Survival at the Edge of Viability

Matthew A. Rysavy MD, PhD
Resident in Pediatrics
University of Wisconsin
Madison, WI

Dr. Rysavy received his MD and PhD in Epidemiology at the University of Iowa in 2015. His thesis was on prognosis in perinatal medicine. Dr. Rysavy is a previous recipient of the New York Academy of Medicine David E. Rogers Fellowship and headed the development of the Evidence-based Medicine curriculum for medical students at the University of Iowa. He is first author of the recent paper "Between-hospital variation in treatment and outcomes in extremely preterm infants" in the New England Journal of Medicine. He is currently a resident in pediatrics at the University of Wisconsin in Madison.

Annual Quality Congress Sunrise Session, Sunday, October 4, 2015
Survival at the Edge of Viability
Objective: Discuss recently published data from the NICHD Neonatal Research Network regarding outcomes for infants born at the margin of viability and the influence of treatment decisions on prognosis statistics.

Key References:
Prognosis for Periviable Birth: Facts, Values, and Decisions
Matthew Rysavy MD, PhD

Disclosures
1. Dr. Rysavy is a resident physician in pediatrics at the University of Wisconsin.
2. He has no financial relationships to disclose.
3. This presentation will not involve discussion of unapproved or off-label, experimental or investigational use of a drug.

Background
Prognosis
• Prognosis = “what to expect”
  – pro = before
  – gnosis = knowing

Prognosis Research
• Interpreted in two lights:
  – For groups — Rates
    “Rate of death after extremely preterm birth is 40 in 100”
  – For individuals* — Risks
    “Risk of death for this extremely preterm infant is 40%”

*For an individual, the rate will be either 0 or 1. Therefore, risk estimated by studying a large group of similar individuals.

Background
There are large differences in mortality among centers in the NICHD Neonatal Research Network (NRN)

Differences in outcomes among hospitals = “center effect”

Stoll BJ et al. Pediatrics 2010;126:443-56
Motivation

Hypothesized that large part of “center effect” results from differences among hospitals in the approach to initiating neonatal active treatment

- Active treatment = any potentially lifesaving treatment after birth (as opposed to comfort care)

Study Description

Participants: Infants born alive at <27 weeks’ gestation at 24 NRN hospitals 2006-2011 (n=4987 infants)

- Included: Inborn liveborn infants, regardless of delivery room resuscitation or admission to NICU
- Excluded: Infants with syndromes or major congenital malformations

Outcomes: Neurodevelopmental impairment (NDI) at 18 to 22 months’ corrected age and mortality before assessment for NDI

- 94% of eligible infants were evaluated at 18-22 months

Analysis: Multivariable hierarchical logistic regression (estimates intraclass correlation coefficient [ICC])

Results

1. Variation in Active Treatment

2. Relationship of Hospital Active Treatment Rate to Outcomes

Results: Variation in Active Treatment

Active treatment varies by gestational age

<table>
<thead>
<tr>
<th>Gestational Age</th>
<th>Proportion of Infants Actively Treated</th>
<th>(95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>22 Weeks</td>
<td>22.1% (18.1-26.8)</td>
<td></td>
</tr>
<tr>
<td>23 Weeks</td>
<td>71.8% (68.5-74.9)</td>
<td></td>
</tr>
<tr>
<td>24 Weeks</td>
<td>97.1% (96.0-98.0)</td>
<td></td>
</tr>
<tr>
<td>25 Weeks</td>
<td>99.6% (98.3-99.8)</td>
<td></td>
</tr>
<tr>
<td>26 Weeks</td>
<td>99.8% (99.4-100)</td>
<td></td>
</tr>
</tbody>
</table>

Results: Variation in Active Treatment

Active treatment varies among hospitals

<table>
<thead>
<tr>
<th>Variance in Active Treatment Attributable to Hospital of Birth (ICC)</th>
<th>Gestational Age</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>22 Weeks</td>
</tr>
<tr>
<td></td>
<td>23 Weeks</td>
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<tr>
<td></td>
<td>24 Weeks</td>
</tr>
<tr>
<td></td>
<td>25 Weeks</td>
</tr>
<tr>
<td></td>
<td>26 Weeks</td>
</tr>
<tr>
<td>22 Weeks</td>
<td>71% (45-88)</td>
</tr>
<tr>
<td>23 Weeks</td>
<td>38% (21-58)</td>
</tr>
<tr>
<td>24 Weeks</td>
<td>23% (6-57)</td>
</tr>
<tr>
<td>25 Weeks</td>
<td>N/A</td>
</tr>
<tr>
<td>26 Weeks</td>
<td>N/A</td>
</tr>
</tbody>
</table>
Results

1. Variation in Active Treatment

2. Relationship of Hospital Active Treatment Rate to Outcomes

Summary of Findings

1. Large variation in initiating treatment for infants born at 22, 23, and 24 weeks’ GA
   — Variation related to hospital of birth and gestational age
2. Increased hospital rates of active treatment associated with increased rates of survival and survival without NDI at 22, 23, and 24 weeks
3. Variation in the approach to active treatment accounts for a large part of the “center effect” on outcome

Importance

1. How do therapy decisions inform prognosis research?
   - Prognosis
   - Diagnosis
   - Therapy

2. Which is the correct prognosis statistic to use in counseling?
   - All infants? Actively treated infants?

Thank you
Prognosis for Periviable Birth: Facts, Values, and Decisions
Matthew Rysavy MD, PhD

What’s Important About This for Patients?

Outcomes after live birth at 22 weeks

<table>
<thead>
<tr>
<th>Outcome</th>
<th>All liveborn infants</th>
<th>Actively treated infants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Survival</td>
<td>5.1%</td>
<td>23.1%</td>
</tr>
<tr>
<td>Survival without severe impairment</td>
<td>3.4%</td>
<td>15.4%</td>
</tr>
<tr>
<td>Survival without moderate or severe impairment</td>
<td>2.0%</td>
<td>9.0%</td>
</tr>
</tbody>
</table>

Active Treatment Definition

Active treatment (neonatal, not obstetric) was defined as receipt of at least one of the following:
- Chest compressions
- Epinephrine
- CPAP or bag-valve-mask ventilation
- Tracheal intubation
- Mechanical ventilation
- Parenteral nutrition

Neurodevelopmental Impairment (NDI) Definition

- **Severe NDI** defined as 1 or more:
  - Bayley-III cognitive score <70
  - Bayley-III motor score <70
  - Severe cerebral palsy
  - Gross Motor Function Classification System Level 4 or 5
  - Bilateral blindness
  - Severe hearing impairment (not correctable with amplification)
- **Moderate NDI** defined as 1 or more:
  - Bayley-III cognitive score 70-84
  - Bayley-III motor score 70-84
  - Moderate cerebral palsy
  - Gross Motor Function Classification System Level 2 or 3

Rates of Active Treatment by GA Day

Methods: Statistical Analysis

- Multivariable hierarchical logistic regression
  - Accounts for clustering among hospitals
  - Adjusts for individual-level characteristics
    - Maternal age
    - Private health insurance
    - Prenatal care
    - Birth weight
    - Infant sex
    - Race/ethnicity
    - Maternal hypertension, preeclampsia or eclampsia
    - Maternal diabetes
    - Chorioamnionitis
    - Plurality
    - 1-minute Apgar score
    - Antenatal corticosteroids
Survival at the Edge of Viability

Joe Kaempf MD
Neonatologist
Chair, Evidence Based Medicine
and Clinical Research
NICU and Women and Children’s Program
Providence St. Vincent Medical Center
Portland, OR

Joe Kaempf MD trained in Pediatrics at the Johns Hopkins Hospital and in Neonatal Perinatal Medicine at the University of Colorado Health Sciences Center. He is currently a member of Northwest Newborn Specialists, and the chair of Evidence Based Medicine and Clinical Research for NNS and the Providence St. Vincent Medical Center NICU and Women and Children’s Program in Portland, OR. Joe has been a co-investigator in several collaborative RCTs, and dozens of NICU CQI projects over the past 25 years, and particularly has enjoyed working with his many excellent Vermont Oxford Network colleagues; friendships that are particularly important. Joe’s special interest is periviability dialogue, composite CQI metrics and outcomes analysis, with a particular passion for cognition, philosophy, and writing.

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Objective: Discuss recently published data from the NICHD Neonatal Research Network regarding outcomes for infants born at the margin of viability and the influence of treatment decisions on prognosis statistics.
Peri viability Shared Decision Making at 22 to 26 Weeks
18 year Single Center Experience

Joe Kaempf MD

I have no financial or commercial conflicts of interest to disclose.

Sample 100 Infants 23 to 24 Weeks in the VON - 2014
88 were resuscitated
47 survived to discharge
20 will have significant NDI
14/27 w/o NDI will have neurobehavioral, educational, and social impairments

So,.....just 13 of the original 88 resuscitated infants will achieve full neurodevelopmental health.

Value Pluralism
Human values are irreducibly diverse, often conflicting, and ultimately incommensurable.
Fundamental tenets of right and wrong are context dependent and hugely arguable within the multiform cultures and circumstances in which we live.

When important values and ethical principles come into conflict – as they often do with premature births – resolution cannot occur by arbitrary rules, or theoretic reason, or compulsion, or physician bias and belief.
Value Pluralism is not relativism, it recognizes that there is no ultimate moral harmony, that conflicts do arise that ultimately cannot be reasoned or adjudicated without the risk of applying arbitrary power differentials, or worse, experimentation.

Moral tenets should not have a hierarchical structure because there are beliefs, goods, and ethical dilemmas without a common currency for measurement.

Shared Decision Making Model
Palliative care at 22 wks
NICU care at 26 wks
Informed Choice at 23, 24, and 25 wks
1996 to 2013
606 live births 22 0/7 - 26 6/7 weeks

138 infants palliative comfort care
22 0/7 - 25 6/7 weeks
1996 – 2013
Not a single complaint/concern/regret communicated to us related to PCC choice from the pregnant woman

Our authentic intendment at Providence is to help clarify what the meaning of extremely premature birth is to the pregnant woman and family, not to negotiate “best interest models” or establish “moral truth”.

18 Years of Shared Decision Making
PSVMC Survival if Resuscitated (N.S. compared to VON):
N/A 21% 59% 78% 87%
PCC ( ) ~70* ~20* ~5* <2 <1
*P < 0.001 compared to PSVMC

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Joe Kaempf MD

AAP Committee on Fetus and Newborn
Antenatal Counseling Regarding Resuscitation and Intensive Care Before 25 Weeks Gestation

1. Peri viability decisions should be consonant with the parents’ wishes
2. In most cases the approach should be shared decision making
3. The primary goal of antenatal counseling is to provide parents with information that will aid their decision making

Roger Soll commentary on Rysavy et al, NEJM NICHD outcomes report:
“…..even with [active] intervention, rates of mortality and morbidity were high with only 9% of these [22 week] infants surviving without moderate or severe impairment, calling into question whether this should be the next important frontier for neonatal intensive care.”

JAMA, September 2015

Physician Conflicts of Interest
Line of Demarcation
Normative Sociology
Risk vs. Uncertainty
Multicultural population, diverse religious beliefs, varied socioeconomic groups
Evidence-based medical decision making vs. moral, religious, and personal choices

Some things are simply the right thing to do yesterday,….today,….and tomorrow.
Breast Feeding
Hand Washing
Skin-to-Skin Kangaroo Care
Shared Decision Making with Parents

References
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Keith J. Barrington MB, ChB
Neonatologist and Clinical Researcher
Sainte Justine University Health Centre
Professor of Pediatrics
University of Montreal
Montreal, Quebec, Canada

Keith J. Barrington is a neonatologist and clinical researcher at Sainte Justine University Health Center in Montréal. He is Professor of Paediatrics at the University of Montréal. He was formerly chair of the Society of Neonatologists of Québec. His particular research interests are in cardiovascular support, in apnea and its treatment, in the ethics of decision making for high risk newborns, and in anything in clinical care that might affect outcomes.

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