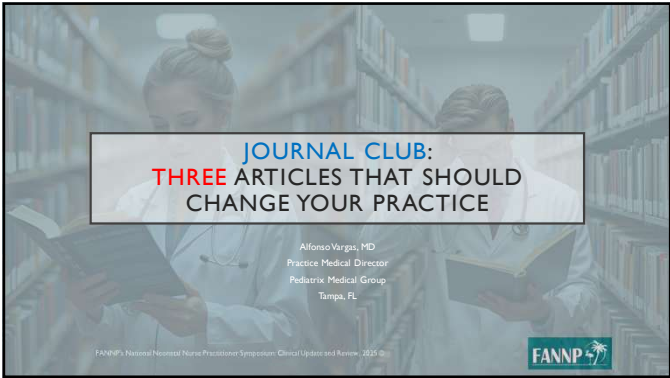
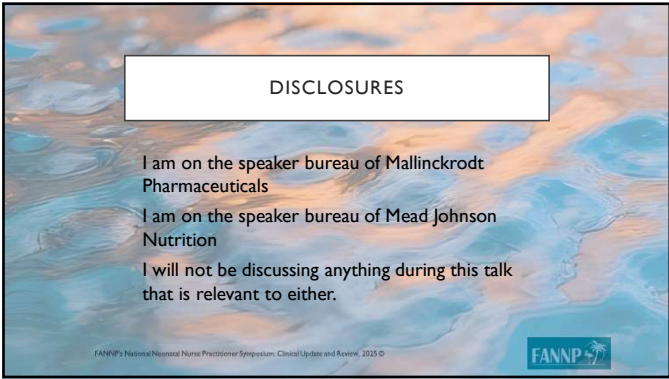


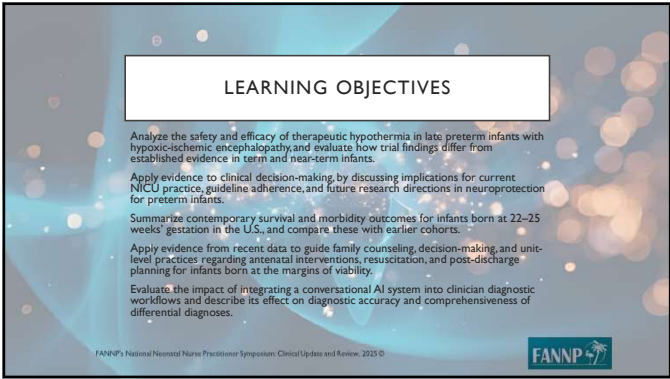
1



2



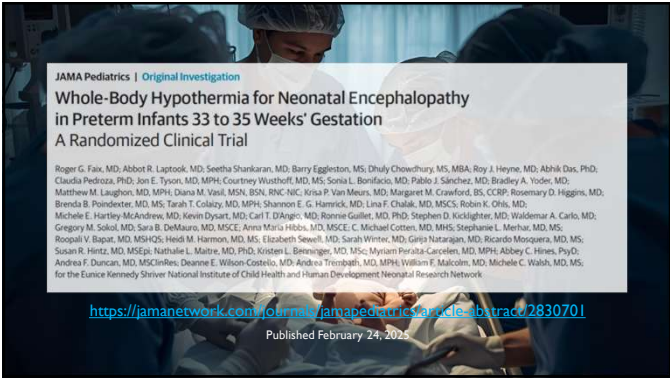
3



4



5



8



9

### MAJOR STUDIES

- **CoolCap trial [2005]** selective head cooling within 5.5 h of age for 72 hrs showed independent protective effect on outcome of **death or disability** in **term infants**.
- **NICHD trial [2005]** whole body cooling showed a significant reduction in the risk of **death** and **moderate to severe disability** at 18 months in **≥36 week infants**.
- **TOBY trial [2008]** whole body cooling showed improvement in **neurologic outcome** in **term infants**.

Systematic review of all three trials showed a significant reduction of combined rate of death and severe disability.

FANNP

10

### AHA GUIDELINES

**2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science**

- It is recommended that **infants born at ≥36 weeks gestation with evolving moderate to severe HIE should be offered therapeutic hypothermia**.

FANNP's National Neonatal Nurse Practitioner Symposium: Clinical Update and Review, 2023 ©

11

**Florida Neonatal Neurologic Network**  
CONNECTING HOPE WITH EXCELLENCE

- FN3 Protocol based on NICHD Whole Body Cooling Protocol
- Protocol distributed to all FN3 sites in the state.
- Protocol was adapted and implemented for use at our institution

FANNP

12

### THERAPEUTIC HYPOTHERMIA AT SJWH

Gestational Age greater than or equal to 35 weeks gestation

Birth weight greater than or equal to 1800 g

Less than or equal to 6 hours since insult occurred

FANNP's National Neonatal Nurse Practitioner Symposium: Clinical Update and Review, 2023 ©

13

**01**

Therapeutic hypothermia (TH) is proven to reduce death and disability in term and near-term infants (≥36 weeks) with hypoxic-ischemic encephalopathy (HIE).

**02**

Despite lack of randomized trial data, TH has been increasingly used off-label in infants <36 weeks' gestation.

**03**

Preterm infants may be more vulnerable to complications of cooling, such as intracranial hemorrhage, NEC, coagulopathy, or hemodynamic instability.

14



JAMA Pediatrics | Original Investigation

**Whole-Body Hypothermia for Neonatal Encephalopathy in Preterm Infants 33 to 35 Weeks' Gestation: A Randomized Clinical Trial**

Roger G. Faix, MD, Abbot R. Laptook, MD, Seetha Shankaran, MD, Barry Eggertson, MS, Dhruv Chowdhury, MS, MBA, Roy J. Heyne, MD, Abhik Das, PhD, Claudia Pedraza, PhD, Jon E. Tyson, MD, MPH, Courtney Wusthoff, MD, MS, Sonia L. Bonifacio, MD, Pablo J. Sanchez, MD, Bradley A. Yoder, MD, Matthew M. Laughon, MD, MPH, Dana M. Vail, MSN, BSN, RNC-NC, Krisa P. Van Meurs, MD, Margaret M. Crawford, BS, CCSP, Rosemary D. Higgins, MD, Brenda B. Poindexter, MD, MS, Tarah T. Colaizy, MD, MPH, Shannon E. G. Hamrick, MD, Lina F. Chalak, MD, MSCS, Robin K. Ohls, MD, Michele E. Hartley-McAndrew, MD, Kevin Dycart, MD, Carl T. D'Angio, MD, Ronnie Guillot, MD, PhD, Stephen D. Kiclighter, MD, Waldemar A. Carlo, MD, Gregory M. Sokol, MD, Sara B. DelMarino, MD, MSCE, Anna Maria Hobbs, MD, MSCE, C. Michael Cortes, MD, MHS, Stephanie L. Mehall, MD, MS, Rogopal V. Bapat, MD, MSHQs, Heidi M. Harmon, MD, MS, Elizabeth Sewell, MD, Sarah Wintner, MD, Garja Natarajan, MD, Ricardo Mosquera, MD, MS, Susan R. Hintz, MD, MSEpi, Nathalie L. Maitre, MD, PhD, Kristen L. Benninger, MD, MSc, Myriam Peraza-Carcelen, MD, MPH, Abbey C. Hines, PhD, Andrea F. Duncan, MD, MSClinRes, Deanne E. Wilson-Costello, MD, Andrea Trembath, MD, MPH, William F. Malcolm, MD, Michele C. Walsh, MD, MS, for the Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network

Faix RG, Laptook AR, Shankaran S, et al. *Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network. Whole-body hypothermia for neonatal encephalopathy in preterm infants 33 to 35 weeks' gestation: a randomized clinical trial.* JAMA. 2024;331(10):e240613. Published online February 24, 2025. doi:10.1001/jama.2024.6613

15

Does therapeutic hypothermia decrease death or disability in preterm infants (33–35 weeks) with moderate to severe HIE?

16

STUDY DESIGN

- **Type:** Multicenter RCT
- **Sites:** 19 NICHD NRN centers in the US
- **Period:** July 2015 – Dec 2022
- **Population:** 168 preterm infants (33–35 weeks GA) with moderate or severe HIE
- **Randomization:** Hypothermia (n=88) vs normothermia (n=80)
- **Outcome:** Composite of death or moderate-to-severe disability at 18–22 months' corrected age

17

RESULTS

- **Demographics:** Mean GA ~34 weeks; baseline characteristics comparable.
- **Primary Outcome:**
  - Hypothermia: 29/83 infants (35%)
  - Normothermia: 20/69 infants (29%)
  - Adjusted RR: 1.11 (95% CrI 0.74–2.00) → 74% probability of harm.
- **Death Alone:**
  - Hypothermia: 18/88 (20%)
  - Normothermia: 9/78 (12%)
  - Adjusted RR: 1.38 (95% CrI 0.79–2.85) → 87% probability of harm.

18

RESULTS

- **Survival with disability:** Similar between groups (13% vs 16%).
- **Exploratory Analyses:**
  - No subgroup (by sex, race, or GA) showed benefit.
  - Many cooled infants overshot to <32°C, but even excluding these, no benefit emerged.
- **Adverse Events:**
  - Rates of bleeding, arrhythmia, infection, NEC, seizures, or other morbidities were comparable between groups.
  - Some metabolic differences (e.g., higher hyperglycemia in cooled infants).

19

- **Enrollment by GA**
  - 33 weeks: 36 infants
  - 34 weeks: 84 infants
  - 35 weeks: 48 infants
- **Primary Outcome (Death or Moderate/Severe Disability)**
  - 33 weeks
    - Higher in hypothermia vs normothermia.
  - 34 weeks
    - Same pattern — more adverse outcomes in hypothermia.
  - 35 weeks
    - Hypothermia showed no benefit
- **Death Alone**
  - 33 weeks
    - No difference.
  - 34 weeks
    - More deaths in hypothermia group.
  - 35 weeks
    - More deaths in hypothermia group.

20

STRENGTHS

- First large RCT in late preterm infants with HIE
- Multicenter, standardized design with blinded outcome assessors
- Careful measures to avoid hyperthermia in the control group.

21

LIMITATIONS

- Moderate sample size (n=168); limited power to detect small effects.
- Some loss to follow-up (11% normothermia, 6% hypothermia).
- Intervention unblinded to clinicians (though outcome assessors were blinded).
- 47 eligible infants were excluded because clinicians opted for hypothermia outside trial.

22

KEY TAKEAWAY

Across **all GA**, hypothermia **did not reduce disability** and tended to increase mortality. The only exception: at **33 weeks**, mortality was not worse with hypothermia, but disability outcomes still were not improved.

23

CONCLUSIONS

01

Hypothermia should not be used for HIE in infants <36 weeks' gestation outside of strict protocols.

02

For 33–35 week infants, cooling may increase mortality without reducing disability.

03

Future research should explore alternative neuroprotective therapies for this vulnerable population.

24

PRACTICE IMPLICATIONS

Re-evaluate	hypothermia use in <36 week neonates—current evidence does not support it
Develop	NICU guidelines to align hypothermia eligibility strictly with evidence
Educate	staff and align practice with new risk data to ensure safety
Highlight	importance of stratifying by GA in neuroprotection trials

25



26


www.nature.com/jp

Journal of Perinatology

ARTICLE

Check for updates

### Therapeutic hypothermia for preterm infants 34–35 weeks gestational age with neonatal encephalopathy

Seh Hyun Kim<sup>1</sup>, Hoda El-shibiny<sup>2</sup>, Terrie Inder<sup>1,2</sup> and Mohamed El-Dib<sup>1,2</sup> <sup>✉</sup>

© The Author(s), under exclusive licence to Springer Nature America, Inc. 2024

**OBJECTIVE:** To evaluate the short-term outcomes and safety of therapeutic hypothermia (TH) for neonatal encephalopathy in preterm infants at 34–35 weeks of gestation.

**STUDY DESIGN:** A matched retrospective cohort study of 20 preterm infants at 34–35 weeks of gestation and 40 infants at 36 weeks of gestation or more who received TH between the years 2015–2021.

**RESULT:** Short-term outcomes of preterm infants at 34–35 weeks of gestation who received TH were comparable with infants at 36 weeks or more of gestation who received TH regarding seizures, intraventricular hemorrhage, blood transfusions, subcutaneous fat necrosis, brain injury on magnetic resonance imaging, and mortality. These findings were consistent when short-term outcomes were adjusted for birthweight.

**CONCLUSION:** TH in preterm infants at 34–35 weeks of gestation is feasible and safe in our study population.

*Journal of Perinatology* (2024) 44:528–531; <https://doi.org/10.1038/s41372-024-01874-x>

27



28

Survival of Infants Born at 22 to 25 Weeks' Gestation Receiving Care in the NICU: 2020–2022



**OBJECTIVE:** To report the contemporary rates of survival, length of stay, and technology dependence at discharge for infants born at 22 to 25 weeks' gestation receiving care in the NICU: 2020–2022.

**DESIGN:** Retrospective cohort study.

**SETTING:** A tertiary care NICU.

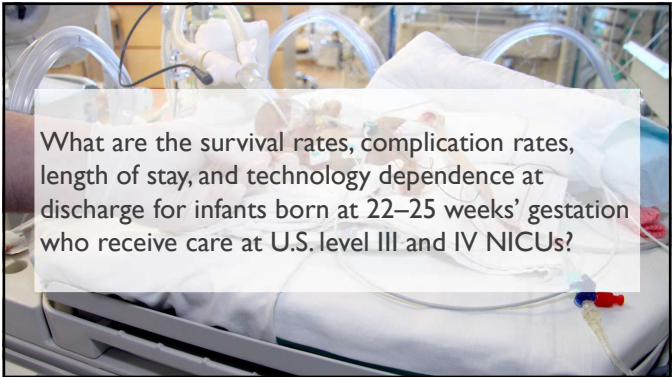
**PARTICIPANTS:** Infants born at 22 to 25 weeks' gestation receiving care in the NICU: 2020–2022.

**MEASUREMENTS AND MAIN RESULTS:** The study included 1,142 infants born at 22 to 25 weeks' gestation receiving care in the NICU: 2020–2022. The median gestational age at birth was 23 weeks (range 22–25 weeks). The median birth weight was 450 g (range 250–1,000 g). The median length of stay was 28 days (range 1–100 days). The median technology dependence at discharge was 1.5 (range 0–10). The survival rate at discharge was 61.6% (95% CI 57.1–66.1%).

**CONCLUSIONS:** The survival rate at discharge for infants born at 22 to 25 weeks' gestation receiving care in the NICU: 2020–2022 was 61.6%.

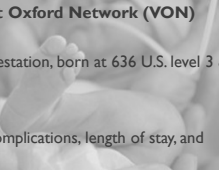
Edwards EM, Ehret DEY, Spill RF, Horbar JD. Survival of Infants Born at 22 to 25 Weeks' Gestation Receiving Care in the NICU: 2020–2022. *Pediatrics*. 2024;154(4):e2024065963. doi:10.1542/peds.2024-065963

31



32

Observational cohort study using the Vermont Oxford Network (VON) Research Repository.



**Population:** 22,953 inborn infants, 22–25 weeks' gestation, born at 636 U.S. level 3 & 4 NICUs (2020–2022).

**Primary outcome:** Survival to hospital discharge.

**Secondary outcomes:** Survival without severe complications, length of stay, and technology dependence at discharge.

33

RESULTS

Active Resuscitation	Overall Survival	Survival If Active Resuscitation
• 22 weeks: 68% (61.6% in 2020 → 73.7% in 2022)	• 22 weeks: <b>24.9%</b>	• 22 weeks: <b>35.4%</b>
• 24 weeks: 99.8%	• 23 weeks: <b>52.8%</b>	• 23 weeks: <b>55.1%</b>
	• 24 weeks: <b>71.1%</b>	• 24 weeks: <b>71.5%</b>
	• 25 weeks: <b>82.1%</b>	• 25 weeks: <b>82.0%</b>

34

RESULTS		
Survival Without Severe Complications	Length of Stay	Technology Dependence at Discharge
<ul style="list-style-type: none"><li>• 22 weeks: <b>6.3%</b></li><li>• 23 weeks: <b>14.4%</b></li><li>• 24 weeks: <b>26.2%</b></li><li>• 25 weeks: <b>40.9–43.2%</b></li></ul>	<ul style="list-style-type: none"><li>• 22 weeks: ~160 days</li><li>• 25 weeks: ~110 days</li></ul>	<ul style="list-style-type: none"><li>• Oxygen:<ul style="list-style-type: none"><li>• 74% at 22 weeks → 45% at 25 weeks.</li></ul></li><li>• G Tube:<ul style="list-style-type: none"><li>• 13% at 22 weeks → 6% at 25 weeks.</li></ul></li><li>• Tracheostomy:<ul style="list-style-type: none"><li>• 4% at 22 weeks → 1–2% at ≥ 23 weeks.</li></ul></li></ul>

35

STRENGTHS
<ul style="list-style-type: none"><li>▪ Large, contemporary cohort</li><li>▪ Nationally representative sample</li><li>▪ Standardized data collection</li><li>▪ Focus on clinically meaningful outcomes</li><li>▪ Temporal trends captured<ul style="list-style-type: none"><li>▪ Showed increasing resuscitation at 22 weeks (from 61.6% in 2020 → 73.7% in 2022).</li></ul></li></ul>

36

LIMITATIONS
<ul style="list-style-type: none"><li>▪ Restricted to level III/IV NICUs</li><li>▪ Observational design<ul style="list-style-type: none"><li>▪ No randomization</li><li>▪ Causality between interventions (e.g., steroids, magnesium, delivery mode) and outcomes cannot be firmly established.</li></ul></li><li>▪ No long-term neurodevelopmental outcomes</li><li>▪ Limited detail on decision-making factors<ul style="list-style-type: none"><li>▪ Hospital-level and provider-level variations in resuscitation practices not fully explained.</li><li>▪ Parental preferences and counseling strategies not captured.</li></ul></li><li>▪ Study period included the COVID-19 pandemic</li></ul>


37

KEY TAKEAWAYS
<ul style="list-style-type: none"><li>▪ Survival at 22 weeks is higher than previously reported</li><li>▪ Survival without severe complications remains low at the earliest gestations.</li><li>▪ Hospital stay is long and resource-intensive.</li><li>▪ Maternal interventions matter.<ul style="list-style-type: none"><li>▪ At 22 weeks, only 41% received both antenatal steroids and magnesium sulfate, compared with ~80% at 25 weeks.</li></ul></li><li>▪ Care is shifting toward greater intervention at the margins of viability.</li></ul>

38

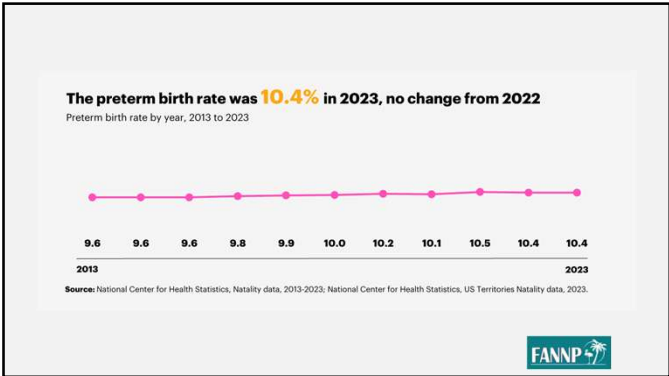
WHY FOCUS ON SMALL BABIES?


39

PRETERM BIRTH IN THE US	2024 MARCH OF DIMES REPORT CARD UNITED STATES
<p>3.6 million births in 2024</p> <p>Approximately 10% preterm</p> <p>Extremely preterm infants (&lt;28 wks) contribute disproportionately to both neonatal and infant mortality</p>	<p>The preterm birth grade was <b>D+</b> in 2023; the worst grades occurred in the southern region of the US</p> <p>Preterm birth rate (born before 37 completed weeks gestation) and grade by state, 2023</p> <p>GRADE AND PRETERM BIRTH RATE</p> <p>FANNP's National Neonatal Nurse Practitioner Symposium: Clinical Update and Review, 2024 ©</p> 

40





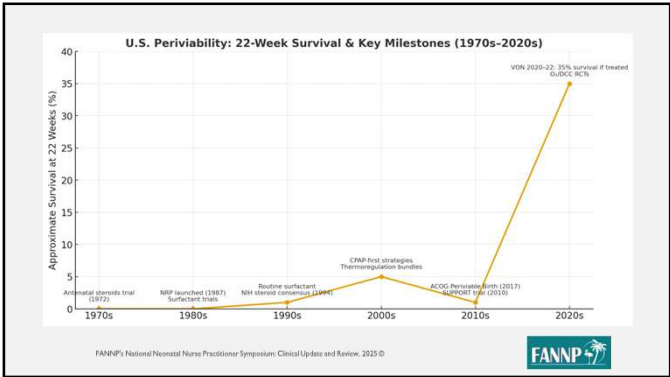
41

Decade	Definition of Periviability	Resuscitation / NICU Practice Trends	Survival at Threshold (22-24 wks)
1970s	Viability cited around 26-28 wks; 'perivable' not yet a standard term.	First RCT of antenatal corticosteroids (1972). No surfactant. Resuscitation inconsistent and center-dependent.	Survival <24 wk essentially 0%; survival expected at 26-28 wk in select centers.
1980s	Lower limit ~24-25 wks in tertiary centers.	NRP launched 1987. Surfactant trials late decade. Antenatal steroid use expanding.	23-24 wk survival rare, highly center-specific; 22 wk almost universally non-survivable.
1990s	Emerging 'periviability' concept, usually 23-24 wks.	Surfactant routine by early 1990s. 1994 NIH consensus drives routine antenatal steroids. NRP uptake expands.	NRN data (1993-): survival at 23-24 wk improving, still uncommon at 22 wk.
2000s	Active care considered at 23-24 wks; 22 wk still rarely resuscitated.	CPAP-first strategies emerge; gentle ventilation; thermoregulation bundles.	NRN 2006-2011: median survival ~5% at 22 wk (if treated), higher at 23-24 wk.
2010s	ACOG 2017 defines perivable birth as 20 0/7-25 6/7 wk. Active care often 22-24 wk.	SUPPORT trial (2010) validates CPAP at birth. NRPPCOR updates emphasize titrated O <sub>2</sub> and deferred cord clamping.	NRN (2000-2011): deaths 97-98% at 22 wk; ~1% survived without NDI (reflects low treatment rates).
2020s	Many centers now offer active care at 22 wk with shared decision-making.	Active treatment at 22 wk rising nationally. DCC standard. 2020 NRP guidelines emphasize targeted O <sub>2</sub> . New RCTs on FiO <sub>2</sub> during DCC.	VON 2020-2022: 22 wk survival 24.9% overall, 35.4% if treated; survival without severe complications 6.3%.

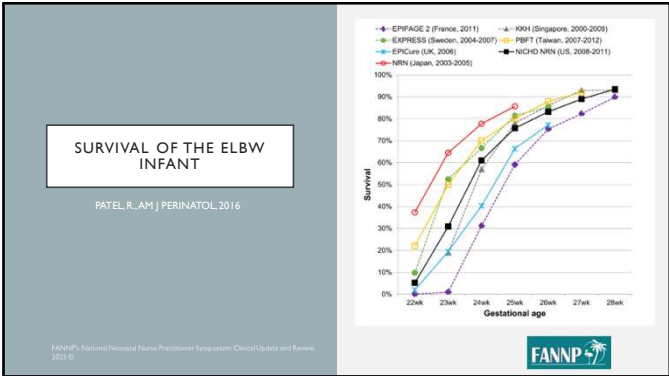
42



43



44



45

Retrospective study from Saitama Medical Center, Japan (2013-2020)  
29 neonates born at 22 weeks gestation  
Actively resuscitated and admitted to the NICU  
Key Findings  
Survival: 82.8% (24/29)  
No delivery room deaths; all infants received active resuscitation

**ARTICLE**  
Management and outcomes of perivable neonates born at 22 weeks of gestation: a single-center experience in Japan  
Yukiko Matsuda<sup>1</sup>, Sei Nishimura<sup>2</sup>, Kazuhiko Kato<sup>3</sup>, and Fumihiko Nishida<sup>4</sup>  
© The Author(s), under exclusive license to Springer Nature America, Inc. 2023

**OBJECTIVE:** We aimed to present the active management and outcomes of infants born at 22 weeks of gestation.  
**STUDY DESIGN:** This retrospective observational study presented the resuscitation methods, management during hospitalization, and outcomes of 29 infants born at 22 weeks of gestation who were actively resuscitated and admitted to our center during 2013-2020.  
**RESULTS:** The survival rate was 82.8% (24/29). Tracheal intubation was performed in all patients, and surfactant was administered for 27 (93.1%). Conventional mechanical ventilation was introduced in 27 (93.1%), and this was changed to high-frequency oscillatory ventilation in more than half by day 4. Surgical treatment of patent ductus arteriosus, necrotizing enterocolitis, and retinopathy of prematurity were required in 4 (13.8%), 5 (16.9%), and 15 (51.7%) patients, respectively. No patient required a tracheostomy or ventriculoperitoneal shunt.  
**CONCLUSIONS:** The overall survival rate and survival rate without morbidities were high among infants born at 22 weeks of gestation.  
Journal of Perinatology (2023) 43:1380-1391. <https://doi.org/10.1038/s41375-023-01706-4>

FANNP's National Neonatal Nurse Practitioner Symposium: Clinical Update and Review, 2023 ©

46

**Doctors Can Now Save Very Premature Babies. Most Hospitals Don't Try.**

Babies born 22 weeks into pregnancy have increasingly better odds of survival—but parents often don't know what's possible

"After her water broke early, doctors told Fatima Goines to prepare for her newborn's death. Goines was 22 weeks into her pregnancy, just past the halfway mark. Doctors at Methodist Hospital in suburban Minneapolis said they couldn't save such a premature baby and that no hospital could. They told her that once the baby girl was born, Goines could hold her until the infant died.

Goines did not want to give up. She checked herself out of Methodist Hospital and, on the recommendation of a fellow mom on [Facebook](#), went to a birthing center connected to Children's Minnesota hospital, 7 miles away from Methodist. After Goines gave birth, doctors there immediately intubated the baby to help her breathe and placed her in an incubator.

Mc'Loni is now a **healthy 4-year-old**, and **has surpassed all the developmental milestones for her age**. "She's doing wonderfully well," said Dr. Thomas George, who directs the Children's Minnesota neonatal intensive care unit."

Wall Street Journal, 8/7/2024

FANPP

47

EXCLUSIVE

HEALTHCARE

## Bill Would Force Hospitals to Warn If They Aren't Equipped to Save Premature Babies

A Wall Street Journal investigation found parents were told nothing could be done for their infants even when other nearby hospitals could offer care

By Liz Gohary [Journal](#)  
July 23, 2020, 9:00 PM EDT

Show

Revis

130

Listen (2 min)


“...would require hospitals to *disclose publicly whether there is a minimal gestational age at which they offer active care for infants*, rather than comfort measures before their death. While many hospitals require lifesaving measures to be given at 25 weeks’ gestational age or above, decisions on whether to attempt to save younger premature infants can vary by hospital or even doctor.”

Wall Street Journal, 7/23/2025

FANNP's National Neonatal Nurse Practitioner Symposium: Clinical Updates and Review, 2025 ©

FANNP

48



<https://www.congress.gov/bills/119/congress-119-overview/2433/text>

(b) **HOSPITAL REQUIREMENT**—Each hospital shall publicly disclose the policy of such hospital regarding the provision of life-saving care to an infant in the case of a premature birth, including—

- (1) whether there is a minimum gestational age at which life-saving care will be provided to an infant in the case of a premature birth;
- (2) whether the decision to provide life-saving care to an infant in the case of a premature birth is made on a case-by-case basis; and
- (3) the process by which the hospital, in the case of a premature birth or expected premature birth, would transfer the infant and mother to the nearest facility with a neonatal intensive care unit that would provide life-saving care to the infant, if the hospital does not have the capacity to provide life-saving care to such infant.

(b) **PRACTITIONER REQUIREMENT**—Each obstetrician, or other health care practitioner, who provides obstetric services to patients, shall, at the first prenatal visit of a patient, disclose to the patient the policy of such hospital in which the obstetrician or practitioner has admitting privileges regarding the provision of life-saving care to an infant in the case of a premature birth, including—

- (1) whether there is a minimum gestational age at which life-saving care will be provided to an infant in the case of a premature birth;
- (2) whether the decision to provide life-saving care to an infant in the case of a premature birth is made on a case-by-case basis; and
- (3) the process by which the hospital, in the case of a premature birth or expected premature birth, would arrange for the transfer the infant and mother to the nearest facility with a neonatal intensive care unit that would provide life-saving care to the infant, if the facility in which the practitioner is providing services does not have the capacity to provide life-saving care to such infant.

49

# SMALL BABY TEAMS

50



51

**DEDICATED ELBW TEAMS**

Single center 67 bed Level IV NICU

28 weeks or < 1000 grams.

Pre-intervention 117 infants, post 232 infants over 3 year period.

Core team with EB guidelines, and checklists.

Care in a distinct unit by a consistent multidisciplinary SBU team

**Decrease in BPD, sepsis, and improved growth.**

Comparative Study > Pediatrics. 2015 Oct;136(4):e1007-15. doi: 10.1593/1542-0067.136.4.e1007. Epub 2015 Sep 7.

**Small Baby Unit Improves Quality and Outcomes in Extremely Low Birth Weight Infants**

Meely Morris <sup>1</sup>, John Patrick Cleary <sup>2</sup>, Antoine Soliman <sup>3</sup>

Affiliations + expand

PMID: 26347427 DOI: 10.1542/peds.2014-2918

**Abstract**

**Objective:** The survival rates for extremely low birth weight (ELBW) infants is many are discharged from the hospital with significant challenges. Our goal objectives for this population by using a multidisciplinary team-based quality approach.

**Methods:** A unique program called the Small Baby Unit (SBU) was established hospital to care for the ELBW infant born at 28 weeks or less and weighing less than 1000 grams. These patients were cared for in a separate location from the main neonatal intensive care unit (NICU) by a dedicated team of neonatologists and nurses. A multidisciplinary team that participates in ongoing education and process-improvement provides care. Evidence-based guidelines and checklists are used.

**Results:** Data from the 2 years before and 4 years after opening the SBU are presented.

FANNP's National Neonatal Nurse Practitioner Symposium: Update and Research 2023 60

**FANNP**

52



PRACTICE IMPLICATIONS

Counseling Families

- Provide updated, data-driven survival and morbidity rates.
- Stress differences between survival with vs. without complications.
- Discuss prolonged hospitalization, technology needs at discharge, and long-term developmental risks.

Standardization of Care

- Develop Small Baby Teams.
- Align obstetric and neonatal management (antenatal steroids, magnesium sulfate use, delivery planning).

Quality Improvement & Equity

- Focus on shared decision-making, clear communication, and family-integrated care.
- Address regional disparities; ensure deliveries occur at level 3/4 NICUs.

Policy Considerations

- Support risk-appropriate perinatal regionalization to reduce care variability.
- Address social determinants of health, parental stress, and financial burdens associated with prolonged NICU stays.

53

BOTTOM LINE

Survival for infants born at 22–25 weeks has improved substantially, particularly at high-level NICUs, but survival without severe morbidity remains low—especially at 22–23 weeks. NICUs must balance aggressive care with realistic counseling, structured “small baby” care programs, and ongoing family-centered, equitable approaches to improve both survival and long-term outcomes.

54

ARTICLE III

55

Artificial Intelligence (AI):  
Computer systems designed to perform tasks requiring human-like intelligence (e.g., pattern recognition, reasoning).

Large Language Models (LLMs):  
A type of AI trained on massive text datasets. They “predict the next word” in context, which allows them to answer questions, write summaries, and even reason through medical cases.

FANNP’s National Neonatal Nurse Practitioner Symposium: Clinical Update and Review, 2023 ©

58

Article

Towards accurate differential diagnosis with large language models

<https://doi.org/10.1006/j4586-025-08888-4>

Received: 19 January 2024

Accepted: 25 February 2023

Published online: 9 April 2023

Open access

A comprehensive differential diagnosis is a cornerstone of medical care that is often

Daniel McDuff<sup>1,2,3,4</sup>, Mike Schwabmann<sup>2,3,4</sup>, Tao Tu<sup>2,3,4</sup>, Anil Palap<sup>2,3,4</sup>, Amy Wang<sup>2,3,4</sup>, Jake Gerrits<sup>2,3,4</sup>, Karen Wright<sup>2,3,4</sup>, Teah Sharma<sup>2,3,4</sup>, Shikhar Arora<sup>2,3,4</sup>, Karan Kulkarni<sup>2,3,4</sup>, Li Heo<sup>2,3,4</sup>, Yong Cheng<sup>2,3,4</sup>, Yan Liu<sup>2,3,4</sup>, & Sara Mahdavi<sup>2,3,4</sup>, Sushant Prakash<sup>2,3,4</sup>, Anupam Pathak<sup>2,3,4</sup>, Christopher Semler<sup>2,3,4</sup>, Shikhar Patel<sup>2,3,4</sup>, David S. Winkler<sup>2,3,4</sup>, Ewa Domoniewska<sup>2,3,4</sup>, Jung Gwakwon<sup>2,3,4</sup>, Jodie Barak<sup>2,3,4</sup>, Katherine Chou<sup>2,3,4</sup>, Greg S. Corrado<sup>2,3,4</sup>, Yossi Matias<sup>2,3,4</sup>, Jike Songsheng<sup>2,3,4</sup>, Alan Karthikesalingam<sup>2,3,4</sup>, & Vivek Natarajan<sup>2,3,4</sup>

59

Can Large Language Models (LLMs), like the **Articulate Medical Intelligence Explorer (AMIE)**, improve the process of making a **differential diagnosis (DDx)**?

Does AMIE perform better than physicians working alone, and can it *help* physicians make better, more comprehensive differential diagnoses?

60

### OBJECTIVES

- Test AMIE's ability to generate accurate and comprehensive DDx lists.
- Compare **standalone AI performance** vs. physicians working without assistance.
- Compare **physician performance with AI assistance** vs. traditional tools (Google, UpToDate, PubMed).
- Explore whether AI can **support, not replace**, clinicians in complex diagnostic reasoning.

61

### METHODS

- Cases:** 302 challenging real-world cases from the *New England Journal of Medicine* Clinicopathological Conferences.
- Participants:** 20 board-certified internal medicine physicians.
- Study design:**
  - Physicians first gave an **unassisted DDx**.
  - Then they were randomized to receive help from:
    - Traditional resources** (search, UpToDate, PubMed).
    - AMIE (LLM)**, with or without additional searches.

62


### EVALUATION

Expert raters scored DDx lists on:


- Accuracy** (did it contain the final diagnosis?).
- Quality** (how close was the DDx to the correct diagnosis?).
- Comprehensiveness** (did it cover all reasonable options?).
- Appropriateness** (fit with the case context).

63


### RESULTS




**AMIE alone:**  
Top-10 accuracy of **59.1%** vs. **33.6%** for unassisted physicians



**Physicians assisted by AMIE:**  
Accuracy improved significantly (top-10 accuracy **51.7%**) compared to physicians with search tools (**44.4%**)



AMIE helped clinicians build **more comprehensive and appropriate DDx lists**.



**Efficiency:**  
Using AMIE took about the same time as search tools (~7 minutes), despite being new to clinicians.

64

### WHY I LIKED THIS PAPER

- Head-to-head design**
  - It directly compares clinician-alone vs. clinician+AI vs. AI-alone.
- Nuanced findings**
  - Shows that **AI can surpass clinicians in isolation**, but **clinician+AI is best**—emphasizing partnership.
- Future relevance**
  - It captures the complexity we face: AI as an augmentation tool, not a wholesale replacement.
- Practical message for providers**
  - The value of AI lies not in replacing us, but in re-shaping workflows to let us practice at the top of our license while AI handles breadth, recall, and pattern-spotting.


65

Study	Setting	Who/What Compared	Primary Finding	Limitation
1) AMIE (Nature, 2025)	302 NEJM CPC cases (simulated)	AI alone vs Clinicians vs Clinicians+AI	Clinicians+AI > clinicians alone; AI alone strong	Simulated, text-only; no outcomes
2) LLM RCT (JAMA NO, 2024)	Physician vignettes (randomized)	Physicians w/LLM vs without; LLM-alone benchmark	LLM access didn't boost MD accuracy; LLM-alone highest	Vignettes; short exposure; small N
3) GPT-4 (NEJM AI)	Complex case challenges (text)	GPT-4 vs aggregate physician readers	GPT-4 exceeded nearly all readers	Self-selected benchmark; no real-world data

### WHAT OTHER STUDIES ARE OUT THERE?

66


IMPLICATIONS FOR HEALTHCARE



**Promise:**

LLMs can help clinicians broaden their diagnostic thinking, reduce missed possibilities, and support education.


Could be especially valuable in **time-sensitive settings** (NICU, ER) or **resource-limited areas**.



**Cautions:**

AI may still “hallucinate” or mislead. AI should be viewed as an **assistant**, **not a replacement**.

**Human** clinical judgment, context, and responsibility remain central.



**Future Directions:**

Integrating multimodal data

Training clinicians to interact effectively with AI.

Ensuring fairness and avoiding health disparities in AI use.


Exploring educational uses—“upskilling” junior staff with broader DDx thinking.

67

- Accurate DDx is essential in neonatal and pediatric care, where presentations can be subtle and time-sensitive.
- AMIE shows that AI can **expand and refine DDx lists**, giving clinicians a safety net for rare or overlooked conditions.
- Nurse practitioners may one day use AI-based tools in daily practice—especially for decision support, education, and identifying red flags.
- Critical thinking and human oversight are **non-negotiable**—AI is a partner, not a replacement.

TAKE HOME MESSAGE

68



69

REFERENCES

- Faix RG, Laptook AR, Shankaran S, et al; Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network. **Whole-body hypothermia for neonatal encephalopathy in preterm infants 33 to 35 weeks' gestation: a randomized clinical trial.** *JAMA Pediatr.* Published online February 24, 2025. doi:10.1001/jamapediatrics.2024.6613
- Edwards EM, Ehret DEY, Soll RF, Horbar JD. **Survival of Infants Born at 22 to 25 Weeks' Gestation Receiving Care in the NICU: 2020–2022.** *Pediatrics.* 2024;154(4):e2024065963. doi:10.1542/peds.2024-065963
- Tu T, Schaekermann M, Palepu A, et al. **Towards accurate differential diagnosis with large language models.** *Nature.* 2025 Apr 9;628(8015):364-372. doi:10.1038/s41586-025-08869-4.

70

10/16/2025

11