



Royal College of
Obstetricians &
Gynaecologists

Perinatal Management of Pregnant Women at the Threshold of Infant Viability (The Obstetric Perspective)

Scientific Impact Paper No. 41

February 2014

Perinatal Management of Pregnant Women at the Threshold of Infant Viability

(The Obstetric Perspective)

1. Background

Delivery at the threshold of viability (23⁺⁰ weeks to 24⁺⁶ weeks of gestation) is a major medical and ethical challenge. It should be preceded by the best possible advice from a multidisciplinary neonatal and obstetric team, which informs parents fully, seeks to achieve a consensus on the best way forward, and provides the best care for the mother and neonate. There is international consensus that at 22 weeks of gestation there is no hope of survival, and that up to 22⁺⁶ weeks is considered to be the cut-off of human viability and for week 25⁺⁰ onwards there is also a general agreement that active management should be offered.¹ Delivery between these two gestational age limits is the most challenging. Given the marked improvement in survival for extremely premature infants as reported in EPICure 1 (1995) and EPICure 2 (2006) studies, more babies below 26 completed weeks of gestation are being admitted to neonatal units in England (an increase of 30%).² There has been an overall increase in survival of 12%; from 40% to 52%.³ Unfortunately this marked improvement in survival has not been associated with a reduction in morbidity, with no change in the proportion of survivors with major short term complications in 1995 and 2006; brain haemorrhage (15% versus 13%), chronic lung disease (75% versus 74%) and treated retinopathy of prematurity (13% versus 21%).

Given the importance of reducing the morbidity associated with extreme prematurity, it is essential that obstetricians optimise all aspects of the peridelivery period at the threshold of viability. Inevitably this includes accurate counselling of likely outcomes, prediction of impending preterm delivery, transferring the woman to an appropriate perinatal unit, promoting fetal maturation, preventing cerebral palsy, as well as optimising the timing, site and mode of delivery whilst minimising the risk of infection and neurological injury. The existing evidence base covering issues specific to the obstetric perinatal management of extremely preterm infants born spontaneously between 23⁺⁰ and 24⁺⁶ weeks of gestation will be summarised. The relevant guidelines⁴⁻⁶ and reports⁷ will be considered, and an opinion on the clinical management of women who are pregnant who are in preterm labour at the extreme of infant viability will subsequently be provided.

2. Evidence

2.1 Prediction of overall birth outcome

Gestational age is the primary determinant of almost all perinatal outcomes. At the threshold of viability as few as 5 extra days in utero can double the chance of survival and greatly increase neurologically intact survival. Accurate and early gestational age estimation by ultrasound is therefore essential, with national guidelines recommending first trimester ultrasound.⁸ Birthweight and female sex are independently positively associated with survival after extremely preterm birth, with greatest survival in those infants born weighing between the 50th and 85th centile.⁹ Estimated fetal weight (EFW) can be derived using ultrasound but the accuracy of EFW measurement is compromised by large intra- and interobserver variability which may be compounded when the membranes have ruptured and the presenting part, head or breech is low in the pelvis. In one systematic review of methods for EFW in low birth weight fetuses, large random errors were reported, and no specific formula was recommended.¹⁰ Similarly although a variety of Doppler indices are frequently used to assess fetal wellbeing their prediction of long term outcome is more limited. A decision to resuscitate a baby born at extreme prematurity should not be based solely on EFW but on consideration of the true birthweight measured immediately after birth, and neonatal vigour.

2.2 *In utero transfer*

Neonatal survival is improved when extreme preterm infants are delivered in an appropriate level neonatal unit. The reason for transfer may also be to optimise management but not necessarily to do everything to achieve neonatal survival when faced with imminent delivery at the limits of viability. Since diagnosis of preterm labour in women with symptoms at extremes of prematurity can be challenging, a number of techniques are available in addition to vaginal examination. The accuracy of these techniques has been summarised in a recent systematic review.¹¹ These techniques include vaginal fetal fibronectin, cervical phosphorylated insulin-like growth factor binding protein-1 and transvaginal ultrasound measurement of cervical length. Use of tests of prediction of preterm labour is dependent on local policies, but it is recommended that at least one of these tests is performed in women presenting with threatened preterm labour at the limits of viability, when in utero transfer to an appropriate level neonatal unit is being considered.⁶

2.3 *The use of ultrasound in threatened or established extreme preterm labour*

Translabial cervical length assessment achieves similar measurements of cervical length to those obtained by transvaginal sonography at 22–24 weeks of gestation.¹² Although there is no evidence for its preferred use in preterm labour at extremes of viability, translabial ultrasound may be a useful alternative to transvaginal ultrasound so as to avoid introduction of the probe into the vagina when bulging of the membranes is suspected. However, there is no correlation between cervical length as measured by translabial ultrasound in women with preterm premature rupture of the membranes, and latency to delivery interval.¹³ There is no evidence for the use of ultrasound in preterm labour at the threshold of viability. Intermittent abdominal ultrasound may be helpful in monitoring fetal viability during labour (to inform the parents and the neonatal team) and to monitor the progress in the second stage of labour such as descent of the presenting part.

2.4 *Maternal and fetal antenatal interventions*

2.4.1 *Prevention of and delaying preterm birth in women with threatened preterm labour*

Given the clear advantages of increasing gestational age on overall survival at extreme prematurity, much attention has been on methods to prevent or delay preterm birth in women who present in threatened preterm labour. Although, prolonging the pregnancy may be inappropriate because of intrauterine infection or placental abruption for some women.

Insertion of a cervical cerclage can be performed as a salvage measure in the case of premature cervical dilatation with exposed fetal membranes in the vagina but is not recommended when a woman is in established preterm labour.¹⁴ Some women who already have a cervical cerclage in place will present with labour symptoms at extreme preterm gestations. The decision to remove the cerclage must be timed carefully to avoid unnecessary trauma to the cervix if the woman labours with the cerclage in situ.

The evidence for use of tocolysis in preterm labour has recently been summarised.¹⁵ Systematic reviews have not distinguished between tocolytic use at the threshold of viability (≤ 26 weeks of gestation) and later preterm gestations. One systematic review concluded that tocolytics were not associated with a significant reduction in births before 30 weeks of gestation¹⁶ and another concluded that oxytocin receptor antagonists such as atosiban did not prevent preterm birth at < 28 weeks of gestation.¹⁷ There are insufficient data available on long term outcomes.

In extreme preterm gestations, a randomised controlled trial (RCT) of atosiban found a higher incidence of perinatal and neonatal death in women at < 24 weeks of gestation who were randomised to atosiban compared to placebo, although numbers were small ($n = 19$).¹⁸ A second study comparing glyceryl trinitrate skin patches with placebo conducted a *priori* sub-analysis according to gestational age and showed that there was a non-significant decreased risk of delivery before 28 weeks of gestation (RR 0.50, 95% CI 0.23, 1.09).¹⁹ A recent systematic review and meta-analysis of nifedipine as a tocolytic agent in women with preterm labour did not stratify for gestational age, and no conclusions could be drawn.²⁰ For women who are already in threatened or established labour with intact membranes, a

recent meta-analysis concluded there was insufficient evidence to advocate the use of progesterone as a tocolytic agent.²¹

2.4.2 Antenatal corticosteroid administration

The many neonatal benefits of antenatal corticosteroids are well established. All women requiring, or at high risk of, impending preterm delivery between 24⁺⁰ and 34⁺⁶ weeks of gestation should receive antenatal corticosteroids.²² This should also be considered for women at the threshold of viability who are at risk of preterm birth. A high quality prospective cohort study showed antenatal corticosteroid use in pregnancies at 23–25 weeks of gestation was associated with a lower rate of death or neurodevelopmental impairment at 18–22 months of age.²³

The question of repeating a course of steroids may arise infrequently in women at the threshold of viability due to the nature of the clinical circumstances. A Cochrane review showed that the short term benefits for babies of less respiratory distress and fewer serious health problems in the first few weeks after birth support the use of repeat dose(s) of prenatal corticosteroids for women still at risk of preterm birth 7 days or more after an initial course. These benefits were associated with a small reduction in size at birth. The current available evidence reassuringly shows no significant harm in early childhood, although no benefit.²⁴

2.4.3 Maternal antibiotic administration

Prematurity is a risk factor for early onset group B streptococcus (GBS) disease for neonates. Recently, the National Institute for Health and Care Excellence (NICE)²⁵ evaluated the evidence for antibiotics to prevent early onset neonatal sepsis. A few studies included focused on extreme preterm gestations.^{26–29} Indicators of suspected or confirmed clinical chorioamnionitis such as intrapartum fever > 38°C, foul-smelling amniotic fluid, leukocytes or bacteria in amniotic fluid, fetal tachycardia or meconium-stained amniotic fluid were identified as risk factors for early onset neonatal infection. It was recommended that intrapartum antibiotic prophylaxis using intravenous benzyl penicillin should be considered in order to prevent early-onset neonatal infection in women in preterm labour with prelabour rupture of membranes.²⁵ For women presenting in preterm labour with intact membranes and with no other risk factors for vaginal GBS infection or indicators of chorioamnionitis, intrapartum antibiotics should not be offered unless they are known to be colonised with GBS.³⁰

2.4.4 Maternal Magnesium sulphate administration

Evidence for the administration of peripartum magnesium infusion to prevent cerebral palsy is lacking at the threshold of viability and more data are needed at these extreme gestations.^{31–34} If a decision has been made for active intervention, then it would seem sensible to consider the use of peripartum magnesium infusion in discussion with the parents. Peripartum magnesium infusion is recommended once 24 weeks of gestation is reached.

2.4.5 Induction of labour

Occasionally it becomes necessary to expedite delivery at the threshold of viability for maternal benefit, for example, when severe chorioamnionitis has developed. Guidelines from NICE³⁵ and Royal College of Obstetricians and Gynaecologists (RCOG)³⁶ on induction of labour in women with preterm prelabour rupture of membranes could only identify studies conducted in women after 29 weeks of gestation and the best method to induce labour at extreme prematurity is currently unknown.

2.5. Interventions for delivery

2.5.1 Role of caesarean section

When immediate delivery is required, for example due to massive antepartum haemorrhage or fulminating preeclampsia, then delivery by caesarean section may be the only option. When there is a choice regarding mode of delivery, caesarean section may intuitively appear less traumatic for the infant, but studies fail to show a significant advantage to the infant in unselected cases and an updated Cochrane review did not stratify preterm births according to their gestation.³⁷

There are even less data about mode of delivery at the threshold of viability, and no RCTs have been conducted as of yet. A retrospective study in the United States of America (USA) showed that delivery of infants between 22–25 weeks of gestation by caesarean section had a reduced neonatal mortality rate, independent of any risk factors, but this was primarily on the day of birth.³⁸ A study in Israel specifically investigating preterm infants < 1500 g, found that caesarean section was not associated with a beneficial effect on survival except in a sub-group who had chorioamnionitis.³⁹

There are no data specifically addressing mode of delivery at the threshold of viability in non-cephalic fetal presentation. There are no data for gestations less than 26 weeks, but one of the trials included in the aforementioned Cochrane review specifically addressed planned caesarean section for preterm breech between 26 and 32 weeks of gestation; however recruitment rates were poor and no conclusions were able to be drawn. The evidence shows that routine caesarean section for the delivery of preterm breech presentation should not be advised and mode of delivery should be discussed on an individual basis with a woman and her partner.

In the case of multiple pregnancies, a population study of otherwise uncomplicated pregnancies compared the outcome of second twins delivered by caesarean section due to breech presentation of the sibling, with those delivered vaginally.⁴⁰ In births before 34 weeks of gestation, second born twins delivered by caesarean section had a lower risk of neonatal death than those delivered vaginally (2.1 versus 9.0%, adjusted OR 0.40, 95% CI 0.17, 0.95) but this study had only low numbers of extremely preterm infants (1.2–1.4% were < 28 weeks of gestation).

The rate of classical caesarean section is inversely related to the gestation. In one cohort study where a classical incision was performed in 1% of all caesarean sections, 20% of incisions were classical at 24 weeks of gestation, < 5% at 30 weeks and < 1% from 34 weeks of gestation.⁴¹ The complications of classical caesarean section are increased risk of scar rupture and subfertility in the future and higher maternal morbidity (bleeding, paralytic ileus)⁴² hence women need to be counseled regarding these issues when classical caesarean section is anticipated.

The present evidence suggests that the method of delivery in extreme prematurity should be based on obstetric or maternal indications rather than perceived outcome of the baby and caesarean delivery cannot be recommended routinely.^{39,43} Delivery of the fetus within the intact gestation sac “*en caul*” is well described as a technique to reduce the trauma during Caesarean delivery, although substantive evidence for this approach is lacking.

2.5.2 Fetal monitoring during labour

At present there is no evidence that continuous or intermittent fetal heart rate monitoring is of benefit in infants at the threshold of viability during labour. Intrapartum continuous fetal heart rate monitoring would seem appropriate during labour for those pregnancies in which active obstetric intervention, such as emergency caesarean section in the presence of a pathological cardiotocography (CTG), and full neonatal support is planned.

2.5.3 Management during labour and obstetric emergencies

Analgesia in labour is an important consideration. Labour at the threshold of viability can occasionally progress rapidly with minimal painful uterine contractions and no requirement for analgesia. More frequently, labours may be more lengthy and painful. There is no evidence that the choice of analgesia (for example, TENS, Entonox, opiates or epidural analgesia) influences the outcome of infants at the threshold of viability.

Keeping the membranes intact during labour and delivery may prevent fetal trauma. There does not appear to be any contraindication to the use of oxytocin to augment labour. Evidence is lacking on the risk of amniotic fluid embolism and induction of labour with intact membranes at the threshold of viability.⁴⁴

Cord prolapse is more common in preterm deliveries, particularly in non-cephalic presentations and should be managed in accordance with current guidelines if cord prolapse were to occur.⁴⁵ In breech deliveries entrapment of the fetal head affects approximately 9.3% of vaginally delivered neonates and

5.6% of neonates delivered by caesarean section at 24–27 weeks of gestation, with maneuvers such as intravenous maternal administration of nitro-glycerine (150–250 µg)⁴⁶ or lateral cervical incisions reported as immediate therapies.⁴⁷ Routine caesarean section in breech deliveries is not recommended however, as mode of delivery was not associated with any difference in adverse neonatal outcomes.⁴⁸

There are no data on the role of episiotomy at the threshold of viability but it may be useful to widen the introitus and aid delivery of the presenting part in non-cephalic presentations.

2.5.4 Delayed cord clamping

Evidence suggests that immediate cord clamping, defined as within the first 30 seconds after birth, reduces placental transfusion and thus lowers neonatal haemoglobin.⁴⁹ For preterm infants immediate cord clamping increases the need for transfusion. The risk of an ultrasound diagnosis of intraventricular haemorrhage is also increased, but the long term significance of this is not yet known. A Scientific Advisory Committee impact paper⁵⁰ published by the RCOG summarises the evidence on delayed cord clamping.

2.6 Resuscitation

At present within the United Kingdom, active resuscitation is attempted for the 84% of infants born alive at 23⁺⁰ to 23⁺⁶ weeks of gestation (Appendix 1). Although largely related to long term survival, the 5 minute Apgar score is associated with short term outcomes in infants born at 23–24 weeks of gestation, with this association being stronger for infants born at 24 weeks.⁵¹ The guidance on optimal resuscitation (clinicians to attend, interventions etc.) is described in regional² and national⁴ documents which are used in conjunction with local network or unit guidelines.

2.7 Long term outcome

Survival rates after birth of extremely preterm infants vary between countries. Differences in the availability of neonatal intensive care and in attitudes towards end of life decisions, such as removal of care, could in part explain these differences. A study compared practices of care and outcomes of infants who were born between 23 and 25 weeks of gestation in 1995 in the British Isles (EPICure) and in 1997–8 in France (EPIPAGE). Despite apparent differences in the modalities in groups with limitation of intensive care, longer term outcomes of infants were not significantly different.⁵² In the EPIPAGE study, which was a prospective observational population-based study in France in 1997, survival to discharge was 0% at 23 weeks, 31% at 24 weeks and 50% at 25 weeks.⁵³

In the EPICure study of 1995, 314 (39%) of 811 infants admitted to neonatal units survived.⁵⁴ Of the survivors 17% had parenchymal cysts and/or hydrocephalus, 14% received treatment for retinopathy of prematurity and 51% needed supplementary oxygen at the expected date of delivery. Failures to administer antenatal steroids and postnatal transfer for intensive care within 24 hours of birth were predictive of a major scan abnormality. Of those surviving, 241 (78%) children were assessed at 6 years of age. At that time, 13% had disabling cerebral palsy, 13% had severe sensory impairment and 21% had an IQ up to 3 standard deviations (SD) less than children that were not born severely preterm.⁵⁵

In EPICure 2,³ 1041 (61%) out of 1687 infants born at 22 to 26 weeks of gestation admitted to neonatal units survived; 16% at 22 weeks, 29% at 23 weeks, 46% at 24 weeks, 69% at 25 weeks and 78% at 26 weeks (the original EPICure study included babies born between 22 and 25 weeks). Of the survivors, outcome data were available for 767/1031 (74%) children at 3 years of age and missing outcomes were imputed to generate a complete dataset for analysis. 724 (70% of survivors and 43% of admissions for neonatal care) had mild or no disability; 150 (14% of survivors and 9% of admissions) had moderate disability, and 157 (15% of survivors and 9% of admissions) had severe disability. Between the two EPICure studies, survival for babies 22–25 weeks of gestation admitted for intensive care had increased by 13%; the proportion of admissions with severe disability had not changed significantly, whereas the proportion surviving without disability as defined rose by 11% ($p < 0.001$). The proportion of surviving admissions rose significantly only for babies born at 24 and 25 completed weeks of gestation (Appendix 1).

2.8 Postnatal management of the mother

There is no available evidence on obstetric postnatal management in terms of investigations or the optimum arrangements for postnatal counselling appointments.

3. Opinion

The limit of viability has been lowered along with advancements in perinatal and neonatal medicine. The viability limit defined in the Japanese Motherhood Protection Act was amended from 24 to 22 completed weeks of gestation in 1991 based on the survival rate of extremely preterm infants.⁵⁶ In contrast in the UK, this has legally remained at 24 weeks due to the poor survival at gestations below this threshold, while in certain European countries it is defined as 26 weeks due to the significant risk of handicap.

The infants born between 23⁴⁰ and 24⁴⁶ weeks of gestation with a birth weight of 500–599 g present the greatest uncertainty surrounding survival and outcome.⁵⁷ For these infants, born at the threshold of viability, the line between patient (parent) autonomy and medical futility is blurred. If the birth weight is < 500 g, resuscitation should only be performed after the most careful of consideration. Infants born at ≥ 25 weeks of gestation and with a birth weight of ≥ 600 g are mature enough to warrant initiation of intensive care as the majority of these babies survive and at least 50% do so without long term disabilities.

Medical decision making becomes even more complex and needs to carefully consider a number of factors and especially the best interests of the child, while maintaining a dialogue with the parents. These factors include appraisal of prenatal data such as EFW and sonographic signs of fetal wellbeing, parental wishes regarding resuscitation and continuing care, evaluation of gestational age, the birth weight and clinical condition at delivery, ongoing assessment of the baby's response to resuscitation and intensive care, and continued involvement of the parents in the decision making process after delivery.

The General Medical Council (GMC)⁵⁸ advice on the parents' wishes in relation to the care of their neonate, although not totally applicable to the prenatal situation, is useful to consider when consulting with parents faced with an extreme preterm birth. The GMC advises clinicians to work in partnership with parents when considering decisions about their child's treatment, sharing with them the information they want or need about their child's condition and options for care, in a way that they can understand. Parental views should be accounted for when identifying options that are clinically appropriate and likely to be in the child's best interests.

It is important when managing the birth of an infant in this 'grey zone' of viability to have a consistent obstetric and neonatal approach. To a degree, the obstetric management will be driven by the plans for neonatal resuscitation agreed with the parents. Alternatively if the neonatologists are not planning to resuscitate the baby then there would be little point in monitoring fetal wellbeing during labour, or for performing a caesarean section to improve outcome. Three scenarios are available, the first; 'active' management with recourse to caesarean section and full resuscitation. The second; 'passive' management in which caesarean delivery is not to be performed but resuscitation will be attempted. And the third; 'palliative' management in which comfort care will be provided if a live birth ensues. For each scenario, there will need to be a discussion regarding other obstetric interventions such as steroids, magnesium sulphate and tocolysis. This is poignant; preterm delivery is unpredictable and a few days can make a huge difference to neonatal survival and outcome.

In the majority of very preterm births the clinician is presented with a woman in spontaneous preterm labour where the power to do much is limited. Less commonly there may be the need for elective delivery at the limits of viability because of imminent danger to the life of the mother, for example severe preeclampsia or even chorioamnionitis. A live infant at the threshold of viability may result from such a delivery, and it is important to agree a plan of management with the parents in conjunction with the neonatal team before birth, should this occur. This plan should consider whether resuscitation or palliative care will be provided. The parents' preference should be considered and discussion should be carefully documented.

Uncommonly there may be the need for elective delivery at the threshold of viability because of imminent danger to the life of the fetus, for example with severe early onset fetal growth restriction. The decision for elective delivery will need to include discussion about the risks of the delivery procedure for the mother, since it will almost certainly be surgical, and a classical caesarean section.

Regardless of the cause of preterm birth, the discussion with parents should centre on whether survival is possible at this gestational age/EFW, and the risks of significant disability considered in detail, in consultation with the multidisciplinary team using the best available data. The mortal, morbid and fertility risks to the mother of such early delivery should also be mentioned, particularly when caesarean section is being considered. At the threshold of viability, this judgment is fluid and multifactorial, and may change on a daily basis should the pregnancy continue. In such a highly charged environment, parental requests for urgent delivery in the face of an appallingly poor fetal prognosis will test the counselling skills of even the most committed perinatal specialist. Conveying the concept that fetal death is not the worst outcome, and that severe neonatal morbidity and maternal and fertility morbidity are also important considerations to the woman and her partner, must be conducted with kindness and sensitivity.

There will need to be discussion with the woman and her partner in advance of the labour so that they are aware of the risk of obstetric emergencies such as cord prolapse, and if possible, to agree the mode of delivery. After the birth, investigations should be performed to determine the cause of spontaneous preterm birth, such as placental histology and microbiology. Couples have many questions after the birth particularly about why the mother went into extreme preterm labour, the risk of recurrence and how to manage a future pregnancy. An appointment should be offered for follow up with an obstetrician with suitable experience to discuss the results and to answer their questions.

Delivery at the threshold of viability can be the greatest dilemma faced by an obstetrician. In many cases there will be little elective decision making, nature has decided intrauterine time has ended. However, given that almost all studies are either underpowered or do not stratify for extreme prematurity the challenge of providing non-evidence based perinatal management at these gestations is likely to continue. A summary from which Units may develop local guidelines is offered in Appendix 2.

References

1. 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;121:193–8.
2. EPICure 2 Perinatal Group. Survival and early morbidity of extremely preterm babies in England: changes since 1995. *Arch Dis Child* 2008;93(Suppl 1):33–4.
3. Costeloe KL, Hennessy EM, Haider S, Stacey F, Marlow N, Draper ES. Short term outcomes after extreme preterm birth in England: comparison of two birth cohorts in 1995 and 2006 (the EPICure studies). *BMJ* 2012;345:e7976.
4. Thames Regional Perinatal Group. *Framework for practice relating to the birth of extremely immature babies (22–26 weeks gestation)*. London;Thames Regional Perinatal Group:1999.
5. Wilkinson AR, Ahluwalia J, Cole A, Crawford D, Fyle J, Gordon A, et al. Management of babies born extremely preterm at less than 26 weeks gestation: a framework for clinical practice at the time of birth. *Arch Dis Child Fetal Neonatal Ed* 2009;94:2–5.
6. Fenton A, Peebles D, Ahluwalia J. *Management of acute in-utero transfers: a framework for practice*. London;British Association of Perinatal Medicine:2008. [http://www.bapm.org/publications/documents/guidelines/IUTs_Jun08_final.pdf]
7. Nuffield Council on Bioethics. *Critical care decisions in fetal and neonatal medicine: ethical issues*. [[http://www.nuffieldbioethics.org/sites/default/files/CCD%20web%20version%2022%20June%2007%20\(updated\).pdf](http://www.nuffieldbioethics.org/sites/default/files/CCD%20web%20version%2022%20June%2007%20(updated).pdf)].
8. Loughna P, Chitty L, Evans T, Chudleigh T. Fetal size and dating: charts recommended for clinical obstetric practice. *Ultrasound* 2009;17:161–7.

9. Effer SB, Moutquin JM, Farine D, Saigal S, Nimrod C, Kelly E, Niyonsenga T. Neonatal survival rates in 860 singleton live births at 24 and 25 weeks gestational age. A Canadian multicentre study. *BJOG* 2002;109:740–5.
10. Dudley NJ. A systematic review of the ultrasound estimation of fetal weight. *Ultrasound Obstet Gynecol* 2005;25:80–9.
11. Honest H, Forbes CA, Durée KH, Norman G, Duffy SB, Tsourapas A, et al. Screening to prevent spontaneous preterm birth: systematic reviews of accuracy and effectiveness literature with economic modelling. *Health Technol Assess* 2009;13:1–627.
12. Cicero S, Skentou C, Souka A, To MS, Nicolaides KH. Cervical length at 22–24 weeks of gestation: comparison of transvaginal and transperineal–translabial ultrasonography. *Ultrasound Obstet Gynecol* 2001;17:335–40.
13. Fischer RL, Austin JD. Cervical length measurement by translabial sonography in women with preterm premature rupture of membranes: can it be used to predict the latency period or peripartum maternal infection. *J Matern Fetal Neonatal Med* 2008;21:105–9.
14. Royal College of Obstetricians and Gynaecologists. *Cervical Cerclage. Green-top Guideline No. 60*. London;RCOG:2011.
15. Royal College of Obstetricians and Gynaecologists. *Tocolysis for Women in Preterm Labour. Green-top Guideline No. 1b*. London;RCOG:2011.
16. Gyetvai K, Hannah ME, Hodnett ED, Ohlsson A. Tocolytics for preterm labor: a systematic review. *Obstet Gynecol* 1999;94:869–77.
17. Papatsonis D, Flenady V, Cole S, Liley H. Oxytocin receptor antagonists for inhibiting preterm labour. *Cochrane Database Syst Rev* 2005;(3):CD004452.
18. Romero R, Sibai BM, Sanchez–Ramos L, Valenzuela GJ, Veille JC, Tabor B, et al. An oxytocin receptor antagonist (atosiban) in the treatment of preterm labor: a randomized, double–blind, placebo–controlled trial with tocolytic rescue. *Am J Obstet Gynecol* 2000;182:1173–83.
19. Smith GN, Walker MC, Ohlsson A, O’Brien K, Windrim R. Randomized double–blind placebo–controlled trial of transdermal nitroglycerin for preterm labor. *Am J Obstet Gynecol* 2007;196:1–8.
20. Conde–Agudelo A, Romero R, Kusanovic JP. Nifedipine for the management of preterm labor: a systematic review and meta–analysis. *Am J Obstet Gynecol* 2011;204:1–20.
21. Su LL, Samuel M, Chong YS. Progestational agents for treating threatened or established preterm labour. *Cochrane Database Syst Rev* 2010;(1):CD006770.
22. Royal College of Obstetricians and Gynaecology. *Antenatal corticosteroids to reduce neonatal morbidity and mortality. Green-top Guideline No. 7*. London;RCOG:2010.
23. Carlo WA, McDonald SA, Fanaroff AA, Vohr BR, Stoll BJ, Ehrenkranz RA, et al. Association of antenatal corticosteroids with mortality and neurodevelopmental outcomes among infants born at 22 to 25 weeks gestation. *JAMA* 2011;306:2348–58.
24. Crowther CA, Harding JE. Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease. *Cochrane Database Syst Rev* 2007;(18):CD003935.
25. National Institute of Health and Clinical Excellence. *Antibiotics for early–onset neonatal infection: antibiotics for the prevention and treatment of early–onset neonatal infection. CG149*. London;NICE:2012.
26. Alexander JM, Gilstrap LC, Cox SM, McIntire DM, Leveno KJ. Clinical chorioamnionitis and the prognosis for very low birth weight infants. *Obstetrics and Gynecology* 1998;91:725–9.
27. Buhimschi CS, Bdel–Razeq S, Cackovic M, Pettker CM, Dulay AT, Bahtiyar MO, et al. Fetal heart rate monitoring patterns in women with amniotic fluid proteomic profiles indicative of inflammation. *Am J Perinatol* 2008;25:359–72.
28. Martius JA, Roos T, Gora B, Oehler MK, Schrod L, Papadopoulos T, et al. Risk factors associated with early–onset sepsis in premature infants. *Eur J Obstet Gynecol Reprod Biol* 1999;85:151–8.

29. Rønnestad A, Abrahamsen TG, Medbø S, Reigstad H, Lossius K, Kaaresen PI, et al. Septicemia in the first week of life in a Norwegian national cohort of extremely premature infants. *Pediatrics* 2005;115:262–8.
30. Royal College of Obstetricians and Gynaecologists. *Prevention of Early Onset Neonatal Group B Streptococcal Disease. Green-top Guidelines No. 36.* London;RCOG:2012.
31. Royal College of Obstetricians and Gynaecologists. *Magnesium Sulphate to Prevent Cerebral Palsy Following Preterm Birth. Scientific Impact Paper No. 29.* London;RCOG:2011.
32. Magpie Trial Follow-Up Study Collaborative Group. The Magpie Trial: a randomised trial comparing magnesium sulphate with placebo for pre-eclampsia. Outcome for women at 2 years. *BJOG* 2007;114:300–9.
33. Marret S, Marpeau L, Zupan-Simunek V, Eurin D, Leveque C, Hellot MF, et al. Magnesium sulphate given before very-preterm birth to protect infant brain: the randomised controlled PREMAG trial. *BJOG* 2007;114:310–8.
34. Rouse DJ, Hirtz DG, Thom E, Varner MW, Spong CY, Mercer BM, et al. A randomized, controlled trial of magnesium sulfate for the prevention of cerebral palsy. *N Engl J Med* 2008;359:895–905.
35. National Institute for Health and Clinical Excellence. *Induction of labour. CG70.* London;NICE:2008
36. Royal College of Obstetricians and Gynaecologists. *Preterm Prelabour Rupture of Membranes. Green-top Guideline No. 44.* London;RCOG:2010.
37. Alfirevic Z, Milan SJ, Livio S. Caesarean section versus vaginal delivery for preterm birth in singletons. *Cochrane Database Syst Rev* 2012;(6):CD000078.
38. Malloy MH. Impact of cesarean section on neonatal mortality rates among very preterm infants in the United States, 2000–2003. *Pediatrics* 2008;122:285–92.
39. Riskin A, Riskin-Mashiah S, Lusky A, Reichman B. The relationship between delivery mode and mortality in very low birthweight singleton vertex-presenting infants. *BJOG* 2004;111:1365–71.
40. Herbst A, Kallen K. Influence of mode of delivery on neonatal mortality in the second twin, at and before term. *BJOG* 2008;115:1512–7.
41. Bethune M, Permezel M. The relationship between gestational age and the incidence of classical caesarean section. *ANZJOG* 1997;37:153–5.
42. Irvine DS, Haddad NG. Classical versus low-segment transverse incision for preterm caesarean section: maternal complications and outcome of subsequent pregnancies. *Br J Obstet Gynaecol* 1989;96:371–2.
43. Haque KN, Hayes AM, Ahmed Z, Wilde R, Fong CY. Caesarean or vaginal delivery for preterm very-low-birth weight (< or =1,250 g) infant: experience from a district general hospital in UK. *Arch Gynecol Obstet* 2008;277:207–12.
44. Knight M, Berg C, Brocklehurst P, Kramer M, Lewis G, Oats J, et al. Amniotic fluid embolism incidence, risk factors and outcomes: a review and recommendations. *BMC Pregnancy Childbirth* 2012;12:7.
45. Royal College of Obstetricians and Gynaecologists. *Umbilical Cord Prolapse. Green-top Guideline No. 50.* London;RCOG:2008.
46. Dufour P, Vinatier D, Puech F. The use of intravenous nitroglycerin for cervico-uterine relaxation: a review of the literature. *Arch Gynecol Obstet* 1997;261:1–7.
47. Royal College of Obstetricians and Gynaecologists. *Breech Presentation, Management. Green-top Guideline No. 20b.* London;RCOG:2006.
48. Robertson PA, Foran CM, Croughan-Minihane MS, Kilpatrick SJ. Head entrapment and neonatal outcome by mode of delivery in breech deliveries from 24 to 27 weeks gestation. *Am J Obstet Gynecol* 1995;173:1171–6.
49. Hutton EK, Hassan ES. Late vs early clamping of the umbilical cord in full-term neonates: systematic review and meta-analysis of controlled trials. *JAMA* 2007;297:1241–52.
50. Royal College of Obstetricians and Gynaecologists. *Clamping of the umbilical cord and placental transfusion. Scientific Impact Paper No. 14.* London;RCOG:2009.

51. Forsblad K, Kallen K, Marsal K, Hellstrom–Westas L. Short–term outcome predictors in infants born at 23–24 gestational weeks. *Acta Paediatrica* 2008;97:551–6.
52. Bodeau–Livinec F, Marlow N, Ancel PY, Kurinczuk JJ, Costeloe K, Kaminski M. Impact of intensive care practices on short–term and long–term outcomes for extremely preterm infants: comparison between the British Isles and France. *Pediatrics* 2008;122:1014–21.
53. Larroque B, Bréart G, Kaminski M, Dehan M, André M, Burguet A, et al. Survival of very preterm infants: Epipage, a population based cohort study. *Arch Dis Child Fetal Neonatal Ed* 2004;89:139–44.
54. Costeloe K, Hennessy E, Gibson AT, Marlow N, Wilkinson AR. The EPICure study: outcomes to discharge from hospital for infants born at the threshold of viability. *Pediatrics* 2000;106:659–71.
55. Costeloe K. EPICure Study Group. EPICure: facts and figures: why preterm labour should be treated. *BJOG* 2006;113(Suppl 3):10–2.
56. Nishida H, Sakuma I. Limit of viability in Japan: ethical consideration. *J Perinat Med* 2009;37:457–60.
57. Seri I, Evans J. Limits of viability: definition of the gray zone. *J Perinat Med* 2008;28(Suppl 1):4–8.
58. General Medical Council. *0–18 years: guidance for all doctors*. [http://www.gmc-uk.org/guidance/ethical_guidance/children_guidance_index.asp].

APPENDIX 1: EPICure 2 Cohort Data

Table 1. Overall outcome by different denominators at each completed week of gestation for EPICure 2 cohort born in England during 2006; disability classified as in Disability and Perinatal Care 1994. (Data from EPICure 2 reproduced with permission of the EPICure Investigators)

Gestational age (Completed weeks)	22	23	24	25	26
Population					
Alive at the onset of labour Δ	272	416	495	550	594
Live birth	152	339	443	521	580
Live birth with stabilisation attempted ∞	41	284	427	514	576
Neonatal care					
Admission for neonatal care	19	217	382	498	571
Deaths in Neonatal care	16	151	204	152	123
Deaths after discharge home	0	3	1	5	1
Survivors to 3 years of age	3	63	177	341	447
Disability					
Survivors with severe disability \S	1	17	37	57	45
Survivors with moderate disability \S	1	14	33	48	54
Survivors without disability \S	1	32	107	236	348
Survival					
From onset of labour	1%	15%	36%	62%	75%
Of live births with attempted stabilisation ∞	7%	22%	42%	66%	78%
Of admissions for neonatal care	16%	29%	46%	69%	78%
Survival without disability					
From onset of labour	0.4%	8%	22%	43%	59%
Of live births with attempted stabilisation ∞	2%	11%	25%	46%	60%
Of admissions for neonatal care	5%	15%	28%	47%	61%
Δ Includes all caesarean sections where the baby was alive when the delivery was initiated.					
∞ Live births for which stabilisation attempted					
\S Numbers imputed from whole dataset					

APPENDIX 2: Planning for Delivery

Early ultrasound scans should be used to best estimate gestational age. Information on estimated fetal weight, while subject to significant inaccuracies in a situation where a few grams may make a difference in the decision to intervene, will help make the best quality decision. Consideration of antenatal fetal Doppler results (umbilical artery, middle cerebral artery, ductus venosus), fetal gender, and the possibility of, infection or congenital anomalies should be used to counsel the parents with regard to outcome, with subsequent delivery planned as informed by these discussions.

Where time allows, the neonatologist should to begin with, present national survival and disability figures and supplement these with local figures and local guidelines/practices at these gestations, while also explaining the difficulty of predicting outcome for the individual pregnancy. If such figures suggest in utero transfer, availability of mother's bed and neonatal cot need to be discussed.

When the decision is made with the parents not to actively resuscitate the baby because there is little chance of survival and it is considered not to be in the baby's interests, palliative care should be planned before birth, in discussion with the neonatal team. Parents should be reassured that all aspects of comfort care and avoidance of suffering for the baby are employed. There should be clear agreement by all in the team on the way forward and every care should be employed to exclude illogical management such as monitoring of a fetus when active resuscitation is not planned.

Discussions with parents, their wishes and the decisions made with the multidisciplinary team on resuscitation and palliative care should be carefully documented in the case notes. There should be a documented plan about when to review these decisions if birth does not ensue as anticipated, since advancing gestational age may change the decisions made for delivery and resuscitation.

Parents should be given the opportunity to visit the neonatal intensive care unit, if the mother's clinical condition allows, to familiarise themselves with care that an extreme preterm infant requires.

For women at risk of delivery at the threshold of viability, transfer of the mother to a perinatal centre with appropriate neonatal intensive care facilities is recommended for pregnancies from 23⁺⁰ weeks of gestation. The reason for transfer should be to optimise management and the aim may not necessarily be to do everything to achieve neonatal survival. A clear plan of what is expected by in utero transfer should be communicated to parents and carers. A pragmatic approach is to consider transfer to perinatal centres in women with symptoms of preterm labour with one or more of the following: cervical length ≤ 15 mm, positive fetal fibronectin (< 50 ng/ml), positive pHIGFBP-1, history of preterm delivery or preterm prelabour rupture of membranes.

Maternal and Fetal Antenatal Interventions

Although tocolysis at the threshold of viability does not appear to confer a short or long term benefit on neonatal outcome, it may be useful for those women who require transfer for neonatal care or time to complete a course of corticosteroids. As most babies delivering at 23 weeks of gestation are likely to receive active stabilisation at birth, antenatal steroids should be given after 22⁺⁶ weeks of gestation unless a policy decision has been taken not to offer active intervention after delivery.

Peripartum magnesium infusion is recommended once 24 weeks of gestation is reached. Before that, it would seem sensible to consider its use if a decision has been made for active intervention.

If the mother is a carrier of GBS, intrapartum intravenous Penicillin should be given.

Monitoring During Labour

If active obstetric intervention in the interests of the fetus is not planned, continuous fetal heart rate monitoring is not advised. In this case, intermittent fetal heart rate auscultation should be used to establish fetal viability during labour, at intervals to be decided on an individual basis. This will assist the neonatal team for the resuscitation.

Continuous fetal heart rate monitoring should be considered when there has been agreement following discussion with the parents, that emergency caesarean section will be performed for a pathological CTG.

Mode of Delivery

Obstetric management, in particular a decision for caesarean section, due to fetal indication must be individualised taking into account the wishes of the parents, and making it clear that a classical caesarean section may be required. It is unusual to deliver by caesarean section before 24 weeks of gestation. However each decision should be on a case-by-case basis on the understanding that if the pregnancy continues, the decision on mode of delivery will need to be reassessed, possibly even on a daily basis.

The surgical complications of Caesarean delivery to mother and baby at such extremes of gestation must be explicit, and even the rarity of hysterectomy and infertility should be mentioned but placed in context. When this information has been given, the couple's views must be added and a final decision on how to proceed is made. At 25⁺⁰ weeks of gestation, newborn survival should be given priority. Although clear evidence for the optimum mode of delivery is unavailable, in cases of spontaneous labour with a single and cephalic fetus, vaginal delivery should be attempted. However if continuous CTG monitoring reveals features of suspected acute fetal compromise/distress, a caesarean section should be performed without delay.

Caesarean delivery at an extreme preterm gestation can be complex and a senior obstetrician should be present. As there is a significant risk of cord prolapse during labour with transverse lie or footling breech presentation at extremely preterm gestations, emergency caesarean section should be discussed with the parents if the decision is taken to opt for active obstetric intervention.

Keeping the amniotic membranes intact may reduce the risk of trauma to the fetus during labour and delivery. If labour is induced, there is no requirement to rupture the membranes. Intravenous oxytocin can be used should labour not progress, without the need for amniotomy.

Ultrasound during labour can be useful to monitor fetal viability and descent of the presenting part through the vagina when the membranes are kept intact.

Episiotomy may be useful to widen the introitus and aid delivery of the presenting part in non-cephalic presentations.

In flexed or extended breech deliveries complications such as an entrapped fetal head may arise, therefore an attendant with suitable experience should be present at delivery.

The risks and benefits of delayed cord clamping should be considered prior to delivery and discussed with the parents and with the neonatal team who will manage neonatal resuscitation to derive a clear plan of management at birth.

Postnatal Care

A postnatal appointment should be offered with an obstetrician with suitable experience to review the circumstances surrounding labour and delivery, the results of investigations and to plan the next pregnancy.

This Scientific Impact Paper was produced on behalf of the Royal College of Obstetricians and Gynaecologists by:

**Dr A Soe MBBS FRCPCH MRCP DCH, Medway Maritime Hospital, Gillingham, Kent;
Dr ALM David MRCOG, London; Mr AD Roberts FRCOG, Burton–Upon–Trent and
Professor K Costeloe MB BCHir FRCP FRCPCH, Blizard Institute, Barts and The London
School of Medicine and Dentistry, London**

and peer-reviewed by:

Bliss for babies born too soon, too small, too sick; British Association of Perinatal Medicine (BAPM);
British Maternal and Fetal Medicine Society (BMFMS); Mr DI Fraser FRCOG, Norwich;
Professor N Marlow BA MBBS DM, University College London, London;
Professor DM Peebles FRCOG, London; RCOG Ethics Committee; RCOG Women's Network;
Royal College of Paediatrics and Child Health (RCPCH); Professor GCS Smith FRCOG, Cambridge
and Mr A Wishart, Producer and Presenter, BBC 2, London.

The Scientific Advisory Committee lead reviewers were:

Professor RA Anderson FRCOG, Edinburgh and Professor SM Nelson MRCOG, Glasgow.

The final version is the responsibility of the Scientific Advisory Committee of the RCOG.

The reviewing process will commence in 2016, unless otherwise indicated.