pineda[3] and Terrie E. Inder[1,2,4]

frontiers | Frontiers in Pediatrics

TYPE Study Protocol
PUBLISHED 12 October 2023
DOI 10.3389/fped.2023.1203579

Reference Group	SENSE Program Groups	
	Low-Risk Group	High-Risk Group
Neonatal Therapy Standard Care	(Standard Care + "SENSE")	(Standard Care + "SENSE-Plus")
Developmentally sensitive bedside care OT or PT/Motor therapy: • 8–34 weeks PMA: total of 1–3 sessions per week • >34 weeks PMA: total of 2–4 sessions per week If known neurological injury or neurologic exam differences, or parent education and support need: consider increasing therapy to 2–4 times/week Neurologic assessments: • Brain MRI at TEA if <28 weeks GA at birth, or >28 weeks GA and additional risk factors per NICU guideline • TIMP at TEA by PT/OT in NICU • TIMP at 3–4 months PMA by OT in outpatient follow-up clinic SLP/Feeding therapy: • 33–34 weeks PMA: 1–2 times/week • >34 weeks PMA: 2–4 times/week Feeding assessment: • Assessment of feeding skills progression with FOIS-P (31) feeding scale	Neonatal therapy and assessment per reference Group, plus the following: • SENSE Program delivery with weekly targets for sensory experiences from enrollment to TEA • Therapist-guided parent training on reading infant's behavioral cues and contingent responses • Therapist-led education on positive auditory experiences (facilitating reading, music exposures per SENSE goals for GA) Neurologic assessments: • Brain MRI every 2 weeks from enrollment until TEA • Premie-Neuro every 2 weeks with MRI • TIMP and HNNE at TEA by PT/OT and research nurse • TIMP at 3–4 months PMA by OT in outpatient follow-up clinic Feeding assessment: • Assessment of feeding skills progression with FOIS-P (31) feeding scale	Neonatal therapy and assessment per Low-Risk Group, plus the following: Enhanced therapy involvement based on serial assessments and imaging results, as follows: • Additional 1–2 skilled OT or PT weekly sessions (totaling service delivery to 4–5 days/week) • Motor therapy goals targeted based on results of formal neurologic assessments, focus on areas requiring further therapist-guided interventions (e.g. postural control, midline orientation, symmetrical movements, motor experience) • OT/PT increased availability to facilitate day-shift routine care times with staff/parents (i.e. facilitation diaper changes, handling time) • Increased reading with infant several times a week (optimal: daily) • Enhanced family education with parent instructional videos

Factors Associated with Outpatient Therapy Utilization in Extremely Preterm Infants - Ponnapakkam et al

Am J Perinatol 2024;41:458–469.

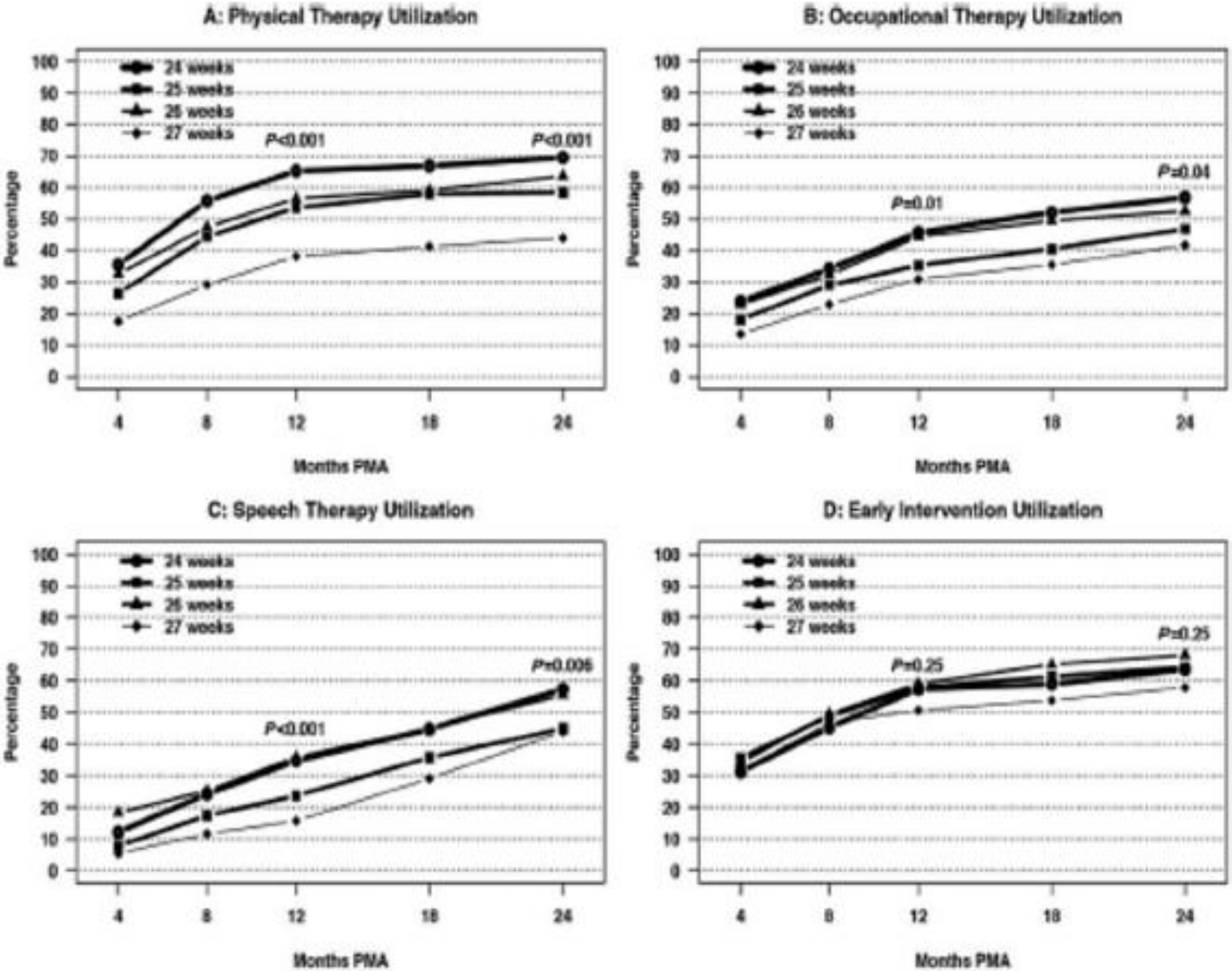
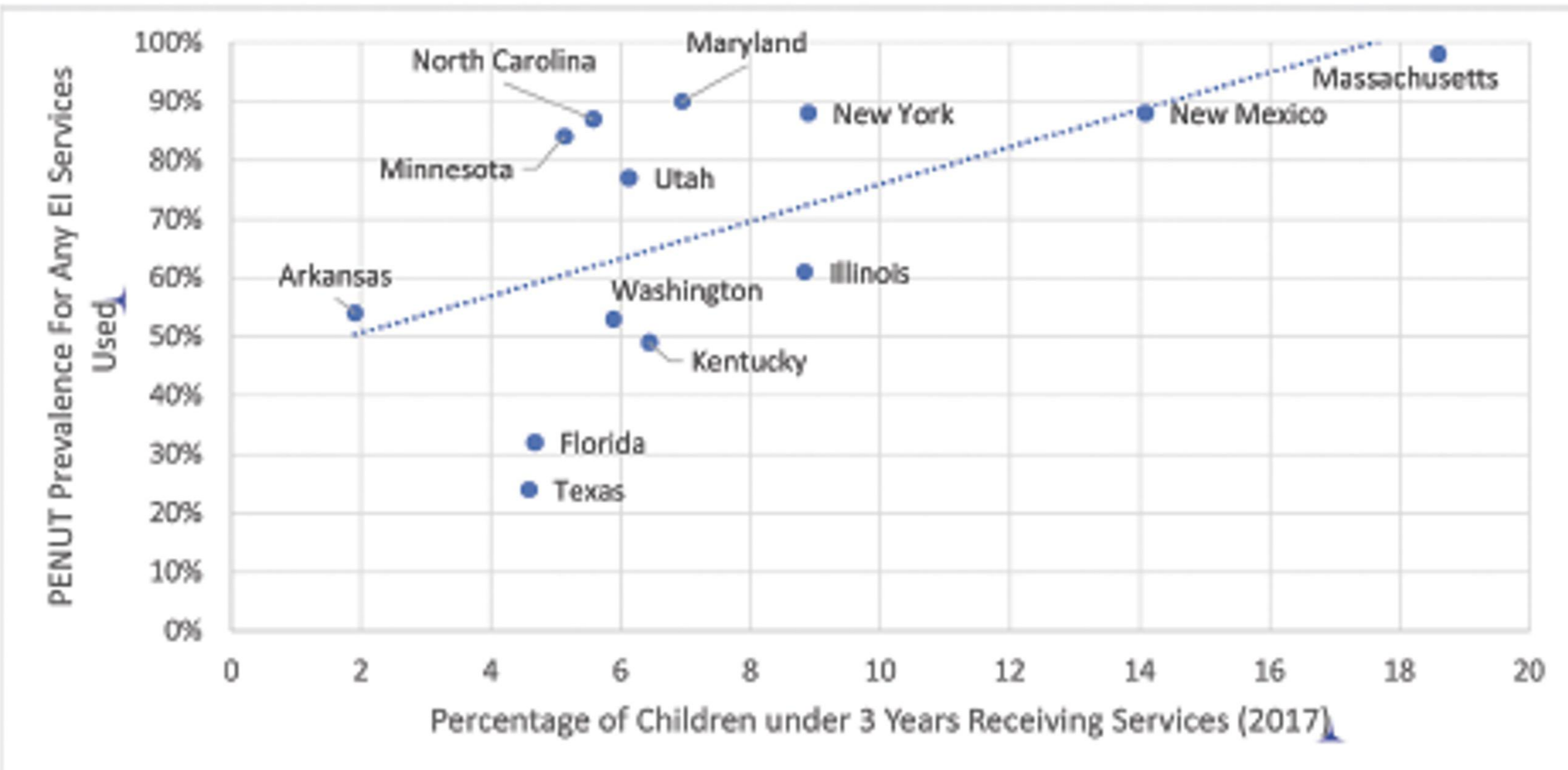


Fig. 3 For all therapy interventions, infants born at 27 weeks gestation utilized services less frequently than more immature infants. p-Values represent a test of global differences across gestational age weeks in the cumulative rate of service utilization through 12 and 24 months, respectively, after the adjustment for treatment with Epo and birth weight Z-score.

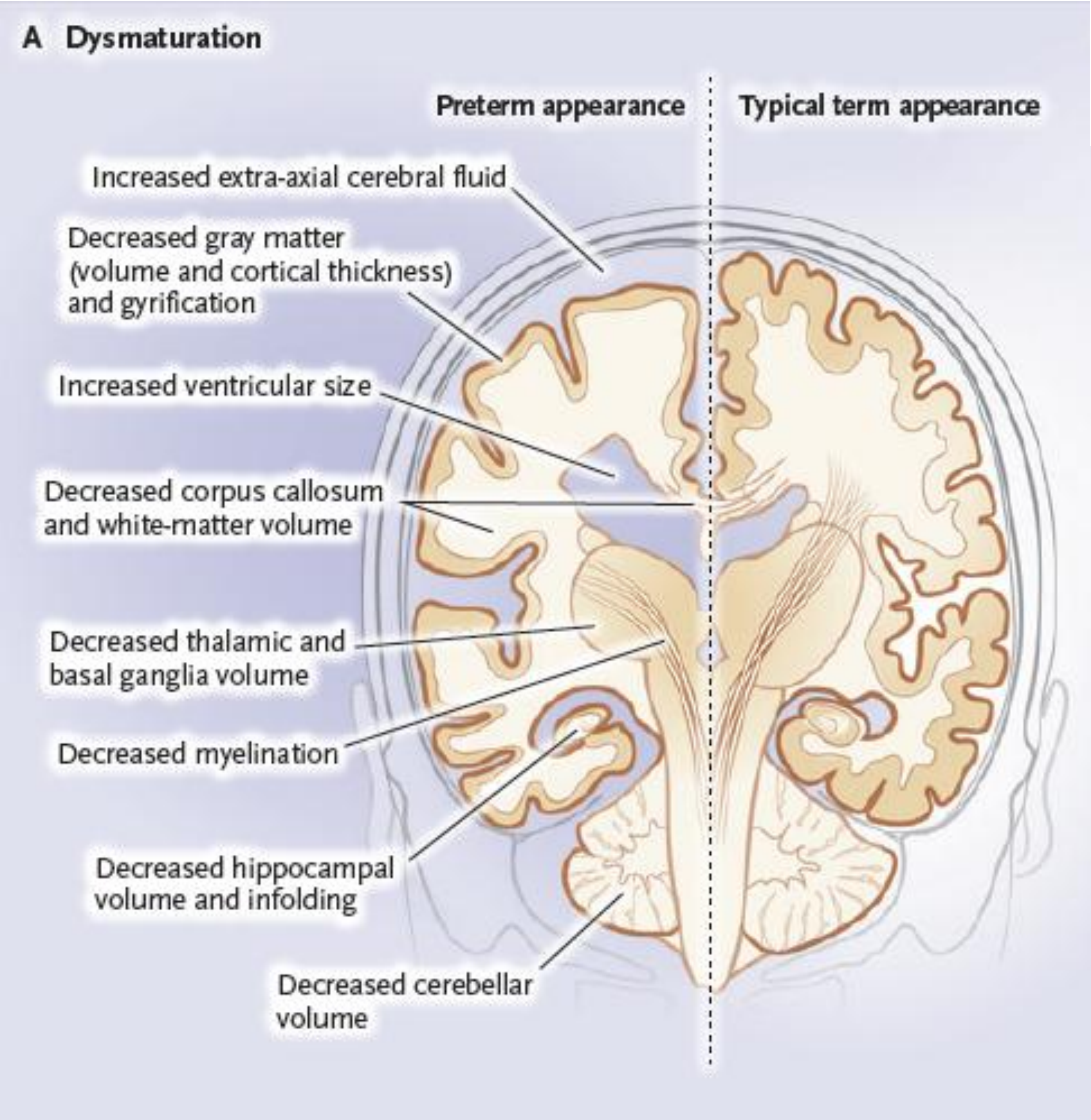
Early intervention services vary

Am J Perinatol 2024;41:458–469.



What else is happening to the brain of the preterm infant - alterations in brain growth and brain development?

Brain Dysmaturation in Prematurity



Defining the Neurologic Consequences of Preterm Birth

Terrie E. Inder, M.B., Ch.B., M.D., Joseph J. Volpe, M.D., and Peter J. Anderson, Ph.D.

N Engl J Med 2023;389:441-53.
DOI: 10.1056/NEJMra2303347

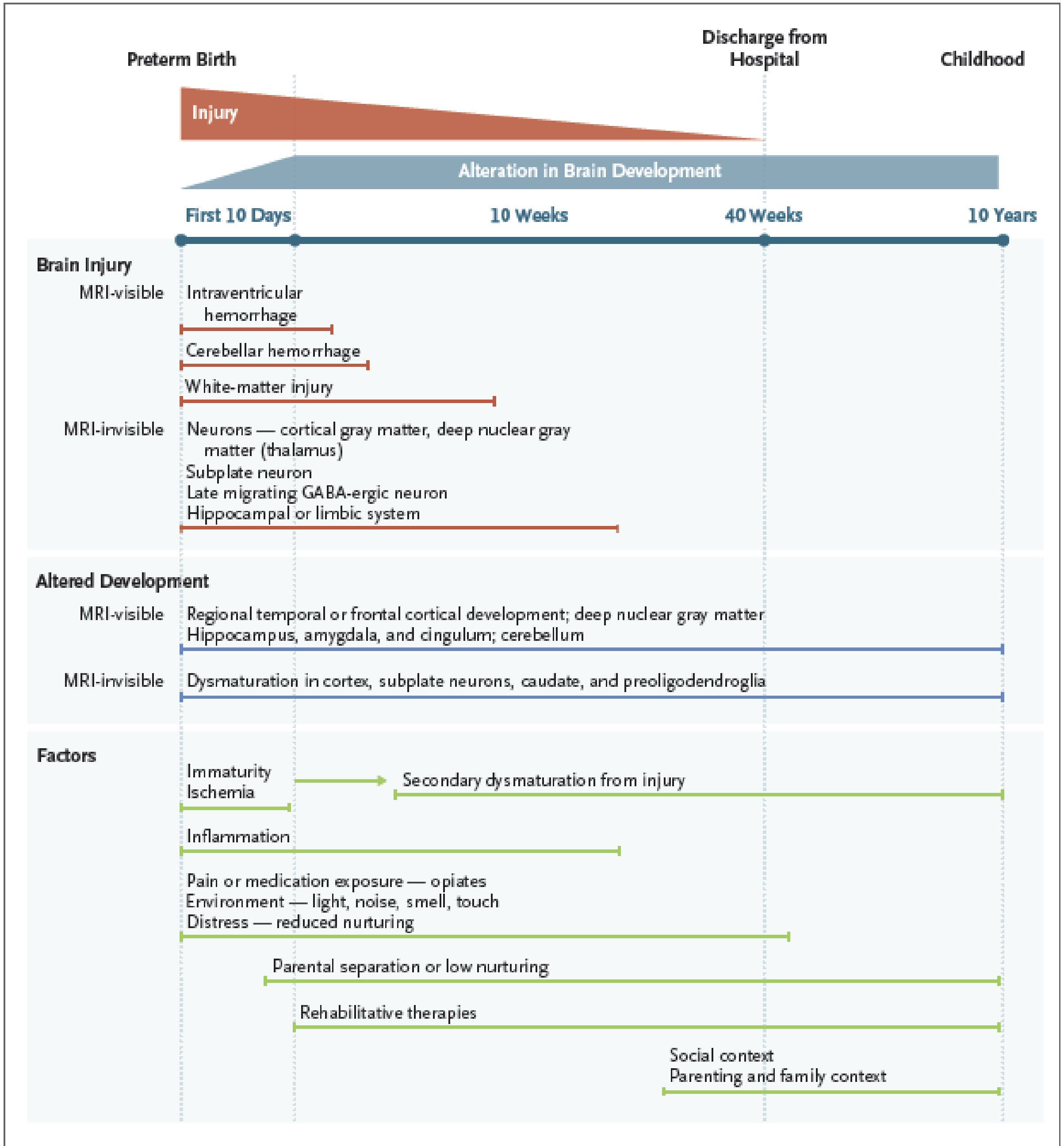


Figure 1. Timeline of Vulnerability or Exposure and Neurologic Consequences of Preterm Birth.
Shown are the key timing, patterns, and factors determining the neurologic consequences of preterm birth. GABA denotes γ-aminobutyric acid, and MRI magnetic resonance imaging.

Defining the Neurologic Consequences of Preterm Birth

Terrie E. Inder, M.B., Ch.B., M.D., Joseph J. Volpe, M.D., and Peter J. Anderson, Ph.D.

N Engl J Med 2023;389:441-53.
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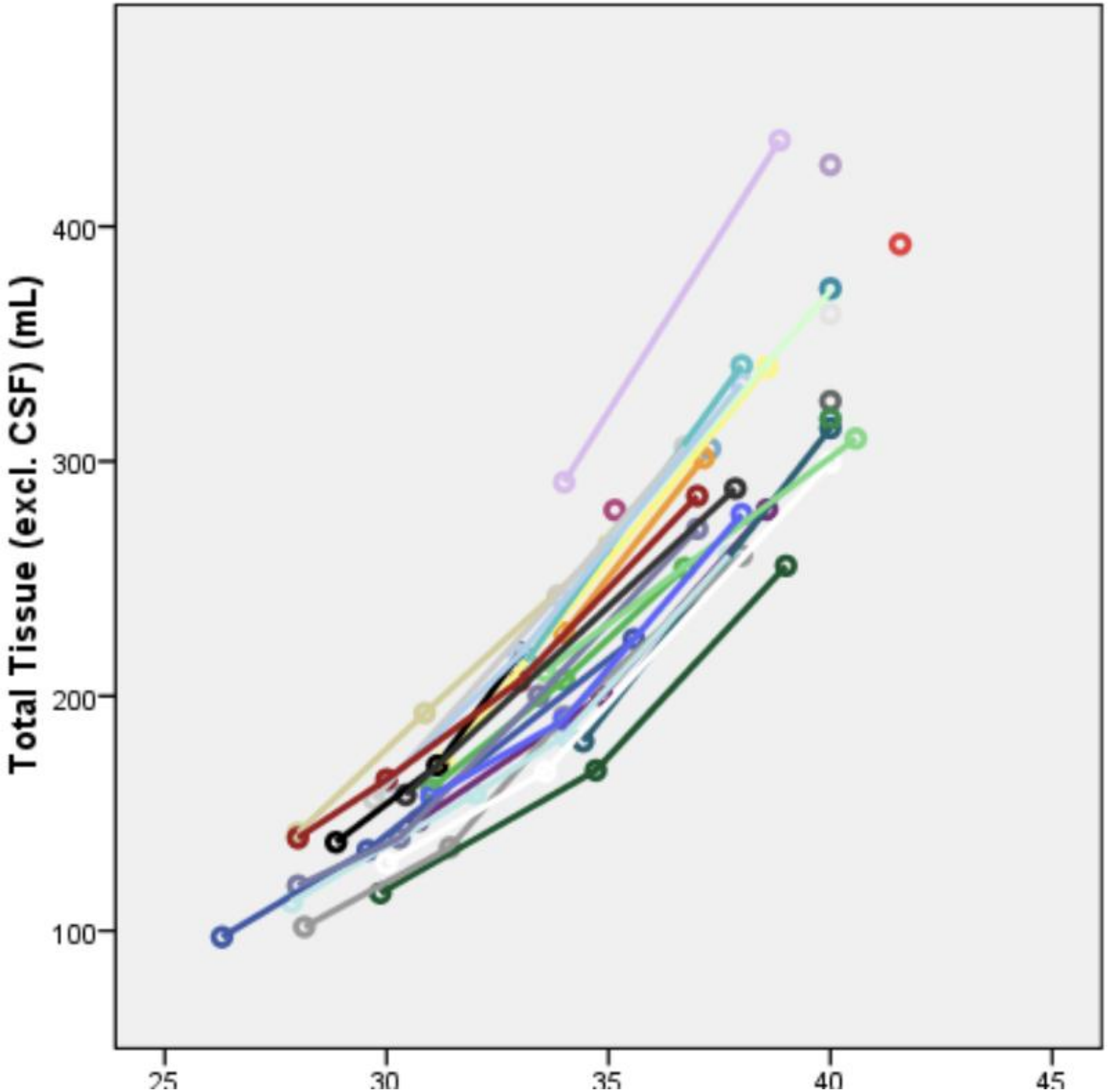


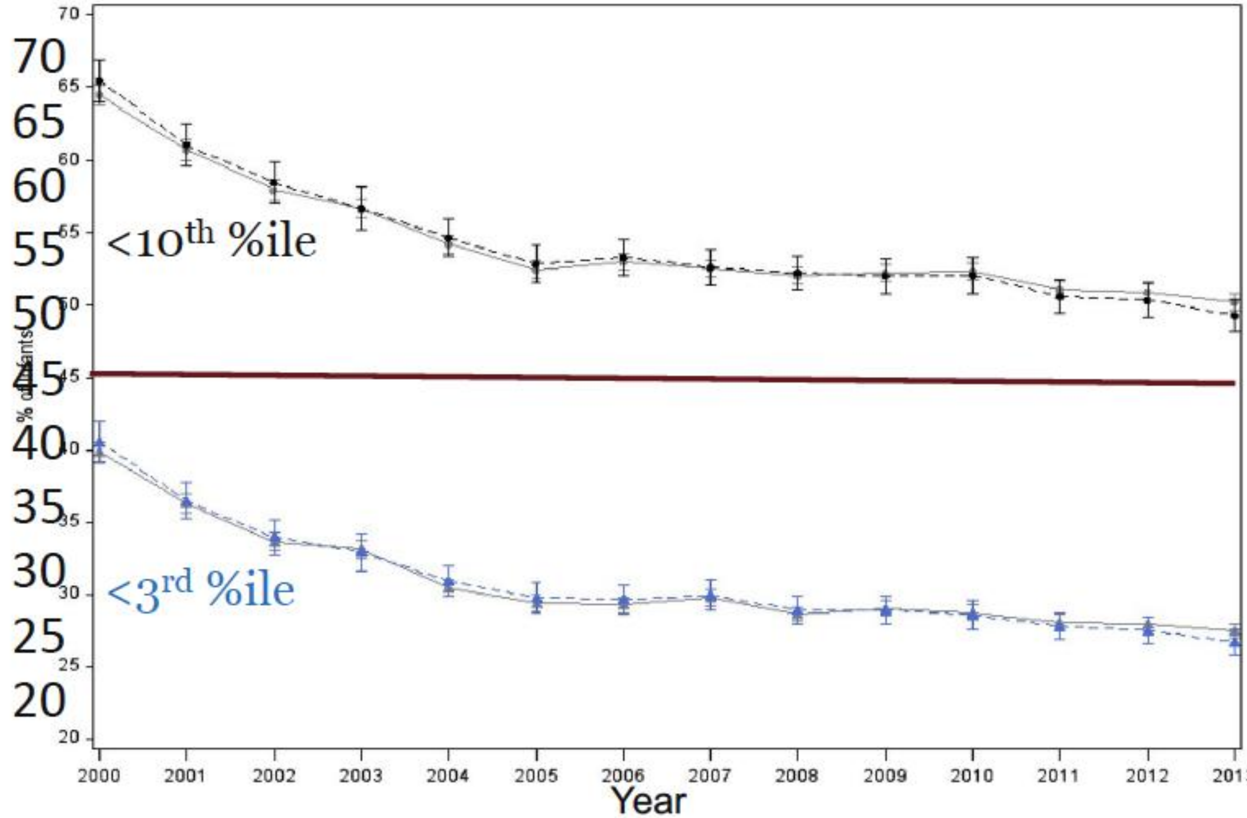
Mathews et al
Pediatr Res. 2018;
83(5):976-981

Inadequate Nutrition is Common

- EUGR – reflects overall inadequate energy intake to meet metabolic demand

Horbar, 2015

% of Infants with EUGR



Summary: Effects of Macronutrient Intake

Macronutrient	Time Period	Brain Size/Growth	Brain Maturation
Energy, Fat			
- Total	DOL 0-14	↑ *growth* of total brain, BG, cerebellum	↑ global maturation/injury score, ↑ white matter maturation
- Enteral	DOL 0-28	↑ cerebellum, BG/thalami	↑ FA in PLIC (w.m.)
- Parenteral		?	?
Protein			
- Total	DOL 0-14	↑ total brain	*no effect*
- Enteral	DOL 0-28	↑ total brain, cerebellum, BG/thalami	↑ white matter maturation
- Parenteral		?	?

*BG = basal ganglia; FA = fractional anisotropy

Tan 2008, Strommen 2015, Schneider, 2018, Beauport 2017, Coviello, 2018

Article

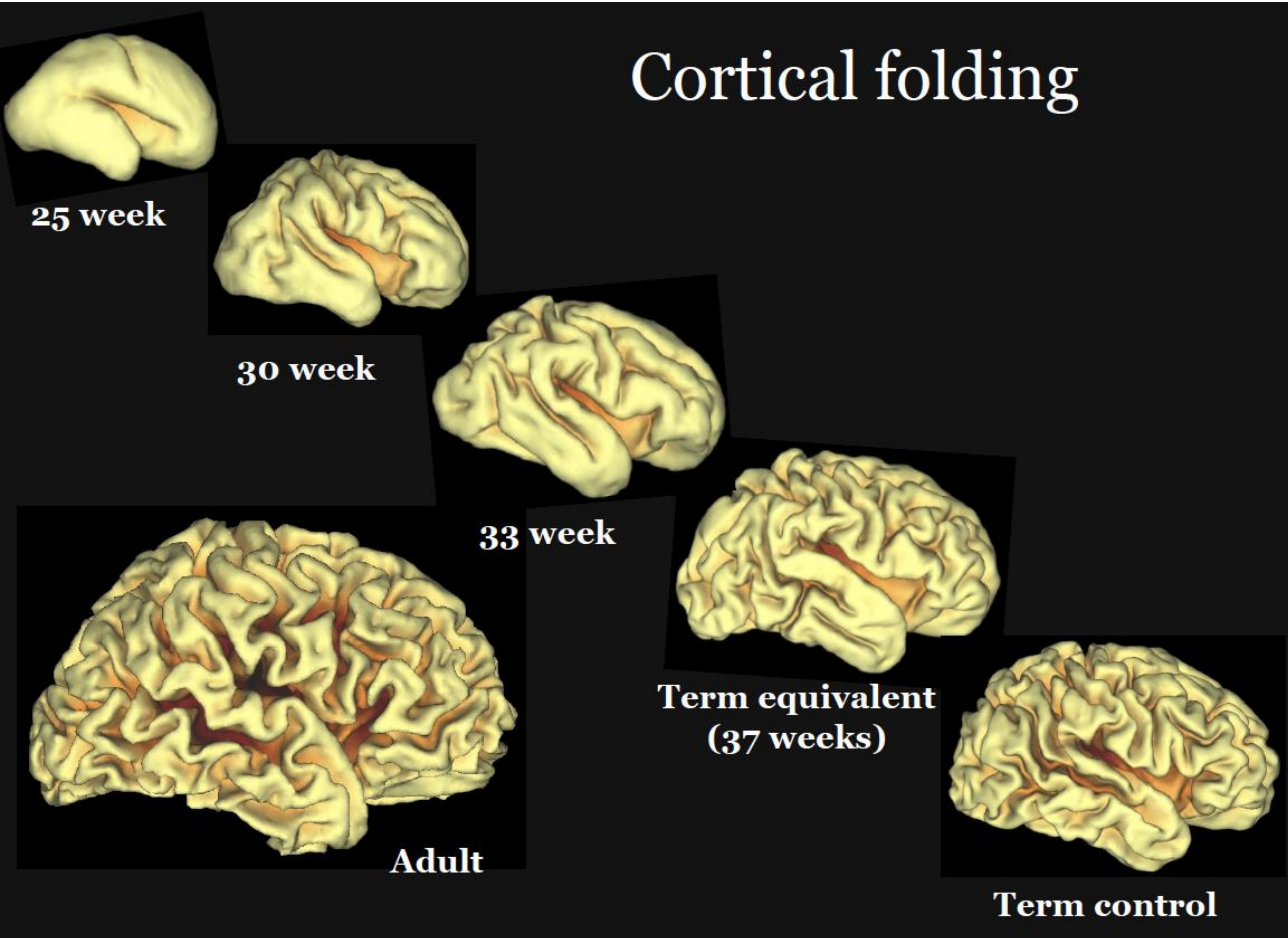
Associations of Macronutrient Intake Determined by Point-of-Care Human Milk Analysis with Brain Development among very Preterm Infants

Children **2022**, *9*, 969. https://doi.org/10.3390/children9070969

- 104 very low birthweight infants (mean GA 28 weeks)
- Human milk analysis of maternal milk (1775 samples - 38/infant)
- Association of greater protein intake (2g/kg/day mother milk vs 1.1 g/kg/day) with larger brain volumes

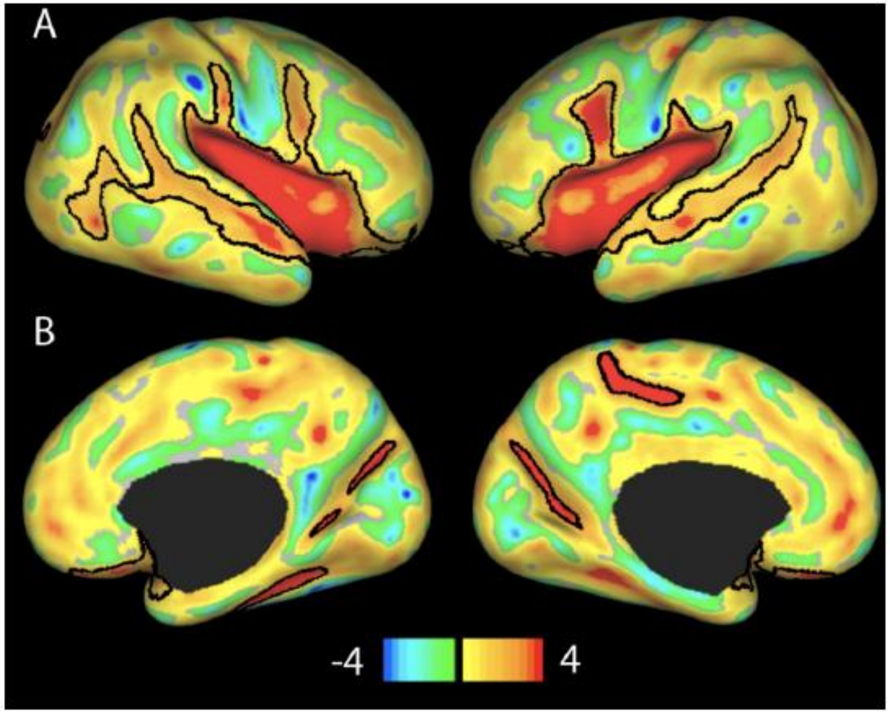
	Estimated Additional Brain Volume in cc (95% CI) for Infants in Top Quintile (>80th Percentile) versus All Other Quintiles (≤80th Percentile) of Macronutrient Intake.					
	Total Brain Volume	Cortical Gray Matter	Deep Gray Matter	White Matter	Hippocampus	Cerebellum
Protein	36.0 * (7.1, 64.8) $p = 0.02$	22.2 * (6.7, 37.8) $p = 0.006$	1.5 * (0.1, 2.9) $p = 0.04$	18.8 (−10.0, 47.6) $p = 0.19$	0.4 (−0.4, 1.1) $p = 0.30$	−1.1 (−3.6, 1.4) $p = 0.37$
Fat	11.7 (−27.6, 51.0) $p = 0.55$	0.6 (−19.3, 20.6) $p = 0.95$	0.2 (−1.8, 2.2) $p = 0.85$	14.1 (−3.4, 31.6) $p = 0.11$	0.2 (−0.6, 1.1) $p = 0.60$	−1.4 (−3.1, 0.2) $p = 0.08$
Carbohydrate	18.7 (−12.0, 49.5) $p = 0.23$	19.9 (−0.8, 33.3) $p = 0.06$	1.6 (−0.1, 3.2) $p = 0.06$	14.6 (−6.8, 36.1) $p = 0.17$	0.4 (−1.0, 1.7) $p = 0.52$	0.9 (−2.8, 4.6) $p = 0.62$
Energy	30.9 * (5.5, 56.4) $p = 0.02$	15.3 * (0.8, 29.9) $p = 0.04$	1.0 (−1.0, 3.0) $p = 0.32$	22.9 * (12.2, 33.4) $p < 0.001$	−0.1 (−1.1, 0.8) $p = 0.81$	−1.0 (−3.4, 1.5) $p = 0.42$

Cortical folding



Comparison of sulcal depth maps

39 weeks

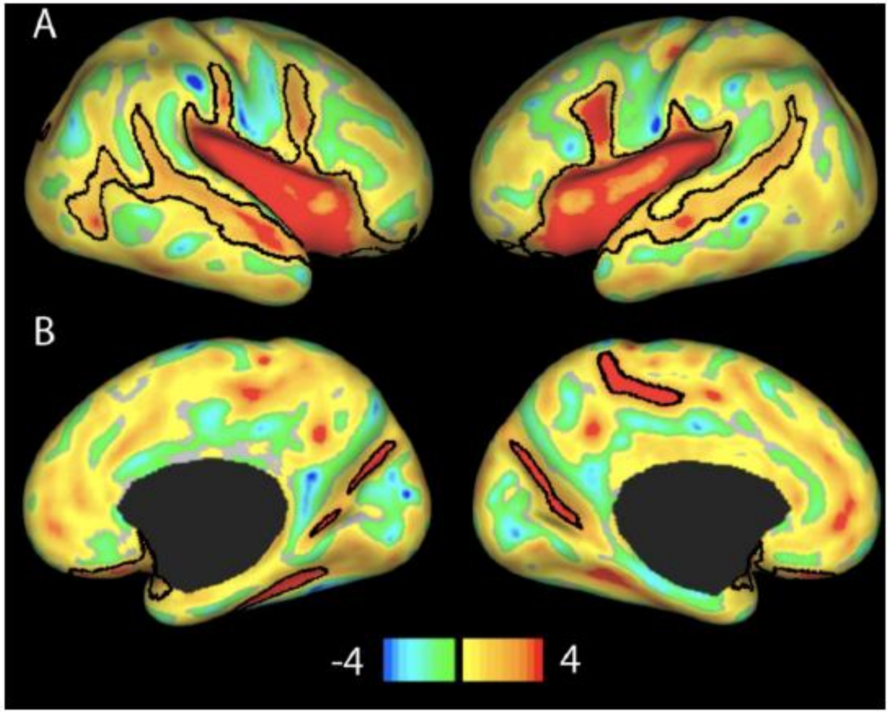


Deeper Sulci in VPT   Deeper Sulci in TC

Zhang, Neil, Inder, van Essen
Neuroimage. 2015 Apr 1;109:469-79

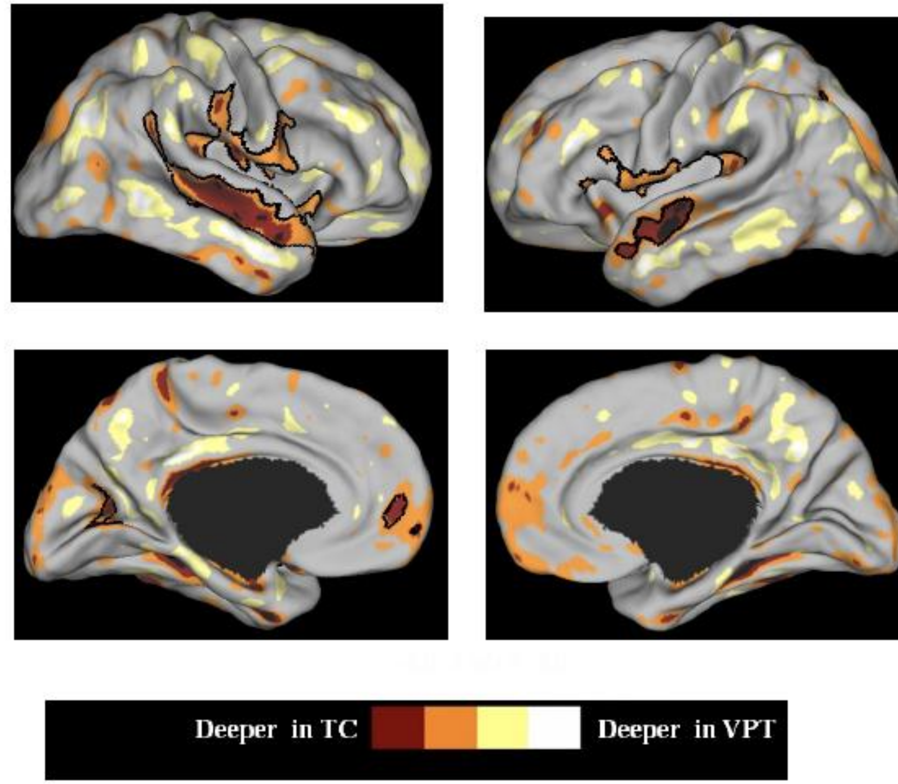
Comparison of sulcal depth maps

39 weeks



Deeper Sulci in VPT Deeper Sulci in TC

7 years



Zhang, Neil, Inder, van Essen
Neuroimage. 2015 Apr 1;109:469-79

They don't catch up - implications for aging

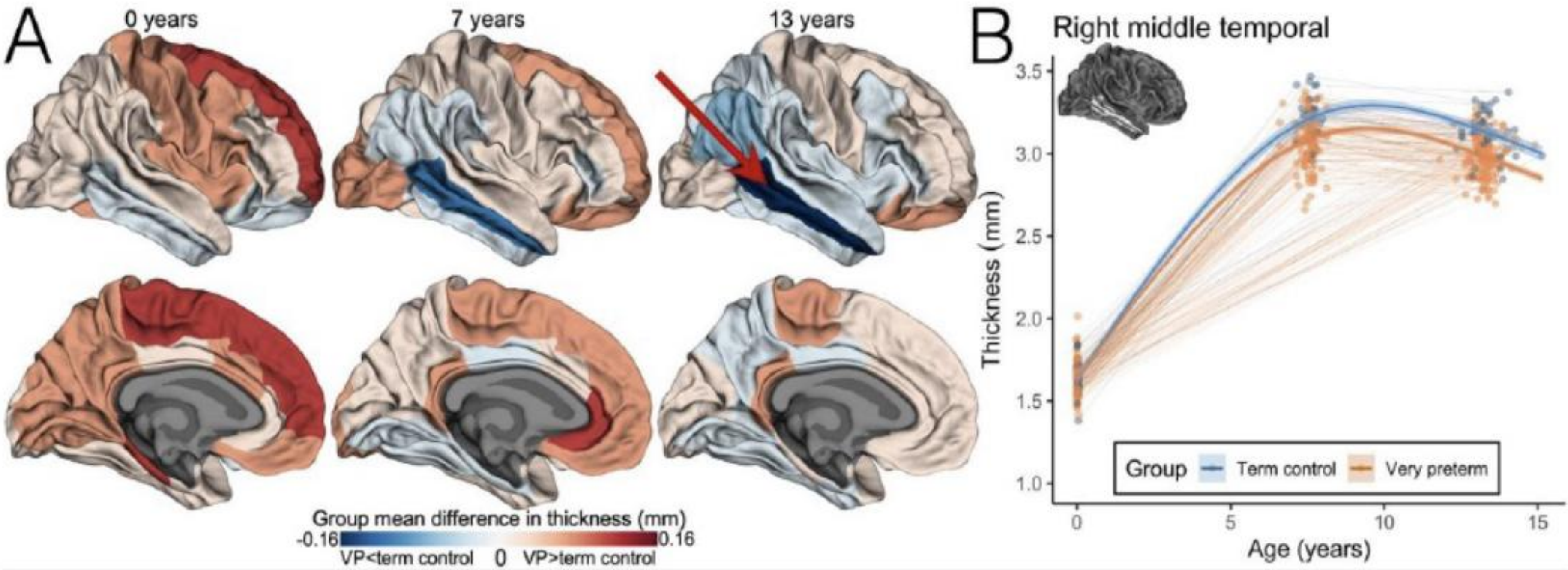


Fig 3. Cortical development at 0, 7 and 13 years in the VIBeS cohort. A. Cross-sectional differences in cortical thickness between the VP and term group. Greater reductions in cortical thickness at 13 years are seen prominently in the lateral temporal region (arrow). B. Developmental trajectory of cortical thickness of the right middle temporal region for the VP and term groups demonstrating the widening of the thickness difference over childhood although the pattern of reductions remains similar.

WHAT FACTORS ARE MEDIATING THE ALTERATIONS IN BRAIN DEVELOPMENT?

EXPERIENCE
STRESS

Pain and Neonatal Stress

Average daily Neonatal Infant Stressor Scale score	
First 14 days (mean ± SD)	**106 ± 13**
First 28 days (mean ± SD)	**102 ± 18**
Admission until term equivalent/discharge (mean ± SD)	**80 ± 12**
Average daily number of procedures	
First 14 days (mean ± SD)	**11 ± 4**
First 28 days (mean ± SD)	**10 ± 5**
Admission until term equivalent/discharge (mean ± SD)	**7 ± 3**

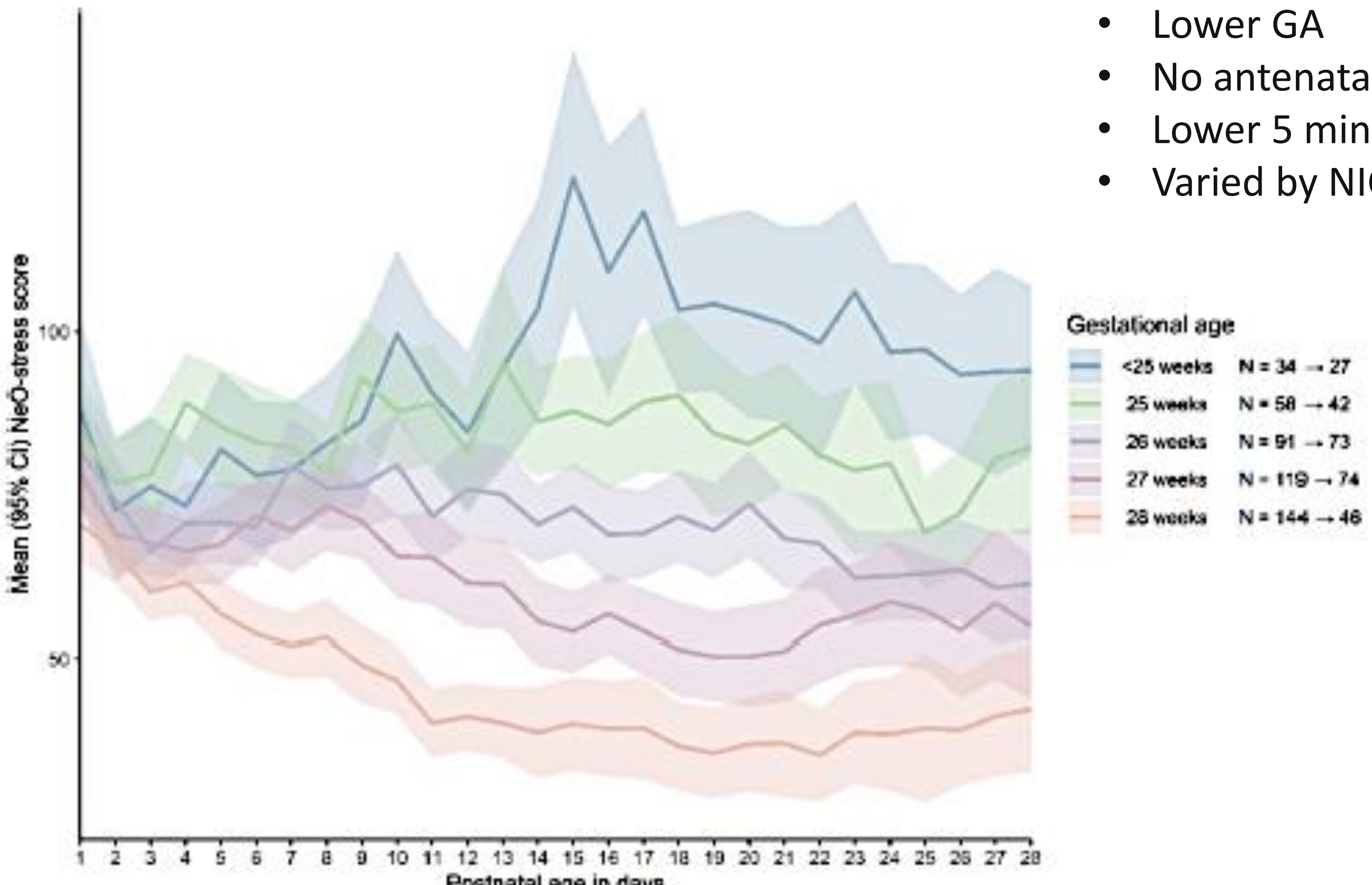
Increased stress associated with decreased frontal lobe width,
Abnormal temporal lobe diffusion and neural networks (after adjusting
for confounders of immaturity, length of ventilation, CRIB score, sepsis +).

Smith G. et al Annals of Neurology 2011

Exposure to clinical stressors during NICU admission in preterm infants

European Journal of Pediatrics (2025) 184:196
https://doi.org/10.1007/s00431-025-06018-7

Naomi J. Meesters[1] · Gerbrich E. van den Bosch[1] · Maria Luisa Tataranno[2] · Chris H. P. van den Akker[3] · Christ-Jan van Ganzewinkel[4] · Judith A. ten Barge[1] · Frank A. B. A. Schuerman[5] · Henriette van Zanten[6] · Willem P. de Boode[7] · Marlou M. A. Raets[8] · Peter H. Dijk[9] · Joost van Rosmalen[10,11] · Marijn J. Vermeulen[12] · Wes Onland[3,13] · Lotte Haverman[14] · Irwin K. M. Reiss[1] · Anton H. van Kaam[3] · Manon Benders[2] · Monique van Dijk[1] · Sinno H. P. Simons[1] on behalf of the HIPPO study group



- Lower GA
- No antenatal steroids
- Lower 5 min Apgar
- Varied by NICU by 30pt

Review

The evolving neurobiology of early-life stress

Matthew T. Birnie[1] and Tallie Z. Baram[1,2,3,*]
[1]Department of Pediatrics, University of California, Irvine, Irvine, CA, USA
[2]Department of Anatomy/Neurobiology, University of California, Irvine, Irvine, CA, USA
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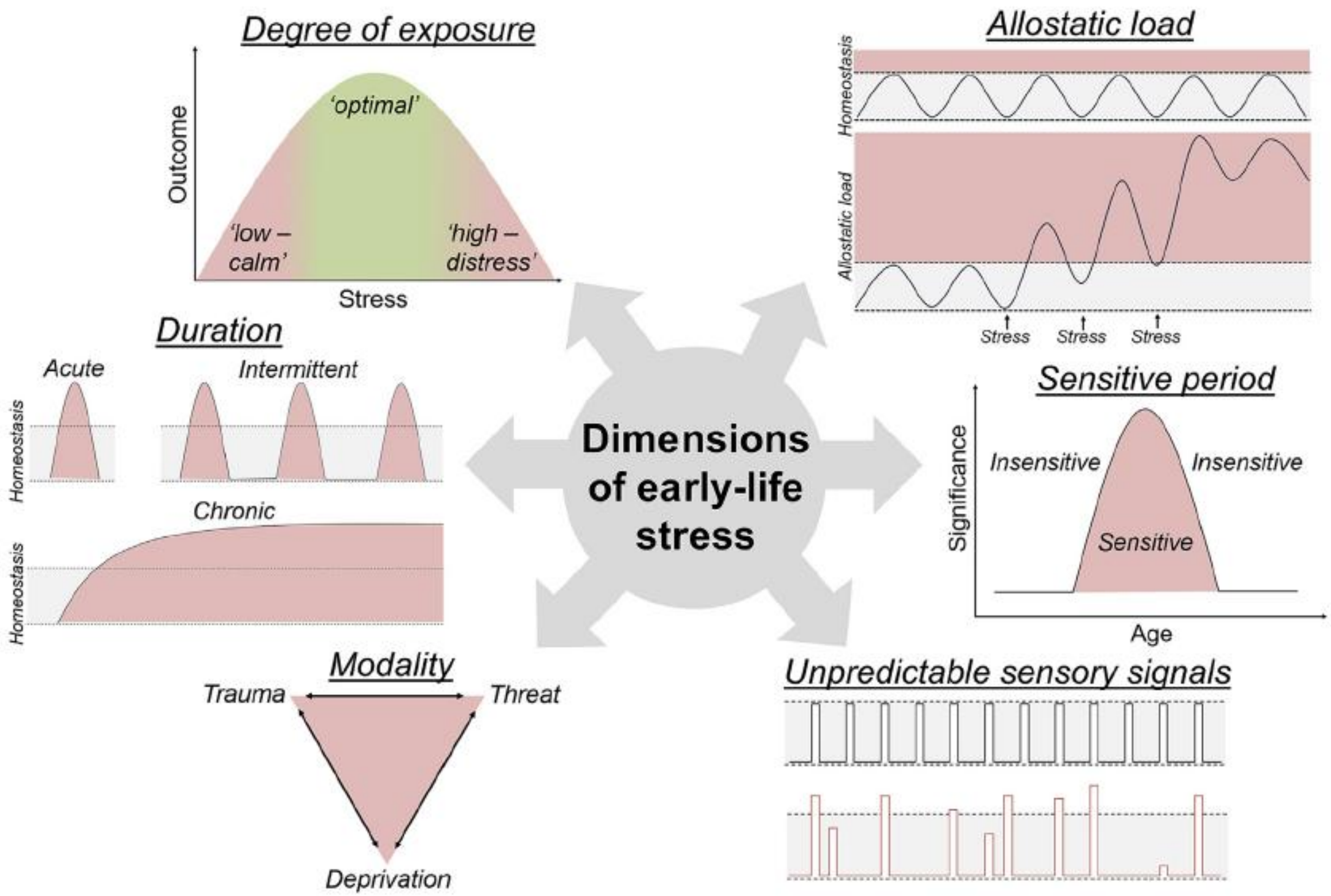
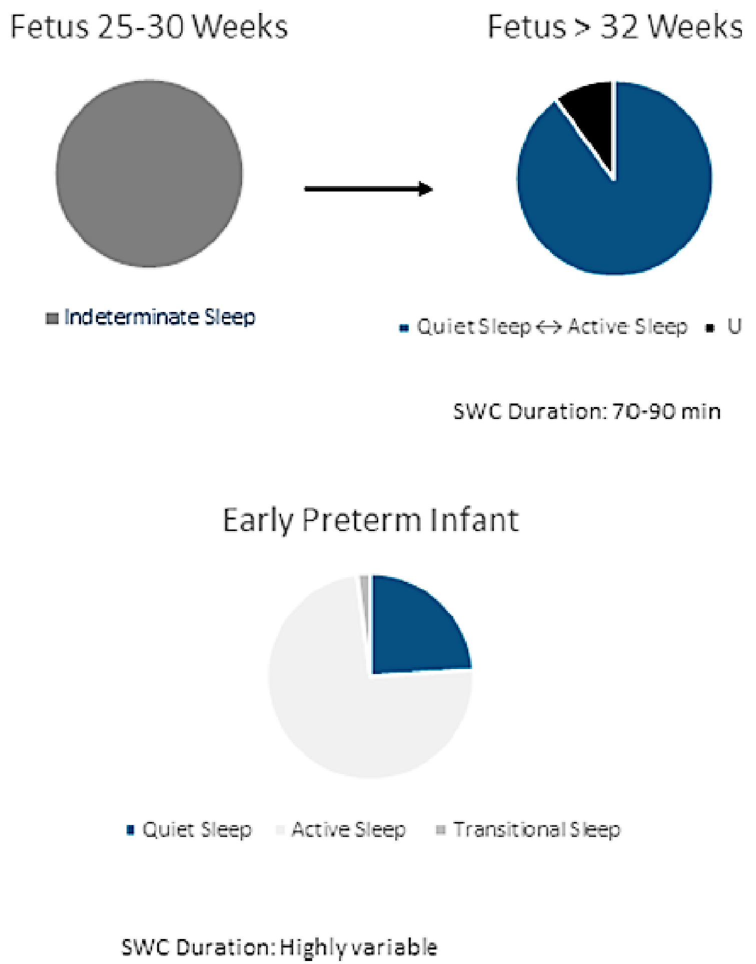
*Correspondence: tallie@uci.edu
https://doi.org/10.1016/j.neuron.2025.02.016



The role of sleep in neonatal neurocritical care and the influence on long-term outcome

Leonie M. Paciello [a], Mirja Quante [b], Hendrik Rosewich [a,c,d,e], Renée A. Shellhaas [f,*]

SEMIN PERINATOL xxx (xxxx) xxx



- Disordered sleep and reduced quiet sleep is associated with adverse cognitive and behavioral outcome
- Marker vs causation is unknown

The Developmental Effects of the NICU Single Patient Room

Study NICU

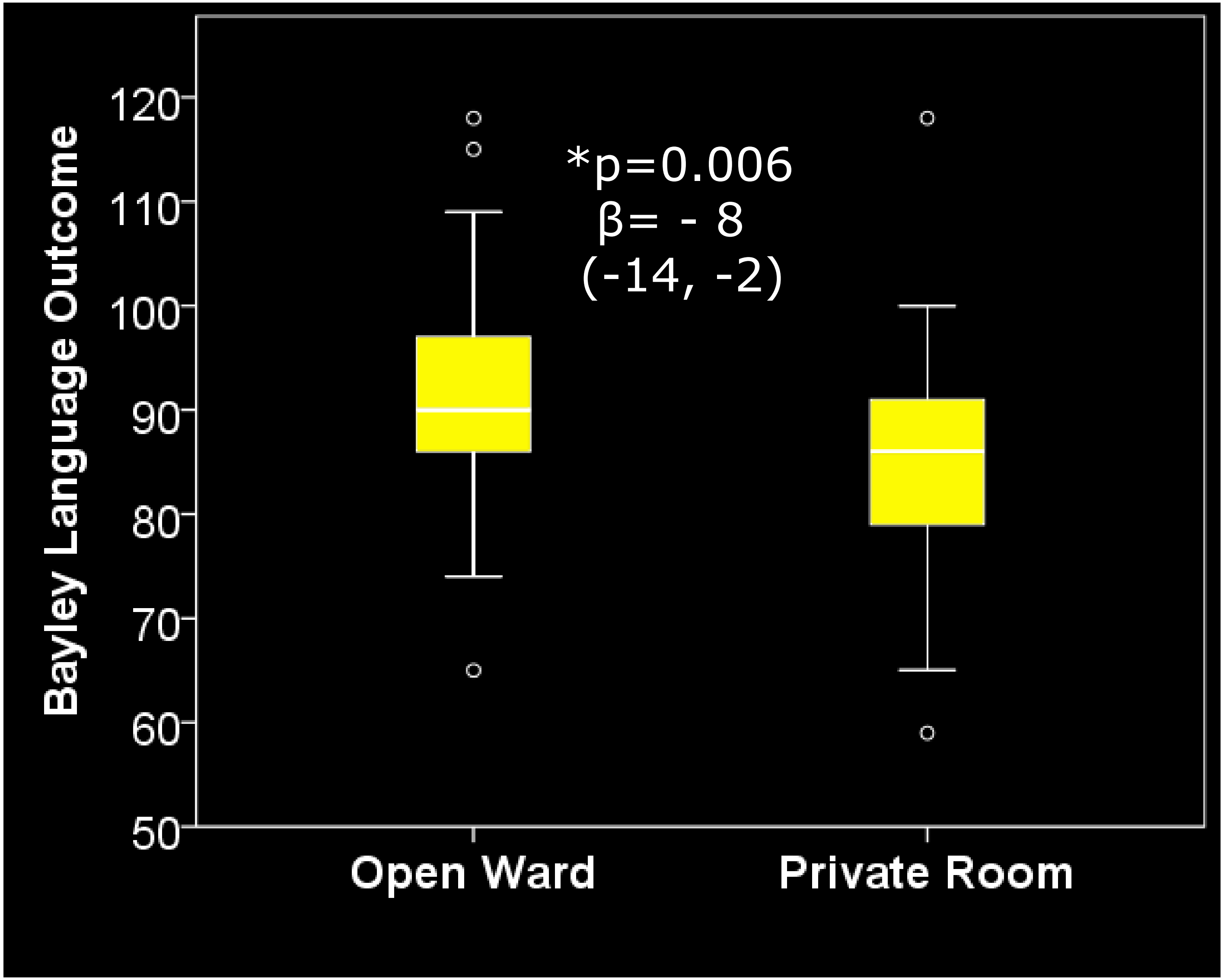
- **½ single patient rooms**
  - 168 square feet
  - 3 walls; 4th wall is a sliding glass door
  - Individualized lighting
  - Parents can visit 24 hours a day
    - Lounger at the bedside for parents to sleep on
- **½ open bay beds**
  - Approx 10-12 beds in 1100 square feet of space
  - General lighting
  - Screens can be pulled to bedside for privacy
  - Parents can visit 24 hours a day
    - Sleep rooms available just outside the NICU

Follow up at age 2 years

- 86 infants (83%) returned for developmental follow-up
  - Mean (SD): 27.4 (2.1) months
- Associations between room type and cognitive, language and motor outcome were explored, while controlling for:
  - CRIB score
  - Cerebral injury
  - Social risk score
  - Family functioning

Alterations in brain structure and neurodevelopmental outcome in preterm infants hospitalized in different neonatal intensive care unit environments.
Pineda RG, et al J Pediatr. 2014 Jan;164(1):52-60.e2.

Language outcome

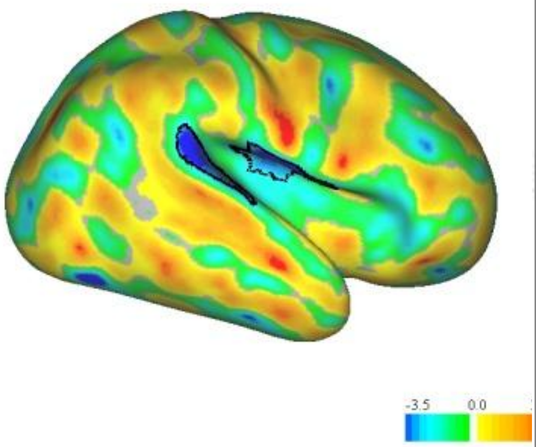


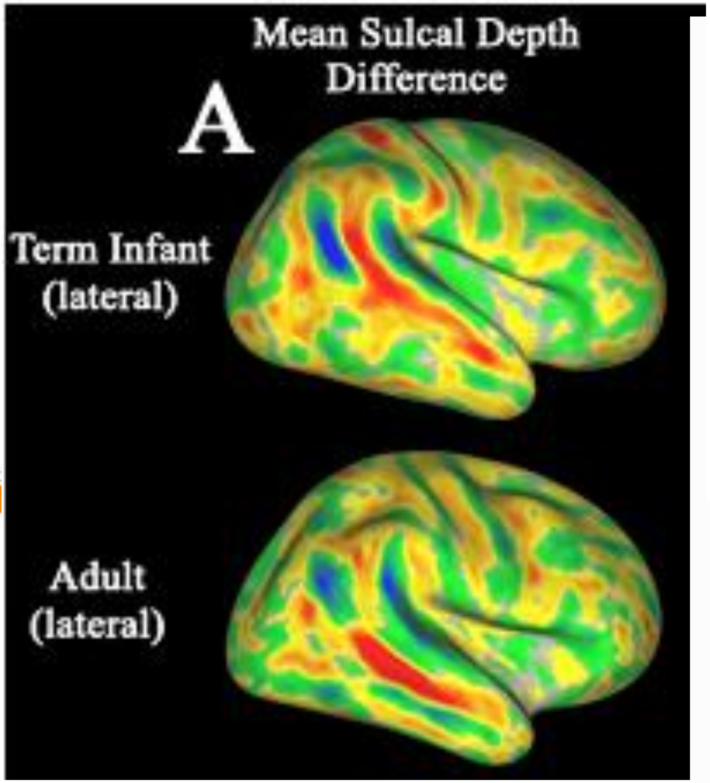
*Linear regression; controlling CRIB, cerebral injury, social risk and family functioning

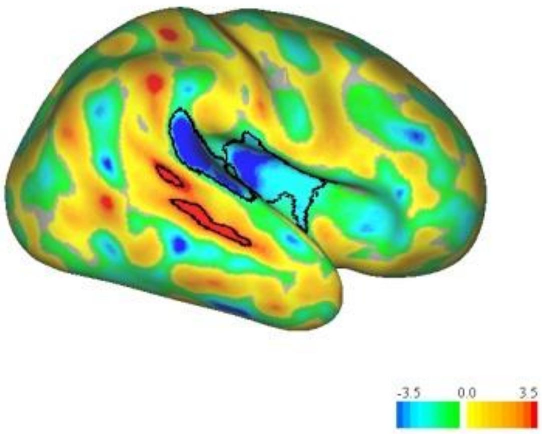
Hemispheric Asymmetries

Single Patient Room

Open Bay

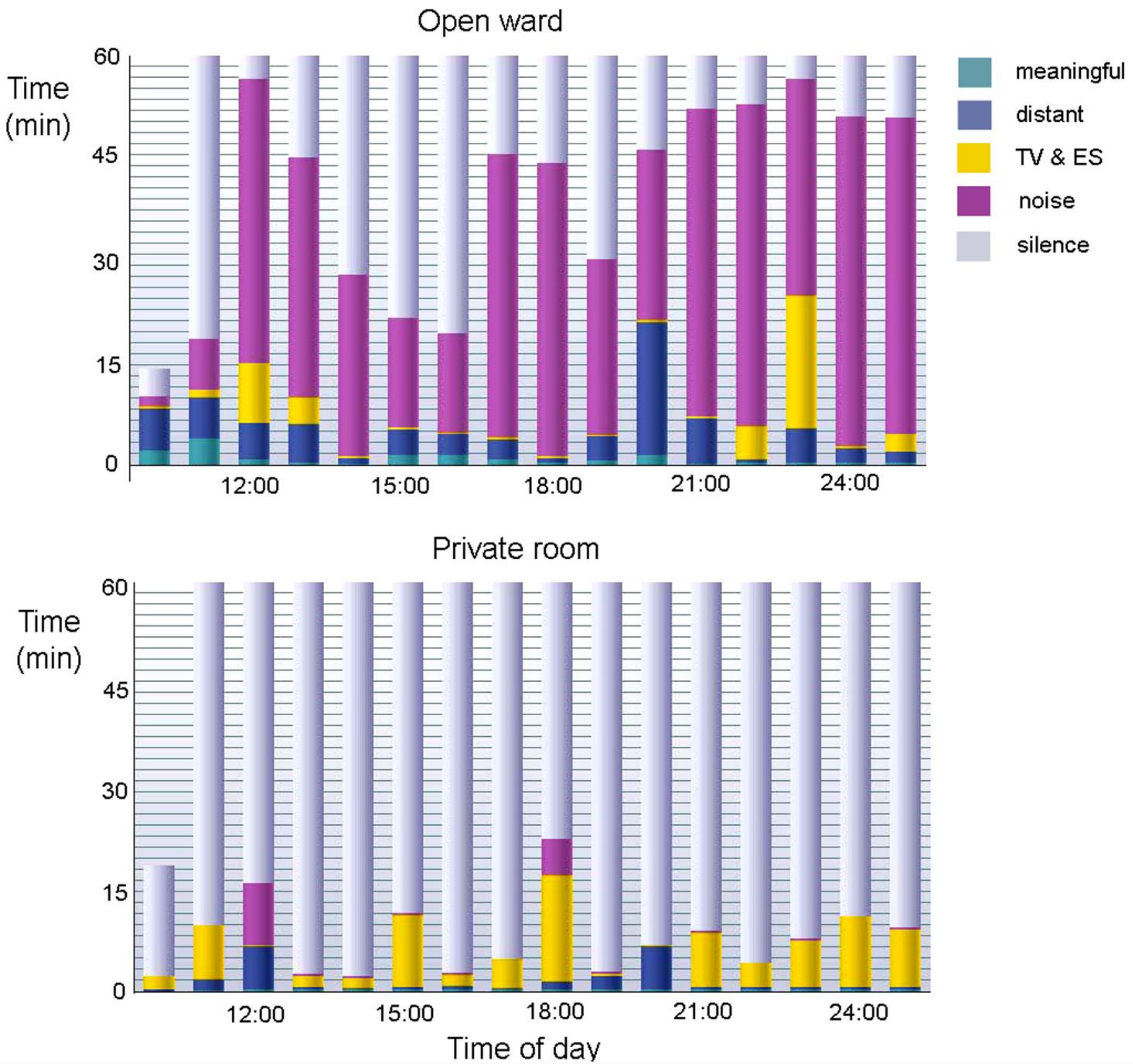






Auditory

- 24 weeks GA - all major elements of cochlea present
- 25 weeks GA - systematic response to auditory input
- 26-30 weeks GA - hair cells present responding to low frequencies and transmit to the brainstem
- 30 weeks GA - auditory system is mature enough to detect complex sounds and distinguish between different speech phonemes to begin language and speech development
- By 35 weeks GA, auditory processing facilitates learning and memory formation
- Implications for NICU:
  - Negative Auditory exposure – Alarms, Mechanical noise
  - Lack of Positive Auditory exposure – Incubator, Human voice


Open ward
Time (min)
60
45
30
15
0
12:00
15:00
18:00
21:00
24:00
meaningful
distant
TV & ES
noise
silence
Private room
Time (min)
60
45
30
15
0
12:00
15:00
18:00
21:00
24:00
Time of day

Auditory Exposure in the Neonatal Intensive Care Unit: Room Type and Other Predictors

Roberta Pineda, PhD, OTR/L[1,2], Polly Durant, MSOT[1], Amit Mathur, MD[2], Terrie Inder, MD[3], Michael Wallendorf, PhD[4], and Bradley L. Schlaggar, MD, PhD[2,5,6,7,8]

(J Pediatr 2017;183:56-66).

Table II. Characteristics of the sound environment by room type

	Room type	Mean (h:min) ± SD	Difference between rooms (h:min) or decibels or number of words
Amount of time spent with meaningful language (in a 16-h period)			
Birth (n = 52)	Private room	0:08 ± 0:09	0:02
	Open ward	0:06 ± 0:07	
30 wk (n = 50)	Private room	0:06 ± 0:05	0
	Open ward	0:06 ± 0:05	
34 wk (n = 48)	Private room	0:17 ± 0:19	0:01
	Open ward	0:16 ± 0:21	
Term (n = 44)	Private room	0:35 ± 0:25	0:04
	Open ward	0:31 ± 0:23	
Amount of time spent with distant language (in a 16-h period)			
Birth (n = 52)	Private room	1:44 ± 1:27	0:17
	Open ward	1:27 ± 1:31	
30 wk (n = 50)	Private room	0:36 ± 0:29	−0:56
	Open ward	1:32 ± 1:27	
34 wk (n = 48)	Private room	0:57 ± 0:46	−0:14
	Open ward	1:11 ± 0:45	
Term (n = 44)	Private room	0:35 ± 0:57	−0:39
	Open ward	1:14 ± 0:49	
Amount of time spent with electronic sounds (in a 16-h period)			
Birth (n = 52)	Private room	0:57 ± 1:11	0:01
	Open ward	0:56 ± 1:36	
30 wk (n = 50)	Private room	0:50 ± 0:58	−1:07
	Open ward	1:57 ± 2:01	
34 wk (n = 48)	Private room	1:25 ± 1:33	−1:59
	Open ward	3:24 ± 4:23	
Term (n = 44)	Private room	2:31 ± 2:10	−2:50
	Open ward	5:19 ± 3:16	

THE JOURNAL OF PEDIATRICS • www.jpeds.com

ORIGINAL ARTICLES

Language Exposure for Preterm Infants is Reduced Relative to Fetuses

Brian B. Monson, PhD[1,2,3,4], Sophie E. Ambrose, PhD[5], Carey Gaede, MSN[4], and Derrick Rollo, DO[4]

. (J Pediatr 2023;262:113344).

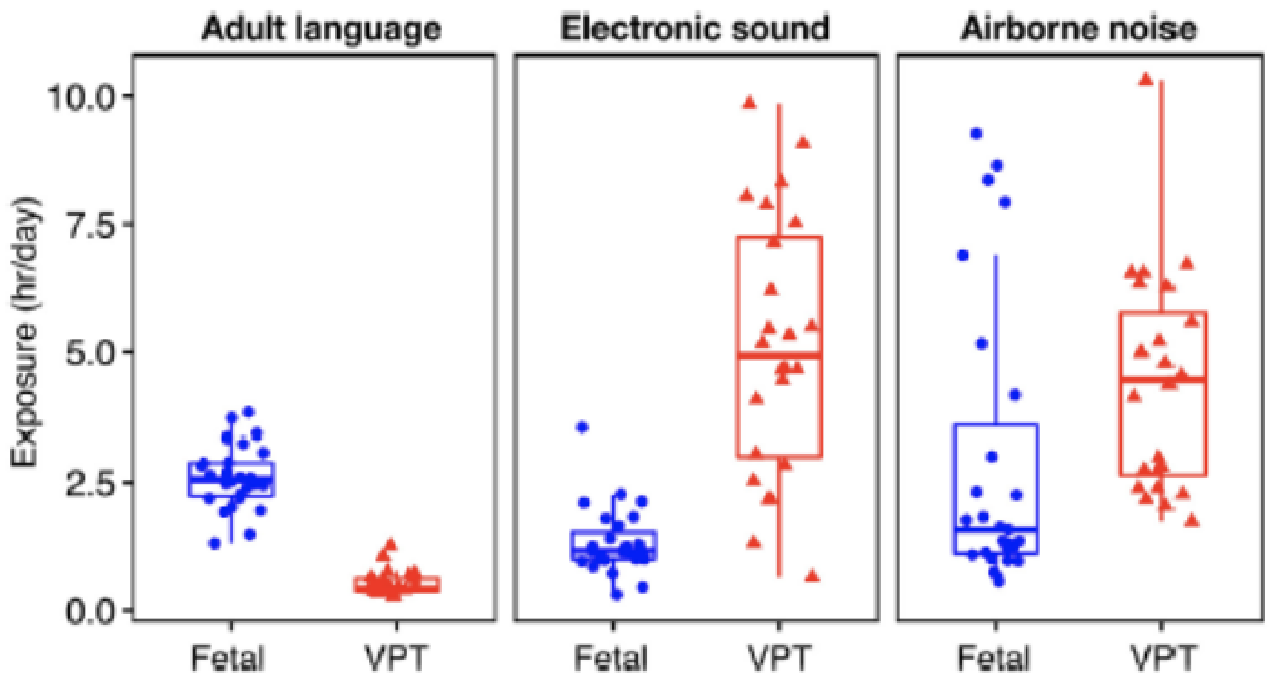
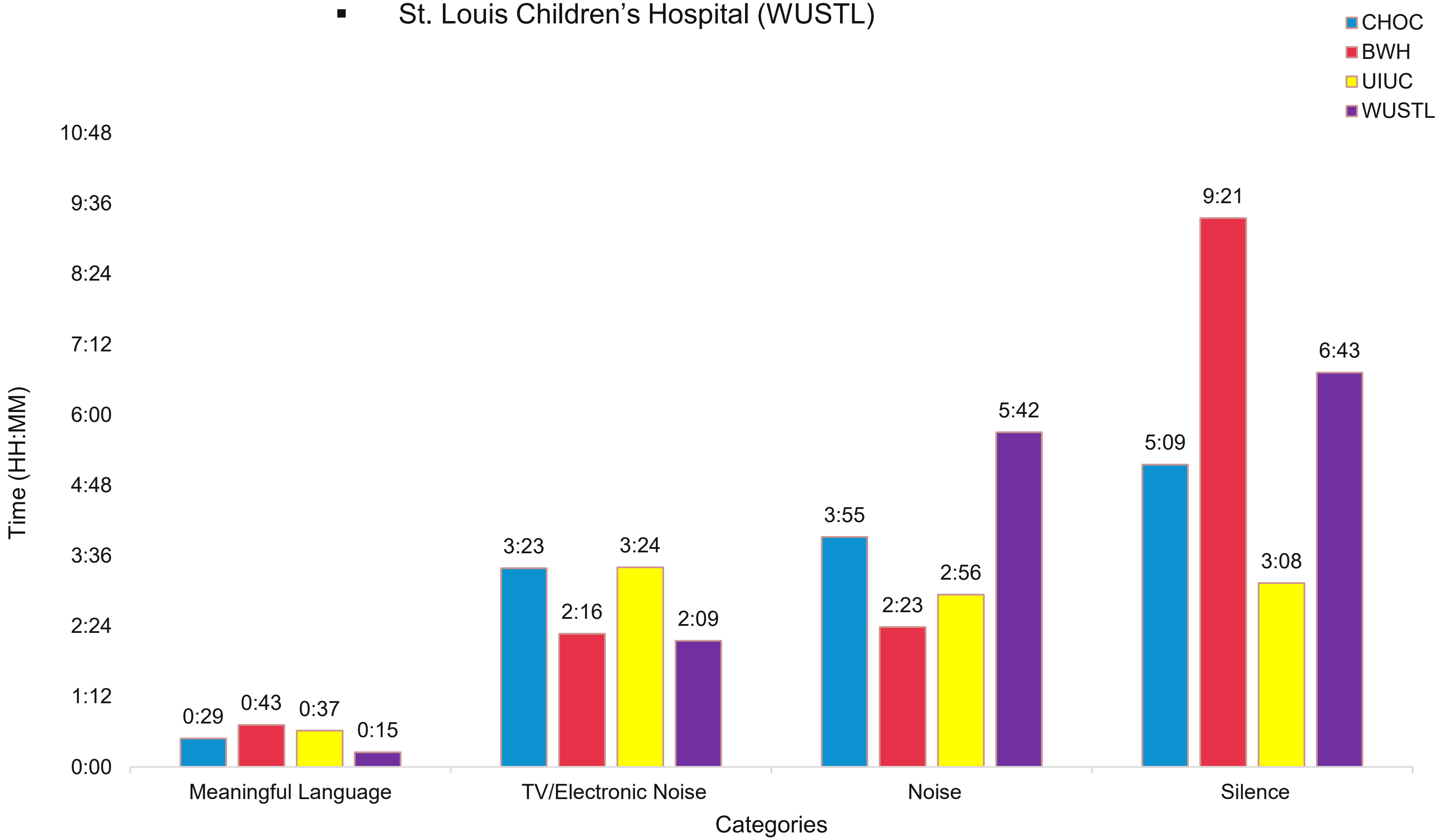


Figure 1. Daily auditory exposures for fetuses (*blue*) and VPT infants (*red*). Values for fetuses represent extrauterine exposures. Each data point represents a daily average for 1 participant. Some pregnant women reported using noise machines to sleep at night, which contributed to the high noise exposure for some fetuses.

Auditory Exposure in the NICU

- Brigham and Women's Hospital (BWH)
- Carle Foundation Hospital (UIUC)
- St. Louis Children's Hospital (WUSTL)



NICU sensory experiences associated with positive outcomes: an integrative review of evidence from 2015–2020

Roberta Pineda[1,2,3], Polly Kellner[1], Rebecca Guth[4], Audrey Gronemeyer[4] and Joan Smith[5]

Journal of Perinatology (2023) 43:837–848; https://doi.org/10.1038/s41372-023-01655-y

	Postmenstrual age (weeks)																	
	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40
Tactile Interventions																		
**Skin-to-skin/Kangaroo care		2	3	4	5	7	7	9	11	11	11	11	11	10	6	4	3	3
Auditory Interventions																		
**Live/recorded music											2	2	2	2	2	1	1	1
**Voice/human sounds			1	1	1	3	4	4	4	4	4	4	2	1	1	1	1	1
Visual Interventions																		
Darkness								2	2	2	1	1	1					
Red light													1	1	1	1	1	
Cycled light						1	2	3	3	2	2	2	2	1	1	1	1	1
Kinesthetic Interventions																		
Passive range of motion						1	1	2	2	2	1	1						
**Guided movement and position changes												1	1	1				
Gustatory/Olfactory Interventions																		
Maternal scent								2	2	2	1	1	1	1				
Multimodal Interventions																		
**Supporting and Enhancing NICU Sensory Experiences	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
**Fontana multisensory program				1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
**Skin-to-skin care + auditory			1	1	1	1	3	4	4	5	5	5	5	5	4	3	2	2
**Massage (with kinesthetic component)						1	1	4	4	5	5	5	6	5	3	3	3	3
**Massage + olfactory								1	1	1	1	1	1	1	1	1	1	1
**Massage + Premature Infant Oral Motor Intervention										1	1	1	1	1				
**Therapeutic static touch + auditory		2	2	2	2	2	3	3	3	3	3	3	3	3	3	3	3	3
Skin-to-skin + range of motion							1	1	1	1	1	1	1	1	1			
**Audio, Tactile, Visual, Vestibular Intervention (ATVV)										1	1	1	1	1	1	1	1	1

Sensory Support: 32 Weeks*

Here are some things to do with your baby each day this week
(as long as tolerated)

Touch

Give at least 2 hours of positive touch each day by doing one or more of these things:

- Provide a hand hug.
- Do kangaroo care (skin-to-skin) for at least 1 hour.
- Hold your baby in a blanket for 15 minutes at a time, or longer if your baby's temperature remains stable.
- Do massage for up to 15 minutes.

Hearing

Give at least 1 ½ hours of positive sound each day by doing one or more of these things:

- Read, sing, and/or speak to your baby (can be broken up into 30 minute periods several times per day).
- Play soft music or recorded voice.

*At the sound of a whisper or quiet conversation.

Smell

Provide at least 3 hours per day of parent scent or the smell of breast milk.

Seeing

- Cycle light to your baby with natural light (or lights on, when there is no natural light) during the day and dim light or darkness at night.
- Avoid direct and bright lights.

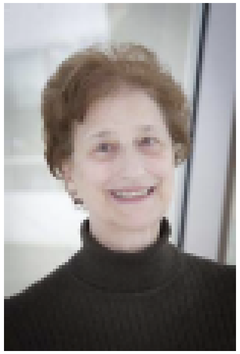
Movement & Body Awareness

- Unwrap your baby and allow stretching and free movement for at least 2 minutes prior to a diaper change at least 3 times per day.
- Allow your baby to experience being in at least 2 different positions for at least 10 minutes each.
- Rock during holding for at least 3 minutes.

Room Type vs Parent presence

The importance of parent presence and involvement in the single-family room and open-bay NICU

It is remarkable how the perception of an optimal environment for preterm infants has evolved since Dr. Julius Hess opened the first premature unit at Sarah Morris Hospital in Chicago in 1914 (1). With the introduction of the incubator and gavage feeding, Dr. Martin Couney first introduced care of the preterm to the public in an exhibit at the 1939 New York Words Fair where visitors paid a fee to view preterm infants in incubators. Wet nurses provided breast milk, and infants were separated from their mothers. In 1960,



Pediatric RESEARCH www.nature.com/pr

COMMENT

Turns out not where but who you're with that really matters

Terrie Eleanor Inder[1]

Pediatric Research (2020) 88:533–534; https://doi.org/10.1038/s41390-020-1040-1

ORIGINAL ARTICLE

Parental presence and holding in the neonatal intensive care unit and associations with early neurobehavior

LC Reynolds[1], MM Duncan[1], GC Smith[2], A Mathur[2], J Neil[2,3,4], T Inder[2,3,4] and RG Pineda[1,2]

Journal of Perinatology (2013) 33, 636–641

www.nature.com/jp

Table 2. Descriptives of independent variables: patterns of visitation and holding

	Minimum	*Maximum*	*Mean*	*s.d.*	*Median*	*Interquartile range*
Hours visited weeks 1–2[a]	0.50	187.50	26.20	29.40	17.00	11.10–28.60
Hours visited weeks 3–4[a]	1.00	141.50	21.26	24.60	13.50	8.40–20.80
Hours visited weeks 5-term[a]	1.50	101.00	20.15	20.81	13.50	9.30–22.50
Hours visited birth-term[a]	1.80	104.07	21.33	20.88	13.90	10.10–23.60
Days visited weeks 1–2[b]	1.00	7.00	5.68	1.25	6.00	5.00–6.80
Days visited weeks 3–4[b]	1.00	7.00	5.07	1.64	5.00	3.50–7.00
Days visited weeks 5-term[b]	1.00	7.00	5.08	1.57	5.40	4.20–6.50
Days visited birth-term[b]	1.33	7.00	5.24	1.35	5.33	4.30–6.40
Days cuddled weeks 1–2[c]	0.00	6.50	1.60	1.67	1.00	0.00–2.60
Days cuddled weeks 3–4[c]	0.00	5.50	2.12	1.75	1.50	0.50–3.50
Days cuddled weeks 5-term[c]	0.00	7.00	2.93	1.68	2.67	1.60–3.90
Days cuddled birth-term[c]	0.00	5.91	2.29	1.47	2.00	1.20–3.10
Skin-to-skin days weeks 1–2[d]	0.00	6.00	0.94	1.27	0.50	0.00–1.50
Skin-to-skin days weeks 3–4[d]	0.00	5.00	1.10	1.38	0.50	0.00–1.50
Skin-to-skin days weeks 5-term[d]	0.00	5.57	0.72	1.13	0.21	0.00–1.00
Skin-to-skin days birth-term[d]	0.00	4.18	0.71	0.94	0.30	0.10–0.90
Day of life of first hold[e]	0.00	76.00	10.30	12.14	5.00	2.00–15.50

Infants response to parents

Inpatient Skin-to-skin Care Predicts 12-Month Neurodevelopmental Outcomes in Very Preterm Infants

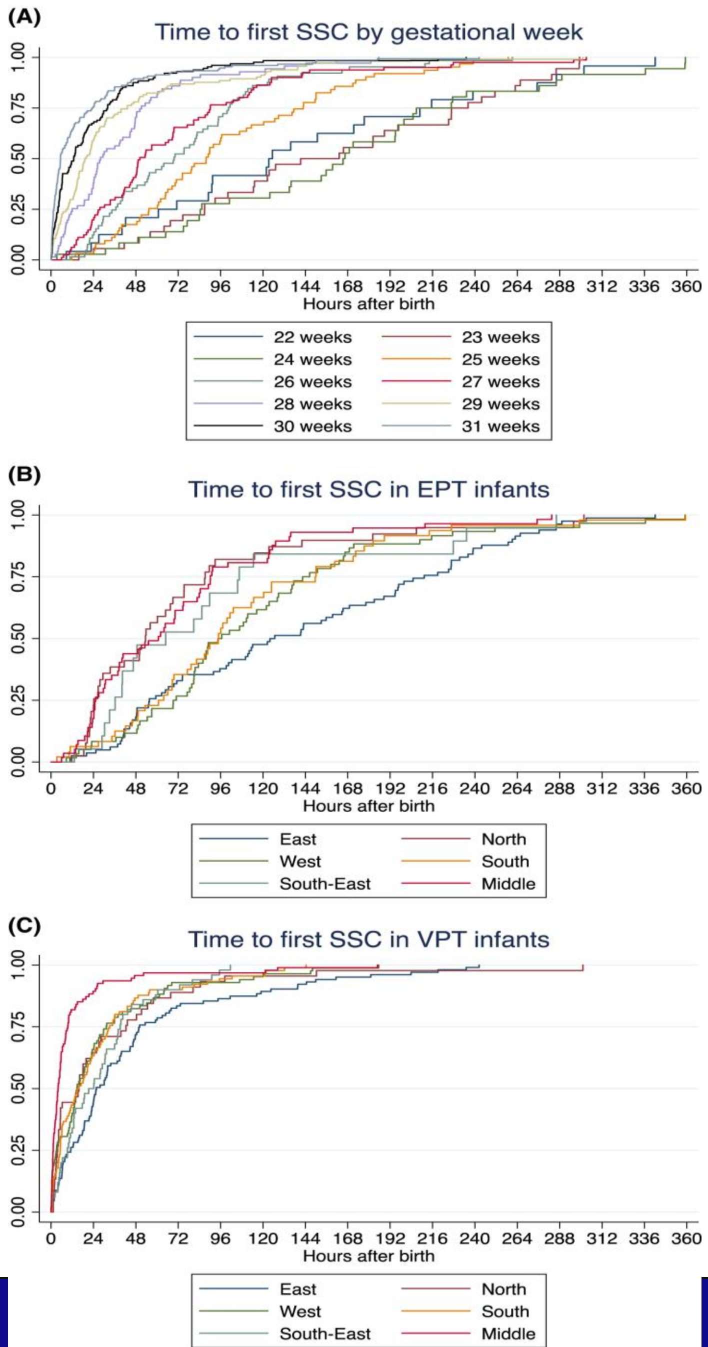
Molly F. Lazarus, BA[1,2], Virginia A. Marchman, PhD[1,3], Edith Brignoni-Pérez, PhD[1,4], Sarah Dubner, MD[1],
Heidi M. Feldman, MD, PhD[1], Melissa Scala, MD[5], and Katherine E. Travis, PhD[1,2]

J Pediatrics 2024; 274:114190

- Total subjects n=181, mean GA 28 weeks, LOS 79 days
- Over their entire stay, infants received average 18 minutes/day of skin-to-skin care.
- Families engaged in skin-to-skin care less than 2 instances/ week (M = 0.25, SD = 0.23)
- Infants from higher SES families experienced more skin-to skin care per day (M = 23.18, SD = 17.57), vs low SES families (M = 11.12, SD = 12.71) (t = 5.34 P < .001).
- Families who visited more frequently tended to perform skin-to-skin care for more minutes/day.
- Skin-to-skin rate uniquely predicted 12-month neurodevelopmental scores after GA, SES, health acuity, and family visitation, with skin-to-skin rate accounting for approximately 6% unique variance.
- A 1% increase in skin to-skin care was associated with 0.09-point increase in 12- month scores. **Thus, on average, a 20-minute increase in the amount of average daily skin-to-skin care was associated with a 10.09-point increase in scores on 12- month neurodevelopmental assessments, more than two-thirds of an SD increase**

Sweden population

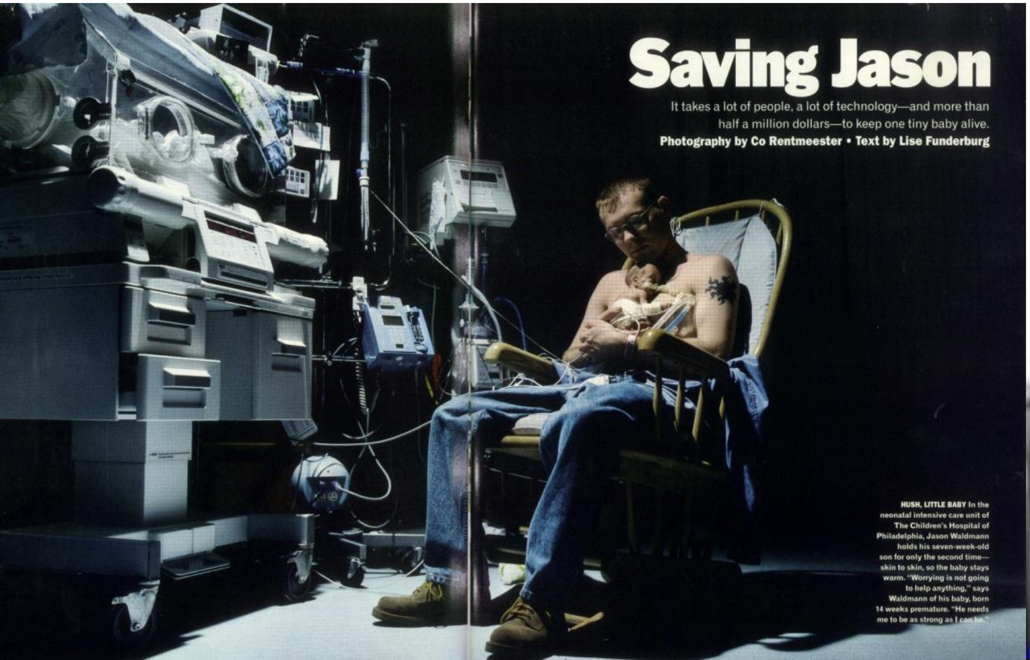
- 1 January 2020 - October 2021
- 1483 EPT and VPT infants
- 22-31 weeks
- GA 22-24 weeks median 100 hours (4 days) time for first skin to skin
- GA 28-32 weeks >75% in first 24 hours
- First 7 days average 3 hours/day
- NICU stay average 6 hrs/day
- Aimed to increase the early skin to skin AND the length of time skin to skin in coming year



Acta Pediatrica Volume111, Issue9
September 2022 Pages 1715-1721

The NICU:
A Window of Opportunity?

The post acute NICU recovery period is a window of opportunity to therapeutically optimize infant development AND support maternal wellbeing/ family adaptation to enhance long term outcomes



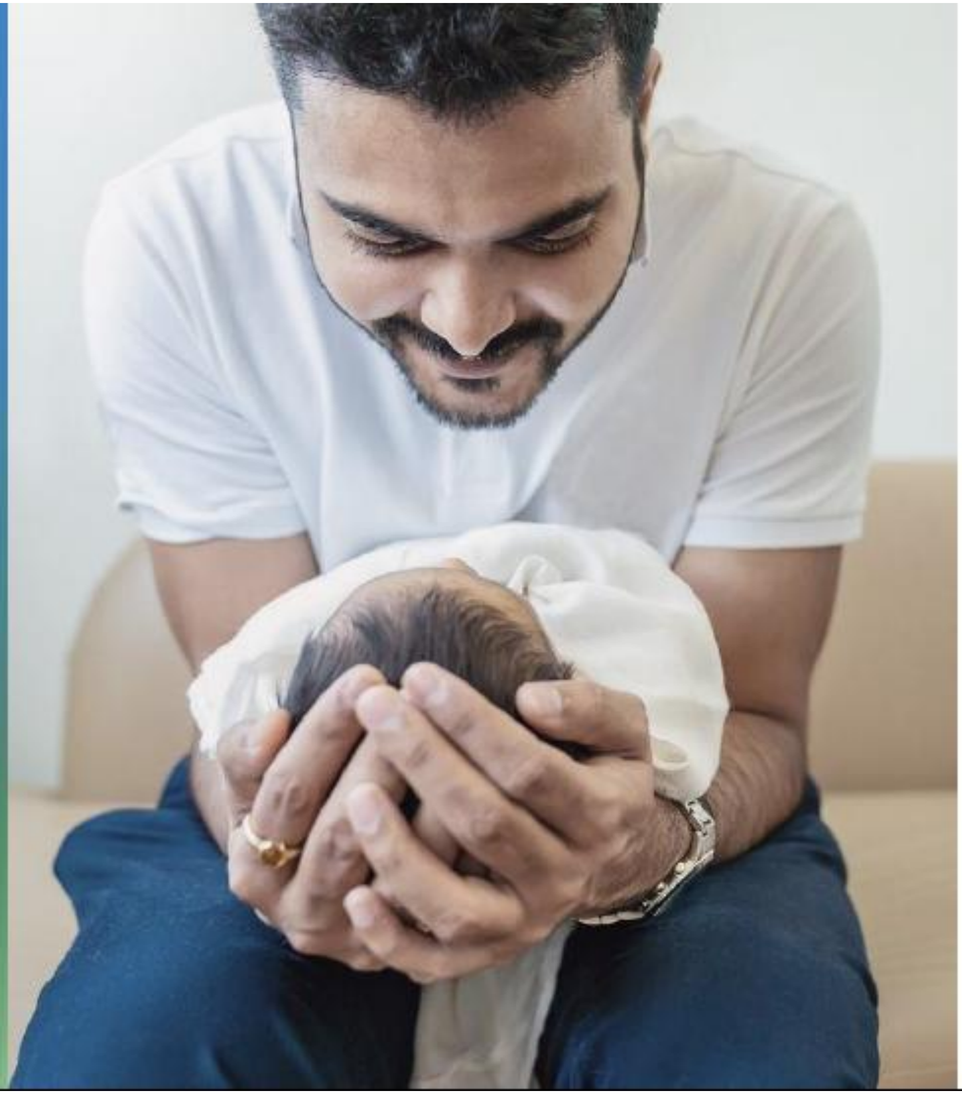
Implications for NICU Parents

NICU parents are at particularly high risk for feelings of loneliness

NICU parents have significantly higher rates of stress, depression, anxiety, and PTSD as compared with controls

	MOTHERS	FATHERS
Anxiety	51%	26%
Depression	31%	12%
Stress	41%	22%

Garg et al., 2023; Kouri et al., 2023; Shetty et al., 2013

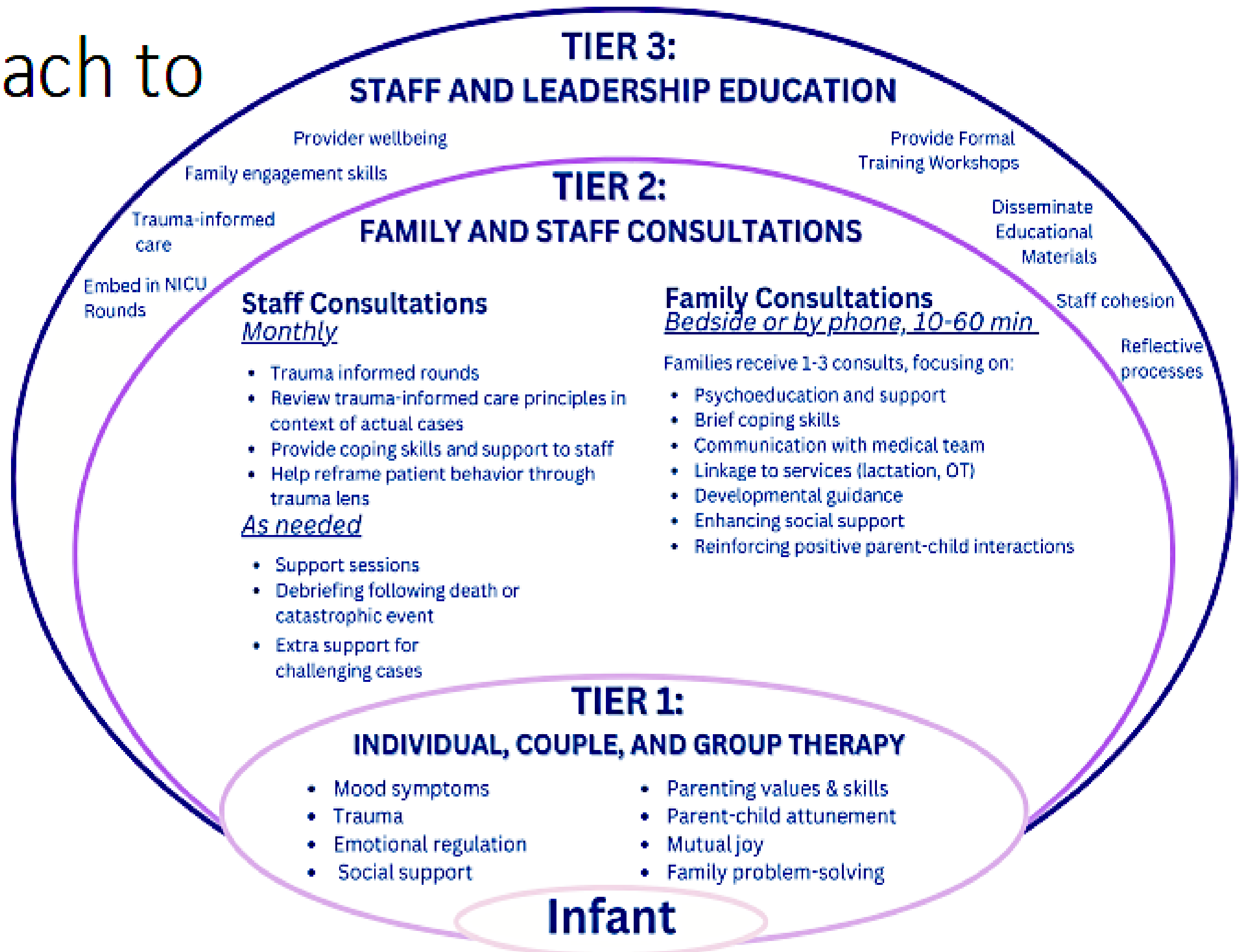


Dad’s Mental Health

- Increased risk of developing mental health challenges as compared with fathers of healthy infants
- Up to one-third of NICU dads experience depressive, anxiety, stress, and posttraumatic stress symptoms
- While mothers’ depressive symptoms tend to improve over the course of the NICU stay, fathers’ depressive symptoms do not

Garfield et al., 2021; Lefkowitz et al., 2019; Mackley et al., 2010

Approach to Care



UCLA Family Development Program Model of Care as presented in:
Morris et al., 2025 oral plenary given at the Gravens High Risk Newborns Conference

Impact of KMC on Maternal Mental Health

- Reduction in depression in the intervention (KMC) group was moderate: SMD=-0.38 (-0.68 to -0.08; 95% CI; I^2=86%; P=0.013), but not in 3 studies on EPNDS.
- Trend toward lower anxiety and parent stress.

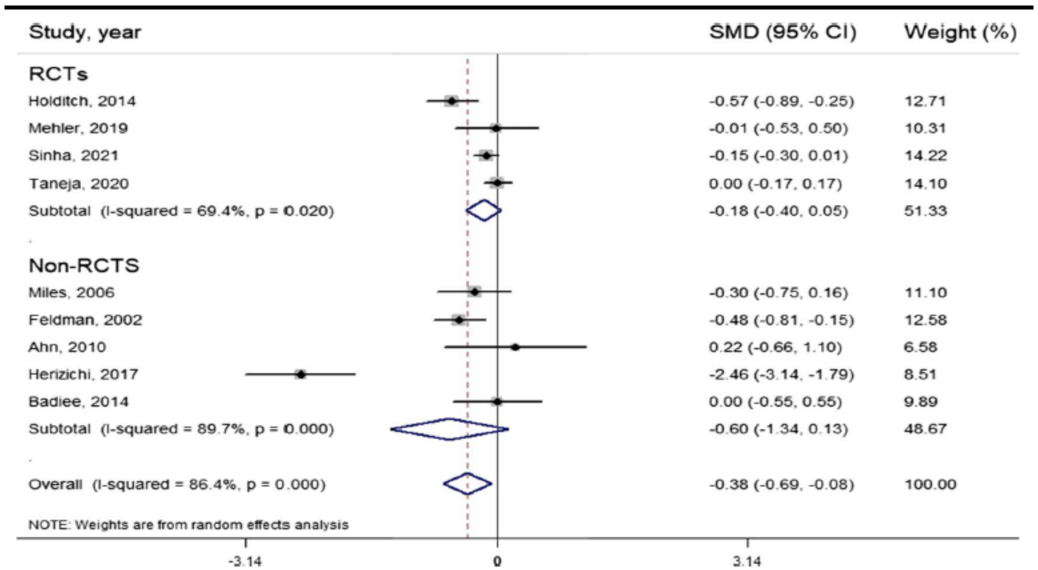
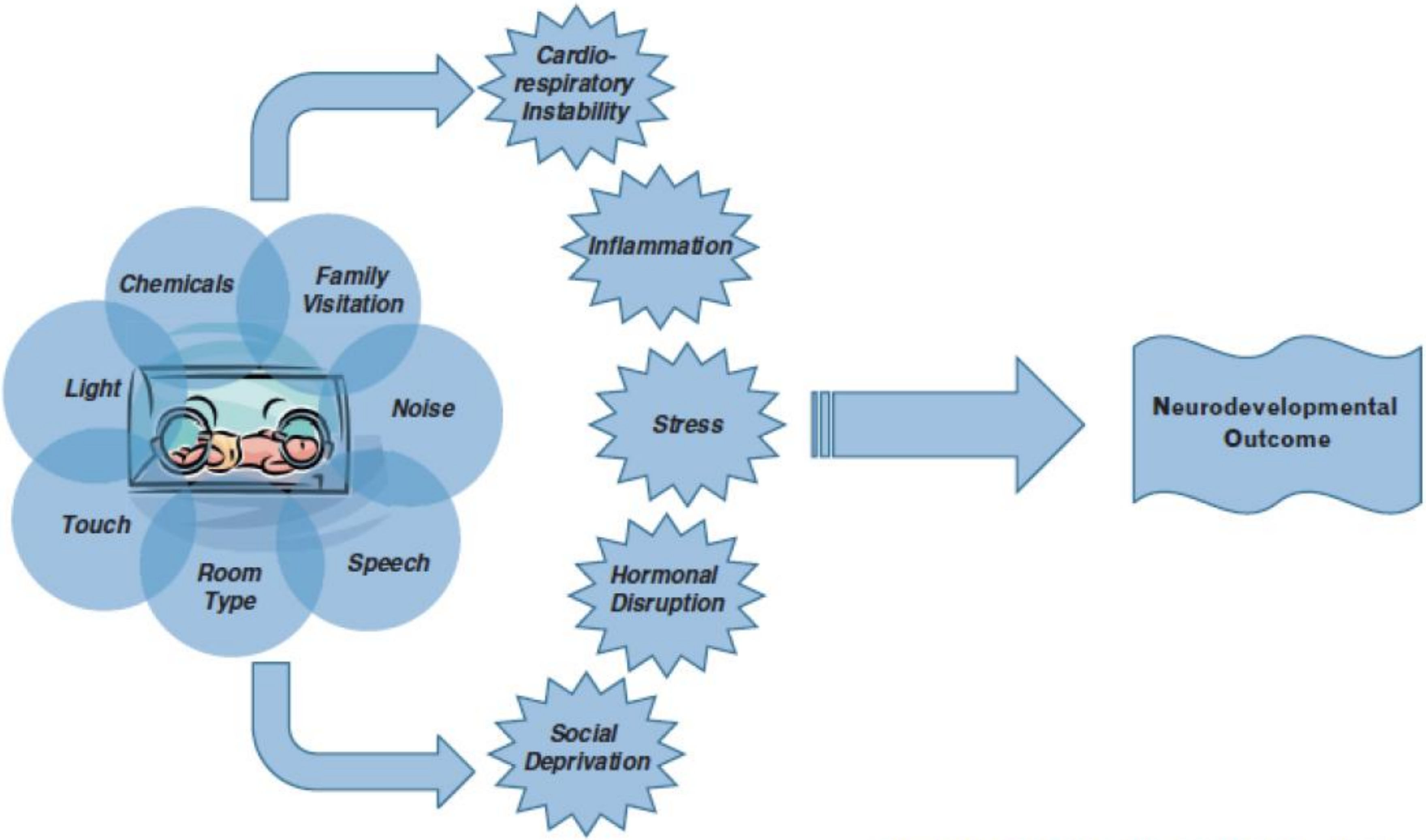


Figure 2. Meta-analysis of the included studies. Notes. SMD, standard mean difference. Results from individual studies were standardized and quality-weighted.

Anwar et al Annals of Medicine & Surgery 2023; *Apr 12;85(6):2841-2848.*

The Impact of the Environment



Curr Opin Pediatr 2015, 27:254–260

The Neonatal Exposome - ”Early life Stress”

- Constructs of Volume (how much) AND of unpredictability

- **Procedural stress and Pain**
  - How is pain assessed systematically?
  - How are procedures balanced in justification?
- **Environmental Stress**
  - Sound, light, alarms,
- **Psychological Stress**
  - Deprivation and family separation

Improving outcomes for preterm infants: Mitigating stress exposure

Marliese Dion Nist *, Nicole Cistone, Rita H. Pickler

SEMIN PERINATOL xxx (xxxx) xxx

Table 1

NICU[a] stressors and strategies to mitigate effects.

Stressor	Mitigation Strategies	Specific Interventions	Considerations for Implementation
Routine nursing care	Cue-based care	• Assess behavioral state prior to caregiving • Avoid awakening infants for routine care • Pace and deliver care based on infant engagement and stress cues	• Training for nurses to interpret infant cues • Effects of workflows and staffing patterns on flexibility in nursing care • Regular interdisciplinary reviews of best practices and unit policies
	Developmental care	• Eliminate or delay unnecessary caregiving activities • Nonpharmacological and pharmacological pain management • Swaddling, positioning, touch following care to promote sleep and recovery	• Evaluation of each infant's daily stress burden and the necessity of specific procedures • Availability of resources and staff to appropriately manage pain • Staffing ratios
Parental Separation	Couplet care	• Maternal postpartum care in the NICU • Neonatal care in the postpartum unit • Combined departments	• Cross-training for nurses • Unit design to accommodate mothers and infants with space for unrestricted access to both patients • Simulation and emergency planning • Phased transition to couplet care
	Parent-infant interaction	• Parent participation in caregiving activities • Skin-to-skin contact	• Education for parents • Staffing ratios to allow for nurse facilitation of skin-to-skin contact • Revisions to NICU protocols • Education for nurses to promote flexibility in care delivery • Comfort of NICU facilities for parents • Staff attitudes regarding parent presence and participation in caregiving

Aljawad *et al. BMC Pediatrics* (2025) 25:291
https://doi.org/10.1186/s12887-025-05620-w

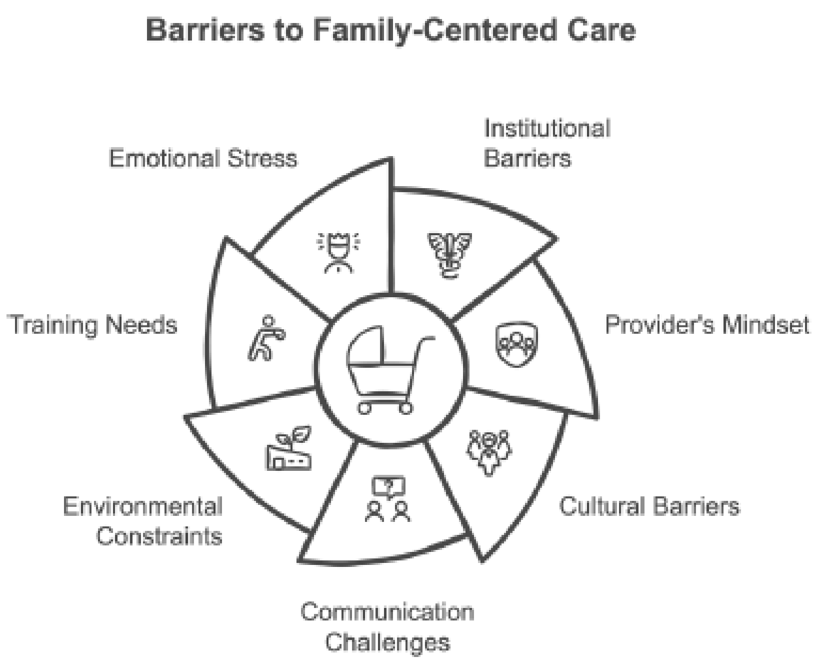
BMC Pediatrics

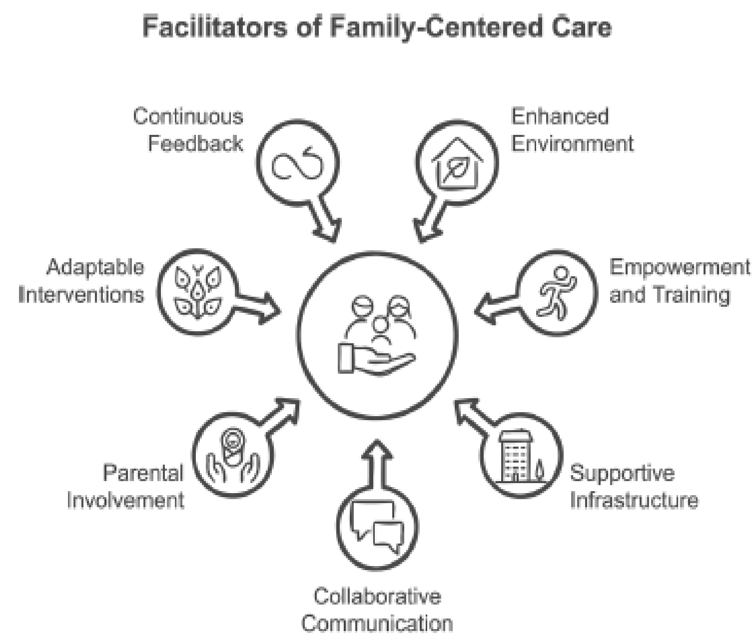
RESEARCH

Open Access

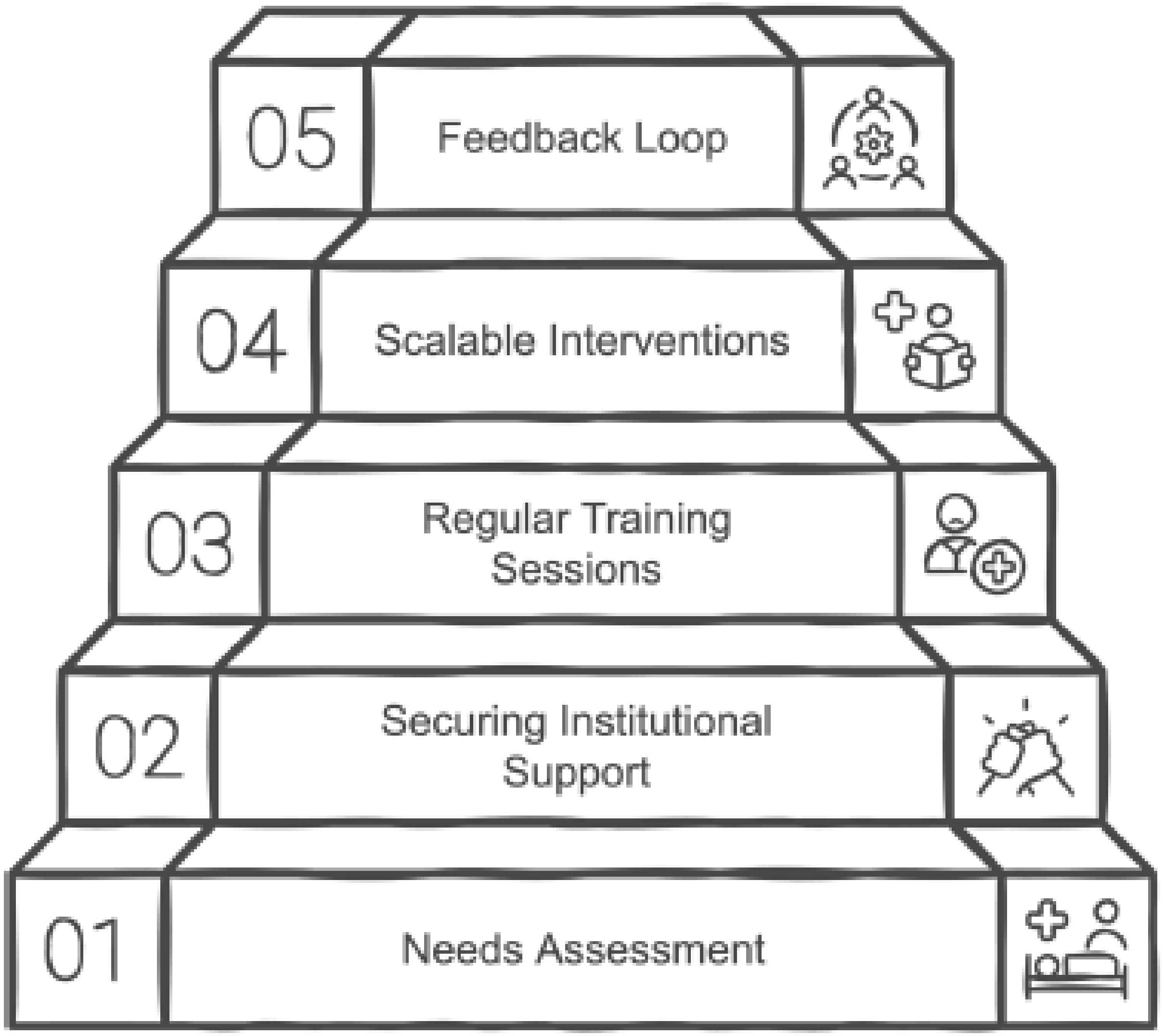
Family-centered care in neonatal and pediatric critical care units: a scoping review of interventions, barriers, and facilitators

Bayan Aljawad[1,2*], Shaima Ali Miraj[1], Furqan Alameri[3,4] and Husam Alzayer[5,6]





Implementing Family-Centered Care



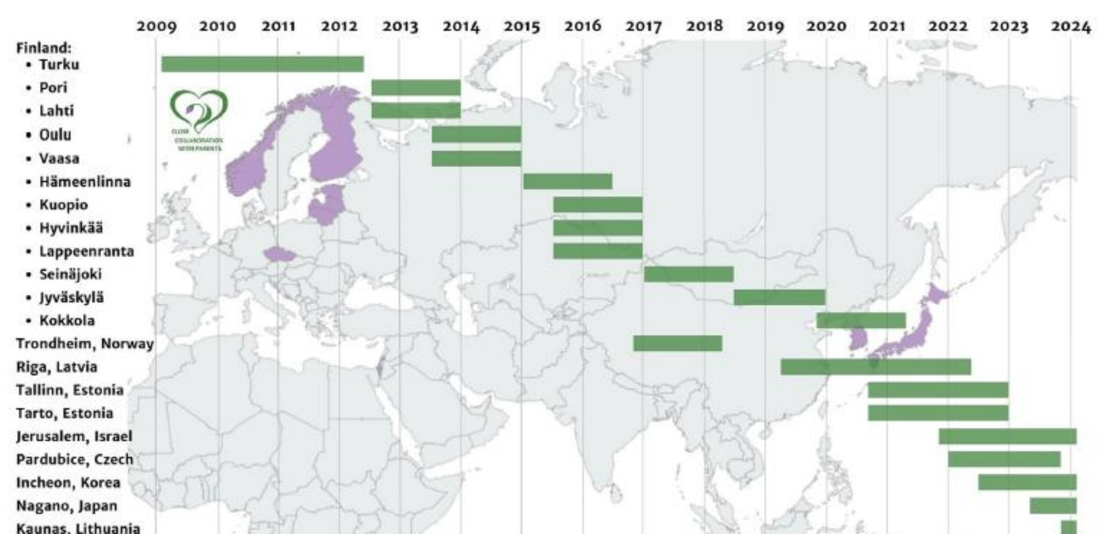
Close Collaboration with Parents—Implementation and effectiveness

Acta Paediatrica. 2025;114:699–709.

Sari Ahlqvist-Björkroth[1] | Anna Axelin[2] | Liisa Lehtonen[3,4]

- The program provides a deeper understanding of
  - observing infants' individual needs,
  - Improved communication with families,
  - integrating parents in care planning and decision-making,
  - and providing emotional support to parents.

8. When and how much	The training for the local mentors consists of 15 workdays, usually within 3 months. Their training starts with 5-day teaching in the teaching centre, continues remotely with 4-h sessions 8 times, and is completed by 5-day teaching in the own unit of the local mentors. The multidisciplinary staff receives training in their unit. Each nurse works with their local mentor for 6 full-day shifts, including 4½ hours of e-learning. Each doctor does six practices with the mentor and e-learning. The mentoring resources can be estimated to be about one man-year for 60 staff members (number of nurses × 6 workdays = the need for mentoring resources).



Close Collaboration with Parents Affects the Length of Stay and Growth in Preterm Infants: A Register-Based Study in Finland

Neonatology 2024;121:351–358
DOI: 10.1159/000535517

Ryo Itoshima[a, b, c] Kjell Helenius[a, b] Sari Ahlqvist-Björkroth[b, d]
Tero Vahlberg[e] Liisa Lehtonen[a, b]

- The adjusted LOS, the primary outcome, was 1.8 days or 6% shorter in the CC group than in the control group (95% confidence interval [95% CI] 0.89–1.00).
- Growth was better in the CC group compared to the control group: adjusted group difference 11.7 g/week (95% CI, 1.4–22.0) for weight, 1.3 mm/ week (95% CI, 0.6–2.0) for length.
- The CC group infants had lower odds of having any unscheduled outpatient visits compared to the control group (adjusted odds ratio 0.81; 95% CI, 0.67–0.98).

Conclusion

- Stress occurs in our very preterm infants and influences brain development and outcomes
- Occurs in three dimensions - procedural, environmental and psychological
- Quantity and unpredictability dimensions are both important
- Modified by parent presence and nurturing for all dimensions
- Implementation of change in NICU culture is challenging and requires resources, education, scalable interventions across a unit that can be measured
- Artificial intelligence may offer “Aura ring” like interpretation for an individual infant of markers of stress, sleep and resilience in the future

Improving outcomes - *with thanks*