Outcomes of infants born at 22-25 weeks’ gestation

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Disclosures

I have no financial conflicts of interest to disclose or resolve
Objectives

At the end of my talk, the learner should be able to:

• Understand the short and long-term outcomes of neonates delivered at a periviable gestation
Periviable Deliveries

- Approx 0.5% of all births occur before the 3rd trimester of pregnancy
- ~12000 babies/yr in the US  
  Martin, NCHS Data Brief 2014
- ACOG, AAP, CPS “make individualized decisions with shared decision making”  
  Cummings, Pediatrics 2015; Raju, J Ob Gyn 2014; Jeffries, Ped Child Health 2012
Survival and (short) Long Term Outcomes

Well, we're both fruit.
## Survival at Extremely Low Gestational Age

<table>
<thead>
<tr>
<th>Study Name, Location, Year at birth, Type of Study</th>
<th>% survive 22 wks</th>
<th>23 wks</th>
<th>24+ wks</th>
</tr>
</thead>
<tbody>
<tr>
<td>NICHD (US, 2006-2011, multicenter)</td>
<td>23</td>
<td>33</td>
<td>57</td>
</tr>
<tr>
<td>VON (US, 1998-2003, multicenter)</td>
<td>4</td>
<td>38</td>
<td>70</td>
</tr>
<tr>
<td>Victoria (AUS, 2005, population based)</td>
<td>3</td>
<td>20</td>
<td>75</td>
</tr>
<tr>
<td>EPIBEL (Belgium, 1999-2000, population-based)</td>
<td>0</td>
<td>2</td>
<td>50</td>
</tr>
<tr>
<td>EPICure (UK, 1995, population-based)</td>
<td>1</td>
<td>10</td>
<td>35</td>
</tr>
<tr>
<td>EPIPAGE (France, 1997, population-based)</td>
<td>0</td>
<td>0</td>
<td>59</td>
</tr>
<tr>
<td>Essen (Germany, 2000-4, hospital-based)</td>
<td>20</td>
<td>33</td>
<td>71</td>
</tr>
<tr>
<td>ETFOL (Denmark, 1994-5, population-based)</td>
<td>0</td>
<td>56</td>
<td></td>
</tr>
<tr>
<td>New South Wales + AUS Capital Territory (AUS, 2007-2011, population-based)</td>
<td>27</td>
<td>60</td>
<td></td>
</tr>
<tr>
<td>EXPRESS Group (Sweden, 2004-7, population-based)</td>
<td>12</td>
<td>54</td>
<td>71</td>
</tr>
<tr>
<td>CNN (Canada, 2013, multicenter)</td>
<td>7</td>
<td>34</td>
<td>62</td>
</tr>
<tr>
<td>Japan NRN (Japan, 2003-5, multicenter)</td>
<td>36</td>
<td>63</td>
<td>81</td>
</tr>
<tr>
<td>Cologne (Germany, 2010-14, hospital-based)</td>
<td>65</td>
<td>72</td>
<td></td>
</tr>
</tbody>
</table>
## ND Outcomes at 18-36 months

<table>
<thead>
<tr>
<th>Study</th>
<th>Death or Neurodevelopmental Impairment (%)</th>
<th>22 weeks</th>
<th>23 weeks</th>
<th>24+ weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>NICHD (US, 18-22 mo, 2007-2011, multicenter)</td>
<td>(84)</td>
<td>(74)</td>
<td>(54)</td>
<td></td>
</tr>
<tr>
<td>VON (US, 18-24 mo, 1998-2003, multicenter)</td>
<td>515/528 (98)</td>
<td>679/916 (74)</td>
<td>1401/3033 (46)</td>
<td></td>
</tr>
<tr>
<td>Victoria (AUS, 24 mo, 2005, population-based)</td>
<td>-</td>
<td>-</td>
<td>196/288 (68)</td>
<td></td>
</tr>
<tr>
<td>EPIBEL (Belgium, 30-42 mo, 1999-2000, population-based)</td>
<td>28/28 (100)</td>
<td>40/41 (98)</td>
<td>142/182 (78)</td>
<td></td>
</tr>
<tr>
<td>EPICure (France, 24 mo, 1997, population-based)</td>
<td>137/138 (99)</td>
<td>230/241 (95)</td>
<td>661/806 (82)</td>
<td></td>
</tr>
<tr>
<td>Essen (Germany, 24-30 mo, 2000-4, hospital-based)</td>
<td>9/10 (90)</td>
<td>12/18 (67)</td>
<td>22/55 (40)</td>
<td></td>
</tr>
<tr>
<td>ETFOL (Denmark, 24 mo, 1994-5, population-based)</td>
<td>-</td>
<td>37/37 (100)</td>
<td>206/349 (59)</td>
<td></td>
</tr>
<tr>
<td>Japan NRN (Japan, 36 mo, 2003-5, multicenter)</td>
<td>60/75 (80)</td>
<td>156/245 (64)</td>
<td>267/737 (36)</td>
<td></td>
</tr>
</tbody>
</table>

All values represent % of survivors evaluated
NDI = CP level 2-5, hearing or visual impairment or DQ < 70

Rysavy NEJM. 2015
Cologne Follow-up at 2 yrs’ corrected age

• Available for 32 infants (of the 58 survivors born at 22-23 weeks GA)

• 50% with normal development (Bayley)

• Of the 16 with developmental delay:
  – 7 (44%) with minor disabilities
  – 9 (56%) with severe disabilities

One in four infants (25%) born at 22 or 23 weeks of gestation who received active care at this single-center, survived the neonatal period without severe complications but 1/3 were severely impaired

Why the Variation in Outcomes?
Is it the moms?
# Maternal Demographics

<table>
<thead>
<tr>
<th></th>
<th>US</th>
<th>Japan</th>
<th>Germany</th>
</tr>
</thead>
<tbody>
<tr>
<td>Homogenous population</td>
<td>No</td>
<td>Yes</td>
<td>Mostly, but immigrants ↑ prematurity</td>
</tr>
<tr>
<td>Healthy pre-pregnancy weight %</td>
<td>53</td>
<td>71</td>
<td>72</td>
</tr>
<tr>
<td>Gestational Diabetes %</td>
<td>2.7-6.8</td>
<td>1.8</td>
<td>1.9-5.3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>NICHD</th>
<th>Japan NRN</th>
<th>Cologne</th>
</tr>
</thead>
<tbody>
<tr>
<td>Teen mom %</td>
<td>13-18%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean maternal age (yrs)</td>
<td></td>
<td></td>
<td>31-32</td>
</tr>
</tbody>
</table>

Rysavy NEJM. 2015  
Variation – Is it the doctors and nurses?
Resident and RN views on resuscitation

- June-October 2002 Québec, Canada
- Survey of
  - 172 Ob/Gyn and Peds residents
  - 136 RNs McGill University Health Centre involved in any neonatal care
- Asked if they would resuscitate in the delivery room:
  - An AGA depressed infant at 24 weeks gestation
  - A preterm infant with 50% predicted survival and if survives, 50% chance normal development and 20-25% chance serious handicap
Respondents who would always resuscitate
Variability in Resuscitation at the Limit of Viability

- 2012 survey AAP neonatologists
- 637 completed surveys (30% response)
- 68% considered 23-week gestation to be the youngest age that should be resuscitated at parental request
- 51% felt that 25-week gestation is the youngest age of obligatory resuscitation even with parental refusal.
Approaches to Periviable Counseling

- Indiana University study with 16 Obs and 15 Neos (faculty and fellows) who consented to participate

- Video encounter with standardized patient: 31 yo with PPROM, not yet laboring at 23 weeks GA

- Analyzed for content (dx, prognosis, steroids, mode of delivery)

- Qualitative analysis of “themes” that emerged
## Complimentary Counseling

<table>
<thead>
<tr>
<th></th>
<th>Obstetricians (%)</th>
<th>Neonatologists (%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk to mom</td>
<td>88</td>
<td>27</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Classical cesarean</td>
<td>63</td>
<td>7</td>
<td>0.005</td>
</tr>
<tr>
<td>Antibiotics</td>
<td>69</td>
<td>20</td>
<td>0.005</td>
</tr>
<tr>
<td>Neonatal complications</td>
<td>44</td>
<td>87</td>
<td>0.044</td>
</tr>
<tr>
<td>Neonatal Resuscitation</td>
<td>69</td>
<td>100</td>
<td>0.024</td>
</tr>
<tr>
<td>Palliative/comfort care</td>
<td>56</td>
<td>93</td>
<td>0.036</td>
</tr>
</tbody>
</table>

Tucker Edmonds J Perinatol 2015
Steroids

- When posed with questions from the standardized patient, both Ob and Neo frequently deferred management conversation to the other specialty.

- Neo-8: “I think the obstetrician needs to talk to you about (steroids)...I don’t want to tell you what the obstetrician is going to do because once again I say one thing and they say something else then you are in the middle and will be really confused.”

- OB-2: “Again, (regarding steroids) because I’m not the primary provider for the baby, I always consult with the intensive care unit neonatologists who are experts at caring for babies at this gestational age.”
## Obstetrical Approach

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<th>Cologne</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any antenatal steroids % at 22 weeks</td>
<td>28</td>
<td>21</td>
<td>93</td>
</tr>
<tr>
<td>Any antenatal steroids % at 23 weeks</td>
<td>67</td>
<td>32</td>
<td>92</td>
</tr>
<tr>
<td>C/S delivery % at 22 weeks</td>
<td>11</td>
<td>42</td>
<td>75</td>
</tr>
<tr>
<td>C/S delivery % at 23 weeks</td>
<td>26</td>
<td>42</td>
<td>84</td>
</tr>
</tbody>
</table>

Rysavy NEJM. 2015
NICHD Rates of Active Treatment by GA

Active treatment included any:
- Surfactant
- Intubation
- Ventilatory support
- Parenteral nutrition
- Epinephrine
- Chest compressions
Eugenics Protection Act Japan

- Review of maternal and infant health system and vital statistics
- Survival rate ELBW infants increased to over 80%
- Viability limit defined by the Eugenic Protection Act was amended in 1991 from 24 to 22 completed weeks of gestation
Osaka Medical Center and Research Institute for Maternal and Child Health - 2009
Mortality 2001-2005

• By Gestational Age
  – 22-23 wk 12%
  – 24-25 wk 12%
  – 26-27 wk 4%
  – Does not include DR deaths

• By Birth Weight
  – <500 gm 52%
  – 500-749 gm 15%
  – 750-999 gm 5%

• No bilateral grade IV IVH in past 5 yrs
Delivery Room Resuscitation - Osaka

- Meticulous, well orchestrated approach
- The infant is the priority
- NICU RN prepares medications & drips (dopamine, dobutamine, calcium infusion, phenobarbital and 5% albumin)
- Neonatologists - 2 attendings at all deliveries
  - Incubator
  - Ventilator, battery, tanks
  - Catheters – PIV, PAL, PICC
  - Medications/drips
Resuscitation Room Characteristics

- Cesarean section delivery in far room
- Baby brought by nurse through double doors into resuscitation room
- Temp in resuscitation room 32°C (= 90°F)
- Special “walls” provide additional heat for the premature infant
Resuscitation Video Clips – 23 and 28wk

• Sequence of resuscitation procedures nearly identical

• 1st Two minutes of life:
  – Weigh baby first, then place on radiant warmer
  – Dry, stimulate, suction oropharynx
  – Pulseox probe, monitor leads, OG tube - gastric aspirate

• Minutes 2-10 of life:
  – Doctor 1 is testing for surfactant deficiency
  – Doctor 2 is performing intubation
  – ETT taped at 3 min 45 sec.
  – Surfactant administered at 4 min 40 sec.
  – Baby placed on ventilator just after 9 min of life
• Minutes 11-20 of life
  – Doctor 1 – obtains **PIV** access
  – Doctor 2 – places **PAL** at 12 min of life. Draw Labs
  – Doctor 1 – places double lumen **PCVL** by 14:40 min of life.

• Minutes 20-60 of life
  – IV fluids and drug infusions started. Phenobarb given.
  – **Echocardiogram** by neonatologist
  – Followed by **head ultrasound** by neo to document IVH
  – **Skin-to-skin contact** between mother and baby occurs after mother’s surgery completed (infection prevention)
  – Baby moved to incubator, on ventilator
  – Finally incubator, ventilator, battery, tanks, IV pumps all **transported to NICU**.
Cologne Patients

Active care
86/106 = 81%
## Box. Key Features of Active Prenatal and Postnatal Care at University of Cologne Medical Centre.

- Use of prenatal steroids after parental counseling from 22 weeks of gestation
- Cesarean delivery with local anesthesia as preferred mode of delivery
- Delayed cord clamping
- Comfort positioning (lateral) of the infant
- Establishment of spontaneous breathing via a stepwise increase in positive end-expiratory pressure
- Less invasive surfactant application
Cologne Limitations

• Single center experience, might not be applicable or transferrable to other centers
• Outcomes data refer to infants who received active care (not to entire population that includes 19% who opted for palliative care)
• Neurodevelopmental outcomes data missing for some patients; may be overestimating results
• Preference for c/s deliveries puts mothers at higher risk with unclear benefit for infant
Outcomes in Adulthood
Worldwide at 19 yrs or older:

- Cerebral palsy 6.2-13.4%
- Blindness 0-13% (before laser surgery)
- Deafness 0-7%
- Lower educational achievement
- Lower job related income
- More social welfare/disability assistance
- More living at home with parents
- More delays in onset of sexual activity, marriage or cohabitation, and reproduction
- Higher prevalence of chronic, physical and mental health issues
- Many of these differences persist into the 4th decade of life
What information to provide patients re: outcomes?

- Significant variation in rates of survival between studies and countries
- Results from other centers/countries may not be applicable (context, resources)
- NICHD Neonatal Research Network: Extremely Preterm Birth Outcome Data website calculator.
  - Not predictive of individual outcomes, ie. An infant’s trajectory may quickly diverge from the prenatal population on which predictions are based (sepsis, hypotension, IVH, etc)
  - Useful predicting survival, but overestimates rates of severe disability

Andrews JPediatr 2016
Counseling Patients

• Institution statistics may be more meaningful than network data or published studies

• Frank discussions between OB and Neonatology before counseling patients, including whether or not to offer antenatal steroids, operative delivery

• Consider an “Active Care Bundle” to be offered to patients who desire “everything be done” to optimize outcomes
Preemie Voices

• Collection of short essays by young men and women born very prematurely describing their lives, challenges and achievements
• Born 1977-1982 Ontario, Canada
• All < 1000 gm at birth
• www.preemievevoicesbook.com
Preemie Voices

• Video clip
References