WORKSHEET for PROPOSED Evidence-Based GUIDELINE RECOMMENDATIONS

Worksheet Author:	**Home Subcommittee:** RC (UK) NLS
Author's Home Resuscitation Council: Resuscitation Council (UK)	**Date Submitted to Subcommittee:** May 28, 2004; Nov 3, 2004; December 8, 2004

STEP 1: STATE THE PROPOSAL. State if this is a proposed new guideline; revision to current guideline; or deletion of current guideline.

Existing guideline, practice or training activity:
Update /revision of current guideline on the use of specific clinical indicators for non-initiation or discontinuation of resuscitation in the delivery room. Indicators for non-initiation include extreme prematurity of <23 weeks (or 24 weeks in some cases), birthweight less than 500g or lethal malformations including anencephaly, and trisomy 18 or 13 (preferably confirmed by antenatal chromosomal analysis).

Current guidelines:

ILCOR : International Guidelines for Neonatal Resuscitation (2000) P.13 states "There are circumstances in which noninitiation or discontinuation of resuscitation in the delivery room may be appropriate……The delivery of extremely immature infants and infants with severe congenital anomalies raises questions about initiation of resuscitation. Noninitiation of resuscitation in the delivery room is appropriate for infants with confirmed gestation <23 weeks or birthweight <400g, anencephaly , or confirmed trisomy 13 or 18. Discontinuation of resuscitative efforts may be appropriate if resuscitation of an infant with cardiorespiratory arrest does not result in spontaneous circulation in 15 minutes. Resuscitation of newly born infants after 10 minutes of asystole is very unlikely to result in survival or survival without severe disability.

UK Newborn Life Support course manual text (2001) P.39 states "It is rare for a baby less than 500g to survive but many show signs of life after birth."

British Association of Perinatal Medicine (2000). Fetuses and Newborn Infants at the Threshold of Viability. A Framework for Practice, states "The increasing potential risk of residual disability or early death associated with decreasing gestational age (especially <26 weeks) raises serious ethical dilemmas in respect of appropriate management. These include whether elective delivery for fetal indication is appropriate or whether intensive care should be provided following delivery, or, alternatively, whether comfort care is more appropriate (warmth, offer of oral nourishment and human contact).
Decisions on management should be based on what is perceived by the parents and their medical advisors to be in the child's best interests, uninfluenced by the child's gender or by religious, eugenic, demographic or financial factors."

Step 1A: Refine the question; state the question as a positive (or negative) hypothesis. State proposed guideline recommendation as a specific, positive hypothesis. Use single sentence if possible. Include type of patients; setting (in-/out-of-hospital); specific interventions (dose, route); specific outcomes (ROSC vs. hospital discharge).

Hypothesis: It is justified to not initiate or to discontinue delivery room resuscitation in extremely preterm babies (gestation <23 weeks and/or weight <500g) due to their poor long term outcome, or in babies with obvious or confirmed lethal malformations or chromosomal abnormalities. The same is true for many babies of <24 weeks gestation who's outcome is also poor.

Step 1B: Gather the Evidence; define your search strategy. Describe search results; describe best sources for evidence.

Terms searched (all mapped to subject (MeSH) headings where appropriate):
Ethics, neonat$ (as last time)
Cardiopulmonary resuscitation, outcome, neonat$ (as last time)
Premature
Baby
Preterm
Pre-term
Stop$
Cease
Discontinue
Noninitiate
Non-initiate

Malformation
There was relatively little new evidence available since the last review in 1999 (see later).
List electronic databases searched (at least MEDLINE (http://igm.nlm.nih.gov/) and hand searches of journals, review articles, and books.

Medline (Ovid); Pubmed, Embase and Cochrane Library ; identified articles searched for additional relevant references

- State major criteria you used to limit your search; state inclusion or exclusion criteria (e.g., only human studies with control group? no animal studies? N subjects > minimal number? type of methodology? peer-reviewed manuscripts only? no abstract-only studies?)

Human studies only. Full published papers. No abstract only reports.

- Number of articles/sources meeting criteria for further review: Create a citation marker for each study (use the author initials and date or Arabic numeral, e.g., "Cummins-1"). If possible, please supply file of best references; End Note 4+ preferred as reference manager, though other reference databases acceptable.

Reference list at end.

Step 2A Worksheet: List of articles meeting selection criteria with their level of evidence

Level of Evidence	List of articles
Level 1	
Level 2	
Level 3	Lemons (2001)
Level 4	Finer (1999a), , Emsley (1998), Fanaroff (1995),Kilpatrick (1997), Tin (1997), Lefebvre (1996), Tyson (1996) Vohr (2004),
Level 5	Noninitiation of resuscitation: Lorenz (2001), Doron (1998), Evans (2001), Costeloe (2000), Sauve (1998), Kramer (1997), O'Shea (1997), Piecuch (1997), Allen (1993), Whyte (1993), Sood (1992) Discontinuation of resuscitation Wyckoff (2000), Finer (1999b), Casalaz (1998), Perlman (1995), Sims (1994), Yeo (1994), Jain (1991), Lantos (1988), Levene (1986), Scott (1976), Steiner (1975)
Level 6	
Level 7	
Level 8	

Step 2B: Critically assess each article/source in terms of research design and methods.

Was the study well executed? Suggested criteria appear in the table below. Assess design and methods and provide an overall rating. Ratings apply within each Level; a Level 1 study can be excellent or poor as a clinical trial, just as a Level 6 study could be excellent or poor as an animal study. Where applicable, please use a superscripted code (shown below) to categorize the primary endpoint of each study. For more detailed explanations please see attached assessment form.

Component of Study and Rating	Excellent	Good	Fair	Poor	Unsatisfactory

Design & Methods	Highly appropriate sample or model, randomized, proper controls **AND** Outstanding accuracy, precision, and data collection in its class	Highly appropriate sample or model, randomized, proper controls **OR** Outstanding accuracy, precision, and data collection in its class	Adequate, design, but possibly biased **OR** Adequate under the circumstances	Small or clearly biased population or model Weakly defensible in its class, limited data or measures	Anecdotal, no controls, off target end-points Not defensible in its class, insufficient data or measures

A = Return of spontaneous circulation C = Survival to hospital discharge E = Other endpoint
B = Survival of event D = Intact neurological survival

Noninitiation of resuscitation

Good: Costeloe (2000), Kramer (1997), O'Shea (1997), Tin (1997)
Fair: Vohr (2004), Lorenz (2001), Evans (2001), Lemons (2001), Finer (1999a), Doron (1998), Emsley (1998), Sauve (1998), Kilpatrick (1997), Piecuch (1997), Lefebvre (1996), Tyson (1996), Fanaroff (1995), Allen (1993), Whyte (1993), Sood (1992)

Discontinuation of resuscitation

Fair: Wyckoff (2000), Finer (1999b), Casalaz (1998), Perlman (1995), Sims (1994), Yeo (1994), Jain (1991), Lantos (1988), Levene (1986)
Poor: Scott (1976), Steiner (1975)

Step 2C: Determine the <u>direction</u> of the results and the statistics: supportive? neutral? opposed?

DIRECTION of study by results & statistics:	**SUPPORT the proposal**	**NEUTRAL**	**OPPOSE the proposal**

Results	Outcome of proposed guideline superior, to a clinically important degree, to current approaches	Outcome of proposed guideline no different from current approach	Outcome of proposed guideline inferior to current approach

Noninitiation of resuscitation

Supportive: Evans (2001), Lemons (2001), Costeloe (2000), Finer (1999a), Doron (1998), Emsley (1998), Sauve (1998), Kilpatrick (1997), Kramer (1997), O'Shea (1997), Piecuch (1997), Tin (1997), Lefebvre (1996), Tyson (1996), Fanaroff (1995), Allen (1993), Whyte (1993), Sood (1992)
Neutral: Vohr (2004), Lorenz (2001)

Discontinuation of resuscitation

Supportive: Wyckoff (2000), Casalaz (1998), Perlman (1995), Sims (1994), Yeo (1994), Jain (1991), Lantos (1988), Levene (1986), Scott (1976), Steiner (1975)
Opposing: Finer (1999b)

Step 2D: Cross-tabulate assessed studies by a) *level*, b) *quality* and c) *direction* (ie, supporting or neutral/ opposing)**; combine and summarize.** Exclude the *Poor* and *Unsatisfactory* studies. Sort the *Excellent, Good,* and *Fair* quality studies by both *Level and Quality of evidence,* and *Direction of support* in the summary grids below. Use citation marker (e.g. author/ date/source). In the *Neutral* or *Opposing* grid use bold font for *Opposing* studies to distinguish them from merely neutral studies. Where applicable, please use a superscripted code (shown below) to categorize the primary endpoint of each study.

Noninitiation of resuscitation
Supporting Evidence

Quality of Evidence	**Excellent**								
	Good				**Tin (1997)[C,D]**	**Costeloe (2000)[C]** **Kramer (1997)[C,E]** **O'Shea (1997)[C,D]**			

	Fair			**Lemons (2001)[C,D]**	**Finer (1999a)[C,E] Emsley (1998)[C,D] Kilpatrick (1997)[C] Tyson (1996)[C,D] Fanaroff (1995)[C,E]**	**Evans (2001)[C] Doron (1993)[C] Sauve (1998)[C,D] Piecuch (1997)[D] Lefebvre (1996)[C,D] Allen (1993)[C,E] Whyte (1993)[C,D] Sood (1992)[C,D]**			
		1	**2**	**3**	**4**	**5**	**6**	**7**	**8**
		Level of Evidence							

A = Return of spontaneous circulation C = Survival to hospital discharge E = Other endpoint
B = Survival of event D = Intact neurological survival

Neutral or Opposing Evidence

Quality of Evidence									
	Excellent								
	Good								
	Fair				**Vohr (2004)[C,D]**	**Lorenz (2001)[C,D]**			
		1	**2**	**3**	**4**	**5**	**6**	**7**	**8**
		Level of Evidence							

A = Return of spontaneous circulation C = Survival to hospital discharge E = Other endpoint
B = Survival of event D = Intact neurological survival

Discontinuation of resuscitation
Supporting Evidence

Quality of Evidence									
	Excellent								
	Good								
	Fair					**Wyckoff (2000)**[C] **Casalaz (1998)**[C,D] **Perlman (1995)**[C] **Sims (1994)**[C,D] **Yeo (1994)**[C,D] **Davis (1993)**[C] **Jain (1991)**[C,D] **Lantos (1988)**[C] **Levene (1986)**[C,D] **Scott (1976)**[C,D] **Steiner (1975)**[C,D]			
		1	**2**	**3**	**4**	**5**	**6**	**7**	**8**
		Level of Evidence							

A = Return of spontaneous circulation C = Survival to hospital discharge E = Other endpoint
B = Survival of event D = Intact neurological survival

Neutral or Opposing Evidence

Quality of Evidence	**Excellent**								
	Good								
	Fair					**Finer (1999b)**[C]			
		1	**2**	**3**	**4**	**5**	**6**	**7**	**8**
		Level of Evidence							

REVIEWER'S PERSPECTIVE AND POTENTIAL CONFLICTS OF INTEREST: Briefly summarize your professional background, clinical specialty, research training, AHA experience, or other relevant personal background that define your perspective on the guideline proposal. List any potential conflicts of interest involving consulting, compensation, or equity positions related to drugs, devices, or entities impacted by the guideline proposal. Disclose any research funding from involved companies or interest groups. State any relevant philosophical, religious, or cultural beliefs or longstanding disagreements with an individual.

I am a Consultant Neonatologist in a Level 3 NNU in the UK. I have been a Consultant for the past 7 years. I am an NLS Instructor in the UK. There are no conflicts of interest, either financial or personal.

REVIEWER'S FINAL COMMENTS AND ASSESSMENT OF BENEFIT / RISK: Summarize your final evidence integration and the rationale for the class of recommendation. Describe any mismatches between the evidence and your final Class of Recommendation. "Mismatches" refer to selection of a class of recommendation that is heavily influenced by other factors than just the evidence. For example, the evidence is strong, but implementation is difficult or expensive; evidence weak, but future definitive evidence is unlikely to be obtained. Comment on contribution of animal or mechanical model studies to your final recommendation. Are results within animal studies homogeneous? Are animal results consistent with results from human studies? What is the frequency of adverse events? What is the possibility of harm? Describe any value or utility judgments you may have made, separate from the evidence. For example, you believe evidence-supported interventions should be limited to in-hospital use because you think proper use is too difficult for pre-hospital providers.

There is little new evidence since the last review and all of the new studies are level 5 evidence only. All of the studies agree that extreme prematurity (<23 weeks or birthweight <400g) or lethal malformation are acceptable reasons not to initiate resuscitation (or to discontinue resuscitation).

Based on poor prognosis, many of the studies suggest that this is also true for babies <24 weeks or birthweight<500g and this is certainly the experience in the UK from the Epicure (Costeloe) and Northern Network (Tin) studies. Whilst this is the majority opinion in the UK it is certainly not a unanimous one.

The conclusions regarding babies <24 weeks gestation seems at odds with data from Finer (1999b), in this

small series many of the babies received drugs without cardiac massage (against NLS teaching in the UK) and the case series did not include ALL babies at this gestation which the 2 UK studies strove to do. Evans (2001) demonstrated that such selection bias can significantly change the results of such studies. Wyckoff (2000) very eloquently summarized the concern that early delivery of cardiac massage and/or drugs may be at the expense of adequate ventilation of these babies and lack of establishment of functional residual capacity (FRC), which is imperative for successful resuscitation.

Preliminary draft/outline/bullet points of Guidelines revision: Include points you think are important for inclusion by the person assigned to write this section. Use extra pages if necessary.

Attachments:

Printed (paper) bibliography; and on diskette using a reference manager. It is recommended that the bibliography be printed in annotated format. This will include the article abstract and any notes you would like to make providing specific comments on the quality, methodology and/or conclusions of the study.

Key figures or tables from evidence-based analysis

Full hard copies of most critical cited papers

Citation List

Citation Marker	Full Citation*
{Allen, 1993 #16}	Allen, M. C., P. K. Donohue, et al. (1993). "The limit of viability--neonatal outcome of infants born at 22 to 25 weeks' gestation." N Engl J Med **329**(22): 1597-601.
{Ballard, 2002 #31}	Ballard, D. W., Y. Li, et al. (2002). "Fear of litigation may increase resuscitation of infants born near the limits of viability." J Pediatr **140**(6): 713-8.
{Costeloe, 2000 #3}	Costeloe, K., E. Hennessy, et al. (2000). "The EPICure study: outcomes to discharge from hospital for infants born at the threshold of viability." Pediatrics **106**(4): 659-71.
{Doron, 1998 #5}	Doron, M. W., K. A. Veness-Meehan, et al. (1998). "Delivery room resuscitation decisions for extremely premature infants." Pediatrics **102**(3 Pt 1): 574-82.
{Emsley, 1998 #6}	Emsley, H. C., S. P. Wardle, et al. (1998). "Increased survival and deteriorating developmental outcome in 23 to 25 week old gestation infants, 1990-4 compared with 1984-9." Arch Dis Child Fetal Neonatal Ed **78**(2): F99-104.
{Evans, 2001 #1}	Evans, D. J. and M. I. Levene (2001). "Evidence of selection bias in preterm survival studies: a systematic review." Arch Dis Child Fetal Neonatal Ed **84**(2): F79-84.
{Fanaroff, 1995 #15}	Fanaroff, A. A., L. L. Wright, et al. (1995). "Very-low-birth-weight outcomes of the National Institute of Child Health and Human Development Neonatal Research Network, May 1991 through December 1992." Am J Obstet Gynecol **173**(5): 1423-31.
{Finer, 1999 #4}	Finer, N. N., J. D. Horbar, et al. (1999). "Cardiopulmonary resuscitation in the very low birth weight infant: the Vermont Oxford Network experience." Pediatrics **104**(3 Pt 1): 428-34.

{Kilpatrick, 1997 #8}	Kilpatrick, S. J., M. A. Schlueter, et al. (1997). "Outcome of infants born at 24-26 weeks' gestation: I. Survival and cost." Obstet Gynecol **90**(5): 803-8.
{Kramer, 1997 #9}	Kramer, W. B., G. R. Saade, et al. (1997). "Neonatal outcome after active perinatal management of the very premature infant between 23 and 27 weeks' gestation." J Perinatol **17**(6): 439-43.
{Lefebvre, 1996 #13}	Lefebvre, F., J. Glorieux, et al. (1996). "Neonatal survival and disability rate at age 18 months for infants born between 23 and 28 weeks of gestation." Am J Obstet Gynecol **174**(3): 833-8.
{Lemons, 2001 #2}	Lemons, J. A., C. R. Bauer, et al. (2001). "Very low birth weight outcomes of the National Institute of Child health and human development neonatal research network, January 1995 through December 1996. NICHD Neonatal Research Network." Pediatrics **107**(1): E1.
{Lorenz, 2001 #32}	Lorenz, J. M., N. Paneth, et al. (2001). "Comparison of management strategies for extreme prematurity in New Jersey and the Netherlands: outcomes and resource expenditure." Pediatrics **108**(6): 1269-74.
{McHaffie, 1998 #33}	McHaffie, H. E. and P. W. Fowlie (1998). "Withdrawing and withholding treatment: comments on new guidelines." Arch Dis Child **79**(1): 1-2.

{O'Shea, 1997 #10}	O'Shea, T. M., K. L. Klinepeter, et al. (1997). "Survival and developmental disability in infants with birth weights of 501 to 800 grams, born between 1979 and 1994." Pediatrics **100**(6): 982-6.

{Piecuch, 1997 #11}	Piecuch, R. E., C. H. Leonard, et al. (1997). "Outcome of infants born at 24-26 weeks' gestation: II. Neurodevelopmental outcome." Obstet Gynecol **90**(5): 809-14.
{Sauve, 1998 #7}	Sauve, R. S., C. Robertson, et al. (1998). "Before viability: a geographically based outcome study of infants weighing 500 grams or less at birth." Pediatrics **101**(3 Pt 1): 438-45.
{Sood, 1992 #18}	Sood, S. and G. P. Giacoia (1992). "Cardiopulmonary resuscitation in very low birthweight infants." Am J Perinatol **9**(2): 130-3.
{Tin, 1997 #12}	Tin, W., U. Wariyar, et al. (1997). "Changing prognosis for babies of less than 28 weeks' gestation in the north of England between 1983 and 1994. Northern Neonatal Network." Bmj **314**(7074): 107-11.
{Tyson, 1996 #14}	Tyson, J. E., N. Younes, et al. (1996). "Viability, morbidity, and resource use among newborns of 501- to 800-g birth weight. National Institute of Child Health and Human Development Neonatal Research Network." Jama **276**(20): 1645-51.
{Vohr, 2004 #30}	Vohr, B. R., L. L. Wright, et al. (2004). "Center differences and outcomes of extremely low birth weight infants." Pediatrics **113**(4): 781-9.
Whyte, 1993 #17}	Whyte, H. E., P. M. Fitzhardinge, et al. (1993). "Extreme immaturity: outcome of 568 pregnancies of 23-26 weeks' gestation." Obstet Gynecol **82**(1): 1-7.

Discontinuation of resuscitation

Citation Marker	Full Citation*
{Casalaz, 1998 #20}	Casalaz, D. M., N. Marlow, et al. (1998). "Outcome of resuscitation following unexpected apparent stillbirth." Arch Dis Child Fetal Neonatal Ed **78**(2): F112-5.
{Davis, 1993 #24}	Davis, D. J. (1993). "How aggressive should delivery room cardiopulmonary resuscitation be for extremely low birth weight neonates?" Pediatrics **92**(3): 447-50.
{Finer, 1999 #19}	Finer, N. N., T. Tarin, et al. (1999). "Intact survival in extremely low birth weight infants after delivery room resuscitation." Pediatrics **104**(4): e40.
{Jain, 1991 #25}	Jain, L., C. Ferre, et al. (1991). "Cardiopulmonary resuscitation of apparently stillborn infants: survival and long-term outcome." J Pediatr **118**(5): 778-82.

{Lantos, 1988 #26}	Lantos, J. D., S. H. Miles, et al. (1988). "Survival after cardiopulmonary resuscitation in babies of very low birth weight. Is CPR futile therapy?" N Engl J Med **318**(2): 91-5.
{Levene, 1986 #29}	Levene, M. I., C. Sands, et al. (1986). "Comparison of two methods of predicting outcome in perinatal asphyxia." Lancet **1**(8472): 67-9.
{Perlman, 1995 #21}	Perlman, J. M. and R. Risser (1995). "Cardiopulmonary resuscitation in the delivery room. Associated clinical events." Arch Pediatr Adolesc Med **149**(1): 20-5.
{Scott, 1976 #27}	Scott, H. (1976). "Outcome of very severe birth asphyxia." Arch Dis Child **51**(9): 712-6.
{Sims, 1994 #22}	Sims, D. G., C. A. Heal, et al. (1994). "Use of adrenaline and atropine in neonatal resuscitation." Arch Dis Child Fetal Neonatal Ed **70**(1): F3-9; discussion F9-10.
{Steiner, 1975 #28}	Steiner, H. and G. Neligan (1975). "Perinatal cardiac arrest. Quality of the survivors." Arch Dis Child **50**(9): 696-702.
{Wyckoff, 2000 #34}	Wyckoff, M. and J. Perlman (2000). "Cardiopulmonary resuscitation in very low birth weight infants." Pediatrics **106**(3): 618-20.
{Yeo, 1994 #23}	Yeo, C. L. and D. I. Tudehope (1994). "Outcome of resuscitated apparently stillborn infants: a ten year review." J Paediatr Child Health **30**(2): 129-33.

Noninitiation of resuscitation

Vohr, B. R., L. L. Wright, et al. (2004). "Center differences and outcomes of extremely low birth weight infants." Pediatrics **113**(4): 781-9.

OBJECTIVE: Previous multicenter studies have shown significant center differences in neonatal characteristics and morbidities. This study evaluated center differences in outcome at 18 to 22 months among extremely low birth weight (ELBW; 401-1000 g) infants after adjusting for demographics and antenatal interventions, and it identified neonatal interventions associated with outcome differences. METHODS: We assessed the outcome of 2478 liveborn infants who were admitted in 1993 and 1994 to the 12 centers of the Neonatal Research Network of the National Institute of Child Health and Human Development; 1483 (60%) infants survived to 18 to 22 months, and 1151 (78%) had comprehensive evaluations. Logistic regression analyses were performed to identify center differences and the association of 4 neonatal interventions--active resuscitation, postnatal steroids, ventilator treatment for < or =27 days, and full enteral feedings < or =24 days--with adverse outcomes (cerebral palsy, low Bayley scores, and neurodevelopmental impairment [NDI]), after adjusting for demographics and antenatal interventions. RESULTS: Using bivariate analyses, significant center differences were identified for mortality, antenatal and postnatal interventions, social and environmental variables, neonatal morbidities, and neurodevelopmental outcomes for the 12 centers. After adjustment for maternal and infant demographics and antenatal interventions, the percentage of ELBW infants who had died or had NDI at 18 to 22 months ranged from 52% to 85%. Active resuscitation and postnatal steroids were associated with increases of NDI of 11.8% and 19.3%, whereas shorter ventilation support and shorter time to achieve full enteral feeds were

associated with decreases in NDI of 20.7% and 17.3%, respectively. CONCLUSION: There are large and disturbing differences among centers in outcomes at 18 to 22 months after adjusting for demographic and antenatal interventions. Center differences in postnatal interventions associated with differences in outcome can provide hypotheses for testing in clinical trials to improve outcome.

Level of Evidence 4 **Quality** Fair **Evidence** Neutral
Comment
Gives us some useful ideas for clinical trials to try and tease out the areas of neonatal care that may contribute to the well described inter-hospital differences but confirms that the need for active resuscitation in these very pre-term babies is associated with significant increased risks of mortality and morbidity.

Ballard, D. W., Y. Li, et al. (2002). "Fear of litigation may increase resuscitation of infants born near the limits of viability." J Pediatr **140**(6): 713-8.
OBJECTIVES: To explore how fear of litigation influences neonatal treatment decisions. STUDY DESIGN: In a mailed survey, we presented a hypothetical vignette of a premature infant to 1000 neonatologists. We asked them to estimate prognosis, indicate appropriate intervention, and respond to parental treatment requests. Subjects were randomly assigned to receive one of two questionnaires, "litigious" or "nonlitigious," which differed only in the description of the infant's parents. RESULTS: The response rate was 63.0%. The vast majority of respondents deferred to parental requests rather than adhering to their best judgment. They deferred whether or not parents requested treatment and whether or not parents were described as litigious (P <.0001). Among those respondents who shifted their resuscitation opinion after parental introduction, respondents to the nonlitigious version were more likely to shift their opinion from "treat" to "do not treat" after parental requests to "use your best judgment" (P <.042). The influence of parental litigiousness was primarily seen among neonatologists who thought that the infant's prognosis was dismal (P <.044). CONCLUSIONS: There is a strong disposition among neonatologists toward respecting parental wishes. This disposition is stronger when neonatologists are given additional reason to be concerned about litigation.

Level of Evidence 8 **Quality** Fair **Evidence** Neutral

Comment: An interesting study which went some way to teasing out the effect of parental attitude on the way that decisions to withhold or withdraw care are made.

Lorenz, J. M., N. Paneth, et al. (2001). "Comparison of management strategies for extreme prematurity in New Jersey and the Netherlands: outcomes and resource expenditure." Pediatrics **108**(6): 1269-74.

OBJECTIVE: To quantify differences in resource expenditure in the perinatal period and long-term outcome of extremely premature infants who received systematically different approaches to neonatal intensive care. METHODS: Perinatal management, mortality, prevalence of disabling cerebral palsy (DCP), and resource expenditure of 2 population-based inception cohorts of extremely premature infants born in the mid-1980s were compared. Electronic fetal monitoring, tocolysis, cesarean section delivery, and assisted ventilation were used to characterize management approaches. Participants included all live births at 23 to 26 weeks' gestation in a 3-county area of central New Jersey (NJ) from 1984 to 1987 (N = 146) and throughout the Netherlands (NETH) in 1983 (N = 142). Mortality and the prevalence of DCP were the primary outcomes. Numbers of hospital days with and without assisted ventilation were the measures of resource expenditure. RESULTS: Electronic fetal monitoring (100% vs 38%), cesarean section (28% vs 6%), and assisted ventilation (95% vs 64%) were all more commonly used in NJ than in NETH. Ten percent of NJ deaths occurred without assisted ventilation, compared with 45% of Dutch deaths. A total of 1820 ventilator days were expended per 100 live births in NJ, compared with 448 in NETH. The increase in the number of nonventilator days (3174 vs 2265 days per 100 live births) did not reach statistical significance. Survival to age 2 (46 vs 22%) and the prevalence of DCP among survivors (17.2 vs 3.4%) were significantly greater in NJ at age 2 than in NETH at age 5. CONCLUSIONS: Near universal initiation of intensive care in NJ, compared with selective initiation of intensive care in NETH, was associated with 24.1 additional survivors per 100 live births, 7.2 additional cases of DCP per 100 live births, and a cost of 1372 additional ventilator days per 100 live births.

Level of Evidence 5 **Quality** Fair **Evidence** Neutral

Comment: An interesting paper comparing what are probably 2 extremes of care in these extremely preterm babies. The authors try to look at the cost of these 2 approaches in terms of mortality, significant morbidity and financial burden of the care provided. I feel that this paper is neutral as it is impossible to balance the extra survival against the increased number of children with DCP even excluding the considerable cost implications in terms of finance and cot occupancy.

Evans, D. J. and M. I. Levene (2001). "Evidence of selection bias in preterm survival studies: a systematic review." Arch Dis Child Fetal Neonatal Ed **84**(2): F79-84.

OBJECTIVE: To determine by how much selection bias in preterm infant cohort studies results in an overestimate of survival. DESIGN: Systematic review of studies reporting survival in infants less than 28 weeks of gestation published 1978-1998. Studies were graded according to cohort definition: A, stillbirths and live births; B, live births; C, neonatal unit admissions. Proportions of infants surviving to discharge were calculated for each week of gestation. RESULTS: Sixty seven studies report data on 55 cohorts (16 grade A, 23 grade B, 16 grade C). Studies that are more selective report significantly higher survival between 23 and 26 weeks of gestation (grade C > grade B > grade A, $p < 0.01$), exaggerating survival by 100% and 56% at 23 and 24 weeks respectively. CONCLUSION: To minimise the potential for overestimating survival around the limits of viability, future studies should endeavour to report the outcome of all pregnancies for each week of gestation (terminations, miscarriages, stillbirths, and all live births)

Level of Evidence 5 **Quality** Fair **Evidence** Supportive

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Comment: An interesting analysis that underlines the importance of collecting data on all pregnancies at each gestation so as to provide more accurate figures with which to counsel parents.

Lemons, J. A., C. R. Bauer, et al. (2001). "Very low birth weight outcomes of the National Institute of Child health and human development neonatal research network, January 1995 through December 1996. NICHD Neonatal Research Network." Pediatrics **107**(1): E1.

OBJECTIVES: To determine the mortality and morbidity for infants weighing 401 to 1500 g (very low birth weight [VLBW]) at birth by gestational age, birth weight, and gender. STUDY DESIGN: Perinatal data were collected prospectively on an inborn cohort from January 1995 through December 1996 by 14 participating centers of the National Institute of Child Health and Human Development Neonatal Research Network and were compared with the corresponding data from previous reports. Sociodemographic factors, perinatal events, and the neonatal course to 120 days of life, discharge, or death were evaluated. RESULTS: Eighty four percent of 4438 infants weighing 501 to 1500 g at birth survived until discharge to home or to a long-term care facility (compared with 80% in 1991 and 74% in 1988). Survival to discharge was 54% for infants 501 to 750 g at birth, 86% for those 751 to 1000 g, 94% for those 1001 to 1250 g, and 97% for those 1251 to 1500g. The incidence of chronic lung disease (CLD; defined as receiving supplemental oxygen at 36 weeks' postmenstrual age; 23%), proven necrotizing enterocolitis (NEC; 7%), and severe intracranial hemorrhage (ICH; grade III or IV; 11%) remained unchanged between 1991 and 1996. Furthermore, 97% of all VLBW infants and 99% of infants weighing <1000 g at birth had weights less than the 10th percentile at 36 weeks' postmenstrual age. Mortality for 195 infants weighing 401 to 500 g was 89%, with nearly all survivors developing CLD. Mortality in infants weighing 501 to 600 g was 71%; among survivors, 62% had CLD, 35% had severe ICH, and 15% had proven NEC. CONCLUSIONS: Survival for infants between 501 and 1500 g at birth continued to improve, particularly for infants weighing <1000 g at birth. This improvement in survival was not associated with an increase in major morbidities, because the incidence of CLD, proven NEC, and severe ICH did not change. However, poor postnatal growth remains a major concern, occurring in 99% of infants weighing <1000 g at birth. Mortality and major morbidity (CLD, severe ICH, and NEC) remain high for the smallest infants, particularly those weighing <600 g at birth.

Level of Evidence 3 **Quality** Fair **Evidence** Supportive.

Comment: These figures are generally similar to those in other studies. Whilst gestational age survival is higher than in EPICure, if Evans and Levene's calculations of likely overestimation are accurate these figures will be similar. Also where there was doubt greater than 2 weeks between LMP and US scan the lower estimate was always used which will overestimate these extremely preterm babies in number.

Costeloe, K., E. Hennessy, et al. (2000). "The EPICure study: outcomes to discharge from hospital for infants born at the threshold of viability." Pediatrics **106**(4): 659-71.

OBJECTIVE: To evaluate the outcome for all infants born before 26 weeks of gestation in the United Kingdom and the Republic of Ireland. This report is of survival and complications up until discharge from hospital. METHODOLOGY: A prospective observational study of all births between March 1, 1995 and December 31, 1995 from 20 to 25 weeks of gestation. RESULTS: A total of 4004 births were recorded, and 811 infants were admitted for intensive care. Overall survival was 39% (n = 314). Male sex, no reported chorioamnionitis, no antenatal steroids, persistent bradycardia at 5 minutes, hypothermia, and high Clinical Risk Index for Babies (CRIB) score were all independently associated with death. Of the survivors, 17% had parenchymal cysts and/or hydrocephalus, 14% received treatment for retinopathy of prematurity (ROP), and 51% needed supplementary oxygen at the expected date of delivery. Failure to administer antenatal steroids and postnatal transfer for intensive care within 24 hours of birth were predictive of major scan abnormality; lower gestation was predictive of severe ROP, while being born to a black mother was protective. Being of lower gestation, male sex, tocolysis, low maternal age, neonatal hypothermia, a high CRIB score, and surfactant therapy were all predictive of oxygen dependency. Intensive care was provided in 137 units, only 8 of which had >5 survivors. There was no difference in survival between institutions when divided into quintiles based on their numbers of extremely preterm births or admissions. CONCLUSIONS: This study provides outcome data for this geographically defined cohort; survival and neonatal morbidity are consistent with previous data from the United Kingdom and facilitate comparison with other geographically based data.

Level of Evidence 5 **Quality** Good **Evidence** Supportive

Comment: This is the largest population based study reported with robust data collection and a complete picture. Whilst still only level 5 it gives compelling evidence about poor survival at <24 weeks and especially at <500g but also admits that survival figures for the US are higher. This study's results and any local data are now routinely used in counseling parents of threshold viable babies in the UK.

Finer, N. N., J. D. Horbar, et al. (1999). "Cardiopulmonary resuscitation in the very low birth weight infant: the Vermont Oxford Network experience." Pediatrics **104**(3 Pt 1): 428-34.

OBJECTIVE: The limited literature available to date suggests that the use of delivery room cardiopulmonary resuscitation (DR-CPR) is associated with very poor outcomes, especially for extremely low birth weight infants. We reviewed the cumulative experience of the Vermont Oxford Network to determine the actual utilization of DR-CPR and the neonatal outcomes of such infants. METHODS: A retrospective review of information available in the Vermont Oxford Network Database for the years 1994 to 1996. The data set was collected from 196 neonatal units who participate in the Network (data for infants 401 to 500 g were from 1996 only). Infants were eligible for study if they received DR-CPR defined as the administration of chest compressions and/or epinephrine in the delivery room as noted on the Vermont Oxford Network Database record. RESULTS: Information regarding survival was available for 27 707 newborns with birth weights from 501 to 1500 g, and 497 infants with birth weights from 401 to 500 g. There were 24 001 (86.6%) survivors. Overall DR-CPR was given to 9.3% of infants from 401 to 500 g and 6% of infants from 501 to 1500 g, 82.1% receiving chest compressions, and 66.7% receiving epinephrine. Survival of infants receiving DR-CPR was 23. 9% for infants of 401 to 500 g, and 63.3% for infants of 501 to 1500 g, compared with 16.7% and 87.9% for infants in these weight groups not receiving DR-CPR. Survival was greater for infants of 501 g or greater without DR-CPR compared with those who received this intervention within each 250-g birth weight subgroup. For infants of <1000 g, survival was 53.8% with DR-CPR compared with 74.9% without. Head ultrasounds were available for 95.5% of all surviving infants and 96.7% of infants who received DR-CPR. Overall, any grade of intraventricular

hemorrhage (IVH) occurred more frequently in infants who received DR-CPR (38%) than in those who did not (21%). Grade 3 or 4 (severe) IVH was seen in 15.3% of infants who received DR-CPR compared with 4.9% of the infants who did not. Overall, survival without severe IVH occurred in 52.2% of DR-CPR infants compared with 81.3% of infants who did not require this intervention. CONCLUSION: The majority of very low birth weight and extremely low birth weight infants who receive DR-CPR survive, and at least half of such infants who survive do not have evidence of severe IVH. Further follow-up studies are required to determine the long-term neurodevelopmental outcome of such infants. The current study does not support the previously noted poor outcome in extremely low birth weight infants who receive DR-CPR.

Level of Evidence 4 **Quality** Fair **Evidence** Supportive

Comment: These data are amongst the largest in number. Data is included from community and tertiary academic centres and may reflect actual practice better than a study from a single academic tertiary centre. The only outcome measures were survival to discharge and incidence and severity of IVH. No information on long term neurodevelopmental outcome is included. It is not apparent from the paper to what extent DR decisions were made about CPR in the 401-500 and 501-750 g groups. Mortality was higher if the infant did not receive CPR. The definition of CPR here is also problematic since there is no indication of how many infants were intubated but did not require CPR, what percentage of these ELBW infants was intubated and responded and what percentage was not intubated, i.e. not resuscitated or did not require intubation. The authors also felt that decisions regarding which newborns were selected for aggressive resuscitation may have had a larger impact on the results than the effectiveness of CPR. This paper tries to respond to earlier reports of CPR being "futile". One could conclude that the data did not support CPR as a therapy that gave a superior result over no CPR. If it is not superior to intubation and mechanical ventilation as far as survival and severe IVH, physicians may not have an obligation to offer the treatment. Many would argue (Wyckoff 2000) that good quality ventilation is the most important therapy: in the UK this need not initially be by intubation but by mask/T-piece system (Newborn Life Support Course).

Doron, M. W., K. A. Veness-Meehan, et al. (1998). "Delivery room resuscitation decisions for extremely premature infants." Pediatrics **102**(3 Pt 1): 574-82.

BACKGROUND: Neonatologists are criticized for overtreating extremely premature infants who die despite invasive and costly care. Withholding resuscitation at delivery has been recommended as a way to minimize overtreatment. It is not known how decisions to forgo initiating aggressive care are made, or whether this strategy effectively decreases overtreatment. OBJECTIVE: To identify whether physicians' or parents' preferences primarily determine the amount of treatment provided at delivery, to examine factors associated with the provision of resuscitation, and to assess whether resuscitation at delivery significantly postpones death in nonsurvivors. METHODS: We evaluated delivery room resuscitation decisions and mortality for all infants born at 23 to 26 weeks gestation at the University of North Carolina Hospitals from November 1994 to October 1995. On the day of delivery, the attending neonatologist completed a questionnaire regarding discussion with the parents before delivery, the prognosis for survival estimated before delivery, the degree of certainty about the prognosis, parents' preference for the amount of treatment at delivery, and the degree of influence exerted by parents and physicians on the amount of delivery room treatment provided. Medical records were reviewed for demographics and hospital course. RESULTS: Thirty-one of 41 infants were resuscitated (intubation and/or cardiopulmonary resuscitation) at delivery. Resuscitation correlated with increasing gestational age, higher birth weight, estimated prognosis for survival greater than or equal to 10%, and uncertainty about prognostic accuracy. Physicians saw themselves as primarily responsible for delivery room resuscitation decisions when the parents' wishes about initiating care were unknown, and as equal partners with parents when they agreed on the level of care. When disagreement existed, doctors always thought parents preferred more aggressive resuscitation, and identified parents as responsible for the increased amount of treatment at delivery. Twenty-four infants died before hospital discharge. The median age at death was 2 days when physicians primarily determined the amount of treatment at delivery, 1 day when parents primarily determined the amount of treatment, and < 1 day when responsibility was shared equally. The median age at death was < 1 day when physicians and parents agreed about the preferred amount of treatment at delivery and 1.5 days when they disagreed. The median age at death was < 1 day when parents' preferences were known before delivery and 4 days when

parents' preferences were unknown. CONCLUSIONS: Physicians resuscitated extremely premature infants at delivery when they were very uncertain about an infant's prognosis or when the parents' desires about treatment were unknown. When parents' preferences were known, parents usually determined the amount of treatment provided at delivery. Resuscitation at delivery usually postponed death by only a few days, decreasing prognostic uncertainty and honoring what physicians perceived were parents' wishes for care, without substantially contributing to overtreatment.

Level of Evidence 5 **Quality** Fair **Evidence** Supportive

Comment: Studied role of parent preference in the resuscitation of threshold viability infants. They were influential in deciding what resuscitation would be offered. Death was delayed 2-3 days by not knowing parental preferences. Physician's prognosis was fairly accurate (no babies survived with an estimated survival <10% and 40% survived where the estimated survival was 10-40%). The authors stressed /the role of withdrawal as a very acceptable option. However holding discussions with the parents, developing a preliminary plan, and obtaining permission from the parents prior to delivery is optimal.

Emsley, H. C., S. P. Wardle, et al. (1998). "Increased survival and deteriorating developmental outcome in 23 to 25 week old gestation infants, 1990-4 compared with 1984-9." Arch Dis Child Fetal Neonatal Ed **78**(2): F99-104.

AIMS: To assess whether changes in survival over time in infants of 23 to 25 weeks of gestational age were accompanied by changes in the incidence of disability in childhood during an 11 year period. METHODS: Obstetric and neonatal variables having the strongest association with both survival to discharge from a regional neonatal medical unit and neurodevelopmental disability in 192 infants of 23 to 25 weeks of gestation, born in 1984 to 1994, were studied as a group and in two cohorts (1984 to 1989 n = 96 and 1990 to 1994 n = 96). The data collected included CRIB (clinical risk index for babies) scores and cranial ultrasound scan findings. The children were followed up at outpatient clinics. RESULTS: Between 1984 and 1989 (cohort 1) and 1990 and 1994 (cohort 2) the rate of survival to discharge increased significantly from 27% to 42% and the rate of disability in survivors increased from 38% to 68%; most of this increase was in mild disability. The proportions of survivors with cerebral palsy did not alter significantly (21% vs 18%), but more survivors with blindness due to retinopathy of prematurity (4% vs 18%), myopia (4% vs 15%) and squints (8% vs 13%) contributed to the increased rate of disability. Clinically significant cranial ultrasound findings and a high CRIB score were strongly associated with death. A high CRIB score was most strongly associated with disability. CONCLUSIONS: The rise in disability with improved survival was not due to cerebral palsy; rather the main contributors were blindness due to retinopathy, myopia, and squint. The causes of these disabilities seem to be linked to high CRIB scores. A system of regular and skilled retinal examination and access to facilities for retinal ablation should be in place in all neonatal units which undertake the care of such extremely preterm infants.

Level of Evidence 4 **Quality** Fair **Evidence** Supportive

Comment: No information about DR resuscitation. Relatively poor 23 week survival against reports from the US and especially as cohort is NICU admissions and not stillbirths+livebirths. This does support other data that increased survival is not necessarily associated with increased numbers of infants with severe cerebral palsy.

McHaffie, H. E. and P. W. Fowlie (1998). "Withdrawing and withholding treatment: comments on new guidelines." Arch Dis Child **79**(1): 1-2.

An interview based study of withdrawing and withholding treatment which included but was not specific to neonatology. It looked at both junior doctors (residents) and consultants (attendings). In general the RCPCH Framework was supported.
Comment: The study suggested that junior doctors find maintaining life in a hopeless situation (whilst they wait for a senior opinion) was one of the most stressful situations we could put them in. It also underlined that where possible such decisions should be team ones including the parents, neonatologists, neonatal nurses, obstetricians and midwives

Sauve, R. S., C. Robertson, et al. (1998). "Before viability: a geographically based outcome study of infants weighing 500 grams or less at birth." Pediatrics **101**(3 Pt 1): 438-45.

OBJECTIVE: The primary objective of this study was to determine the likelihood of long-term survival and avoidance of disabilities in a geographically based population of infants born at 20 weeks gestation or more and weighing 500 g or less at birth. STUDY DESIGN: This was a 12-year historical cohort follow-up study of all infants born in this gestational age and birth weight category in the Province of Alberta, Canada, between 1983 and 1994. Data were collected from certificates of live births or stillbirths, death certificates, hospital records, and longitudinal multidisciplinary follow-up examinations. RESULTS: One thousand one hundred ninety-three infants were of 20 weeks gestation or more, weighed 500 g or less, and were born between 1983 and 1994. Eight hundred eleven (68.0%) were stillborn and 382 (32.0%) were born alive. Among the latter, neonatal intensive care was provided in 113 (29.6%) and withheld in 269 (70.4%). The infants receiving intensive care were of heavier birth weight, later gestational age, higher antenatal risk scores, were more likely to be born in a level III center, to have received antenatal steroids, and to have been delivered by cesarean section. Of the infants receiving intensive care, 95 (84. 1%) died and 18 (15.9%) were discharged alive, but 5 of these died after discharge because of respiratory complications. The infants discharged alive had later gestational age, were more likely to be small for gestational age, singletons, treated with antenatal steroids, and to have been delivered by cesarean section. Maternal indications were described in the majority of cesarean sections done for live-born infants. The 13 infants who were long-term survivors were followed at ages 12 and 36 months adjusted age. Four had no serious disabilities, 4 had one disability (cerebral palsy or mental retardation), and 5 had multiple disabilities (cerebral palsy plus mental retardation with blindness in 2 cases and deafness in 1 case). CONCLUSION: The majority of infants born at gestational age 20 weeks or more weighing <500 g were stillborn. Among live births, neonatal intensive care was withheld in 70% and initiated in 30%. Of the latter, 11% survived to 36 months of age, and of these, 4 infants (31%), most of whom are small for gestational age, female infants, avoided major disabilities but 9 (69%) had one or more major disabilities. Survivors are prone to rehospitalizations early in life, slow growth, feeding problems, and minor visual difficulties; rates of learning-related and behavioral problems at school age are not yet known. Implications. Parents and caregivers faced with the impending delivery of an infant in this gestational age/birth weight category should understand that survival without multiple major disabilities is possible but rare. They should be made aware of local population-based results and not just isolated reports.

Level of Evidence 5 **Quality** Fair **Evidence** Supportive

Comment: Overall we can calculate that only 1% of all babies of this size in this study survived intact. Unable to define outcomes based on gestational age or specific birth weight categories. No indication of whether DR mortality was from no resuscitation or lack of response. 17/18 of the babies who survived until discharge were growth retarded. There was no increase in age at death over time. It seems fair to conclude that the infant <500 grams is still "previable", even though very small numbers survived.
The authors summarise “parents and caregivers faced with the impending delivery of an infant in this gestational age/weight category should understand that survival is possible but rare without multiple major disabilities”.

Kilpatrick, S. J., M. A. Schlueter, et al. (1997). "Outcome of infants born at 24-26 weeks' gestation: I. Survival and cost." Obstet Gynecol **90**(5): 803-8.

OBJECTIVE: To determine neonatal survival, short-term morbidities, and cost per survivor in pregnancies delivered at 24-26 weeks' gestation in a center in which antenatal steroids and exogenous surfactant are standard care. METHODS: A retrospective cohort study compared survival, short-term outcome, and initial hospital charges for pregnancies delivered at 24-26 weeks during 1990-1994. We calculated hospital costs for each year by using the corresponding institutional cost-charge ratio. RESULTS: There were 138 infants after excluding those with severe anomalies. Survival was 43%, 74%, and 83% at 24, 25, and 26 weeks, respectively (P = .006). The majority of women received antenatal steroids, and the majority of surviving neonates received exogenous surfactant. Severe retinopathy of prematurity and chronic lung disease decreased significantly from 24 to 26 weeks (P < or = .026). The likelihood of having a surviving infant

without chronic lung disease or severe retinopathy of prematurity was 35% at 24 weeks and 78% at 26 weeks. Hospital costs for the 29 nonsurvivors were $1.46 million and for the 94 surviving infants were $16.9 million. The cost per day was similar at each gestational age, whereas the cost to produce a survivor was $294,749, $181,062, and $166,215 at 24, 25, and 26 weeks, respectively. CONCLUSION: Survival at 24 weeks was only 43% despite treatment with antenatal steroids and exogenous surfactant. The cost per survivor for infants born at 24 weeks was higher than the cost for those born after 1 more week in utero. Outcome improved markedly between 24 and 26 weeks, and small differences in gestational age lead to large economic differences. All efforts should be attempted to prolong pregnancy, and if prolongation is unsuccessful, treatment options including nonintervention should be available to parents of 24-week gestations.

Comment: Paper stresses importance of communication and discussion with parents and among obstetricians and pediatricians and also that all efforts should be made to prolong pregnancy.

Kramer, W. B., G. R. Saade, et al. (1997). "Neonatal outcome after active perinatal management of the very premature infant between 23 and 27 weeks' gestation." J Perinatol **17**(6): 439-43.

OBJECTIVE: To record the effect of aggressive perinatal management on neonatal outcome in the very premature infant. METHODS: A retrospective chart review of 114 infants born between 23 and 27 weeks' gestation, managed by one perinatal transport service at one hospital between July 1989 and December 1993. Fetuses > 23 weeks' gestation were considered viable and were managed with tocolytics, antibiotics, and surfactant at the discretion of the treating physician. Morbidity and mortality rates in the first 6 months, including stillbirths were analyzed. A major neurologic condition was defined as ultrasonographic evidence of grade 3 or 4 intraventricular hemorrhage or periventricular leukomalacia. RESULTS: Both neonatal mortality rate and the incidence of stillbirths decreased with advancing gestational age. Of 24 infants born at 23 weeks' gestation, 33% were stillborn and 13% were alive at 6 months. This survival rate improved to 48% for infants delivered at 24 weeks' gestation, and to 68%, 75%, and 71% for those delivered at 25, 26, and 27 weeks' gestation, respectively. The percentage of infants who survived without a major neurologic condition increased with advancing gestational age at delivery from 13% at 23 weeks' gestation to 40% at 24 weeks, 48% at 25 weeks, 70% at 26 weeks, and 71% at 27 weeks. The incidence of retinitis of prematurity, respiratory complications, and days spent in the hospital decreased with greater gestational age. CONCLUSIONS: An active plan of management for all gestations of > 23.9 weeks seems appropriate.

Comment: As with many other studies this one (which includes stillbirths) shows a very high mortality in the <24 week group despite aggressive tocolysis and intensive care. It is not clear whether the centre then adopted this as its own policy.

O'Shea, T. M., K. L. Klinepeter, et al. (1997). "Survival and developmental disability in infants with birth weights of 501 to 800 grams, born between 1979 and 1994." Pediatrics **100**(6): 982-6.

OBJECTIVE: Because the survival rate has increased for extremely low birth weight neonates, many have raised the concern that the rate of developmental disability among survivors will also increase. To address this concern, we analyzed changes over time in survival and major neurosensory impairment in a sample of extremely low birth weight infants born between July 1, 1979, and June 30, 1994. METHODS: The study sample included 513 infants with birth weights of 501 to 800 g who were cared for in either of the two neonatal intensive care units that serve a 17-county region in northwest North Carolina and who were born to mothers residing in that region. At 1 year of age (corrected for gestation), survivors were examined by a pediatrician and were tested using the Bayley Scales of Infant Development. Major neurosensory impairment was defined as cerebral palsy, a Bayley Mental Developmental Index <68, or blindness. A total of 209/216 (97%) of survivors were examined at 1 year of age. Epoch of birth was defined as follows: epoch 1, July 1, 1979 to June 30, 1984; epoch 2, July 1, 1984 to June 30, 1989; and epoch 3, July 1, 1989 to June 30, 1994. RESULTS: Survival rates for epochs 1, 2, and 3 were, respectively, 24/120 (20%), 63/175 (36%), and 129/218 (59%). In contrast, the proportions with a major neurosensory impairment did not increase over time; rates for successive epochs were 6/24 (25%), 17/61 (28%), and 26/124 (21%). Rates of cerebral palsy were 3/24 (13%), 12/61 (20%), and 9/124 (7%); rates of delayed mental development were 4/24 (17%), 12/61 (20%), and 17/124 (14%); and rates of blindness were 2/24 (8%), 0/62, and 5/124 (4%),

respectively. CONCLUSIONS: This analysis suggests that the increasing survival of extremely low birth weight neonates since the late 1970s has not resulted in an increased rate of major developmental problems identifiable at 1 year of age.

Comment: Relatively large numbers (26 at 23 weeks, 53 at 24 weeks) with fairly complete follow-up. Significant survival at 23 weeks is noted but this is babies admitted to NICU only and therefore a highly selected group. However in view of the large numbers and excellent follow up this is an important study.

Piecuch, R. E., C. H. Leonard, et al. (1997). "Outcome of infants born at 24-26 weeks' gestation: II. Neurodevelopmental outcome." Obstet Gynecol **90**(5): 809-14.

OBJECTIVE: To assess the neurodevelopmental outcome of infants born at 24-26 weeks' gestation. METHODS: One hundred thirty-eight nonanomalous infants were born at our hospital after pregnancies of 24-26 weeks' gestation between 1990 and 1994. Ninety-four infants survived to discharge and 86 were followed in a nursery follow-up program for outcome. Associations between gestational age and neurodevelopmental outcome and risk factors and outcome were analyzed. Mean age at follow-up was 32 months. RESULTS: The frequency of cerebral palsy did not differ significantly in the three groups (11, 20, and 11% at 24, 25, and 26 weeks, respectively). The incidence of normal cognitive outcome was associated significantly with gestational age at birth (28, 47, and 71% normal at 24, 25, and 26 weeks, respectively). Poor neurologic outcome was associated with the medical risk factor of intracranial hemorrhage grade 3 or 4 or periventricular leukomalacia. Poor cognitive outcome was correlated with both medical and social risk factors; however, there was an association between poor cognitive outcome and lower gestational age ($P < .05$), regardless of the relationships of any other risk factors to cognitive outcome. CONCLUSION: Although the incidence of cerebral palsy was low in these three groups, the high percentage of infants born at 24 and 25 weeks' gestation with cognitive deficits is concerning.
Comment: The relationship of poor cognitive outcome persisted even when controlling for other factors such as medical and social risk. Mild to moderate cognitive delay (rather than severe) was associated with high social risk (and also CLD). The authors could perhaps surprisingly not show an association between outcome and birthweight, which is contrary to most other published studies.

Tin, W., U. Wariyar, et al. (1997). "Changing prognosis for babies of less than 28 weeks' gestation in the north of England between 1983 and 1994. Northern Neonatal Network." Bmj **314**(7074): 107-11.

OBJECTIVE: To investigate the changing prognosis for babies of less than 28 weeks' gestation. DESIGN: A prospective, collaborative, population based survey. SETTING: The former Northern Regional Health Authority. SUBJECTS: All the births between 1983 and 1994 at 22 to 27 completed weeks' gestation to women normally resident in the region. MAIN OUTCOME MEASURES: Miscarriage, stillbirth, death in the first year of life, and disability in survivors. RESULTS: There were 479070 registered births in the study period. No baby of 22 weeks' gestation survived; only eight (4%) of the 197 babies of 23 weeks who were alive at the onset of labour survived for a year-a proportion that did not change during the study period. Survival among other babies of less than 28 weeks improved progressively between 1983-6 and 1991-4, but administration of artificial surfactant to babies requiring ventilation from mid-1990 was associated with further improvement in survival only in those over 25 weeks' gestation. Babies of 24 weeks required three times as much high dependency care per survivor as babies of 27 weeks (76 v 26 days). The rate of severe disability in the one year survivors of less than 26 weeks' gestation (30/123; 24%) was similar to that seen in the sampled survivors of 26 and 27 weeks (29/108; 27%); the proportion disabled did not change significantly during the study period. All the children born in 1983, 1987, and 1991 were later reassessed in greater detail: 10% (13/136) seemed destined for a continuing life of total dependency. CONCLUSIONS: Gestation, if accurately assessed, can give a woman facing very preterm delivery a clear indication of the prognosis for her baby and help her judge the appropriateness of accepting obstetric intervention and sustained perinatal support.

Comment: A well designed and executed study which gives good data for counselling for the UK. Survival at 24-27 weeks had improved over the 12 year period but disability rates (25%) had remained unchanged. Overall 10% of survivors were thought unlikely to become independently mobile or to communicate effectively due to their profound disabilities. Again this complete data from ALL births

suggests that intact survival at <24 weeks is extremely rare in the UK.

Lefebvre, F., J. Glorieux, et al. (1996). "Neonatal survival and disability rate at age 18 months for infants born between 23 and 28 weeks of gestation." Am J Obstet Gynecol **174**(3): 833-8.

OBJECTIVE: Our purpose was to determine gestational age-specific outcomes of infants born in a period of surfactant use. STUDY DESIGN: All 465 consecutive births between 23 and 28 weeks' gestation in a tertiary center from 1987 to 1992 were analyzed prospectively. At 18 months' corrected age, 217 of 254 (85%) survivors were evaluated. RESULTS: From 1987 and 1988 to 1991 and 1992 there was an increase in survival for infants born at 24 weeks (from 0% to 33% p = 0.17), 25 to 26 weeks (38% to 71%, p < 0.005), and 27 to 28 weeks (66% to 84%, p < 0.05). At each weekly interval from 24 to 28 weeks of gestation the respective incidence of normality was 44%, 71%, 57%, 76% and 72% (not significant) and the respective mean developmental quotient was 91 +/- 17, 89 +/- 25, 90 +/- 24, 96 +/- 15 and 96 +/- 14 (not significant). CONCLUSIONS: Gestational age was strongly associated with outcome in terms of survival. Overall, 70% of children followed up were developing within the normal range.

Comment: Unable to tell how whether resuscitation was attempted for those <500 grams. Study is based on gestational age (that is more difficult to accurately assess) but poor outlook for babies born at 23 weeks is similar to results from other studies.

Tyson, J. E., N. Younes, et al. (1996). "Viability, morbidity, and resource use among newborns of 501- to 800-g birth weight. National Institute of Child Health and Human Development Neonatal Research Network." Jama **276**(20): 1645-51.

OBJECTIVES: To assess risk factors affecting viability and analyze the effects of mechanical ventilation (MV) on neonatal outcome and resource use among extremely premature infants. DESIGN: Inception cohort study. SETTING: Neonatal intensive care units of the 12-center National Institute of Child Health and Human Development Neonatal Research Network. PARTICIPANTS: A total of 1126 infants with a birth weight of 501 to 800 g born in network centers between January 1, 1994, and December 31, 1995. MAIN OUTCOME MEASURES: Observed survival; maximum estimated survival (assuming the same survival among infants who died without MV as among infants in the same risk category who received MV); observed and maximum estimated survival without severe brain injury (either interventricular echodensity with ventricular dilation or parenchymal echodensity); hospital stay; resource investment. RESULTS: Overall mortality was 43%; mortality in infants without MV was 93%. A total of 15% of all the infants died without MV. Females, small-for-gestational-age infants, and infants whose mothers received antenatal steroids had an advantage in survival with MV equivalent to an increase in birth weight of 90 g, 57 g, and 67 g, respectively. The corresponding advantage of these infants in survival without severe brain injury was 107 g, 97 g, and 64 g, respectively. Females in the lowest birth-weight group were more likely to die without MV than were larger males with a similar estimated likelihood of survival with MV. Mean hospital stay was 115 days for the survivors, values much greater than the 17.9-day standard for 501- to 800-g survivors under the diagnosis related group system. Resource investment was considerable (127 hospital days per survivor and 148 days per survivor without severe brain injury), but, like outcome, varied markedly between risk categories. Had MV been used for all infants who died, we estimate a substantial increase in resource use and a maximum of 8 additional survivors (no more than 6 without severe brain injury per 100 infants with a birth weight of 501 to 800 g. CONCLUSIONS: Although recommendations to initiate or forgo MV for extremely premature infants have often focused on 1 factor (birth weight or gestational age), multiple factors should be considered. Other factors being equal, our analyses support use of MV for females at a minimum birth weight approximately 100 g lower than that for males. The current diagnosis related group reimbursement system can be expected to compromise resources for 501- to 800-g infants who would benefit from MV. Such care entails considerable resource use, although the cost per life-year gained is likely to be considerably less than that for many adults given intensive care. Our findings can be used to facilitate more appropriate treatment decisions, determine adequate resources, and better inform the debate about the benefits and burdens of intensive care for extremely premature newborns.

Comment: This is a large database of tiny babies. However, there are no data for newborns < 500 g birth weight. The assumption that survival rates for resuscitated babies could be applied to those not resuscitated

is questionable as there likely was selection bias. They emphasize that based on their data, resuscitation decisions should be based on gender, growth status and use of maternal steroids in addition to birth weight and gestational age. Whilst it is important to optimize care (eg maternal steroids) it is imperative that each individual case is considered on its own merits. Prenatal estimation of fetal weight/growth can be unreliable.

Fanaroff, A. A., L. L. Wright, et al. (1995). "Very-low-birth-weight outcomes of the National Institute of Child Health and Human Development Neonatal Research Network, May 1991 through December 1992." Am J Obstet Gynecol **173**(5): 1423-31.

OBJECTIVES: Our goals were to determine the mortality risk for infants weighing 501 to 1500 gm according to gestational age, birth weight, and gender and to document birth weight-related changes in mortality and morbidity over a 5-year time period. STUDY DESIGN: In this observational study perinatal data were prospectively collected by the 12 participating centers of the National Institute of Child Health and Human Development Neonatal Research Network from May 1991 through December 1992 and compared with the corresponding data from 1987 through 1990. Standard definitions were used to record sociodemographic factors, perinatal events, and the neonatal course to 120 days of life, discharge, or death. RESULTS: The 1991 and 1992 cohort included 4279 in-born infants. Among their mothers 10% were < 18 years old; 55% were black, 31% were white, and 11% were Hispanic; 14% had received no prenatal care; and 20% had received antenatal corticosteroids. Multiple gestations accounted for 20% of the births. Fifty percent of the infants were delivered by cesarean section. During 1991 and 1992 the overall survival for infants weighing 501 to 1500 gm at birth was 81%, compared with 74% in 1987 and 1988. Survival at birth weight 501 to 750 gm was 44%; it was 81% at 751 to 1000 gm, 92% at 1001 to 1250 gm, and 95% between 1251 and 1500 gm. Female infants had a significantly greater chance of surviving than male infants at similar birth weights and gestational ages. At any given gestational age, smaller infants were less likely to survive. Survival in all birth weight categories increased between 1987 and 1992, without accompanying increases in medical morbidity. Major morbidity increased with decreasing birth weight and included late-onset septicemia 22%, chronic lung disease (oxygen dependence at 36 weeks' corrected age) 18%, severe intraventricular hemorrhage (grades III and IV) 11%, and necrotizing enterocolitis 5%. Twelve percent of all infants were treated with corticosteroids for chronic lung disease, including 36% of infants who were oxygen dependent at age 28 days. The mean length of hospital stay was 69 days for survivors and 18 days for infants who died. CONCLUSIONS: Mortality for infants between 501 and 1500 gm at birth has declined over the past 5 years. There are interactions between birth weight, gestational age, gender, and survival rate. This increase in survival was not accompanied by an increase in medical morbidity.

Comment: Data are now quite dated, but numbers are large and 12 tertiary academic centers are represented. Again data is liveborns admitted to NICU only so survival figures may well be significant overestimates. No information is available on newborns < 500 g birth weight. The study emphasizes the importance of gender in estimating survival. 80% of mothers were not treated with steroids which is a much higher figure than we would expect today. The population was 55% black, 31% white and 11% Hispanic and would be certainly unrepresentative of the population of most European countries.

Allen, M. C., P. K. Donohue, et al. (1993). "The limit of viability--neonatal outcome of infants born at 22 to 25 weeks' gestation." N Engl J Med **329**(22): 1597-601.

BACKGROUND. With improved survival of preterm infants, questions have been raised about the limit of viability. To provide better information and counseling for parents of infants about to be delivered after 22 to 25 weeks' gestation, we evaluated the mortality and neonatal morbidity of preterm infants born at these gestational ages. METHODS. We studied retrospectively all 142 infants born at 22 to 25 weeks' gestation (as judged by best obstetrical estimate) from May 1988 through September 1991 in a single hospital. Mortality in the first six months, including stillbirths, and neonatal morbidity (i.e., the presence of intracranial pathologic conditions, chronic lung disease, and retinopathy of prematurity) were analyzed. RESULTS. Fifty-six infants (39 percent) survived for six months. Survival improved with increasing gestational age; none of 29 infants born at 22 weeks' gestation survived, as compared with 6 of 40 (15 percent) born at 23 weeks, 19 of 34 (56 percent) born at 24 weeks, and 31 of 39 (79 percent) born at 25 weeks. There were seven stillbirths at 22 weeks' gestation and four stillbirths at 23 weeks. The more

immature the infant, the higher the incidence of neonatal complications as determined by the number of days of mechanical ventilation, the length of the hospital stay, and the presence of retinopathy of prematurity, periventricular or intraventricular hemorrhage, or periventricular leukomalacia. Only 2 percent of infants born at 23 weeks' gestation survived without severe abnormalities on cranial ultrasonography, as compared with 21 percent of those born at 24 weeks and 69 percent of those born at 25 weeks. CONCLUSIONS. We believe that aggressive resuscitation of infants born at 25 weeks' gestation is indicated, but not of those born at 22 weeks. Whether the occasional child who is born at 23 or 24 weeks' gestation and does well justifies the considerable mortality and morbidity of the majority is a question that should be discussed by parents, health care providers, and society.

Comments: Study population now 12 years ago. Resuscitation decisions made in the DR by neonatologist (but presumably not the same one for all). No clear policy on resuscitation at <24 weeks so presumably some variability between neonatologists. However study has included stillbirths so survival figures should be more accurate. Infant intubated only if vigorous or responded to bag-mask ventilation. High DR loss at 23 weeks but this is perhaps not too unusual at this gestation. All data based on gestational age and not on birth weight. Whilst assessment of gestational age based on obstetrical estimate is not always accurate pragmatically GA is more important as fetal weight estimation is even more inaccurate and awaiting birthweight means it is difficult to provide accurate information parentally.

Whyte, H. E., P. M. Fitzhardinge, et al. (1993). "Extreme immaturity: outcome of 568 pregnancies of 23-26 weeks' gestation." Obstet Gynecol **82**(1): 1-7.

OBJECTIVE: To provide guidelines to the perinatologist regarding extremely premature infants based on the experience of the University of Toronto Newborn Service (two high-risk perinatal units and one outborn neonatal intensive care unit), with a catchment area of 60,000 deliveries annually. METHODS: The study included all births or admissions in the Newborn Service from January 1, 1982 to June 30, 1987 with gestational age determined by the best obstetric estimate of gestational age, ranging from 23-26 completed weeks. The obstetric records were reviewed and the surviving infants followed prospectively for a minimum of 2 years after delivery. RESULTS: Analysis of the neonatal and 2-year follow-up data on 568 infants born between 23-26 weeks' gestation revealed a 39% mortality rate, which increased with decreasing gestation. The highest mortality rates occurred following complicated pregnancies, including fetal growth restriction. Intact survival increased with increasing gestational age, from 11% at 23 weeks to 50% at 26 weeks. There was a marked improvement in both mortality and morbidity by 25 completed weeks. CONCLUSIONS: The results suggest that an aggressive approach before 24 completed weeks' gestation is not warranted. From a total of 60,000 live births per year, only one child born at 23 weeks' gestation and three at 24 weeks were free of major handicap at 2 years.

Comment: Includes an entire geographical area. Fairly large numbers of infants with good follow up data at 18 months to two years. The higher intact survival rate in the outborn center for 23-24 week babies probably reflects a referral selection bias. Older data, but consistent with other data concerning very low intact survival at 23 weeks gestation.

Sood, S. and G. P. Giacoia (1992). "Cardiopulmonary resuscitation in very low birthweight infants." Am J Perinatol **9**(2): 130-3.

Of 191 patients with birthweight less than 1500 gm admitted to our neonatal intensive care unit in a 2-year period, 41 underwent cardiopulmonary resuscitation (CPR). Eleven of 41 very low birthweight (VLBW) (27%) survived to be discharged. None of the infants who received CPR after 72 hours of life survived. Also, all infants who underwent CPR, both in the delivery room and neonatal intensive care unit (NICU), died. The most significant factor distinguishing survivors from nonsurvivors was the demonstration of vasopressor unresponsive hypotension 20 hours prior to CPR in the latter group. This study confirmed the very poor survival rate after CPR in VLBW infants. We conclude that performance of CPR in patients with vasopressor unresponsive hypotension or previous delivery room resuscitation should be considered a rescue or experimental treatment and parents should be given the option of no resuscitation. Future research efforts should be directed to better the understanding and treatment of cardiovascular dysfunction prior to cardiac arrest.

Comment: Numbers are very small. Data were not analyzed by birth weight category, although they say their data support Lantos' opinion that survival is poor after resuscitation of infants < 1000 g birth weight. Few of the babies were resuscitated in the DR. Differs from Lantos in that outcome was worse if arrest occurred > 72 hrs of age.

Wyckoff, M. and J. Perlman (2000). "Cardiopulmonary resuscitation in very low birth weight infants." Pediatrics **106**(3): 618-20.

A letter commenting on an earlier article (Finer 1999a) but showing the authors' data from their own institution over a 3 year period (1996-1998). The authors emphasized the importance of adequate ventilation to establish FRC and were concerned that moving early to ECM and/or epinephrine may compromise this (and suggested that the NRP guidelines were often not being followed).

Comment: The authors underline the importance of following the NRP guidelines during resuscitation so that ECM/epinephrine are not given at the expense of adequate ventilation and that other factors such as antenatal steroid usage, prophylactic surfactant delivery and the effect of low Apgar score (<2 and by implication "asphyxia") were taken into account. 7.5% of the babies 501-750g vs 2% of those 1251-1500g required ECM in the delivery room

Finer, N. N., T. Tarin, et al. (1999). "Intact survival in extremely low birth weight infants after delivery room resuscitation." Pediatrics **104**(4): e40.

OBJECTIVE: None of the 20 previously reported infants weighing <750 g at birth who received cardiopulmonary resuscitation (CPR) in the delivery room (DR) survived. To clarify whether such resuscitation is futile in our center, we evaluated our experience with DR-CPR over a 4-year period. STUDY DESIGN: We retrospectively reviewed the outcomes of all inborn infants with birth weights <1000 g at University of California, San Diego Medical Center from January 1993 to December 1996. Surviving infants and matched control infants were followed for </=40 months' adjusted age using standardized neurodevelopmental assessments. RESULTS: Of the infants with birth weight <1000 g born during this period, 29% (51/177) died, including 44% of those <750 g and 16% of those >/=750 g. Overall, 19 infants received DR-CPR, of whom 12 were <750 g. Of the infants who received DR-CPR, 79% (15/19) survived, including 10 of 13 infants <750 g and 5 of 6 infants >/=750 g. Of the 15 survivors, 10 were followed beyond 10 months' adjusted age (median: 28 months). At last examination, 70% were both neurologically and developmentally normal. Two infants had cerebral palsy with mild cognitive and severe motor developmental delay. Of 7 infants with birth weight <750 g, 6 had normal neurodevelopmental outcomes. The mean composite mental and motor scores of DR-CPR survivors were 93 +/- 10 and 89 +/- 25, respectively. No differences were found in neurologic or developmental outcome between DR-CPR survivors and control infants matched for gestational age, sex, and year of birth. CONCLUSIONS: Our results indicate that intact survival is possible for infants weighing <750 g at birth after DR-CPR.

Comment: These findings are somewhat at odds with other studies. However we know nothing about the ethnicity of these babies (which may be important) and the authors admit that "we were unable to document either the specific indications for chest compressions or epinephrine administration in the DR or the time course of the resuscitative efforts". Indeed of the 10 survivors <750g 7 received epinephrine without cardiac compressions. This would be contraindicated if following the current UK Newborn Life Support course recommended method for resuscitation.

Casalaz, D. M., N. Marlow, et al. (1998). "Outcome of resuscitation following unexpected apparent stillbirth." Arch Dis Child Fetal Neonatal Ed **78**(2): F112-5.

There are few data to inform a decision to resuscitate babies who are unexpectedly stillborn. The outcome for 42 successfully resuscitated stillborn children, of whom 62% survived to be discharged home, is reported. Of the survivors, a poor outcome with severe disability was found in 23% (including one postneonatal death), equivocal outcome was found in 15% (two mild hypertonia; two with mild hemiplegia and no associated other disability) and 62% were free of any impairment at follow up 20 months to 8 years later. In 39 (93%) fetal problems had been identified and the resuscitation team was present at delivery.

Poor outcome was associated with late return of heart beat, delayed respirations, neonatal acidaemia and early onset of seizures. Of the unexpected apparent stillbirths successfully resuscitated, 52% died or survived severely disabled, 10% had an equivocal outcome, but 36% survived apparently intact. Therefore, vigorous resuscitation is clearly indicated in these circumstances.

Comment: Need to be cautious about use of term stillborn. These and other studies address infants who apparently died recently. Rate of successful resuscitation 42/45 much higher than Jain's study where 31/93 died in the DR. Therefore the two definitions or patient populations may not be comparable. There are very few premature infants in this group, but prematurity did not apparently alter the prognosis. They identified late return of heartbeat, delayed respiration's, and acidemia as poor prognostic factors. 93% of these deliveries were anticipated and trained personnel were present. The poor prognosis described in those babies who had no HR at 10 minutes has been previously described and is an indication in itself to contemplate discontinuation.

Perlman, J. M. and R. Risser (1995). "Cardiopulmonary resuscitation in the delivery room. Associated clinical events." Arch Pediatr Adolesc Med **149**(1): 20-5.

OBJECTIVES: To determine (1) what percentage of infants require chest compressions and medications as part of resuscitation in the delivery room, (2) the associated clinical events contributing to neonatal depression, and (3) the neonatal outcome of such children. DESIGN: Observational study. SETTING: Urban county hospital. RESULTS: For 2 years, 39 (0.12%) of 30,839 infants were administered chest compressions and/or epinephrine as part of cardiopulmonary resuscitation in the delivery room. Fifteen were term infants and 24 were premature. Five term infants had evidence of severe fetal acidemia (FA) (umbilical cord arterial pH < 7.00 and/or base deficit > or = -14 mEq/L); two died secondary to severe brain injury, and the neurologic examinations showed abnormalities in the three survivors. The 10 infants without severe FA exhibited an uncomplicated neonatal course. Five infants had evidence of severe FA; the neurologic examination showed abnormalities in four. Of the remaining 19 infants without severe FA, four died and five additional infants have moderate to severe brain injury. Abnormal outcome was more likely to occur with severe FA ($P < .002$). The presumed clinical events contributing to the neonatal depression were severe FA (n = 10), malpositioning of the endotracheal tube (n = 5), and ineffective or improper initial ventilatory support (n = 24). CONCLUSIONS: Cardiopulmonary resuscitation in the delivery room, resulting in administration of chest compressions and medications, is a rare event. Approximately one third of the infants had evidence of severe FA; in the remaining two thirds, ineffective or improper initial ventilatory support was the presumed mechanism for the continued neonatal depression. The appropriate therapeutic response to continuing neonatal depression should be to optimize ventilatory support before administering chest compressions or medications.

Comment: Small numbers of premature infants. Grade II IVH is included as an abnormal outcome. Their data supports that need for CPR frequently results from inadequate ventilation and that in the depressed neonate good and adequate ventilatory support should be the priority. Outcome was particularly poor for premature infants with severe fetal acidemia. Unfortunately that data are rarely available while the resuscitation is ongoing.

Sims, D. G., C. A. Heal, et al. (1994). "Use of adrenaline and atropine in neonatal resuscitation." Arch Dis Child Fetal Neonatal Ed **70**(1): F3-9; discussion F9-10.

One hundred and five infants treated with adrenaline or atropine, or both, as part of resuscitation on 124 occasions were studied retrospectively. Adrenaline was administered to 98 infants, in 40 of whom it was in combination with atropine, and seven infants received atropine alone. Twenty infants were treated solely on the delivery unit, 81 on the neonatal medical unit, and four in both places. Twelve infants treated on the delivery unit and 13 treated on the neonatal unit survived. Follow up studies showed that 13 infants were handicapped with nine severely handicapped. Extreme prematurity, the need for early or repeated resuscitation using these drugs, particularly for episodes of collapse without a clear precipitating cause, and asystole rather than bradycardia were associated with a worse outcome. Evidence is accumulating to support a view that the use of these drugs for resuscitation at birth and in the first week of life of extremely preterm infants may be inappropriate.

Comments: Small numbers and older time period limit this study. However, these data are consistent with other data concerning high risk for death and disability among extremely premature infants receiving CPR/drugs. Follow up was erratic. Does not help answer the question of when to stop resuscitation in the DR as the denominator is survivors of DR resuscitation but suggests that if drugs are required in extreme prematurity during resuscitation outlook is likely to be very poor.

Yeo, C. L. and D. I. Tudehope (1994). "Outcome of resuscitated apparently stillborn infants: a ten year review." J Paediatr Child Health **30**(2): 129-33.

This study addresses the dilemma of whether to attempt resuscitation of the previously undiagnosed fresh stillborn infant and evaluates factors predictive of survival and long-term outcome. We reviewed the clinical spectrum, immediate complications and long-term outcome of 45 successfully resuscitated apparently stillborn infants (34 term, 11 preterm) who were admitted to the Intensive Care Nursery. Significant obstetric and intrapartum events were identified in 34 (75%) infants while 11 (25%) had no apparent risk factors. Of the 39 infants with neonatal complications, 37 had hypoxic-ischaemic encephalopathy (HIE: Sarnat stage 1 in 5, stage 2 in 15, stage 3 in 17); 12 (27%) had oliguria, 10 (22%) had hypotension, 7 (16%) experienced hypoglycaemia, 4 (9%) had disseminated intravascular coagulopathy (DIC) and 1 (2%) had persistent pulmonary hypertension of the newborn (PPHN). Fourteen infants (31%) died in the neonatal period and four (9%) died during infancy. Risks of death and adverse neurodevelopment were significantly increased in infants with stage 2 or 3 HIE ($P < 0.005$). Follow-up assessment of 24 of the 27 surviving infants revealed a normal outcome in 15 (63%), severe disability in six (25%), moderate disability in two (8%) and mild disability in one (4%) infant. The positive predictive value of stage 2 or 3 HIE was 70% for mortality and 80% for morbidity. One-third (15/45) of successfully resuscitated apparently stillborn infants were normal at follow-up assessment and the outcome for these infants was predicted with complete accuracy by the stage of HIE present during the neonatal period.

Comment: Similar results to other studies, i.e., "stillborn" infants can survive intact. Apgar of 0 at 5 minutes carried very poor prognosis, but numbers were small. Apgar of 1-3 at 5 minutes had much better prognosis. There is no data about Apgar scores at 10 min. While numbers are small, there was not a disadvantage to birth weight <2500 g or even <1500 g.

Davis, D. J. (1993). "How aggressive should delivery room cardiopulmonary resuscitation be for extremely low birth weight neonates?" Pediatrics **92**(3): 447-50.

Case record review of all 156 infants born <1000 grams in a single regional perinatal centre from June 1989-May 1992. 15 of 25 infants weighing <500 grams and 4 of 62 weighing 501-750 g did not have active intervention in the DR (mean gestational age 22.4 weeks, mean birth weight 436 g). For the 10 infants <500 g in whom resuscitation was attempted, 8 received only intubation. None survived. 59% of babies who weighed 501-750 g who responded to airway management survived. However, of those who required additional measures, none survived. Of infants 501-750 g with Apgar scores 0-3 at 5 minutes, 0 of 21 survived. This improved in the 751-1000 gram group to 3/8 (38%).

Comments: Data is now >10 years old. Larger series for this specific weight group than other studies. However, small numbers in each weight category. Data consistent with other data with predictors of poor outcome being birth weight <500 g and need for cardiac compressions and drugs in babies 500-750 g. An additional predictor would be lack of response to resuscitation (Apgar score 0-3 at 5 minutes) in babies 500-750 g.

Jain, L., C. Ferre, et al. (1991). "Cardiopulmonary resuscitation of apparently stillborn infants: survival and long-term outcome." J Pediatr **118**(5): 778-82.

To determine the outcome of apparently stillborn infants who received cardiopulmonary resuscitation, we studied the short- and long-term outcome of 93 infants who had an Apgar score of 0 at 1 minute of age and were resuscitated at birth. Sixty-two (66.6%) responded and left the delivery room alive; 26 (42%) of the 62 infants died in the neonatal period and 36 infants were discharged home; of the 36 infants, three

subsequently died during infancy. Of the 33 survivors, ten were lost to follow-up after discharge. Developmental assessment of 23 of 33 long-term survivors revealed normal outcome in 14 (61.7%), abnormal results in 6 (26%), and suspect status in 3 (13%). Fifty-eight infants had an Apgar score of 0 at greater than or equal to 10 minutes of age and all except one died; the surviving infant has an abnormal developmental outcome. We conclude that 39% of apparently stillborn infants who were resuscitated survived beyond the neonatal period and that 61% of the 23 survivors who were available for developmental follow-up had normal development at the time of last examination. Survival was unlikely if there was no response after 10 minutes of resuscitation.

Comment: Retrospective, multi-institution study with some question about definition of terms and population. Limited to stillborn population. Small numbers of premature infants. Further clarification of response not possible, e.g. what if Apgar is only 1 or 2 at ten minutes. Rate of failure of CPR was higher in level II centres and higher than in the study by Casalaz where 42/45 survived resuscitation in the DR.

Lantos, J. D., S. H. Miles, et al. (1988). "Survival after cardiopulmonary resuscitation in babies of very low birth weight. Is CPR futile therapy?" N Engl J Med **318**(2): 91-5.

We conducted a retrospective study of outcome after cardiopulmonary resuscitation (CPR) in babies of very low birth weight. Of 158 such babies (birth weight, less than 1500 g) admitted to a neonatal intensive care unit in 1985, 49 (31 percent) underwent CPR. Low birth weight, low Apgar scores, birth asphyxia, pulmonary interstitial emphysema, hyaline membrane disease, and severe intraventricular hemorrhage were associated with the need for CPR. None of the 38 babies who received CPR in the first three days of life survived. Four of the 11 babies who received CPR after the first 72 hours survived. Three of the four survivors had residual neurologic deficits. Survival rates after CPR in infants of very low birth weight are lower than those in older children or adults. CPR may therefore be considered a nonvalidated therapy in this population. If the results of our study are confirmed, CPR should not be instituted automatically in very-low-birth-weight babies as though it were a validated treatment. Instead, it should be administered upon parents' advance informed consent to experimental treatment.

Comment: Only an NICU population and hence not necessarily easy to extrapolate to the DR setting. Data is now 18 years old. Total number and numbers in each weight category are very small. Differs from that of Sood et al whose data demonstrated a worse prognosis in those requiring CPR after 72 hrs.

Levene, M. I., C. Sands, et al. (1986). "Comparison of two methods of predicting outcome in perinatal asphyxia." Lancet **1**(8472): 67-9.

In a follow-up study of 122 full-term infants in whom postasphyxial encephalopathy occurred the incidence of death or severe handicap was 1 in 1000 deliveries. The abilities of two methods of diagnosing intrapartum asphyxia to predict outcome at a median age of 2.5 years were compared. A decision matrix calculation was undertaken to assess the sensitivity and specificity of low Apgar score and postasphyxial encephalopathy. A 10 min Apgar score less than or equal to 5 was the most sensitive of six different Apgar ratings in predicting adverse outcome (sensitivity 43%, specificity 95%) but even this was much less sensitive than the presence of moderate or severe encephalopathy in predicting death or severe handicap (sensitivity 96%).

Comment: Apgar scores that are immediately available in the DR were more specific than encephalopathy that evolves over time. Unfortunately, the sensitivity of Apgar scores was low. Numbers were very small in each Apgar category. I am not sure this adds anything to our decision making as most people would continue resuscitation with an Apgar > 5.

Scott, H. (1976). "Outcome of very severe birth asphyxia." Arch Dis Child **51**(9): 712-6.

The aim of this study was to establish the outcome of very severe birth asphyxia in a group of babies intensively resuscitated at birth. 48 infants, born between 1966 and 1971 inclusive, were selected; 15 were apparently stillborn and 33 had not established spontaneous respirations by 20 minutes after birth. One-half of them died, but 3 to 7 years later three-quarters of the survivors are apparently normal. Later handicap

was associated with factors leading to prolonged partial intrapartum asphyxia, while acute periods of more complete asphyxia were not necessarily harmful.
Comment: Numbers are very small. Resuscitation protocols were significantly different from the NRP protocol and were carried out by individuals of varying skill levels. Many deaths were from causes other than asphyxia, such as HMD. However, even in the significant past, intact survival following severe perinatal depression was possible.

Steiner, H. and G. Neligan (1975). "Perinatal cardiac arrest. Quality of the survivors." Arch Dis Child **50**(9): 696-702.

Steiner, H., and Neligan, G. (1975). Archives of Disease in Childhood, 50, 696. Perinatal cardiac arrest: quality of the survivors. Twenty-two consecutive survivors of perinatal cardiac arrest have been followed to a mean age of 4 1/4 years, using methods of neurological and developmental assessment appropriate to their ages. 4 showed evidence of gross, diffuse brain-damage (2 of these died before the age of 3 years). These were the only 4 survivors of the first month of life who took more than 30 minutes to establish regular, active respiration after their heartbeat had been restored. The arrest in these cases had occurred during or within 15 minutes of delivery, and followed antepartum haemorrhage, breech delivery, or prolapsed cord. The remaining 18 were free of any evidence of brain damage. In the majority of these the arrest had occurred during shoulder dystocia or exchange transfusion, or was unexplained; the heartbeat had been restored within 5 minutes in most cases, and regular, active respiration had been established within 30 minutes thereafter in all cases.

Comment: Very small numbers and a mixture of babies arresting at different times. Obviously old data and lack of standard resuscitation protocols. There is no control for confounding factors such as maternal medications or anesthetics that might depress respiration.

Citation Marker	Full Citation*
Vohr (2004)	Vohr BR, Wright LL, Dusick AM, Peritt R et al Center differences and outcomes of extremely low birthweight infants Pediatrics, 2004, 113, 781

A review of 8 centres from the NICHD database looking at outcome of babies born weighing 401-1000g in 1993 and 1994. The study includes only liveborn babies but importantly looked at outcome at 18-22 months with a just acceptable follow up of 78% of the cohort. There was a marked difference in outcome and survival between the units but the need for active resuscitation at birth was associated with a significant increased risk of death, psychomotor and neourodevelopmental impairment and cerebral palsy.

*CommentLevel of evidence: * Quality: * Supportive*

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