Periviability

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Disclosures

None

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Outline

- Historical review
- Trends in periviable survival & variables impacting survival
- Antenatal consultation
- Antenatal periviable management
- Perspectives of former preterm infants

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Neonatology History

We trust we have been forgiven for coining the words, "neonatology" and "neonatologist." We do not recall ever having seen them in print. The one designates the art and science of diagnosis and treatment of disorders of the newborn infant, the other the physician whose primary concern lies in the specialty. … We are not advocating now that a new subspecialty be lopped from pediatrics … yet such a subdivision … [has] as much merit as does pediatric hematology.

—A. J. Schaffer, 1960

Diseases of the Newborn

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Neonatology History - 1963

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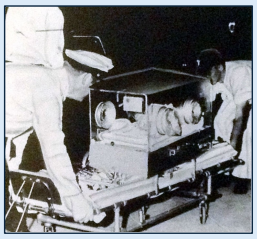
Neonatology History - 1963


The Boston Globe
BABY SPED TO BOSTON
Has Trouble Breathing; Kennedy Stands by Here
Whole World Taken By Littlest Kennedy
'He's a Kennedy —He'll Make It'
Powers to Head N.H. Sweeps



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Martha Lott – Born 1961

Martha's Story

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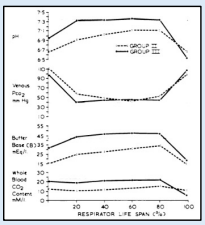
Neonatology History - 1964

- Delivoria-Papadopoulos & Swyer, "Assisted Ventilation in Terminal Hyaline Membrane Disease"
- 18 infants with "terminal and apparently hopeless cases of RDS"

TABLE 1

INITIAL CLINICAL AND BIOCHEMICAL STATUS (VENOUS BLOOD) OF 18 INFANTS DIVIDED INTO THREE GROUPS OF 6 PATIENTS ON BASIS OF INCREASING SEVERITY

Clinical Group	I	II	III
Respiratory arrest	5	3	1
Heart	Arrest 3	Arrest 3 or Rate 20	Arrest 1 or Rate 60
Cyanosis	Pallid	Mottling	Livid
pH	6·5	6·75	6·75
P_vCO_2 (mm.Hg)	100	100	100
Buffer base (mEq l.)	15·0	20·0	20·0



Delivoria-Papadopoulos & Swyer, 1964

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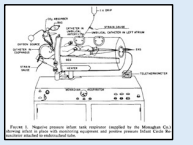
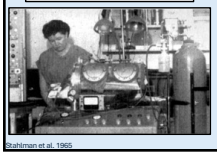
Neonatal History - 1965





CLINICAL DETAILS OF TWENTY INFANTS WITH RESPIRATORY FAILURE TREATED WITH IPPR

Case No. and Sex	Birth Weight (kg.)	Gestation (wk.)	Complications of Pregnancy or Delivery	Mode of Delivery	Age at Onset of IPPR (hr.)	Total Hours on Ventilator	Age at Death (hr.)
Group I							
1	M	1·6	32	Footling breech	Vaginal	6	101	109
2	F	1·4	30	Twin pregnancy	Cesarean	6	11	17
3	F	1·4	27	Uncontrolled diabetes, hydramnios	Cesarean	6	21	30
4	F	1·7	35		Vaginal	4	82	88
5	F	1·5	33	Uncontrolled diabetes	Cesarean	6	100	115
6	M	1·0	30	Precipitous delivery	Vaginal	6	18	24
Group II								
7	M	2·0	34		Vaginal	498	126	130
8	M	1·7	32	Uncontrolled diabetes	Vaginal	18	12	30
9	M	1·7	30	Surgical removal ureteral stone	Vaginal	18	13	48
10	M	1·2	31	Twin pregnancy	Vaginal	30	58	199
11	M	1·2	29	Placenta praevia	Cesarean	42	4	79
12	M	1·9	34		Cesarean	417	164	Lived
13	M	1·9	34		Cesarean	417	164	Lived
14	ME	1·9	33	Uncontrolled diabetes, toxaemia	Cesarean	18	72	Lived
15	F	1·8	33	Premature rupture membrane	Vaginal	49	176	Lived
16	M	1·7	40	Severe birth asphyxia	Vaginal	50	48	Lived
17	M	2·1	36	Placenta praevia	Cesarean	42	192	Lived
18	M	1·1	30		Cesarean	41	96	Lived

Stahlman et al. 1965

Delivoria-Papadopoulos et al. 1965

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Why the Focus on the Lungs?

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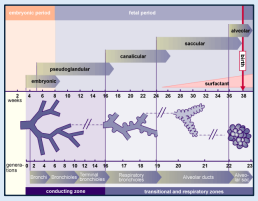
What limits the periviable threshold?

- Canalicular Stage (16-25 weeks)
  - Mesenchymal thinning
  - Respiratory bronchioles
  - Primitive alveolar/capillary network
  - Type II pneumocytes – surfactant
  - Fetal breathing



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Periviability: Trends in Survival

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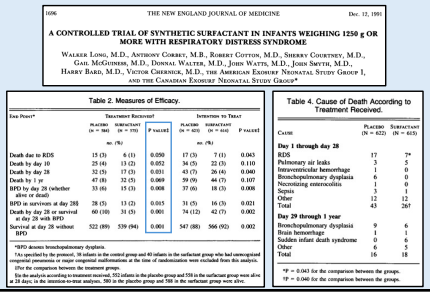
Surfactant Trials



A CONTROLLED TRIAL OF SYNTHETIC SURFACTANT IN INFANTS WEIGHING 1250 g OR MORE WITH RESPIRATORY DISTRESS SYNDROME

Table 2. Measures of Efficacy.

End Point*	Treatment Received† Placebo (N = 561)	Surfactant (N = 559)	P value‡	Intention to Treat Placebo (N = 651)	Surfactant (N = 642)	P value‡
	no. (%)			no. (%)		
Death due to RDS	15 (3)	6 (1)	0.050	17 (3)	7 (1)	0.043
Death by day 10	25 (4)	13 (2)	0.052	34 (5)	22 (3)	0.110
Death by day 28	32 (5)	17 (3)	0.031	43 (7)	26 (4)	0.040
Death by 1 yr	47 (8)	32 (5)	0.069	59 (9)	44 (7)	0.107
BPD by day 28 (whether alive or dead)	33 (6)	15 (3)	0.008	37 (6)	18 (3)	0.008
BPD in survivors at day 28§	28 (5)	13 (2)	0.015	31 (5)	16 (3)	0.021
Death by day 28 or survival at day 28 with BPD	60 (10)	31 (5)	0.001	74 (12)	42 (7)	0.002
Survival at day 28 without BPD	522 (89)	539 (94)	0.001	547 (88)	566 (92)	0.002

*BPD denotes bronchopulmonary dysplasia.
†As specified by the protocol, 38 infants in the control group and 40 infants in the surfactant group who had unrecognized congenital pneumonia or major congenital malformations at the time of randomization were excluded from this analysis.
‡For the comparison between the treatment groups.
§In the analysis according to treatment received, 552 infants in the placebo group and 558 in the surfactant group were alive at 28 days; in the intention-to-treat analysis, 580 in the placebo group and 588 in the surfactant group were alive.

Table 4. Cause of Death According to Treatment Received.

Cause	Placebo (N = 622)	Surfactant (N = 615)
Day 1 through day 28		
RDS	17	7*
Pulmonary air leaks	3	5
Intraventricular hemorrhage	1	0
Bronchopulmonary dysplasia	6	0
Necrotizing enterocolitis	1	0
Sepsis	3	1
Other	12	12
Total	43	26†
Day 29 through 1 year		
Bronchopulmonary dysplasia	9	6
Brain hemorrhage	1	1
Sudden infant death syndrome	0	6
Other	6	5
Total	16	18

*P = 0.043 for the comparison between the groups.
†P = 0.040 for the comparison between the groups.

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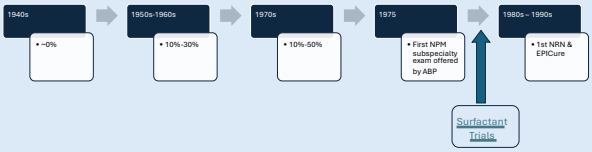
Periviability: Trends in Survival



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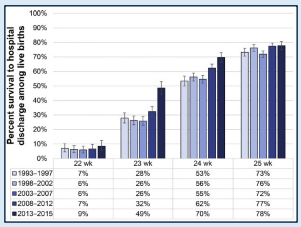
Periviability: Trends in Survival

All liveborn infants regardless of treatment initiation



	22 wk	23 wk	24 wk	25 wk
1993-1997	7%	28%	53%	73%
1998-2002	8%	26%	56%	76%
2003-2007	6%	26%	55%	72%
2008-2012	7%	32%	62%	77%
2013-2015	9%	40%	70%	78%

Stoll et al. 2015

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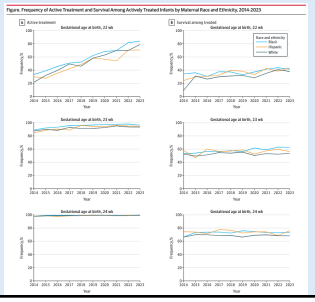
Periviability: Trends in Survival



Boghossian et al. 2025

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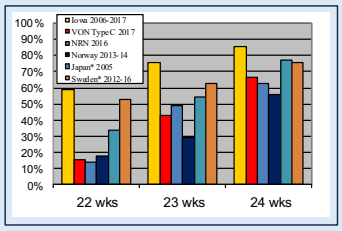
Current Survival Statistics



Klein, Iowa

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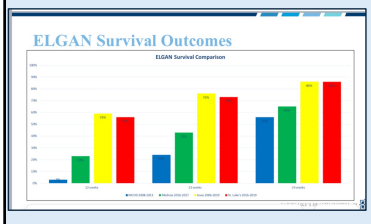
Current Survival Statistics



GA	Delivered	Survived n (%)	Survived/of those given ICU care (%)
22	16	3 (11)	3/4 (75)
23	27	8 (29)	8/21 (38)
24	51	26 (51)	26/47 (55)
25	45	39 (87)	39/42 (93)
26	50	45 (90)	45/49 (92)
27	79	68 (86)	68/79 (86)

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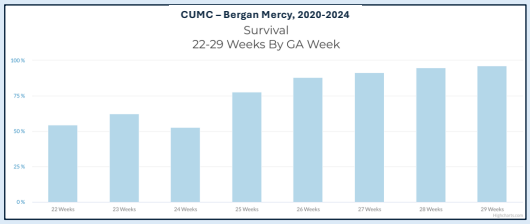
Current Survival Statistics



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Why the Variability?

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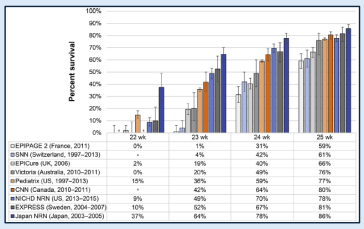
Periviability: Variability in Reporting



	22 wk	23 wk	24 wk	25 wk
EPIPAGE 2 (France, 2011)	0%	1%	31%	59%
SNN (Switzerland, 1997–2013)	-	4%	42%	61%
EPICure (UK, 2006)	2%	19%	40%	66%
Victoria (Australia, 2010–2011)	0%	20%	49%	76%
Pediatrix (US, 1997–2013)	15%	36%	59%	77%
CNN (Canada, 2010–2011)	-	42%	64%	80%
NICHD NRN (US, 2013–2015)	9%	46%	70%	78%
EXPRESS (Sweden, 2004–2007)	10%	52%	67%	81%
Japan NRN (Japan, 2003–2005)	27%	64%	78%	86%

Patel et al. 2017

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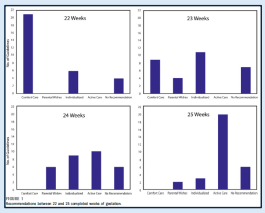
Variability in Recommendations



- Systematic review: Delivery room care of periviable infants
  - Primary outcome: rating of recommendation from comfort care to active care
  - Included 31 guidelines from 23 countries

Guillen et al. 2015

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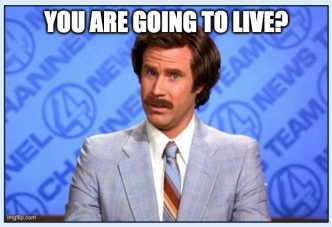
Predicting Mortality & Morbidity



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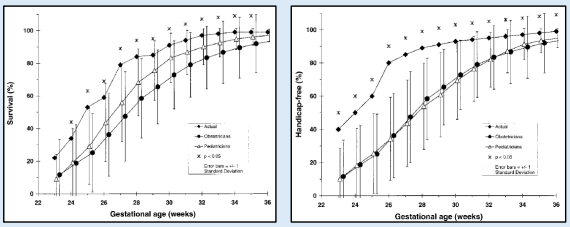
Predicting Mortality & Morbidity



Morse et al. 2009

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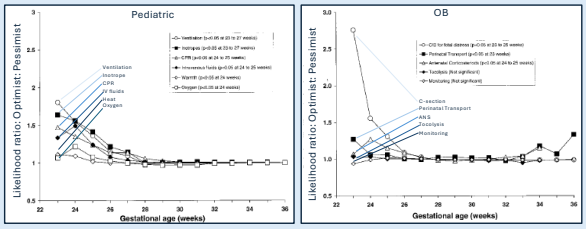
Predicting Mortality & Morbidity



Morse et al. 2000

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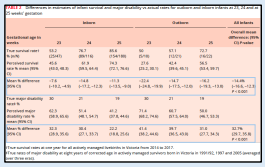
Predicting Mortality & Morbidity



- Perceived vs True Outcomes: 22-23 weeks
  - Survey: Midwives, RN, Neonatologists, OB at tertiary and non-tertiary hospitals
  - Underestimate survival: 14%
  - Overestimate disability: 33%

Boland et a. 2022

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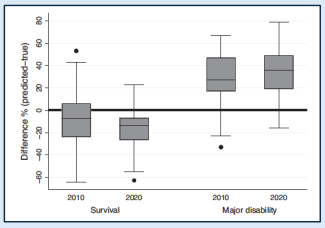
Predicting Mortality & Morbidity



Boland et a. 2022

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What is Morbidity?

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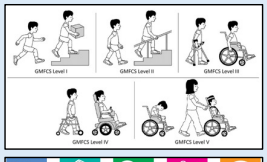
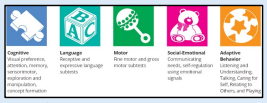
Morbidity





Bayley Scales of Infant and Toddler Development

Neurodevelopmental Impairment Categorization

Mild: Bayley III cognitive & motor >85 & GMFCS level 0-1
Mod: Bayley III cognitive & motor >70, <85 & GMFCS level 2-3
Severe: Bayley III cognitive & motor <70 & GMFCS level 4-5, bilateral blindness, bilateral severe hearing impairment

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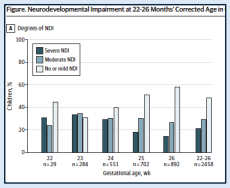
Morbidity Trends at Periviability

- Prospective NICHD NRN data:
  - ~2,600 infants 22-26weeks between 2013-2016 with follow up at 22-26 months
- Mild:
  - Bayley III cognitive & motor >85 & GMFCS level 0-1
- Moderate:
  - Bayley III cognitive & motor >70, <85 & GMFCS level 2-3
- Severe:
  - Bayley III cognitive & motor <70 & GMFCS level 4-5, bilateral blindness, bilateral severe hearing impairment



Bell et al. 2022

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Morbidity Severity with Time

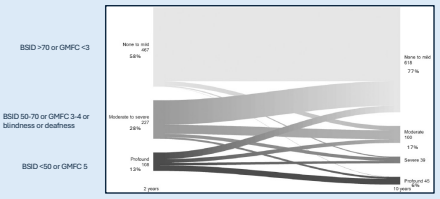

TABLE 2 Outcomes of Children With None to Mild NDI at 10 Years of Age

10 y Outcome	Stable	Improvement From 2 to 10 y		
	None to Mild (n = 439)	Moderate to Severe to None to Mild (n = 144)	Profound to None to Mild (n = 38)	P
IQ[a] median (IQR)	96 (86–106)	93 (84–100)	90 (79–97)	<.0001
Latent profile analysis group = 1 or 2, n (%)[b]	409 (94)	125 (85)	28 (72)	<.0001
Cerebral palsy,[b] n (%)	11 (2.5)	12 (8.3)	7 (17.9)	<.0001
Pediatric quality of life inventory, median (IQR)	86 (79–95)	80 (69–91)	82 (67–92)	<.0001

Taylor et al., 2021

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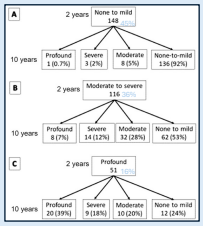
Morbidity Severity with Time: 23-25 weeks

SUPPLEMENTAL TABLE 5 NDI by Gestational Age: 2 Years

NDI	Gestational Age, wk				
	23 (n = 38)	24(n = 122)	25(n = 162)	26(n = 201)	27(n = 279)
None to mild, n (%)	11 (29)	62 (51)	79 (48)	131 (65)	184 (66)
Moderate to severe, n (%)	21 (55)	35 (29)	62 (38)	45 (22)	64 (23)
Profound, n (%)	6 (16)	25 (21)	21 (13)	25 (12)	31 (11)

SUPPLEMENTAL TABLE 6 NDI by Gestational Age: 10 Years

NDI	Gestational Age, wk				
	23 (n = 38)	24(n = 122)	25(n = 162)	26(n = 201)	27(n = 279)
None to mild, n (%)	18 (47)	78 (64)	119 (73)	154 (77)	249 (89)
Moderate, n (%)	9 (24)	18 (15)	25 (15)	33 (16)	15 (5)
Severe, n (%)	4 (11) 53%	12 (10) 36%	10 (6) 31%	6 (3)	7 (3)
Profound, n (%)	7 (18) 53%	14 (12) 36%	8 (5) 31%	8 (4)	8 (3)



Taylor et al., 2021

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Periviability: Current Recommendations

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Periviability: Current Recommendations

TABLE
Summary of American College of Obstetricians and Gynecologists and Society for Maternal-Fetal Medicine guidelines for intervention with threatened periviable birth

Intervention	20 0/7 to 21 6/7 wk	22 0/7 to 22 6/7 wk	23 0/7 to 23 6/7 wk	24 0/7 to 24 6/7 wk	25 0/7 to 25 6/7 wk
Neonatal assessment for resuscitation	Not recommended 1A	Consider 2B	Consider 2B	Recommended 1B	Recommended 1B
Antenatal corticosteroids	Not recommended 1A	Consider 2C	Consider 2B	Recommended 1B	Recommended 1B
Magnesium sulfate for neuroprotection	Not recommended 1A	Not recommended 1A	Consider 2B	Recommended 1B	Recommended 1B
Antibiotics to prolong latency during expectant management of PPROM	Consider 2C	Consider 2C	Consider 2B	Recommended 1B	Recommended 1B
Intrapartum antibiotics for group B streptococci prophylaxis	Not recommended 1A	Not recommended 1A	Consider 2B	Recommended 1B	Recommended 1B
Cesarean delivery for fetal indication	Not recommended 1A	Not recommended 1A	Consider 2B	Consider 1B	Recommended 1B

PPROM, preterm prelabor rupture of membranes.
Adapted from Cahill et al.[1] 2021 and Obstetric Care Consensus No. 6: Periviable birth.[2]
Society for Maternal-Fetal Medicine. Management of periviable and previable preterm prelabor rupture of membranes. Am J Obstet Gynecol 2024.

SMFM, 2024

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Antenatal Consultation at Periviability

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Antenatal Consultation at Periviability: Current Recommendations

TABLE 2
Recommendations for periviable birth

Recommendations	Grade of Recommendations
Based on anticipated neonatal or maternal complications, antepartum transport to a center with advanced levels of neonatal or maternal care is recommended when feasible and appropriate.	Best practice
Prenatal and postnatal counseling regarding anticipated short-term and long-term neonatal outcome should take into consideration anticipated gestational age at delivery, as well as other variables that may alter the likelihood of survival and adverse newborn outcomes (eg, fetal sex, multiple gestation, the presence of suspected major fetal malformations, antenatal corticosteroid administration, birth weight, and response to initial newborn resuscitation).	Best practice
Family counseling should be provided by a multidisciplinary team that includes obstetrician–gynecologists and other obstetric providers, maternal–fetal medicine specialists, if available, and neonatologists who can address their individual and shared considerations and perspectives. Maternal and neonatal outcomes should be considered. Follow-up counseling should be provided when there is relevant new information about the maternal and fetal status or the newborn's evolving condition.	Best practice
A predelivery plan, made with the parents, family, or both, should be recognized as a general plan of approach, which may be modified as the neonate's condition and response is evaluated by the neonatal providers. A recommendation regarding assessment for resuscitation is not meant to indicate that resuscitation should always either be undertaken or deferred, or that every possible intervention need be offered. A stepwise approach concordant with neonatal circumstances and condition and with parental wishes is appropriate. Care should be reevaluated regularly and potentially redirected based on the evolution of the clinical situation.	Best practice

Recommendations regarding specific interventions, tailored to gestational age and other clinical data, and taking into account individual family preferences and values, are summarized in Table 3.
ACOG. Periviable birth. Am J Obstet Gynecol 2016.

ACOG, 2017

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Antenatal Consultation at Periviability: Current Recommendations

Optimize outcomes → deliver at a center with expertise in BOTH maternal and neonatal periviable care

⬇️

Provide multi-disciplinary counseling

⬇️

Have a *plan*

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Antenatal Consultation at Periviability: Having a Plan

"Everyone has a plan until they get hit in the mouth."
Mike Tyson

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Periviable Consultation

- Provide parents with most accurate prognosis possible.
- Tailored to each family and their individual case
- Emphasize that statistics, if given, are specific to this gestational age and improve with each additional DAY of pregnancy

Janvier et al. 2012

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Antenatal Consultation at Periviability: Avoid Data Dumping

- "At 24 weeks, survival is 50-70%. If the baby survives, she has a 40-50% chance of no disability, 20-30% chance of major disability, and 40-50% chance of minor disability."

Janvier et al. 2012

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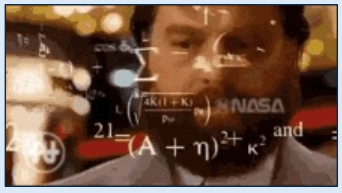
Antenatal Consultation at Periviability: Avoid Data Dumping



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Antenatal Consultation at Periviability: Avoid Data Dumping

1. People don't understand statistics
2. Stating statistics introduces framing bias

Janvier et al. 2012

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Framing Effect

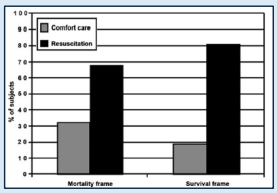
Imagine now that you (or someone close to you) are pregnant. You have just come back from a trip and notice that you are having cramps. You are worried because you are at only 23 weeks which is very premature. Up until now your pregnancy has been normal. You visit your doctor who tells you that you are going into premature labor and that you may deliver in the next 36 hours. Your doctor admits you to the hospital and tries to help stop your labor. You ask your doctor what usually happens when babies are born this early. Your doctor tells you:

At 23 weeks, which is how far along you are in your pregnancy, 25 out of 100 babies will survive if provided intensive care. Of those who survive, 15 out of the 25 babies will not have severe developmental disabilities. With comfort care, all babies born this early would die. However, the baby's suffering would be minimized.

Your doctor asks you what option you want to choose.

- ○ I would want the doctors to provide the baby intensive care.
- ○ I would want the doctors to provide the baby comfort care.

There is no right or wrong answer. Both options are respected and legal.



- Positively framed vignette (ABOVE) providing **survival** and **lack of disability** statistics
- Negatively framed vignette was identical with exception of providing **death** and **disability** statistics

Haward et al., 2008

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Antenatal Consultation at Periviability: Avoid Data Dumping

1. People don't understand statistics
2. Stating statistics introduces framing bias
3. Percentages describe outcomes for a group of infants, parents want to know outcome for their baby (0 or 100%)
4. Life and death decisions are not made using only rationale statistics, emotions play a significant role

Janvier et al., 2012

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Playbook for Periviable Consultation

- Introduction
  - Introduce self/role
  - Assure all family members/support people are present (if feasible)
  - Sit down (eye level preferred)
  - BE NORMAL: ask sex, name (if known) and use name not "fetus" in consult
    - Ask about family – other children, where they live, +/- employment
  - Discuss goals of consultation (i.e. develop a plan)

Krakauer & Anani, 2022

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Playbook for Periviable Consultation

- Situational assessment
  - Elicit parents' current understanding.
  - Re-affirm current knowledge and fill in gaps of obstetrical factions and reason(s) for consult
  - Introduce the role of the NICU and provide reassurance
  - LISTEN
    - what questions do you have?
    - Do you have any previous experience with prematurity?
    - What concerns you the most?

Krakauer & Anani, 2022

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Playbook for Periviable Consultation

- Provide Information
  - What information is most helpful to you?
    - Details or "big picture"
  - Tailor conversation to their needs
  - Talk about role of a parent in the NICU – breast feeding, bedside cares, kangaroo care, involvement with therapy teams

Krakauer & Anani, 2022

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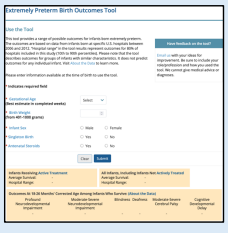
Outcome Tool



- Center specific data is preferred
- NICHD Outcomes calculator can help if center data not available
- ***data from 2006-2012***

NICHD Outcomes Tool

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Playbook for Periviable Consultation

- Decision making
  - Circle back on values
    - "After hearing the information thus far, what is most important to you?"
  - Discuss potential trajectories (intensive care, comfort care, "trial of life") and reassure family all trajectories are loving decisions they are making for their child.
    - "I know this is not easy but understand you do not need to make this decision alone. My role is to help you, and I am happy to provide recommendations as well."
  - Summarize understanding of parents' wishes
  - Reassure family consult is ongoing and can answer any future questions

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Antenatal Factors Impacting Outcomes

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Antenatal Factors Impacting Outcomes

Modifiable
- Antenatal Steroids
- Magnesium
- Mode of Delivery
- Cord management

Not Modifiable
- GA
- Birth weight
- Sex
- Singleton vs Multiple

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Antenatal Factors Impacting Outcomes: ANS

Table 2. Survival Rates, by Gestational Age at Birth

Gestational Age, wk	No. of Survivors/Total No. of Infants (%)		Risk ratio	
	Postnatal Life Support Alone	Postnatal Life Support With ANS Exposure	RR (95% CI)	aRR (95% CI)[a]
22	89/503 (17.7)	210/546 (38.5)	2.17 (1.75-2.70)	2.11 (1.68-2.65)
23	391/1097 (35.6)	2884/5210 (55.4)	1.55 (1.43-1.69)	1.54 (1.40-1.70)
24	667/1119 (59.6)	6640/9312 (71.3)	1.20 (1.14-1.26)	1.18 (1.12-1.25)
25	834/1101 (75.7)	8983/10 925 (83.0)	1.10 (1.06-1.13)	1.11 (1.07-1.14)
22-25	1981/3820 (51.9)	18 717/25 892 (72.3)	1.39 (1.35-1.44)	1.37 (1.32-1.42)

Proactive neonatal treatment at 22 weeks of gestation: a systematic review and meta-analysis

Carl H. Backes, MD, Brian K. Rivera, MD, Leana Pavlek, MD, Lindsey J. Rosr, MD, Molly K. Ball, MD, Eli T. Zettler, BS, Charles V. Smith, PhD, Jeffrey A. Bridge, PhD, Edward F. Bell, MD, Heather A. Frey, MD, MSci

Key findings

The pooled prevalence of survival among live-born infants who were delivered at 22 weeks of gestation and provided proactive neonatal treatment (resuscitation and intensive care) was 29.0% (95% confidence interval, 17.2–41.6; 31 studies.

- Survival (P<.01):
  - ANS: 39%
  - No ANS: 19.5%

Ehret et al. 2018 Backes et al. 2021

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Benefits of Betamethasone

Table 1 Immaturity of organs of normal fetuses at 24 weeks' gestation responsible for morbidity and mortality

Lungs	About 250,000 saccules, no alveoli Poor microvascular development No surfactant Minimal matrix in tissue
Kidneys	Very low renal blood flow and glomerular filtration Low sodium reabsorption Inability to concentrate
Gut	Low digestive enzymes Poorly developed peristalsis
Skin	Minimal cornification Poor barrier function
Brain	Immature respiratory control
Immune system	Inadequate responses to infection

Corticosteroid impact by organ system

- Lung
  - Surfactant production
  - Fluid clearance
  - Improved capillary permeability
  - Mesenchymal thinning
- Brain
  - Enhanced myelination
  - Maturation of BBB
  - Decrease ischemic change
- Skin
  - Keratinization
- Liver
  - Glycogen synthesis
- Intestine
  - Gland and villi maturation
  - Increase protein absorption
  - Enhanced digestion
- Pancreas
  - Enhanced insulin responsiveness
- Kidney
  - Improved filtration, sodium reabsorption, concentrating ability

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Antenatal Factors impacting outcomes: Magnesium

Table 2. Outcomes Assessed at Follow-up.

Outcome	Magnesium Sulfate (N = 1041)	Placebo (N = 1095)	Relative Risk (95% CI)	P Value
	no./total no. (%)			
All pregnancies				
Moderate or severe cerebral palsy or death[a]	118/1041 (11.3)	128/1095 (11.7)	0.97 (0.77–1.23)	0.80
Moderate or severe cerebral palsy alone	20/1041 (1.9)	38/1095 (3.5)	0.55 (0.32–0.95)	0.03
Death alone	99/1041 (9.5)	93/1095 (8.5)	1.12 (0.85–1.47)	0.41
Pregnancies without major congenital anomalies				
Moderate or severe cerebral palsy or death[a]	100/997 (10.0)	117/1060 (11.0)	0.91 (0.71–1.17)	0.47
Moderate or severe cerebral palsy alone	18/997 (1.8)	34/1060 (3.2)	0.56 (0.32–0.99)	0.04
Death alone	83/997 (8.3)	86/1060 (8.1)	1.03 (0.77–1.37)	0.85
Scores on the Bayley Scales of Infant Development				
Psychomotor Development Index <70	134/876 (15.3)	146/919 (15.7)	0.98 (0.79–1.21)	0.83
Psychomotor Development Index <85	299/876 (34.1)	315/919 (34.3)	1.00 (0.88–1.13)	0.95
Mental Development Index <70	165/876 (18.8)	171/919 (18.6)	1.01 (0.83–1.23)	0.90
Mental Development Index <85	406/876 (46.3)	427/919 (46.5)	1.00 (0.90–1.10)	0.96

- Mechanism unclear:
  - BP and normalizing CBF
  - Antioxidant effects
  - Anti-inflammatory effects

Rouse et al. 2008 (BEAM Trial)

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Antenatal Factors impacting outcomes: Magnesium +/- ANS

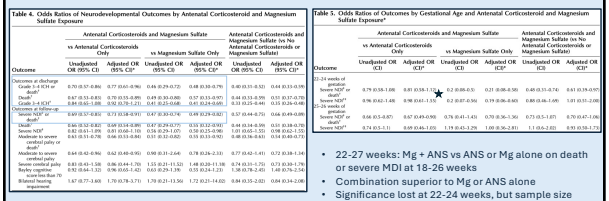

Table 4. Odds Ratios of Neurodevelopmental Outcomes by Antenatal Corticosteroid and Magnesium Sulfate Exposure

Outcome	Antenatal Corticosteroids and Magnesium Sulfate vs Antenatal Corticosteroids Only: Unadjusted OR (95% CI)	Antenatal Corticosteroids and Magnesium Sulfate vs Antenatal Corticosteroids Only: Adjusted OR (95% CI)a	Antenatal Corticosteroids and Magnesium Sulfate vs Magnesium Sulfate Only: Unadjusted OR (95% CI)	Antenatal Corticosteroids and Magnesium Sulfate vs Magnesium Sulfate Only: Adjusted OR (95% CI)a	Antenatal Corticosteroids and Magnesium Sulfate (vs No Antenatal Corticosteroids or Magnesium Sulfate): Unadjusted OR (95% CI)	Antenatal Corticosteroids and Magnesium Sulfate (vs No Antenatal Corticosteroids or Magnesium Sulfate): Adjusted OR (95% CI)a
Outcomes at discharge						
Grades 3 or 4 IVH or death[b]	0.70 (0.57-0.86)	0.77 (0.61-0.96)	0.46 (0.29-0.72)	0.48 (0.30-0.79)	0.40 (0.31-0.52)	0.44 (0.33-0.59)
Death[c]	0.67 (0.53-0.83)	0.70 (0.53-0.89)	0.49 (0.30-0.80)	0.57 (0.33-0.97)	0.44 (0.33-0.59)	0.51 (0.37-0.70)
Grade 3 or 4 IVH[c]	0.84 (0.60-1.18)	0.92 (0.63-1.33)	0.61 (0.32-1.18)	0.61 (0.28-1.32)	0.53 (0.34-0.82)	0.59 (0.36-0.98)
Outcomes at follow-up						
Severe NDI[d] or death[c]	0.69 (0.57-0.83)	0.73 (0.58-0.91)	0.47 (0.30-0.74)	0.49 (0.29-0.82)	0.57 (0.44-0.75)	0.66 (0.49-0.88)
Death[c]	0.66 (0.52-0.82)	0.69 (0.53-0.89)	0.47 (0.29-0.77)	0.55 (0.32-0.93)	0.44 (0.34-0.59)	0.51 (0.38-0.70)
Severe NDI[d]	0.82 (0.61-1.09)	0.91 (0.66-1.24)	0.56 (0.29-1.07)	0.58 (0.25-1.36)	1.01 (0.65-1.55)	0.98 (0.62-1.55)
Moderate to severe cerebral palsy or death[e]	0.63 (0.51-0.78)	0.66 (0.53-0.84)	0.51 (0.32-0.82)	0.55 (0.33-0.92)	0.48 (0.36-0.63)	0.54 (0.40-0.73)
Moderate to severe cerebral palsy[e]	0.64 (0.42-0.96)	0.62 (0.40-0.95)	0.90 (0.31-2.64)	0.78 (0.26-2.33)	0.77 (0.42-1.41)	0.72 (0.38-1.34)
Severe cerebral palsy or GMFCS level 4 or 5[e]	0.83 (0.43-1.58)	0.86 (0.44-1.70)	1.55 (0.21-11.32)	1.48 (0.20-11.18)	0.74 (0.31-1.75)	0.73 (0.30-1.79)
Bilateral hearing impairment	0.92 (0.64-1.33)	0.96 (0.65-1.42)	0.63 (0.29-1.39)	0.53 (0.24-1.23)	1.38 (0.78-2.45)	1.48 (0.76-2.84)

Table 5. Odds Ratios of Outcomes by Gestational Age and Antenatal Corticosteroid and Magnesium Sulfate Exposure[a]

Outcome	Antenatal Corticosteroids and Magnesium Sulfate vs Antenatal Corticosteroids Only: Unadjusted OR (CI)	Antenatal Corticosteroids and Magnesium Sulfate vs Antenatal Corticosteroids Only: Adjusted OR (CI)a	Antenatal Corticosteroids and Magnesium Sulfate vs Magnesium Sulfate Only: Unadjusted OR (CI)	Antenatal Corticosteroids and Magnesium Sulfate vs Magnesium Sulfate Only: Adjusted OR (CI)a	Antenatal Corticosteroids and Magnesium Sulfate (vs No Antenatal Corticosteroids or Magnesium Sulfate): Unadjusted OR (CI)	Antenatal Corticosteroids and Magnesium Sulfate (vs No Antenatal Corticosteroids or Magnesium Sulfate): Adjusted OR (CI)a
22–24 weeks of gestation						
Severe NDI[d] or death[c]	0.79 (0.58–1.08)	0.81 (0.58–1.12)	0.2 (0.08–0.5)	0.21 (0.08–0.58)	0.48 (0.31–0.74)	0.61 (0.39–0.97)
Death[c]	0.96 (0.62–1.48)	0.98 (0.61–1.57)	0.2 (0.07–0.56)	0.19 (0.06–0.60)	0.85 (0.46–1.59)	1.01 (0.51–2.00)
25–26 weeks of gestation						
Severe NDI[d] or death[c]	0.66 (0.5–0.87)	0.67 (0.49–0.90)	0.76 (0.41–1.43)	0.79 (0.36–1.76)	0.73 (0.5–1.07)	0.70 (0.47–1.06)
Death[c]	0.74 (0.5–1.1)	0.69 (0.46–1.03)	1.19 (0.43–3.29)	1.00 (0.36–2.81)	1.1 (0.6–2.02)	0.93 (0.50–1.72)

- 22-27 weeks: Mg + ANS vs ANS or Mg alone on death or severe MDI at 18-26 weeks
- Combination superior to Mg or ANS alone
- Significance lost at 22-24 weeks, but sample size extremely small

Gentile et al. 2020

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Antenatal Factors Impacting Outcomes: Mode of Delivery

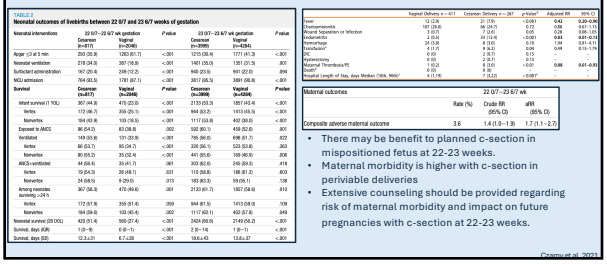

TABLE 2
Neonatal outcomes of livebirths between 22 0/7 and 23 6/7 weeks of gestation

Neonatal interventions	22 0/7–22 6/7 wk gestation: Cesarean (n=817)	22 0/7–22 6/7 wk gestation: Vaginal (n=2046)	P value	23 0/7–23 6/7 wk gestation: Cesarean (n=2995)	23 0/7–23 6/7 wk gestation: Vaginal (n=4284)	P value
Apgar ≤3 at 5 min	269 (35.9)	1283 (61.7)	<.001	1215 (38.4)	1771 (41.3)	<.001
Neonatal ventilation	278 (34.8)	387 (18.8)	<.001	1401 (39.0)	1351 (27.5)	.001
Surfactant administration	197 (25.4)	249 (12.2)	<.001	940 (31.5)	941 (22.0)	.004
NICU admission	764 (93.5)	1741 (87.1)	<.001	2817 (95.5)	3681 (86.8)	<.001
Survival	**Cesarean (n=817)**	**Vaginal (n=2046)**	**P value**	**Cesarean (n=3000)**	**Vaginal (n=4284)**	**P value**
Infant survival (1 YOL)	367 (44.9)	470 (23.0)	<.001	2133 (53.3)	1857 (43.4)	<.001
Vertex	172 (46.7)	356 (75.7)	<.001	944 (63.2)	1413 (65.5)	<.001
Nonvertex	194 (43.9)	103 (16.5)	<.001	1117 (53.8)	422 (30.0)	<.001
Exposed to AMCS	80 (54.2)	83 (38.8)	.002	552 (80.1)	438 (52.8)	.001
Ventilated	149 (53.9)	131 (33.9)	<.001	799 (66.0)	698 (51.7)	.022
Vertex	66 (53.7)	85 (24.7)	<.001	308 (66.1)	533 (53.8)	.063
Nonvertex	80 (55.2)	35 (32.4)	<.001	441 (65.8)	169 (45.9)	.006
AMCS+ventilated	44 (64.4)	35 (41.7)	.081	303 (82.0)	245 (59.3)	.418
Vertex	19 (54.3)	20 (48.1)	.631	115 (58.8)	186 (81.2)	.003
Nonvertex	24 (68.5)	9 (29.0)	.013	193 (83.3)	59 (66.1)	.138
Among neonates surviving >24 h	367 (58.3)	470 (49.8)	.001	2133 (61.7)	1857 (58.9)	.010
Vertex	172 (67.9)	356 (61.4)	.059	944 (81.5)	1413 (68.9)	.109
Nonvertex	194 (59.0)	103 (45.4)	.002	1117 (62.1)	422 (37.0)	.049
Neonatal survival (28 DOL)	429 (51.4)	560 (27.4)	<.001	2424 (80.6)	2149 (50.2)	<.001
Survival, days (IQR)	1 (1–9)	0 (0–1)	<.001	2 (0–114)	1 (0–1)	<.001
Survival, days (SD)	12.3 (±37	6.7 (±26	<.001	186.6 (±43	13.8 (±37	<.001

	Vaginal Delivery n = 671	Cesarean Delivery n = 267	p Value[a]	Adjusted RR	95% CI
Fever	12 (2.0)	21 (7.9)	<0.001	0.41	0.20–0.85
Chorioamnionitis	107 (26.8)	49 (24.7)	0.71	0.98	0.67–1.43
Wound Separation or Infection	3 (0.7)	7 (2.6)	0.05	0.28	0.08–1.03
Endometritis	2 (0.5)	10 (12.9)	<0.001	0.03	0.01–0.13
Hemorrhage	4 (1.0)	8 (3.0)	0.06	0.34	0.11–1.11
Transfusion	4 (1.0)	9 (4.2)	0.04	0.19	0.13–1.14
DIC	0 (0)	2 (0.7)	0.15	–	–
Hysterectomy	0 (0)	2 (0.7)	0.15	–	–
Maternal Thrombosis/PE	1 (0.2)	8 (3.0)	<0.01	0.08	0.01–0.83
Death	0 (0)	2 (0.7)	–	–	–
Hospital Length of Stay, days Median (10th, 90th)[a]	4 (3,14)	7 (5,22)	<0.001[a]	–	–

Maternal outcomes	22 0/7 – 23 6/7 wk		
	Rate (%)	Crude RR (95% CI)	aRR (95% CI)
Composite adverse maternal outcome	3.6	1.4 (1.0–1.9)	1.7 (1.1–2.7)

- There may be benefit to planned c-section in mispositioned fetus at 22-23 weeks.
- Maternal morbidity is higher with c-section in periviable deliveries
- Extensive counseling should be provided regarding risk of maternal morbidity and impact on future pregnancies with c-section at 22-23 weeks.

Cesaru et al. 2021

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Prenatal Factors impacting outcomes: Umbilical Cord Management

- Delayed cord clamping (DCC) is an established intervention proven to reduce mortality, IVH, and BPD
- Concern that non-vigorous extremely preterm infants are harmed by delaying resuscitation with 30-60 seconds of cord clamping
- In such situations, placental transfusion via cord milking provides a more rapid alternative
- Early trials showed no difference in outcomes between the two interventions

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Antenatal Factors Impacting Outcomes: Umbilical Cord Management

- Multi-national RCT DCC vs cord milking 24-31 wks
- Primary outcome: Death OR Severe IVH
- Early trial discontinuation
  - Biggest impact was severe IVH rate – most pronounced at 22-26 weeks
- No difference in other DR interventions to explain outcomes

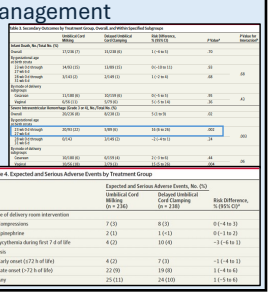

Table 4. Expected and Serious Adverse Events by Treatment Group

	Expected and Serious Adverse Events, No. (%)		
	Umbilical Cord Milking (n = 236)	Delayed Umbilical Cord Clamping (n = 235)	Risk Difference, % (95% CI)[a]
Type of delivery room intervention			
Compressions	7 (3)	8 (3)	0 (−4 to 3)
Epinephrine	2 (1)	1 (<1)	0 (−1 to 2)
Polycythemia during first 7 d of life	4 (2)	10 (4)	−3 (−6 to 1)
Sepsis			
Early onset (≤72 h of life)	4 (2)	7 (3)	−1 (−4 to 1)
Late onset (>72 h of life)	22 (9)	19 (8)	1 (−4 to 6)
Any	25 (11)	24 (10)	1 (−5 to 6)

Kuthethur 2019

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Prenatal Factors impacting outcomes: Umbilical Cord Management

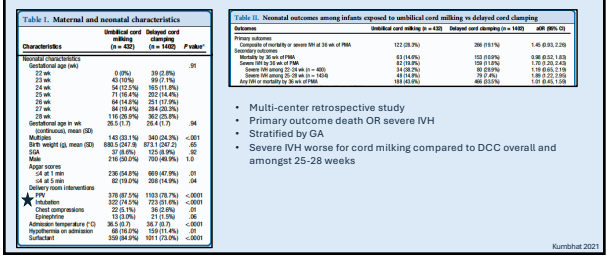

Table 1. Maternal and neonatal characteristics

Characteristics	Umbilical cord milking (n = 422)	Delayed cord clamping (n = 1402)	P value*
Neonatal characteristics			
Gestational age (wk)			.91
22 wk	0 (0%)	39 (2.8%)	
23 wk	43 (10%)	99 (7.1%)	
24 wk	54 (12.5%)	165 (11.8%)	
25 wk	71 (16.4%)	202 (14.4%)	
26 wk	64 (14.8%)	251 (17.9%)	
27 wk	64 (15.4%)	284 (20.3%)	
28 wk	116 (26.9%)	362 (25.8%)	
Gestational age in wk (continuous), mean (SD)	26.5 (1.7)	26.4 (1.7)	.94
Multiples	143 (33.1%)	340 (24.3%)	<.001
Birth weight (g), mean (SD)	880.5 (247.9)	873.1 (247.2)	.65
SGA	37 (8.8%)	125 (8.9%)	.92
Male	216 (50.0%)	700 (49.9%)	1.0
Apgar scores			
≤4 at 1 min	236 (54.8%)	669 (47.9%)	.01
≤4 at 5 min	82 (19.0%)	208 (14.9%)	.04
Delivery room interventions			
PPV	378 (87.5%)	1103 (78.7%)	<.0001
Intubation	322 (74.5%)	723 (51.6%)	<.0001
Chest compressions	22 (5.1%)	36 (2.6%)	.01
Epinephrine	13 (3.0%)	21 (1.5%)	.06
Admission temperature (°C)	36.5 (0.7)	36.7 (0.7)	<.0001
Hypothermia on admission	66 (16.0%)	159 (11.4%)	.01
Surfactant	359 (84.5%)	1011 (73.0%)	<.0001

Table 11. Neonatal outcomes among infants exposed to umbilical cord milking vs delayed cord clamping

Outcome	Umbilical cord milking (n = 422)	Delayed cord clamping (n = 1402)	aOR (95% CI)
Primary outcomes			
Composite of mortality or severe IVH at 36 wk of PMA	122 (28.3%)	396 (28.1%)	1.45 (0.93, 2.26)
Secondary outcomes			
Mortality by 36 wk of PMA	63 (14.6%)	133 (9.5%)	0.98 (0.52, 1.83)
Severe IVH by 36 wk of PMA	82 (19.0%)	199 (14.2%)	1.75 (1.20, 2.43)
Severe IVH among 22–26 wk (n = 400)	34 (38.2%)	80 (28.9%)	1.19 (0.65, 2.19)
Severe IVH among 25–26 wk (n = 1434)	48 (14.8%)	79 (7.4%)	1.88 (1.22, 2.90)
Any IVH or mortality by 36 wk of PMA	151 (43.9%)	466 (33.2%)	1.31 (0.45, 1.59)

- Multi-center retrospective study
- Primary outcome death OR severe IVH
- Stratified by GA
- Severe IVH worse for cord milking compared to DCC overall and amongst 25-28 weeks

Kumbhat 2021

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Neonatal Management

The known, unknown, maybe known, thought to be known, potentially known

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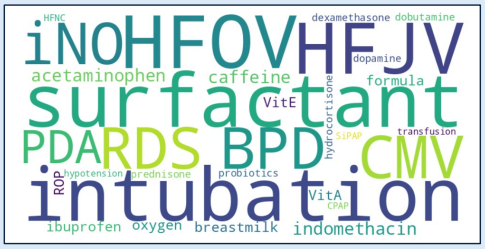

61

"The Known"…or at least "The Studied"

- 400+ systematic reviews
- Protocols for reviews in process
- In-depth analysis with citations for each study in each review
- Not all reviews provide answers…

High frequency jet ventilation versus high frequency oscillatory ventilation for pulmonary dysfunction in preterm infants

Overall: This review found no evidence for comparison of the superiority or harmful side effects of HFJV over HFOV, or of HFOV over HFJV, in infants at risk for or having breathing difficulty due to RDS.

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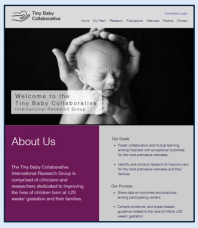
Additional Periviability Resource



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ELBW/Extreme Prematurity Protocols

- Protocols tailored to all infants born <28 weeks or <1kg
  - Antenatal
  - Delivery room
  - Respiratory
  - Feeding
  - Lines
  - Neuro care
- But periviable neonates?

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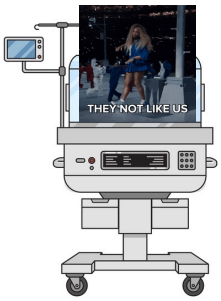

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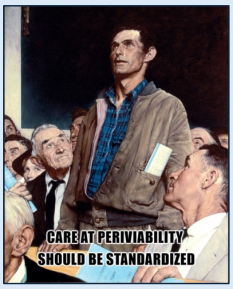

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It's the little things. A framework and guidance for programs to care for infants 22–23 weeks' gestational age

Laura B. Bernardini[1,14], Helen Healy[2,3,4,15], Ashley N. Battarbee[5], Elizabeth Brennick[1], Paige Church[2], Leeann R. Pavlek[6], Thea Tagliaferro[7], Colm Travers[3], Kourtney Vier[8], Jennifer Walsh[1], Matthew A. Rysavy[9] and the Tiny Baby Collaborative Steering Committee*

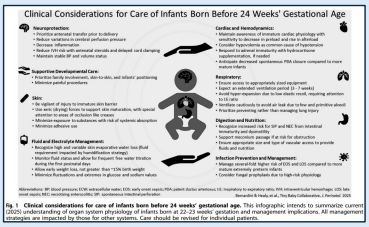

Fig. 1 **Clinical considerations for care of infants born before 24 weeks' gestational age.** This infographic intends to summarize current (2025) understanding of organ system physiology of infants born at 22–23 weeks' gestation and management implications. All management strategies are impacted by those for other systems. Care should be revised for individual patients.

Bernardini & Healy, et al., The Baby Collaborative, J. Perinatol. 2025

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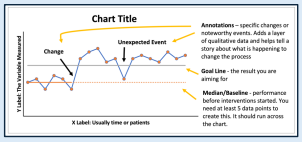
Standardization of Care

- Development of Tiny Baby team
  - OB, MFM, NICU "stakeholders"
- Protocolization of care
  - Based on best available data AND local capabilities/comfort
- Protocolization
  - Learn to do something and do it well
  - Improves outcomes
  - Reduces variability
  - Produces better data for QI



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Standardization of Care

The impact of standardization of care for neonates born at 22–23 weeks gestation

Faris N. Al Ghanaibeh[1,2,10], DonnaMaria E. Cortezzo[3,4,5,6,7], Amy T. Nathan[1,2] and James M. Greenberg[1,2]

Table 4. Morbidities & resource utilization across the study period.

	2015–2017 n = 33	2018–2020 n = 71	2021–2023 n = 66	p value*
Neonates who did not experience early death (n = 170)				
IVH (n = 123)[a]	15 (38%)	29 (69%)	26 (47%)	0.273
Severe IVH (n = 123)[a]	10 (26%)	21 (50%)	17 (31%)	0.754
PDA (n = 170)	20 (61%)	41 (58%)	33 (50%)	0.595
NEC (n = 170)	**8 (24%)**	**8 (11%)**	**5 (8%)**	**0.025**
Neonates who survived (n = 68)				
IVH	10 (32%)	16 (48%)	12 (40%)	
Severe IVH	7 (27%)	10 (26%)	6 (20%)	0.367
PDA	**17 (90%)**	**27 (82%)**	**19 (63%)**	**0.026**
NEC	**8 (32%)**	**4 (12%)**	**2 (7%)**	**0.021**
Grade III BPD	3 (19%)	5 (15%)	2 (7%)	0.299
Severe ROP	5 (26%)	7 (21%)	4 (13%)	0.249
Abdominal Surgery	5 (26%)	4 (12%)	3 (10%)	0.650
Home Oxygen	8 (42%)	14 (42%)	8 (27%)	0.225

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Perspectives of Former Premies

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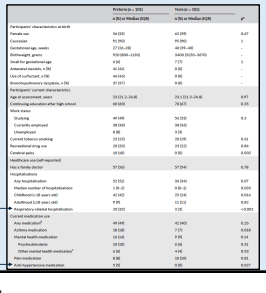
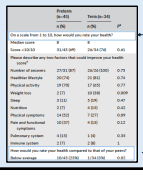
Perspectives of Former Premies



- Study-reported healthcare utilization of former preterm and term individuals –now young adults
- No difference in rating of health BUT
- Former premies more likely to rate their health worse compared to their peers



Girard-Block 2021

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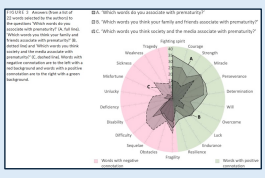
Perspectives of Former Premies



- Full line: self-description
- Dotted line: family description
- Dashed line: society description

Girard-Block 2023

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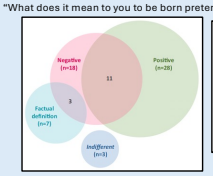
Perspectives of Former Premies

"What does it mean to you to be born preterm?"

I have the impression I should not be alive (if science was not what it was) so I feel I should live my life at a 110% pace and consider myself lucky. I am very dynamic, energetic, determined and have wind under my wings. I feel this "force" and this attitude that "nothing can stop me" comes from a long time ago.
(27-year-old female, with 2 adverse health conditions)

They say I am courageous, a go-getter and a fighter.
(21-year-old male, with cerebral palsy and 2 adverse health conditions)



Being preterm meant more steps to get through. But this helped me become a person who is strong and patient. All the problems I have gone through (medical, at school, etc) are small compared to others who lived through worse. I think it is one of the reasons I became a teacher. I know what it means to have difficulties, pain, anxiety and fear. But in general, I always had doctors who were supportive, and my family helped give me nice life experiences.
(27-year-old female, with 3 adverse health conditions)

Essentially it is a more difficult start than average. But I also consider it like a hurdle that enabled me to acquire (unconsciously) strength and adaptation skills.
(27-year-old female, with 3 adverse health conditions)

Girard-Block 2022

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Parental Perspectives of Former Premies

Box 1 Example of parental quotes for the main themes invoked when describing positive impacts of prematurity on them or their family

Improved outlook on life, such as gratitude and change of perspective (48%)
'My child's a miracle in our lives and his strength and resilience give me strength and resilience'.
'We have a new perspective on life. We focus on what is important'.
'My daughters' birth has helped me learn to focus on the present situation along with learning that nothing is impossible. Seeing, walking, talking and doing something as simple as breathing is just so amazing. We are so lucky'.
'Her courage has helped me gain perspective on what was important and changed my life. We remember every day that all the moments with our children are precious'.
'We no longer take life for granted. We enjoy each and every moment'.
Stronger family relationships (31%)
'Our son made our family and couple much stronger'.
'I feel that we were such a strong team with my husband during the hospital stay. Today, this has made us much stronger in everyday life'.
'I have stronger bonds and connection with my wife'.
'The positive intensity with which I dedicate myself to my family, this has replaced my priorities in the good order, in relationships, at work and other problems…'
'I have learned that I am stronger than I thought, me and my couple'.
The gift of the child (28%)
'Being the parent of this child in a family filled with love'.
'The chance of being his father'.
'She is such a gift, so much love'.
'This child is a miracle. A ray of sun in our lives'.

Box 2 Example of parental quotes for the main themes invoked when describing negative impacts of prematurity on them or their family

Stress and fear (42%)
'The fear of losing them still. The hypervigilance that continues since I left the hospital'.
'I am way more concerned and stressed when she goes sick'.
'The constant fear something will happen to her'.
'They were so fragile. There was so much stress, disappointments and anguish'.
'It was almost traumatic stress. I was there at wat, every day, to save our child'.
'It was a traumatic experience. The fear of my life'.
'It was permanent stress. Fear of death and not doing the right things as a parents'.
Loss of equilibrium due to the child's medical fragility (35%)
'The first year was so difficult. I was so alone and isolated during my maternity leave'.
'The frequent hospital visits, especially during the first year'.
'So many appointments, so many sleepless nights when she is sick'.
'A chaotic family life'.
'So little time for me […] stress on our couple'.
Concerns about developmental outcomes including the child's future (18%)
'Although he is doing amazingly well there is still a lot of anxiety on what the future will hold'.
'I am still concerned about her development, school, the future'.
The child's vulnerability (15%)
'He gets sick so quickly'.
'She is so fragile. We need to stay isolated to avoid infections'.

Table 2 Frequency of most frequent positive and negative themes invoked: impacts in relation to child's level of NDI

Positive impacts			
Most frequent themes invoked	**No NDI n=148**	**Mild-moderate NDI n=61**	**Significant NDI n=47**
Better outlook on life	66 (45)	33 (54)	19 (40)
Stronger family connectedness	53 (36)	15 (25)	11 (23)
Gift of the child	34 (23)	16 (26)	17 (36)
Negative impacts			
Most frequent themes invoked	**No NDI n=125**	**Mild-moderate NDI n=54**	**Significant NDI n=48**
Stress and fear	59 (47)	22 (41)	14 (29)*
Loss of equilibrium	44 (35)	16 (30)	20 (42)
Developmental concerns	21 (17)	11 (20)	14 (29)
Child's vulnerability	15 (12)*	11 (20)	16 (33)*

Data presented as number (%).
248 parents of 213 children participated; they provided 285 individual responses (some parents had twins and triplets). Both parents answered the questionnaire for 71 children; n=256 parent-child answers with main positive themes invoked; n=227 parent-child answers with main negative themes invoked; parents could invoke more than one theme.
*P value <0.05 by logistic regression.
NDI, neurodevelopmental impairment.

Jarvaise et al. 2023

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Questions?

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