Care at the Edge of Viability: Medical and Ethical Issues

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KEYWORDS

- Periviability • Ethics • Decision-making • Extreme prematurity

MEDICAL ISSUES

General Considerations

When critically examining the ethical issues for infants born extremely preterm, at 22 to 25 weeks' gestation, a review of neonatal outcomes and its limitations is necessary to help families and the perinatal community in making shared informed decisions. The complexity of this process must take into consideration the chances for survival when such an early birth occurs, the range of complications experienced by these infants once born, and the impact of both acute and long-term health and developmental care needs for the infant and families. The woman or couple must interpret this information within their moral framework, deciding which course of action—comfort care or resuscitation with a trial of intensive care—should be pursued in the delivery room.

Informed decision-making requires knowledge about fetal development at this critical period, including the degree of physiologic development necessary to sustain life outside the womb, even with currently available therapies. Not only are infants born in this periviable period susceptible to injury sustained from preterm birth but also their neurodevelopmental processes are changed so that the normal migration and connectivity patterns in the brain are altered permanently, leading to errors in brain development. No technological advancements have been able to address this insult to development. Thus, although survival has improved for these extremely preterm babies, the neurologic and developmental sequelae they experience have not. In addition, the potential for survival at 22 to 25 weeks is not an all-or-none phenomenon. Biologic variability in organ maturation and function among individual fetuses contributes

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to difficulty in accurately predicting the likelihood of a particular outcome before the infant's birth. Discussion must therefore encompass not only what is possible but also what is probable in terms of treatment options and outcomes.[1] Maternal health and pregnancy complications further affect survival rates and long-term outcomes. Education and support are essential for the perinatal team members to assure they offer appropriate consistent information and assistance to families.

Injury versus alterations in development: prematurity versus immaturity

Developmentally, at 22 weeks' gestation, although all major organs are present, their structure and function are at different phases and extremely immature. This circumstance poses significant challenges for physicians trying to promote survival with minimal morbidity. Unique to infants born at 22 to 25 weeks' gestation and different from older preterm infants is the structural and developmental immaturity of the lungs and brain. Damage to these organs and secondarily to the gastrointestinal tract has the greatest impact on the chance for survival and the degree of functional impairment. In particular, normal neuronal migration, starting at 18 weeks, is arrested at birth and does not continue to follow the same pattern as in children who remain in utero or in later-born preterm infants whose neurons have completed migration. Although review of the developmental contribution of each organ system is beyond the scope of this article, interventions proven efficacious for older preterm infants may be physiologically and developmentally ineffective in the extremely immature baby.

Methodological themes important to review

Statistics The manner in which outcome statistics are reported affects how outcome data are interpreted. Survival statistics are significantly higher if only infants admitted to the intensive care unit are considered (10/100), compared with all live births (10/150) or with all live births and still births (10/200).[2] Likewise, rates of disability reported for all live births (eg, 10/100 = 10%) versus rates reported on only those who survive (eg, 10/40 = 25%) will be different if a large number of infants die before discharge.[3] The specific denominators used to describe these rates vary based on institutional and national policies, making comparability between cohorts difficult.[4]

Birth weight versus gestational age Until recently, most cohort analyses have focused on birth weight categories. These cohorts include infants who are more developmentally mature but are small for gestational age. Cohorts whose upper limits include older infants will seem to have better survival statistics than cohorts whose upper limits are younger.[5] Gestational age definitions are themselves subject to uncertainty based on dating methods.[6] The National Institutes of Health Center for Child Health and Human Development (NICHD) Neonatal Research Network[7] notes that a difference of 100 g is equivalent in survival to an additional 1 week in utero, and an additional day in utero increases survival by 4%.[8] Because of these difficulties, the outcomes literature has started to report cohorts with gestational ages.

Differences in management styles Survival statistics can also reflect delivery room management styles and can vary by center and within regions and countries. Proactive strategies have resulted in increased live births and survival rates compared with less-aggressive management styles.[9–11] Some international comparisons of varied management approaches have shown increased morbidities in the total population,[9] whereas others have reported similar rates of morbidities.[10,11] It has been argued that management strategies can result in self-fulfilling prophecies, whereby less-aggressive management at lower gestational ages results in decreased survival.[6]

Cohorts: center, multicenter, regional, international Regional cohorts representing tertiary referral centers with large sample sizes may be subject to referral biases, which can be resolved by using geographic (population-based) cohorts. Center-specific cohorts collect detailed data but may have limited sociodemographic diversity making generalization difficult. Epoch comparisons allow for evaluation of trends over time reflecting changing management strategies and survival indices.

MEDICAL OUTCOMES

Survival to Hospital Discharge

Table 1 summarizes survival rates by gestational age for live born infants reported in the United States,[12,13] Europe,[14–18] Canada,[19] and Japan.[20,21] These data illustrate the worldwide variation in survival rates based on nation-specific approaches to care and when data are presented for the entire population, live births, or neonatal intensive care unit (NICU) admissions. A review of the NICHD database reveals survival rates of 6% for infants at 22 weeks, 26% at 23 weeks, 55% at 24 weeks, and 72% at 25 weeks.[12] These rates are comparable to 2009 data from the Vermont Oxford Neonatal Network (VON), a multicenter multinational database; reported survival rates were 5% at 22 weeks, 33% at 23 weeks, and 61% at 24 weeks.[13] Of the infants in the NICHD cohort who survived, 100% at 22 weeks' gestation experienced morbidity at discharge, 92% at 23 weeks, and 91% at 24 weeks. Survival at 22 weeks' gestation was significantly more likely to be influenced by delivery room resuscitation practices than at 25 weeks, suggesting potentially higher survival rates if all infants been resuscitated.

In the EPICure study, a population-based cohort of infants born between 20 and 25 weeks' gestation in the United Kingdom and Ireland during 1995, 1%, 11%, 26%, and 44% of infants born at 22, 23, 24, and 25 weeks' gestation, respectively, were discharged alive from the NICU.[14] Some studies provide survival data as all births and all live births[15] or admissions to the NICU.[16] The Swedish EXPRESS group, who reported on live births, showed that survival rates were higher at 22 and 23 weeks than the NICHD or VON cohorts: 12% at 22 weeks, 54% at 23 weeks, 71% at 24 weeks, and 82% at 25 weeks. Survival rates at 1 year were 9.8%; 53%, 67%, and 82%, respectively.[15] In the Norwegian Extreme Prematurity Study, survival rates among NICU admissions were 39% at 23 weeks, 60% at 24 weeks, and 80% at 25 weeks. No infants at 22 weeks were admitted to the NICU, and the risk of not being resuscitated increased with decreasing gestational age.[16]

Neurodevelopmental Outcomes After Extremely Preterm Birth

Numerous outcome studies have been reported in recent years from single-center, multicenter, and national cohorts of extremely preterm children. Significant variation exists in outcomes, partly related to the chronologic age at evaluation, criteria used to classify disability and functional capacity, and attrition among the group whose outcome is described. The two largest cohorts of children born since the mid-1990s for whom sequential outcome data by week of gestation are cited are the NICHD Neonatal Network and EPICure Study Group. The earliest outcomes that correlate with later severe disability are reported at 18 to 22 months' and at 30 months' corrected age by the NICHD[22] and EPICure Group, respectively.[14] Subsequent time points when outcomes have been reported are 6 to 8 years of age[23,24] and 10 to 12 years of age.[25] Assessments at 8 years of age most accurately predict academic achievement and performance outcomes into young adulthood.

Table 1
Survival rates to hospital discharge among infants born 22 to 25 weeks' gestation

Cohort	Year	Denominator	22 Wk	23 Wk	24 Wk	25 Wk
NICHD (United States)[12]	2003–2007	Live births	6%	26%	55%	72%
VON (Multinational)[13]	2009	Live births	5%	33%	61%	—
Canadian Neonatal Network (Chan et al, 2001)[19]	1996–1997	Population-based	1%	17%	44%	68%
EPIBel (Vanhaesebrouck et al, 2004)[18]	1999–2000	Population-based	0%	6%	29%	56%
EPICure (United Kingdom, Ireland)[14]	1995	Population-based (LB + SB)	1%	11%	26%	44%
EXPRESS (Sweden)[15]	2004–2007	Live births	12%	54%	71%	82%
		Population-based	7%	34%	60%	73%
Norwegian Infant Study[16]	1999–2000	Admissions to NICU	0	39%	60%	80%
		Population-based	0	16%	44%	66%
Switzerland (Fischer et al, 2009)[17]	2000–2004	Population-based	0%	5%	30%	50%
Japan: Single Center[20]	1991–2006	Live births	25%	47%	50%	—
Japan: Multicenter[21]	2003		36%	75%	75%	

Abbreviations: LB, live birth; NICU, Neonatal Intensive Care Unit; SB, Stillbirth.

The NICHD has reported that the likelihood of a favorable outcome with neonatal intensive care can be better estimated by evaluating four factors in addition to gestational age: female or male sex, exposure or nonexposure to antenatal corticosteroids, single versus multiple birth, and birth weight.[7] The infant's sex not only impacts the chance for survival but also has implications for longer-term cognitive and functional outcomes.[26] **Table 2** provides an overview of the rates of death and severe neurodevelopmental impairment among infants enrolled in the NICHD Network. Death or severe to profound disability is common among the few survivors born at 22 weeks' gestation. Similarly, intact outcomes for infants at 23 and 24 weeks' gestation are extremely poor. By 25 weeks' gestation, however, greater equipoise is seen, as rates of death and severe disability approach 50%.[7]

Hintz and colleagues[27] recently reported that early childhood neurodevelopmental outcomes are not improving for infants born before 25 weeks' gestation. Despite advances in perinatal care practices, infants born between 2002 and 2004 did not experience fewer adverse outcomes (moderate-severe cerebral palsy [11% vs 14.9%], cognitive impairment [IQ<70; 44.9% vs 51%], or developmental delays [50.1% vs 58.7%]) at 18 to 22 months' corrected age compared with an earlier cohort of infants born between 1999 and 2001.

The EPICure Study Group has reported longitudinal outcome data through 11 years of age for their population of 4004 infants born in 1995. Of this group, 811 infants with gestational ages less than 26 weeks were admitted to the NICU; 314 babies survived to hospital discharge. Among survivors, 92% (283/302), 78% (241/308), and 71% (219/307) were evaluated at 30 months' corrected age, 6 years, and 11 years of age, respectively. Neurocognitive outcomes and composite disability rates are summarized in **Table 3**.[24,26] Overall, only 16% of survivors between 22 and 25 weeks' gestation are disability-free; 39% have mild impairments that affect functioning, with 45% exhibiting moderate to severe impairments. Extremely preterm children have a mean IQ significantly below that of their classmates (83.7 [SD 18.0] vs 104.1 [SD 11.1]), modified only slightly through controlling for socioeconomic status and

Table 2
Rates of death and severe neurodevelopmental impairment among infants enrolled in the NICHD Network

		Outcomes at 18–22 Months' Corrected Age		
Gestational Age (Completed Wk)	**Death Before NICU Discharge**	**Death**	**Death/Profound Neurodevelopmental Impairment**	**Death/Moderate to Severe Neurodevelopmental Impairment**
Outcomes for all infants in the sample				
22 wk	95%	95%	98%	99%
23 wk	74%	74%	84%	91%
24 wk	44%	44%	57%	72%
25 wk	24%	25%	38%	54%
Outcomes Only for Mechanically Ventilated Infants in the Sample				
22 wk	79%	80%	90%	95%
23 wk	63%	63%	76%	87%
24 wk	40%	41%	55%	70%
25 wk	23%	24%	37%	54%

Data from Tyson JE, Parikh NA, Langer J, et al. Intensive care for extreme prematurity: moving beyond gestational age. N Engl J Med 2008;358:1672–81.

Table 3
Neurocognitive function and degree of disability at 6 years,[24] and 11 years[26]

Outcome Age 6 Y	≤23 Wk	24 Wk	25 Wk	Outcome Age 11 Y	≤23 Wk	24 Wk	25 Wk
Cognition (%)				Cognition (%)			
No disability	25	21	33	No disability	35	26	34
Severe disability	25	27	17	Mild	26	27	30
				Moderate	22	26	25
				Severe	17	21	10
Neuromotor (%)				Neuromotor (%)			
No disability	70	75	79	No disability	78	78	86
Cerebral palsy	16	19	10	Cerebral palsy, mild	9	9	7
				Cerebral palsy, moderate	4	4	2
				Cerebral palsy, severe	9	9	5
Overall disability (%)				Overall disability (%)			
No disability	12	14	24	No disability	13	16	17
Severe disability	25	29	28	Mild	39	30	44
No disability (original birth cohort)	1	3	8	Moderate	26	33	28
				Severe	22	21	11

excluding children untestable because of severe impairments (20 vs 15.5 points difference).

The infants sex and gestational age have independent effects on outcomes. Serious disability was more common among extremely preterm boys (53%) than preterm girls (38%), with boys scoring eight points lower than girls. Serious disability was identified in 53% of children born at 23 to 24 weeks' gestation compared with 39% of children born at 25 weeks. Mean cognitive scores at 23, 24, and 25 weeks' gestation were 82.9 (SD 21.2), 79.6 (20.8), and 86.1 (15.3), respectively. Among children with significant disability, 75% had impairment in one domain (cognition, vision, hearing, neuromotor function), 17% in two domains, and 8% in three.[26]

Studies in a single center in Japan, where all infants receive intensive care beginning at 22 weeks' gestation, showed that 67% (2 of 3 survivors) had significant neurologic disability and 100% had cerebral palsy. At 23 and 24 weeks' gestation the risks of disability were 40% and 45%, respectively, and risks for cerebral palsy were 62% and 28%, respectively.[20]

Health and Behavioral Outcomes

Poor health outcomes affect preterm infants more than term controls[28,29] and show gestational age effects.[30] Behavioral differences, including autism spectrum disorder, and inattention type attention deficit hyperactivity disorder (ADHD)[31] are more prevalent among preterm infants.[30] Adult psychiatric disorders, schizophrenia, and externalizing and internalizing behaviors are up to 10-fold more likely to occur in low-birth-weight children.[30] Preterm children have been reported to either show fewer risk-taking behaviors[28,32] or be similar to the general population.[30] These studies, however, reflect preterm adolescents/young adults who were more mature at birth.

Social Relationships and Quality of Life Perceptions

Despite these differences, many studies show higher-than-anticipated overall quality of life perceptions by the preterm individuals and their families.[32] Patterns of adjustment give surprisingly favorable perceptions of quality of life for many preterm adolescents and young adults,[29,31] despite the lower likelihood of finding a life partner,[30] increased perceived difficulties in romantic relationships and finding a job, lesser scholastic achievement, and poorer athletic abilities.[33] Other reports suggest no differences in overall independence and social relationships.[34] Self-reports of quality of life by preterm adolescents are high despite parental reports of more frequent issues with depression and ADHD.[31] A meta-analysis focused on quality of life studies highlighted the differences in self-reports and parental reports. In general, self-reports suggest no differences between the teen/young adulthood perception of quality of life and term controls despite objective measures and parental reports suggesting the contrary.[35]

ETHICS

Overview

The four cardinal principles of beneficence, nonmaleficence, autonomy, and justice that guide medical ethics frequently conflict when questions related to neonatal intensive care and delivery room management arise for extremely preterm infants. These principles are briefly defined in **Table 4** followed by discussion about the tensions inherent in neonatal decision-making. Professional guidelines are reviewed and a culturally and ethically sensitive approach to decision-making offered.

Table 4
Ethical Principles

Beneficence	Duty of the physician to take action to prevent harm or actively promote welfare of the patient[70]
Nonmaleficence	Duty of the physician to "above all (or first) do no harm."[70] Passive action[70]
Autonomy Respect for Autonomy[a]	"Self"- auto and "rule"-nomos[59] "…at minimum, to acknowledge that person's right to hold views, to make choices and to take actions based on personal values and beliefs."[59] Norm guiding medical decision-making for competent patients[41]
Distributive Justice	Balance between the patients' rights to medical care and the fair allocation of resources and social burdens within society[59]

[a] For neonates, respect for autonomy applies to surrogate decision-making, accepted to be the parent's responsibility, acting on behalf of the best interests of the child.[61]

Principles

Table 4 defines the principles of beneficence, nonmaleficence, autonomy, and justice.

Framework for Ethical Decision-Making

Sound evidence-based ethical decisions cannot be made without evaluating what is known and predictable and what is unknown and unpredictable.[36] The struggle in decision making for these marginally viable infants begins with the data. When outcomes are clearly beneficial[37] or "predictably good enough,"[38] there is little ethical conflict and treatment is mandatory.[38,39] When treatment is deemed futile[37] and society judges the cost to be unacceptably high relative to benefit,[39] then it is mandatory not to provide treatment. In fact, as argued by Paris and Reardon,[40] it should be considered ethical and moral to not offer options for futile treatment because this undermines patient autonomy, misinforming patients that options exist when they do not. When outcomes are "uncertain" or "ambiguous,"[37,38] however, society might reasonably, although not universally, consider the cost to be acceptable in relation to the value.[39] Treatment choices should be available and explained to the decision makers.

The health care team should thoroughly assess the mitigating factors that may influence prognosis. A fetus' initial prognosis may change based on complicating antenatal and/or postnatal factors. Thus, open and transparent multidisciplinary communication between health professionals and the family is crucial to sustain trust and foster collaborative decision-making. Given the uncertainty and unpredictability of outcomes and significant associated health burdens for the infant and family, the perinatal community supports a process of shared decision-making between the physician and the family. Parents of extremely immature infants are permitted to interpret information within the context of their own moral values.[41,42] The exact gestational ages at which these boundaries are set have been shown to vary among physicians, disciplines, health care institutions, and countries.[43,44] The tensions inherent in neonatal decision-making must be explored to understand the variability in professional guidelines.

TENSIONS IN ETHICAL NEONATAL DECISION-MAKING FOR EXTREMELY PRETERM INFANTS

Futility: Is it a Legitimate Concept to Justify Care Boundaries for Extremely Immature Infants?

The inherent limitations must be understood when defining futility. Quantitative definitions propose labeling futile interventions as those consistently resulting in treatment failures when provided consecutively to 100 patients.[45] Operationalizing this definition in the context of the extremely immature neonate is problematic given limitations in the outcomes evidence and ethical concerns in obtaining this data.[36] Defining futility qualitatively attempts to isolate the term *futile* from judgments related to the value of the intended outcome, which are values inevitably heterogeneous in any society.[46] Futility can also be defined as qualitative effects to the "whole person" rather than brief effects of treatment.[45,47,48] However, this effect/benefit dyad is inseparable from the values assigned to the effectiveness of a particular outcome.[46]

Futility arguments based on distributive justice rest on cost analyses, assessment of benefits and burdens, and the ability to predict outcomes.[46,47] A review of hospitalization and posthospitalization costs in industrialized countries has shown increased health care cost trends with decreasing gestational age and birth weight, increasing survival and morbidities at lower gestational ages, and costs far exceeding what would be anticipated based on the proportion of infants born.[49–51] In addition, hidden costs such as sibling effects and the impact on family functioning are rarely considered.[36,49] The question becomes whether these resources would be better allocated toward preventive measures to decrease rates of preterm birth.[52] Unfortunately, factors predictive of resource expenditures before birth remain elusive and therefore cannot be used in a decision analysis.[42,53–57]

Lastly, attempts at resolving the futility debate balance concepts of best interests, patient autonomy and physician duties. Kopelman[58] argues that the best interests standard depends on assessments of benefits and burdens; maximizing short- and long-term interests while allowing subjective latitude as long as an objective minimum standard of care is met. This standard weighs the rights and duties of the patient against rights and duties to others. She argues that the "Best Interests' Standard permits within socially sanctioned limits, and established rights and duties, individualized decision-making including attention to such decisions as when to seek to maintain biologic life and when to seek comfort care." Discussions of physician duties often cite the Hippocratic Oath, which states "I will use treatment to help the sick according to my ability and judgment, but I will never use it to injure or wrong them."[59] Implicit are principles of beneficence and nonmaleficence. When the patients' best interests are not clear and are potentially harmed is when conflict with physician duties arises and attempts to define futility begin. However, no consensus has been obtained with this approach, reiterating the multidimensional "complex network of relational obligations, which can be negotiated in one way under certain circumstances and in another way when the situation changes."[47]

These arguments, however, are not meant to imply that all demands for treatment should be honored. Physicians have an obligation to protect patients from treatment that involves risk for inexcusable harm without ultimately altering imminent, inevitable death.[6] Fine and colleagues[60] note that no clear guidance is available from professional organizations on conflict resolution when parents want to continue treatment that physicians feel does not further the infant's best interests.

The authors suggest that using "futility" as a reason for limiting care is misleading and too dependent on subjective interpretations. In constructing the boundaries of the "gray zone," it would be preferable to describe limits based on care that minimally promotes a socially and culturally defined goal, congruent with a family's moral framework, and ethically acceptable based on empirical outcomes evidence and evidence-based best interests principles. The burden of proof would then no longer lie in showing that a treatment fails but rather that a treatment meets an acceptable level of success with respect to the defined goal.

Surrogate Decision-Making: The Concept and Role of the Parent

For patients who lack decisional capacity, the medical community advocates for a surrogate decision-maker. In adult populations, this representative makes decisions believed to be consistent with the patient's wishes, executing "substituted judgment." For infants, whose wishes are unknown, decision-making uses the best interests standard, and the representatives who can best ascertain these interests are generally accepted to be the infant's parents.[61] They are expected to possess adequate knowledge and information to make informed decisions, be committed to the child's interests while emotionally stable, and be able to make reasoned judgments.[59] This role is rarely disputed unless physicians feel the parents do not meet these qualifications.

Determining a child's best interests is complex. It requires an assessment of how a "reasonable person" (or the infant as an older individual) would weigh the benefits and burdens of disabilities and overall perceptions about quality of life.[62] Furthermore, perceptions of disability are often presumed worse by those without disability.[63] Whether the best interests of the child should be considered in isolation of the family's interests is also disputed,[64] because burdens on families after the birth of an extremely preterm infant are significant.[65]

Shared Decision-Making: The "Responsibility"

Many professional organizations support a process of shared decision-making between the physician and the parents[66–69] under conditions of uncertainty in which significant burdens to the infant and family could ensue. What exactly is shared decision-making: a process, a decisional responsibility, or both? The authors argue that it should be a process with decisional responsibility based on parental preferences. Without fulfilling certain requirements in this process, the resulting decisional outcomes can be biased. Shared decision-making does not preclude autonomous decision-making. Rather, by fulfilling the tenets of informed consent, the processes of shared decision-making support autonomous decision making.

Informed consent requires adherence to five principles: disclosure, comprehension, voluntariness, competence, and decision or consent.[70] Disclosure requires that complete information about the treatment and its risks, and the risks and benefits of forgoing treatment, is communicated.[70,71] The inherent challenge is that the extent of the disclosure can be based either on professional standards,[70] reasonable person standards (information that a minimum number of people would deem important in making these decisions),[72] or a subjective standard in which the physician decides what information is the most salient to share.[70] Comprehension signals the decision-maker's capacity to assimilate and articulate this information. Voluntariness reflects the decision maker's right to be free of any coercive influences on their decision. Competence requires an ability to integrate the information and assimilate it in terms that are both accurate and relevant to the circumstances, weighing benefits and burdens, to come to a consistent choice. Finally the last step, the consent or decision signifies autonomous decision-making.

Shared decision making also requires a reciprocal exchange of information. Physicians should communicate medical information objectively to the parent in exchange for information about the parent's values and moral ideals.[41] Informed consent and shared decision making have been suggested to differ in the final tenet: consent or decision. In shared decision making, the physician's role has been proposed to include active participation, sharing in the decisional responsibility, and providing recommendations. In the informed consent model, patients or surrogate decision makers make the decision independently without physician recommendations.[73,74]

In principle, processes supporting informed consent and autonomous decision-making are the norm. In practice, several leading ethicists have suggested that this last step, the end-of-life decision-making responsibility, can be too overwhelming for some parents,[75,76] especially as it relates to withdrawal of care for neonates. Unquestionably, asking surrogates to physically sign a do not resuscitate order increases stress and produces feelings akin to "signing a death warrant."[77] The anguish, psychological distress, and suffering that accompany these end-of-life decisions are important to recognize because despite the ethical equivalence of withdrawal and noninitiation of care, the psychological consequences have the potential to be widely divergent.[75] This fact suggests that the "wait and see approach," which itself is disputed as an effective prognostic tool,[42,54–57] may have limited applicability in this difficult decision.

Despite hesitations concerning the burdens of parental responsibility, studies of parental perceptions about end-of-life decision-making after withdrawal of care from sick neonates showed that most parents felt it was their responsibility, as part of their parental duty, to make these decisions on behalf of their infant.[78–80] These beliefs remain consistent over time; parental guilt was not related to withdrawal of care but rather to their less-active participation in the decision-making process.[79]

Families' exhibit varied decision-making preferences. Zupancic and colleagues,[81] identified that physicians are poor at determining which decision-making style families favor. Respecting a family's right to determine their desired level of participation in decision-making is both legal and ethical. If a family chooses not to participate in decision-making, this should be respected as an autonomous decision; under these circumstances forcing a decision disrespects their choices.[82] Qualitative research has shown that when parents are confronted with a decision-making style that differs from their expectations, they are less confident about their decisions.[83] Even when the decision-making approach is less autonomous, physicians have a responsibility to explore and formulate management decisions consistent with the parent's moral framework. Parents must be engaged in a process of consent and assent: consent to give the physicians decisional discretion and assent for the actual management decision.

Assent Versus Consent: The Role of Physician Recommendations

The difference between assent and consent is subtle. Assent traditionally means concurrence of opinion, whereas consent usually denotes permission. Assent requires physician recommendation, whereas it can be argued to be discretionary in a consent process. Physician recommendations have been criticized for introducing bias based on physician values, perpetuating a perceived power hierarchy between the physician and the patient.[84,85] Clinically, both assent and consent models have been described in end-of-life decision-making in adult and neonatal settings.[74,83] In neonatal settings, two paradigms are common: one in which a physician neutrally presents objective information, allowing parents to decide independently to consent to a particular course of action, and another in which physicians propose a course of action to which parents assent. The fact that two paradigms exist is not surprising given the lack of consensus among professional organizations.[67] The American Academy of Pediatrics (AAP) Committee on Bioethics advocates for a negotiated model, in which parental moral values guide decision-making, whereas the AAP Committee on Fetus and Newborn suggests an expertise model, in which physicians are more directive in assessing the best interests of the infant.[68,69,86] In adult end-of-life decision-making, four practices have been described: physicians taking an informative role, a facilitative role, a collaborative role, or a directive role.[74] Physicians seldom deviated from their consultative styles, rarely giving recommendations even when requested by surrogates.[74,83]

For parents who favor active participation in decision-making without physician recommendations, consent models may be appropriate, whereas for those who desire a more passive role, assent models with physician recommendations may be preferable. Assent models can incorporate physician recommendations either by asking for agreement or concurrence with a proposed plan of action or requiring dissent to a proposed course of action, also known as *default* models. The difference between these approaches rests on whether the parent must make an active decision. Use of defaults (disagreement with the proposed course of treatment) may be an important communication strategy under certain circumstances, lessening the burden of decision-making feared by some parents. Feudtner and colleagues[87] suggest that when a child's death is imminent and the goal is to determine whether to halt or continue therapy, using default options would not be unreasonable because they would permit parents to achieve a desired goal without needing to actively decide to withdraw care.[87] However, processes involving default models for a recommended course of care can exert powerful effects on decisional behaviors, and therefore must be used with caution.

Quality of Life Versus Sanctity of Life

Subjective judgments about quality of life and sanctity of life are central to decision-making. Parents must rapidly assimilate medical information under conditions of uncertainty, incorporating quality of life and sanctity of life perceptions, to judge the overall value of a particular decision. They may be at a disadvantage if long-term issues were not addressed prenatally,[88] because their attention is directed toward the immediate effects of interventions without consideration of long-term consequences.[88,89] Unintentionally failing to address the longer-term outcomes and their meaning to families may lead to misperceptions about future expectations.

What is quality of life and who is best suited to make these assessments? Quality of life might be considered a minimum standard for life beyond biologic existence. That minimum standard is not easy to define, is highly subjective, and varies based on who is making the assessment.[34] According to the social sciences, a minimal standard would require sufficient functioning to engage in life tasks that bring enjoyment and satisfaction.[90] Others suggest a minimum standard requires "capacity for symbolic interaction and communication" or "potential for cognitive development and interaction."[91,92]

Sanctity of life also has inconsistent definitions. Vitalists' mark conception as the initiation of life, whereas others, such as the Nuffield Council on Bioethics, "…regard the moment of birth, which is straight forward to identify, and usually represents a significant threshold in potential viability, as the significant moral and legal point of transition for judgments about preserving life." The Nuffield Council makes no statement on the moral status of the embryo or fetus.[66] Even with this variability, these concepts can be operationalized through identifying how they motivate decision-making. Physicians can then assist parents in maximizing those goals.[93] Difficulty arises when these values are not clearly identified or when they are present in degrees.

Maternal Versus Fetal Rights

Unique to the obstetrician's role is the dual responsibility of caring for two patients, the mother and fetus, simultaneously. Historically, a focus of maternal–fetal conflicts has involved maternal refusal of treatments deemed clearly beneficial for the fetus, such as refusal of a cesarean section for a term fetus at risk. On balance is a woman's right to autonomy versus the best interests of the fetus. Professional guidelines recommend that although everything possible must be attempted to protect the best interests of the fetus, these interests are insufficient to override the pregnant woman's right to autonomy. The American College of Obstetricians and Gynecologists has stated that "respect for the right of individual patients to make their own choices about their health care is fundamental."[94] Risk/benefit analyses can help justify strong recommendations, and even warrant assent approaches under these circumstances, but cannot take away a woman's right to decide what happens to her body.

The impending birth of an extremely preterm fetus has an added dimension related to personhood: at what point does a fetus possess rights and liberties? Related to this argument, and poignantly controversial, are questions surrounding the spectrum and overlap of the pregnant woman's termination rights against viability boundaries for the fetus. The perinatal team is acutely aware of the legal and political landscape, making this apparent inconsistency especially treacherous to navigate.

Can a Physician Refuse to Resuscitate?

Mercurio[6] explores three potential reasons why physicians can refuse resuscitation based on the principles of futility, distributive justice, and best interests. Futility has been rejected for reasons cited previously. Distributive justice, he also argues, is difficult for an individual physician to justify until society has upheld the idea of withholding intensive care based on resource allocation. The third argument justifies refusal based on the best interests of the infant. This stance is supported by the Hippocratic Oath and professional medical organizations. On forgoing life-sustaining medical treatment, the AAP Committee on Bioethics endorses overriding parental decisions when "those views clearly conflict with the interests of the child."[68] Best interests standards have been the primary guide for treatment decisions in never-competent patients, whose wishes and desires are unknown[95] and surrogates are charged with guarding those interests. However, a surrogate's decisions can be questioned when unilateral demands for, or refusal of, treatments conflicts with the patient's best interests.[96]

Can a Physician Refuse to Perform a Cesarean Section for an Extremely Preterm Fetus?

Competing principles of beneficence, nonmaleficence, and patient autonomy complicate matters for the perinatal/obstetric team caring for the woman and fetus. This conflict can be approached in two ways: first, weighing the risks and benefits for both patients, and then evaluating whether the intention and the likely result based on medical evidence are equivalent and acceptable. Ultimately, physicians reserve the right to use their own medical judgment and refuse to perform a procedure deemed harmful and of no benefit to a patient. The risk for harm can be immediate or long-term. Certainly any risk likely to result in imminent death should not be considered mandatory or ethical and would violate the principle of nonmaleficence. Even when harm is not an immediate consequence of an intervention, if no realistic probability of the desired outcome exists based on sound medical evidence and multidisciplinary assessments, then it is reasonable for a physician to override a patient's demand for treatment that is without clear benefit.

Unique Circumstances: Medical Decision-Making During the Prenatal Consultation

The threatened delivery of an extremely preterm fetus poses complicated medical and ethical challenges for physicians and families. The information available for deliberation is incomplete, may not reflect current management for this unique population of infants, and must be communicated under less-than-ideal circumstances of emotional distress and time constraints.[97,98] Personal beliefs, values, knowledge about outcomes, and emotional exhaustion caused by conflicts over treatment decisions by members of the woman's health care team may influence how information is presented to families and the type of support offered.[99]

During the consultation, physicians must explore the parent's values and expectations about decision-making, respecting their autonomy as surrogate decision-makers. Physicians should follow best interests standards and begin a process of shared decision-making, with responsibility for decisions dictated by parental preferences. Parents must rapidly assimilate new and evolving information and determine how their moral framework will guide their deliberation. When appropriate, recommendations can be given and models of assent followed. All members of the perinatal team must participate in the consultation process, bridging gaps for parents as they transition from antenatal to postnatal care issues. The multidisciplinary deliberations must be transparent for parents to understand potential uncertainties compounding the evolving clinical prognoses and to avoid feelings of mistrust. Boundaries of care should be constructed based on best available evidence and decisional discretion permitted for gestational ages when clinical and ethical equipoise exists.

Practically speaking, most of the empirical work on decision-making for extremely preterm infants during the prenatal consultation has focused on physician behaviors and parental recall, knowledge, and satisfaction with the process of prenatal consultation.[100,101] Only a few studies have focused specifically on the parental decision-making process.[80,83] Physician behavior, however, is a poor proxy for parental preferences. Survey assessments delineating physician practices have shown inconsistencies in resuscitation of infants born between 23 and 24 weeks, which cannot be attributed solely to variations in parental preferences, because nearly half of the physicians do not alter their behavior based on parental preferences.[43,44,64,81,88,102–104]

Perceptions of a good outcome can vary among disciplines. Despite this discrepancy, however, recommendations for delivery room management are frequently more similar among disciplines than not.[104] Initial obstetric assessments of prognosis, however, can dictate whether neonatal consultations are obtained.[105] Neonatal and obstetric assessments of prognosis can act independently or can interplay, impacting behaviors across disciplines.

Several studies have queried parents retrospectively about which factors have been most helpful to them when withdrawing life support from their children/infants. These studies are prone to retrospective biases based on the infant's outcome and parental adjustment. Some studies report on thematically related but intrinsically different decisions. Nonetheless, they inform the medical community about issues parents find important: clear information; visual deterioration; repetitive conversations; pain and suffering; the infant's bleak prognosis[78,79]; reliance on spirituality, hope,[80] and religion[106,107]; and parents' own interpretations of the infant's condition.[80,83] The parents' frame of reference is different from the physicians': parents view decisions initially from the perspective of the impending loss of the pregnancy and their chance at parenthood. Parents express the need for support and the opportunity to explore the meaning of uncertainty to augment the factual information provided. In contrast, physicians approach decisions from a medical perspective already focused on the to-be-born infant.[83,108] Only when the decision-making style fits their expectations do parents become confident in their decisions. Few physicians believe that discussing nonmedical facts with parents is part of their role, resulting in little exploration of parental values. This lack of communication compromises their ability to help parents interpret risks and benefits according to the family's moral framework.[109] Clearly, under conditions of emotional distress, what is communicated shows poor concordance with what is heard or remembered.[80,81,103,110] If parents cannot recall that they had a choice, how can the process be informed? External factors may influence their perception of options.[107] Physicians may be reluctant to offer choices based on their beliefs.[64] Parents who present to a tertiary care center may expect that the only option is resuscitation and may not be informed of the contrary.[98]

Research optimizing risk communication has been limited. The general public's awareness of issues related to extreme prematurity is limited,[89] and is impacted by the way in which information is presented.[107] A series of investigators and parents have advocated for increased education of the general public, especially those who are pregnant,[89] and for consideration of initiatives to create advance directives for pregnancies threatened with preterm delivery.[111] If the goal is to optimize parental decision-making and permit parents to make decisions consistent with their own moral framework, then continued research is needed into the process, factors that impede or promote an informed decision, and strategies to maximize consistent and stable decisions for parents. As stated by Paris and Reardon,[112] "treatment decisions for extremely premature newborns whose course is uncertain or ambiguous remains with those who bear responsibility for the infant — the parents."

Professional Guidelines

Principles of justice preclude physicians individually determining the limits of viability. Rather, professional medical organization guidelines provide standards based on which individualized factors can be considered in an attempt to provide decision-makers with some prognostic guidance.[7] International guidelines are remarkably similar, supporting parental discretion at 23 and 24 weeks. Several countries suggest resuscitation and intensive care is experimental at less than 23 weeks' gestation, supporting provision of compassionate care.[113] A few countries consider providing resuscitation or intensive care on parental insistence at 22 weeks' gestation (United Kingdom, Germany, Canada, United States). At greater than 25 weeks' gestation, most countries support intensive care, with the Netherlands considering care mandatory at 26 weeks and essentially mandatory at 25 weeks.[113] Parental expectations of participation in medical decisions about infants born extremely preterm vary by country.[43,114] Recommendations for parental involvement, the degree to which physicians direct care, and views on trials of therapy also vary. Within the United States, several state initiatives have attempted to construct guidelines; however, professional organizations struggle to provide guidance without making treatment mandatory, because this has the potential to increase liability risks when taken out of context. Some organizations designate boundaries based on short-term burdens of pain and suffering (Switzerland); others on long-term consequences. Many countries do not stratify based on gestational age; those that do not base recommendations on assessments made and information gained after birth or based on trials of intensive care (Germany, Singapore).[113]

Obstetric recommendations range from aggressive management that includes intrapartum fetal monitoring, tocolysis, glucocorticoids, and cesarean delivery to nonintervention. Intermediate approaches that attempt to avoid an operative delivery may be used, but add further complexity to the decision process because the fetus may experience additional compromise. The challenge for the obstetrician is identifying the fetus for which nonintervention is the appropriate option given a poor prognosis versus the fetus who would fare well if the intrapartum care was managed intensively.[115] Cesarean section for fetal indications is generally not recommended at less than 25 weeks' gestation, and antenatal steroids, although recommended[116] from 24 weeks' gestation, are inconsistently administered. In their comparison of international guidelines, Pignotti and Donzelli[113] noted that none of the reviewed practice parameters addressed antenatal corticosteroid administration at less than 24 weeks' gestation, with the United States recommending use after 24 weeks and the Netherlands after 25 weeks.

Whenever possible, the use of local data should be incorporated in prenatal consultations, adhering to social and cultural norms. Constructing intrainstitutional guidelines is an important way to support parental decision-making. Inconsistent messages received from different providers have been shown to increase parental distress.[117] To address this issue, a multidisciplinary effort to improve the quality of prenatal consultations and decisional satisfaction was successfully undertaken in Oregon. It provided caregivers an opportunity to incorporate their expertise with local and national outcomes and create clear and effective communication interventions to improve consistency and quality among providers.[117] These standardized evidence-based guidelines encompass obstetric and neonatal care options specific to the periviable period, offering counseling recommendations for pregnancies less than 27 weeks, including gestations less than 23 weeks.[115]

SUMMARY

Decision-making for extremely immature preterm infants at the margins of viability is ethically, professionally, and emotionally complicated. Expectant parents are suddenly thrust onto an emotional roller coaster, needing to urgently decide the fate of their unborn child while their thought processes are confounded by feelings of guilt, grief, and disbelief. They must not only incorporate the uncertainty of the medical prognostic information but also balance this new information against their values and moral framework, questioning the meaning of life and altering their world order. For some parents this may be their first experience with this decisional process, whereas for others it is a road too familiar.

This ethical dilemma has reached new dimensions as technology collides with the margins of human physiologic capacity. Interventions previously shown to improve outcomes may be of trivial benefit to these extremely immature infants. The professional community has not given definitive recommendations, appropriately leaving decisional discretion to the physician and the woman/couple to jointly decide care options at gestational ages at which the burdens of survival are significant and risks of burdensome long-term outcomes are not inconsequential. The heterogeneity of societal values and parental preferences should guide the physician–parent encounter, and the processes of shared decision-making should be encouraged.

The authors encourage that a standard for prenatal consultation be developed that would incorporate an assessment of parental decision-making preferences and styles, a communication process involving a reciprocal exchange of information, and effective strategies for decisional deliberation, guided by and consistent with parental moral framework. They recommend that all professional caregivers who provide perinatal consultations or end-of-life counseling for extremely preterm infants be sensitive to these issues and be taught flexibility in counseling techniques adhering to consistent guidelines. Emphasis must shift away from physician beliefs and behaviors about the boundaries of viability. Research must be focused on parental decisional processes to understand how they construct a minimally acceptable outcome and make life and death decisions under conditions of prognostic uncertainty.

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REFERENCES

1. Blackmon L. Biologic limits of viability: implications for clinical decision making. Neoreviews 2003;4(6):e140–6.
2. Evans DJ, Levene MI. Evidence of selection bias in preterm survival studies: a systematic review. Arch Dis Child Fetal Neonatal Ed 2001;84:F79–84.
3. Hack M, Wilson-Costello D. Trends in the rates of CP associated with neonatal intensive care of preterm children. Clin Obstet Gynecol 2008;51(4):763–74.
4. Draper ES. Evaluating and comparing neonatal outcomes. Arch Dis Child Fetal Neonatal Ed 2010;95:F158–9.
5. Lorenz JM, Wooliever DE, Jetton JR, et al. A quantitative review of mortality and developmental disability in extremely premature newborns. Arch Pediatr Adolesc Med 1998;152:425–35.
6. Mercurio MR. Physicians' refusal to resuscitate at borderline gestational age. J Perinatol 2005;25:685–9.
7. Tyson JE, Parikh NA, Langer J, et al. Intensive care for extreme prematurity-moving beyond gestational age. N Engl J Med 2008;358:1672–81.
8. Fanaroff AA, Stoll BJ, Wright LL, et al. Trends in neonatal morbidity and mortality for very low birthweight infants. Am J Obstet Gynecol 2007;196:147, e1–8.
9. Lorenz JM, Paneth N, Jetton JR, et al. Comparison of management strategies for extreme prematurity in New Jersey and the Netherlands: outcomes and resource expenditure. Pediatrics 2001;108:1269–74.
10. Håkansson S, Farooqi A, Holmgren PA, et al. Proactive management promotes outcome in extremely preterm infants: a population based comparison of two perinatal management strategies. Pediatrics 2004;114:58–64.
11. Saigal S, den Ouden L, Wolke D, et al. School-age outcomes in children who were extremely low birth weight from four International population-based cohorts. Pediatrics 2003;112:943–50.
12. Stoll BJ, Hansen NI, Bell EF, et al. Neonatal outcomes of extremely preterm infants from the NICHD Neonatal Research Network. Pediatrics 2010;126:443–56.
13. Hobar JD, Carpenter J, Kenny M, et al. Very Low Birth Weight (VLBW) database summary for infants 501–1500 grams. Available at: https://nightingale.vtoxford.org/summaries.aspx. Accessed January 4, 2011.
14. Wood NS, Marlow N, Costeloe K, et al. Neurologic and developmental disability after extremely preterm birth. N Engl J Med 2000;343:378–84.
15. Express Group. One year survival of extremely preterm infants after active perinatal care in Sweden. JAMA 2009;301(21):2225–33.
16. Markestad T, Kaaresen P, Rønnestad A, et al. Early death, morbidity, and need of treatment among extremely premature infants. Pediatrics 2005;115:1289–98.
17. Fischer N, Steurer MA, Adams M, et al. Survival rates of extremely preterm infants: (gestational age <26 weeks) in Switzerland: impact of the Swiss guidelines for the care of infants born at the limit of viability. Arch Dis Child Fetal Neonatal Ed 2009;94:F407–13.
18. Vanhaesebrouck P, Allegaert K, Bottu J, et al. The EPIBEL Study: outcomes to discharge from hospital for extremely preterm infants in Belgium. Pediatrics 2004;114:663–75.

19. Chan K, Ohlsson A, Synnes A, et al. Survival, morbidity, and resource use of infants of 25 weeks' gestational age or less. Am J Obstet Gynecol 2001;185:220–6.
20. Iijima S, Arai H, Ozawa Y, et al. Clinical patterns in extremely preterm (22 to 24 weeks of gestation) infants in relation to survival time and prognosis. Am J Perinatol 2009;26:399–406.
21. Kusauda S, Fujimura M, Sakuma I, et al. Morbidity and mortality of infants with very low birth weight in Japan: center variation. Pediatrics 2006;118:e1130–8.
22. Hintz SR, Kendrick DE, Vohr BR, et al. Changes in neurodevelopmental outcomes at 18 to 22 months' corrected age among infants of less than 25 weeks' gestational age born in 1993–1999. Pediatrics 2005;115:1645–51.
23. Marlow N, Hennessy EM, Bracewell MA, et al. Motor and executive function at 6 years of age after extremely preterm birth. Pediatrics 2007;120:793–804.
24. Marlow N, Wolke D, Bracewell MA, et al. Neurologic and developmental disability at six years of age after extremely preterm birth. N Engl J Med 2005;352(1):9–19.
25. Johnson S, Hennessy E, Smith R, et al. Academic attainment and special educational needs in extremely preterm children at 11 years of age: the EPICure study. Arch Dis Child Fetal Neonatal Ed 2009;94:F283–9.
26. Johnson S, Fawke J, Hennessey E, et al. Neurodevelopmental disability through 11 years of age in children born before 26 weeks' gestation. Pediatrics 2009; 124:e249–57.
27. Hintz SR, Kendrick DE, Wilson-Costello DE, et al. Early-childhood neurodevelopmental outcomes are not improving for infants born at 25 weeks' gestational age. Pediatrics 2011;127:62–70.
28. Hack M, Flannery DJ, Schluchter M, et al. Outcomes in young adulthood for very low birth weight infants. N Engl J Med 2002;346:149–57.
29. Saigal S, Stoskopf B, Boyle M, et al. Comparison of current health, functional limitations and health care use of young adults who were born with extremely low birth weight and normal birth weight. Pediatrics 2007;119:e562–73.
30. Moster D, Lie RT, Markestad T. Long term medical and social consequence of preterm birth. N Engl J Med 2008;359:262–73.
31. Saigal S, Pinelli J, Hoult L, et al. Psychopathology and social competencies of adolescents who were extremely low birth weight. Pediatrics 2003;111:969–75.
32. Hille E, Weisglas-Kuperus N, van Goudoever JB, et al. Functional outcomes and participation in young adulthood for very preterm and very low birthweight infants: the Dutch Project on preterm and small for gestational age infants at 19 years of age. Pediatrics 2007;120:e587–95.
33. Grunau RE, Whitfield MF, Fay TB. Psychosocial and academic characteristics of extremely low birth weight (<800gm) adolescents who are free of major impairment compared with term-born control subjects. Pediatrics 2004;114:e725–32.
34. Saigal S, Stoskopf B, Pinelli J, et al. Self perceived health related quality of life of former extremely low birth weight infants at young adulthood. Pediatrics 2006; 118:1140–8.
35. Zwicker JG, Harris SR. Quality of life of formerly preterm and very low birth weight infants from preschool age to adulthood: a systematic review. Pediatrics 2008;121:e366–76.
36. Tyson JE, Stoll BJ. Evidence-based ethics and the care and outcome of extremely premature infants. Clin Perinatol 2003;30:363–87.
37. Abram MB. Deciding to forego life-sustaining treatment: a report on ethical, medical, and legal issues in treatment decisions. Washington, DC: President's

Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research; 1983. p. 218–9.

38. Lantos JD, Meadow WL. Neonatal bioethics: the moral challenges of medical innovation. Baltimore (MD): Johns Hopkins University Press; 2006.
39. Tyson JE. Evidenced-based ethics and the care of premature infants. Future Child 1995;5(1):197–213.
40. Paris JJ, Reardon FE. Physician refusal of requests for futile or ineffective interventions. Camb Q Healthc Ethics 1992;1:127–34.
41. Charles C, Whelan T, Gafni A, et al. What do we mean by partnership in making decisions about treatment. BMJ 1999;319(7212):780.
42. Leuthner SR, Lorenz JM. Can rule-based ethics help in the NICU? Available at: http://virtualmentor.ama-assn.org/site/archives.html. Accessed June 28, 2011.
43. De Leeuw R, Cuttini M, Nadai M, et al. Treatment choices for extremely preterm infants: an international perspective. J Pediatr 2000;137:608–15.
44. Partridge JC, Freeman H, Weiss E, et al. Delivery room resuscitation decisions for extremely low birth weight infants in California. J Perinatol 2001;21:27–33.
45. Schneiderman LJ, Jecker NS, Jonsen AR. Medical futility: its meaning and ethical implications. Ann Intern Med 1990;112(12):949–54.
46. Truog RD, Brett AS, Frader J. The problem with futility. N Engl J Med 1992;326: 1560–4.
47. Helft PR, Siegler M, Lantos J. The rise and fall of the futility movement. N Engl J Med 2000;343:293–6.
48. Veatch RM, Spicer CM. Medically futile care: the role of the physician in setting limits. Am J Law Med 1992;18:15–36.
49. Petrou S, Eddama O, Mangham L. A structured review of the recent literature on the economic consequences of preterm birth. Arch Dis Child Fetal Neonatal Ed 2011;96:F225–32. DOI: 10.1136/adc.2009.161117.
50. Cuevas KD, Silver DR, Brooten D, et al. The cost of prematurity: hospital charges at birth and frequency of rehospitalizations and acute care visits over the first year of life. Am J Nurs 2005;105:56–64.
51. Gilbert WM, Nesbitt TS, Danielsen B. The cost of prematurity: quantification by gestational age and birth weight. Obstet Gynecol 2003;102:488–92.
52. Zupancic JA. Dangerous economics: resource allocation in the NICU. Can Med Assoc J 1992;146(6):1073–6.
53. Ardagh M. Futility has no utility in resuscitation medicine. J Med Ethics 2000;26: 396–9.
54. Meadow W, Lagatta J, Andrews B, et al. Just in time: ethical implications of serial predictions of death and morbidity for ventilated premature infants. Pediatrics 2008;121:732–40.
55. Meadow W, Frain L, Ren Y, et al. Serial assessment of mortality in the neonatal intensive care unit by algorithm and intuition: certainty, uncertainty and informed consent. Pediatrics 2002;109(5):878–87.
56. Singh J, Fanaroff J, Andrews B, et al. Resuscitation in the gray zone of viability: determining physician preferences and predicting infant outcomes. Pediatrics 2007;120:519–26.
57. Donovan EF, Tyson JE, Ehrenkranz RA. Inaccuracy of Ballard scores before 28 weeks' gestation. National Institute of Child and Human Development Neonatal Research Network. J Pediatr 1999;135(2):147–52.
58. Kopelman L. The best interests standard for incompetent or incapacitated persons of all ages. J Law Med Ethics 2007;35(1):187–96.

59. Beauchamp TL, Childress JF. Principles of biomedical ethics. 5th edition. New York: Oxford University Press; 2001.
60. Fine RL, Whitfield JM, Carr BL, et al. Medical futility in the neonatal intensive care unit: hope for a resolution. Pediatrics 2005;116:1219–22.
61. American Academy of Pediatrics Committee on Fetus and Newborn. The initiation or withdrawal of treatment for high-risk newborns. Pediatrics 1995;96: 362–4.
62. Campbell AG, McHaffie HE. Prolonging life and allowing death: infants. J Med Ethics 1995;21(6):339.
63. Saigal S, Stoskopf BL, Feeny D, et al. Differences in preferences for neonatal outcomes among health care professionals, parents and adolescents. JAMA 1999;281(21):1991–7.
64. Peerzada JM, Richardson DK, Burns JP. Delivery room decision-making at the threshold of viability. J Pediatr 2004;145(4):492–8.
65. Forman V. This lovely life. New York: Houghton Mifflin Harcourt Publishing Company; 2009.
66. Critical Care Decisions in Fetal and Neonatal Medicine. Ethical issues: Nuffield Counsel on Bioethics. Available at: www.nuffieldbioethics.org. Accessed April 6, 2010.
67. Leuthner SR. Decisions regarding resuscitation of the extremely premature infant and models of best interest. J Perinatol 2001;21:193–8.
68. AAP Committee on Bioethics. Guidelines on forgoing life-sustaining medical treatment. Pediatrics 1994;93:532–6.
69. AAP Committee on Bioethics. Ethics and the care of critically ill infants and children. Pediatrics 1996;98:149–52.
70. Faden RR, Beauchamp TL. A history and theory of informed consent. New York: Oxford University Press; 1986.
71. Kon AA. Healthcare providers must offer palliative treatment to parents of neonates with hypoplastic left heart syndrome. Arch Pediatr Adolesc Med 2008;162(9):844–9.
72. Feudtner C. Ethics in the midst of a therapeutic evolution. Arch Pediatr Adolesc Med 2008;162(9):854–7.
73. Emanuel EJ, Emanuel LL. Four models of the physician-patient relationship. JAMA 1992;267:2221–6.
74. White DB, Malvar G, Karr J, et al. Expanding the paradigm of the physician's role in surrogate decision-making: an empirically derived framework. Crit Care Med 2010;38:743–50.
75. Paris JJ, Graham N, Schreiber MD, et al. Has the emphasis on autonomy gone too far? Insights from Dostoevsky on parental decision making in the NICU. Special section: the power of choice: autonomy, informed consent and the right to refuse. Camb Q Healthc Ethics 2006;15:147–51.
76. Montello M, Lantos J. The Karamazov complex: Dostoevsky and DNR orders. Perspect Biol Med 2002;45:190–9.
77. Sulmacy DP, Sood JR, Texlera K, et al. A prospective trial of a new policy eliminating signed consent for do not resuscitate orders. J Gen Intern Med 2006;21: 1261–8.
78. McHaffie HE, Laing IA, Parker M, et al. Deciding for imperiled newborns: medical authority or parental autonomy? J Med Ethics 2001;27:104–9.
79. McHaffie HE, Lyon AJ, Hume R. Deciding on treatment limitation for neonates: the parents' perspective. Eur J Pediatr 2001;160:339–44.

80. Boss RD, Hutton N, Sulpar LJ, et al. Values parents apply to decision-making regarding delivery room resuscitation for high risk newborns. Pediatrics 2008; 122:583–9.
81. Zupancic JA, Kirpalani H, Barrett J, et al. Characterizing doctor-parent communication in counseling for impending preterm delivery. Arch Dis Child Fetal Neonatal Ed 2002;87:F113–7.
82. Meisel A, Kuczewski M. Legal and ethical myths about informed consent. Arch Intern Med 1996;156:2521–6.
83. Payot A, Gendron S, Lefebvre F, et al. Deciding to resuscitate extremely premature babies: how do parents and neonatologists engage in the decision? Soc Sci Med 2007;64:1487–500.
84. Truog RD. Doctor if this were your child what would you do? Commentary. Pediatrics 1999;103(1):153–5.
85. White DB, Evans LR, Bautista CA, et al. Are physicians' recommendations to limit life support beneficial or burdensome? Am J Respir Crit Care Med 2009; 180:320–5.
86. AAP, Committee on Fetus and Newborn and ACOG, Committee on Obstetric Practice. Perinatal care at the threshold of viability. Pediatrics 1995;96: 974–6.
87. Feudtner C, Munson D, Morrison W. Framing permission for halting or continuing life-extending therapies. Virtual Mentor 2008;10(8):506–10.
88. Schroeder J. Ethical issues for parents of extremely premature infants. J Paediatr Child Health 2008;44:302–4.
89. Martinez AM, Partridge JC, Yu V, et al. Physician counseling practices and decision making for extremely preterm infants in the Pacific Rim. J Paediatr Child Health 2005;41:209–14.
90. McCullough LB. Neonatal ethics at the limits of viability. Pediatrics 2005;116: 1019–21.
91. Rhoden NK. Treatment dilemmas for imperiled newborns: why QOL counts. S C Law Rev 1985;58(6):1283–347.
92. Robertson JA. Extreme prematurity and parental rights after baby doe. Hastings Cent Rep 2004;34:32–9.
93. Chiswick M. Parents and end of life decisions in neonatal practice. Arch Dis Child Fetal Neonatal Ed 2001;85:1–3.
94. American College of Obstetricians and Gynecologists. Ethical decision making in obstetrics and gynecology. Available at: http://www.acog.org/from_home/publications/ethics/co390.pdf. Accessed June 17, 2011.
95. Caplan A, Cohen CB. Imperiled newborns. Hastings Cent Rep 1987;17(6):1–52.
96. Paris JJ, Schreiber MD. Parental discretion in refusal of treatment for newborns: a real but limited right. Clin Perinatol 1996;23:573–81.
97. Harrison H. Counseling parents of extremely premature babies. Lancet 1997; 349(9047):289.
98. Janvier A, Barrington KJ. The ethics of neonatal resuscitation at the margins of viability: informed consent and outcomes. J Pediatr 2005;147:579–85.
99. Yoon JD, Rasinski KA, Curlin FA. Conflict and emotional exhaustion in obstetricians and gynecologists: a national survey. J Moral Educ 2010;36:731–5.
100. Paul DA, Epps S, Leef KH, et al. Prenatal consultation with a neonatologist prior to preterm delivery. J Perinatol 2001;21:431–7.
101. Blanco F, Suresh G, Howard D, et al. Ensuring accurate knowledge of prematurity outcomes for prenatal counseling. Pediatrics 2005;115:e478–87.

102. Doron MW, Veness-Meehan KA, Margolis LH, et al. Delivery room resuscitation decisions for extremely premature infants. Pediatrics 1998;102(3):574–82.
103. Keenan H, Doron M, Seyda B. Comparison of mothers' and counselors' perceptions of pre-delivery counseling for extremely premature infants. Pediatrics 2005;116(1):104–11.
104. Lavin JP, Kantak A, Ohlinger JM, et al. Attitudes of obstetric and pediatric health care providers toward resuscitation of infants who are born at the margins of viability. Pediatrics 2006;118:S169–76.
105. Martinez AM, Weiss E, Partridge JC, et al. Management of extremely low birth weight infants: perceptions of viability and parental counseling practices. Obstet Gynecol 1998;92:520–4.
106. Hammerman C, Kornbluth E, Lavie O, et al. Decision making in the critically ill neonate: cultural background v individual life experiences. J Med Ethics 1997; 23:164–9.
107. Haward MF, Murphy RO, Lorenz JM. Message framing and perinatal decisions. Pediatrics 2008;122:109–18.
108. Britt DW, Evans WJ, Mehta SS, et al. Framing the decision: determinants of how women considering multifetal pregnancy reduction as a pregnancy-management strategy frame their moral dilemma. Fetal Diagn Ther 2004; 19(3):232–40.
109. Bastek TK, Richardson DK, Zupancic JA, et al. Prenatal consultation practices at the border of viability; a regional survey. Pediatrics 2005;116:406–13.
110. Koh TH, Jarvis C. Promoting effective communication in neonatal intensive care units by audiotaping doctor-patient conversations. Int J Clin Pract 1998;52:27–9.
111. Catlin A. Thinking outside the box: prenatal care and the call for a prenatal advanced directive. J Perinat Neonatal Nurs 2005;19:169–76.
112. Paris J, Reardon F. Bad cases make bad law: HCA vs. Miller is not a guide for resuscitation of extremely premature newborns. J Perinatol 2001;21(8):541–4.
113. Pignotti MS, Donzelli G. Perinatal care at the threshold of viability: an international comparison of practical guidelines for the treatment of extremely preterm births. Pediatrics 2008;121:e193–8.
114. Orfali K. Parental role in medical decision-making: fact or fiction? A comparative study of ethical dilemmas in French and American neonatal intensive care units. Soc Sci Med 2004;58(10):2009–22.
115. Tomlinson MW, Kaempf JW, Ferguson LA, et al. Caring for the pregnant woman presenting at periviable gestation: acknowledging the ambiguity and uncertainty. Am J Obstet Gynecol 2010;202:529.e1–6.
116. Effect of corticosteroids for fetal maturation on perinatal outcomes. NIH Consens Statement 1994;12(2):1–24.
117. Kaempf JW, Tomlinson M, Arduzza C, et al. Medical staff guidelines for periviability pregnancy counseling and medical treatment of extremely premature infants. Pediatrics 2006;117:22–9.