Preterm deliveries are increasing in absolute numbers and as a proportion of all births. According to NHS data for England in 2006, 2000 births—0.3% of all births—were extremely preterm (23-25+6 weeks’ gestation). Similar numbers are reported by other western European countries. Preterm births have increased by 20% over the past two decades in the United States, mainly because of the 42% increase in twin births. Advances in neonatal intensive care for babies born at the margins of viability have improved survival, but these infants are more likely to have long term morbidities and to use healthcare resources extensively in the first 2 years of life. Data from the Neonatal Research Network show that babies born before 26 weeks’ gestation spend at least 111 days in hospital during infancy and incur intensive care costs of more than £100 000 (€114 000; $160 000). An emotional and financial burden is often placed on families and community support systems. One or more family member may leave paid work to care for the baby, or skilled day care providers may help care for a child with serious ongoing medical conditions.

Disability is highest in extremely preterm infants, but the numbers of children with disability and the implications for public health and social care are greatest in children born moderately prematurely. Although extremely premature infants are cared for perinatally as inpatients, any clinician who deals with pregnant women could benefit from an awareness of advances in care and the evidence that underpins best practices to advise, refer, and support women who are at risk of or have had an extremely preterm delivery.

**Why are babies born extremely preterm?**
This may occur because of spontaneous preterm vaginal delivery, when planned delivery before 26 completed weeks is the safest option for delivering the baby alive (almost never carried out before 24 weeks), or when planned early delivery is necessary because of maternal illness. Complications that can cause spontaneous preterm delivery include rupture of membranes, chorioamnionitis, placental abruption, polyhydramnios, and multiple pregnancy. Reasons for an intended delivery include fetal distress, severe pre-eclampsia, acute or chronic maternal conditions such as renal disease, decompensation of congenital heart disease, or connective tissue disorders. Severe early onset fetal growth restriction at 24-26 weeks does not normally lead to intended delivery because the outcome of growth restricted premature babies less than 450 g is poor.

**Why has survival improved for these infants?**
The administration of maternal antenatal corticosteroids has become standard practice—a systematic review and large cohort study have shown that this is associated with increased survival in moderately preterm and extremely preterm infants. Improvements within organised neonatal and perinatal networks for pre-delivery (in utero) transfer enable the fetus to be delivered at a specialist centre with appropriate resources and
Potential antenatal interventions to reduce prematurity

- Legislation to reduce the number of embryos transferred into the uterus during in vitro fertilisation (already present in the UK)
- Measurement of fetal fibronectin and assessment of cervical length by transvaginal ultrasound may help define which women admitted to the delivery unit require transfer to a specialist unit. Their role in this context has not yet been defined
- Cervical cerclage or progesterone prophylaxis may benefit women at risk of preterm delivery

Information about numbers of extremely preterm infants surviving to hospital discharge in a particular neonatal database should be qualified, because data can be reported as the proportion of all births, all live births, or all babies admitted to neonatal intensive care that survive. When using survival statistics in counselling or decision making, clinicians should consider which cohort is most applicable to the clinical situation. For example, it would be most relevant to consider the proportion of all neonates who survive when engaging in a prenatal discussion on the delivery unit with parents.

What is the long term outcome for these infants?

Many infants have serious disabilities that affect quality of life. Magnetic resonance imaging of the central nervous system shows that up to 80% of premature infants have diffuse white matter injury. Outcome studies use varied definitions of impairment, including any abnormal neurological finding, changes in coordination, cerebral palsy, blindness, deafness, or cognitive deficits. The data all reflect practice at least five and, in many cases, more than 10 years ago. The further into childhood the neurological evaluation is performed, the more predictive it will be of adult function. Statistics on neurodevelopmental impairment can be difficult to put into context; for example, a Finnish multicentre trial found that 43% of children had any neurological abnormality, but only 14% had function limiting cerebral palsy at 2 years. If profound impairment includes an IQ more than two standard deviations below the mean, uncorrectable blindness or deafness, or cerebral palsy that precludes ambulation, then about a third of those born at 23-24+6 weeks, and a half of those born at 25-26+6 weeks, survive without profound impairment.

Two recent national cohort studies from the UK and France provide data on survival and long term neurodevelopmental outcome. Epicure is the first UK national study of long term outcome for babies born at 23 weeks’ gestation or less. Disability was common, and follow-up at 8 years has given insight into school performance. The children who were extremely preterm scored an average of 24 points lower on cognitive testing than their age matched school peers (IQ 82 v 106). The Epipage study group studied a similar cohort of preterm infants and reported that the incidence of cognitive and neurological impairment at 5 years increased with decreasing gestational age. Preterm infants are at risk of other long term morbidities; very low birthweight babies (<1500 g) are more likely to develop insulin resistance, glucose intolerance, and hypertension in early adult life. Respiratory prob-

What is the chance of survival for these infants?

The lowest gestation at which survival is possible is currently 22 weeks. However, it is rare for a baby born this early to survive without serious morbidity in the neonatal period and long term disability.

Survival data are available from the United Kingdom, France, northern Europe, and the US for extremely preterm births from the mid-1990s to 2003 (table). Most neonates born at 22 weeks’ gestation were not resuscitated; survival varied from 0% to 5%. Survival increased greatly with each successive week of gestation: at 23 weeks’ gestation, 11-43% survived until discharge from hospital; this improved to 26-61% at 24 weeks’ gestation and 44–77% at 25 weeks.

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NICHD = National Institute of Child Health and Human Development.
A clinician's perspective

I began bleeding at home on the evening that I gave birth to Elijah. I was just starting to enjoy the pregnancy and then the baby was already out. I hadn’t heard of anybody giving birth at less than seven months, but Elijah was born at 23 weeks and 6 days’ gestation, weighing just 680 g. I was in shock when the doctors tried to discuss whether to resuscitate my baby, but I think the right decision was made. I come in each day happy to see him. If we get good news I go home happy. If the news is bad, such as when he recently needed surgery for patent ductus arteriosus ligation, I go home upset. During the pregnancy, I had dreams of how wonderful it would be to experience the birth of my baby and to take him home with me. Now, I feel I have to let go of those dreams and start another chapter of my life. It took 10 days before my husband began taking pictures of Elijah. We were both so afraid to become attached. Elijah is now 30 days old and we take a photo every day.

Karen Faminial (about her son Elijah), Bottisham, Cambridge

pah problems such as asthma can persist throughout childhood, and growth usually remains below average. Immediate neonatal morbidities such as chronic lung disease, necrotising enterocolitis, patent ductus arteriosus, retinopathy of prematurity, and late onset sepsis have not changed substantially in incidence.

Obstetric decision making when extreme preterm delivery is likely

Difficult management decisions around the time of delivery need a multidisciplinary approach involving the parents, midwives, obstetric staff, and paediatric staff. This must include a plan for delivery (mode of delivery and fetal monitoring) and for managing the baby afterwards, either by active intervention or palliative care. An accurate gestational age, ideally from a 10-14 week ultrasound, should be ascertained. A recent scan describing the estimated fetal weight, presentation, amniotic fluid, and—in fetal growth restriction—Doppler arterial and venous blood flow indices is invaluable for tailoring management to individual circumstances. Corticosteroids should be given to the mother if delivery is expected within 48 hours. Tocolytics are sometimes given to delay early spontaneous preterm labour—to allow time for transfer to a specialist neonatal care unit or for steroids to take effect—although no benefit on perinatal mortality has been shown.

Evidence on which to base a decision on vaginal delivery or caesarean section at 24-26 weeks is scant. No adequate randomised studies exist because of recruitment difficulties. Some trials have indicated that caesarean section confers a survival advantage, whereas others have found no difference. If spontaneous vaginal delivery is anticipated, the indications for an operative delivery should be discussed with the parents. If the parents do not want operative intervention, the fetal heart rate should probably not be monitored. When delivery is planned, a caesarean section is usually performed rather than induction of labour so that the baby is born under optimal condition. In tertiary obstetric practice, operative intervention may be considered after 25+0 weeks’ gestation. Before 26 weeks, however, a classic caesarean is often performed, in which a vertical incision is made in the uterus because the lower uterine segment is poorly developed. This increases the risk of uterine rupture in a subsequent pregnancy and mandates future delivery by caesarean.

What guidance can be given about active resuscitation versus palliative care?

The decision not to begin intensive care for an extremely preterm infant is an important and difficult judgment. Staff must tell the parents if a baby is unlikely to survive or will have a high risk of severe disability and discuss the purpose of resuscitation with them. The Nuffield Council on Bioethics and the British Association of Perinatal Medicine have issued recent resuscitation guidelines. Resuscitation is not recommended at 22 weeks’ gestation, whereas 23-24 weeks is a “grey area” in which the decision relies heavily on parental wishes and the clinical condition of the baby. Doctors should remember that parents are more likely than professionals to favour intervention.

What other factors influence survival?

Factors other than gestational age at birth influence survival. The US Neonatal Research Network study published in 2008 confirmed the findings from large international databases. A birth weight more than 100 g above the average for gestation, female sex, and adequate administration of antenatal steroids all improved the chances of survival. Delivery by caesarean was also associated with increased survival, although this may be influenced by surgery being performed in more favourable circumstances or an association between chorioamnionitis and vaginal birth. Multiple birth and birth outside a specialist centre reduced survival, but race and ethnicity did not.

Ongoing support for families

The decision of whether to resuscitate, the effect of long term morbidities, and the loss of a baby can place serious psychological pressures on parents. The average length of hospital stay is 111 days at
25 weeks’ gestation, and this rises to 222 days at 22 weeks’ gestation. Parents often rely on neonatal nurses to help them cope with their baby’s illness and establish their role as caregivers. Parent support groups are a useful resource for both parents and staff. Developmental care programmes help support parents during hospital stay and after discharge. Irrespective of the outcome, it is usual practice to provide follow-up obstetric debriefing and discussion of risks for future pregnancies. If the child has died, bereavement support can be offered both in hospital and in community settings.

Ongoing community and paediatric support must be available for these babies as they grow, to identify developmental delays and to intervene when, for example, learning difficulties and speech problems occur. It should not be forgotten, however, that many extremely preterm babies who survive the neonatal period will live healthy and fulfilling lives.

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Patient consent obtained.


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ADDITIONAL EDUCATIONAL RESOURCES

Information resources for health professionals

British Association of Perinatal Medicine (www.bapm.org.uk)—Information on neonatal networks and the management of in utero transfers

Nuffield Council on Bioethics (www.nuffieldbioethics.org/go/ourwork/neonatal/introduction)—Considers the ethical problems raised by critical care decisions in fetal and neonatal medicine

Information resources for parents

BLISS (www.bliss.org.uk)—Special care baby charity that provides free information and advice to families

SANDS (www.uk-sands.org)—Charity that supports parents whose baby has died during pregnancy or after birth