EXTREMELY LOW BIRTH WEIGHT

Ethical aspects in the care and study of infants at the borderline of viability

Stephen Baumgart, MD
Division of Neonatology
Department of Pediatrics

Hippocrates

Children born at the 8th month are not so viable as at the 7th

The father of medicine as envisioned by a Byzantine artist

Hebrew Tradition

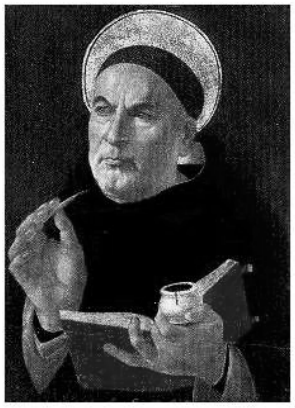
- **Naming on the 8th day**
- **Circumcision is performed symbolizing the covenant between Abraham and God**
- **Death at 40 days remains "stillborn"**

Hebrew Tradition

On family values

“The Jews see to it that their numbers increase. It is a deadly sin to kill a born or unborn child, and they think that eternal life is granted to those who die in battle or execution.”

Roman Historian TACITUS, A.D. 56-117



St. Thomas Aquinas

[1227-1274]

At the 25th week, infants assume human appearance, and the Holy Spirit enters in

Pius IX

[1792-1878]

Doctrine of Immaculate Conception, life begins at conception

In the Constitution *Ineffabilis Deus* of 8 December, 1854, Pius IX pronounced and defined that the Blessed Virgin Mary "in the first instance of her conception, by a singular privilege and grace granted by God, in view of the merits of Jesus Christ, the Saviour of the human race, was preserved exempt from all stain of original sin."

The Last Century

- 1930 ***American Academy of Pediatrics*** recognizes premature birth as other than a lethal birth defect (***weaklings***)
- 1950 ***World Health Organization*** defines prematurity as birth at a ***weight*** <2,500 grams
- 1980 United States Government commissions ***cost*** accounting of medical technologies applied to premature infants

"Melissa"

born 1980 at 23-5/7 wks, 530 grams

- Neonatology has become a new sub-specialty of Pediatrics
- NICU's are built
- Fertility medicine creates "special" babies

Recognize a Moral Issue

- ***Moral*** – Pertaining to the principles of ***right and wrong***; right conduct, or virtue
- ***Ethical*** – Conforming to ***accepted principles*** of right and wrong, especially those governing the conduct of a profession, as medicine
- A ***moral conflict*** goes deeper than ***legal or institutional concerns***; deals with dignity, rights, and future hopes

Principles

- ***Autonomy*** **– Respect infant *and* parent**
- ***Nonmaleficence*** **– "*Primum non nocere*"**
- ***Beneficence*** **– "Do the right thing"[Spike Lee, 1989]**
- ***Justice*** **– Is cost to society justified?**
- ***Truth*** **– Don't try to protect parents**
- ***Medical futility*** **– Are risks/benefits of intervention disproportionate?**
  - ***May reach consensus***
  - ***Never reach unanimity***

Duty – Formalist Approach

Emannuel Kant [1724-1804]

- **Looks at the nature of the act itself (medical intervention), and at duties (to preserve life), and at rights (infant and parent to receive care)**
- **Consequences (outcomes) are irrelevant, or of minor consideration**

Utilitarianism – Consequentialist Approach

John Stuart Mill [1806-1873] and Jeremy Bentham [1748-1832]

- **Looks only at consequences to determine ethical acceptability**
- **But, you must assess *all* possible consequences (*both* good and bad)**

Casuistry – Testing Proportionality

Case-based Ethics

- How do risks and benefits compare?
- Are they proportionate or disproportionate?
- How have similar cases been treated in the past?
- What were the outcomes?
- How does this case differ from past cases?

Published Guidelines for Pediatric End-of-Life Decisions

Solomon, et al, Pediatrics;116:2005

- 1. Though distressing, the distinction between witholding and withdrawing life support is moot.
- 2. Medically supplied food and fluids can be stopped, like any intervention, when their burdens outweigh their benefits.
- 3. Opioids are appropriate for pain, even if hastens death: Research shows respiratory depression rare when titrated properly even at high doses.
- 4. Paralytic agents should never be initiated during the withdrawal of life-support.
- 5. Brain death criteria, like cardiac cessation does not require family's permission for withdrawal of ventilator support.
- 6. Dead-donor rule, *not* permanently unconscious.

Relevant Information

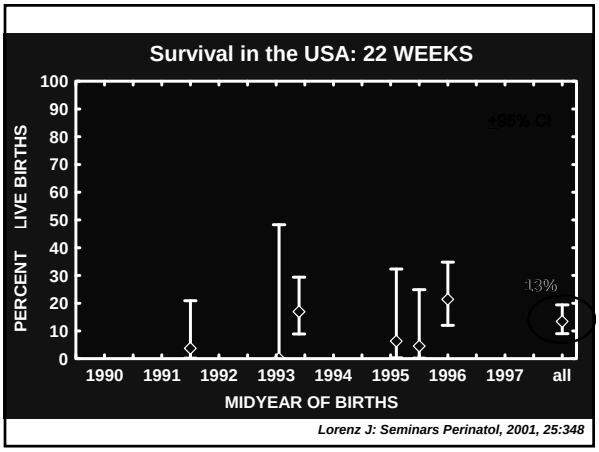
- Mortality/survival rates
- Long-term outcomes — functions limited, health related quality of life (HRQL)
- Effects on the Family
- Economics — cost to families & to society

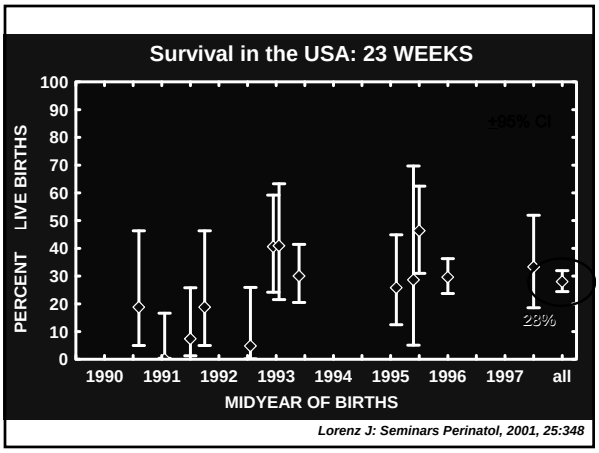
Outcomes in ELBW Babies

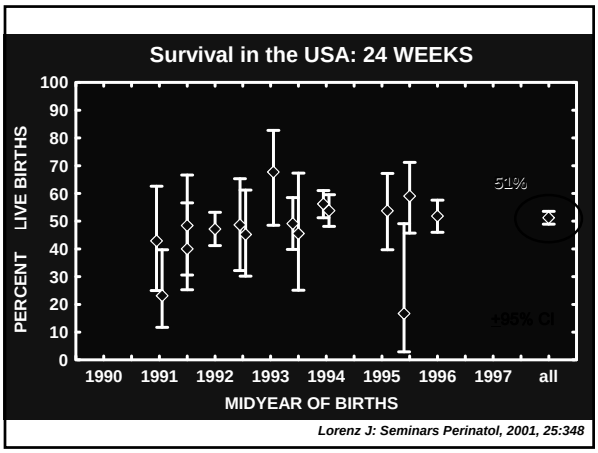
Lorenz J: Seminars Perinatol 2001, 25:348

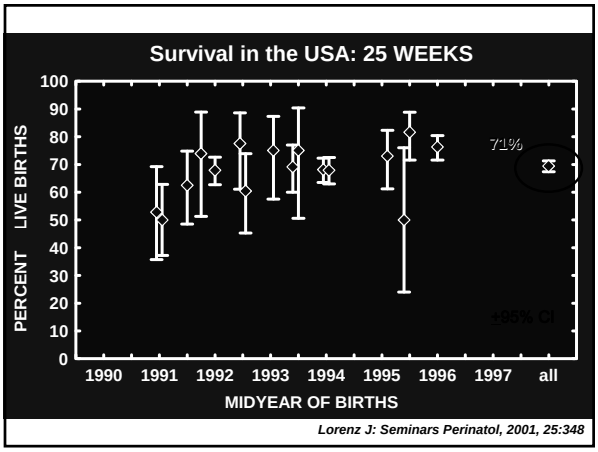
- **English literature 1970 through 2000**
- **Reporting mortality and developmental outcome for infants <27 weeks GA**
- **Direct examination and formal testing of >75% of survivors at ≥18 months of age**

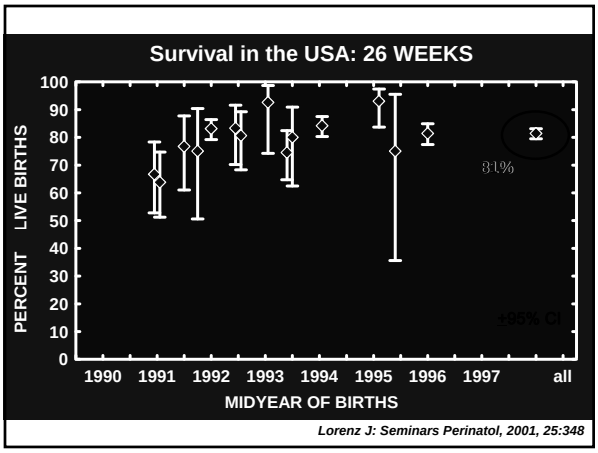
⇒ **26 reports of 30 cohorts**






Survival in the USA: 24 WEEKS
PERCENT LIVE BIRTHS
100
90
80
70
60
50
40
30
20
10
0
51%
±95% CI
1990 1991 1992 1993 1994 1995 1996 1997 all
MIDYEAR OF BIRTHS
Lorenz J: Seminars Perinatol, 2001, 25:348


Survival in the USA: 25 WEEKS
PERCENT LIVE BIRTHS
100
90
80
70
60
50
40
30
20
10
0
71%
±95% CI
1990 1991 1992 1993 1994 1995 1996 1997 all
MIDYEAR OF BIRTHS
Lorenz J: Seminars Perinatol, 2001, 25:348


Survival in the USA: 26 WEEKS
PERCENT LIVE BIRTHS
100
90
80
70
60
50
40
30
20
10
0
81%
±95% CI
1990 1991 1992 1993 1994 1995 1996 1997 all
MIDYEAR OF BIRTHS
Lorenz J: Seminars Perinatol, 2001, 25:348

Summary, Survival of the Extremely Premature Newborn Infant

North American studies, 1990's

Gestation	Mean	Range
22 weeks	13 %	0 – 21 %
23 weeks	28 %	0 – 46 %
24 weeks	51 %	17 – 68 %
25 weeks	71 %	50 – 82 %
26 weeks	81 %	74 – 93 %

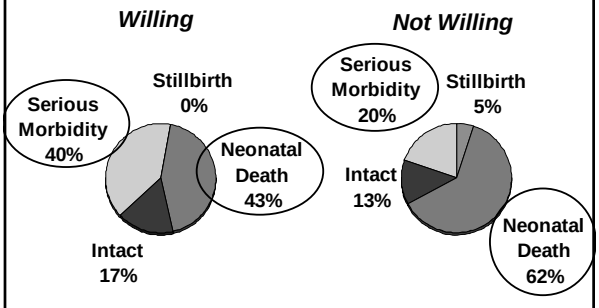
Lorenz J: Seminars Perinatol, 2001, 25:348

Marked Variability in Rates of Disabilities for Survivors

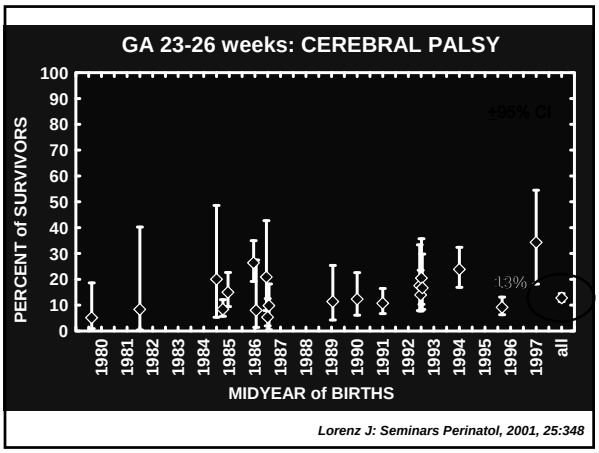
- Chance – only 7 cohorts with >100 survivors
- Heterogeneity among cohorts
- Heterogeneity in criteria for defining disabilities
- Heterogeneity in perinatal morbidities associated with increased risk
- Variations in perinatal/neonatal management (aggressive *vs* passive)

Neonatal Outcomes

Obstetrician's willingness to intervene

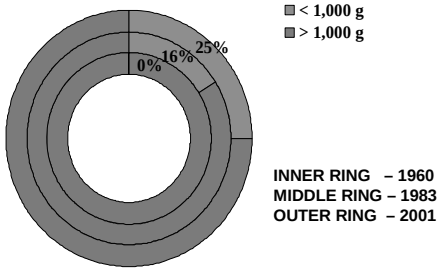


Bottoms S: MFMU-AJOG 1997



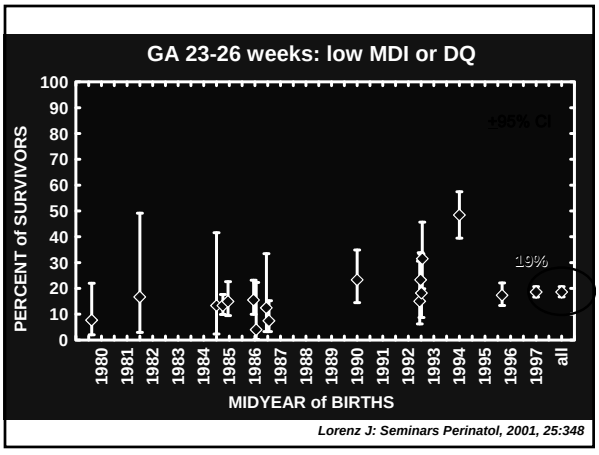
Lorenz J: Seminars Perinatol, 2001, 25:348

THE INCREASING PROPORTION OF CP FROM ELBW INFANTS

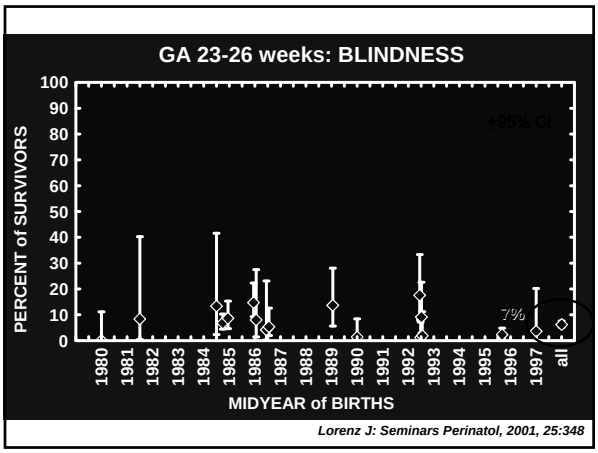


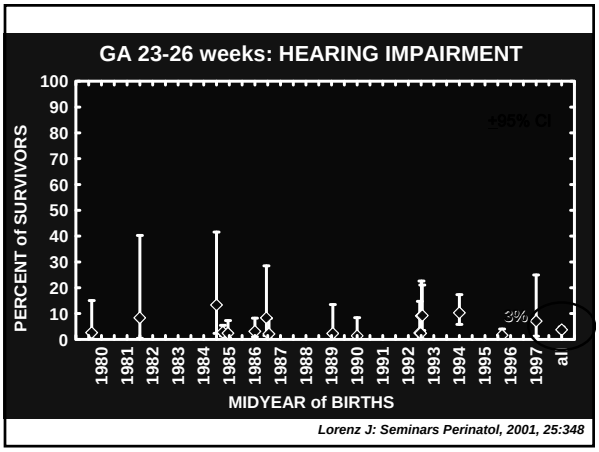
INNER RING – 1960
MIDDLE RING – 1983
OUTER RING – 2001

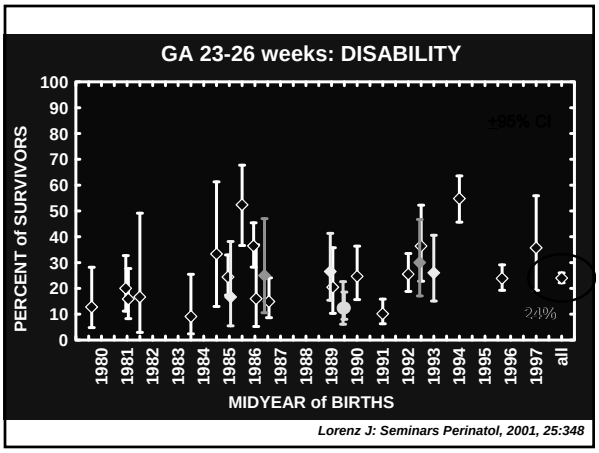
Lorenz J: Seminars Perinatol, 2001, 25:348



Lorenz J: Seminars Perinatol, 2001, 25:348


GA 23-26 weeks: BLINDNESS
PERCENT of SURVIVORS
100
90
80
70
60
50
40
30
20
10
0
±95% CI
7%
1980
1981
1982
1983
1984
1985
1986
1987
1988
1989
1990
1991
1992
1993
1994
1995
1996
1997
all
MIDYEAR of BIRTHS
Lorenz J: Seminars Perinatol, 2001, 25:348


GA 23-26 weeks: HEARING IMPAIRMENT
PERCENT of SURVIVORS
100
90
80
70
60
50
40
30
20
10
0
±95% CI
3%
1980
1981
1982
1983
1984
1985
1986
1987
1988
1989
1990
1991
1992
1993
1994
1995
1996
1997
all
MIDYEAR of BIRTHS
Lorenz J: Seminars Perinatol, 2001, 25:348


GA 23-26 weeks: DISABILITY
PERCENT of SURVIVORS
100
90
80
70
60
50
40
30
20
10
0
±95% CI
24%
1980
1981
1982
1983
1984
1985
1986
1987
1988
1989
1990
1991
1992
1993
1994
1995
1996
1997
all
MIDYEAR of BIRTHS
Lorenz J: Seminars Perinatol, 2001, 25:348

Summary of Outcomes Research in ELBW Babies

Gestational age, weeks	Death[1]	Survival *with* disability[2]	Survival *without* disability
22	87 %	?	?
23	72 %	11 %	17 %
24	49 %	18 %	33 %
25	31 %	19 %	50 %
26	19 %	20 %	61 %

[1] 13 reports of births *in* tertiary care perinatal centers in the USA from 1988-1997

[2] 10 reports of live births *in* tertiary care perinatal centers in Canada, USA, Australia from 1977-1995

Usual Guidelines for Intervention Are Based on Gestation

Tyson JE, NICHD Workshop, March 2004, privileged communication

>25 weeks GA, initiate intervention

≤22 weeks, forego interventon

23-24 weeks, decide with parents

Between 20-27 weeks, an error of as much as 3 weeks or as little as 1 week can change the decision to initiate intervention

Errors in Estimating Gestational Age

Tyson JE, Neonatal Network

- **Variability in cycle length (LMP): 2 SD = 40 days for 2 years after menarche, decreasing to 10 days in healthy adult women**
- **>10% likelihood of fertility each day of cycle from day 6-21**
- **At each week by LMP, estimated gestation varied between 7-11 weeks (95% CI)**
- **Mean Pediatric estimates (revised Ballard) exceeded Obstetric estimates (LMP) by 1.3 – 1.9 weeks**

Alternative Use of Birth Weight

Tyson JE, Neonatal Network

Risk group, 501-600g	Observed Network survival	Maximum reported survival	Observed unimpaired survival	Maximum reported unimpaired survival
Male	22%	37%	4%	7%
Female	40%	52%	18%	24%
All	32%	46%	13%	18%

Intervention for All Infants 501-600g

Tyson JE, NICHD Workshop, March 2004

- Males: Need to treat >33 infants to produce 1 extra survivor without major impairment
  - Hospital stay >178 days per survivor
  - >890 days per unimpaired survivor
- Females: Need to treat >16 girls to produce 1 extra survivor without major impairment
  - Hospital stay >138 days per survivor
  - >301 days per unimpaired survivor

Outcomes of 401-500g ELBW Infants?

Tyson JE, NICHD Workshop, March 2004

Survival to discharge home in Neonatal Network centers:

Overall	16%
Females	21%
Males	9%

Hypothetical guidelines for intervention, emphasizing concern for parental autonomy & infant suffering …

Tyson, NICHD Workshop, March 2004

- ***Unreasonable*** **if <23 wks GA or <400g (Text of Neonatal Resuscitation, AAP)**
- ***Investigational*** **if estimated likelihood of survival without major impairment <25%**
- ***Optional*** **if estimated likelihood is 25-49%**
- ***Mandatory*** **if estimated likelihood is ≥50%.**

- **Investigational:**
  - **SGA girls <550g**
  - **AGA girls & SGA boys <650g**
  - **AGA boys <750g**
- **Optional:**
  - **SGA girls 550-649g**
  - **AGA girls & SGA boys 650-749g**
  - **AGA boys 750-850g**
- **Mandatory:**
  - **SGA girls ≥650g**
  - **AGA girls & SGA boys ≥750g**
  - **AGA boys ≥ 850g**

Threshold values lowered 50g for antenatal steroids; and 50g for future improvements in outcome

Effects on Family

- **Divorce rates and death rates (from natural and unnatural causes) are higher in the parents of disabled children**
- **Impact on neglected siblings and family finances are poorly quantified**

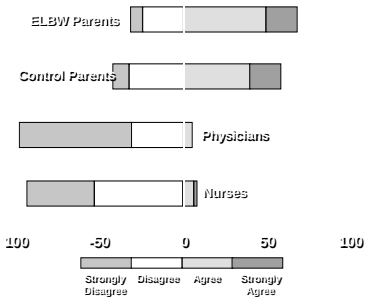
Self-Perceived Health Status and HRQL of ELBW and Control Teenagers at Adolescence

Saigal S: JAMA 1996, 276:453

- **Mean utility scores of functional impairment (1.00 is perceived perfect function) were only slightly lower for the ELBW cohort (0.87 ± 0.26 *vs* 0.93 ± 0.11, P<.02)**
- **A similar proportion of ELBW and control teenagers gave utility ratings of >0.95 (71% *vs* 73%)**

Agreement of parents and professionals to the statement: "Attempts should be made to save every infant regardless of birth weight."

Streiner DL: Pediatrics 2001, 108:152

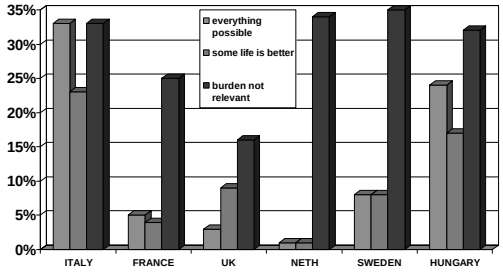


DO YOU AGREE WITH THE FOLLOWING STATEMENTS?

Rebagliato M, et al: Neonatal End-of-Life Decision Making: Physicians' Attitudes … in 10 European Countries. JAMA 2000, 284:2451

- **Because human life is sacred, everything possible should be done to ensure a neonate's survival, however severe the prognosis.**
- **Even with severe mental disability, some life is better than no life at all.**
- **The burden that a disabled child will represent for the family is not so relevant when making ethical decisions for the neonate.**

PROPORTION OF NEONATOLOGISTS AGREEING WITH THREE QUESTIONS



Cost of Intensive Care for ELBW Infants 500-749g

(1985-1991)

BW (g)	#	#CC	#Live (%)	Cost (K)	Cost/ Infant (K)	Cost/ Survivor (K)
500-549	19	9	3 (16)	$1,685	$89	$1,685
550-599	21	3	5 (24)	$2,189	$104	$407
600-649	12	2	6 (50)	$1,726	$144	$288
650-699	18	3	11 (61)	$2,684	$149	$244
700-749	30	1	17 (57)	$7.671	$247	$426
Total	100	18	42 (42)	$15,954	$158	$363

Pomerance, *et al*. Pediatr Res 1993; 33:2314

Cost Comparisons

	ELBW[1] 500-750g	Liver transplant[2]	Neonatal ECMO[3]
Year(s)	1985-1991	1987	1989
Expected survival [without intervention]	0%	0%	20%
Observed survival	58% [to discharge]	69% [to 1 year]	83% [to 1 year]
Cost/case	$158,000 [mean]	$204,000 [median]	$120,000 [median]
Cost/survivor	$363,000	$295,000	$144,578

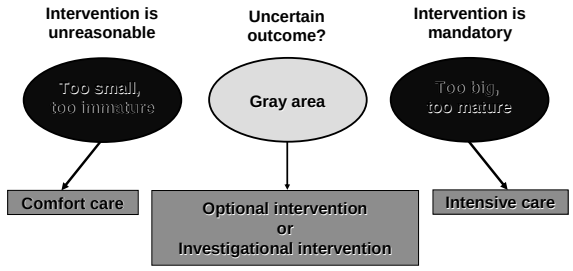
1 Pomerance, *et al*: Peds Res 1993; 33:2314
2 Hotta SS: Health Tech Assessment Reports – Liver transplant. US DHHS, PHS, AHCPP 1990
3 Schwartz, *et al:* NICHD Workshop on Diffussion of ECMO Tech, #93-3399, 1993

Make a Judgement: Interventions for ELBW Babies Fit into One of Four Categories

Tyson, et al: JAMA 1996, 276:1645

- Unreasonable
- Mandatory
- Optional
- Investigational

Consistently Apply ELBW Interventions to the Category Chosen

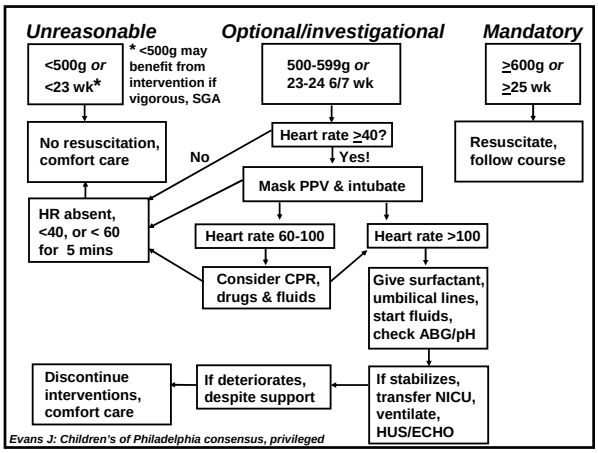


Evans J: Children's of Philadelphia consensus on the ELBW newborn, privileged communication

Care Based on Outcomes

Category	Examples	Parental involvement	Duties of society
Unreasonable outcome	Infants <23 wks	Be informed and given time to understand & accept prognosis and grieve	No professional or societal obligation for NICU care – give comfort care
Uncertain outcome	Infants 23–25 wk	Understand risks & benefits of treatment alternatives	Treatment provided only with the consent of parents; continually recess burden *vs* benefit
Mandatory	Infant >25 wk	Understand risks and benefits of treatment and their obligation to provide treatment	Obliged to provide treatment

Adapted from Lawrence University Program in Biomedical Ethics and Wisconsin Health Decisions. *Guidelines for the Responsible Use of Intensive Care.* Appleton, WI, 1998



Proposal for Outcomes Research in Optional Cases

- Explain that intensive care in these circumstances is optional.
- Explain that more information about risks, benefits, outcomes and costs is needed in order for parents to make better informed decisions.
- Request that every family participate in research-oriented follow-up, whether they opt for intensive care or not.
- Follow-up should focus on families — siblings as well as parents and babies.

Assess Effects of Intervention on Families of Marginally Viable Infants

Follow and assess all parents, *including those whose infants died*:

- Depression, anxiety, & quality of life (utilities)
- Serious adverse effects – loss of employment, separation/divorce, alcohol or drug abuse, major illness or accident
- Potential benefits to parents (greater fulfillment, closer marriage and family ties)

Finis

EPICure Study

Wood, *et al*. NEJM 2000; 343:378.

- **Prospective study 4004 births at 20-25 weeks, UK & Ireland over 10 months in 1995**
- **Antepartum death rate 70%**
- **30% live births died at delivery, 43% died before discharge**
- **Follow-up at median 30 months:**
  - **49% no disability**
  - **25% severe disability**
  - **23% other disability (unrelated to GA)**

Survival Without Disability

EPIcure

Week	Total #	% Live Births	% NICU Admits	NNT [assumes no intact survivors without intervention]
22	138	0.7%	5%	20-142
23	241	5%	8%	12.5-20
24	382	12%	15%	6.7-8.3
25	424	23%	27%	3.7-4.3

EPICure Outcomes at 6 Years

Bracewell, 2002

Gestation	23 weeks	24 weeks	25 weeks
Disability*	29%	33%	29%

*** 59 infants evaluated, 25% of 240 who survived to discharge**