

Survival of extremely premature babies in a geographically defined population: prospective cohort study of 1994-9 compared with 2000-5

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ABSTRACT

Objective To assess changes in survival for infants born before 26 completed weeks of gestation.

Design Prospective cohort study in a geographically defined population.

Setting Former Trent health region of the United Kingdom.

Subjects All infants born at 22+0 to 25+6 weeks' gestation to mothers living in the region. Terminations were excluded but all other births of babies alive at the onset of labour or the delivery process were included.

Main outcome measures Outcome for all infants was categorised as stillbirth, death without admission to neonatal intensive care, death before discharge from neonatal intensive care, and survival to discharge home in two time periods: 1994-9 and 2000-5 inclusive.

Results The proportion of infants dying in delivery rooms was similar in the two periods, but a significant improvement was seen in the number of infants surviving to discharge ($P<0.001$). Of 497 infants admitted to neonatal intensive care in 2000-5, 236 (47%) survived to discharge compared with 174/490 (36%) in 1994. These changes were attributable to substantial improvements in the survival of infants born at 24 and 25 weeks. During the 12 years of the study none of the 150 infants born at 22 weeks' gestation survived. Of the infants born at 23 weeks who were admitted to intensive care, there was no significant improvement in survival to discharge in 2000-5 (12/65 (18%) in 2000-5 v 15/81 (19%) in 1994-9).

Conclusions Survival of infants born at 24 and 25 weeks of gestation has significantly increased. Although over half the cohort of infants born at 23 weeks was admitted to neonatal intensive care, there was no improvement in survival at this gestation. Care for infants born at 22 weeks remained unsuccessful.

INTRODUCTION

Current UK legislation limits abortion to before 24 weeks' gestation unless there are specific medical issues. It has been suggested that because of improvements in medical care for such babies this limit should be lowered. During discussions in a House of Commons select committee to review the legislation it was recognised that published peer reviewed UK evidence is lacking to answer the question of whether the survival of infants born at 23 or 24 weeks has

improved in recent years. We compared the survival of infants in a geographically defined population born before 26 weeks' gestation in 1994-9 and 2000-5.

METHODS

Participants

We included in the study infants alive at the onset of labour, born between 1 January 1994 and 31 December 2005 and before 26 completed weeks' gestation, and born to a mother whose normal home address was within the former Trent health region. The Trent region has a population of about 4.6 million, with about 55 000 births a year. Sixteen hospitals within the region provide maternity and neonatal services.

Outcome measures

The outcome measures were stillbirth or miscarriage, death without admission to neonatal intensive care, death before discharge from neonatal intensive care and survival to discharge home.

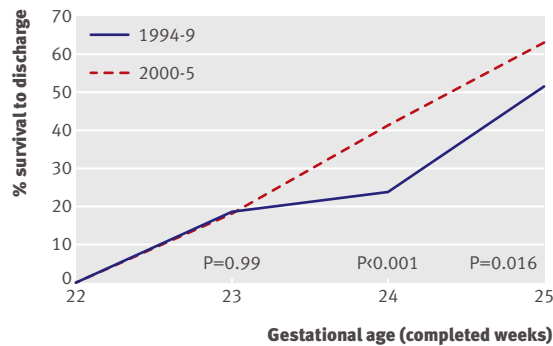
Data collection

A register of all babies born at or before 32 weeks or requiring intensive care has existed in Trent since February 1990. Neonatal nurses prospectively collect data during regular visits to neonatal units. Gestation of infants is allocated by using the following hierarchy: mother certain of her dates (most reliable); early dating scan; late dating scan; postnatal examination (least reliable). Systems are also in place to obtain data about babies of Trent origin cared for outside the regional boundaries.¹

We determined the number of miscarriages or stillbirths and deaths of infants without admission to a neonatal unit from the national confidential inquiry. This collates data from various sources about all infants delivered after 22 weeks' gestation either born dead or who died in the first year of life.^{1,2}

Statistical analysis

We compared two periods of six years: 1994-9 and 2000-5 inclusive. We assessed the significance of differences in outcomes between the two reported time periods and determined birth rates with the overall regional births data from the Office for National Statistics.



Percentage survival to discharge by gestational age for infants admitted to neonatal intensive care, 1994-9 compared with 2000-5

RESULTS

Comparison of time periods

Total births for the two periods were 339 774 in 1994-9 and 317 473 in 2000-5. During the two periods of the study similar numbers of infants in the relevant gestation groups were either born dead or died in delivery rooms, suggesting no major change in attitude to care during labour or assessment after birth of these infants. Of the infants born at 22 and 23 weeks, 58% (133/229) and 63% (126/200) died in the delivery room in each of the time periods, respectively, while slightly fewer (13% (59/453) *v* 10% (46/469) of the infants born at 24 and 25 weeks did so. See [bmj.com](#).

There was a marked improvement between the two time periods in the survival to discharge of the infants born at 24 and 25 weeks who were admitted to intensive care (figure). This amounted to an improvement from 24% to 41% ($P<0.001$) in the 24 week group and from 52% to 63% ($P=0.016$) in the 25 week group. These improvements were not seen in those born at 22 and 23 weeks. In both time periods none of the infants born at 22 weeks and admitted to neonatal intensive-care survived to discharge. The rate of survival to discharge after admission also changed little for infants born at 23 weeks' gestation, being 18.52% in 1994-9 and 18.46% in 2000-5.

Use of resources

The total number of days spent on the neonatal unit rose during the second period in relation to births at each week of gestation except for babies admitted at 22 weeks. It was only in this group that there seemed to have been a move to less aggressive care.

DISCUSSION

This analysis of data from the Trent region of the UK showed no improvement in the survival of babies admitted to neonatal intensive care born before 24 weeks' gestation. In those born at 24 and 25 weeks, however, there was a markedly different pattern of improving survival. This suggests a significant improvement in the care of these slightly more mature infants.

Our findings cannot be explained by a change in practice as similar numbers died in the delivery room in both time periods (1994-9 and 2000-5). We have no

mechanism for differentiating those deaths that occurred because aggressive resuscitation failed from those where such resuscitation was considered inappropriate. Despite a slight fall (from 55% to 50%) in the proportion of infants who were admitted to a neonatal unit at 23 weeks' gestation, our results indicate no change in the attitude to those admitted. In 1994-9, 78/81 infants (96%) received intensive care compared with 62/65 infants in 2000-5 (95%) ($P=0.78$). The remaining infants received palliative care alone.

When clinicians consider the appropriateness of intensive care for extremely premature infants they often use the survival figures and developmental outcomes of the EPICure study.³ This study was a prospective cohort study of all infants born at 20-25 completed weeks' gestation in the UK and Ireland during a 10 month period beginning in March 1995. It has recently been repeated.

Our survival figures for the whole period 1994-2005 are similar to those reported from 1995 by the EPICure group.³ In the EPICure study, deaths in the delivery room accounted for 84%, 46%, 22%, and 16% of infants born alive at 22, 23, 24, and 25 weeks' gestation, respectively. The corresponding figures in our study were 84%, 48%, 15%, and 9%. Similarly, survival to discharge occurred in 9%, 20%, 34%, and 52% of the EPICure infants admitted to a neonatal intensive care unit at 22, 23, 24, and 25 weeks' gestation, respectively, with our corresponding figures being 0%, 18%, 34%, and 57%. Follow-up data from the EPICure cohort have indicated high rates of long term morbidity among children born at 23 and 24 weeks' gestation.^{4,5}

Trent is reasonably representative of the UK as a whole. It is therefore unlikely that our data are substantially at variance with outcomes of neonatal intensive care across the UK. Population based studies from northern Europe have reported similar rates of survival. In Scandinavia rates are generally a little higher, with the best of these reporting 40% survival at 23 weeks for babies admitted to intensive care.

The use of resources associated with the care provided to babies in our study markedly increased between the two time periods. This trend has major implications for the neonatal service as a whole.

Strengths of study

We used up to date information with robust methods of data collection. Data verification procedures maximised the quality and completeness of the data. Using data from the entire region increases statistical precision and removes some of the potential for bias in the results of an observational study.⁶ We also used the confidential inquiry database of stillbirths and deaths in the delivery room to ensure we knew and appropriately classified the outcome of all infants alive at the onset of labour or delivery.

The approach to estimation of expected date of delivery and gestation changed over the period of the study, with most current pregnancies undergoing a dating scan compared with perhaps 50% at the start of the study period. This could have introduced systematic bias which we avoided by having just eight trained

WHAT IS ALREADY KNOWN ON THIS TOPIC

Survival rates in infants born before 26 weeks' gestation are relatively low

Recent reports from individual centres of improved survival of extremely premature babies are hard to interpret because of inclusion bias and variation in case mix

WHAT THIS STUDY ADDS

By looking at changes in survival over time in a whole population this study provides data free of inclusion bias and case mix effects

Survival rates in infants born at 24 and 25 weeks' gestation have clearly improved in the past 12 years

Survival rates in those born at 23 weeks' gestation have not changed, and intensive care for babies born at 22 weeks remains unsuccessful

and experienced nurses who used the same algorithm throughout collection of data.

Weaknesses

There was a relatively small number of babies born at 22 and 23 weeks' gestation. While this might be why we could not show improving survival in the smallest babies, the similarity of the survival rates at 22 and 23 weeks is compelling. Application of a retrospective calculation of sample size shows that the cohort was large enough to detect a difference of 13% in the survival rates of the infants born at 23 weeks in the two periods.

Our findings concur with the view of Hack and Fanaroff, who suggested in 2000 that the limit of viability had been reached.⁷ Large improvements in the survival to discharge of admitted babies born at 24 and 25 weeks (to 41% and 63%, respectively) in the most recent time period suggests that a blanket policy of not resuscitating these infants is inappropriate. In the

UK a widespread consultation has suggested guidelines for the approach to individual infants based on gestational age.⁸

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Competing interests: None declared.

Ethical approval: Local research ethics committee approval was obtained for each of the centres at the beginning of the Trent Neonatal Survey. In 2004 approval was obtained from the Trent multicentre research ethics committee. The neonatal survey obtained section 60 approval under the Health and Social Care Act for its programmes in 2002. The Patient Information Advisory Group also gave approval for collection of data without consent.

Provenance and peer review: Not commissioned; externally peer reviewed.

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Nortriptyline plus nicotine replacement versus placebo plus nicotine replacement for smoking cessation: pragmatic randomised controlled trial

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ABSTRACT

Objective To test the efficacy of nortriptyline plus nicotine replacement therapy compared with placebo plus nicotine replacement therapy for smoking cessation.

Design Pragmatic randomised controlled trial.

Setting National Health Service stop smoking service clinics.

Participants 901 people trying to stop smoking.

Interventions Participants chose their nicotine replacement product, including combinations of nicotine replacement therapy, and received behavioural support. Nortriptyline was started one to two weeks before quit day, with the dose increased from 25 mg to 75 mg daily for eight weeks and reduced if not tolerated.

Main outcome measures Primary outcome was prolonged confirmed abstinence at six months. Secondary outcomes were prolonged abstinence at 12 months, drug use, severity of side effects, nicotine withdrawal symptoms, and urges to smoke.

Results 72 of 445 (16%) people using nortriptyline and 55 of 456 (12%) using placebo achieved prolonged abstinence at six months (relative risk 1.34, 95% confidence interval 0.97 to 1.86). At 12 months the corresponding values were 49 (11%) for nortriptyline and 40 (9%) for placebo (1.26, 0.84 to 1.87). 337 (79%) people in the nortriptyline arm and 325 (75%) in the placebo arm were taking combination treatment on quit day, median 75 mg per day in both groups. More people in the nortriptyline arm than in the placebo arm took lower