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# Temporal trends of in-utero and early postnatal transfer of extremely preterm infants between 2011-2016: A UK population study

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**Objective**

Early postnatal transfer (PNT) of extremely preterm infants is associated with adverse outcomes compared to in-utero transfer (IUT). We aimed to explore recent national trends of IUT and early PNT.

**Design**

Observational cohort study using the National Neonatal Research Database.

**Setting**

Neonatal units in England, Scotland and Wales.

**Patients**

Extremely preterm infants $23^{+0}$ to $27^{+6}$ weeks gestation admitted for neonatal care from 2011-2016.

**Main Outcome**

The incidence of IUT or PNT within 72 hours of life. Secondary outcomes included mortality, hospital transfer level between centres and temporal changes across two equal epochs, 2011-2013 (Ep1) and 2014-2016 (Ep2).

**Results**

14,719 infants were included (Ep1=7,363 and Ep2=7,256), 4,005 (27%) underwent IUT and 3,042 (20.7%) PNT. IUTs decreased significantly between epochs from 28.3%

(Ep1=2,089) to 26.0% (Ep2=1,916) (OR 0.90, 95%CI 0.84-0.97, p<0.01). Conversely, PNTs increased from 19.8% (Ep1=1,416) to 21.5% (Ep2=1,581) (OR 1.11, 95%CI 1.02-1.20, p=0.01). PNTs between intensive care centres increased from 8.1% (Ep1=119) to 10.2% (Ep2=161, p=0.05). Mortality decreased from 21.6% (Ep1=1,592) to 19.3% (Ep2=1,421) (OR 0.90, 95%CI 0.83-0.97, p=0.01). Survival to 90 days of age was significantly lower in infants undergoing PNT compared to IUT (Hazard ratio 1.31, 1.18-1.46), with the greatest differences observed in infants <25 weeks gestational age.

**Conclusions**

In the UK, IUT of extremely preterm infants has significantly decreased over the study period with a parallel increase in early PNT. Strategies to reverse these trends, improve IUT pathways and optimise antenatal steroid use could significantly improve survival and reduce brain injury for these high-risk infants.

## INTRODUCTION

Centralised neonatal intensive care improves the outcomes of high-risk infants. [1 2] In 2003, UK neonatal services were re-organised into managed clinical networks to provide centralised intensive care. [3] National guidance was developed advising extremely preterm infants, i.e. <28 weeks gestational age (GA), should be delivered and cared for in intensive care centres (level 3 neonatal intensive care unit (NICU)) to reduce mortality and severe morbidity. [4 5] These changes have led to a significant reduction in mortality, although this has not yielded improvements in survival without neurodisability. [1 6 7]

Extremely preterm infants born in centres with a co-located NICU i.e., they are either booked and born there or are booked elsewhere and undergo in-utero transfer (IUT), have reduced mortality and morbidity compared to those undergoing early postnatal transfer (PNT) into an NICU. [6 8-10] This has resulted in the adoption of IUT as the optimal standard of care for extremely preterm infants where feasible. [11] However, maternal clinical instability, precipitous preterm delivery and barriers to IUT [12] mean PNT can be unavoidable. In addition to the increased mortality, PNT of extremely preterm infants is associated with other adverse outcomes including an increased risk of severe IVH, [13-16] also associated with increased mortality and a worse neurodevelopmental outcome. [17] This can have a long-term impact on the quality of life of the child and their family, as well as a significant cost to society. [15 18]

The cause of excess severe brain injury in extremely preterm infants undergoing early PNT remains unclear but is likely to be multifactorial. The perinatal period is a high-risk

time with most IVH's occurring in the first few days of life, [19 20] coincident with when they are most likely to undergo PNT. [21] It has been proposed that the transport process itself may contribute to the increased morbidity observed in these infants due to the exposure to an adverse environment, including excessive noise, vibration and temperature instability. [22-26] Appropriate IUT where possible could improve survival without significant disability.

Improving neonatal outcomes is a key driver for many health services including in the UK where the government aims to reduce mortality and halve brain injury in newborns by 2025. [5] To achieve this, multiple areas and strategies will need to be explored, including the care of extremely preterm infants at high risk of death or significant brain injury. [27-29] There are a lack of national data on IUT and PNT in the UK, [30] understanding these patterns could provide invaluable data for service optimisation and potential strategies to improve IUT. The primary aim of this study was to establish the incidence of infants <28 weeks GA who undergo either IUT or PNT. The secondary aims were to compare mortality rates, evaluate changes over time and the patterns of inter-hospital transfers.

## METHODS

### Study Design and participants

This is an observational cohort study of prospectively routinely recorded clinical data obtained from the National Neonatal Research Database (NNRD). The NNRD is a validated database containing data on demographic details, antenatal care and

postnatal outcomes on all neonatal admissions in the UK. [31] [32] Data were analysed on all extremely preterm infants born from $23^{+0}$ to $27^{+6}$ weeks' gestation that were admitted to neonatal units in England, Scotland and Wales between 2011 and 2016. Infants were identified as undergoing PNT within 72 hours of life from the data fields "Discharge destination", "Admission time" and "Discharge time". IUT infants were identified if their booking hospital code did not match the place of birth hospital code. Hospital care level was determined from the "Place of birth NHS code" data field. Hospital levels in the UK are level 1 (special care baby units, low dependency care), level 2 (local neonatal units, mainly high dependency care) and level 3 (neonatal intensive care units, tertiary units caring for sickest babies). Infants born at home, with missing hospital codes (therefore IUT status cannot be determined), missing hospital admission episodes and those with erroneous data (implausible birth weight) were excluded.

**Outcomes**

The primary aim was to establish the incidence of IUT and PNT within 72 hours of age for extremely preterm infants. The secondary aims were mortality, hospital transfer levels between referring and receiving centres and temporal changes across two equal epochs, 2011-2013 (Ep1) and 2014-2016 (Ep2).

**Statistical Analysis**

The population was separated into two equal epochs (Ep1 from 2011-2013 and Ep2 from 2014-2016) to evaluate temporal changes. Mann-Whitney U test was used for group analysis to compare changes between epochs. Odds ratio (OR) and confidence

intervals (CI) were calculated with significance set as $p<0.05$. Kaplan-Meier method was used to evaluate survival of infants over time for infants who were either IUT or early PNT. Hazard ratios were calculated using log-rank test to compare curves. Statistical analysis was performed using Stata SE (StataCorp, Version 15) and GraphPad Prism (Version 9).

## RESULTS

During the study period, 14 719 extremely preterm infants were admitted to neonatal units. Of these 7 363 were in Ep1 and 7 356 in Ep2 (Supplementary Figure 1). A total of 4005 (27%) infants underwent IUT with a significant decrease in numbers between epochs from 28.3% to 26% (Ep1=2089 and Ep2=1916; OR 0.90, 95% CI 0.84-0.97, $p<0.01$). Conversely, 3042 (20.7%) infants had early PNT, a significant increase between epochs from 19.8% to 21.5% (Ep1=1461 and Ep2=1581; OR 1.11, 95% CI 1.02-1.20, $p=0.01$). The percentage total of all IUT and PNTs by GA between the two epochs are shown in Figure 1 and Supplementary Table 1. Maternal and neonatal characteristics are shown in Supplementary Table 2.

Overall, Level 2 to Level 3 PNTs were most prevalent accounting for 63.3% (n=1924), an increase between epochs of 13.3% (Table 1). The early PNT of infants between Level 3 NICUs has seen the greatest proportional increase of 35% from Ep1 to Ep2. There were no differences in median gestational age (Ep1 26 weeks (IQR 25-27) and Ep2 26 weeks (IQR 25-27), $p=0.30$) or birthweight (Ep1 890g (IQR 750-1000), Ep2 845g (715-956), $p=0.18$) between level 3 to level 3 transferred infants over time (Supplementary Table 3).

Overall, there was no difference in the proportion of infants who received a full course of antenatal steroids between epochs, irrespective of transportation subgroup (64.6% vs 65.3%, p=0.36). However, for infants who underwent PNT there was a significant increase between Ep1 from 40% (n=578) and Ep2 at 43.3% (n=685) (p<0.01, Table 2).

## Mortality

### *Mortality by place of birth*

A total of 3013 (20.5%) infants died during the study period, with a significant decrease between Ep1 (n=1592, 21.6%) and Ep2 (n=1421, 19.3%) (OR 0.90, 95% CI 0.83-0.97, P=0.01). Infants born at 23 and 24 weeks GA showed the greatest benefit from birth in a level 3 intensive care centre with lower mortality compared to birth in either a level 1 or 2 centre (Table 3).

Following early PNT, 686 (22.8%) infants died. The proportion of these infants who died following PNT from a level 3 to another level 3 centre has significantly increased between epochs (Ep1 5.6% (n=20) vs Ep2 9.7% (n=31); OR 1.83 (1.02-3.29), p=0.04 (Supplementary Table 4). There was no significant difference in demographic characteristics or antenatal steroid course between epochs for these infants (Supplementary Table 5).

### *Survival by transfer status*

Overall, infants who underwent PNT were significantly less likely to survive to day 90 of life compared to infants who had an IUT (Hazard ratio 1.31 (1.18 – 1.46)). Infants born

at 23- and 24-weeks GA showed the greatest benefit from IUT with significantly higher 90-day survival compared to early PNT (Figure 2).

## DISCUSSION

This study aimed to describe the current national trends of IUT and PNT of extremely preterm infants. We found the incidence of IUT has significantly decreased over time and this was associated with an increase in early PNT within 72 hours of life. Almost 45% of the highest risk infants (those born at 23- and 24-weeks GA) who required transfer into a tertiary centre for delivery, underwent early PNT rather than IUT. Mortality in the PNT group was significantly higher and this appears to be greatest in infants born at 23- and 24-weeks' gestation.

This UK population study is the largest to date to quantify the current trends in the centralised approach to the management of extremely preterm infants. The recent Saving Babies' Lives Version Two care bundle highlights the importance of optimising the place of birth for preterm infants to reduce both morbidity and mortality. [33] However, there are several barriers to undertaking IUT, such as the length of time required by staff with other roles to facilitate transfers, lack of available maternal and neonatal beds within the same hospital and concerns regarding imminent delivery. [12] Careful consideration is required to determine which women can be safely transferred using midwifery and obstetric expertise, as well as better predictors of preterm delivery. [34 35] The majority of women in threatened preterm labour do not deliver within 24 hours of presentation [36-38] and infants rarely deliver during transportation. [34 36 39] This suggests

the window of opportunity for IUT may be greater than currently perceived and improving care pathways could help reverse the declining IUT rate.

The significant increase in early PNTs could reduce survival and expose a greater proportion of vulnerable infants to an increased risk of severe IVH. [13-15] The reduction in successful IUTs may be in part due to difficulties undertaking the IUT pathway, as unlike for neonatal transport provision, a co-ordinated centralised network service has yet to be developed. Additionally, lack of NICU cot capacity can further contribute to the need for PNT [40] and this may be reflected in the significant increase with NICU to NICU transfers over time.

Our results are consistent with previous studies that demonstrate improved survival with birth in a centre with an NICU and following IUT compared to early PNT. [6 9] This benefit was greatest for those at the extremes of viability. Recent UK guidance [41] advocates a change in practice towards more proactive management of infants at the lowest gestational ages. We were unable to account for factors such as the lower rates of antenatal steroid use observed in PNT infants, which are known to improve outcomes, although in previous studies accounting for this the higher risk remained.[13 14] Our study highlights the necessity of strategies to improve IUT pathways for these infants to improve outcomes along with timely antenatal steroids where the risk of preterm delivery is significant.

The gestational split on IUT and PNT suggests that an increasing number of infants at 23 weeks GA are undergoing IUT. However, the pattern appears reversed for all other gestations, a worrying trend considering this makes up the greatest proportion of infants <28 weeks. The increase in mortality for infants who underwent level 3 to level 3 transfers is concerning. Given these infants should receive similar standards of care at both centres and there was no difference in demographic background or antenatal steroid administration, this raises the concern regarding early PNT as a contributing factor although other causes, such as transfer for surgery, could also be important.

**Strengths**

A major strength of this study is the large number of infants included using prospectively collected data from all neonatal units in the UK. This enables evaluation of trends for the whole population at a national level and allows for variation in management across neonatal networks. Since data are prospectively entered on a daily basis, this allows accurate evaluation of timing of PNT and changes in outcomes over time.

**Limitations**

The main limitations of our study include the lack of ability to determine the exact reason for PNT over potential IUT, as this is not recorded within the database. However, we found a significant increase in the number of early PNT infants who received a full course of antenatal steroids, which would suggest these mothers were inpatients at the referring centre for at least a period of 24 hours prior to delivery, during which an IUT may have been feasible. As data is not collected on reasons why an IUT

did not occur, we cannot speculate further on this but prospective recording of this should be considered to identify and learn from any missed opportunities. Furthermore, we did not obtain data on the cause of death, as this was a descriptive study on patterns of transfer, which could help understand the indications for transfer.

A further limitation to our study is the assumption that infants born in a different centre to where they were booked were IUTs, as the NNRD does not directly record IUT. We acknowledge the overall number is likely to be less due to transfer of care to a level 3 centre for clinical reasons during the pregnancy or the mother could have been out of region (e.g. on holiday) prior to delivery. However, the number of these infants is likely to remain unchanged over time, therefore the overall trend is unlikely to change. We also acknowledge that we were unable to account for the number of mother's who were IUT but did not subsequently deliver and infants who were IUT and died in the delivery room as these data are not recorded within the NNRD.

In addition, the NNRD only records infants who survive to neonatal unit admission. Infants at the extremes of gestational age who do not undergo IUT may be less likely to be offered active care at non-intensive care centres or die in the delivery room. We were unable to account for these deaths in our study, whereas those infants at the lowest gestational ages who underwent IUT to a centre with an NICU are more likely to have active management, successful stabilisation following birth and admission to the NICU. This is reflected by the reduced initial survival of infants who underwent IUT compared to early PNT within the first 24 hours of life in our study.

Although the NNRD is a validated database and uses strict measures to ensure erroneous data is minimised, it relies on clinicians to input data. Therefore, we acknowledge some data entry error may remain.

## Conclusion

Outcomes for extremely preterm infants are better following IUT rather than PNT. During this six-year study period in the UK, the incidence of IUT has decreased over time with an increase in early PNTs, especially between intensive care centres. Mortality is greater in extremely preterm infants who undergo early PNT and there is increasing evidence the adverse transport environment is associated with a higher risk of severe IVH. Currently, in the UK, there is a national drive to increase the number of extremely preterm infants born in a centre with an NICU, a focus on better preterm birth recognition, staff training, streamlined IUT pathways and shared multi-disciplinary learning. This study provides baseline data to measure the impact of this programme going forward. Further evaluation of the potential benefits of a centralised referral system alongside up to date maternity bed and neonatal cot status to facilitate the co-ordination of this care pathway is required. These interventions could reduce unnecessary early PNTs and the associated risks to improve survival and long-term neurodevelopmental outcomes in high-risk infants.

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Electronic patient data recorded at participating neonatal units that collectively form the United Kingdom Neonatal Collaborative (UKNC) are transmitted to the Neonatal Data

Analysis Unit (NDAU) to form the National Neonatal Research Database (NNRD). DS had full access to all the data in the study and take full responsibility for the integrity of the data and accuracy of the data analysis.

We are grateful to all the families that agreed to the inclusion of their baby's data in the NNRD, the health professionals who recorded data and the NDAU team.

**Contributions**

LJS and DS made substantial contributions to the concept, planning, design of the study and acquisition of data. LJS and DS analysed and interpreted the data. All authors assisted in drafting and editing the manuscript. All authors approved the final version for publication.

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**Competing interests**

The authors have no conflict of interest. The sponsor had no involvement in the conduct of this study.

**Ethics approval**

Ethical approval was given by the London – City and East Research Ethics Committee (REC: 17/LO/1822).

## Data availability statement

All data were extracted and supplied by the NDAU and are available from the corresponding author on reasonable request and with permission of the study team and NDAU.

What is already known on this topic:

- Extremely preterm infants undergoing in-utero transfer (IUT), into level 3 intensive care centres, have reduced mortality and morbidity compared to infants undergoing postnatal transfer (PNT)
- Early PNT of extremely preterm infants is associated with an increased risk of severe intraventricular haemorrhage
- Improving perinatal and long-term neurodevelopmental outcomes is a key driver for many health services including in the UK

What this study adds:

- The rate of IUT of extremely preterm infants within the UK has decreased over time, with an associated increase in early PNT
- Early PNT of extremely preterm infants between level 3 neonatal intensive care centres has increased
- Infants undergoing IUT into intensive care centres have improved 90-day survival compared to those undergoing PNT, with the greatest difference in those <25 weeks' gestation

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**Table 1**. Referring and receiving neonatal unit levels for all postnatally transferred extremely preterm infants within 72 hours of age in the UK

| Unit level | | Epoch 1 n=1461 | Epoch 2 n=1581 | | |
|---|---|---|---|---|---|
| **Referring** | **Receiving** | **PNT infants n (%)** | **PNT infants n (%)** | **% change** | **p value** |
| L3 | L3 | 119 (8.1) | 161 (10.2) | + 35.3 | 0.05 |
| L2 | L3 | 902 (61.7) | 1022 (64.6) | +13.3 | 0.09 |
| L1 | L3 | 317 (21.7) | 279 (17.6) | -12.0 | <0.01 |
| L3 | L2 | 25 (1.7) | 31 (2.0) | +24.0 | 0.61 |
| L2 | L2 | 36 (2.5) | 32 (2.0) | -11.1 | 0.41 |
| L1 | L2 | 34 (2.3) | 22 (1.4) | -35.3 | 0.06 |
| MLU | L2 | 2 (0.1) | 0 (0) | n too small | - |
| MLU | L3 | 16 (1.1) | 14 (0.9) | n too small | - |
| Missing | Missing | 9 (0.6) | 19 (1.2) | - | - |

PNT, postnatal transport; L3, Level 3; L2, Level 2; Level 1; MLU, Midwife-led unit

**Table 2.** Comparison of antenatal steroid course between in-utero transferred (IUT) and postnatally transferred (PNT) extremely preterm infants between 2011 – 2016 (Data are n (%))

| | Epoch 1 (2011 – 2013) | | Epoch 2 (2014 – 2016) | |
|---|---|---|---|---|
| | **IUT n=2089** | **PNT n=1461** | **IUT n=1916** | **PNT n=1581** |
| **No steroids** | 87 (4.2) | 365 (25.0) | 57 (3.0) | 268 (17.0) |
| **Incomplete course** | 225 (10.8) | 465 (31.8) | 208 (10.9) | 550 (34.8) |
| **Complete course** | 1717 (82.2) | 578 (40.0) | 1597 (83.4) | 685 (43.3) |
| **Unknown/missing** | 56 (2.7) | 53 (3.6) | 54 (2.8) | 78 (4.9) |

**Table 3:** Comparison of births and deaths by level of birth centre for extremely preterm infants born in the UK from 2011-2016

| Gestation (weeks) | Level 1 (n=660) | Level 2 (n=3804) | Level 3 (n=10053) |
|---|---|---|---|
| **23** | | | |
| Births | 44 (6.6) | 236 (6.2) | 814 (8.1) |
| Deaths[a] | 30 (68.2)** | 156 (66.1)** | 400 (49.1) |
| **24** | | | |
| Births | 111 (16.8) | 548 (14.4) | 1781 (17.7) |
| Deaths[a] | 51 (45.9)** | 207 (37.8)* | 589 (33.1) |
| **25** | | | |
| Births | 122 (18.5) | 633 (16.6) | 2056 (20.4) |
| Deaths[a] | 28 (23.0) | 147 (23.2) | 416 (20.2) |
| **26** | | | |
| Births | 180 (27.3) | 879 (23.1) | 2589 (25.8) |
| Deaths[a] | 30 (16.7) | 122 (13.9) | 367 (14.2) |
| **27** | | | |
| Births | 203 (30.8) | 1508 (39.6) | 2813 (28.0) |
| Deaths[a] | 19 (9.4) | 131 (8.7) | 253 (9.0) |

Data are n (%) of births at each unit level
Comparison with level 3 centres, data analysed using chi squared test: *p<0.05, **P<0.01
[a] Data are n (%) of total birth per gestational week

## FIGURE LEGENDS

**Figure 1.** Comparison of in-utero transfer (IUT) and postnatal transfer (PNT) within 72 hours of life between Epoch 1 (2011-2013) and Epoch 2 (2014-2016) by gestational age (IUT n=4005, PNT n=3042)

**Figure 2.** Kaplan-Meier survival curves by gestational week for infants born at $23^{+0}$-$27^{+6}$ weeks who had in-utero transfer (IUT) or postnatal transfer (PNT) within the first 72 hours of life

**Supplementary Online Content**

# Temporal trends of in-utero and early postnatal transfer of extremely preterm infants between 2011-2016: A UK population study

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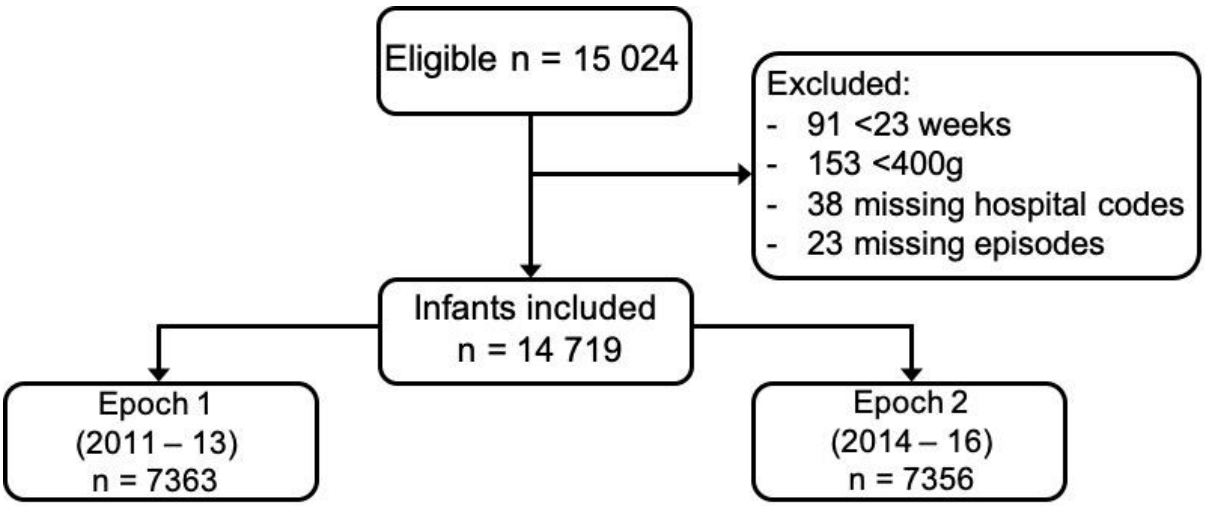
**Supplementary Figure 1.** Flowchart of study population demonstrating included/excluded for extremely preterm infants admitted to neonatal units in the UK




**Supplementary Table 1:** Incidence of in-utero and postnatal transfer for extremely preterm infants born between 2011 and 2016 in the UK

| | **Epoch 1 (n = 7363)** | | **Epoch 2 (n = 7356)** | |
|---|---|---|---|---|
| **Gestation (weeks)** | **IUT (n = 2089)** | **PNT (n = 1461)** | **IUT (n = 1916)** | **PNT (n = 1581)** |
| 23 – $23^{+6}$ | 124 (1.7) | 121 (1.6) | 137 (1.9) | 111 (1.5) |
| 24 – $24^{+6}$ | 391 (5.3) | 295 (4.0) | 370 (5.0) | 298 (4.1) |
| 25 – $25^{+6}$ | 470 (6.4) | 338 (4.6) | 407 (5.5) | 360 (4.9) |
| 26 – $26^{+6}$ | 560 (7.6) | 381 (5.2) | 500 (6.8) | 418 (5.7) |
| 27 – $27^{+6}$ | 544 (7.4) | 326 (4.4) | 502 (6.8) | 394 (5.4) |

IUT, In-utero transfer; PNT, Postnatal transfer

**Supplementary Table 2.** Comparison of demographic and clinical variables for extremely preterm infants who underwent in-utero transfer (IUT) or postnatal transfer (PNT) within 72 hours of life

| | Epoch 1 (n=7363) | | Epoch 2 (n=7356) | |
|---|---|---|---|---|
| **Variable** | **IUT (n=2089)** | **PNT (n=1461)** | **IUT (n=1916)** | **PNT (n=1581)** |
| Smoking/Alcohol/Drugs | 339 (16.2) | 321 (22.0) | 335 (17.4) | 331 (20.9) |
| Pre-eclampsia | 35 (1.7) | 15 (1.0) | 92 (4.8) | 34 (2.2) |
| Risk factors of early infection[a] | 521 (24.9) | 200 (13.7) | 574 (30.0) | 262 (16.6) |
| Gestational diabetes | 26 (1.2) | 11 (0.8) | 30 (1.6) | 24 (1.5) |
| Antepartum haemorrhage[b] | 283 (13.5) | 232 (15.9) | 260 (13.6) | 219 (13.9) |
| Gender (Male) | 1153 (55.2) | 851 (58.3) | 1015 (53.0) | 857 (54.2) |
| Birthweight (grams) | 795 (676 – 930) | 815 (690 – 945) | 790 (660 – 946) | 820 (700 – 960) |
| Gestation (weeks) | 26 (25 – 27) | 25 (24 – 26) | 26 (24 – 27) | 26 (24 – 26) |
| Mode of delivery | | | | |
| NVD | 1135 (54.3) | 875 (60.0) | 982 (51.3) | 925 (58.5) |
| Em CS no labour | 435 (20.8) | 245 (16.8) | 447 (23.3) | 278 (17.6) |
| Em CS in labour | 320 (15.3) | 252 (17.2) | 280 (14.6) | 276 (17.5) |
| El CS no labour | 63 (3.0) | 9 (0.6) | 63 (3.2) | 9 (0.6) |
| El CS in labour | 12 (0.6) | 6 (0.4) | 10 (0.5) | 7 (0.4) |
| Instrumental | 33 (1.6) | 19 (1.3) | 40 (2.1) | 15 (1.0) |
| Missing | 91 (4.3) | 55 (3.8) | 94 (4.9) | 71 (4.5) |
| Intraventricular haemorrhage[c] | 679 (32.5) | 576 (39.4) | 745 (38.8) | 721 (45.6) |

NVD, Normal vaginal delivery; Em CS, Emergency caesarean section; El CS, Elective caesarean section
Data are n (%) or median (interquartile range)
[a] Maternal pyrexia, prolonged rupture of membranes, chorioamnionitis, group B streptococcus, urinary tract infection
[b] Placental abruption, placenta praevia or other antepartum haemorrhage
[c] Data represents any grade of intraventricular haemorrhage or germinal matrix haemorrhage. Data extracted from "principle diagnosis at discharge" data field and grade of intraventricular haemorrhage from recorded cranial ultrasound scans
Data items gestational diabetes, preeclampsia, risk factors for sepsis, alcohol/drugs/smoking and antepartum haemorrhage variables are collected using a tick box, so not possible to accurately determine missing data from absence of a characteristic

**Supplementary Table 3.** Gestational age of infants who were postnatally transferred from level 3 to level 3 hospitals within 72 hours of age over time

| Gestation (weeks) | Total infants (n = 280) | Epoch 1 (n = 119) | Epoch 2 (n = 161) |
|---|---|---|---|
| 23 | 10 (3.5) | 6 (5.0) | 4 (2.5) |
| 24 | 40 (14.3) | 13 (10.9) | 27 (16.8) |
| 25 | 48 (17.1) | 17 (14.3) | 31 (19.3) |
| 26 | 83 (29.6) | 38 (31.9) | 45 (28.0) |
| 27 | 99 (35.4) | 45 (37.8) | 54 (33.5) |

Data are n (%)

**Supplementary Table 4**. Deaths by place of referring and receiving neonatal unit levels for all postnatally transferred extremely preterm infants within 72 hours of age in the UK

| Unit level | | Epoch 1 n = 364 | Epoch 2 n = 322 | |
|---|---|---|---|---|
| Referring | Receiving | Deaths n (%) | Deaths n (%) | p value* |
| L3 | L3 | 20 (5.5) | 31 (9.6) | 0.04 |
| L2 | L3 | 242 (66.5) | 218 (67.7) | 0.92 |
| L1 | L3 | 78 (21.4) | 57 (17.7) | 0.22 |
| L3 | L2 | 1 (0.3) | 3 (0.9) | 0.26 |
| L2 | L2 | 9 (2.5) | 5 (1.6) | 0.40 |
| L1 | L2 | 4 (1.1) | 3 (0.9) | 0.83 |
| MLU | L2 | 1 (0.3) | 0 | 0.35 |
| MLU | L3 | 6 (1.6) | 2 (0.6) | 0.21 |
| Missing | Missing | 3 (0.8) | 3 (0.9) | 0.88 |

L3, Level 3; L2, Level 2; Level 1; MLU, Midwife-led unit
* Data analysed using chi squared test

**Supplementary Table 5.** Demographic characteristics of extremely preterm infants who underwent early level 3 to level 3 postnatal transfer and died

| | **Total infants n = 51[a]** | **Epoch 1 n = 20[a]** | **Epoch 2 n = 31[a]** | **p value*** |
|---|---|---|---|---|
| Gender (male) | 32 (62.7) | 10 (50) | 22 (71) | 0.13 |
| Birth weight (grams) | 768 (630-880) | 772 (573-895) | 768 (630-855) | 0.85 |
| Gestation (weeks) | | | | 0.66 |
| 23 | 7 (13.7) | 4 (20.0) | 3 (9.7) | |
| 24 | 13 (25.5) | 5 (25.0) | 8 (25.8) | |
| 25 | 9 (17.6) | 2 (10.0) | 7 (22.6) | |
| 26 | 9 (17.6) | 3 (15.0) | 6 (19.4) | |
| 27 | 13 (25.5) | 6 (30.0) | 7 (22.6) | |
| Antenatal Steroids | | | | 0.08 |
| None | 8 (16.0) | 2 (10.0) | 6 (20.0) | |
| Incomplete | 11 (22.0) | 2 (10.0) | 9 (30.0) | |
| Complete | 29 (58.0) | 14 (70.0) | 15 (50.0) | |
| Missing | 2 (4.0) | 2 (10.0) | 0 | |
| Age at transfer | | | | <0.01 |
| <24 hours | 29 (56.9) | 14 (70.0) | 15 (48.4) | |
| 24-48 hours | 7 (13.7) | 3 (15.0) | 6 (19.4) | |
| 48-72 hours | 15 (29.4) | 3 (15.0) | 10 (32.3) | |
| Day of Death | | | | <0.01 |
| 0-3 days | 6 (11.8) | 4 (20.0) | 2 (6.5) | |
| 3-7 days | 11 (21.6) | 2 (10.0) | 9 (29) | |
| 7-14 days | 12 (23.5) | 5 (25.0) | 7 (22.6) | |
| 14-21 days | 5 (9.8) | 3 (15.0) | 2 (6.5) | |
| >21 days | 17 (33.3) | 6 (30.0) | 11 (35.5) | |

[a] Data are n (%) or median (interquartile range)

[b] Categorical data analysed using chi squared test, non-normally distributed continuous data analysed using Mann-Whitney U test