NATIONAL PERINATAL PRACTICE GUIDELINE

Perinatal Care of Extremely Preterm Baby at The Threshold of Viability

Document title: Perinatal care of extremely preterm baby at the threshold of viability

Version 1.0

Release Date: April 2021

Review date: April 2025

Purpose: To provide national general guidance regarding Obstetric and neonatal interventions for threatened and imminent periviable birth and general approach to resuscitation and intensive care measures for periviable infants by best estimate of gestational age.

Applicability: All Health professionals in Bahrain public and private maternity and neonatal services.

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Commissioned by: Quality and Clinical Guidelines Committee, Supreme Council of Health

Abbreviations	
IVH	Intraventricular Hemorrhage
CTG	Cardiotocography
C/S	Cesarean section
GA	Gestational Assessment

Table for definitions

Definitions	
Term	**Definition**
Periviable (Limit of viability)	The stage of fetal maturity that ensures a reasonable chance of extrauterine survival, (defined by NICHD as 20 $^{+0/7}$ through 25 $^{+6/7}$ weeks of gestation.
Fetus	Describe the baby before birth.
Baby	Describe the baby after birth.
Parents	Refers to the mother and the father.
Life sustaining Intervention/Resuscitation	Any intervention used in obstetric and neonatal management that has the aim of sustaining life of the fetus/baby e.g., epinephrine, CPAP, Mechanical ventilation.
Palliative care (comfort care)	Obstetric and neonatal management when the aim is not to attempt to sustain the life of the fetus/baby, but to focus on the baby's comfort.
NICU	A designated neonatal intensive care unit.
Best interest	In caring for the vulnerable infants who lack autonomy in decision-making and who have no competence, the ethical principles of non-maleficence and beneficence should prevail to ensure justice in the care they deserve and promote their well-being and refraining from causing harm.

Disclaimer

This guideline is intended as a guide and provided for information purposes only. This national guideline has been prepared to promote and facilitate standardization and consistency of practice, using a multidisciplinary approach. The information has been prepared using a multidisciplinary approach with reference to the best information and evidence available at the time of preparation. No assurance is given that the information is entirely complete, current, or accurate in every respect.

The guideline is not a substitute for clinical judgement, knowledge and expertise, or medical advice. Variation from the guideline, taking into account individual circumstances, may be appropriate.

This guideline does not address all elements of standard practice and accepts that individual clinicians are responsible for:

- Providing care within the context of locally available resources, expertise, and scope of practice regulated by National Health Regulatory Authority, Kingdom of Bahrain (NHRA).

- Supporting consumer rights and informed decision making, including the right to decline intervention or ongoing management.

- Advising consumers of their choices in an environment that is culturally appropriate and which enables comfortable and confidential discussion. This includes the use of interpreter services where necessary.

- Meeting all legislative requirements and professional standards as regulated by NHRA.

- Applying standard precautions, and additional precautions as necessary, when delivering care.

- Documenting all care in accordance with mandatory and NHRA requirements, to the maximum extent permitted by law, all responsibility and all liability (including without limitation, liability in negligence) for all expenses, losses, damages and costs incurred for any reason associated with the use of this guideline, including the materials within or referred to throughout this document being in any way inaccurate, out of context, incomplete or unavailable.

Background:

Peri-viability also referred to as the "***limit of viability***" is defined as the stage of fetal maturity that

ensures a reasonable chance of extrauterine survival (broadly defined by National Institute of Child Health and Human Development (NICHD) as 20 $^{0/7}$ through 25 $^{6/7}$ weeks of gestation). [1,2,3] Approximately 0.5% of all births occur before the third trimester of pregnancy (<28 weeks), and these very early deliveries result in the majority of neonatal deaths and more than 40% of infant deaths.[4] With active intervention, most infants born at 26 weeks and above have a high likelihood of survival, and virtually none below 22 weeks will survive.[1] The survival data for births at 22, 23, 24, and 25 weeks of gestation were 6%, 26%, 55%, and 72%, respectively, at initial discharge from the hospital.[3] The chance of survival thus increases dramatically over these few weeks. In addition to the high risk of death in the immediate newborn period, children born at the limit of viability have a high risk of permanent disability. An understanding of both of these risks is essential to parental counseling and decision-making, with regard to attempted resuscitation and provision of life-sustaining measures in the newborn intensive care unit (NICU).[1-11]

Introduction:

The birth of an extremely preterm baby is a stressful experience for the parents and family.[1] Birth at these gestations also presents enormous challenges for the healthcare team. Although neonatal survival rates have improved dramatically over the last few decades, significant morbidity is still common. As the gestational age decreases, morbidity and mortality increase dramatically. [2-5]

Outcome data from many countries around the world confirm both improved survival and neurodevelopment outcomes for extremely preterm babies.[1-14] While there is no single global or national consensus regarding resuscitation, there is a trend toward offering postnatal life support at these extremely preterm gestations.[14]

Prevention of preterm birth remains a focus for healthcare in the Kingdom of Bahrain. However, where birth at extremely preterm gestational age is unavoidable, individualized care led by experienced clinicians and informed by the best available evidence and contemporary healthcare practices is essential.

The guideline is designed to aid clinical decision-making in the context of anticipated or actual premature birth below 26 weeks 'gestation, survival and morbidity of extremely preterm infants born will be reviewed. In addition, a management approach for infants born in the previable period, based upon prognosis, will be presented.

Purpose of the guideline:

The purpose of this guideline is to:

- Promote consistency in perinatal counseling
- Promote family centered counseling
- Promote informed ethical decision-making
- To provide national general guidance regarding Obstetric and Neonatal interventions for

threatened and imminent peri-viable birth and general approach to resuscitation and intensive care measures for peri-viable infants by best estimate of gestational age.

This guideline is considered a living document and will be reviewed frequently to assess alignment with contemporary practices.

Target Audience

Health professionals in kingdom of Bahrain public and private maternity and neonatal services.

Patient population

All extreme preterm babies in the edge of viability, defined as the stage of fetal maturity that ensures a reasonable chance of extrauterine survival (broadly defined by National Institute of Child Health and Human Development (NICHD) as 20 $^{0/7}$ through 25 $^{6/7}$ weeks of gestation). [1,2,3]

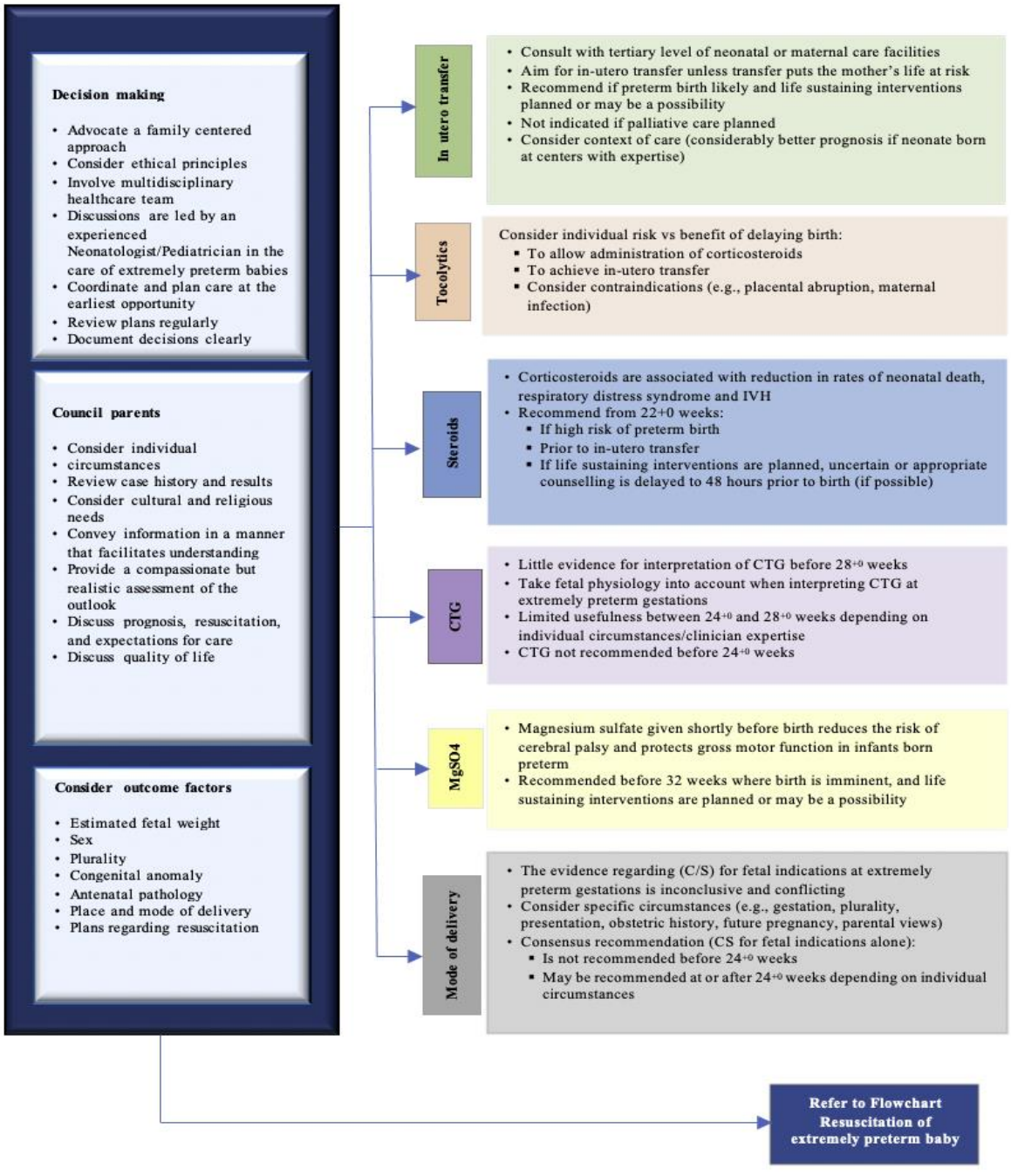
Executive summary:

1. This Framework has been developed by a multidisciplinary working group in the light of the evidence of improving outcomes for babies born before 26 completed weeks of gestation and evolving national and international changes in the approach to their care.
2. The recommended general approach to resuscitation and intensive care measures for peri-viable infants is as follows:
    a. **Below 22 weeks gestation** – Resuscitation is not offered or provided due to the zero or near-zero chance of survival.
    b. **$22^{0/7}$ to $23^{6/7}$ weeks gestation** – Resuscitation is considered and offered to parents, unless there is major pathology or risk factors in addition to extreme prematurity.
    c. **24 weeks gestation and higher** – Resuscitation is recommended.
    d. **Uncertain gestational age** – Life sustaining interventions should be initiated until the clinical course is clearer, further management will be individualized based on the clinical condition of the baby and the response to initial resuscitation. Discuss the baby's condition, clinical assessment and decision making with the family as soon as possible.

3. Exceptions may be made at the discretion of the attending clinician if there is additional compelling evidence that significantly worsens the prognosis (e.g., certain congenital anomalies or profound growth restriction).

Flow Chart 1: Antenatal care where birth imminent or indicated at the limit of viability

Inform the family that initiation of antenatal interventions does not oblige nor necessarily equate to a final decision for life sustaining interventions after birth especially at extremely preterm or uncertain gestations



Flow chart 2: Consensus approach to resuscitation of an extremely preterm baby at the limit of viability.[1]

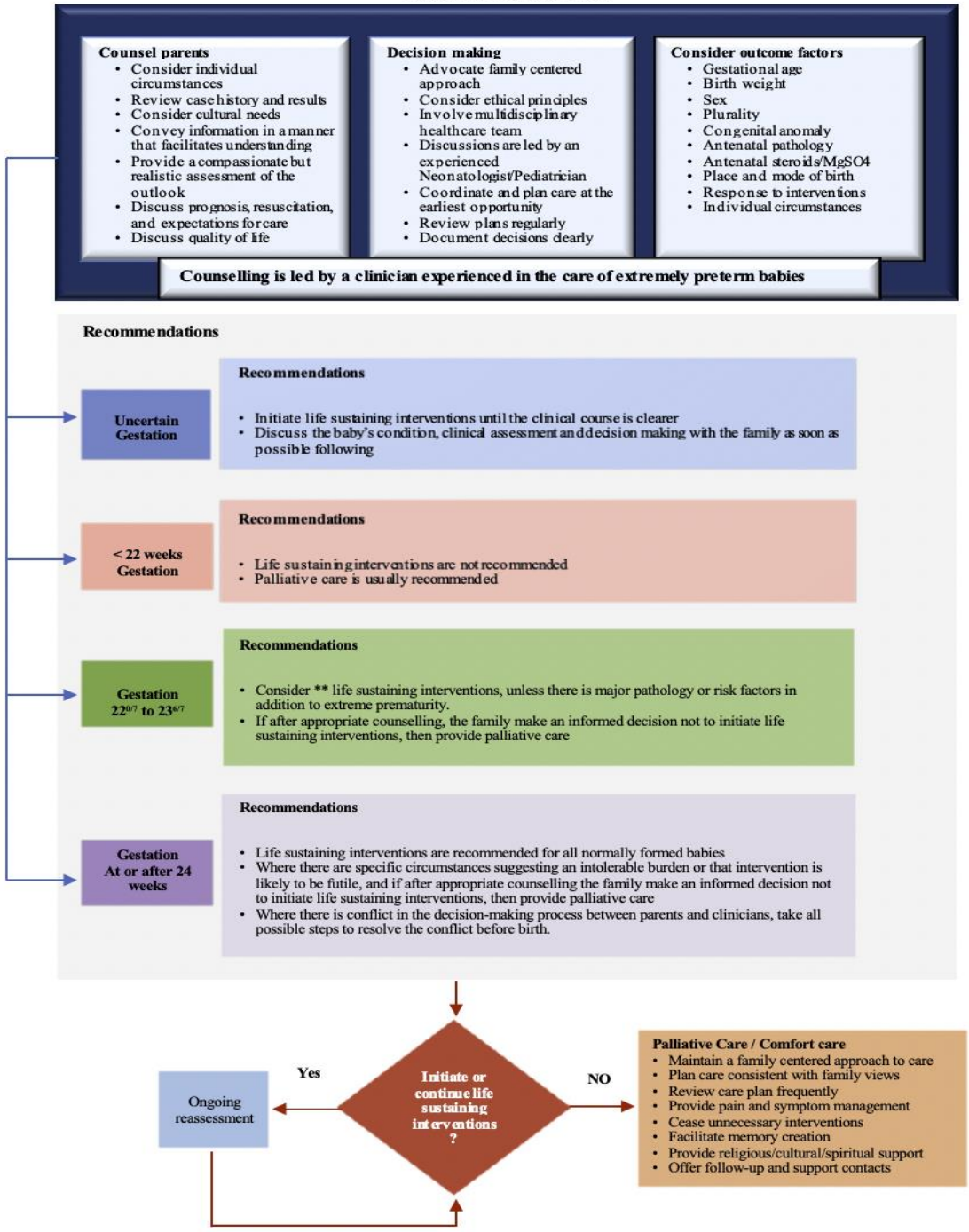


Table 1: General Guidance Regarding Obstetric Interventions for threatened and imminent Periviable Birth by Best Estimate of Gestational Age*					
Gestational Age	**20 0/7 weeks to 21 6/7 weeks**	**22 0/7 weeks to 22 6/7 weeks**	**23 0/7 weeks to 23 6/7 weeks**	**24 0/7 weeks to 24 6/7 weeks**	**25 0/7 weeks to 25 6/7 weeks**
Neonatal assessment for resuscitation	Not recommended 1A	Consider** 2B	Consider** 2B	Recommended 1B	Recommended 1B
Antenatal corticosteroids	Not recommended 1A	Not recommended 1A	Consider 2B	Recommended 1B	Recommended 1B
Tocolysis for preterm labor to allow for antenatal corticosteroid administration	Not Recommended 1A	Not recommended 1A	Consider 2B	Recommended 1B	Recommended 1B
Magnesium sulfate for neuroprotection	Not recommended 1A	Not Recommended 1A	Consider 2B	Recommended 1B	Recommended 1B
Antibiotics to prolong latency during expectant management of preterm prom if delivery is not considered imminent	Consider 2C	Consider 2C	Consider 2B	Recommended 1B	Recommended 1B
Intrapartum antibiotics for group B streptococci prophylaxis	Not recommended 1A	Not recommended 1A	Consider 2B	Recommended 1B	Recommended 1B
Cesarean delivery for fetal indication	Not recommended 1A	Not recommended 1A	Consider 2B	Recommended 1B	Recommended 1B

Adapted from: Obstetric Care Consensus No. 6. Periviable birth. American College of Obstetricians and Gynecologists (ACOG) and the Society for Maternal-Fetal Medicine (SMFM) October 2017

*Appendix1**refer to (when to consider life-sustaining intervention/Resuscitation or Palliative / Comfort care)

Grade of Recommendation:

1A. Strong recommendation. High quality evidence

1B. Strong recommendation. Moderate quality evidence

1C. Strong recommendation. Low quality evidence

2A. Weak recommendation. High quality evidence

2B. Weak recommendation. Moderate quality evidence

2C. Weak recommendation. Low quality evidence

Key Points:

1. Fetal gestational age, as currently estimated, is an imprecise predictor of neonatal survival, a margin of error from a few days to two weeks.[2-4]

2. 22 weeks of gestation is generally accepted as the lower threshold of viability.[1-4]

3. Base gestational age on ultrasound measurements of the crown-rump length at 8–12 weeks (accuracy +/- 4 days) and/or history of the last menstrual period (accuracy -6 to +14 days) or if conception date is known, e.g. (IVF) [4], certainty of gestational age is discussed in supplementary Appendix 2.

4. **Uncertain gestational age** – Life sustaining interventions should be initiated until the clinical course is clearer, further management will be individualized based on the clinical condition of the baby, discuss the baby's condition, clinical assessment and decision making with the family as soon as possible.[1-5]

5. Although most infants delivered between 22- and 24-weeks 'gestation will die in the neonatal period or have significant long-term neurodevelopmental morbidity, outcomes in individual cases are difficult to predict.[12-17]

6. Outcomes of infants delivered at 22 to 24 weeks of gestation vary significantly from center to center.[12-17]

7. Because of the uncertain outcomes for infants born at 22 to 24 weeks 'gestation, it is reasonable that decision-making regarding the delivery room management is individualized and family-centered, taking into account known fetal and maternal conditions and risk factors as well as parental beliefs regarding the best interest of the child.[1-5]

8. All deliveries should be conducted in labor room.

9. The most senior pediatrician/Neonatologist available at the time of birth should be present for any delivery around the threshold of viability whether or not active resuscitation is planned.

10. Attitudes vary not only between providers and parents but also among physicians and staff, ongoing interdisciplinary communication and written policies and procedures can promote consistent, timely, and effective counseling[18-28]

11. Optimal decision-making regarding resuscitating preterm baby in the threshold of viability can be promoted through joint discussions between the parents and both the obstetric and neonatal care providers whenever possible.[27-29]

12. Factors to consider when counseling parents include their ability to comprehend the situation, language preference, cultural and/or religious considerations, and family support structure. If the parent has limited English/Arabic proficiency, an interpreter should be used. Visual aids and outcome data based on local institutional experience may be helpful when communicating concepts such as mortality and morbidity.[27]

13. Optimal use of the limited time available, as well as the recognition and management of potential barriers to effective communication, will facilitate an effective discussion of anticipated outcomes and options.[30-31]

14. Clinical learners may benefit from observing these prenatal counseling sessions. In addition, other educational tools, such as simulations, can be used to help them gain experience in such situations.[27-29]

15. When a joint decision is made not to resuscitate a newborn infant, comfort care is appropriate, as is encouraging the family to spend time with the dying/deceased newborn infant. Providing religious, psychosocial, and/or palliative care support may assist families at this difficult time.[20]

METHODS AND ETHICAL CONSIDERATION

When to Consider life-sustaining intervention/Resuscitation OR Palliative / Comfort care.

A key ethical consideration for decisions about instituting life-sustaining intervention /Resuscitation for an extremely preterm baby is the baby's prognosis i.e., the risk of an acceptable (or unacceptable) outcome if active management is undertaken.[5, 27-32]

If there is a plan to provide life- sustaining treatment for the baby, then the pregnancy and birth should be managed with the aim of optimizing the baby's condition at birth and subsequently.

Ethical principles:

Four commonly held broad ethical principles form a framework within which moral decision-making can occur.[20, 27-32]

These principles are outlined in **Table 2**

Table 2: Ethical Principles

PRINCIPLE	CONSIDERATION
NON-MALEFICENCE	• Requires that harm not be inflicted intentionally and is closely linked to the imperative to minimize harm.
BENEFICENCE	• Refers to a moral obligation to act for the benefit of others, helping them to further their important and legitimate interests, at times preventing or removing possible harm. • Harm may result from treatment that in other circumstances would be clinically appropriate and beneficial. This implies a constant need to determine the levels of potential harm and benefits of life-sustaining interventions and to ensure that the benefits outweigh the harms.
AUTONOMY	• Autonomous individuals are entitled to make their own decisions and life choices. Extremely premature babies must rely on others to make decisions for them.
JUSTICE	• Prescribes actions that are fair to those involved suggests that like cases should be treated alike and that variations in management must be justified by relevant clinical and/or evaluative conditions.

RISK-BASED APPROACH TO DECISION- MAKING

A stepwise approach to decision-making, involves three key stages:

1. Assessment of the risk for the baby if delivery occurs, incorporating both gestational age and factors affecting fetal and/or maternal health (modified risk assessment) and using extremely preterm birth outcome Tool developed by NICHD Neonatal research network. (Appendix 3)[5]

2. Counselling parents, and their involvement in decision-making.

3. Agreeing and communicating a management plan.

STEP1

Modified risk assessment

Accurate information about the current pregnancy, including assessment of both fetal and maternal health should be used to refine gestation-based risk of absolute survival and survival without severe impairment.[5-7]

A range of factors are associated with increased or decreased risk:

A. Fetal factors

Fetal factors which may increase risk include

- Male sex
- Multiple pregnancy
- Congenital anomaly
- Poor fetal growth
- Severely abnormal fetal Doppler
- Twin to twin transfusion syndrome

B. Clinical conditions

That pose additional risk and have been associated with increased mortality and morbidity include:

- Prolonged pre-labor rupture of membranes before 24 weeks of gestation and
- Clinical evidence of chorioamnionitis.[6-7]

C. Therapeutic strategies

Factors associated with improved survival and neonatal outcomes as well as reduced risk of childhood impairment, even before 24 weeks of gestation.[8-9]

- Administration of antenatal steroid
- Administration of Magnesium sulfate

D. Clinical setting

Survival is highest at these extreme preterm gestations in centers with experienced staff, well-equipped, and higher patient numbers.[5]

Following full history taking and risk assessment, generally the fetus/baby will fall into one of the following categories: extremely high risk; high risk; moderate risk. A proposed visual tool for refinement of risk is illustrated in figure1.[5]

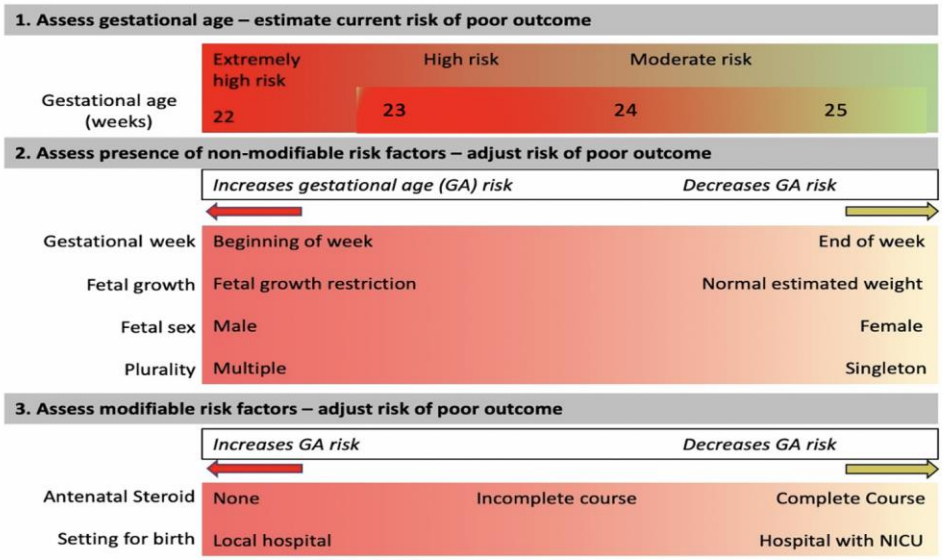


Figure 1 visual tool for refinement of risk

Adapted from: Perinatal management of extreme preterm birth before 27 weeks of gestation: a framework for practice. Mactier H, Bates SE, Johnston T; BAPM Working Group. Arch Dis Child Fetal Neonatal Ed. 2020 May;105(3):232-239.

- There is no objective way of defining a risk as "extremely high" versus 'high' and families differ in the outcome that they regard as unacceptably poor.[5]
- Risk assessment may need to be modified in the light of the parents' knowledge, views and values.[5,7]
- It is important that parents are offered choices and supported to make decisions appropriate for their individual preferences.[5,2]

Box 1 Risk Categories

***Extremely high risk*:** Babies with a >90% chance of either dying or surviving with severe impairment if active care is instigated would fit into this category. For example, this would include:

► Babies at 22^{+0} to 22^{+6} weeks of gestation with unfavorable risk factors.

► Some babies at 23+0 to 23^{+6} weeks of gestation with unfavorable risk factors, including severe fetal growth restriction.

► (Rarely) babies ≥24^{+0} weeks of gestation with significant unfavorable risk factors, including severe fetal growth restriction.

***High risk*:** Babies with a 50–90% chance of either dying or surviving with severe impairment if active care is instituted would fit into this category. For example, this would include:

► Babies at 22^{+0} to 23^{+6} weeks of gestation with favorable risk factors.

► Some babies ≥24^{+0} weeks of gestation with unfavorable risk factors and/or comorbidities.

***Moderate risk*:** Babies with a <50% chance of either dying or surviving with severe impairment if active care is instituted would fit into this category. For example, this would include:

► Most babies ≥24^{+0} weeks of gestation.

► Some babies at 23^{+0} to 23^{+6} weeks of gestation with favorable risk factors.

Adapted from: Perinatal management of extreme preterm birth before 27 weeks of gestation: a framework for practice. Mactier H, Bates SE, Johnston T; BAPM Working Group. Arch Dis Child Fetal Neonatal Ed. 2020 May;105(3):232-239.

- For women presenting to a non-tertiary maternity and neonatal center, assessment of risk should include early discussion with the relevant referral center.
- For pregnancies from 22^{+0} weeks of gestation, decisions should not be based on gestational age alone.
- Within a multiple pregnancy, the risk may differ between fetuses and so each should be considered as an individual. This means appropriate management may not be the same for each baby, even with the same gestational age.
- If birth occurs prior to 22^{+0} weeks of gestation, active obstetric and neonatal management is not appropriate.

Extremely high risk

For babies with an extremely high risk of death or of survival with unacceptably severe impairment despite treatment, palliative (comfort care) would be in the best interests of the baby and life-sustaining treatment should not be offered.[5]

High risk

For babies with a >50% risk of death or of surviving with unacceptably severe impairment despite treatment, it is uncertain whether life sustaining interventions/ resuscitation is in the best interests of the baby and their family.[5]

- Parents should be counselled carefully, and parental wishes should inform a joint decision to provide either active or palliative treatment.
- A senior neonatal /pediatric practitioner who has previously met the parents should be available, if possible, to attend the birth and supervise implementation of the agreed plan.

Moderate risk

For babies with a <50%risk of death or of survival with unacceptably severe impairment, active management would be in the best interests of the baby. A senior neonatal /pediatric practitioner should attend the birth.[5]

STEP 2

Counseling parents and decision- making

- Whenever possible, parents should be involved in planning an extremely preterm birth.
- The planning consultation should include senior clinical staff from the obstetric, midwifery and a senior neonatal /pediatric practitioner available who will be caring for the mother and her baby before, during and after the birth.
- The assessed category of risk to the baby (including the inherent uncertainty around this) should be conveyed sympathetically and with clarity, and the hopes and expectations of parents explored with honesty and compassion in a realistic way. [5,27]
- Clear, balanced information should be shared (figure 2) and management options discussed.[5]
- Time should be allowed for clarification and questions, and parents offered the opportunity to revisit discussions with the perinatal team at any point.[27]

STEP 3

Agreeing a management plan

- Following consultation with parents, initial management of the birth will follow one of two pathways: life-sustaining intervention/Resuscitation or palliative (comfort care) (figure 2).[12,27]
- Consistency in obstetric and neonatal management is essential, either to ensure that the baby is born in the best possible condition or to avoid unnecessary intervention.[11]
- The agreed plan should be clearly documented and communicated to all members of the obstetric and neonatal teams who may be involved in care of the family.
- The challenges inherent in making a binary decision from a continuum of risk should not be underestimated and categorization of risk should always be undertaken by the most senior clinicians available.[27]
- Parents should be counselled that the plan for management will be reviewed and may need to change based on the clinical condition of the baby before, at or after birth, or subsequently in a NICU.[5]

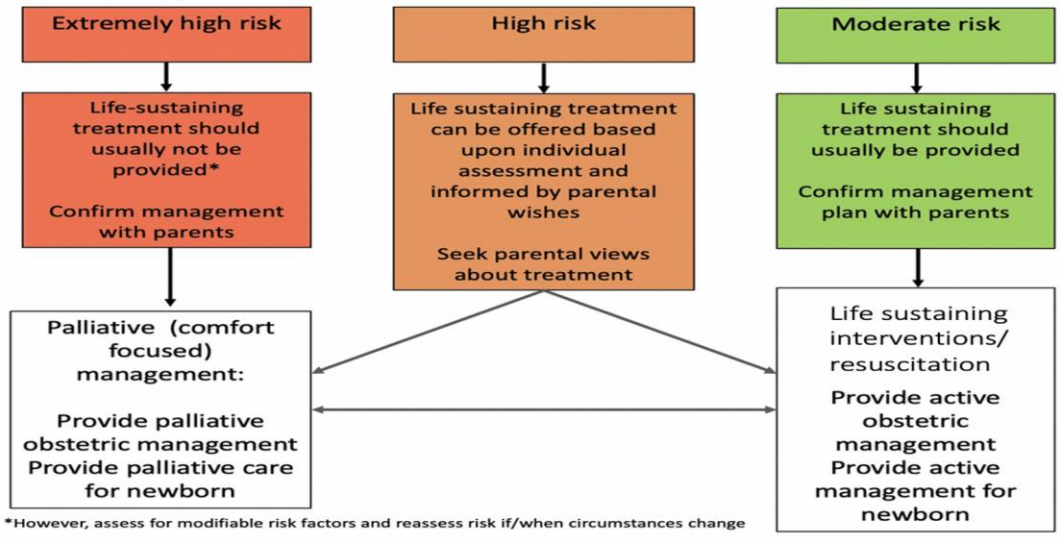


Figure 2: Decision-making around management of delivery, following risk assessment and after consultation with parents.

Special considerations

In utero transfer

- Transfer to a maternity facility co-located with a NICU should be considered at the earliest opportunity when active management is planned.[1,5]
- All transfers should be discussed with the receiving team, and parents should be made aware that the prognosis (and therefore management) may be revised following in utero transfer to a center with greater experience of managing extremely preterm birth (eg, following detailed ultrasound scanning).[5,11-12]
- Communication and agreed plans should be documented in full (including in the maternity handheld record) and, when relevant, clearly communicated with the receiving centre.[11]
- The agreed plan of management should be revised regularly if pregnancy continues. [5,11]

- Parents should also be helped to appreciate that the baby may be born in unexpectedly poor, or unexpectedly good condition, and the implications of this for what care might be appropriate. [5,11]
- When active care is planned and time allows, parents should be given an opportunity to visit the neonatal unit and to meet staff and should receive information and support regarding expressing breast milk. [11-12]

Uncertain gestational age

- If gestational age is uncertain, (i.e., no dating ultrasound scan) but thought to be > 22^{+0} weeks, an ultrasound scan by an experienced sonographer should be carried out if time permits.[1,5,12]
- If the fetal heart is heard during labor, a senior Pediatrician/Neonatologist experienced in stabilization of extremely preterm babies should attend the birth, the baby should be delivered into a plastic bag, and an estimate made of gestation, unless the baby is clearly < 22^{+0} weeks of gestation, and/or estimated (or weighed) at < 350g.[11,28]
- Subsequent management will be dictated by the clinical condition of the baby, the response to stabilization maneuvers and parental views and expectations.[1,5]
- In this scenario, it is likely that the parents will have had little, (if any) time to consider the situation and so it may be appropriate to proceed with initiating life sustaining interventions/resuscitation and to reassess the situation in the ensuing minutes, hours and days.[5]
- Assessment of either gestation or risk of poor outcome based on condition at birth is not reliable.[10, 30-32]

Acute Management upon making decision:

1) If Resuscitation/life sustaining intervention was decided

- Stabilization and support for transition should be carried out by, or under the direct supervision of, the most senior member of the neonatal/pediatric team available at the time of birth, and in accordance with NRP (Neonatal resuscitation program) algorithm, noting specific recommendations for preterm infants.[1-5]
- Ideally, this team includes a physician and a neonatal nurse or midwife that are experienced in stabilization of extremely preterm babies and led by a consultant/ Fellow neonatologist if available.[30-32]

- The team should be aware of parental wishes/views, but when the baby is born in unexpectedly poor, or unexpectedly good condition, it is reasonable for the attending neonatologist/Pediatrician to proceed with care in the baby's best interests.[20]
- Deferred cord clamping for at least 60 s should be routine practice (unless contraindicated), and particular attention should be paid to the maintenance of normothermia, with the use of a plastic bag and/ or other methods of delivering thermal care, and skin protection.[3-5]
- Stabilization and supported transition with lung inflation, using an appropriately sized facemask, should be initiated.
- ***Clinical assessment in the delivery room is not a good predictor of survival in extremely preterm babies*** if there is no response to mask ventilation, and any doubt around the adequacy of ventilation, the baby should be intubated.[5,20,30-32]
- The most important intervention is establishment of adequate lung recruitment, and the most important measure of success is heart rate.[1-5]
- Use of advanced measures for resuscitation including cardiac massage and endotracheal or intravenous epinephrine are rarely required following extreme preterm birth.[1-5]
- Where babies are born in much poorer condition than expected, it may be appropriate to reconsider the planned provision of active management and to move to palliative care.[20]
- Absent heart rate or severe bradycardia persisting despite effective cardiopulmonary resuscitation for more than few minutes is associated with high rates of mortality and neurodevelopmental impairment in extremely preterm babies, hence the most senior experienced attending professional should decide if or when attempts to stabilize and/or resuscitate the baby should stop.[1-5]
- Following successful stabilization of the baby, the mother should be supported to express breast milk as early as possible, with ongoing facilitation of parental contact and family involvement as partners in care.[5]

2) If Palliative (Comfort care) management was decided

The aim of palliative (Comfort care) is to support the parents and their baby and to avoid interventions that may cause discomfort, pain or separation of the baby from the parents. This should not necessitate in utero transfer.[27-32]

A senior pediatrician should be present at delivery to provide a brief assessment of the baby's condition at birth and to support midwifery staff and the family.

Table 3: Palliative care	
ASPECT	**CONSIDERATIONS**
Planning care	• Conduct a thorough assessment of the baby's clinical condition • Develop an agreed care plan with the family, including as appropriate to the circumstances: ▪ Resuscitation ▪ Postnatal care ▪ After death care ▪ Discuss the advantages of post-mortem examination in confirming specific pathology and for informing future pregnancies • Discuss the possibility that the baby may live for many hours or days • Review and adjust the plan at frequent intervals to ensure the goals of care are being met • Include social worker/psychological supports in care planning • Document decisions in detail to ensure a clear and unambiguous understanding by the healthcare team and the family
Newborn care	• Handle baby gently and carefully • Provide wraps for cuddling and holding baby • Offer skin to skin contact • Offer opportunities and support the family's wishes to engage in care provision (e.g., nappy changes, bathing, cuddling/holding)
Nutrition/hydration	• Insertion of a gastric tube for feeding is not usually recommended at extremely preterm gestations • Maintain oral hygiene and comfort (e.g., moisten lips)
Review all interventions	• During the transition to palliative care, removal of technological supports may be considered (e.g., monitors and/or alarms, mechanical ventilation, removal of invasive lines and endotracheal tube) • Where an intravenous line has previously been sited, generally, leave it • in situ to assist with the administration of pain-relieving medication • Supplemental oxygen is not necessary but could be provided if parents' desire. • Suction secretions as necessary • Review whether continued administration of individual medications (e.g., Antibiotics, inotropes) contribute to the comfort of the baby • Stop all unnecessary interventions and observations and actively consider interventions that increase comfort • Provide sensitive emotional support and reassurance to parents throughout the dying process and afterwards

Recommendations:

The AAP Committee on Fetus and Newborn (COFN) revised guidelines for antenatal counselling regarding resuscitation at extremely low GA suggest that predictions provided to parents facing resuscitation decisions should not be based on gestational age **alone** but need to take into account relevant maternal and fetal factors, as well as parental choice and values.[2,4]

The following conclusions were included in these guidelines:

- Joint discussion prior to high-risk birth (if possible) to promote optimal decision making.
- Care providers need to consider** the ability of parents to understand the clinical situation, including language proficiency, if the care providers believe there is no chance of survival for a given infant, then attempted resuscitation offers no benefit to the infant and should not be initiated, one example of this may be confirmed gestational age less than 22 weeks.
- If there is an agreement between parents and care providers that intensive measures will not improve the chance of survival, or pose an unacceptable burden to the child, then those measures will not be escalated and can be withheld. An example of this may include birth between 22-24 weeks gestation.
- Decisions and management should be reviewed before and after birth with parents, with reconsideration of plans based on changes in risk to the fetus/infant and discussion should be clearly documented.
- Although fetal GA is an imprecise predictor of neonatal survival, 22 weeks gestation is generally accepted as the lower threshold of viability. Comfort care should be provided for all cases below 22 weeks gestation at birth.
- Most infants from 22 to 24 weeks gestation will either die in the neonatal period or have significant NDI (Neuro-Developmental index). However, outcomes for individual cases are difficult to predict. As a result, it is reasonable that decision making regarding resuscitative efforts be individualized.

**Refer to (When to consider life-sustaining intervention/Resuscitation or Palliative / Comfort care)

The recommended general approach to resuscitation and intensive care measures for periviable infants is as follows:

1. **Below 22 weeks gestation** – life sustaining interventions/Resuscitation is not offered or provided due to the zero or near-zero chance of survival.
2. **$22^{0/7}$ to $23^{6/7}$ weeks gestation** – life sustaining interventions/Resuscitation is considered** and offered to parents unless there is major pathology or risk factors in addition to extreme prematurity.
3. **24 weeks gestation and higher** – life sustaining interventions/Resuscitation is provided.
4. **Uncertain gestational age** –Life sustaining interventions should be initiated until the clinical course is clearer, further management will be individualized based on the clinical condition of the baby and the response to initial resuscitation. Discuss the baby's condition, clinical assessment and decision making with the family as soon as possible.

- Exceptions may be made at the discretion of the attending clinician if there is additional evidence that significantly worsens the prognosis (e.g, certain congenital anomalies, or profound growth restriction).

**refer to when to consider life sustaining intervention/resuscitation or palliative (comfort care)

Auditing and monitoring

An audit of all admissions of extreme preterm babies born at the threshold of viability will be conducted in yearly basis, which will include the gestational age, birth weight, gender, multiple or single pregnancy, antenatal steroids ,and the presence of (PPROM) Prolonged prelabour rupture of membranes , or /and fetal Doppler abnormalities , or /and chorioamnionitis, inborn or outborn delivery , and other risk factors of each preterm infant, and review the decision taken for each to monitor the adherence to this guideline and then review the outcome and the subsequent recommendations.

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Appendix1

Table 4: Grading Recommendations			
Grade of Recommendation	Clarity of risk/benefit	Quality of supporting evidence	Implications
1A. Strong recommendation. High quality evidence	Benefits clearly outweigh risk and burdens, or vice versa	Consistent evidence from well performed randomized, controlled trials or overwhelming evidence of some other form. Further research is unlikely to change our confidence in the estimate of benefit and risk.	Strong recommendation, can apply to most patients in most circumstances without reservation
1B. Strong recommendation. Moderate quality evidence	Benefits clearly outweigh risk and burdens, or vice versa	Evidence from randomized, controlled trials with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very strong evidence of some other form. Further research (if performed) is likely to have an impact on our confidence in the estimate of benefit and risk and may change the estimate.	Strong recommendation, likely to apply to most patients
1C. Strong recommendation. Low quality evidence	Benefits appear to outweigh risk and burdens, or vice versa	Evidence from observational studies, unsystematic clinical experience, or from randomized, controlled trials with serious flaws. Any estimate of effect is uncertain.	Relatively strong recommendation; might change when higher quality evidence becomes available
2A. Weak recommendation. High quality evidence	Benefits closely balanced with risks and burdens	Consistent evidence from well performed randomized, controlled trials or overwhelming evidence of some other form. Further research is unlikely to change our confidence in the estimate of benefit and risk.	Weak recommendation, best action may differ depending on circumstances or patients or societal values
2B. Weak recommendation. Moderate quality evidence	Benefits closely balanced with risks and burdens, some uncertainly in the estimates of benefits, risks and burdens	Evidence from randomized, controlled trials with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very strong evidence of some other form. Further research (if performed) is likely to have an impact on our confidence in the estimate of benefit and risk and may change the estimate.	Weak recommendation, alternative approaches likely to be better for some patients under some circumstances
2C. Weak recommendation. Low quality evidence	Uncertainty in the estimates of benefits, risks, and burdens; benefits may be closely balanced with risks and burdens	Evidence from observational studies, unsystematic clinical experience, or from randomized, controlled trials with serious flaws. Any estimate of effect is uncertain.	Very weak recommendation; other alternatives may be equally reasonable.

Wolters Kluwer. Smarter decisions. Better care. Waltham, MA: UpToDate. https://www.uptodate.com/home/grading-tutorial (accessed 5/Jan/2020).[30]

Appendix 2
Accuracy of Gestational age

- The argument for mandating a neonatal assessment of gestational age at delivery is essentially based on a belief in the uncertainty of gestational age measurements.
- Although there can be some discussion and advanced care planning with prospective parents on their wishes, decisions should be contingent on the neonatologist's/Pediatrician assessment at birth in the delivery room.
- The argument is that estimates of gestational age can vary, sometimes up to 1 to 2 weeks gestation, which leads to uncertainty, and therefore may not be reliable for prognostication.
- This has important implications, especially if the range of accuracy can place a newborn at either end of the guideline thresholds. There are, however, more and less accurate assessment tools.
- There is evidence supporting that obstetric modality of dating are superior to a well-trained neonatal clinician's assessment of gestational age by examination.
- In fact, research on accuracy of the Ballard examination revealed that clinicians overestimated gestational age by 2 weeks, with a range of +/- 4 weeks.
- This is evidence that the neonatal examination is the least accurate assessment and should never override obstetric dating.
- Although obstetric dating has its level of uncertainty, it must be acknowledged that the epidemiologic outcome data used in developing existing consensus guidelines are based on similar uncertainties, and thus they remain applicable.
- Finally, the most recent guidelines now acknowledge one should not look at gestational age alone but take into account other factors that help predict outcome (gender, singleton, steroids, weigh).

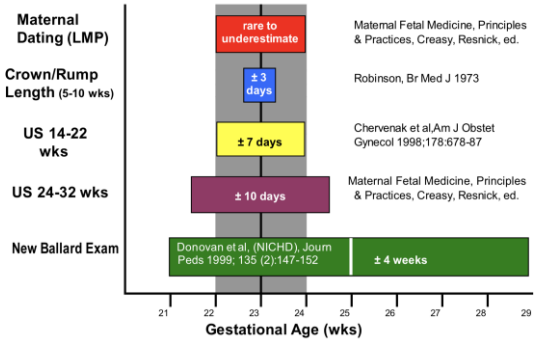

Figure 5 Accuracy of gestational age assessment tools.[31]

Appendix 3

Estimates of survival:

The impact of factors on survival and the probability of a reasonable outcome in infants at or below 25 weeks' gestation was illustrated by a report from the Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network, which evaluated survival and neurodevelopmental outcome for 4446 infants.

A web-based tool based upon this study and the large body of data generated is available to estimate the chance of survival and disability for extremely preterm newborns: *(www.nichd.nih.gov/about/org/der/branches/ppb/programs/epbo/Pages/epbo_case.aspx)*

This tool is not intended to be predictive of individual infant outcomes, but rather provides a range of possible outcomes based on patient characteristics and is applicable only at birth. While it may prove helpful for parental counselling and clinical decision-making regarding resuscitation, this tool is not intended to be the sole basis for care decisions, so the clinician must consider other relevant factors when counselling parents regarding management decisions. Clinicians should consider whether other factors are present that could impact the outcome, such as the adverse effects of long-standing fetal compromise and/or maternal and fetal infection, and the potential positive effects of intensive intervention.

Multiple regression analysis showed that, in addition to increasing GA, the following **four** were associated with improved survival and outcome:

1. Female sex
2. Use of antenatal glucocorticoids
3. Singleton birth
4. 100g increments in birth weight at a given GA

Congenital anomaly:

The outcome or prognosis associated with a significant fetal anomaly may be worsened by extreme prematurity. Examples include (but are not limited to) complex heart disease, diaphragmatic hernia, significant bowel disease.

Antenatal Pathologies:

Poor outcome associated with but not limited to:

1. Birth weight less than the 2nd percentile
2. Premature prolonged rupture of membranes

3. Severely abnormal fetal Doppler
4. Chorioamnionitis
5. Twin to twin transfusion syndrome
6. Multiple pregnancies

Morbidities:

Significant morbidities that occurred in infants 22 to 25 weeks gestation who survived their initial neonatal intensive care unit (NICU) admission include:

1. Severe intraventricular hemorrhage (IVH) (i.e., grade III and IV)
2. Periventricular leukomalacia (PVL)
3. Necrotizing enterocolitis (NEC)
4. Bronchopulmonary dysplasia (BPD
5. Severe retinopathy of prematurity (ROP) (i.e., ≥ Stage 3)
6. Late-onset infection
7. Neurodevelopmental impairment (NDI)

Most surviving infants less than 26 weeks gestation are likely to have significant morbidity, and the risk of more than one morbidity increases with decreasing gestational age.

Neurodevelopmental outcome:

Poor neurodevelopment outcome is a major long-term complication of periviable survivors and includes impaired cognition and motor and neurosensory deficits. A follow-up study of a cohort of infants born at 22–26 weeks of gestation in England in 2006 found a progressive decrease in the proportion of children at age 30 months with severe or moderate impairment (defined as cerebral palsy, blindness, profound hearing loss, or developmental quotient 2SDs or more below the mean) with increasing gestational age at birth: 45% at 22–23 weeks, 30% at 24 weeks, and 17% at 25 weeks of gestation.

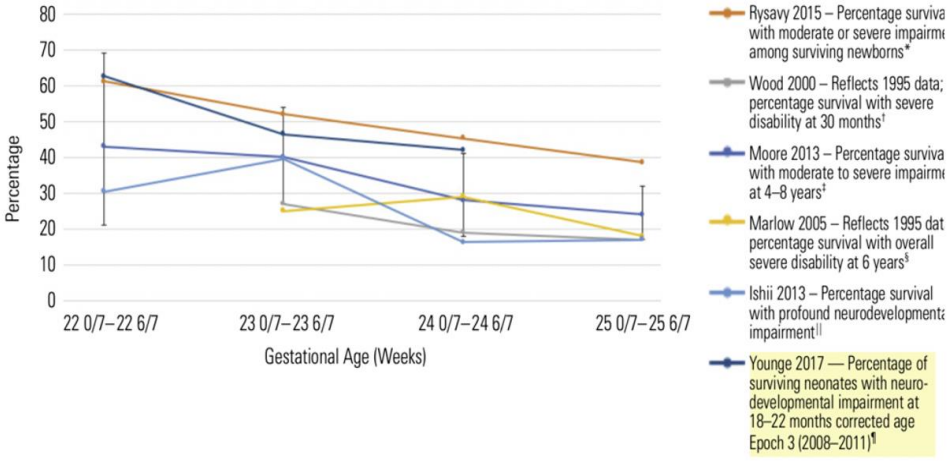

Figure 4: Percentage of surviving neonates with severe or moderate disability by gestational age.

Similarly, a recent systematic review found that the incidence of moderate-to-severe neurodevelopmental impairment among survivors at 4–8 years decreased progressively with each week gained in gestational age at birth: 43% at 22 weeks, 40% at 23 weeks, 28% at 24 weeks, and 24% at 25 weeks of gestation; notably, although the combined rate decreased, the rate of severe neurodevelopmental impairment alone did not decrease significantly with increasing gestational age in this study.

In 2017, a study described survival and neurologic outcomes among more than 4,000 births from 2001 to 2011 that were between 22 weeks and 24 weeks of gestation at 11 centers in the United States.[14] The authors reported that the rate of survival and survival without neurodevelopmental impairment increased over this period whereas the rate of survival with such impairment did not change, arguing that the observed overall increase in survival was not simply a tradeoff for life with significant impairment. The absolute change in survival without impairment was just 4%, however, and most neonates in the most recent 2008–2011 epoch died (64%) or were severely impaired (16%).

Among those born at $22^{+0/7}$- $22^{+6/7}$ weeks, death rates were 97–98% with just 1% surviving without neurodevelopmental impairment. In contrast from 2008 to 2011 at $24^{+0/7}$ weeks to 24 $^{+6/7}$ weeks of gestation, 55% of neonates survived, and 32% survived without evidence of neurodevelopmental impairment at 18–22 months of corrected age. Overall, these data led the authors to conclude that "despite improvements over time, the incidence of death, neurodevelopmental impairment, and other adverse outcomes remains high".

In considering all these outcome studies, it also should be emphasized that although summary data often are grouped into segments of weeks, outcomes for deliveries at the extreme may be closer to those of the adjacent week than to those at the other extreme of the same week (e.g., outcomes at $23^{+6/7}$ weeks may be more similar to those at $24^{+0/7}$ weeks than to those at $23^{+0/7}$ weeks of gestation).