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Extended Research Article

Optimising neonatal services for very preterm births between 27^{+0} and 31^{+6} weeks gestation in England: the OPTI-PREM mixed-methods study

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Dedicated to all babies born preterm, their families and their healthcare teams.

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Abstract

Aim: To investigate, for preterm babies born between 27^{+0} and 31^{+6} weeks gestation in England, optimal place of birth and early care.

Design: Mixed methods.

Setting: National Health Service neonatal care, England.

Methods: To investigate whether birth and early care in neonatal intensive care units (tertiary units) compared to local neonatal units (non-tertiary units) influenced gestation-specific survival and other major outcomes, we analysed data from the National Neonatal Research Database, for 29,842 babies born between 27^{+0} and 31^{+6} weeks gestation and discharged from neonatal care between 1 January 2014 and 31 December 2018. We utilised an instrumental variable (maternal excess travel time between local neonatal units and neonatal intensive care units) to control for unmeasured differences. Sensitivity analyses excluded postnatal transfers within 72 hours of birth and multiple births. Outcome measures were death in neonatal care, infant mortality, necrotising enterocolitis, retinopathy of prematurity, severe brain injury, bronchopulmonary dysplasia, and receipt of breast milk at discharge. We also analysed outcomes by volume of neonatal intensive care activity. We undertook a health economic analysis using a cost-effectiveness evaluation from a National Health Service perspective and using additional lives saved as a measure of benefit, explored differences in quality of care in high compared with low-performing units and performed ethnographic qualitative research.

Results: The safe gestational age cut-off for babies to be born between 27^{+0} and 31^{+6} weeks and early care at either location was 28 weeks. We found no effect on mortality in neonatal care (mean difference −0.001; 99% confidence interval −0.011 to 0.010; $p = 0.842$) or in infancy (mean difference −0.002; 99% confidence interval −0.014 to 0.009; $p = 0.579$) ($n = 18{,}847$), including after sensitivity analyses.

A significantly greater proportion of babies in local neonatal units had severe brain injury (mean difference −0.011; 99% confidence interval −0.022 to −0.001; $p = 0.007$) with the highest mean difference in babies born at 27 weeks (−0.040). Those transferred in the first 72 hours were more likely to have severe brain injury. For 27 weeks gestation, birth in centres with neonatal intensive care units reduced the risk of severe brain injury by 4.2% from 11.9% to 7.7%. The number needed to treat was 25 (99% confidence interval 10 to 59) indicating that 25 babies at 27 weeks would have to be delivered in a neonatal intensive care unit to prevent one severe brain injury.

For babies born at 27 weeks gestation, birth in a high-volume unit (> 1600 intensive care days/year) reduced the risk of severe brain injury from 0.242 to 0.028 [99% confidence interval 0.035 to 0.542; $p = 0.003$; number needed to treat = 4 (99% confidence interval 2 to 29)].

Estimated annual total costs of neonatal care were £262 million. The mean (standard deviation) cost per baby varied from £75,594 (£34,874) at 27 weeks to £27,401 (£14,947) at 31 weeks. Costs were similar between neonatal intensive care units and local neonatal units for births at 27^{+0} to 29^{+6} weeks gestation, but higher for local neonatal units for those born at 30^{+0} to 31^{+6} weeks. No difference in additional lives saved were observed between the settings. These results suggested that neonatal intensive care units are likely to represent value for money for the National Health Service. However, careful interpretation of this results should be exercised due to the ethical and practical concerns around the reorganisation of neonatal care for very preterm babies from local neonatal units to neonatal intensive care units purely on the grounds of cost savings.

We identified a mean reduction in length of stay (1 day; 95% confidence interval 1.029 to 1.081; $p < 0.001$) in higher-performing units, based on adherence to evidence- and consensus-based measures. Staff reported that decision-making to optimise capacity for babies was an important part of their work. Parents reported valuing their baby's development, homecoming, continuity of care, inclusion in decision-making, and support for their emotional and physical well-being.

Conclusions: Birth and early care for babies ≥ 28 weeks is safe in both neonatal intensive care units and local neonatal units in England. For anticipated births at 27 weeks, antenatal transfer of mothers to centres colocated with neonatal intensive care units should be supported. When these inadvertently occur in centres with local neonatal units, clinicians should risk assess decisions for postnatal transfer, taking patient care requirements, staff skills and healthcare resources into consideration and counselling parents regarding the increased risk of severe brain injury associated with transfer.

Study registration: This study is registered as Current Controlled Trials NCT02994849 and ISRCTN74230187.

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Supplementary material can be found on the NIHR Journals Library report page (https://doi.org/10.3310/JYWC6538).

Supplementary material has been provided by the authors to support the report and any files provided at submission will have been seen by peer reviewers, but not extensively reviewed. Any supplementary material provided at a later stage in the process may not have been peer reviewed.

List of abbreviations

BAPM	British Association of Perinatal Medicine
BLISS	The national charity for babies born premature or sick
BMF	breast milk feeds at discharge
BPD	bronchopulmonary dysplasia
CRG	Clinical Reference Group
EPR	electronic patient records
HRG	healthcare resource group
ICD-10	*International Statistical Classification of Diseases and Related Health Problems*, Tenth Revision
IMD	Index of Multiple Deprivation
IRAS	Integrated Research Application System
IV	instrumental variable
LNU	local neonatal unit
LOS	length of stay
NDAU	Neonatal Data Analysis Unit
NEC	necrotising enterocolitis
NICU	neonatal intensive care unit
NIV	non-invasive ventilation
NNAP	National Neonatal Audit Programme
NNRD	National Neonatal Research Database
NNT	number needed to treat
OPCS	Operating Procedure Codes Supplement
PPI	patient and public involvement
RCPCH	Royal College of Paediatrics and Child Health
REC	Research Ethics Committee
ROP	retinopathy of prematurity
SBI	severe/serious brain injury
SCBU	special care baby units
TPN	total parenteral nutrition

Plain language summary

Preterm babies are at risk of death and serious long-term problems. For babies born at ≤ 26 weeks, we know outcomes are better with birth and care in tertiary maternity and neonatal units. We do not know whether this is true for the next most vulnerable group, born between 27 and 31 weeks. In England, these babies are born and cared for in either neonatal intensive care units (tertiary) or local neonatal units (non-tertiary).

We did

OPTI-PREM explored whether outcomes for babies born between 27 and 31 weeks differed based on where they were born and cared for. We studied national neonatal data, costs of care, staff and parents' perspectives, quality of care and outcomes. A parent panel guided us.

We found

Outcomes were similar for babies born between 28 and 31 weeks. Severe brain injury was identified more in babies born in local neonatal units. A higher proportion was in babies born at 27 weeks and babies who were transferred within 72 hours after birth. To prevent one baby from developing severe brain injury, 25 babies would need to be cared for in neonatal intensive care units as opposed to local neonatal units at 27 weeks gestation. There was no difference in National Health Service neonatal costs for babies born at 27 weeks (~£76,000) between neonatal intensive care units and local neonatal units. £0.26 billion per year was spent on National Health Service neonatal care for babies born between 27 and 31 weeks in England.

Staff managed decision-making, to ensure space for babies. Parents valued their baby's development, homecoming, continuity of care, being included, and having their emotional and physical well-being supported.

Our findings suggest babies between 28 and 31 weeks can safely be born and cared for in either local neonatal units or neonatal intensive care units. However, to minimise risk of brain injury, births at 27 weeks should be in maternity units colocated with neonatal intensive care units. Transfers of babies after birth should be avoided where possible.

Scientific summary

Background

Recent global evidence indicates that place of birth matters for survival and morbidity advantages for extremely preterm babies born at ≤ 26 weeks gestation. This has shaped national policy. We do not know whether this benefit extends to the next most vulnerable group, born between 27^{+0} and 31^{+6} weeks gestation (hereafter referred to as born at 27–31 weeks). Globally these may be managed in different types of neonatal facilities. In England, they may be born into maternity units colocated with either neonatal intensive care units (NICU, also known as tertiary neonatal units) or local neonatal units (LNU, also known as non-tertiary neonatal units) and cared for in these. NICU can provide higher intensity of care than LNU, but both have facilities to support babies born at < 32 weeks gestation. Occasionally, they may be born outside these units, but, if viable, are quickly transferred for care in either. Current practice makes no distinction between care in either, as these babies, while vulnerable, do not all require the highest intensity of care. The decision about where an individual babies is born is based on maternal choice at booking, presentation to the nearest hospital and bed/staff capacity at the time of delivery. However, these two types of neonatal unit differ in facilities, staffing and staff skill-mix for care of very preterm babies.

Evidence on the most appropriate setting for post-delivery care has been lacking, and questions have been raised around whether, within this cohort of babies born at 27–31 weeks gestation, the optimal care setting could vary across the gestational age range. They account for ~12% of all preterm births and four times the throughput in neonatal units compared to babies born at ≤ 26 weeks gestation. They are a sizeably important group for whom the optimal care setting should be investigated if survival is to be maximised and morbidity minimised.

Aim
To investigate the best place of birth and early care for preterm babies born at 27–31 weeks gestation in England, so that this evidence can be used to inform and optimise neonatal healthcare delivery in England.

Study design
Mixed-methods study comprising five workstreams.

Setting
Neonatal units in England.

Workstream 1: A clinical outcomes study: the impact of place of birth and early care on mortality and morbidity in very preterm babies born at 27–31 weeks gestation in England

Objective
For very preterm babies born at 27–31 weeks gestation in England, and admitted to neonatal units, does birth in maternity units colocated with NICU or LNU offer a survival and/or morbidity advantage?

Design
National population-based cohort study using quality-assured electronic recorded patient data held within the National Neonatal Research Database (NNRD). For mortality the time horizon was 1 year, and for this, NNRD data were linked with mortality information from NHS Digital, Office for National Statistics. For morbidity, the time horizon was the hospital stay, prior to discharge from neonatal care.

Participants
Eighteen thousand eight hundred and forty-seven preterm babies born at between 27–31 weeks gestation in maternity units colocated with NICU compared with LNU in England, who were discharged from or died in neonatal care between 1 December 2014 and 31 December 2018. Neonatal care was assigned to unit designation at admission, and early care, to place of care in the first 72 hours of life.

Methods

We conducted overall and gestation-specific analyses, and adjusted for measured confounders of sex, birthweight z-score, multiplicity, mode of delivery, ethnicity, maternal age and indices of multiple deprivation. We used an instrumental variable approach to control for unmeasured differences between units. The instrument selected was maternal excess travel time between NICU and LNU. We performed sensitivity analyses excluding early postnatal transfers (at 24 hours and up to 72 hours after birth), and multiple births. We also analysed outcomes by volume of neonatal intensive care activity. We studied the outcomes of death in neonatal care, and the first year of life (infant mortality), necrotising enterocolitis (NEC), retinopathy of prematurity (ROP), severe/serious brain injury (SBI), bronchopulmonary dysplasia (BPD), and a care process, the receipt of any breast milk feeds at discharge from neonatal care (BMF). We calculated adjusted mean proportions in each unit with associated mean differences and 99% confidence interval (CI).

Results

Mortality: We included 18,847 babies (10,379 born into maternity units colocated with NICU and 8468 with LNU). Five hundred and seventy-four babies (3.0%) died while in NICU/LNU care, and a further 121 after discharge from neonatal care, within their first year of life (total infant mortality; 3.7%). There was no effect of place of birth on mortality in neonatal care (mean difference −0.001; $p = 0.842$) nor infant mortality (mean difference −0.002; $p = 0.579$). This lack of effect remained after sensitivity analyses.

Morbidity: 18,273 babies survived to discharge. The overall rate for NEC was 2.6%, ROP 1.7%, SBI 3.9% and BPD 10%. 55.9% received BMF. We observed an increase in SBI in babies born in maternity units colocated with LNU (mean difference −0.011; $p = 0.007$). The highest mean difference in gestation-specific SBI was in the group of babies born at 27 weeks gestation (−0.040); those who were transferred in the first 72 hours were more likely to have SBI. Statistical significance was lost after exclusion of early postnatal transfers ($n = 1545$; mean difference −0.002; $p = 0.554$) for the whole group, and then separately, on exclusion of all babies born at 27 weeks gestation (mean difference −0.008; $p = 0.037$). For babies born at 27 weeks gestation, birth in maternity services colocated with NICU reduced the risk of SBI from 11.9% to 7.7%, a reduction of 4.2%. This represented a number needed to treat (NNT) of 25 (99% CI 10 to 59) indicating that 25 babies would need to be delivered in NICU rather than LNU, to prevent one SBI at 27 weeks gestation. For babies born at 27 weeks gestation, birth in a high-volume unit (> 1614 intensive care days/year) reduced the risk of SBI from 0.242 to 0.028 [99% CI 0.035 to 0.542; $p = 0.003$; NNT = 4 (99% CI 2 to 29)].

There was no effect of place of birth on ROP, NEC or BMF. There was a higher likelihood of BPD in births in maternity units colocated with NICU (mean difference 0.018; $p = 0.006$). This remained after exclusion of early transfers (mean difference 0.029; $p \leq 0.001$) and was lost on exclusion of babies born at 27 weeks gestation (mean difference 0.011; $p = 0.065$).

Conclusions

The threshold above which birth and early care can safely be provided close to home, in either NICU or LNU, is 28 weeks gestation. We identified an increased likelihood of SBI in babies born in maternity units colocated with LNU. This appeared to be related to postnatal transfer too. As degree of illness at birth cannot always be predicted for babies born very preterm, our data indicate an urgent need to support antenatal transfers of mothers with expected preterm births at 27 weeks gestation to maternity units colocated with NICU. Where births at 27 weeks gestation inadvertently occur in LNU settings, clinicians should risk assess decisions for transfer.

Workstream 2: A clinical quality of care study addressing unit differences (independent of unit designation as neonatal intensive care unit or local neonatal unit) and impact on neonatal outcomes in very preterm babies born at 27–31 weeks gestation in England

Objective

To investigate the relationship between care provided (irrespective of unit designation) and outcomes for very preterm babies born at 27–31 weeks gestation.

Methods

We identified two areas to explore quality of neonatal care: (a) adherence to prespecified targets or benchmarks for clinical care measures, defined within the National Neonatal Audit Programme (NNAP), and data completion for these on the electronic patient records, and (b) benchmarking in the upper quartile for additional early preterm care evidence-based measures that could be extracted from our OPTI-PREM data set. We categorised units as high performing for quality of care based on their meeting of prespecified targets set by the NNAP for different measures, and for being above the upper quartile for benchmarking exercises. We developed a hierarchical list and compared those units above the top quartile (high-performing units) with those below the upper quartile (lower-performing units). We compared the demographic profiles and unit characteristics and conducted multivariate analyses (linear and logistic regression) exploring associations with length of stay and pre-discharge mortality.

Results

We identified a mean reduction in length of stay of 1 day for babies born at 27–31 weeks gestation in units within the top quartile, for high-performing units (95% CI 1.029 to 1.081; $p < 0.001$). We did not find a significant difference in pre-discharge mortality. Units in high areas of social deprivation and those with fewer staff were less likely to be higher-performing units.

Limitations

Our sample size was restricted to 1 year of the OPTI-PREM cohort, to limit the effect of unit change in care processes and structure on quality of care delivered.

Conclusions

If duration of hospital stay is influenced by the quality of care provided in units, our observations have patient-flow and cost-saving implications for neonatal units and the NHS.

Workstream 3: (a) Cost of neonatal care provided for very preterm babies born at 27–31 weeks gestation in neonatal intensive care unit and local neonatal unit in England within the National Health Service setting

Objective

To estimate neonatal costs to hospital discharge for very preterm babies born at 27–31 weeks gestation in NICU and LNU.

Design

Retrospective analysis of resource use data recorded within the NNRD.

Patients

Babies born at 27–31 weeks gestation in England and discharged from a neonatal unit between 1 April 2014 and 31 December 2018.

Main outcome measures

We costed days receiving different levels of neonatal care, along with other specialised clinical activities. We present mean resource use and costs per baby by gestational age at birth, along with total costs for the cohort.

Results

We used data for 28,154 very preterm babies born at 27–31 weeks gestation and estimated the annual total costs of neonatal care to be £262 million. 95% of costs were attributable to routine daily care provided by units. The mean (standard deviation) cost per baby of daily care varied by gestational age at birth; £75,594 (£34,874) at 27 weeks as compared with £27,401 (£14,947) at 31 weeks.

Conclusions

The findings presented here are a useful resource to stakeholders including NHS managers, clinicians, researchers and policy-makers.

Workstream 3: (b) A cost-effectiveness analysis: comparing the costs and effects of care for very preterm babies born at 27–31 weeks gestation in neonatal intensive care unit compared with local neonatal unit in England within the National Health Service setting

Objective

We quantified and compared the costs and effects of care provided to preterm babies born at 27–31 weeks gestation in NICU compared with LNU in England.

Methods

We analysed data from theNNRD for very preterm babies born at 27–31 weeks gestation, admitted to neonatal units in England and discharged between 1 January 2014 and 31 December 2018. We costed data on the daily levels of neonatal care provided to each baby and on key healthcare interventions, using unit costs from established sources. Survival status at neonatal unit discharge was our measure of health outcome. To facilitate an unbiased comparison of NICU and LNU, we adjusted for measured confounders and used an instrumental variable approach to account for unmeasured confounders.

Results

We did not observe a difference in mortality between babies admitted to NICU compared with LNU. The mean cost of babies managed in NICU (£45,860 SE = £313) was lower than the cost of babies managed in LNU (£48,393, SE = £386) [mean cost difference −£2534 (99% CI −£4096 to −£971)]. The costs of care for babies born at 27–29 weeks gestation were not significantly different between NICU and LNU. Costs were only significantly lower for babies born in NICU at later gestations (30 and 31 weeks) and were driven by differences in the durations of different levels of care provided.

Conclusions

Redirecting care of less sick very preterm babies to NICU to reduce costs may be challenging. Instead, research is needed to understand the reasons for the differences in the durations of intensive care between settings.

Workstream 4: A qualitative ethnographic study exploring place of care decision-making and the perspectives of parents and clinicians, for very preterm babies born at 27–31 weeks gestation in neonatal intensive care unit and local neonatal unit in England

Objective

To assess staff and parent perspectives on place of care for very preterm births at 27–31 weeks gestation in England.

Design

We undertook qualitative studies using an ethnographic approach that included observations of routine behaviours in their natural settings ('work-as-done' rather than 'work-as-imagined') and interviews with staff and parents.

Participants

Parents of babies born at 27–31 weeks gestation from across all geographic areas in England (retrospective and contemporaneous); staff working in four LNU and two NICU, in two neonatal operational delivery networks, and in neonatal transport teams.

Results

Staff were dealing with multiple priorities, making decisions in a rapidly evolving, time-consuming, unstandardised way. The complexities of decision-making and enacting place of care decisions, contextualising decisions and integrating managerial thinking into their decision-making processes was evident. For parents, being able to care for their baby while on the neonatal unit was a priority. Transfer of a baby disrupted parental care and parenthood. It carried with it multiple stresses, including getting to know and to trust the new unit, and the impact of being far from home. Access to practical and emotional support was limited for parents. Optimising their baby's development and preparing for homecoming were important to parents.

Conclusions

Place of care discussions should include assessment of the burden placed on staff, and parents of various socioeconomic backgrounds, and the consequent ability to maintain continuity of care in the face of disruptions. Discussions and reviews of how resources are employed in neonatal units are required to optimise efficiency of staff working, and improve experiences of neonatal care for babies, parents and families.

Workstream 5: Stakeholder engagements on OPTI-PREM findings

Objective

To engage with stakeholders regarding investigation, findings and implications of findings from OPTI-PREM.

Design

We held multiple meetings with stakeholders from national bodies, regional networks and individual units. These were individuals involved in decision-making for delivery of NHS neonatal service provision of neonatal and obstetric clinical care, managers, operational delivery network leads, researchers, parents and members of the public. We presented at neonatal and obstetric meetings to discuss the project, results, and to obtain peer review in the form of comments and constructive criticism from these presentations.

Results

Scientific evidence was shared and considered timely, highly relevant and robust. Key stakeholders engaged, supported the OPTI-PREM project, and participated in discussions on potential implications of our findings. Ideas, critiques and suggestions have been considered and actioned where appropriate within this report. This engagement is ongoing.

Conclusions

OPTI-PREM findings provide timely, important scientific evidence for policy-makers and stakeholders to utilise, in optimising neonatal health care for very preterm babies born at 27–31 weeks gestation. Our findings align with the NHS 2023 3-year delivery plan for maternity and neonatal services in England.

Study registration

This study is registered as Current Controlled Trials NCT02994849 and ISRCTN74230187.

Funding

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Chapter 1 Introduction

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Background

The structure of neonatal units in England

In England care for sick neonates is supported by NHS Specialised Commissioning. It is delivered by neonatal units clustered in and managed through 10 neonatal operational delivery networks. These neonatal units are designated either as neonatal intensive care units (NICU), local neonatal units (LNUs) or special care baby units (SCBU) based on their resources, staffing and capabilities.[3,4] NICU are tertiary units colocated within maternity services that have specialist obstetric and feto-maternal medicine services. NICU have resources and staff to provide tertiary level care for sick babies with varying complexities of clinical conditions, and across all gestational ages at birth. LNU provide care for neonates in their local catchment area; these are not configured to provide long-term intensive care, but can provide emergency care, and short-term intensive support for sick babies. They are considered non-tertiary units. In general, they care for those who do not demand the very highest intensity of neonatal care. SCBU provide care, ideally close to the family home, usually for those born at > 32 weeks gestation. They provide only the lowest intensity of neonatal care.

Clinical profile of very preterm babies

When compared with their extremely preterm counterparts born between 23^{+0} and 26^{+6} weeks gestation (hereafter referred to as born at 23–26 weeks), very preterm babies born between 27^{+0} and 31^{+6} weeks gestation (hereafter referred to as born at 27–31 weeks gestation) tend to have a more favourable prognosis. The effects of immaturity *per se* are often less profound in the group born at 27–31 weeks gestation compared to those on the threshold of viability, born at 23–26 weeks.[5] Unless considered non-viable in the delivery suite, babies born at 27–31 weeks gestation are *always* admitted to a neonatal unit for care, as they are too immature for immediate transfer home or for routine care in a postnatal ward. They are a heterogeneous group; birth in this range is associated with varying but substantial adverse outcomes and differing mortality for each week of gestational age.[5] Many studies that have included babies born at 27–31 weeks gestation were conducted many years ago and were designed to clarify the effects of very low birthweight rather than prematurity on outcomes.

Very preterm babies have shown a relatively greater increase in survival over the past two decades compared with less mature babies.[5] A gradient of risk, with rates of mortality and morbidity increasing from birth at 31 to 27 weeks gestation, has been observed.[5] These place increasing demands on neonatal services and have likely led to changes in the profile of neonatal morbidity, hospitalisation and outcome, the details of which have not yet been captured for UK cohorts.

Very preterm babies: where are they born and cared for in England?

For babies born extremely preterm, at 23–26 weeks gestation, management in a NICU or high-volume neonatal unit confers significant benefit for survival to discharge;[6] this has shaped policy for these babies in England.[7] Similar findings have been observed in other parts of the world.[8–12] In contrast, there is limited evidence to guide the location of care for the next most vulnerable group of very preterm babies, born at 27–31 weeks gestation. Current policy indicates that they can be born and cared for in either NICU or LNU setting, but their care pathways are undefined, and their birth and care is spread, often arbitrarily, across the two settings. In 2013 neonatal data analysis unit (NDAU) data for England shows (unpublished), ~48% were born into maternity services colocated with NICU, and ~41% with LNU. Currently, this translates to care across 43 NICU and 75 LNU in England. Those inadvertently born into maternity services attached to SCBU are transferred to NICU or LNU for ongoing care. In a narrative review of the impact of place of birth and care for this cohort of babies,[13] there appears to be a lack of clarity and consensus not just in England, but globally, on the best place of birth and care for very preterm babies.

The main driver for NHS neonatal care pathways for the very preterm baby born in the UK comes from gestation-specific analyses for extremely preterm babies born at 23–26 weeks gestation.[6] There are currently no data on the optimal location of birth and care for preterm babies born at 27–31 weeks gestation, by designation of unit or any other characteristic, although there is limited evidence that mortality and the most prevalent morbidity outcomes for very preterm births, namely necrotising enterocolitis (NEC), retinopathy of prematurity (ROP) and bronchopulmonary dysplasia (BPD), are similar between LNU and NICU.[11] However, it is not known whether location of care makes a difference to *gestation-specific* outcomes. While the type of care provided by LNU and NICU overlaps considerably, the complexity of problems that can be managed in each differs.[5] We do not know if some babies, such as those who are more preterm or sick, may benefit from care in NICU, which manage the most complex conditions and complications, or whether others, less sick or more mature, may benefit more from care in LNU, focused on lower intensity care, closer to home.

At present, the chief determinant of where a pregnant woman receives antenatal care and gives birth between 27 and 31 weeks gestation, and therefore where her baby receives initial care, is the hospital where she chose to book for antenatal care. This may be in a maternity service colocated with NICU, LNU or SCBU. This is usually the centre closest to her home and is not necessarily determined by the anticipated degree of illness or complexity of care required for her or her baby. For most women at the time of booking for pregnancy care, the risk of pregnancy complications and/or preterm delivery is unpredictable. Where an antenatal reason for continued care in a maternity centre colocated with NICU is noted, and/or there is an anticipated need for NICU support for the baby, these pregnant women are triaged in utero for appropriate ongoing care.

National Health Service England service specifications for neonatal critical care (intensive, high-dependency and special care) E08/S/a[7] outlined for LNU that anticipated singleton births before 26^{+6} weeks gestation, multiple births before 27^{+6} weeks gestation and births where the estimated birthweight is < 800 g should be transferred to maternity services colocated with NICU. Babies born critically ill requiring ongoing intensive care for more than 48 hours should be discussed with NICU. In many cases this has led to transfer to NICU. These recommendations have been consolidated in the Neonatal Critical Care Review,[14] and a recent national neonatology report[15] has explored this further. Bed/cot capacity for care of both mother and baby are major determinants for place of care for these babies. Where all these conditions are met, LNU may triage babies to NICU in the antenatal period (in utero) or in the postnatal period (ex utero), per protocol, as dictated by the NHS service specifications.

Healthcare burden of very preterm births

These babies accounted for approximately 12% of all viable preterm births in England in 2013 (6242/51,000[1]). They utilise over 304,893 bed-days/year, constituting over a third of all bed-days offered to babies in neonatal units in England in 2013 and 2014.[16] This is more than twice the neonatal unit bed-days utilised by babies born at 23–26 weeks gestation, and 4–5 times the numbers of babies born at 23–26 weeks gestation in England. Their mortality in neonatal care in England was 30 per 1000 neonatal admissions (NDAU unpublished data, 181 deaths/5991 admissions in 2014) and their infant mortality, 26/1000 live births.[17] They spend a median of 44 days in neonatal care and are discharged at a median of 36.4 weeks post conceptional age.[18] Survivors at 31 weeks gestation utilise a median of 34 hospital bed-days for their initial neonatal care, while those at 27 weeks gestation, a median of 79 days (for those born at 27 weeks gestation).[19,20]

Economic cost of care

Preterm births (< 37 weeks gestation) generate a substantial healthcare cost, initially during the neonatal hospital stay, and subsequently through increased risks of long-term neurodevelopmental, cognitive, behavioural and physical health problems.[21–23] The overall cost of care for preterm babies in England and Wales was estimated at £2.946 billion in 2006.[24] At that time, the initial hospitalisation costs for preterm babies < 33 weeks gestation was £57,726 [95% confidence interval (CI) 28,779 to 94,868][25] per baby. Current estimates of the costs associated with births between 27 and 31 weeks gestation are lacking for England. Recent literature suggests an inverse relationship between healthcare costs and gestational age.

Mean [standard deviation (SD)] initial hospitalisation costs from Canada for example[26] were estimated at $101,757 ($61,788), $82,719 ($55,321), $59,428 ($44,395), $45,229 ($35,330) and $35,699 ($30,822) for babies born at 27, 28, 29, 30 and 31 weeks gestation, respectively (2017 Canadian $). In Finland, costs were estimated to range from €88,188 per infant born at 26–27 weeks gestation, €56,588 per infant born at 28–29 weeks gestation and €35,147 per infant born at 30–31 weeks gestation (2008 Euro €).[21]

National Health Service hospital costs are high in England, with specialised neonatal intensive care ranging from £776 to £1810 per day and high-dependency care from £709 to £1243 per day, over the past 5 years[1,27,28] depending on the neonatal network in which care is delivered. With increased survival in very preterm babies, the costs of their neonatal and childhood course are unknown. Specifically, for LNU and NICU in England, it is unknown whether care is delivered more cost-effectively in one or the other type of unit. Cost-effective healthcare delivery is a key priority in the NHS; this information is essential in any attempt to optimise neonatal services for very preterm babies, born at 27–31 weeks gestation in England.

Limited healthcare resources mean that alongside assessments of clinical effectiveness, consideration also needs to be given to the cost-effectiveness of alternative care settings for babies born at 27–31 weeks gestation. Survival following preterm birth has improved, and hospital care is costly. The 2021–2 daily cost for neonatal intensive care in the NHS was around 50% higher than for neonatal high- dependency care (£1810 vs. £1243) reflecting the more specialist, intensive and costly management.[28] It is crucial therefore that the appropriate setting and level of care is identified for babies born at 27–31 weeks gestation. If care for less sick preterm babies is unnecessarily provided within NICU, there is an opportunity cost in terms of the health that is foregone by not using these resources in a more appropriate way. Equally, it is important to ensure that sicker preterm babies are not under-supported in LNU, as this could potentially result in prolonged intensive care and ultimately greater morbidity and mortality. At the time of writing and to the best of our knowledge, there have been no previously published analyses assessing the cost-effectiveness of different neonatal care settings for preterm births at any gestational age.

Parent perspectives on place of birth, care and transfers between units

The experience of giving birth to a preterm baby, and parenting a baby receiving neonatal care, can be extremely stressful and often has a negative psychological impact on parents.[29,30] Parents experience moral distress related to caring for a sick baby, and stress associated with separation from their baby, loss of parental role,[31] inconsistent staffing,[32] transfers, and lack of communication and/or involvement in daily decision-making.[33–35] Studies have documented the importance of parental (especially maternal) participation in caring for their baby;[36] satisfaction has been associated with involvement in decision-making processes, respect and empathy from staff, attentive communication, and continuity of treatment and care.[37,38] Within highly medicalised neonatal care facilities, and relevant to preterm babies born at 27–31 weeks gestation, 'parenthood' may be disrupted, with control no longer belonging to parents, and often significant parental trauma.[39,40]

Much of the qualitative research on experiences of preterm delivery and neonatal care has focused on transfers of babies between different levels of neonatal unit, within or between hospitals. Transfers occur not only in response to babies' clinical needs, but may occur to maximise cot utilisation across neonatal networks.[41] Although there is a lack of definitive evidence regarding the psychological impact of transfers on clinical outcomes for neonates,[42] it is recognised that transfers are stressful and emotional for parents,[43,44] create uncertainties, often separate parents from their baby, and disrupt parenthood.[45] Effective communication between staff and parents about transfer processes can help parents feel more comfortable and in control of transfer decisions,[43,46] but parents have reported feeling excluded from such decisions.[42,46] Maternal stress has been related to maladaptive parenting and to long-term developmental problems in the child.[32,47] There are minimal data on parental perspectives on place of care in the UK, and none specifically in relation to unit designation in very preterm babies.

Staff perspectives on care and place of care of very preterm babies

Staff perspectives are important to understand, to drive optimisation of care for this cohort. Staff also experience moral distress in caring for sick preterm babies, and organisational infrastructure is an important facilitator to enable nurses to develop trusting relationships with parents.[48] Several studies have focused on nurses' support for maternal closeness and attachment, which are important for both mothers and babies.[49,50] Challenges for nurses include balancing the importance of facilitating and promoting closeness with the baby's ability to handle stimulation,[50] and managing the work involved in maximising parents' involvement while also attending to the baby's biomedical needs.[51] Studies including both parent and staff perspectives have found that these may be at variance. In the context of very preterm babies, staff perspectives on place of birth and care have not been described.

Rationale for OPTI-PREM

A study addressing these aspects of neonatal care meet the following current NHS neonatal service delivery needs:

1. *Response to new evidence about outcomes associated with place of neonatal care for preterm infants*: Improved survival outcomes for those born at 23–26 weeks gestation when managed in a NICU/high-volume neonatal unit[6,11] must drive investigation of whether similar benefits exist for very preterm babies (born at 27–31 weeks gestation), who are also high risk for neonatal mortality, morbidity and long-term adverse outcomes, and about whom very little is known.
2. *Configuration and optimisation of neonatal services:* The potential benefits and challenges of centralisation of neonatal care and how best to optimise it are the focus of discussions in neonatal health service delivery in England. To fully inform this dialogue, data are required on place of birth and care for all very preterm babies, not only those born at ≤ 26 weeks gestation.
3. *Optimising cost-effectiveness of neonatal care:* Differences in facilities, resources and staffing means there are likely to be inherent differences between LNU and NICU in costs and in the way in which care is provided for babies with similar problems at similar gestational ages. The impact of such variation on short- or long-term outcomes and, as a result, accurate estimates of cost-effectiveness need to be explored in any attempt to optimise neonatal service delivery.
4. *Partnerships between parents and clinicians:* Increasing importance is being placed on service user involvement in decision-making within the NHS and this is now an expectation of the public. Partnership with parents in decision-making about their infants' care following preterm birth is important, but their voices have not yet been effectively heard. Both parents and clinicians have important insights because of their experience in navigating this complex and sensitive healthcare setting.
5. *The need for national guidance:* Despite NHS specifications E08/S/a,[7] there is substantial variation between units and neonatal networks in the way that care is provided for very preterm babies. Evidence-based national recommendations from professional bodies do not exist.

Very preterm babies are a vulnerable, heterogeneous group, with a high mortality rate in the neonatal period and infancy. Currently in the UK they may be cared for in either LNU or NICU, but their optimum place of birth and care has not been defined. Unlike their more immature counterparts, there are no gestation-specific data detailing their mortality and morbidity when managed in LNU compared to NICU. Healthcare costs for these babies are unknown and the opinions and perspectives of parents and staff relating to place of birth have not been investigated.

This NIHR HS&DR project therefore set out to establish whether the designation (type) of unit in which neonatal care is delivered influences outcomes for these babies, and whether benefits of NICU care in relation to survival and morbidities that have already been identified for babies born at 23–26 weeks gestation extend to those born up to 31 weeks gestation. It also explored whether it is safer and more cost-effective for very preterm babies to be cared for in LNU, and whether there is a set point within this range at which care can equitably be provided in either LNU or NICU. Perspectives of staff and parents in co-contributing to strategies for optimal care were included throughout.

Aim

The overarching aim was to optimise neonatal service delivery for babies born at 27^{+0} to 31^{+6} weeks gestation.

Objectives

Primary objective:

- For preterm babies born at 27–31 weeks gestation and admitted into a neonatal unit for care (population), does care in NICU (intervention), when compared to care in LNU (comparator), result in improved gestation-specific survival (primary outcome) up to 1 year of age, and reduced neonatal major morbidities (secondary outcomes)?

Secondary objectives:

- For preterm babies born at 27–31 weeks gestation and admitted into a neonatal unit for care

  a. are there key differences in clinical care provided in LNU and NICU, and are these associated with differences in outcomes?
  b. where is it most cost-effective to care for these babies from an NHS perspective (LNU or NICU)?
  c. what are parents' perspectives regarding place of care, and how can these be used to guide decision-making about place of care?
  d. what are LNU and NICU clinicians' perspectives regarding place of care, and how can these be used to guide decision-making about place of care?

The study findings were intended to form the basis of discussions with the British Association of Perinatal Medicine (BAPM), the Neonatal Clinical Reference Group (CRG), Neonatal Specialised Commissioning services and the national charity for babies born premature or sick (BLISS)[52] as relevant stakeholders to

- help develop recommendations for the optimal, most cost-effective place of care for babies born at 27–31 weeks gestation. BAPM, BLISS, The Royal College of Paediatrics and Child Health (RCPCH) and the Neonatal CRG were aware of, and supportive of, this work.

Chapter 2 Project structure and governance

OPTI-PREM was a mixed-method, longitudinal study comprising five workstreams, underpinned and supported by a Parent Advisory Panel recruited through BLISS, and a Study Steering Committee. Our protocol has been previously published and the project structure is outlined in *Figure 1*.

Research ethics approval

This project was approved by the North East Tyne and Wear South REC 17/NE/0800 on 17 March 2017 [Integrated Research Application System (IRAS) 212304]. Ethics approval for use of the National Neonatal Research Database (NNRD[53]) for this research was obtained through a proportionate (expedited) review through the NHS Research Ethics Committee (NREC), for workstreams 1, 2, 3 and 5. A full review was conducted for workstream 4. For NNRD data, the National Research Ethics Service (10/H0803/151) and the Ethics and Confidentiality Committee of the National Information Governance Board [ref ECC-05(f)/2010] approved utility of the database. The NNRD was created in 2007 to support activities including audit, evaluation, and research in neonatology, and is maintained by the NDAU at Imperial College, London.[53] It is available for use by other investigators. For study purposes, unidentifiable, anonymous data was obtained from the NNRD and transferred to the Wolfson Institute of Preventive Medicine (Queen Mary University of London) using the NHS Net. CAG approval to link the OPTI-PREM data set extracted from the NNRD with NHS Digital Hospital Episode Statistics and mortality was obtained on 7 November 2014 (19/CAG/0104; DARS-NIC-125031-Z3D7S-v0.13).

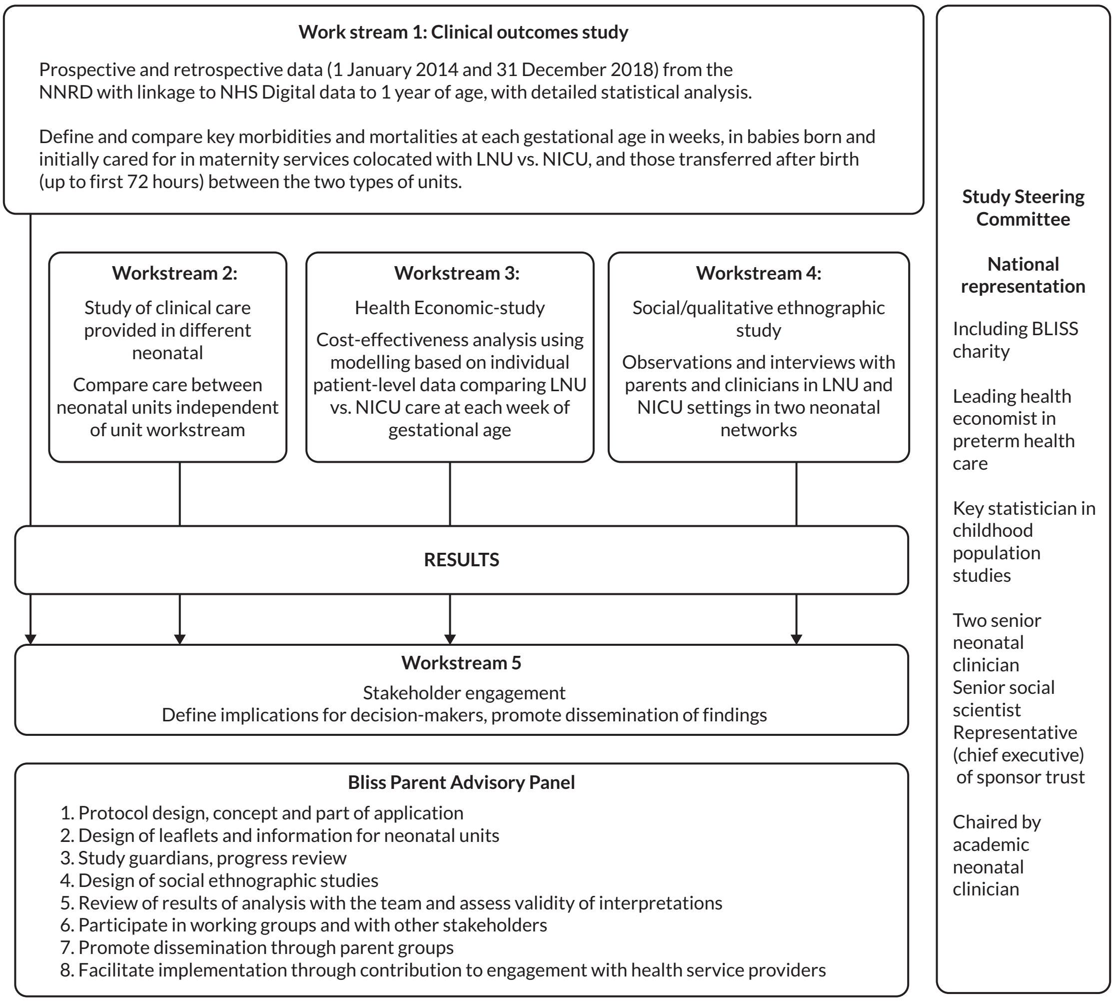

FIGURE 1 OPTI-PREM project structure.

Consent

All NICU and LNU in England were informed of the study and offered the opportunity to 'opt out' of having their unit data included in our analyses. Data on babies from units who opted out were removed before the pseudo-anonymised data set was transferred from NDAU to the study team at the Universities of Oxford and Leicester. Study posters, unit leaflets and parent information leaflets were made available during the study period. Distribution of project details to neonatal units, and unit consent for use of routinely collected unit data captured within the NNRD (for the study period 1 January 2014–31 December 2018), began in July 2017. For the period between August 2017 and August 2018, we were able to include the OPTI-PREM within the UK Clinical Research Network (CRN) Portfolio of research studies. All babies born at 27–31 weeks gestation and admitted for neonatal care were eligible for being recorded as contributing to CRN research activity. As accrual numbers of research participants influence the allocation of CRN research funding to centres, this had a positive effect on unit participation.

Parents of babies who were admitted to neonatal units from the time that we had begun notifying units about the project (July 2017) to the end date of NNRD data capture (31 December 2018) were offered the opportunity to opt out, on behalf of their baby, of the inclusion of their data in the study. Information about opting out was provided through unit posters, unit leaflets and parent information leaflets. It was not feasible to retrospectively seek individual consent from parents whose babies had been discharged from neonatal care before July 2017, when we began groundwork for the project (data period 1 January 2014–31 December 2018). Units displayed information for parents on the NNRD, and the NDAU, which contained information on the general concept of opt-out studies. Additional explicit informed consent was required for the qualitative study in workstream 4, and this is described later.

Study management

Steering Committee

The project was supported by a study steering committee comprising seven members. This was led by a senior academic neonatologist (Birmingham) and included specialists working across England in relevant fields relating to the mixed-methodology study. These were a clinical neonatologist (Bristol), a health economist with expertise in preterm costs of care (Warwick and Oxford), a senior statistician involved in longitudinal follow-up studies in children (Bradford), a senior research engagement officer from BLISS (London), a senior social scientist (Cambridge), and the chief executive of the sponsor trust.

Co-investigators

Co-investigators met 3 monthly initially to refine methodology, and thereafter to share progress within their workstream, and to discuss challenges. Each team worked in parallel. The project team met with the study steering committee 11 times during the project, with additional ad hoc meetings between the project chief investigator and study steering committee chair, to provide updates and share information. Discussions were held about the justification of need for no-cost extensions for the project, and to assist in development of the applications for these extensions. Meetings were co-ordinated through the chief investigator. Workstream 2 supported the development of a PhD studentship, which was successfully completed.

Chapter 3 Patient and public involvement

Aim

The aim of patient and public involvement (PPI) was to ensure that the voices of parents, families and babies were represented in OPTI-PREM.

Methods

Background (preparatory work)

We first undertook preparatory work with parents from the Midlands and followed this with recruitment of a definitive independent panel.

Recruitment to parent panel

Parents were recruited through BLISS. Parents were invited, though BLISS social media [Facebook (Facebook, Inc., Menlo Park, CA, USA); initially sent out by BLISS then readvertised by interested parent support organisations such as NeoMates[54]] to submit an email to the chief investigator, outlining their suitability to represent parents on the OPTI-PREM parent panel. The chief investigator reviewed all applications and included those who met the inclusion criteria. These were parents who:

a. had a very preterm baby
b. replied to the request for interview
c. were able to invest time reviewing the protocol and contributing either face to face or through virtual media.

We were keen to have a diverse as possible representation of parents in the panel. The panel was refreshed in 2020. This was because some parents were not either not contactable, returned to work, or their babies had grown into toddlers and other priorities took over.

Recruitment to Study Steering Committee

The chief investigator approached BLISS for representation on the panel. The research engagement officer accepted the offer of a place on the Study Steering Committee. BLISS also provided a letter of support, submitted as supporting evidence to the NIHR, through its chief executive.

Recruitment to the national stakeholder event

An advert using BLISS social media was sent out inviting parents to participate in the stakeholder event held in April 2022.

Involvement of parents in OPTI-PREM

Parents were included either as part of the full panel, or through the parent panel lead, at all stages of the project. This included:

a. protocol review
b. development of posters and parent information leaflets for the overall project
c. detailed involvement in workstream 4
d. representation at OPTI-PREM study steering committee and collaborator meetings
e. review of results for face validity
f. participation in stakeholder meetings
g. contribution to implications for decision-makers
h. contribution to scientific output on the project
i. anticipated contribution to the public dissemination phase of the findings of OPTI-PREM.

Results

Preparatory work

In preparing for the NIHR funding application, we held a volunteer focus group discussion, co-ordinated with BLISS. This discussion was held with parents of very preterm infants born at 27–31 weeks gestation in England and cared for in the Black Country. This sought to explore parental perceptions on neonatal care and movement of their babies between types of neonatal units and to evaluate how best to engage parents in a project aiming to refine neonatal service delivery.

Parents reported that prior to having had a very preterm baby, they did not have any significant understanding of these types of neonatal units, or how and why this could have relevance to their babies' outcomes: *'I originally thought that all hospitals in the NHS were the same'*; *'I did not know that different hospitals had different abilities to care for babies'*. They supported research into defining the best place for delivery and care of very preterm babies, and how best to support families whose very preterm babies were being cared for in hospital. Parents felt that research based on place of birth was valid with clinical outcome being their main concern. They noted the importance of considering parent perspectives in developing strategies on where babies should be cared for, and recommended broadening recruitment for parents nationally, with the help of BLISS.

Recruitment

As a result, we sent out a national advertisement through BLISS social media platform (Facebook). Forty-two parents responded to this from around the country, and 10 were selected to form a parent advisory panel. The panel comprised both mothers and fathers, including parents with twins and a neonatal death, all born very preterm, within the gestational age range of 27–31 weeks.

Training

The original panel received a day of training (face to face and virtual) in which the principles of public engagement in clinical research (INVOLVE)[55] the project protocol, and guidance for preparing parent information leaflets were reviewed.

Participation in OPTI-PREM meetings

This was followed by further parent panel meetings (with face-to-face and virtual participants) in which the project protocol and plans for the study were reviewed. In total we had parent representation in 27 separate meetings: 6 parent group meetings, 11 Study Steering Committee meetings, and 10 OPTI-PREM collaborator meetings. It was not possible to have all parents present at all study steering committee and collaborator meetings. The parent panel chair and BLISS representative fulfilled these roles.

The panel contributed to development of parent information leaflets, unit information leaflets, posters, photographs of their baby (with consent) for the online website and posters. In workstream 4 (see *Chapter 8*) they participated in developing the ethnographic component of the study regarding the most appropriate aspects to study, and questions to ask in the qualitative workstream. The parent panel chair was part of the interview panel in the appointment of the senior qualitative researcher employed to undertake the qualitative work on the project.

The parent panel acted as study guardians and assessed face validity of the work as it was progressing. They contributed to working group and stakeholder discussions on the results, discussions to determine implications for practice at a national level with respect to place of birth for very preterm babies, and dissemination of information to parents.

The parent panel was separate to the parents interviewed for workstream 4, who formed part of the study population. These will be described later.

Discussion and conclusions

The inclusion of the parent panel to OPT-PREM study design added value and contributed to the integrity of the project's intent. It offered the project team reassurance that the voice of parents, families and babies were considered at all stages. Throughout the project, the lived experience of parents brought a reminder to the team of the practical issues that parents and families faced, and why it was so important for the project to be completed to the best possible standard and make a difference to the lives of babies and their families. At the same time, through stakeholder discussions in which parents shared their lived experience not just with the study team, but with all stakeholders that attended (25 April 2022), parents were able to reach decision-makers, clinicians and managers across different geographic regions (see *Chapter 9*). This was a powerful contribution, for which parents were acknowledged, for sharing their practical issues. Similarly, including parents in the project and meetings, contributed to their increased awareness of the complexities of decision-making around capacity and resources in neonatal and maternity services around the country. Refreshing the panel in 2020 was an inadvertent bonus for the project, as the input remained more contemporaneous to the practices in neonatal units.

Reflection and critical perspective

Overall, the inclusion of PPI in the project was positive, and aligned well with the NIHR-INCLUDE strategy.[56] The OPTI-PREM team are reassured that the voices of parents, families and babies have been represented. This representation, however, was biased, because we used one portal for recruitment of parents to the parent panel, that is BLISS. Parents who had not subscribed to the organisation, or were unaware of or unable to use social media for whatever reason, were not offered the opportunity to participate, by default.

As discussed in *Chapter 12*, there is more work to be done to ensure that the voices of minority groups, different socioeconomic groups and electronic/virtual media capabilities are incorporated. As we learn more about health inequity and inequality in perinatal services,[57–60] we believe that a stronger, more inclusive foundation is required for all future perinatal projects. Efforts to improve PPI require sustained focus, funding and advocacy by NHS, professional and societal organisations.

Chapter 4 Workstream 1: a clinical outcomes study

The impact of place of birth and early care on mortality and morbidity.

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Introduction

We address the primary research question of whether place of birth, by designation of unit as NICU or LNU, matters for preterm babies born at 27–31 weeks gestation. We study this for outcomes of mortality and key morbidities published in the literature for preterm births and added a measure of clinical care process[62] to assess difference in the culture of care provided between units.

Aim

To evaluate differences in mortality and morbidity outcomes by type of unit of birth and early care in the first 72 hours of life of very preterm babies (born at 27–31 weeks gestation) in England.

Study design

Retrospective large-scale data analysis exploring and comparing outcomes between babies born and cared for initially in maternity services colocated with NICU compared with LNU, using routinely collected national data.

Objective

To assess, for preterm babies born at 27–31 weeks gestation and admitted to neonatal units in England (population), whether birth into maternity services colocated with NICU (intervention) compared to LNU (comparator) and early care in the first 72 hours in the respective neonatal units offered a gestation-specific:

i. survival advantage while in neonatal care and up to 1 year of age (outcome), and
ii. reduction in major neonatal morbidity (outcome).

Methods

Data source

Data were obtained from the NNRD. All NHS neonatal units in England used their electronic patient record (EPR) supplier systems to routinely submit detailed information to the NNRD on the outcomes of and clinical care provided to babies. Submitted data are quality-assured and curated to a research standard. NNRD data comprise demographics, diagnoses, health outcomes, daily interventions (including the level of care, namely intensive, high-dependency, special, or normal care, provided each day) and treatments administered during the inpatient episode of care. We used data collected for babies admitted to neonatal units in England. This baby-level data set was linked by NHS Digital Office for National Statistics[63] for mortality data, for up to 1 year of age.

The OPTI-PREM cohort comprised preterm babies born at 27–31 weeks gestation born in maternity services colocated with a NICU or an LNU in England, and who were discharged from or died in neonatal care between 1 December 2014 and 31 December 2018. We selected date of discharge as opposed to date of birth, so that we could have a defined end date for data extraction from the NNRD.

Outcome variables

Primary outcomes were death in neonatal care and death during the first year of life (infant mortality). Secondary outcomes were important neonatal outcomes [ROP, severe/serious brain injury (SBI), NEC, BPD], and one measure of clinical care process [receipt of any breast milk feeds at discharge from neonatal care (BMF)]. We compared outcomes between babies born in maternity services colocated with NICU with those in services colocated with LNU.

Definitions

Severe retinopathy of prematurity: a baby with Stage 3+ ROP[64] in one or both eyes. All babies who had laser surgery were also included on the assumption that they would have Stage 4 ROP to warrant surgery.

Severe/serious brain injury: a baby having one or more of the following at any time while in neonatal care: periventricular leukomalacia, unilateral or bilateral grade 3 or 4 intraventricular haemorrhage, porencephalic cysts or hydrocephalus.

Necrotising enterocolitis: a baby undergoing surgical treatment/laparotomy for NEC while in neonatal care, with information extracted from the abdominal X-ray table in the NNRD data and supplemented with information reviewed in the entries on daily data of NEC. Cases where suspected NEC was recorded were excluded.

Bronchopulmonary dysplasia: oxygen dependence at 36 weeks post menstrual age, and a requirement for oxygen for at least 80% of the days before reaching 36 weeks post menstrual age. Babies who were discharged before 36 weeks post conceptional age were regarded as not oxygen dependent. The data were extracted using the added oxygen variable within the daily data. It was clinically accepted that babies who were oxygen dependent would not be discharged before 36 weeks gestation in England.

Receipt of any breast milk feeds at time of discharge from neonatal unit *(BMF)*: was extracted from the final day records on the NNRD.

Place of care for babies: a baby's care was assigned to NICU or LNU according to whether the maternity service in which they were born was colocated with NICU or LNU.

Composite outcomes: outcomes for ROP, SBI, NEC, BPD and death were combined to describe the composite adverse outcomes for babies.

Statistical methods

Sample size

We estimated a sample size of approximately 26,250 based on 6000 births per year and a 48% NICU and 41% LNU split between place of birth. We assumed an in-unit mortality of approximately 5%, giving over 1000 deaths in the sample. Assuming 5.0% of babies in the NICU died before discharge, this anticipated sample size of 26,250 admissions would give a minimum detectable difference of 2.6% in mortality for the LNU with at least 80% power at the two-sided 5% significance level in a simple comparison. The inclusion of over 1000 deaths in the study was expected to provide sufficient statistical power to investigate the potential predictors of mortality and morbidity.[1]

Measured and unmeasured confounders

In the absence of a randomised allocation of babies to each 'neonatal unit type', we considered that appropriate statistical methods were required to address the biases that would likely arise from a non-randomised comparison of outcomes of babies receiving care in each unit type. To control for measured confounders, we used propensity score matching to create a sample of babies managed in each setting, who were balanced in terms of neonatal and maternal characteristics. The following observed neonatal and maternal characteristics were used in the matching exercise and were selected after discussions at multiple OPTI-PREM collaborator and study steering committee meetings: gestational age; sex; birthweight z-score; multiplicity; maternal ethnicity; maternal age; index of multiple deprivation (IMD) score and mode of delivery.[65,66] The result of this matching exercise (see *Report Supplementary Material 1*) suggested that we had limited information about measured confounders. For instance, preterm babies born into maternity services colocated with NICUs could be more complex due to high-risk maternal and fetal illnesses compared to those delivered in services colocated with LNU. The NNRD contains limited maternal clinical data to conduct an adjusted analysis of all confounders of importance. In addition, the potential existence of unobserved characteristics that varied by unit type could result in biased estimates of outcomes, if left unaddressed. To account for the available measured confounders and additional unmeasured confounding, an instrumental variable (IV) approach was used.[67,68]

The instrumental variable approach

With this approach, the aim is to identify a variable that supports women giving birth to their preterm baby in a particular setting and that naturally controls for observable and unobservable confounders. This variable is referred to as an instrument, and in line with previous work we considered that the difference in the distances between the mother's residential postcode and her nearest NICU postcode, and the mother's residential postcode and her nearest LNU postcode (known henceforth as the excess travel time to a NICU) would likely be an appropriate IV.[9] Details of how this variable was generated for babies in the study are provided in *Report Supplementary Material 2*. To be considered an appropriate IV, a variable should be highly correlated with the independent variable of interest (in this case the 'unit type') but have no direct effect on the outcomes of interest (mortality and complications). Crucially, an IV should not be related to the unobservable confounders biasing the estimate between the independent variable of interest and the outcome. In the context of each of the requirements for an IV outlined above, data have previously shown that high-risk women will likely deliver in a NICU if they are living closer to a hospital with a NICU, and thus we hypothesised that excess travel time to a NICU would be highly correlated with 'unit type'.[9] We also considered that excess travel time to a NICU would not have a direct impact upon infant costs and outcomes, except through the route of whether the baby was delivered in a NICU or an LNU. Finally, it is highly unlikely that excess travel time to a NICU would be related to any unobserved confounders as women generally do not choose to live close to a hospital with a NICU in case they ever have a preterm birth. Excess distance is thus likely to be randomly distributed across the cohort. Travel time to a facility is a common candidate of instrument in epidemiological studies with observational data.[69]

To assess the strength of our chosen instrument, we evaluated (1) whether there was a strong correlation between 'unit type' and excess travel time, and (2) whether the instrument distributed measured confounders equally using the median of the excess travel time distribution across the whole cohort as a cut-off value. We then estimated our IV models for primary and secondary outcomes using bivariate probit regression. The choice of the bivariate probit instead of the standard probit model was the binary nature of 'unit type' (NICU or LNU).[70] The models also included the measured confounders used in the matching exercise and described above.

To account for the multiple comparisons used within our analyses, we set the CIs for statistical significance for all analyses at 99% ($p \leq 0.01$).

Morbidity and care process outcomes

We extracted key morbidity outcomes and the BMF care process outcome from the diagnoses, daily data on the NNRD, discharge summary and other relevant data entries. We assumed that when no morbidity was entered in the daily data, diagnoses, discharge summary or recorded elsewhere it was assumed that there was no event rather than missing data, except for ROP. All babies < 32 weeks gestation are nationally mandated to have a ROP screening examination at 4–6 weeks of age. Therefore, where this was not recorded on the data extract, we presumed it to be missing data. These babies were removed from the ROP analyses. For the analyses on ROP, BPD and BMF we also excluded babies who had died while in neonatal care. For morbidities of SBI and NEC, we included babies who had died while in neonatal care.

Sensitivity analyses

We undertook sensitivity analyses to explore data from prespecified subgroups of babies. These were defined in our statistical analysis plan and undertaken for mortality and morbidity outcomes.

a. Early transfers: to ensure that our results were not influenced disproportionately by babies who were born in a LNU but who were critically unwell and required clinical transfer of care to a NICU, we repeated the analyses after excluding (1) babies who were transferred in the first 24 hours, and (2) those transferred in the first 72 hours of life. We chose a 72-hour cut-off based on the NHS specifications for neonatal services, which recommend that critically ill babies in an LNU should be transferred to a NICU, or that their condition should be discussed with the neonatal team in a NICU for ongoing care after 48 hours of stabilisation.[7] We added a further 24 hours to accommodate the logistics of the actual transfer process. We defined 'early transfers' as babies who were transferred out and were receiving care in a location other than that into which the baby was born, in the first 24 hours, and up to the first 72 hours of life. We also excluded babies who had died in the first 24 and up to the first 72 hours from analyses. We considered the babies who were not transferred and had not died within this 72-hour time frame to be representative of those receiving early care in their respective units.
b. Singleton compared with multiple pregnancies: to account for maternity services colocated with a NICU being more likely to deal with complex multiple pregnancies, which carry a higher risk of neonatal mortality, we repeated our analyses excluding all babies born to mothers with multiple pregnancies.

Analysis independent of neonatal intensive care unit–local neonatal unit unit designation

To avoid overlooking higher-performing LNUs that were working as NICUs and vice versa, we undertook a further analysis comparing mortality outcomes for babies born and cared for in high-volume compared with low-volume neonatal units.[11] We defined high-volume units as above the uppermost quartile for number of intensive care bed-days offered to babies born at < 32 weeks gestation during the OPTI-PREM 5-year study period. Units below the uppermost quartile were defined as low-volume units.

Results

Summary statistics

From the NNRD data extraction of 29,842 preterm babies born at 27–31 weeks gestation and discharged from neonatal care between 1 January 2014 and 31 December 2018, a total of 18,847 babies were studied (*Figure 2*). Births outside of NICU and LNU, babies with known congenital anomalies (see *Appendix 1*, *Table 31*) and missing data were excluded (see *Report Supplementary Material 3*), resulting in 10,379 babies born in maternity services linked to NICU and 8468 to LNU. A comparison of this cohort to the group with missing data (n = 7438) is outlined in *Appendix 2*, *Table 32*. They were similar regarding gestational age, place of birth and mortality outcome. Our data compared favourably when we compared the birth statistics for the latter 3 years of our cohort with data reported to the Office for National Statistics of all very preterm babies born in England between 2016 and 2018 (see *Appendix 3*, *Table 33*).

Twice as many preterm babies born at 27 weeks gestation were born in maternity services colocated with NICU and admitted to NICU compared to LNU [*Table 1*: 1507 (14.5%) compared with 777 (9.2%)]. This difference decreased as gestational age in weeks increased, reaching equivalent numbers by preterm birth at 29 weeks, with higher numbers of births at 31 weeks gestation in LNU compared with NICU (34% compared with 28%). Preterm babies born and admitted into NICU were smaller in weight, had similar sex distribution, median Apgar scores at 5 minutes, receipt of antenatal steroids and admission temperatures compared to those preterm babies born and admitted to LNU. There was a higher proportion of mothers of mixed or ethnic minority groups, higher levels of social deprivation scores and higher caesarean section rates in mothers who delivered their preterm babies in maternity services colocated with NICU (*Table 1*). However, when defining the cohort against the median differential time of excess travel] [median (range) 3.91 (–130.36 to 74.11) minutes], the groups appeared to be balanced (standardised differences < 0.1) (*Table 2*). This was noted in all categories except IMD scores, which is an acceptable imbalance linked to urbanicity when using distance instruments.[72]

Mortality outcomes

There were 574 deaths (3.0%) while in NICU and LNU care, and a further 121 deaths (3.7% total mortality) in the first year of life after discharge from neonatal care. Babies admitted to NICU had a higher unadjusted mortality while receiving neonatal care (3.8% for NICU admission compared with 2.2% for LNU admission; $p < 0.001$) and higher

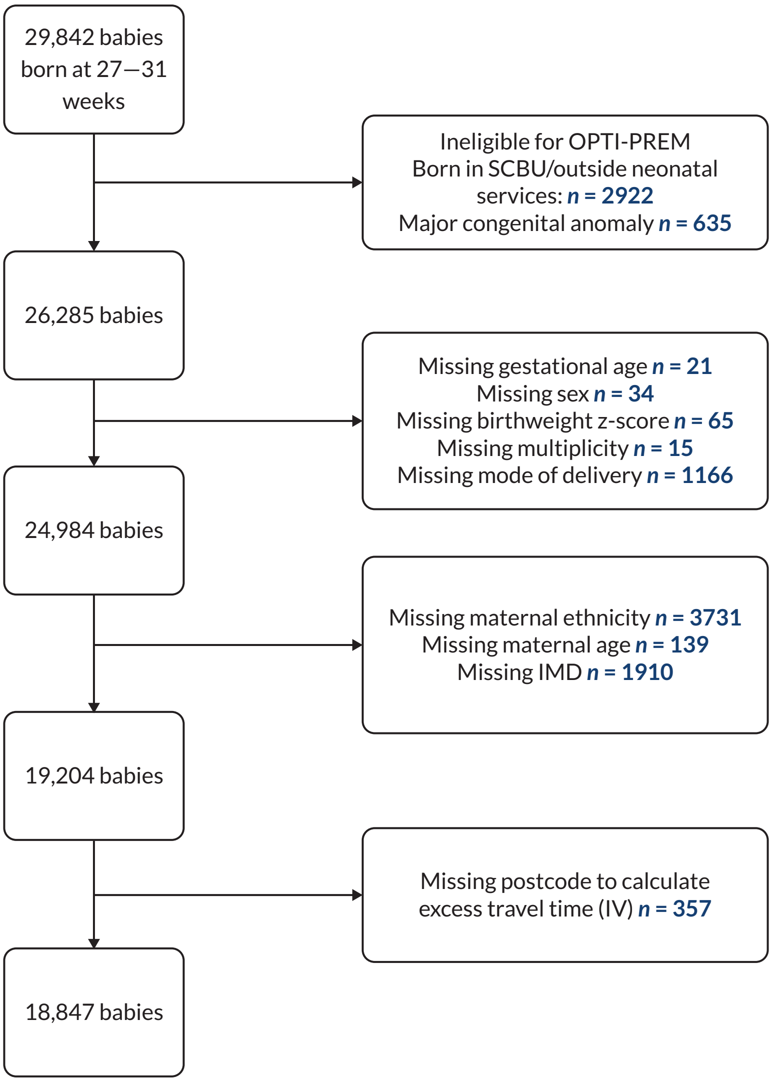

FIGURE 2 OPTI-PREM data study flow chart.

unadjusted infant mortality (4.5% for admissions to NICU and 2.7% for LNU admissions; $p < 0.001$; *Table 1*). When comparing neonatal characteristics by median differential travel time to a NICU, the covariates were balanced indicating similar covariate distribution of measured and potentially unmeasured confounders (see *Table 2*).

After adjusting for measured and unmeasured confounders, the mean difference for mortality between babies born in maternity services colocated with NICU compared with LNU while receiving specialised neonatal care was −0.001 (99% CI −0.011 to 0.010; $p = 0.842$), and for infant mortality −0.002 (99% CI −0.014 to 0.009; $p = 0.579$). Comparisons for both the overall group of babies born at 27–31 weeks gestation, and for each week of gestation, did not reveal significant differences (*Table 3*).

Sensitivity analyses

Early transfers

A total of 12,831 (68.1% of 18,847) babies received all their neonatal care in one unit (wholly owned). Of the 6016 babies that were transferred to another unit, 720 (12.0%) babies were transferred in the first 24 hours of life, and 1545 (25.6%) in the first 72 hours of life. One out of every two babies (49.7%) born at 27 weeks gestation were transferred between units while in neonatal care, of which 13.6% occurred in the first 72 hours of life. This was much higher when compared to babies born at 31 weeks gestation, where 22.7% were transferred overall, with 6.4% in the first 72 hours of life (see *Table 4*). Overall, there was a high rate (31.9%) of movement between units for this cohort (*Table 4*).

TABLE 1 Neonatal and maternal characteristics by place of birth (maternity unit attached to a NICU or a LNU) using WS1 cohort

	NICU (*n* = 10,379)		LNU (*n* = 8468)	
Neonatal characteristics				
Gestational age, n (%)				
27 weeks	1507	(14.5)	777	(9.2)
28 weeks	1773	(17.1)	1258	(14.9)
29 weeks	1885	(18.2)	1527	(18.0)
30 weeks	2348	(22.6)	2031	(24.0)
31 weeks	2866	(27.6)	2875	(34.0)
Birthweight (g), mean (SD)	1286	(342.5)	1356	(312.4)
Male sex, *n* (%)	5658	(54.5)	4659	(55.0)
Singleton, *n* (%)	7254	(69.9)	6318	(74.6)
Temperature on admission, mean (SD)	36.9	(0.6)	36.8	(0.6)
Missing[a]	100		70	
Apgar score at 5 minutes, median (10th, 90th centile)	9	(6 to 10)	9	(6 to 10)
Missing	667		557	
Antenatal steroids provided, n (%)	9538	(92.7)	7737	(92.0)
Missing	98		62	
Died in neonatal care, n (%)	391	(3.8)	183	(2.2)
27 weeks	120	(8.0)	48	(6.2)
28 weeks	115	(6.5)	57	(4.5)
29 weeks	53	(2.8)	36	(2.4)
30 weeks	41	(1.8)	23	(1.1)
31 weeks	62	(2.2)	19	(0.7)
Died in 1 year, n (%)	468	(4.5)	227	(2.7)
27 weeks	141	(9.4)	53	(6.8)
28 weeks	127	(7.2)	66	(5.3)
29 weeks	70	(3.7)	42	(2.8)
30 weeks	52	(2.2)	34	(1.7)
31 weeks	78	(2.7)	32	(1.1)
Died in neonatal unit (singletons)	300	(4.1)	156	(2.5)
Died in neonatal unit (multiples)	91	(2.9)	27	(1.3)
Died in 1 year (singletons)	353	(4.9)	183	(2.9)
Died in 1 year (multiples)	115	(3.7)	44	(2.1)
Maternal characteristics				
C-section, n (%)	7132	(68.7)	5625	(66.4)

TABLE 1 Neonatal and maternal characteristics by place of birth (maternity unit attached to a NICU or a LNU) using WS1 cohort (*continued*)

	NICU (*n* = 10,379)		LNU (*n* = 8468)	
Maternal ethnicity, n (%)				
White	7457	(71.8)	6338	(74.8)
Black	956	(9.2)	712	(8.4)
Asian	1532	(14.8)	1106	(13.1)
Mixed	210	(2.0)	149	(1.8)
Other	224	(2.2)	163	(1.9)
Maternal age, mean (SD)	31	(6.3)	31	(6.2)
Maternal quintiles of IMD, n (%)				
Least deprived 1st Q	1304	(12.6)	1210	(14.3)
2nd Q	1447	(13.9)	1318	(15.6)
3rd Q	1630	(15.7)	1677	(19.8)
4th Q	2246	(21.6)	2086	(24.6)
Most deprived 5th Q	3752	(36.2)	2177	(25.7)

C, caesarean; Q, quintile.
a Any temperature < 33 or > 39 °C was regarded as missing.

TABLE 2 Neonatal and maternal characteristics by median differential travel time to a NICU

	Differential travel time[a]				
	< 3.9 minutes (*n* = 9420)		≥ 3.9 minutes (*n* = 9427)		Standardised difference[b]
Neonatal characteristics					
Gestational age, n (%)					0.020
27 weeks	1115	(11.8)	1169	(12.4)	
28 weeks	1505	(16.0)	1523	(16.2)	
29 weeks	1718	(18.2)	1694	(18.0)	
30 weeks	2210	(23.5)	2169	(23.0)	
31 weeks	2872	(30.1)	2869	(30.4)	
Birthweight (g), mean (SD)	1320	332	1314	330	0.016
Male sex, *n* (%)	5146	(54.6)	5171	(54.9)	0.005
Singleton, *n* (%)	6821	(72.4)	6751	(71.6)	0.018
Temperature on admission, mean (SD)	36.9	(0.6)	36.8	(0.6)	0.102
Missing[a]	87		83		
Apgar score at 5 minutes, median (10th, 90th centile)	9	(6 to 10)	9	(6 to 10)	0.021

continued

TABLE 2 Neonatal and maternal characteristics by median differential travel time to a NICU (*continued*)

	Differential travel time[a]				
	< 3.9 minutes (*n* = 9420)		≥ 3.9 minutes (*n* = 9427)		Standardised difference[b]
Missing	617		607		
Antenatal steroids provided, n (%)	8577	(91.9)	8698	(93.0)	0.041
Missing	87		73		
Died in neonatal care, n (%)	288	(3.1)	286	(3.0)	0.001
27 weeks	80	(7.2)	88	(7.5)	0.014
28 weeks	83	(5.5)	89	(5.8)	0.014
29 weeks	43	(2.5)	46	(2.7)	0.013
30 weeks	35	(1.6)	29	(1.3)	0.021
31 weeks	47	(1.6)	34	(1.2)	0.038
Died in 1 year, n (%)	346	(3.7)	349	(3.7)	0.002
27 weeks	95	(8.5)	99	(8.5)	0.002
28 weeks	93	(6.2)	100	(6.6)	0.015
29 weeks	53	(3.1)	59	(3.5)	0.022
30 weeks	45	(2.0)	41	(1.9)	0.011
31 weeks	60	(2.1)	50	(1.7)	0.025
Died in neonatal unit (singletons)	227	(3.3)	229	(3.4)	0.004
Died in neonatal unit (multiples)	61	(2.4)	57	(2.1)	0.015
Died in 1 year (singletons)	269	(3.9)	267	(4.0)	0.001
Died in 1 year (multiples)	77	(3.0)	82	(3.1)	0.006
Maternal characteristics					
C-section, n (%)	6304	(66.9)	6453	(68.5)	0.033
Maternal ethnicity, n (%)					
White	6827	(72.5)	6968	(73.9)	0.070
Black	794	(8.4)	874	(9.3)	
Asian	1420	(15.1)	1218	(12.9)	
Mixed	192	(2.0)	167	(1.8)	
Other	187	(2.0)	200	(2.1)	
Maternal age, mean (SD)	30.7	(6.2)	31.0	(6.2)	−0.060
Maternal quintiles of IMD, n (%)					
Least deprived 1st Q	1091	(11.6)	1423	(15.1)	0.305
2nd Q	1242	(13.2)	1523	(16.2)	
3rd Q	1439	(15.3)	1868	(19.8)	
4th Q	2033	(21.6)	2299	(24.4)	
Most deprived 5th Q	3615	(38.4)	2314	(24.5)	

C, caesarean.
a Instrument used for this study, representing additional distance women would need to travel beyond nearest LNU to arrive at a hospital with NICU. Median differential travel time was 3.9 minutes.
b Absolute standardised difference of ≥ 0.10 generally indicates that covariates are imbalanced between groups.[71]

TABLE 3 Association between place of birth (maternity unit attached to a NICU or a LNU) and overall and gestational age-specific mortality while in neonatal care and at 1 year using an IV

	Number of cases	Sample size	NICU mean proportion (SE)[a]	LNU mean proportion (SE)[a]	Mean difference (99% CI)	*p*-value for difference
Died in neonatal unit						
Overall	574	18,847	0.030 (0.002)	0.031 (0.003)	−0.001 (−0.011 to 0.010)	0.842
27 weeks	168	2284	0.069 (0.008)	0.086 (0.021)	−0.017 (−0.081 to 0.048)	0.508
28 weeks	172	3031	0.052 (0.006)	0.068 (0.013)	−0.016 (−0.056 to 0.024)	0.302
29 weeks	89	3412	0.023 (0.004)	0.032 (0.007)	−0.009 (−0.031 to 0.014)	0.307
30 weeks	64	4379	0.014 (0.003)	0.016 (0.004)	−0.002 (−0.017 to 0.013)	0.734
31 weeks	81	5741	0.018 (0.003)	0.009 (0.002)	0.009 (−0.002 to 0.019)	0.028
Died at year one						
Overall	695	18,847	0.036 (0.002)	0.038 (0.003)	−0.002 (−0.014 to 0.009)	0.579
27 weeks	194	2284	0.083 (0.009)	0.089 (0.020)	−0.005 (−0.071 to 0.060)	0.836
28 weeks	193	3031	0.057 (0.006)	0.078 (0.013)	−0.021 (−0.062 to 0.021)	0.202
29 weeks	112	3412	0.029 (0.004)	0.040 (0.008)	−0.010 (−0.035 to 0.014)	0.269
30 weeks	86	4379	0.018 (0.003)	0.023 (0.005)	−0.005 (−0.023 to 0.013)	0.487
31 weeks	110	5741	0.022 (0.003)	0.015 (0.003)	0.007 (−0.006 to 0.019)	0.163

SE, standard error.
a Adjusted for gestational age (when analysing the overall cohort); sex; birthweight z-score; multiplicity; mode of delivery; maternal ethnicity; maternal age andIMD. Statistical significance was set at $p \leq 0.01$.

TABLE 4 Descriptive distribution of transfers between units within the OPTI-PREM cohort

Gestational age in weeks	Total births	Number transferred at 72 hours (%)	Number transferred at any time[a] (%)
27	2284	310 (13.6)	1136 (49.7)
28	3031	322 (10.6)	1208 (39.9)
29	3412	274 (8.0)	1127 (33.0)
30	4379	271 (6.2)	1239 (28.3)
31	5741	368 (6.4)	1306 (22.7)

a Babies who were transferred more than once were captured once on the counts.

We did not detect a significant difference in mortality during neonatal care and up to 1 year of age when sensitivity analyses were conducted excluding early transfers in the first 24 hours of life (mean difference 0.000; 99% CI −0.011 to 0.010; $p = 0.915$ while in neonatal care; mean difference −0.002; 99% CI −0.014 to 0.010; $p = 0.659$ for mortality up to the first year of life), and in the first 72 hours of life (mean difference 0.002; 99% CI −0.009 to 0.013; $p = 0.634$ for mortality while in neonatal care and mean difference 0.000; 99% CI –0.012 to 0.012; $p = 0.961$ for mortality up to 1 year of age). Similarly, when we considered the group who had either been transferred and/or had died in the first 24 hours, or in the first 72 hours of life, and excluded these from the analysis, we found no difference in mortality outcomes between NICU and LNU for our cohort.

Singleton compared with multiple pregnancies

There were 456 deaths while in neonatal care and a further 80 deaths after discharge up to the end of the first year of life (3.9%) in singleton babies ($n = 13,572$). There were 118 deaths while in neonatal care and a further 41 deaths (3.0%)

in the first year of life of babies born in multiple pregnancies (*n* = 5275) in the OPTI-PREM cohort. No effect was found when only singleton births were analysed while in neonatal care and in the first year of life. We were unable to replicate the analyses for multiple pregnancies as the sample size did not fit the model.

Analysis independent of NICU-LNU designation

High-volume units for intensive care days (IC days) were units in the uppermost quartile and offered between 11,647 and 8068 IC days to babies born at 27–31 weeks gestation over the 5-year period. This averaged to > 1614 IC days per year. Low-volume units were therefore those that offered ≤ 1614 IC days per year.

When comparing mortality outcomes for the OPTI-PREM cohort, between high- and low-volume units based on the uppermost quartile of IC days versus lower three quartiles of ICU days provided, and independent of NICU and LNU designation, no significant differences were observed (*Table 5*).

Morbidity outcomes

Severe brain injury was documented in 735 (3.9%) of the 18,847 babies studied, ROP in 297 (1.65%) of 17,930 babies, BPD in 1819 (10.0%) of 18,273, NEC in 490 (2.6%) of 18,847. 10,220 (55.9%) of 18,273 babies received BMF at discharge from neonatal care.

Severe/serious brain injury

There was a significant difference with a higher proportion of SBI in babies born and cared for in a LNU (mean difference −0.011; 99% CI −0.022 to −0.001; $p = 0.007$, *Table 6*). The highest mean difference in gestation-specific SBI was in the group of babies born at 27 weeks gestation (−0.040). 14.5% (45/310) of preterm babies born at 27 weeks gestation and transferred in the first 72 hours of life had SBI, compared to 3.5% (13/368) of those born at 31 weeks gestation and transferred in the first 72 hours of life.

TABLE 5 Association between place of birth (high-volume IC days vs. low-volume IC days) and overall and gestational age-specific mortality while in neonatal care and at 1 year using IV model (*n* = 18,781[a])

	High-volume mean proportion	SE	Low-volume mean proportion	SE	Difference in proportion	99% CI	*p*-value for difference
Died in NNU							
Overall	0.022	0.005	0.036	0.006	−0.016	−0.049 to 0.016	0.200
27 weeks	0.038	0.013	0.121	0.045	−0.101	−0.309 to 0.108	0.213
28 weeks	0.028	0.010	0.086	0.025	−0.072	−0.203 to 0.059	0.155
29 weeks	0.014	0.006	0.047	0.031	−0.043	−0.196 to 0.110	0.466
30 weeks	0.009	0.003	0.020	0.006	−0.013	−0.045 to 0.019	0.298
31 weeks	0.021	0.009	0.012	0.002	0.007	−0.014 to 0.029	0.365
Died in 1 year							
Overall	0.024	0.005	0.046	0.006	−0.026	−0.062 to 0.010	0.067
27 weeks	0.047	0.021	0.124	0.045	−0.089	−0.313 to 0.135	0.305
28 weeks	0.028	0.008	0.103	0.025	−0.096	−0.223 to 0.031	0.052
29 weeks	0.017	0.006	0.059	0.030	−0.056	−0.200 to 0.088	0.320
30 weeks	0.012	0.005	0.026	0.008	−0.018	−0.061 to 0.025	0.290
31 weeks	0.020	0.009	0.019	0.003	0.001	−0.026 to 0.029	0.919

IC days, intensive care days; SE, standard error.
a *n* = 18,781 due to small number of missing units with number of care days. Low/high-volume neonatal units were defined by the number of intensive care days provided for babies born < 32 weeks gestation during the OPTI-PREM study. Those above the upper quartile for provision of IC days per year were classed as high volume (> 1614 IC days per year) and those below the upper quartile (< 1614 IC days/year) being classified as low volume units.

TABLE 6 Association between place of birth (maternity unit attached to a NICU or a LNU) and key overall and gestational age-specific secondary outcomes using IV model

	NICU mean (SE) proportion	LNU mean (SE) proportion	Difference in proportion	Lower 99% CI	Upper 99% CI	*p*-value for difference
SBI						
Overall	0.034 (0.002)	0.046 (0.003)	−0.011	−0.022	−0.001	0.007[a]
27 weeks	0.077 (0.008)	0.119 (0.020)	−0.040	−0.096	0.017	0.071
28 weeks	0.051 (0.006)	0.070 (0.009)	−0.019	−0.051	0.013	0.123
29 weeks	0.037 (0.005)	0.051 (0.007)	−0.014	−0.039	0.011	0.161
30 weeks	0.022 (0.003)	0.032 (0.005)	−0.010	−0.029	0.008	0.160
31 weeks	0.015 (0.003)	0.016 (0.003)	0.000	−0.013	0.013	0.986
BPD						
Overall	0.107 (0.004)	0.089 (0.004)	0.018	0.001	0.035	0.006[a]
27 weeks	0.349 (0.017)	0.270 (0.027)	0.080	−0.023	0.183	0.045
28 weeks	0.222 (0.014)	0.172 (0.016)	0.051	−0.018	0.119	0.056
29 weeks	0.103 (0.009)	0.089 (0.011)	0.013	−0.031	0.058	0.439
30 weeks	0.044 (0.006)	0.031 (0.005)	0.013	−0.011	0.038	0.169
31 weeks	0.012 (0.002)	0.017 (0.003)	−0.005	−0.015	0.006	0.227
ROP Stage 3+						
Overall	0.017 (0.002)	0.016 (0.002)	0.002	−0.007	0.010	0.610
27 weeks	0.064 (0.009)	0.050 (0.013)	0.015	−0.040	0.070	0.485
28 weeks	0.025 (0.006)	0.021 (0.008)	0.003	−0.028	0.035	0.777
29 weeks	0.011 (0.003)	0.013 (0.004)	−0.002	−0.017	0.014	0.785
30 weeks	0.013 (0.004)	0.008 (0.002)	0.005	−0.010	0.020	0.378
31 weeks	0.003 (0.001)	0.006 (0.002)	−0.003	−0.008	0.003	0.216
NEC						
Overall	0.026 (0.002)	0.026 (0.003)	0.000	−0.011q	0.011	0.957
27 weeks	0.061 (0.008)	0.045 (0.011)	0.018	−0.031	0.066	0.346
28 weeks	0.050 (0.008)	0.046 (0.009)	0.004	−0.033	0.042	0.771
29 weeks	0.020 (0.004)	0.031 (0.008)	−0.010	−0.038	0.018	0.337
30 weeks	0.016 (0.004)	0.017 (0.005)	−0.001	−0.019	0.018	0.904
31 weeks	0.012 (0.003)	0.010 (0.002)	0.001	−0.010	0.013	0.763
Any morbidity[b] or died						
Overall	0.184 (0.004)	0.178 (0.006)	0.006	−0.016	0.028	0.501
27 weeks	0.475 (0.017)	0.448 (0.029)	0.027	−0.080	0.133	0.521
28 weeks	0.338 (0.015)	0.315 (0.019)	0.023	−0.054	0.100	0.446
29 weeks	0.174 (0.011)	0.191 (0.014)	−0.016	−0.072	0.040	0.450

continued

TABLE 6 Association between place of birth (maternity unit attached to a NICU or a LNU) and key overall and gestational age-specific secondary outcomes using instrumental variable model (*continued*)

	NICU mean (SE) proportion	LNU mean (SE) proportion	Difference in proportion	Lower 99% CI	Upper 99% CI	*p*-value for difference
30 weeks	0.100 (0.008)	0.088 (0.008)	0.012	−0.025	0.049	0.407
31 weeks	0.054 (0.005)	0.056 (0.006)	−0.002	−0.024	0.021	0.851
Breast milk at discharge						
Overall	0.559 (0.006)	0.558 (0.007)	0.001	−0.028	0.031	0.903
27 weeks	0.476 (0.018)	0.511 (0.031)	−0.035	−0.148	0.079	0.428
28 weeks	0.529 (0.016)	0.534 (0.020)	−0.005	−0.085	0.075	0.865
29 weeks	0.555 (0.015)	0.516 (0.017)	0.038	−0.033	0.110	0.164
30 weeks	0.587 (0.013)	0.565 (0.014)	0.022	−0.037	0.081	0.335
31 weeks	0.587 (0.012)	0.607 (0.011)	−0.020	−0.069	0.029	0.294

a Statistically significant at $p < 0.01$.
b ROP or oxygen dependency or SBI or NEC; SE, standard error.

Statistical significance was not maintained after exclusion of early postnatal transfers for the whole group (early transfers up to 72 hours $n = 1545$; mean difference −0.002, 99% CI −0.013 to 0.08; $p = 0.554$), and then separately, after exclusion of all babies born at 27 weeks gestation (mean difference −0.008; 99% CI −0.019 to 0.002; $p = 0.037$) (*Table 7*).

For babies born at 27 weeks gestation, birth in maternity services colocated with NICU (tertiary neonatal unit) reduced the risk of SBI from 11.9% to 7.7%, a reduction of 4.2%. This translated into a number needed to treat (NNT) of 25 (99% CI 10 to 59) indicating that 25 babies at 27 weeks gestation would need to be delivered in a NICU, rather than a LNU to prevent one SBI.

High-versus low-volume analysis

We analysed SBI by high-versus low-volume units (using the IV approach and adjusting for confounders), defined by the uppermost quartile for IC care days provided compared to the lower three quartiles (see *Report Supplementary Material 4*). For the SBI analysis, high-volume units were defined as those offering ≥ 8304 IC days/5 years, or approximately > 1614 IC days/year, and low-volume units < 8304 days/5 years or ≤ 1614 IC days/year. There was a significant difference with a lower proportion of SBI in babies born and cared for in high-volume units compared to low-volume units (mean difference −0.065; 99% CI −0.121 to −0.009; $p = 0.003$). For babies born at 27 weeks gestation, birth in a high-volume unit reduced the risk of SBI from 0.242 to 0.028, a mean difference of 0.289 (99% CI 0.035 to 0.542; $p = 0.003$). Here the NNT for 27 weeks was 4 (99% CI 2 to 29), indicating that four babies at 27 weeks gestation would need to be delivered in a high-volume unit, to prevent one SBI.

Statistical significance was lost after exclusion of early postnatal transfers up to 72 hours for the whole group (mean difference −0.0423; 99% CI −0.093 to 0.008; $p = 0.029$) and then separately, after exclusion of all babies born at 27 weeks gestation (mean difference −0.045; 99% CI −0.096 to 0.005; $p = 0.019$). Four thousand five hundred and ninety-seven babies were in units considered high volume by the above definition; these units were all NICU (see *Report Supplementary Material 4*).

We further analysed high- versus low-volume units comparing the upper three quartiles for IC days to the lowermost quartile for IC days provided by units per year. Against this definition, high-volume units were those offering ≥ 2197 IC days/5 years or approximately ≥ 440 IC days/year and low-volume units < 2197 days/5 years or < 440 IC days/year. There were no significant differences in SBI rates (mean difference −0.010; 99% CI −0.026 to 0.006; $p = 0.115$) (see

TABLE 7 Association between place of birth (maternity unit attached to a NICU or a LNU) and key secondary outcomes using IV model

	Number of cases	Sample size	NICU mean proportion (SE)	LNU mean proportion (SE)	Mean difference (99% CI)	*p*-value for difference
Any morbidity[a] or died	3407	18,847	0.184 (0.004)	0.178 (0.006)	0.006 (−0.016 to 0.028)	0.501
ROP Stage 3+	297	17,930	0.017 (0.002)	0.016 (0.002)	0.002 (−0.007 to 0.010)	0.610
BPD	1819	18,273	0.107 (0.004)	0.089 (0.004)	0.018 (0.001 to 0.035)	0.006
NEC	490	18,847	0.026 (0.002)	0.026 (0.003)	0.000 (−0.011 to 0.011)	0.957
SBI	735	18,847	0.034 (0.002)	0.045 (0.003)	−0.011 (−0.022 to −0.001)	0.007
BMF	10,220	18,273	0.559 (0.006)	0.558 (0.007)	0.001 (−0.028 to 0.031)	0.903
Excluding babies born at 27 weeks						
Any morbidity[a] or died	2344	16,563	0.143 (0.004)	0.140 (0.005)	0.003 (−0.018 to 0.024)	0.706
ROP Stage 3+	174	15,891	0.011 (0.002)	0.011 (0.002)	0.001 (−0.007 to 0.008)	0.825
BPD	1137	16,157	0.075 (0.003)	0.064 (0.004)	0.011 (−0.004 to 0.027)	0.065
NEC	363	16,563	0.021 (0.002)	0.023 (0.003)	−0.002 (−0.012 to 0.009)	0.684
SBI	529	16,563	0.028 (0.002)	0.037 (0.003)	−0.008 (−0.019 to 0.002)	0.037
BMF	9185	16,157	0.570 (0.007)	0.564 (0.007)	0.005 (−0.025 to 0.036)	0.657

SE, standard error.
a ROP or BPD or SBI or NEC.

Note
Babies may have more than one morbidity and so may appear as a case in multiple analyses. ROP excludes 574 babies who died and 343 missing ROP records; BPD excludes 574 babies who died; BMF excludes 574 babies who died.

Report Supplementary Material 4) between high- and low-volume units using this definition. Here 13,969 babies were in units considered high-volume units (comprising both NICU and LNU), and 4812 in low-volume units (comprising only LNU) (see *Report Supplementary Material 4*).

Bronchopulmonary dysplasia

The rate of BPD was higher in the overall group born into maternity services colocated with NICU (mean difference 0.018; 99% CI 0.001 to 0.035; $p = 0.006$ workstream 1, *Table 6*). This significance remained after excluding early transfers at 24 and up to 72 hours of life (mean difference for early transfers up to 72 hours was 0.029; 99% CI 0.011 to 0.047; $p < 0.001$). The highest mean difference in gestation-specific BPD was in the group of babies born at 27 weeks gestation (−0.080). When preterm babies born at 27 weeks gestation were excluded from the overall BPD analyses, the significant difference seen in overall BPD was lost (mean difference 0.011; 99% CI −0.004 to 0.027; $p = 0.065$).

There was no effect of place of birth on ROP, NEC or BMF. For NEC, ROP, BMF and composite outcomes, we did not detect a statistical difference overall or on analysis at each week of gestational age between babies born into maternity services colocated with NICU compared with LNU, even after exclusion of babies transferred within 24 and 72 hours after birth. Similarly, there was no significant difference when analysing only singleton births.

Discussion

Using robust IV analysis, we found for preterm babies born at 27–31 weeks gestation in England, that there was no survival advantage for birth in NICU (tertiary) compared with LNU (non-tertiary) settings, either during neonatal care or in the first year of life. However, there was a higher proportion of SBI in those babies born in maternity services colocated with LNU. We identified that these observations were driven by babies born at 27 weeks and those transferred out of LNU in the first 72 hours of life. To prevent one case of SBI, 25 babies would need to be cared for in NICU instead of LNU at this gestation.

When we investigated the volume of work undertaken by units, we found that units (which turned out to be all NICU) providing > 1614 IC days per year for babies born < 32 weeks gestation were associated with significantly lower SBI. Here, to prevent one case of SBI, four babies would need to be cared for in a high-volume NICU instead of other units at 27 weeks gestation.

Based on current practices, care for babies born at 28–31 weeks gestation in England in LNU appears to be equitable to that of NICU, even when transfers are excluded. Our findings suggest therefore that the safe threshold for care in either LNU or NICU for very preterm births in England is 28 weeks gestation. This finding has important implications for policy-makers considering optimising health service delivery for preterm babies in England. It provides scientific evidence to support implementation of the 2023 NHS 3-year delivery plan for maternity and neonates.[73]

Findings in context

While we identified a higher proportion of SBI in babies born at LNU and postnatal transfer, we cannot assign causality of the SBI entirely to the transfer process itself. Determining the contributions to SBI from 1) whether these babies were predisposed to this for reasons associated with their degree of illness, 2) the care received in LNU, or 3) the postnatal transfer process is not possible from our data, nor from other studies that have identified a higher likelihood of SBI in those very preterm babies transferred postnatally. Regardless, these observations are concerning, and together suggest that care for anticipated preterm births at 27 weeks gestation should be redirected to maternity services colocated with NICU in the antenatal period.

Severe brain injury in preterm babies can be associated with neurological findings ranging from mild developmental delay to severe cerebral palsy. The short- and long-term impact for preterm babies and their families,[74] and in terms of neurological, psychological, educational and economic cost[75–84] to society is substantial. If we can prevent one preterm baby born at 27 weeks gestation having SBI, the cost savings to the NHS, to babies, families and society would be substantial, considering the intensity of healthcare support required and high healthcare costs for cerebral palsy,[85,86] a known outcome following SBI in preterm births.

The observation of a higher proportion of SBI in postnatal transfers in our study adds to growing evidence of the risks for very preterm babies being born in the wrong place, and postnatally transferred to tertiary centres. In a study of 17,577 preterm births in England, Helenius *et al.*[87] identified an increased risk of SBI in upward transfers in the first 48 hours of life. In a study of very preterm babies born at < 32 weeks in Western Australia, Davis *et al.* noted a higher rate of combined brain injury (10.7% compared with 6.0%) in outborn compared with inborn babies. In OPTI-PREM, we were unable to delineate the reasons for transfer, that is whether the early transfers in our LNU cohort represented (a) upward transfers only, from LNU to NICU for a higher intensity of care, or (b) as dictated by local protocol or included (c) transfers for capacity reasons.[87,88]

During the period of the study, a few neonatal operational delivery networks encouraged antenatal transfer of mothers expected to deliver at 27–28 weeks gestation to maternity services colocated with NICU, or postnatal transfer to NICU. National recommendations for anticipated multiple births at < 28 weeks were to triage mothers to maternity services colocated with NICU,[7,14] and for babies requiring > 48 hours of intensive care support in a LNU to be discussed with teams at NICU for potential postnatal transfer and care in NICU.[7] These factors partly explain the observation of almost twice as many babies born at 27–28 weeks being born in maternity services colocated with NICU compared to LNU and may have masked any potential negative effect that birth in maternity services colocated with LNU may have held. We were unable to identify in utero transfers within the OPTI-PREM cohort data set, to adjust for this observation.

Strengths and limitations

A major strength of this study is its use of large-scale, national, operational data, analysing over a million daily patient records, utilising a robust IV to address unmeasured confounders, while findings are supported by sensitivity analyses.

The alternative of a prospective randomised controlled study in this cohort would be unethical, costly and not feasible. We were unable to study four major maternal medical confounders (pregnancy induced hypertension, diabetes, chorioamnionitis and multiple pregnancies compromised by twin-to-twin transfusion) because of incomplete recording of maternal details (see *Chapter 6*) on the neonatal database. Our adjustments relied on key measured confounders including indices of multiple deprivation (as most NICU are historically located in areas of higher social deprivation in England), sensitivity analyses for transfers and multiple births. We used a robust IV approach to account for the unmeasured confounders of fetal and maternal illness that could have resulted in a higher proportion of ill preterm babies being born in NICU compared with LNU by virtue of being redirected there antenatally or in labour. It is reassuring that on utility of the median excess travel time to describe the covariates, the groups appeared balanced, indicating similar covariate distribution of measured and (potentially) unmeasured confounders. We excluded a high number of babies due to incomplete data, but sensitivity analyses were reassuring, in identifying that the cohort excluded due to missing data was similar demographically and in clinical condition at birth (Apgar at 5 minutes, and admission temperature) to the cohort that was finally studied. We also excluded babies transferred in the first 24 hours and those that had died in the first 24 hours to account for the inadvertent baby born too ill, which may have biased our assessments. A further strength of the study is capturing mortality outcomes to 1 year through linkage with NHS Digital Hospital Episode Statistics for mortality. We did not use Apgar scores or neonatal clinical risk index for babies scores in the adjustments as we considered these an effect of care related to place of birth.

Deaths in the delivery suite could not be studied because of incomplete entries on the neonatal electronic records; linking NNRD neonatal unit admission data with our 20 existing maternity databases was not feasible during the study period. There is also the potential for data quality to be reduced as it relied on routinely collected EPR data. Further limitations are described in *Risk of bias of estimated treatment effect in primary and secondary outcomes*.

We identified a significant association with BPD in those born in maternity services colocated with NICU. This appeared to be intrinsic to NICU, not due to early postnatal transfers, and contributed to by those born at 27 weeks gestation. In comparison to SBI, we considered this a less impactful observation, and one that could be potentially influenced by variations in care processes between units over the period of the study, as well as by the indirect impact of social deprivation. Further clinical evaluation and qualitative work is required to understand the differences in quality of neonatal care provided around weaning from oxygen, and BPD.

Risk of bias of estimated treatment effect in primary and secondary outcomes

Due to the unpredictability of preterm birth, a randomised clinical trial format could not be utilised to answer the research questions that were being explored by OPTI-PREM. As a non-randomised study, the project is subject to the following biases:

Confounding bias

Limited knowledge on known maternal confounders that could affect treatment effect

We had limited data on some maternal comorbidities which may have influenced presentation and care in maternity care in centres colocated with NICU, and therefore influenced the degree of illness in the baby at birth, and subsequent outcomes. For example, there were 10,736 (38.1%) missing entries for maternal diabetes, 10,460 (37.1%) missing entries for maternal hypertension, and 10,595 (37.6%) for maternal infection. As a result, our matching exercise failed and the use of an IV approach to account for unmeasured and available measured confounders was employed primarily. IV methodology is subject to limitations, but we have mitigated against these by using a strong instrument, and also placing the results of our study in the current context and previous evidence available in preterm and critical care research, and not simply in isolation.[72,89]

Addressing maternal confounders through sensitivity analyses and adjusting for measured confounders

We performed sensitivity analyses accounting for multiple pregnancies (and twin-to-twin transfusions) which could have been redirected to NICU for antenatal care, and in whom outcomes may be more adverse between NICU and

LNU. We adjusted for severe intra-uterine growth restriction, which is a manifestation of degree of maternal and fetal illness, and therefore may be different between babies born and cared for in NICU and LNU by using a birthweight z-score. We did not account for differences in degree of illness of baby at birth by using the Apgar score in our adjustments as we considered this to be a measure of the care provided by teams at resuscitation in LNU and NICU, which is what the project was intending to explore.

Unknown confounders

The use of the IV method also addressed unknown unmeasured confounders that could have skewed babies born in NICU having worse outcome by virtue of other maternal and fetal comorbidities, and other factors related to NICU and LNU. We excluded babies with known congenital anomalies (see *Appendix 1*, *Table 31*) to further reduce a treatment effect bias that could have arisen from the redirection of expectant mothers with major fetal congenital anomalies to highly specialised fetal medicine units, which are colocated with NICU in England.

Differences in IMD distribution between groups were still observed across the IV instrument. It is common and is recognised that the use of distance measures (excess travel time) as instrument result in ethnicity and deprivation imbalances.[90] In our study, we believe that this reflects the current geographic distribution of NICU (more socially deprived areas) and LNU.

Selection bias

This is low, as all babies born between the study period were included in the analysis, except for data from one unit, and 10 babies, whose parents declined consent. We could not determine exact number of babies that were excluded in the single unit that opted out of OPTI-PREM, which was classified as a LNU during the study period. On average 64 babies per year were cared for in LNU (see *Chapter 2*), which means that for the cohort ~1% of the sample was not selected (64 babies per year × 5 years).

However, we lost a large component of the sample to use our statistical methods (IV). When we compared maternal/baby characteristics of the final sample versus the original, they were broadly similar.

Our study was designed only to compare outcomes in those that survived to receive neonatal care and excluded deaths in the delivery suite or outside of hospital. This could have been influenced by the decision to provide sustaining life support or resuscitation support in LNU versus NICU. However, for babies born at 27–31 weeks gestation, this is clinically less of an issue as all babies are required to be offered care, unlike those born at 22–23 weeks gestation, where the decision on providing life sustaining support can be varied based on place of birth.[91–95]

Information bias

We consider this bias to be low, as the information on place of birth was always present, and the primary outcome of mortality was noted for all babies as they all required a discharge summary from the neonatal EPR, and we used national statistics for mortality up to a year.

For our secondary outcomes, we were limited by accuracy of data entry in the routinely collected EPRs. We mitigated against this by searching the database using information located in more than one field (e.g. for the definition of NEC), to derive our definitions.

Reporting bias

Our project report aligns with the published protocol,[1] in which we meet the set objective. The risk for this is low.

Summary points from OPTI-PREM clinical outcomes study, workstream 1

What was already known prior to the study

- Care for extreme preterm births ≤ 26 weeks gestation offers a survival advantage and morbidity advantage if born in maternity services colocated with NICU and cared for in NICU.

- There is no evidence to support best place of birth and early care for the next most vulnerable group, that is very preterm babies born at 27–31 weeks gestation. We do not know if there is a threshold below which care offers survival and morbidity advantages in NICU or vice versa.

What the OPTI-PREM study adds

- There is no survival advantage for birth and early care in NICU compared with LNU for babies born at 27–31 weeks gestation in England.
- Babies born at 27 weeks gestation, and who were transferred out of LNU in the first 72 hours of life, were more likely to have SBI.
- Therefore, in England the threshold for safe birth and early care in neonatal units in either NICU or LNU (perhaps closer to home) is 28 weeks.
- We calculated that 25 babies at 27 weeks gestation would need to be delivered in a NICU, to prevent one SBI.
- Our secondary calculation was that four babies at 27 weeks gestation would need to be delivered in a high-volume unit (> 1614 ICU care days per year) to prevent one SBI.

How the OPTI-PREM study may potentially influence policy

(See *Chapters 9* and *10*).

- Review of resources to support antenatal triage of all anticipated preterm births at 27 weeks gestation in maternity services colocated with NICU.
- Clinical judgement for all inadvertent births at 27 weeks gestation in maternity services colocated with LNU, regarding transfers.
- These will need to be risk-assessed for clinical benefit against risk of SBI ± parental stress.
- Capacity transfers, or routine protocol-driven transfers, in well preterm babies born at 27 weeks out of neonatal units may not represent optimal practice.

Chapter 5 Workstream 2: a clinical quality of care study

Addressing differences that may impact on neonatal outcomes, independent of unit designation as NICU and LNU.

Introduction

In *Chapter 4* we explored whether unit designation, that is NICU compared with LNU, impacted on outcomes for very preterm babies. In this chapter, we explore whether unit designation matters at all. We investigate whether differences in the quality of clinical care provided influence outcome, independent of unit designation as LNU or NICU.

Aim

To explore the relationship between quality of early neonatal care and neonatal outcomes, for babies born at 27–31 weeks gestation, in England.

Objectives

i. to choose the most appropriate measures of quality of care to study, and
ii. to explore a relationship between these measures of quality of care and neonatal outcomes, for preterm babies born at 27–31 weeks gestation.

Method

Study design

We conducted a retrospective analysis exploring the relationship between quality of care provided in neonatal units (independent of unit designation) and neonatal outcomes for babies born at 27–31 weeks gestation in England. We explored quality of care by studying the neonatal unit adherence structural and care process measures of quality of care.[62] The measures chosen were based on the hierarchy of scientific evidence available and/or nationally considered best practice. Our hypothesis was that units that paid attention to this would have better outcomes.

The study design was selected following an initial unsuccessful attempt to engage NICU and LNU in a questionnaire-based survey on unit practices. This survey was conducted between July and November 2018; only seven of 20 units (10 NICU and 10 LNU) responded. As a result of the poor response, we focused on other measures of quality of care, as described below. Details of the survey questionnaire can be obtained from the chief investigator, on request.

Choosing the measures of quality of care

a. We reviewed
   i. measures within the National Neonatal Audit Programme (NNAP) (prespecified targets or benchmarking exercises set for 2018)[96] (see *Report Supplementary Material 5*) and
   ii. evidence-based and national consensus measures in early preterm care, from data captured in the OPTI-PREM neonatal data set (hereafter called 'OPTI-PREM data set measures').[97–103]

We categorised units by assessing how well they adhered to these measures, and the degree of data completion for NNAP measures. We considered units that adhered best, and had the most complete data sets, to be 'higher performing', and those that did not, to be 'lower performing'. We utilised quartiles within the data set to categorise these.

b. We compared two defined outcomes captured in the OPTI-PREM data set, in units that were high or lower performing, to explore a relationship between differences in measures of quality of care between these units, and neonatal outcomes.

Rationale for selection of the measures

Rationale for using NNAP measures: the NNAP[96] is a national clinical audit. It is run on behalf of the NHS, by The RCPCH, and is commissioned by the Healthcare Quality Improvement Partnership. It sets audit measures which are either prespecified standards or benchmarking exercises. These are based on published evidence or consensus for best practice in neonatology. A publicly available annual report provides comparison charts for each neonatal unit's adherence with each measure. Part of the purpose of the NNAP is to identify outliers, which can result in regulatory action from the Care Quality Commission, if adherence to a locally produced action plan is poor. As a result, NNAP audit measures have become standards defining good quality of neonatal health care. Adherence to national guidance in the form of NNAP audit measures reflects organisational culture to improve outcomes and deliver good patient care. This involves fulfilling the requirements of each measure, and sufficient data completion to allow accurate monitoring. Because these measures were to be used as surrogate markers for neonatal unit quality of care, the data did not need to be specific to babies born at 27–31 weeks gestation.

Rationale for using non NNAP measures: these were measures extracted from the OPTI-PREM neonatal data set. We selected variables relating to early preterm care, due to increasing recognition of the importance of these in optimising outcomes for preterm babies.[97–103]

Data source

i. For NNAP measures we downloaded publicly available NNAP data for 2018 from the RCPCH website: https://nnap.rcpch.ac.uk/annual-reports.aspx.
ii. OPTI-PREM data set measures and outcomes were extracted from the OPTI-PREM data set described in workstream 1. We used 2018 data. We limited this to 1 year, to minimise the effect of variation in structure and care process measures through change of leadership, protocols, staff, etc.

Data variables

i. NNAP: We utilised the audit measures that were captured by NNAP in 2018 (see *Report Supplementary Material 5*).
ii. OPTI-PREM data set measures: We selected six variables (measures) relating to early preterm care to study.
    a. receipt of any antenatal steroids
    b. normothermia within an hour of neonatal admission
    c. percentage receiving non-invasive ventilation (NIV), of all babies receiving respiratory support) on day 1 of life
    d. percentage requiring intensive care support on day 1 of life, receiving 1 : 1 nursing support
    e. receipt of mother's breast milk on day 1 of life
    f. delayed cord clamping at birth.

Data completion for National Neonatal Audit Programme measures

We excluded measures which had no missing data (minimising inappropriate separation of mother and term, and late to moderate preterm babies, nurse staffing). We also excluded measures where the percentage of missing data was < 10% (antenatal steroids, BPD, breastmilk feeding at discharge home, promoting normal temperature on admission for very preterm babies), and for the remaining included measures, we only counted units as having missing data if their percentage of missing data was ≥ 10%. Failure to exclude these measures/units would have increased the volatility of any analysis, where missing data for a very small number of patients (even one) could impact whether units are in the category of having missing data versus not having missing data. Bloodstream infection and central line associated bloodstream infection were excluded because information on degree of missing data by neonatal unit was not available.

This left a final list of NNAP audit measures to be used to categorise units according to data completion:

i. Antenatal magnesium sulphate.
ii. Parent consultation within 24 hours of admission.
iii. Parental presence at consultant ward rounds.
iv. On-time screening for ROP.
v. NEC.
vi. Follow-up at 2 years of age.

To define unit adherence through data completion, and since there were no standards for acceptable levels of data completion, we adopted the following approach:

We selected those above the uppermost quartile for missing data versus those below the uppermost quartiles against which to assess outcomes. We excluded measures for those variables where there was mainly 100% data completion as a 'top quartile' for data completion was not possible to define here.

Figure 3 outlines the cohort for WS2. A schematic showing demographic parameters chosen for inclusion in workstream 2 analysis is outlined in *Appendix 4*, *Figure 11*.

Inclusion and exclusion criteria

For NNAP data, we selected only units classified as NICU and LNU. We excluded:

i. units with data for < 10 patients
ii. units who had requested the NNAP not to make their data publicly available
iii. variables related to outcome, when assessing adherence to NNAP audit measures[99]
iv. variables with > 10% levels of missing data, when assessing adherence to NNAP audit measures
v. variables with unknown levels of missing data
vi. variables with all units having > 90% data completion when assessing data completion for NNAP audit measures.

For OPTI-PREM data set measures, we excluded:

i. babies not born in a NICU or LNU
ii. babies discharged in 2014–7
iii. babies with data other than from their first episode of care
iv. babies without a recorded gestational age
v. babies born in units with < 10 babies born at 27–31 weeks gestation and outlier units for data completion
vi. babies with significant congenital anomalies (see *Appendix 1*, *Table 31*) (for multivariate analysis only)
vii. variables with > 10% missing data.

Statistical methods

After categorising units by measures of quality of care, and defining quartiles, we compared the demographic neonatal and unit profiles of our comparator groups. This was to identify significant differences that could introduce bias or confounding when conducting analyses on associations with outcomes. To assess whether there were significant differences between the patient populations, chi-squared, Fisher's exact tests and weighted two sample *t*-tests were utilised as appropriate.

Multivariate analyses were conducted to explore associations between adherence with OPTI-PREM data set measures or NNAP audit measures, and outcomes of mortality and LOS while in neonatal care. These analyses were conducted for the cohort (27–31 weeks gestation) and not by individual weeks gestation. To adjust for known, measured confounders the following variables were included in the multivariate analysis: gestational age, birthweight, gender, multiplicity of pregnancy, IMD score, resuscitation at birth requiring adrenaline or cardiac massage and place of birth. In the analyses involving the binary outcome variable, mortality, logistic regression was used, and for the continuous outcome variable, LOS, linear regression was used. For these regression analyses, the clustering of babies was not considered in the analysis.

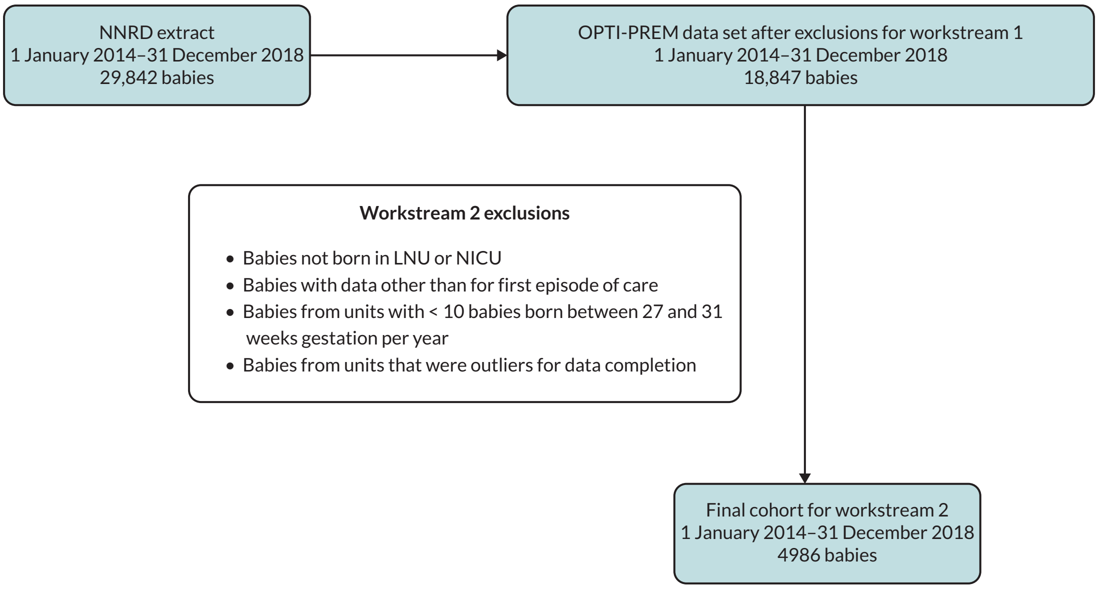

FIGURE 3 Flow diagram outlining the cohort for workstream 2.

This workstream was supported by a clinical researcher undertaking a PhD with the Department of Health Sciences at the University of Leicester. As a result of the COVID-19 pandemic, and his return to support clinical care, the anticipated analyses on other key outcomes, as undertaken in workstream 1 (ROP, SBI, NEC, BPD and BMF) could not be addressed. For the same reason, multivariate analysis was undertaken for unit adherence, and univariate analysis only, for data completion.

Choosing outcome measures

We chose two outcome measures (both of which had 100% data completion):

- Mortality (pre-discharge)
- Length of stay (LOS)

We had initially planned to also interrogate major morbidity outcomes, but due to the impact of the COVID pandemic, this was not possible within the time frame of the study for this workstream.

Results

The cohort

Workstream 2 cohort of OPTI-PREM comprised 4986 eligible babies.

Description of cohort and selection of measures

Of the 185 neonatal units in England, 65 SCBU were excluded, leaving 119 [44 NICU (37%) and 75 LNU (63%)] units and data for 4986 babies available for study. The distribution of gestational age, birthweight, multiplicity and IMD score mirrored that of workstream 1.

In our workstream 2 cohort an average of 64 babies/unit, born at 27–31 weeks gestation, were born in NICU compared to 30 babies/unit in LNU. This difference was largely due to a higher proportion of babies born at 27 and 28 weeks gestation being born in NICU (70.3% and 59.1% born in NICU vs. 29.7% and 40.9% born in LNU, respectively, $p \le 0.01$). Babies born in NICU weighed 75 g less than those born in LNU (mean birthweight for NICU was 1279 g compared with for LNU, 1354 g; $p \le 0.01$). The IMD score was higher for NICU than LNU ($p \le 0.01$).

Two avenues for assessing adherence to measures were explored, based on unit culture and adherence to evidence-based or consensus-based practice:[62]

a. unit adherence to NNAP measures [units meeting prespecified targets (yes/no) and units in the upper quartile for benchmarking exercises (yes/no)]. Within this we also explored data completion for NNAP measures selected
b. unit adherence to other early care measures supporting optimal preterm care, with variables extracted from the OPTI-PREM data set [units meeting prespecified targets (yes/no)].

The selection of these measures, and how we determined the upper quartiles, are described below.

Selecting measures of quality of care

Unit adherence to National Neonatal Audit Programme measures

After exclusions, our sample size for adherence to NNAP measures of quality of care was 98 units, and 4594 babies.

We identified the following NNAP measures for analysis:

i. Antenatal steroids (prespecified target 85%).
ii. Antenatal magnesium sulphate (benchmarking measure).
iii. Promoting normal temperature on admission for very preterm babies (prespecified target 90%).
iv. Minimising inappropriate separation of mother and late to moderate preterm baby (benchmarking measure).
v. Minimising inappropriate separation of mother and term baby (benchmarking measure).
vi. Parent consultation within 24 hours of admission (prespecified target 100%).
vii. On-time screening for ROP (prespecified target 100%).
viii. Receipt of BMF at time of discharge from neonatal care (benchmarking measure).
ix. Nurse staffing: number of shifts with enough staff to meet 'total' nurse specifications required for shift (prespecified target 100%).

We ordered units that met the audit threshold for prespecified targets (yes/no) and benchmarking measures (% of babies that met the measure) from highest to lowest into a hierarchical list. Of the nine measures considered, no unit had adherence to all nine or eight of the nine measures (*Table 8*). Based on their distribution, above the upper quartile which we defined as 'higher-performing' units were those units meeting 4 or more of the above measures (i.e. 'yes' for meeting prespecified measure, or above the upper quartile for the benchmark, or both), and < 4 as 'lower-performing'

TABLE 8 Determining the upper quartile for adherence to NNAP measures

Number of audit measures	Number of units meeting pre-set standard or above the top quartile for benchmarking exercises	Categorisation of units	NICU and LNU distribution
9	0	Higher-performing units: units meeting threshold/in top quartile for 4 or more measures) (*n* = 21)	NICU *n* = 6 LNU *n* = 15
8	0		
7	2		
6	1		
5	4		
4	14		
3	37	Lower-performing units: units not meeting threshold/in top quartile measures) (*n* = 77)	NICU *n* = 36 LNU *n* = 41
2	25		
1	13		
0	2		

TABLE 9 Determining the quartiles for missing data for NNAP measures

Number of audit measures	Number of units	Categorisation of units	NICU and LNU distribution
0	44	Higher-performing units: units not in top quartile/any missing data for 2 or more measures (n = 83)	NICU n = 36 LNU n = 47
1	39		
2	10	Lower-performing units: units in top quartile/any missing data for 2 or more measures (n = 17)	NICU n = 7 LNU n = 10
3	3		
4	3		
5	1		
6	0		

TABLE 10 Selection of NNAP measures for assessing quality of care in neonatal units caring for very preterm babies born at 27–31 weeks gestation in England

NNAP audit measure	NNAP adherence to prespecified standard or benchmark	NNAP data completion
Antenatal steroids	Selected	Excluded due to > 90% data completion
Antenatal magnesium sulphate	Selected	Selected
Promoting normothermia within an hour of admission for very preterm babies	Selected	Excluded due to > 90% data completion
Minimising separation of mother and baby for late and moderate preterm baby	Selected	Excluded due to 100% data completion[a]
Minimising separation of mother and baby for term baby	Selected	Excluded due to 100% data completion[a]
Parent consultation within 24 hours of admission	Selected	Selected
On-time screening for ROP	Selected	Selected
Breast milk feeding at discharge	Selected	Excluded due to > 90% data completion
Nurse staffing[b]	Selected	Excluded due to 100% data completion[a]
BPD	Excluded due to relating to final outcomes	Excluded due to > 90% data completion
NEC	Excluded due to relating to final outcomes	Selected
Bloodstream infection	Excluded due to unknown % missing data	Excluded due to unknown % missing data
Central line associated bloodstream infection	Excluded due to unknown % missing data	Excluded due to unknown % missing data
Parental presence at ward rounds	Excluded due to unknown % missing data	Selected
Follow up at 2 years of age	Excluded due to unknown % missing data	Selected

a Where there was 100% data completion for all units, an upper quartile was not possible to determine.
b Proportion of nursing shifts that were numerically staffed according to guidelines and service specification.

units. Twenty-one neonatal units met the criteria for 'higher performing' and the remaining 77 were classified as 'lower performing' against adherence to overall NNAP audit measures.

Unit data completion for National Neonatal Audit Programme audit measures

For assessment on data completion, 100 neonatal units met the inclusion criteria. There was 100% data completion for the categories of minimising inappropriate separation of mother and term, and late to moderate preterm, babies and nurse staffing. There were < 10% missing data in the categories of antenatal steroids, BPD, breastmilk feeding at discharge home, and promoting normal temperature on admission for very preterm babies. We therefore excluded these measures from the analysis since missing data for a very small number of patients (even one) could impact categorisation of units. We also excluded bloodstream infection and central line associated bloodstream infection as information on degree of missing data by neonatal unit was not available. We identified the list of NNAP audit measures to categorise units according to data completion as:

i. Antenatal magnesium sulphate.
ii. Parent consultation within 24 hours of admission.
iii. Parental presence at consultant ward rounds.
iv. On-time screening for ROP.
v. NEC.
vi. Follow-up at 2 years of age.

We created two hierarchical lists, in which the units were ordered by data completion and split into two groups based on upper quartile, or with any missing data for 2 or more audit measures (*n* = 17), and higher-performing units those with any missing data for < 2 audit measures (*n* = 83) (*Table 9*). *Table 10* details the NNAP measures against those utilised in our study to assess quality of care.

Crude summary statistics on categorising units into higher and lower performing based on adherence to NNAP measures, and data completion are described in *Tables 11* and *12*. There was no difference between the cohorts, except for IMD.

Unit adherence (upper quartiles of performance) to other early care measures from the OPTI-PREM data set

Of the six variables chosen, two were excluded due to a high proportion of missing data. These were delayed cord clamping at birth, and receipt of mother's milk on day 1 of life. The remaining four variables were used to define quartiles for: any dose of antenatal steroids given;[102] normothermia temperature measured within 1 hour of admission to the neonatal unit;[101] ratio/percentage of babies given NIV of all those requiring ventilatory support on day 1 of life;[100] and ratio/percentage of babies requiring intensive care (IC) provided with 1 : 1 nursing care on day 1 of life.[108] We categorised 'higher-performing' units as being in the top quartile for adherence for two or more measures, and 'lower-performing' units as those with adherence to less than two measures. Thirty-three units met the criteria for 'higher-performing', and 80 for 'lower-performing' units.

Crude unadjusted summary statistics of categorisation of units into higher- or lower-performing units based on other early care measures from OPTI-PREM are described in *Table 13*. There was a higher proportion of LNU, and lower deprivation by IMD, in the higher-performing group.

Distribution of overall outcomes for the cohort

Pre-discharge mortality

Overall pre-discharge from neonatal care unadjusted mortality was 3.3%. This ranged from 7.7% for babies born at 27 weeks gestation, to 1.5% in those born at 31 weeks gestation. When separating by gestational week, and designation of unit of birth (NICU vs. LNU), a consistent trend was seen for increased mortality across the gestational age range in NICU (see *Table 14*). This was true for surgical and non-surgical NICU.

Length of stay

The unadjusted overall length of neonatal unit stay (LOS) was 54 days; this ranged from a mean of 36 days for babies born at 31 weeks gestation, to 84 days for babies born at 27 weeks gestation. When separating LOS for babies by

TABLE 11 Summary statistics of higher-compared with lower-performing units by adherence to NNAP measures

Adherence with NNAP audit measures		High performing		Lower performing		*p*
Number of units		21		77		
Unit designations	LNU	15	(71.4%)	41	(53.2%)	0.136
	NICU (all)	6	(28.6%)	36	(46.8%)	
	NICU (surgical)	2	(9.5%)	18	(23.4%)	0.670
	NICU (non-surgical)	4	(19.0%)	18	(23.4%)	
Number of babies		889	(19.4%)	3705	(80.6%)	
Birthweight (weighted average, in grams)		1314		1305		0.944
Unknown or incorrect birthweight		*n* = 12 (0.3%)				
Gestational week	27	102	(11.5%)	498	(13.4%)	0.137
	28	124	(13.9%)	592	(16.0%)	
	29	162	(18.2%)	680	(18.4%)	
	30	207	(23.3%)	833	(22.5%)	
	31	294	(33.1%)	1102	(29.7%)	
Gender	Male	481	(54.1%)	2065	(55.7%)	0.367
	Female	408	(45.9%)	1636	(44.2%)	
	Unknown gender	*n* = 4 (0.1%)				
Multiplicity	1	658	(74.0%)	2700	(72.9%)	0.555
	≥ 2	231	(26.0%)	999	(27.0%)	
	Unknown multiplicity	*n* = 6 (0.55%)				
Significant congenital anomalies		18	(2.0%)	113	(3.0%)	0.080
Apgar score at 5 minutes (weighted average of medians)		9		9		
Unknown Apgar score at 5 minutes		*n* = 6 (0.1%)				
Quintiles of IMD	1 (most deprived)	188	(21.1%)	1234	(33.3%)	< 0.001[a]
	2	214	(24.1%)	799	(21.6%)	
	3	173	(19.5%)	610	(16.5%)	
	4	141	(15.9%)	492	(13.3%)	
	5 (least deprived)	155	(17.4%)	435	(11.7%)	
	Unknown IMD	*n* = 153 (3.3%)				
Resuscitation involving cardiac massage or adrenaline		18	(2.0%)	107	(2.9%)	0.164
Unknown resuscitation status		*n* = 303 (6.6%)				

a significance was set at 99% CI, $p < 0.01$.

TABLE 12 Summary statistics of higher-compared with lower-performing units by missing data for NNAP measures

Missing data for NNAP audit measures		Lower performing		Higher performing		*p*
Number of units		17		83		
Unit designations	LNU	10	(58.8%)	47	(56.6%)	1.000
	NICU (all)	7	(41.2%)	36	(43.4%)	
	NICU (surgical)	4	(23.5%)	17	(20.5%)	0.700
	NICU (non-surgical)	3	(17.6%)	19	(22.9%)	
Number of babies		891	(18.9%)	3831	(81.1%)	
Birthweight (weighted average, in grams)		1306		1308		0.988
Unknown or incorrect birthweight		*n* = 12 (0.3%)				
Gestational week	27	97	(10.9%)	512	(13.4%)	0.259
	28	146	(16.4%)	588	(15.3%)	
	29	166	(18.6%)	701	(18.3%)	
	30	196	(22.0%)	880	(23.0%)	
	31	286	(32.1%)	1150	(30.0%)	
Gender	Male	460	(51.6%)	2139	(55.8%)	0.025
	Female	430	(48.3%)	1689	(44.1%)	
	Unknown gender	*n* = 4 (0.1%)				
Multiplicity	1	662	(74.3%)	2793	(72.9%)	0.400
	≥ 2	228	(25.6%)	1033	(27.0%)	
	Unknown multiplicity	*n* = 6 (0.1%)				
Significant congenital anomalies		29	(3.3%)	104	(2.7%)	0.353
Apgar score at 5 minutes (weighted average of medians)		9		9		
Unknown Apgar score at 5 minutes		*n* = 535 (10.7%)				
Quintiles of IMD	1 (most deprived)	300	(33.7%)	1177	(30.7%)	0.010[a]
	2	223	(25.0%)	849	(22.2%)	
	3	126	(14.1%)	660	(17.2%)	
	4	99	(11.1%)	539	(14.1%)	
	5 (least deprived)	113	(12.7%)	473	(12.3%)	
	Unknown	*n* = 163 (3.5%)				
Resuscitation involving cardiac massage or adrenaline		18	(2.0%)	111	(2.9%)	0.148
Unknown resuscitation status		*n* = 300 (6.4%)				

a Significance was set at 99% CI, $p < 0.01$.

TABLE 13 Summary statistics of higher-compared with lower-performing units by adherence to OPTI-PREM data set measures

OPTI-PREM data set measures		Higher performing		Lower performing		p
Number of units		33		80		
Unit designations	LNU	26	(78.8%)	44	(55.0%)	0.011[a]
	NICU (all)	7	(21.2%)	36	(45.0%)	
	NICU (surgical)	3	(9.1%)	18	(22.5%)	1.000
	NICU (non-surgical)	4	(12.1%)	18	(22.5%)	
Number of babies		1254	(25.2%)	3732	(74.8%)	
Average number of babies born per unit		38		47		0.062
Birthweight (weighted average in grams)		1330		1306		0.081
Unknown or incorrect birthweight		*n* = 12 (0.2%)				
Gestational week	27	145	(11.6%)	479	(13.0%)	0.757
	28	200	(15.9%)	566	(15.2%)	
	29	231	(18.4%)	674	(18.2%)	
	30	288	(23.0%)	850	(23.0%)	
	31	390	(31.1%)	1128	(30.5%)	
Gender	Male	718	(57.3%)	2028	(54.3%)	0.068
	Female	535	(42.7%)	1701	(45.6%)	
	Unknown gender	*n* = 4 (0.08%)				
Multiplicity	1	938	(74.9%)	2711	(72.6%)	0.128
	≥ 2	314	(25.0%)	1017	(27.3%)	
	Unknown multiplicity	*n* = 6 (0.1%)				
Significant congenital anomalies		24	(1.9%)	113	(3.0%)	0.041
Apgar score at 5 minutes (weighted average of medians)		9		9		
Unknown Apgar score at 5 minutes		*n* = 535 (10.7%)				
Quintiles of IMD	1 (most deprived)	306	(24.4%)	1225	(32.8%)	< 0.001[a]
	2	254	(20.3%)	877	(23.5%)	
	3	236	(18.8%)	610	(16.3%)	
	4	175	(14.0%)	504	(13.5%)	
	5 (least deprived)	238	(19.0%)	390	(10.5%)	
	Unknown IMD_Q	*n* = 171 (3.4%)				
Resuscitation involving cardiac massage or adrenaline		25	(2.0%)	110	(2.9%)	0.069
Unknown resuscitation status		*n* = 316 (6.3%)				

a significance was set at 99% CI, $p < 0.01$.

TABLE 14 Pre-discharge mortality trends for WS2 cohort

	NICU			LNU			
Gestational week at birth	**Mortality (pre-discharge)**	**Patient total**	**(%)**	**Mortality (pre-discharge)**	**Patient total**	**(%)**	***p***
27	36	446	(8.1)	13	184	(7.1)	0.680
28	30	457	(6.6)	12	309	(3.9)	0.120
29	16	485	(3.3)	9	427	(2.1)	0.278
30	18	625	(2.9)	8	523	(1.5)	0.130
31	18	791	(2.3)	6	739	(0.8)	0.022
27–31	118	2804	(4.2)	48	2182	(2.2)	< 0.001[a]

Significance was set at 99% CI, *p* = 0.01.
a Crude, unadjusted.

TABLE 15 Length of neonatal stay trends for WS2 cohort

	Mean (LOS – days)				
Gestational week at birth	**All units (SD)**	**NICU**	**LNU**	**Difference (days, 95% CI)**	***p***
27	84 (27)	86	80	6.6 (2.5 to 10.6)	< 0.001[a]
28	71 (25)	72	70	2.2 (−2.9 to 7.3)	0.390
29	58 (23)	60	57	3.1 (−0.8 to 6.9)	0.104
30	47 (18)	49	46	3.1 (0.5 to 5.6)	0.015
31	36 (15)	38	35	2.9 (0.4 to 5.4)	0.02
27–31	54 (26)	57	50	6.9 (4.9 to 9.0)	< 0.001[a]

a Significance was set at 99% CI; *p* < 0.01.

gestational week, and designation of unit of birth, a consistent trend was seen for increased LOS in NICU versus LNU across the gestational age range (*Table 15*).

Analysis of outcomes by adherence to quality of care measures

Pre-discharge mortality

a. *Adherence to NNAP audit measures*: on univariate analysis of pre-discharge mortality, comparing higher-performing units versus lower-performing units, we detected a difference (2.2% compared with 3.6%; *p* = 0.04) for the whole cohort of babies. We could not identify a gestation-specific difference. On multivariate analyses, this difference lost significance (aOR 1.22, 95% CI 0.43 to 1.35) (see *Table 16*).
b. *Data completion for NNAP measures:* we did not detect a significant difference either for the whole cohort (4.0% compared with 3.2%; *p* = 0.21), or at each gestational age in weeks at birth, for data completion of NNAP audit measures (see *Table 16*) on univariate analysis. Multivariate analysis was not conducted for data completion for NNAP measures due to restrictions of time during the PhD process as a result of the COVID pandemic.
c. *Adherence to other early care measures from the OPTI-PREM data set*: We did not detect any significant difference on adherence to OPTI-PREM data set measures, between higher-performing and lower-performing neonatal units (aOR 1.22, 95% CI 0.78 to 1.93) (*Table 16*).

TABLE 16 A comparison of pre-discharge neonatal mortality outcomes in units classified as higher performing compared with lower performing

	Higher-performing units			Lower-performing units			
Gestational age in weeks at birth	Mortality (pre-discharge)	Patient total	(%)	Mortality (pre-discharge)	Patient total	(%)	
Pre-discharge mortality compared with adherence to NNAP measures of quality of care							
27	7	102	(6.8)	41	498	(8.2)	p = 0.341[a]
28	6	124	(4.8)	33	592	(5.6)	
29	3	162	(1.9)	19	680	(2.8)	
30	2	207	(1.0)	20	833	(2.4)	
31	2	294	(0.7)	22	1102	(2.0)	
27–31	20	889	(2.2)	135	3705	(3.6)	
Pre-discharge mortality compared with data completion for NNAP measures of quality of care[b]							
27	39	512	(7.6)	8	97	(8.2%)	p = 0.207[a]
28	33	588	(5.6)	9	146	(6.2%)	
29	17	701	(2.4)	6	166	(3.6%)	
30	15	880	(1.7)	7	196	(3.6%)	
31	18	1150	(1.6)	6	286	(2.1%)	
27–31	122	3831	(3.2)	36	891	(4.0%)	
Pre-discharge mortality compared with adherence to early care measures from OPTI-PREM data set							
27	16	145	(11.0)	33	485	(6.8)	p = 387[a]
28	9	200	(4.5)	33	566	(5.8)	
29	5	231	(2.2)	20	681	(2.9)	
30	4	288	(1.4)	22	860	(2.6)	
31	2	390	(0.5)	22	1140	(1.9)	
27–31	36	1254	(2.9)	130	3732	(3.5)	

a Significance was set at 99% CI; $p < 0.01$.
b Univariate analysis was undertaken only; see COVID statement page 34.

Length of stay

a. *Adherence to NNAP audit measures*: we detected a significant difference between the two groups, on univariate analysis of LOS and adherence to NNAP audit measures. The number of hospital days in neonatal care was significantly lower in higher-performing neonatal units for the total cohort of babies born at 27–31 weeks (difference in weighted mean LOS 3.7 days, 95% CI 0.6 to 6.8; $p = 0.02$). On multivariate analysis using linear regression to explore associations between adherence with the NNAP audit measures and LOS, we found a difference of 1 day, that is shorter hospital stay in neonatal care for babies in the group of units that were higher-performing compared to lower-performing units (95% CI 1.029 to 1.081; $p < 0.001$) (see *Table 17*). The variables entered into the linear regression model explained 46.2% of the variation in LOS.
b. *Data completion for NNAP measures*: for data completion for NNAP audit measures, we did not detect differences across the whole cohort, or at each gestational age in weeks (see *Table 17*) on univariate analysis. Multivariate analysis was not conducted for data completion for NNAP measures due to restrictions of time during the PhD process as a result of the COVID pandemic.

TABLE 17 A comparison of LOS in neonatal units between higher-performing compared with lower-performing neonatal units

Gestational age in weeks at birth	Higher-performing units	Lower-performing units	Difference (days, 95% CI)	
LOS in neonatal care compared with adherence to NNAP measures of quality of care				
27	84	84	0.3 (−5.5 to 6.0)	$p < 0.001$[a]
28	70	72	1.6 (−4.3 to 7.4)	
29	57	59	1.5 (−3.4 to 6.5)	
30	45	48	3.3 (0.0 to 6.6)	
31	35	37	2.4 (−0.6 to 5.4)	
27–31	52	55	3.7 (0.6 to 6.8)	
LOS compared with data completion for NNAP measures of quality of care[b]				
27	85	80	4.8 (−1.4 to 11.1)	$p = 0.164$
28	73	67	5.4 (−0.9 to 11.7)	
29	59	58	0.4 (−5.0 to 5.7)	
30	47	46	1.0 (−2.7 to 4.6)	
31	37	37	0.3 (−3.0 to 3.5)	
27–31	55	52	2.4 (−1.1 to 5.9)	
LOS compared with adherence to early care measures from OPTI-PREM data set				
27	80	85	5.6 (0.7 to 10.4)	$p = 0.007$[a]
28	69	72	2.4 (−2.5 to 7.4)	
29	57	59	1.4 (−2.7 to 5.4)	
30	47	47	0.9 (−1.9 to 3.8)	
31	34	37	3.4 (1.0 to 5.8)	
27–31	52	55	3.1 (0.4 to 5.8)	

a Significance was set at 99% CI; $p < 0.01$.
b Univariate analysis was undertaken only; see COVID statement page 34.

Note
LOS: weighted mean rounded to nearest day for babies by gestational week of birth when categorising units based on adherence with NNAP audit measures.

c. *Adherence to other early care measures from the OPTI-PREM data set*: on analysis of LOS for the composite measures in the OPTI-PREM data set (steroids, temperature, ventilation, nursing), we found a significant difference. LOS was significantly shorter in those units that were higher-performing compared to those lower-performing units (difference in weighted mean LOS 3.1 days, 95% CI 0.4 to 5.8; $p = 0.02$). On multivariate analysis, the LOS for babies in neonatal units in the higher-performing group was 1 day shorter than for the low-performing group. This was statistically significant (95% CI 1.008 to 1.053; $p = 0.007$) (*Table 17*). The variables entered into the linear regression model explained 46.7% of the variation in LOS.

Exploring differences between higher-performing and lower-performing neonatal units

When analysing the cohorts to compare high- and lower-performing units, we noted that there was a significantly higher proportion of LNU in the higher-performing units ($p = 0.01$) for the analysis using the early care measures from the OPTI-PREM data set.

The increased ratio of LNU : NICU in 'high' performing units was only statistically significant for the ratio/percentage of babies requiring intensive care (IC) provided with 1 : 1 nursing care on day 1 of life. For two other measures relating to use of NIV in babies requiring ventilatory support, and normal temperature within 1 hour of admission, this relationship did not reach statistical significance. Overall, for the combination of measures (high performing being defined as in the top quartile for two or more measures out of the four), the ratio of LNU : NICU was increased and statistically significant.

Notably, using the early care measures from the OPTI-PREM data set there was a higher proportion of normothermia in the first hour of admission to neonatal unit, and use of non-invasive respiratory support on day 1 in babies needing respiratory support, where there was no active resuscitation with adrenaline/cardiac massage.

The proportion of babies in each quintile for the IMD_Q, within higher-performing compared with lower-performing units, was also significantly different for adherence to these measures. There was a significant trend towards a less deprived population of patients being in units that were 'higher performing' ($p < 0.01$) (*Table 18*).

Discussion

We explored quality of care within units, using measures of quality of care that were evidence-based, or considered best practice nationally. We explored the culture of units, through how much they aligned with these measures. We investigated whether these were associated with two clinical outcomes: mortality, and LOS while in neonatal care, for babies born at 27–31 weeks gestation in the OPTI-PREM cohort.

We identified higher-performing units for our defined measures of quality of care, by assessing their adherence to prespecified national audit targets and using a quartile structure for measures that were national benchmarking exercises. We found that higher-performing units had a shorter duration of hospital stay of at least 1 day, when compared to those graded as lower performing by our study definitions. When we looked at this in detail, we found that for the OPTI-PREM data set measures, the proportion of LNU : NICU was higher in higher-performing units, and that this was noted for the combined measures and 1 : 1 nursing alone. The higher-performing LNU were also in areas of less deprivation, by IMD scores.

Findings in context

Overall, our exploratory findings support our hypotheses. Units that are striving to comply with national guidance in the form of NNAP audit measures and practice evidence-based care would be expected to have better outcomes for their babies, and this could result in the small but significant difference in LOS. It could also be that units who work hard to comply with national audit, evidence-based and consensus best practice measures are likely to have differences in the structure and process of care that contribute to shorter LOS, that we were unable to measure. These could include for example, early implementation of BMF, more opportunities for parents to provide skin-to-skin care, discharge home on nasogastric tube feeding, and/or availability of community neonatal nurse outreach support.

For OPTI-PREM data set measures, the differences noted are plausible. LNU are smaller volume than NICU,[11] and care for fewer ill babies overall compared to NICU.[15] Therefore, we might expect that LNU would prioritise 1 : 1 nurse staffing for babies that require intensive care on day 1 of life. This association might explain why LNU are disproportionately represented in the top quartile for this measure when using OPTI-PREM data set measures. Our work highlights the importance of identifying the most appropriate measures of quality of care. What we infer from our work is that where babies are likely to be more ill, adherence to highest quality of care as judged by our study criteria, was less likely to be achieved.

The observation of a significant trend towards a less deprived population of patients in units in the top quartile is important. This is unlikely to be direct and unifactorial, and more likely to be related to systemic differences in structures and processes of care between units and the wider healthcare system in more affluent compared with deprived areas.[109,110]

The implications of these preliminary results, if validated, could be substantial. Assuming that the shortened day is a day of special care (with carer present), and that neonatal units are reimbursed ~£535 by NHS England to provide this care, this could represent a substantial cost saving to the NHS in England. It is likely that the effects we are seeing extend beyond the cohort of babies born at 27–31 weeks gestation, to all babies admitted into neonatal care.

TABLE 18 Comparison of patient populations when categorising units according to OPTI-PREM data set measures (steroids, temperature, ventilation, nursing)

OPTI-PREM data set measures		Higher performing		Lower performing		*p*
Number of units		33		80		
Unit designations	LNU	26	(78.8%)	44	(55.0%)	0.011[a]
	NICU (all)	7	(21.2%)	36	(45.0%)	
	NICU (surgical)	3	(9.1%)	18	(22.5%)	1.000
	NICU (non-surgical)	4	(12.1%)	18	(22.5%)	
Number of babies		1254	(25.2%)	3732	(74.8%)	
Average number of babies born per unit		38		47		0.062
Birthweight (weighted average – g)		1330		1306		0.081
Unknown or incorrect birthweight		*n* = 12 (0.2%)				
Gestational week	27	145	(11.6%)	479	(13.0%)	0.757
	28	200	(15.9%)	566	(15.2%)	
	29	231	(18.4%)	674	(18.2%)	
	30	288	(23.0%)	850	(23.0%)	
	31	390	(31.1%)	1128	(30.5%)	
Gender	Male	718	(57.3%)	2028	(54.3%)	0.068
	Female	535	(42.7%)	1701	(45.6%)	
	Unknown gender	*n* = 4 (0.08%)				
Multiplicity	1	938	(74.9%)	2711	(72.6%)	0.128
	≥ 2	314	(25.0%)	1017	(27.3%)	
	Unknown multiplicity	*n* = 6 (0.1%)				
Significant congenital anomalies		24	(1.9%)	113	(3.0%)	0.041
Apgar score at 5 minutes (weighted average of medians)		9		9		
Unknown Apgar score at 5 minutes		*n* = 535 (10.7%)				
Quintiles of IMD	1 (most deprived)	306	(24.4%)	1225	(32.8%)	< 0.001[a]
	2	254	(20.3%)	877	(23.5%)	
	3	236	(18.8%)	610	(16.3%)	
	4	175	(14.0%)	504	(13.5%)	
	5 (least deprived)	238	(19.0%)	390	(10.5%)	
	Unknown IMD_Q	*n* = 171 (3.4%)				
Resuscitation involving cardiac massage or adrenaline		25	(2.0%)	110	(2.9%)	0.069
Unknown resuscitation status		*n* = 316 (6.3%)				

a Statistical significance was set at 99% CI, $p < 0.01$ for OPTI-PREM.

Being able to discharge babies 1 day earlier would influence cot capacity and therefore movement within and between neonatal units. Our findings suggest that there is substantial value in promoting best quality of care in neonatology through adherence to evidence-based and consensus best practice measures in England. Enhancing this may optimise not just neonatal outcomes, but overall health service delivery and costs of care for sick and preterm babies in England.

Strengths and limitations

Our study uses a robust method of assessing quality of care and provides a model for further studies evaluating quality of neonatal service delivery using routinely collected operational data through the NNRD. Our results suggest that units that have better adherence with the NNAP audit measures, and/or practice more evidence-based medicine (according to our chosen measures), have a reduced LOS by an average of 1 day, for babies born at 27–31 weeks gestation. These results must be interpreted with caution. The multivariate analyses allowed for adjustment of important confounding variables, but less than half of the variance in outcomes was explained by the models. Several important, recognised confounders were excluded from consideration due to lack of data (e.g. condition of baby at birth, mother's health status pre- and during pregnancy, ethnicity, etc.), and we have not adjusted for unknown confounding factors through use of an IV approach as in workstream 1. We did not find an association between mortality and quality of care as defined by our study. This may be due to small sample size, as the overall mortality was 3.3%. Therefore, while plausible, this exploratory workstream requires further validation with a larger data set and adjusting for measured and unmeasured confounders for degree of illness of baby.

Summary points from OPTI-PREM clinical quality of care study, workstream 2

What was already known prior to the study

- Quality of neonatal care, in relation to structure, care processes and clinical practices does influence neonatal outcomes.
- Whether this quality of neonatal care is independent of unit designation is unknown.
- There are no data on whether quality of care provided by neonatal units caring for very preterm babies born at 27–31 weeks gestation can influence outcomes, independent of unit designation.

What this study adds

- We developed a novel use of national targets and benchmarking exercises to stratify units according to high-performing compared with lower-performing units for quality of care.
- We found a statistically significant difference in LOS for high-performing units.
- Units in high areas of social deprivation and those with less staff were less likely to meet standards of best practice.
- Our work needs validation through larger studies and accounting for unmeasured confounders.

Chapter 6 Workstream 3: cost of neonatal care analysis

The cost of neonatal care for preterm babies born at 27–31 weeks gestation in England.

Introduction

In this workstream, the overall cost of neonatal care (see *Chapter 6*), and a comparison of the cost-effectiveness of care in NICU and LNU settings (see *Chapter 7*), for babies born at 27–31 weeks gestation are investigated. This is an understudied cohort, and there are no correlates for cost-effectiveness analyses for very preterm births, globally. In addressing best place of care, we considered that if there were no differences in mortality and major morbidity, and there was equivalence in parental perspectives, then cost of care and cost-effectiveness of care would become important components in defining best place of care for NHS neonatal health service delivery. In this chapter we detail the overall cost burden to the NHS of initial neonatal unit care for very preterm babies and identify the key contributors to these costs.

Aim and objective

To identify, for babies born preterm at 27–31 weeks gestation and admitted to a neonatal unit in England, the overall costs of care up to neonatal unit discharge, and the main contributors to costs of care.

Methods

Study design

Retrospective analysis of resource use data recorded within the NNRD.

Data source

Data from the NNRD extract for OPTI-PREM, on preterm babies born at 27–31 weeks gestation and who were discharged from neonatal unit care or died while in neonatal care between 1 January 2014 and 31 December 2018.

Inclusion and exclusion criteria

In addition to admissions into NICU or LNU (which have resources to care for this group of very preterm babies), our cohort included babies who were inadvertently not born in maternity services colocated with LNU or NICU but were later transferred to these for continued care. Babies missing daily intervention records or for whom daily records were available, but level of care data had not been recorded, were excluded from the analysis.

Data variables

The NDAU team provided a final extraction of the relevant NNRD data fields for the cohort on 5 October 2020. Daily intervention data and treatment episode data were received in two separate data sets and were linked by means of participant identification number. Data were imported into the statistical software Stata and were manipulated such that for each baby, a daily intervention record (which included the level of care provided) was available for each day of the admission episode.

Resource use and costs

We conducted the cost analysis from the perspective of the NHS in England. We calculated the costs associated with the routine daily neonatal care received by each baby, by multiplying the number of days spent receiving each level of care, by level-specific national average bed-day costs. We sourced this from the 2018–9 National Schedule of NHS Costs.[28] We derived each bed-day cost by costing the daily care items included in its corresponding neonatal critical care healthcare resource group (HRG). These are groupings of clinical activities made based on diagnosis and procedure codes. They are the 'units' of health care for which providers, in this case neonatal units, receive payment. HRG costs are assigned based on nationally estimated tariffs which were developed to at least cover the cost of high-quality and cost-effective care. We used the following neonatal bed-day costs: intensive care (HRG XA01Z), high-dependency care (HRG XA02Z), special care without carer resident alongside baby (HRG XA03Z), special care with carer resident alongside baby (HRG XA04Z), and normal care (HRG XA05Z). Costs are shown in *Appendix 5*, *Table 34* and further information can be sourced within the NHS.[111]

The neonatal HRG does not contain all high-cost major activities. To capture high-cost specialised items, in consultation with clinical experts we selected the top five major cost non-routine procedures captured within the NNRD offered to our cohort. These were surfactant replacement therapy, utility of nitric oxide, use of total parental nutrition (TPN) (more than 14 days), palivizumab and surgical care. We identified types of neonatal surgery from corresponding operating procedure codes supplement (OPCS) and *International Statistical Classification of Diseases and Related Health Problems*, Tenth Revision (ICD-10) codes for costing purposes. We identified costs for other activities which were obtained from the published literature and through discussions with experts, as detailed in *Appendix 5*, *Table 34*. We assumed that the NNRD data for these five non-routine procedures were complete, and where there was no entry in the corresponding data set fields, we took this to mean that the procedure did not take place.

Statistical analysis

To describe neonatal and maternal characteristics, we used counts and proportions and means and SD for categorical and continuous variables respectively. We undertook all analyses of resource use data and costs by gestation in weeks at birth. We used means (SD) to summarise days provided at each level of care. We made counts of the numbers of babies for whom non-routine procedures were recorded, along with the number of cases (e.g. surgeries) or days (e.g. for nitric oxide, and TPN) for which such treatment was given. We reported total costs for the cohort and for each gestation in weeks at birth.

A secondary analysis used multiple imputations to assess routine care costs at each level (intensive care, high-dependency care, etc.) for babies with missing daily record and level of care data. An imputation model was constructed, that included complete data on baseline baby and maternal characteristics, and the total cost of care provided at each level of care (intensive care, high-dependency care, special care without carer, special care with carer and normal care). We imputed costs for each level of care for babies with missing data. Baseline characteristics included gestational age at birth, gender, number of fetuses, birthweight, neonatal death, maternal age and mode of delivery. All baseline covariates were subject to a small number of missing data that were imputed using conditional mean imputation prior to inclusion in the imputation model. A predictive mean matching estimation using chained equations with 50 imputations was implemented.[112] Mean estimates and estimates of standard errors (SEs) were combined between imputed data sets using Rubin's rule[113] without any adjustment. Combined mean cost estimates and adjusted SE by gestational week across imputed data sets are shown to report the results of the multiple imputation analysis. We conducted our analyses using Stata MP.[114]

Results

These have been previously reported.[104]

We received a NNRD data extraction for 29,842 neonates. This accounted for 1,512,446 daily records and 46,746 episode (admitted to a specific unit) records. We removed babies with missing daily record information (*n* = 1292) and with missing data on the HRG code for daily care provided (*n* = 377). Our final cohort included in the cost analysis was therefore 28,173 babies (94% of the starting cohort of 29,842) (*Figure 4*). We included babies with congenital anomalies as they contribute to the costs of care. In *Table 19* we summarise the characteristics of the babies and their mothers. When we compared between babies included in the analysis and those excluded due to missing data (*n* = 1669) we found that babies excluded were more likely to be born at earlier gestations (e.g. 17% vs. 12% were born at 27 weeks) (see *Appendix 6*, *Table 35*). However, the birth statistics for our cohort compared favourably to those of all very preterm

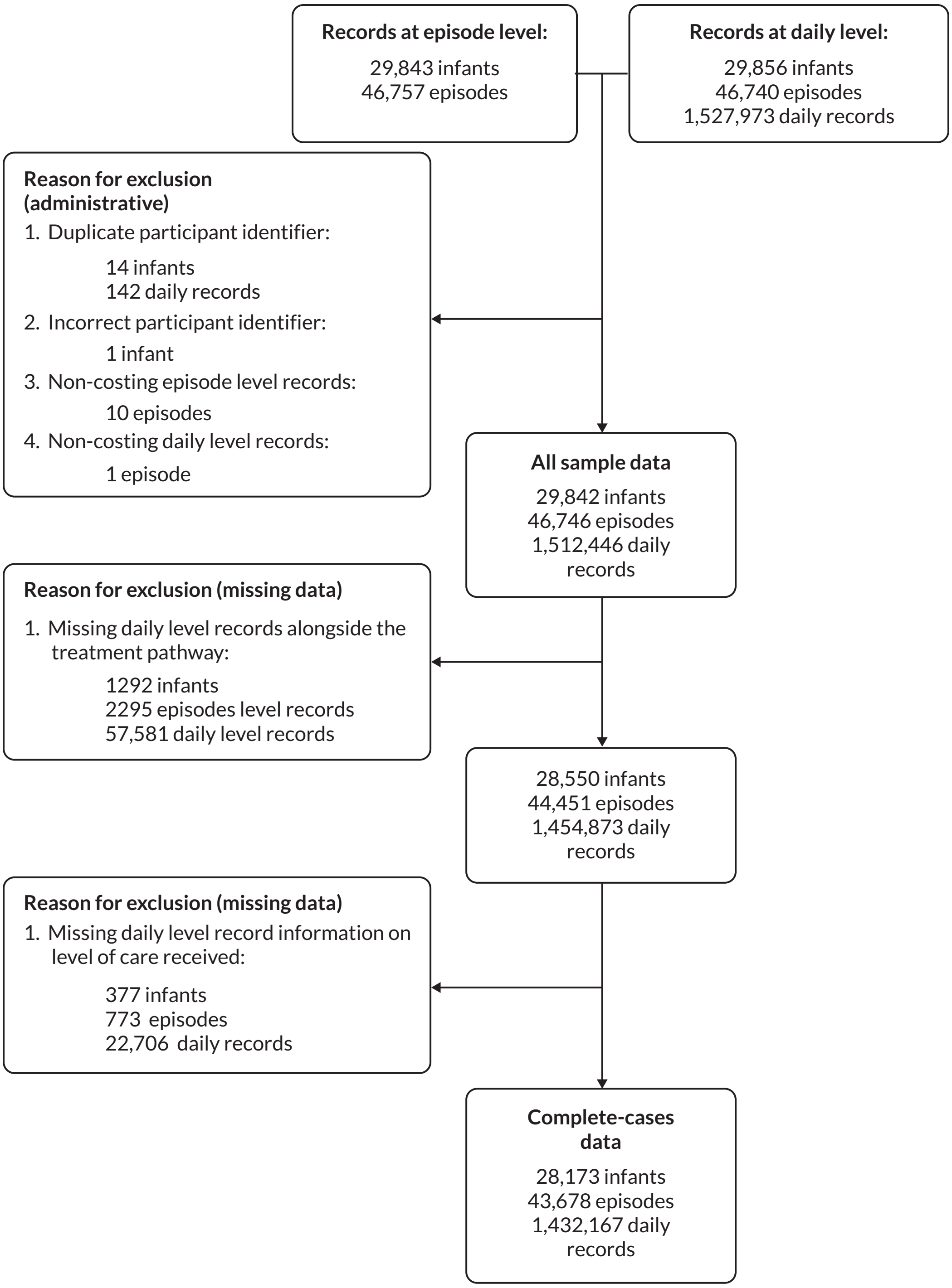

FIGURE 4 Flow of NNRD data available to estimate neonatal care costs in the OPTI-PREM cohort.

TABLE 19 Neonatal and maternal characteristics used in the costing analysis

	Cohort (*n* = 28,173); *n* (%)
Neonatal characteristics	
Gestational age at birth	
27 weeks	3296 (11.7)
28 weeks	4370 (15.5)
29 weeks	5036 (17.9)
30 weeks	6625 (23.5)
31 weeks	8827 (31.3)
Missing	*19 (0.1)*
Gender of baby	
Male	15,363 (54.5)
Female	12,755 (45.3)
Missing	*55 (0.2)*
Number of fetuses	
Singleton birth	20,555 (73.0)
Multiple birth	7598 (27.0)
Missing	*20 (0.1)*
Birthweight (g) – mean (SD)	1330.2 (332.2)
Missing	*82 (0.3)*
Apgar score at 5 minutes – mean (SD)	8.1 (1.8)
Missing	*2877 (10.2)*
Died in neonatal care	985 (3.5)
Missing	*0 (0.0)*
Maternal characteristics	
Age (years) – mean (SD)	30.7 (6.3)
Missing	*279 (1.0)*
Ethnicity	
White	17,647 (62.6)
Black	2011 (7.1)
Asian	3144 (11.2)
Mixed	433 (1.5)
Other	483 (1.7)
Missing	4455 (15.8)
Diabetes	2378 (8.4)
Missing	10,736 (38.1)
Hypertension	3506 (12.4)

continued

TABLE 19 Neonatal and maternal characteristics used in the costing analysis (*continued*)

	Cohort (*n* = 28,173); *n* (%)
Missing	10,460 (37.1)
Infection	3029 (10.6)
Missing	10,595 (37.6)
Mode of delivery	
Vaginal – spontaneous	8200 (29.1)
Vaginal – instrumental	765 (2.7)
Caesarean section	17,691 (62.3)
Missing	*1517 (5.4)*
Quintiles of IMD	
1st Q, least deprived	3355 (11.9)
2nd Q	3761 (13.4)
3rd Q	4516 (16.0)
4th Q	5930 (21.1)
5th Q, most deprived	8057 (28.6)
Missing	2554 (9.1)

Q, quintile.

babies born in England between 2016 and 2018 (data compiled by the Office for National Statistics; see *Appendix 3*, *Table 33*).

Resource use

In *Table 20* we show the mean (SD) duration of days spent receiving each level of daily care according to gestational age at birth. There was a consistent inverse relationship between gestational age at birth and the intensity of daily care provided. *Figure 5* plots the mean durations along with mean overall LOS on the neonatal unit and illustrates the longer durations of higher intensity care (and indeed overall neonatal care) provided to babies born at earlier gestations. For example, babies born at 27 weeks spent on average of 18.1 days (SD = 15.7 days) receiving intensive care and 26.8 days (SD = 22 days) receiving high-dependency care, while babies born at 31 weeks received an average of 3.33 days (SD = 6.7 days) of intensive care and 5.1 days (SD = 7.5 days) of high-dependency care. Also of note is that across all gestational age at birth groups, days spent receiving special care without a carer present accounted for the largest proportion of days spent on the neonatal unit. *Table 21* presents the number of babies who underwent hospital transfers and received key non-routine procedures, again by gestational age at birth. Greater resource utilisation among infants born at earlier gestations can be seen.

Costs

The mean (SD) cost per baby for the various levels of care and non-routine procedures are shown by gestational age at birth in *Table 22* using a complete-case analysis. As expected, and given the observations for resource use, costs can be seen to increase as gestational age at birth decreases. Mean (SD) routine daily care costs for a baby born at 27 weeks, for example, were, at £75,594 (£34,874), 2.8 times greater than the costs for a baby born at 31 weeks [£27,401 (£14,974)]. The final column in *Table 22* shows that for the 2014–8 cohort, just over 50% of total costs were

TABLE 20 Summary of type and duration of daily care received by very preterm babies during neonatal unit admissions in England for the period 2014–8

Gestational age at birth	Level of care provided (HRG Code)				
	Intensive care (XA01Z)	High-dependency care (XA02Z)	Special care without carer (XA03Z)	Special care with carer (XA04Z)	Normal care (XA05Z)
27 weeks gestation (n = 3296)					
Number of days of care	59,494	88,212	100,770	5113	0
Number of babies receiving care	3275	3065	3021	1681	0
Mean (SD) duration of care (days)[a]	18.1 (15.7)	26.8 (22.0)	30.5 (18.0)	1.5 (2.5)	0.0 (0.0)
95% CI	17.9 to 18.2	26.6 to 27.0	30.4 to 30.7	1.5 to 1.6	0.0 to 0.0
Median (range) duration of care (days)[a]	14.0 (0.0 to 174.0)	23.0 (0.0 to 243.0)	30.5 (0.0 to 161.0)	1.0 (0.0 to 31.0)	0.0 (0.0 to 0.0)
28 weeks gestation (n = 4370)					
Number of days of care	59,440	83,399	141,630	7345	4
Number of babies receiving care	4298	4050	4097	2268	1
Mean (SD) duration of care (days)[a]	13.6 (13.4)	19.1 (19.5)	32.4 (16.5)	1.7 (3.0)	0.0 (0.1)
95% CI	13.5 to 13.7	18.9 to 19.2	32.2 to 32.6	1.6 to 1.7	0.0 to 0.0
Median (range) duration of care (days)[a]	11.0 (0.0 to 246.0)	14.0 (0.0 to 203.0)	33.0 (0.0 to 127.0)	1.0 (0.0 to 44.0)	0.0 (0.0 to 4.0)
29 weeks gestation (n = 5036)					
Number of days of care	47,728	57,613	165,090	8449	0
Number of babies receiving care	4774	4631	4868	2671	0
Mean (SD) duration of care (days)[a]	9.5 (10.2)	11.4 (14.1)	32.8 (13.8)	1.7 (3.0)	0.0 (0.0)
95% CI	9.4 to 9.6	11.4 to 11.5	32.6 to 32.9	1.6 to 1.7	0.0 to 0.0
Median (range) duration of care (days)[a]	8.0 (0.0 to 258.0)	7.0 (0.0 to 196.0)	33.0 (0.0 to 119.0)	1.0 (0.0 to 45.0)	0.0 (0.0 to 0.0)
30 weeks gestation (n = 6625)					
Number of days of care	36,599	51,479	199,283	11,428	3
Number of babies receiving care	5196	5724	6471	3582	1
Mean (SD) duration of care (days)[a]	5.5 (7.1)	7.8 (11.1)	30.1 (12.1)	1.7 (2.9)	0.0 (0.0)
95% CI	5.5 to 5.6	7.7 to 7.8	29.9 to 30.2	1.7 to 1.8	0.0 to 0.0
Median (range) duration of care (days)[a]	4.0 (0.0 to 133.0)	5.0 (0.0 to 213.0)	30.0 (0.0 to 115.0)	1.0 (0.0 to 37.0)	0.0 (0.0 to 3.0)
31 weeks gestation (n = 8827)					
Number of days of care	29,094	44,547	219,355	14,948	9

continued

TABLE 20 Summary of type and duration of daily care received by very preterm babies during neonatal unit admissions in England for the period 2014–18 (*continued*)

Gestational age at birth	Level of care provided (HRG Code)				
	Intensive care (XA01Z)	High-dependency care (XA02Z)	Special care without carer (XA03Z)	Special care with carer (XA04Z)	Normal care (XA05Z)
Number of babies receiving care	5124	7055	8672	4718	2
Mean (SD) duration of care (days)[a]	3.3 (6.7)	5.1 (7.5)	24.9 (10.5)	1.7 (2.8)	0.0 (0.1)
95% CI	3.3 to 3.3	5.0 to 5.1	24.7 to 25.0	1.7 to 1.7	0.0 to 0.0
Median (range) duration of care (days)[a]	1.0 (0.0 to 201.0)	3.0 (0.0 to 154.0)	24.0 (0.0 to 240.0)	1.0 (0.0 to 36.0)	0.0 (0.0 to 7.0)

CI, parametric confidence interval using Poisson distribution.
a Estimated across all babies within a gestational age group.

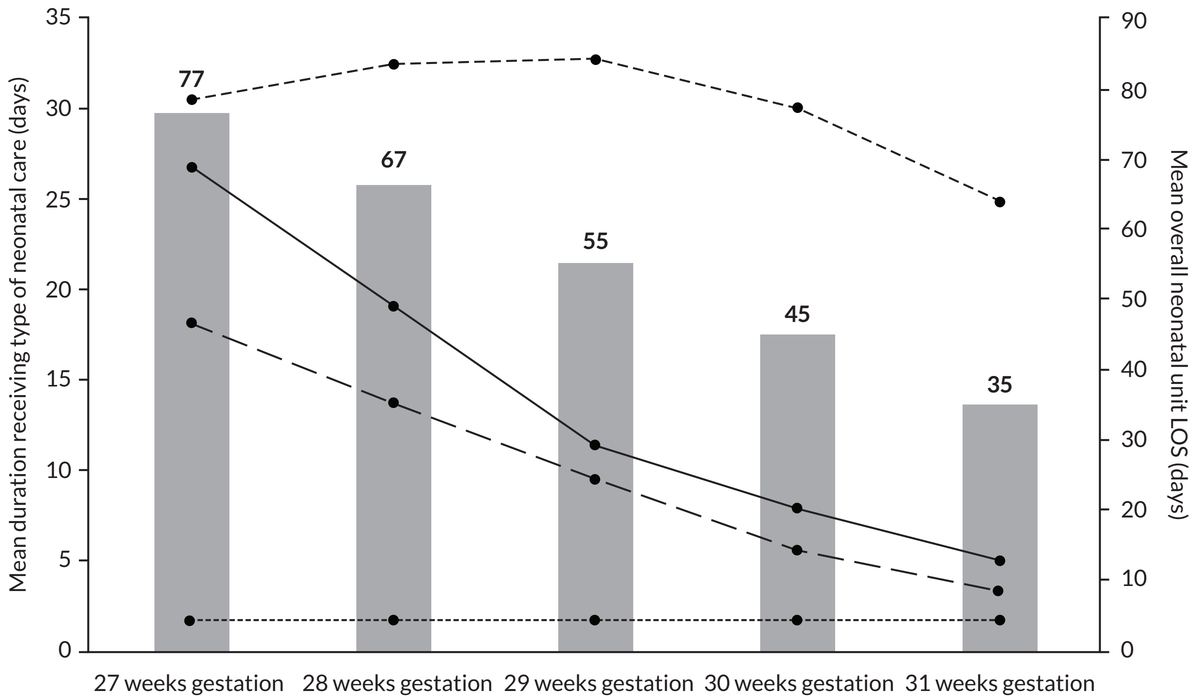

FIGURE 5 Mean duration vs. overall LOS by age of gestation. This figure is reproduced with permission from Yang *et al.*[104] This is an Open Access article distributed in accordance with the terms of the Creative Commons Attribution (CC BY 4.0) licence, which permits others to distribute, remix, adapt and build upon this work, for commercial use, provided the original work is properly cited. See: https://creativecommons.org/licenses/by/4.0/. The figure includes minor additions and formatting changes.

TABLE 21 Counts of hospital transfers, surgeries and days receiving other non-routine procedures during neonatal admissions for very preterm babies in England for the period 2014–8

	27 weeks gestation*n* = 3296	28 weeks gestation*n* = 4370	29 weeks gestation*n* = 5036	30 weeks gestation*n* = 6625	31 weeks gestation*n* = 8827
Hospital transfer within 24 hours of birth[a]					
Number of transfers	287	330	293	286	311
Number (%) of babies receiving	276 (8.4%)	323 (7.4%)	286 (5.7%)	282 (4.3%)	307 (3.5%)

TABLE 21 Counts of hospital transfers, surgeries and days receiving other non-routine procedures during neonatal admissions for very preterm babies in England for the period 2014–8 (*continued*)

	27 weeks gestation*n* = 3296	28 weeks gestation*n* = 4370	29 weeks gestation*n* = 5036	30 weeks gestation*n* = 6625	31 weeks gestation*n* = 8827
Hospital transfer after 24 hours of birth[a]					
Number of transfers	872	836	713	659	571
Number (%) of babies receiving	654 (19.8%)	665 (15.2%)	593 (11.8%)	588 (8.9%)	523 (5.9%)
Nitric oxide					
Number of days of care	1333	1363	953	918	660
Number (%) of babies receiving	425 (12.9%)	467 (10.7%)	360 (7.1%)	419 (6.3%)	326 (3.7%)
Surfactant replacement					
Number of days of care	5932	6561	5525	4201	3667
Number (%) of babies receiving	2743 (83.2%)	3258 (74.6%)	3023 (60.0%)	2677 (40.4%)	2386 (27.0%)
TPN					
Number of days of care (over 14 days' use)	20,182	17,919	11,200	7525	5074
Number (%) of babies receiving	1391 (42.2%)	1411 (32.3%)	990 (19.7%)	692 (10.4%)	515 (5.8%)
Palivizumab					
Number of days of care	90	103	52	31	14
Number (%) of babies receiving	77 (2.3%)	68 (1.6%)	38 (0.8%)	26 (0.4%)	12 (0.1%)
ROP surgery					
Number of days of care	116	53	36	34	15
Number (%) of babies receiving	91 (2.8%)	45 (1.0%)	32 (0.6%)	30 (0.5%)	15 (0.2%)
Neonatal surgery[a]					
Number of surgeries	291	283	203	175	169
Number (%) of babies receiving	255 (7.7%)	266 (6.1%)	185 (3.7%)	162 (2.4%)	161 (1.8%)

a For these items, numbers recorded are reported. For remaining items total number of days receiving treatment are reported.

TABLE 22 Mean (SD) per baby and total neonatal care costs (2018–9 UK £) for very preterm babies in England over the period 2014–8 using complete-case analysis (*n* = 28,154)[a]

	27 weeks gestation (*n* = 3296)	28 weeks gestation (*n* = 4370)	29 weeks gestation (*n* = 5036)	30 weeks gestation (*n* = 6625)	31 weeks gestation (*n* = 8827)	
Resource use item	**Mean (SD) cost per baby**	**Mean (SD) cost per baby**	**Mean (SD) cost per baby**	**Mean (SD) cost per baby**	**Mean (SD) cost per baby**	**Total neonatal care costs (percentage) for 2014–8**
Level of daily care						
Intensive care	£27,690 (£24,039)	£20,865 (£20,473)	£14,548 (£15,603)	£8482 (£10,887)	£5062 (£10,235)	£356,747,496 (27.3%)
High-dependency care	£26,956 (£22,157)	£19,221 (£19,584)	£11,523 (£14,203)	£7828 (£11,186)	£5083 (£7567)	£327,832,878 (25.0%)
Special care without carer	£20,187 (£11,880)	£21,407 (£10,921)	£21,659 (£9110)	£19,875 (£8019)	£16,423 (£6939)	£546,285,433 (41.7%)
Special care with carer	£761 (£1235)	£826 (£1454)	£824 (£1453)	£847 (£1444)	£831 (£1378)	£23,230,160 (1.8%)
Normal care	£0 (£0)	£0.47 (£31)	£0 (£0)	£0.23 (£19)	£0.52 (£40)	£8224 (0.0%)
Total level of care costs	£75,594 (£34,874)	£62,319 (£30,841)	£48,554 (£23,426)	£37,033 (£18,276)	£27,401 (£14,947)	£1,254,104,191 (95.8%)
Hospital transfers	£1120 (£1435)	£886 (£1277)	£712 (£1148)	£566 (£997)	£423 (£860)	£18,660,165 (1.4%)
Non-routine procedures						
Nitric oxide	£105 (£557)	£81 (£436)	£49 (£354)	£36 (£312)	£19 (£148)	£1,356,929 (0.1%)
Surfactant replacement	£1006 (£2052)	£933 (£1980)	£784 (£1970)	£497 (£995)	£351 (£1340)	£17,742,128 (1.4%)
TPN > 14 days use	£930 (£2203)	£609 (£1838)	£316 (£1398)	£147 (£883)	£71 (£550)	£8,919,898 (0.7%)
Palivizumab	£172 (£1188)	£152 (£1518)	£74 (£1007)	£40 (£716)	£16 (£467)	£2,022,625 (0.2%)
ROP surgery	£61 (£398)	£21 (£223)	£12 (£165)	£8.9 (£138)	£2.9 (£71)	£439,674 (0.03%)
Neonatal surgery	£456 (£2053)	£358 (£1844)	£206 (£1325)	£135 (£996)	£107 (£934)	£5,946,767 (0.5%)
Total non-routine procedures costs	£2730 (£4594)	£2153 (£4228)	£1442 (£3333)	£864 (£2143)	£567 (£1955)	£36,428,021 (2.78%)
Total neonatal care costs for 2014–8						*£1,309,192,377*
Annual total neonatal costs						*£261,838,475*

a Nineteen babies had missing gestational age information.

attributable to the provision of intensive and high-dependency care, with a further 42% coming from the provision of special care (without a carer). Further exploration of the composition of total costs in *Figure 6* reveals variation by gestational age at birth. Almost 70% of total costs for babies born at 27 weeks were associated with the use of intensive and high-dependency care, while the proportion decreased to only 36% for babies born at 31 weeks. The usage, and thus cost of special care (without a carer present), increases with increasing gestational age at birth. The results of the multiple imputation analysis for the level of care costs (see *Report Supplementary Material 6*) were similar to the complete-case analysis. Across all gestational at birth groups, non-routine procedures accounted for only a very small proportion of total costs.

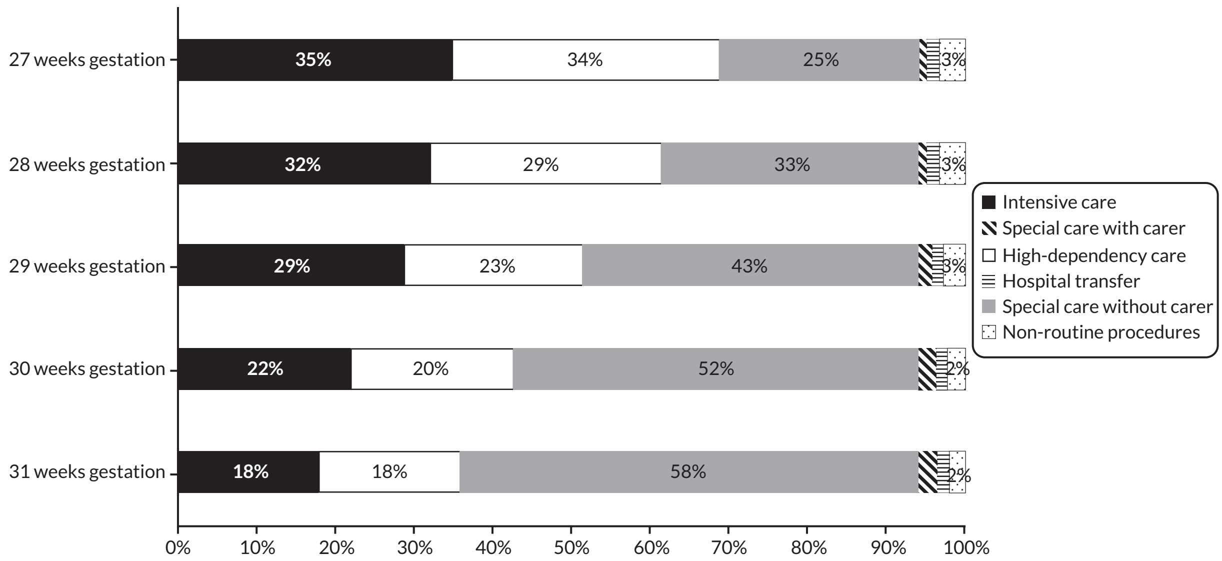

FIGURE 6 Distribution of level of care costs as a proportion of overall costs by age of gestation. This figure is reproduced with permission from Yang *et al.*[104] This is an Open Access article distributed in accordance with the terms of the Creative Commons Attribution (CC BY 4.0) licence, which permits others to distribute, remix, adapt and build upon this work, for commercial use, provided the original work is properly cited. See: https://creativecommons.org/licenses/by/4.0/. The figure includes minor additions and formatting changes.

The overall total cost estimated for the complete-case cohort (*n* = 28,154) over the 5 years from 2014 to 2018 (£1.3 billion in *Table 3*) suggests the annual costs of neonatal care for babies born at 27 and 31 weeks gestation and admitted to a neonatal unit in England to be around £262 million, with the provision of routine daily care on these units accounting for 96% (£252 million) of overall costs. Using the overall sample of 29,842 infants would increase the total cohort costs and the estimates of annual total costs shown in *Table 3* from £1,309,192,377 to £1,394,308,706 and the annual total cost from £262 million to £279 million.

Discussion

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Main findings

Analyses at the level of the individual baby revealed the main cost drivers to be the daily neonatal care provided to support babies. Analyses by gestational age at birth provided further evidence of the previously reported inverse relationship between resource use and healthcare costs and the degree of prematurity, with care for a baby born at 27 weeks estimated to cost almost three times more than for a baby born at 31 weeks.[23] Our work also provides valuable information on the contribution of different resource components to overall costs and illustrates how the mix of intensive care required by these babies varies with gestational age at birth.

A small number of studies have previously estimated neonatal care costs for preterm babies, one of the most recent being by Rios *et al.*[26] in Canada which also used individual patient-level resource use data from a neonatal database (the Canadian Neonatal Network Database) and included around 8000 babies born at 27 and 31 weeks gestation. A comparison between the costs estimated for the babies in this Canadian study and the costs presented here (currency conversion from Can $ to UK £ made using Purchasing Power Parities) revealed the Canadian cost estimates to be consistently lower across all gestational age groups.[115] The most obvious explanation for these differences lies with the scope of the neonatal databases used by each study and the resulting implications for duration of neonatal unit stay. In general Rios *et al.*[26] reported consistently lower mean lengths of stay for all gestational ages compared to our estimates due to their focus on intensive care units and the exclusion of the costs of care in lower dependency neonatal units. Thus, their[26] estimates do not reflect the true costs of healthcare provision for this group of babies.

In 2009, Mangham *et al.*[25] used a decision analytic model to estimate neonatal costs for a hypothetical cohort of preterm babies born in England and Wales.[25] Model parameters were sourced from various cohort studies and the mean cost for a very preterm baby (< 33 weeks) was estimated to be £57,726 (95% CI 28,779 to 94,868) (2006 GBP). With that analysis using a different methodology, reporting results for a wider gestational age range, and now being well over a decade old, comparisons with the estimates reported here are challenging. While a number of more recent UK studies have been published on the costs of preterm birth, these works have focused specifically on births at other gestations (i.e. moderate and late preterm births or extremely preterm births).[22,25,116] One reassuring finding however is that the costs of neonatal care for very preterm births presented here fall between the costs reported for moderate/late preterm infants and for extremely preterm infants in the UK.

Strengths and limitations

This study makes several contributions to the published literature. Firstly, existing UK cost estimates for neonatal care following very preterm birth are over a decade old and so are unlikely to reflect current standards of practice.[25] This study provides up-to-date figures based on a large cohort of more than 28,000 babies who were discharged from or died within neonatal units across England between 2014 and 2018. Secondly, previous UK cost studies in the area have mainly relied on data synthesised from secondary sources to estimate costs. In utilising the NNRD, this study has been able to employ detailed and quality-assured individual participant data derived from EPRs. Furthermore, the data set offered a unique opportunity to capture near population-wide data (and thus costs) on day-to-day care provided across all neonatal units without imposing any additional burden on study participants. Thirdly, the richness of the data set permitted us not only to cost routine daily care provided at differing levels of intensity, but also to consider the cost implications of a number of major non-routine procedures, which are not captured within the HRG codes for neonatal critical care. Finally, by generating up-to-date estimates of the mean resource use and costs of neonatal care for very preterm babies in England, this study provides valuable data of interest to a range of stakeholders, including NHS managers, clinicians providing care, researchers assessing the economic implications of therapies and interventions to prevent and treat preterm birth, and decision-makers charged with implementing new policies and allocating resources.

A few limitations must also be acknowledged. This study considered only healthcare costs associated with the initial period of hospitalisation, though the economic consequences of preterm birth extend over prolonged periods of time, in some cases over the lifetime of the individual.[24,25,117] Preterm birth can lead to additional health care as well as social care needs and special educational needs throughout childhood.[83,118] Further research is needed to adequately capture these wider costs accurately, including the economic costs to families while their preterm baby was hospitalised, and then throughout their lives. A further limitation is the exclusion from the analysis of babies with missing data on daily care provision, who were shown to have been born at earlier gestations than babies with complete data (see *Appendix 6*, *Table 34*). While these babies accounted for only 6% of the initial NNRD cohort and data showed no differences in gestational age at birth between the babies with complete data and all very preterm births registered in England (see *Report Supplementary Material 7*), we observed small significant differences in baseline characteristics between babies with missing and complete data. We conducted a multiple imputation approach to understand the implications of these differences and our results suggested limited impact of the missing data in the overall cost results.

Conclusions

This study has generated up-to-date estimates of the costs of providing neonatal care to very preterm babies in England. Resource use and costs vary by gestational age at birth. The outputs from this work can be used to inform clinical and budgetary service planning and ensure the efficient allocation of healthcare resources.

Summary points from OPTI-PREM cost of care, workstream 3

What was already known prior to the study

- We do not have current cost estimates for very preterm care in England.
- These are required to inform policy-makers on most appropriate place of care for very preterm babies born at 27–31 weeks gestation.

What this study adds

- We have provided a detailed cost analysis at individual baby level, and for all very preterm babies born at 27–31 weeks gestation.
- The major costs of care are due to daily care costs.
- In England we spend approximately 0.25 billion GBP on care for preterm babies born at 27–31 weeks gestation.

How this study may affect policy

(See *Chapters 9* and *10*)

- This is a valuable resource to help decision-makers in resource allocation, to optimise neonatal service delivery for this cohort.
- To guide research assessing the economic implications of preventing preterm births.

Chapter 7 Workstream 3: comparing the costs and effects of care

In NICUs and LNUs for very preterm babies in England: a retrospective analysis of a national birth cohort.

Introduction

Our OPTI-PREM programme of work employed a mixed-methods design to identify the optimal setting in which to provide care at birth for very preterm babies born at 27–31 weeks gestation. In *Chapter 4* we used the NNRD, to evaluate whether being born into maternity services colocated with NICU compared with LNU and admitted to their neonatal unit for care affected mortality (while in neonatal care and in infancy) and key secondary neonatal morbidity outcomes. In *Chapter 6* we estimated total costs of care for very preterm babies born at 27–31 weeks gestation and admitted to all but one neonatal unit in England. We identified that total costs were ~0.25 billion GBP per year, that costs were driven by daily costs of care and that costs of care were inversely proportional to gestational age at birth. Using the same data sources, we then conducted an allied assessment of the cost-effectiveness of care in each type of unit from an NHS perspective and using additional number of lives saved as measure of benefit in the economic evaluation. We report our findings in this section.

Aim and objective

To estimate the cost-effectiveness of care of very preterm babies born at 27–31 weeks gestation and admitted to NICU compared with LNU, in England, up to discharge from neonatal care.

Methods

We utilised individual patient-level data on admissions to all but one of the neonatal units in England, for babies born at 27–31 weeks gestation and who were discharged or died between 1 January 2014 and 31 December 2018. In addition, the cohort also included babies who were inadvertently not born in a hospital with a LNU or NICU, but who were later transferred to one of these for continued care. Admissions were identifiable through the NNRD, as described in *Chapter 5*. Data for the analysis were extracted from the NNRD on 5 October 2020.

Resource use and costs

We conducted the analysis from the perspective of the NHS in England. The time horizon was up to the end of neonatal unit care. To calculate the costs associated with the routine daily neonatal care received by each baby, we multiplied the number of days spent receiving each level of care by level-specific national average bed-day costs sourced from the 2018–9 National Schedule of NHS Costs.[28] We used HRG codes, and their unit costs as described in *Chapter 6*. We included five high-cost non-routine procedures as described in *Chapter 6*, that is nitric oxide, surfactant replacement, total parental nutrition (TPN) (over 14 days of use), palivizumab use and surgical care. Similarly, we identified types of neonatal surgery from their corresponding OPCS and ICD-10 codes for costing purposes, and costs for other activities were obtained from various sources as detailed in *Appendix 5*, *Table 34*. Again, the NNRD data for these five non-routine procedures were assumed to be complete, with no entry in the corresponding data set fields taken as an indication that the procedure did not take place.

Survival

Given the retrospective nature of the analysis, we used survival status at the end of neonatal care as the measure of outcome for the cost-effectiveness analysis, with incremental effectiveness expressed as the number of lives saved.

Statistical analysis

As per the statistical analysis methods used for the OPTI-PREM clinical analyses and described in *Chapter 4*, comparisons of costs and effects between unit types were made after adjusting for measured confounders, and also unmeasured confounders using an IV approach. We utilised the same measured confounders (see *Chapter 4*) and the same IV – excess travel time to a NICU. Our IV model was estimated using two-stage linear least squares for the cost (continuous) variables and seemingly unrelated bivariate probit regression for the mortality (binary) variable. The choice of the bivariate probit instead of the standard probit model was the binary nature of 'unit type' (NICU or LNU). We also conducted a sensitivity analysis and ran costs and mortality models without any measured confounders to understand the impact of this adjustment on the overall results.

For information and the benefit of the reader, we present unadjusted crude means and mean differences between 'unit types', and an analysis adjusted for measured confounders only.

Results

Figure 7 describes the flow of study participants. Records were initially extracted for 29,842 babies born at 27–31 weeks gestation and discharged from neonatal unit care between 1 January 2014 and 31 December 2018. Following exclusion of ineligible cases (n = 3557) and those with missing data (n = 7673), the final analysis was performed using data from 18,612 babies.

Table 23 presents maternal and baby baseline characteristics of the final complete-case sample and those excluded due to missing data. In general, we observed similar distribution between both samples for the majority of characteristics. However, the complete-case analysis sample has slightly more multiple births and caesarean sections, and comparatively a smaller proportion of white women. *Table 24* shows baseline characteristics by neonatal unit type. These data show babies managed within NICU were born at earlier gestations and had a lower birthweight than those born within LNU. Mothers of babies cared for in NICU were also less likely to be of white ethnicity and to have higher levels of deprivation.

Figure 8 details the distribution of excess travel time to NICU of the IV used within the analysis to adjust for unmeasured confounders. The median excess travel time was estimated to be 3.9 minutes suggesting on average women lived slightly closer to a LNU than to a NICU in our sample. *Table 25* shows the baseline characteristics of the cohort when recategorised according to the median IV < 3.9 or IV > 3.9. The groups were well-balanced across most characteristics with an absolute standardised difference < 0.15, with the exception of the IMD, which showed a higher proportion of the most deprived mothers living in closer proximity to a NICU than to a LNU.

Costs

Appendix 7, *Table 36* presents an unadjusted analysis of the mean number of days for which babies cared for in NICU and LNU received different intensities of care. As expected, significantly longer durations of intensive care, high-dependency care and special care were observed with NICU. However, after adjusting for measured confounders (see *Appendix 8*, *Table 37*), differences in intensive and high-dependency care were no longer present. *Table 26* presents the final analysis in which resource use and costs were adjusted for both measured confounders and unmeasured confounders using an IV approach. For each care setting, mean (SE) resource use and costs are reported along with mean cost differences (99% CI). On average, and compared to babies cared for in LNU, those managed in NICU spent fewer days receiving intensive care and high-dependency care, and more days receiving special care. Costing these daily levels of care resulted in a mean per baby cost of NICU-based care of £44,177 and LNU-based care of £46,179 [mean cost difference −£2003 (99% CI −£3432 to −£573)]. This difference in the levels of care provided accounted for 80% (£2003/£2534) of the lower overall total neonatal cost with NICU as compared to LNU, shown in the final row of *Table 26*. Lower costs of hospital transfers and other major non-routine procedures in the NICU setting accounted for the remaining 20%.

Table 27 shows the final analysis adjusted mean total cost of neonatal care for each setting by week of gestation at birth. Costs were significantly lower in the NICU setting for babies born at 30 and 31 weeks gestation. *Appendix 9*,

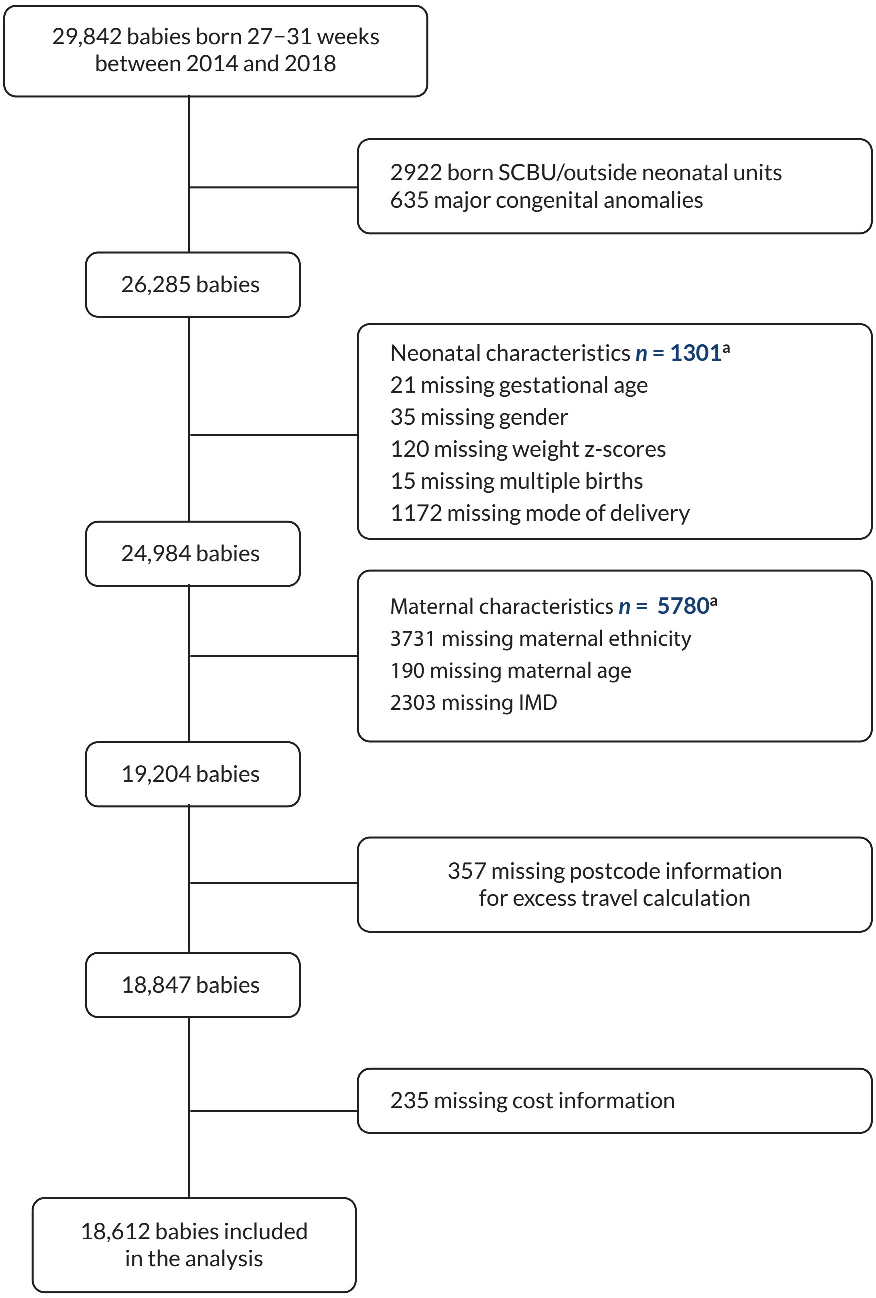

FIGURE 7 Flow of NNRD babies included in the health economic analysis. a, Missing neonatal and maternal characteristics were not mutually exclusive and it was possible to have missing information in more than one characteristic.

TABLE 23 Maternal and baby baseline characteristics of final sample compared with those excluded due to missing data

	Complete-case sample (*n* = 18,612)		Sample with missing data (*n* = 11,230)	
	n	%	*n*	%
Neonatal characteristics				
Baby born in NICU	10,241	55.0	4628	55.7
Gestational age at birth				
27 weeks	2243	12.1	1337	11.9
28 weeks	2985	16.0	1689	15.1

TABLE 23 Maternal and baby baseline characteristics of final sample compared with those excluded due to missing data (*continued*)

	Complete-case sample (*n* = 18,612)		Sample with missing data (*n* = 11,230)	
	n	%	*n*	%
29 weeks	3372	18.1	1953	17.4
30 weeks	4327	23.2	2652	23.7
31 weeks	5685	30.5	3577	31.9
Missing	0		22	
Phenotypic sex of the baby				
Male	10,186	54.7	6155	55.0
Female	8426	45.3	5035	45.0
Missing	0		40	
Birthweight (g), mean (SD)	1318	(331)	1343	(338)
Apgar score at 5 minutes, mean (SD)	8.2	(1.7)	8.1	(1.8)
Multiple birth	5208	28.0	2831	25.2
Mode of delivery				
Vagina l- spontaneous	5484	29.5	3273	33.0
Vagina l- instrumental	532	2.9	293	2.9
Caesarean section	12,596	67.7	6364	64.1
Missing	0		1300	
Died during neonatal stay	568	3.1	439	3.9
Maternal characteristics				
Maternal age, mean (SD)	31	(6.2)	31	(6.3)
Maternal ethnicity				
White	13,627	73.2	5099	78.9
Black	1638	8.8	464	7.2
Asian	2611	14.0	674	10.4
Mixed	353	1.9	99	1.5
Other	383	2.1	129	2.0
Missing	0		4765	
IMD quartile				
Q1 least deprived	2487	13.4	1011	11.9
Q2	2724	14.6	1245	14.7
Q3	3265	17.5	1570	18.5
Q4	4280	23.0	2038	24.0
Q5 most deprived	5856	31.5	2617	30.9
Missing	0		2749	

Q, quintile.

TABLE 24 Neonatal and maternal characteristics by place of birth (maternity unit attached to a NICU or a LNU) using WS3 cohort

	NICU (*n* = 10,241)		LNU (*n* = 8371)	
	n	%	*n*	%
Neonatal characteristics				
Gestational age at birth				
27 weeks	1478	14.4	765	9.1
28 weeks	1750	17.1	1235	14.8
29 weeks	1858	18.1	1514	18.1
30 weeks	2315	22.6	2012	24.0
31 weeks	2840	27.7	2845	34.0
Chromosomal sex of the baby				
Male	5578	54.5	4608	55.0
Female	4663	45.5	3763	45.0
Birthweight (g), mean (SD)	1287	(343)	1357	(312)
Apgar score at 5 minutes, mean (SD)	8.1	(1.7)	8.2	(1.7)
Multiple birth	3085	30.1	2123	25.4
Mode of delivery				
Vaginal – spontaneous	2932	28.6	2552	30.5
Vaginal – instrumental	265	2.6	267	3.2
Caesarean section	7044	68.8	5552	66.3
Died during neonatal stay	386	3.8	182	2.2
Maternal characteristics				
Maternal age, mean (SD)	31	(6.2)	31	(6.3)
Maternal ethnicity				
White	7360	71.9	6267	74.9
Black	941	9.2	697	8.3
Asian	1513	14.8	1098	13.1
Mixed	205	2.0	148	1.8
Other	222	2.2	161	1.9
IMD quartile				
Q1 least deprived	1290	12.6	1197	14.3
Q2	1425	13.9	1299	15.5
Q3	1601	15.6	1664	19.9
Q4	2216	21.6	2064	24.7
Q5 most deprived	3709	36.2	2147	25.6

Q, quintile.

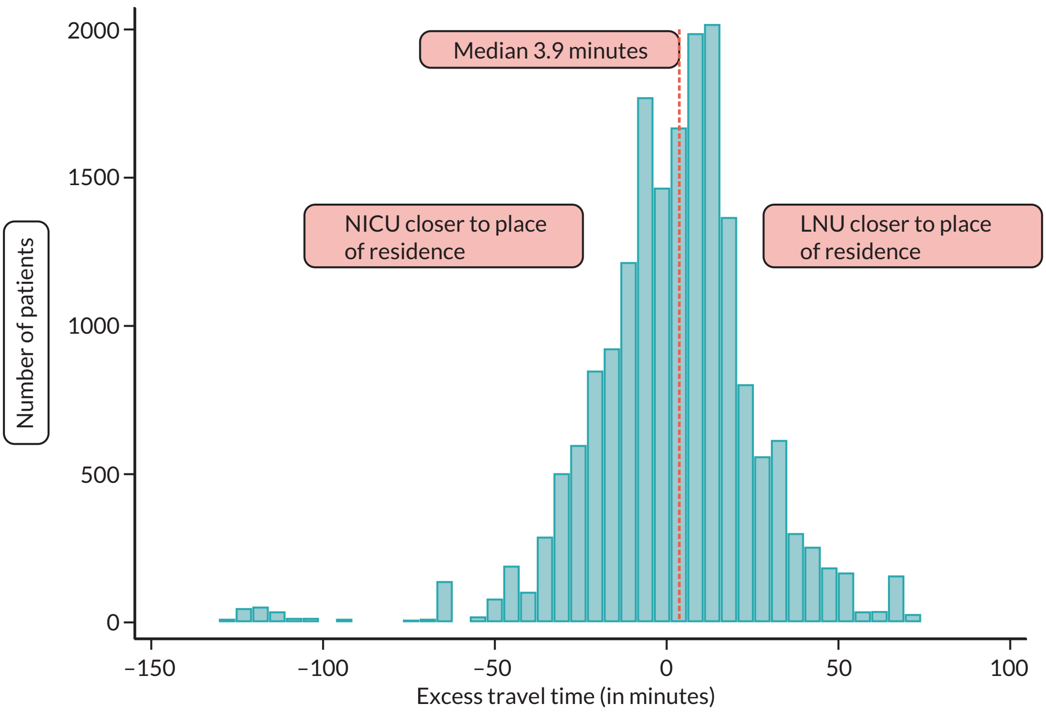

FIGURE 8 Cohort distribution of the IV used in the analysis – excess travel time to a NICU as compared with a LNU.

TABLE 25 Neonatal and maternal characteristics by median differential travel time to a NICU

	Differential travel time (travel time to NICU – travel time to LNU)				
	≤ 3.9 minutes		> 3.9 minutes		
	n	%	*n*	%	Absolute standardised difference
Neonatal characteristics					
Gestational age at birth					
27 weeks	1077	11.7	1166	12.4	0.022
28 weeks	1462	15.9	1523	16.2	0.008
29 weeks	1670	18.2	1702	18.1	0.003
30 weeks	2164	23.5	2163	23.0	0.012
31 weeks	2818	30.7	2867	30.4	0.007
Male	5018	54.6	5168	54.9	0.006
Female	4173	45.4	4253	45.1	0.006
Birthweight (g), mean (SD)	1322	(332)	1315	(330)	0.020
Multiple birth	2529	27.5	2679	28.4	0.020
Mode of delivery					
Vaginal – spontaneous	2775	30.2	2709	28.8	0.031
Vaginal – instrumental	260	2.8	272	2.9	0.0060
Caesarean section	6156	67.0	6440	68.4	0.030
Died during neonatal stay	279	3.0	289	3.1	0.006

continued

TABLE 25 Neonatal and maternal characteristics by median differential travel time to a NICU (*continued*)

	Differential travel time (travel time to NICU – travel time to LNU)				
	≤ 3.9 minutes		> 3.9 minutes		
	n	%	*n*	%	Absolute standardised difference
Maternal characteristics					
Maternal age, mean (SD)	31	(6.2)	31	(6.2)	0.048
Maternal ethnicity					
White	6675	72.6	6952	73.8	0.027
Black	772	8.4	866	9.2	0.028
Asian	1376	15.0	1235	13.1	0.055
Mixed	182	2.0	171	1.8	0.015
Other	186	2.0	197	2.1	0.007
IMD quintile					
Q1 least deprived	1071	11.7	1416	15.0	0.097
Q2	1220	13.3	1504	16.0	0.076
Q3	1396	15.2	1869	19.8	0.121
Q4	1970	21.4	2310	24.5	0.074
Q5 most deprived	3534	38.5	2322	24.6	0.303

TABLE 26 Adjusted mean (SE) neonatal resource use and cost by care setting and mean cost difference (99% CI)[a]

	Mean (SE) resource use per baby		Mean (SE) cost per baby		Mean cost difference (99% CI)
Resource item	NICU setting	LNU setting	NICU setting	LNU setting	(NICU minus LNU)
Levels of daily care					
Intensive care days	7.94 (0.128)	9.13 (0.145)	£12,150 (£196)	£13,980 (£222)	−£1829 (−£2758 to −£900)[b]
High-dependency days	11.42 (0.187)	12.38 (0.235)	£11,504 (£189)	£12,468 (£237)	−£964 (−£1926 to −£2.21)[b]
Special care (no carer) days	30.02 (0.182)	28.46 (0.219)	£19,841 (£120)	£18,810 (£145)	£1032 (£437 to £1627)[b]
Special care (carer) days	1.38 (0.040)	1.87 (0.053)	£681 (£20)	£922 (£26)	−£241 (−£347 to −£136)[b]
Normal ward days	0.00 (0.001)	0.00 (0.000)	£0 (£0)	£0 (£0)	£0 (£0 to £1)
Total cost of daily care	–	–	£44,177 (£288)	£46,179 (£351)	−£2003 (−£3432 to −£573)[b]
Other high-cost procedures					
Number of days with nitric oxide	0.22 (0.018)	0.16 (0.020)	£56 (£5)	£42 (£5)	£14 (−£7 to £35)
Number of days with TPN (over 14 days use)	1.92 (0.115)	2.75 (0.147)	£282 (£17)	£399 (£22)	−£117 (−£204 to −£29)[b]
Number of times palivizumab given	0.01 (0.002)	0.01 (0.003)	£64 (£16)	£66 (£23)	−£2 (−£96 to £91)
Number of ROP surgeries	(0.002)	0.01 (0.002)	£18 (£3)	£14 (£3)	£4 (−£9 to £17)

TABLE 26 Adjusted mean (SE) neonatal resource use and cost by care setting and mean cost difference (99% CI) (*continued*)

Resource item	Mean (SE) resource use per baby		Mean (SE) cost per baby		Mean cost difference (99% CI)
	NICU setting	LNU setting	NICU setting	LNU setting	(NICU minus LNU)
Number of neonatal surgeries	0.06 (0.006)	0.08 (0.007)	£190 (£17)	£237 (£22)	−£48 (−£134 to £39)
Proportion receiving surfactant replacement	0.48 (0.007)	0.54 (0.008)	£571 (£15)	£716 (£19)	−£145 (−£208 to −£82)[b]
Number of hospital transfers	0.40 (0.012)	0.59 (0.016)	£503 (£16)	£740 (£20)	−£237 (−£319 to −£155)[b]
Total neonatal healthcare costs	–	–	£45,860 (£313)	£48,393 (£386)	−£2534 (−£4096 to −£971)[b]

a Model adjusted for gestational age; sex; birthweight z-score; multiplicity; mode of delivery; maternal ethnicity; maternal age and IMD score in the IV model.
b Statistically significant at $p < 0.01$.

TABLE 27 Adjusted mean (SE)[a] total neonatal cost by care setting and mean cost difference (99% CI), by week of gestation at birth

Weeks gestation at birth	Mean (SE) cost per baby NICU setting	Mean (SE) cost per baby LNU setting	Mean cost difference between NICU and LNU (99% CI)
27 weeks (*n* = 2243)	£80,015 (£1309)	£81,631 (£2439)	−£1616 (−£10,352 to £7120)
28 weeks (*n* = 2985)	£65,156 (£1040)	£67,790 (£1356)	−£2634 (−£8016 to £2748)
29 weeks (*n* = 3372)	£49,308 (£719)	£52,448 (£863)	−£3140 (−£6671 to £391)
30 weeks (*n* = 4327)	£37,161 (£446)	£39,531 (£567)	−£2370 (−£4598 to −£142)[b]
31 weeks (*n* = 5685)	£26,955 (£395)	£29,231 (£387)	−£2276 (−£4041 to −£510)[b]

a Adjusted for sex; birthweight z-score; multiplicity; mode of delivery; maternal ethnicity; maternal age and IMD score in the IV model.
b Statistically significant at $p < 0.01$.

Table 38 shows the associated mean number of days provided at each level of intensity and week of gestation at birth and reveals that the significant differences in overall costs are driven by differences in intensive care days at 30 weeks and intensive care, high-dependency and special care days at 31 weeks.

Effects

Table 28 shows the proportions of deaths at neonatal discharge in each care setting, for the overall cohort of 18,612 and by weeks of gestation at birth. Across all babies, there was no difference in death proportions between care settings. Similarly, no differences were observed when analysing mortality data by gestational age at birth.

Cost-effectiveness

Figure 9 plots, for the overall cohort, the difference in mean costs and difference in mean effects between NICU and LNU care settings on the cost-effectiveness plane. Difference in mean effects were expressed as additional number of babies surviving to facilitate interpretation. The point plotted is in the lower half of the plane, reflecting the cost saving in the NICU setting, but it is also close to the origin of the *x*-axis, illustrating the absence of any difference in infant mortality. Also shown are the 95% CIs around the differences and a 95% confidence ellipse illustrating the likely

TABLE 28 Adjusted overall and gestational age-specific mortality while in neonatal care

Weeks gestation at birth	Number of deaths	Cohort size	Mean proportion (SE) of deaths[a] NICU setting	Mean proportion (SE) of deaths[a] LNU setting	Mean difference (99% CI)
Overall	568	18,612	0.03 (0.002)	0.03 (0.003)	0.001 (−0.012 to 0.009)
27 weeks	165	2243	0.07 (0.008)	0.09 (0.022)	−0.020 (−0.085 to 0.046)
28 weeks	171	2985	0.05 (0.006)	0.07 (0.013)	−0.017 (−0.058 to 0.024)
29 weeks	88	3372	0.02 (0.004)	0.03 (0.007)	−0.009 (−0.032 to 0.013)
30 weeks	64	4327	0.01 (0.003)	0.02 (0.004)	−0.002 (−0.017 to 0.013)
31 weeks	80	5685	0.02 (0.003)	0.01 (0.002)	0.009 (−0.002 to 0.019)

a Adjusted for gestational age (when analysing the overall cohort); sex; birthweight z-score; multiplicity; mode of delivery; maternal ethnicity; maternal age and IMD score in the IV model.

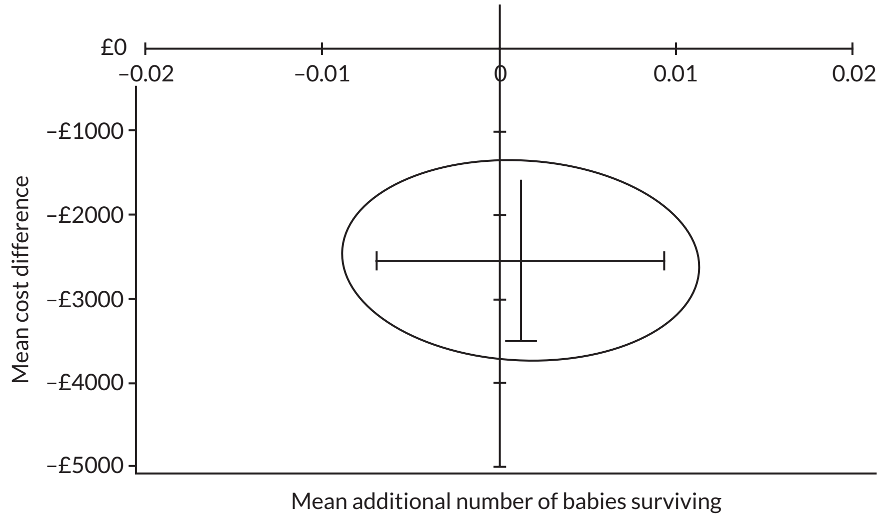

FIGURE 9 Mean cost and effect differences and associated uncertainty between NICU and LNU care settings plotted on the cost-effectiveness plane.

uncertainty of the 95% of the joint distribution of cost and effect differences. The latter suggested that uncertainty on the joint distribution of costs and effects lies in the south-east and south-west of the cost-effectiveness plane. Almost 100% of the joint density of costs and effects wase below willingness to pay for health gain between £50,000 and £100,000.

Sensitivity analysis

Appendix 10, *Table 39* shows the results of the overall and gestation-specific mortality and total costs using an IV model without any adjustment to measured confounders. The results suggested that very little or negligible adjustment was needed using measured confounders in the IV model.

Discussion

Utilising high-quality data from a national database and an IV modelling approach, this study has compared the costs and mortality to discharge of babies born 27–31 weeks gestation in NICU and LNU settings. To the best of our knowledge, no previous studies have assessed the cost-effectiveness of these care settings for preterm babies born at this or indeed any other gestational age.

Findings in context

The results generated by this work require careful interpretation and placing within the context of the organisation of neonatal unit services in England as well as the nature of preterm birth per se. If solely following the conventions of cost-effectiveness analysis, these data appear to advocate for NICU units, suggesting that the setting of post-delivery neonatal care does not impact infant survival but that when care is provided in a NICU, and particularly so for babies born at 30 and 31 weeks gestation, significant cost savings can be realised. In practice however, it would be challenging to try to redirect the post-delivery care of many of these babies from LNU to NICU. The geographical dispersion of neonatal care units within England provides one reason for this. NICU tend to be housed within large, tertiary, city-based hospitals and a great many pregnant women do not live in close proximity to these hospitals. Another and related reason is that unlike a planned elective procedure for which a date and location can be arranged in advance, a preterm birth is an unexpected and frightening event for a woman, who will therefore most likely present to her local hospital regardless of the type of associated neonatal unit. Finally, shifting the care of large numbers of 'less sick' preterm babies to cots within NICU units solely for the purposes of saving costs would be considered unethical and detrimental to those preterm babies born at earlier gestations, for whom care within a NICU is essential for their survival.

Recognising both practical and ethical constraints to the reorganisation of neonatal care for babies born at 27–31 weeks gestation, it would perhaps be prudent to use the findings from this work, which have been able to detail where such cost differences arise, to hypothesise why they might arise. *Table 26* showed that 80% of the mean total cost difference observed between NICU and LNU was attributable to variations in the intensity of care provided to babies daily. Babies cared for in NICU spent just over 1 day longer receiving special care, while those in LNU received around 1 day more of intensive care and high-dependency care. A range of factors with the potential to vary by type of neonatal unit could explain these findings. For example, and as noted above, NICUs are usually located within large tertiary hospitals that often have specialist obstetric and feto-maternal medicine services, and where staff are experienced in managing preterm babies with a range of complex conditions. Highly skilled and specialised clinicians at these sites may be adept at recognising and making timely amendments to the intensity of care required by less sick babies in the unit. Further, in these larger hospitals with greater capacity, staff may more easily be able to facilitate such changes. In smaller LNU with fewer beds, a timely step down of care may prove challenging, with resulting delays, if bed occupancy in the unit is high or at capacity.

The gestation-specific cost estimates shown in *Table 27* would support these hypotheses. While costs for babies born at the earliest gestations (27, 28 and 29 weeks), and thus requiring the highest levels of care, were not significantly different between NICU and LNU settings, costs for babies born at 30 and 31 weeks gestation, and who may be considered 'less sick', were significantly lower with NICU care. Additionally, within LNU, the duration of usage of TPN was longer, and the total amount of surfactant replacement was higher than in NICU. Further mixed-methods research should seek to fully understand the reasons for the observed differences in care practices between NICU and LNU along with whether any of these factors are modifiable such that the management of babies in both types of units could be more closely aligned and cost savings safely realised.

The discussion generated thus far is based upon the observation that there would appear to be no difference in baby mortality between each setting of care. Alongside mortality, however, it is also important to consider the morbidity of these babies. Key morbidities were assessed as secondary outcomes for the OPTI-PREM clinical effectiveness analysis and included ROP at Stage 3+, oxygen dependency, NEC, SBI and breast milk at discharge (see *Chapter 4*). Small yet statistical differences in the proportions of babies with oxygen dependency (1.8% more in NICU) and with SBI (1.1% more in LNU) were observed, with these differences driven by the 11% of babies in the cohort born at 27 weeks gestation. When analysing data only for the 89% of babies born at later gestations, no differences between care settings for any of the morbidities studied were detected.

Placing this research within the context of existing work in the field is challenging, because as noted previously, we are not aware of any other studies that have formally compared the costs and effects of NICU and LNU care for preterm babies. It is possible however to compare certain aspects of this work, and in particular the costing components, with other studies in this field.

Limitations

This study has several limitations, most of which stem from the retrospective cohort approach used for the analysis. The obvious drawback is the lack of a randomised comparison and the risk of bias this exposes the analyses to. We attempted to minimise these risks as much as possible by using appropriate statistical analysis techniques to account for measured as well as unmeasured confounders. Using IV techniques, we were able to generate study groups, which aside from the setting of neonatal care, were well-balanced in terms of mother and baby characteristics (see *Table 1*).

The retrospective approach taken also limited the study outcomes to those available within the NNRD. This analysis used survival status at discharge from the neonatal unit as its measure of effectiveness, which led to further challenges around how to interpret and explore the uncertainty seen in the results. Cost-effectiveness analyses typically measure the effect of an intervention in terms of the number of life-years or quality-adjusted life-years (QALYs) gained. Established threshold or ceiling values reflecting the maximum amount that society is willing to pay for one of these units of outcome (e.g. one QALY) are frequently used by analysts to interpret their results and to construct cost-effectiveness acceptability curves for the purposes of quantifying the level of confidence in their findings.[119,120] As the unit of effect in this case is lives saved, which are not commensurate with life-years saved, such analyses could not be conducted here.

The time horizon used for the study was also dictated by the availability of data and may be considered too short given that the health implications of preterm birth are known to extend through early and late childhood and into adulthood.[121,122] If differences exist in the levels of longer-term morbidity experienced by babies treated in each setting, then the implications of such differences ought to be captured and included in the analysis. Although it was not possible to observe these data, the OPTI-PREM secondary analysis of key morbidities showed no real differences between settings and thus provides some reassurance that this is unlikely to be the case.

Around 38% (*n* = 11,230) of the original 29,842 babies available for the analysis were excluded because they were not eligible or because of missing data due to neonatal or maternal characteristics, missing postcode information to estimate excess travel or missing cost information. Most of the missing data were due to missing mode of delivery (4%), maternal ethnicity (13%) and IMD (8%). Similar rates of missingness have been observed in previous studies using NNRD data for the period of time utilised in OPTI-PREM.[123,124] Some babies in our study had one or more of these characteristics missing that were needed in the modelling to adjust for measured confounders resulting in a significant drop in the final sample size included in the analysis. We explored whether the baseline characteristics of the complete-case sample were somewhat different from the sample with missing data. Our descriptive analysis reported in *Table 1* suggested that only minor differences were observed in the distribution of multiple births, caesarean sections and maternal ethnicity. This was further explored in our sensitivity analysis where we removed measured confounders from the IV model and derived a sample excluding only missing data due to missing postcodes or cost data. This resulted in a data set with a sample of 25,352 babies for the overall and age-specific mortality and a sample of 25,046 babies for the total costs. The results of this analysis were virtually the same as the complete-case analysis suggesting the little or negligible impact of adding measured confounders to the model. To some extent, this was expected as we showed in *Table 25* that groups were well-balanced in terms of neonatal and maternal characteristics when using our IV. Our conclusion to this evaluation is that the sample excluded due to missing data was not significantly different from the complete-case sample and that missing data impacted very little our overall results.

Conclusions

To the best of our knowledge, this is the first study to compare the costs and outcomes of babies born at 27–31 weeks gestation in either NICU or LNU and using high-quality data from a national cohort. Results from OPTI-PREM suggested no difference between the settings in terms of baby outcomes at neonatal unit discharge but identified that those babies born at later gestations (30 and 31 weeks) in NICU had shorter durations of intensive and high-dependency care than their counterparts born in LNU. Factors specifically related to the organisation of neonatal care including the location, size and staff present in these units may explain these findings.

Practical and ethical concerns surround the redirecting of neonatal care for very preterm babies from LNU to NICU purely on the grounds of cost savings. Further mixed-methods research should seek to understand the reasons for the observed differences in care practices between NICU and LNU along with whether any of these factors are modifiable such that the management of babies in both types of units could be more closely aligned and cost savings safely realised.

Summary points from OPTI-PREM costs and effects of care study, workstream 3

What was already known prior to the study

- We are not aware of any previous studies comparing the costs and effects of care provided to very preterm babies born in NICUs and LNUs.
- Such work is required to inform policy-makers on the most appropriate place of care for very preterm babies born at 27–31 weeks gestation.

What this study adds

- The costs of care for babies born at 27–29 weeks gestation were not significantly different between NICU and LNU.
- Costs were significantly lower for babies born into NICU settings at 30 and 31 weeks. These were driven by differences in the durations of different levels of care provided (intensive care and special care days).

How this study may affect policy

- Research is needed to understand the reasons for the differences in the durations of intensive care between settings and how care processes can be more aligned.

Chapter 8 Workstream 4: a qualitative ethnographic study

Exploring place of care decision-making, and the perspectives of parents and clinicians, of preterm babies born at 27–31 weeks gestation.

Introduction

In this workstream we explore parent and staff perspectives regarding place of care. Very preterm babies born at 27–31 weeks gestation, if viable, are always admitted to neonatal units for ongoing care. As their time in hospital may be prolonged, this can be a frightening, highly stressful period for parents, families and staff. We considered therefore, that their perspectives, from having had the lived experience of hospital care and caring for this cohort of babies in both NICU and LNU settings, would provide invaluable insights that could inform best place of birth and care for very preterm babies in England.

Aim

To assess staff and parent perspectives on place of care for preterm births between 27 and 31 weeks gestation in England.

Objectives

To address the following unanswered research questions:

i. What factors do parents think should guide decision-making about where babies are cared for, and how does this happen in practice?
ii. What are clinicians' perspectives and practices around decision-making about place of care?
iii. What are the impacts on parents and families of this decision, and any subsequent change in care location?
iv. How can parents best be supported at this time?

Methods

Study design

This was a qualitative study using an ethnographic approach[125] that included observations of routine behaviours in their natural settings ('work-as-done' rather than 'work-as-imagined')[126–128] and interviews with staff and parents.

Data were initially collected in real time in two neonatal operational delivery networks, involving six neonatal units: two units were NICU (one per network) and four were LNU (two per network). Here, parents with their babies receiving contemporaneous neonatal care, and staff, were observed and interviewed. To broaden the parent perspectives and to include different geographical regions, further interviews were conducted with parents of very preterm babies born at 27–31 weeks gestation with experience of preterm neonatal care in England ('retrospective' perspectives).

Recruitment

Healthcare professionals working in the six neonatal units were introduced to the study by members of the OPTI-PREM project team. The healthcare professionals made parents aware of the study. The OPTI-PREM qualitative researcher then approached parents for consent for participation in the study. All eligible parents (i.e. those with a baby born at 27–31 weeks) who had a baby on the units during periods of observation, and all doctors and nurses working at the units on observation days were approached for interview.

Involvement of parents for 'retrospective' interviews was sought through the charity, BLISS,[52] utilising their social media channels. In response to the first general appeal, offers of participation were primarily from parents motivated to provide good feedback about care provided to their baby. Subjective assessment by the researchers suggested that these parents benefited from a relatively high socioeconomic status. In order to engage a broader, and more representative, sample of parents, a second appeal specifically sought parents whose experience had been 'particularly challenging for practical reasons (e.g. finances, family, culture/religion, English language skills, employment), in addition to their concerns about their baby's medical condition and care'. In doing so, we hoped to target and encourage the participation in our study of parents from demographic groups that are recognised to be under-represented in research.

Verbal consent was obtained from both staff and parents for observation; written consent was obtained for interview. At all times, it was made clear that participation was voluntary and that accounts would be anonymised.

Data collection and analysis

Data were collected and analysed by experienced social scientists. Fieldwork included 280 hours of observations (of ward rounds, daily clinical activities and discussions, and transfers across the six neonatal units) and unstructured discussions with staff and parents. The observer also took written notes unobtrusively and then debriefed with another member of the team. Some of these debrief sessions were audio recorded and transcribed, while others were written debriefs.

We also completed semistructured interviews with staff (see *Table 29* and *Report Supplementary Material 8*), and interviews with parents on the units and the wider group of parents who had recent experience of neonatal care at other units across England (see *Figure 10*). Interviews were either face-to-face or by telephone, lasted up to 1 hour and were audio recorded. A topic guide developed through literature review and discussions within the project team (including parent representatives) was used, but conversations were also guided by issues raised by participants. Observations and interviews were transcribed verbatim, and anonymised. The researchers undertook thematic analysis using a constant comparative approach to address the research questions stated above. NVivo software (QSR International, Warrington, UK) was used to code and organise data.

Inclusion criteria

Participants (parents and clinicians) who were willing and able to give informed consent were included. Participation was voluntary and it was made clear to parents that declining did not compromise the care they or their babies received. Written information was developed for both parents and clinicians invited to participate. Informed consent for participation obtained – verbal for observations and written for interviews.

Results

Overview of data

Fieldwork involved 280 hours of observation across the six neonatal units over a total of 35 days. *Table 29* outlines the staff interviewed, and *Report Supplementary Material 8* shows the observation framework utilised for the ethnographic work in the six neonatal units. *Figure 10* details the cohort of parents recruited for interview from the six neonatal units (real time) and more widely across England (retrospective). The latter included parents from the South West of England, East of England, West Midlands, East Midlands, South East of England, Yorkshire and Humber, North East of England and North West of England. Included within our parent interviews were two cases in which the baby had sadly died. We interviewed parents of babies born across the gestational age spectrum of OPTI-PREM (parents of five babies born at 27 weeks gestation, two at 28 weeks, five at 29 weeks, four at 30 weeks and six at 31 weeks gestation).

TABLE 29 Distribution of staff interviews

Interviews with neonatal unit staff				
Site	**Designation**	**Clinical role**	**Training level/band**	**Participant numbers**
Site 1	NICU	Doctor	Consultant	1
Site 2	NICU	Doctor	Registrar	1
		Nurse	Unknown	1
Site 3	LNU	Doctor	Registrar	1
		Nurse	Band 7 or higher	2
Site 4	LNU	Doctor	Consultant	1
		Nurse	Band 7 or higher	1
Site 5	LNU	Doctor	Consultant	1
Site 6	LNU	Doctor	Consultant	1
		Nurse	Band 7 or higher	1
		Nurse	Band 6 or lower	1
Other (working across sites)		Transport Nurse		3
Total staff interviewed				15

The interview schedules for staff, and real time and retrospective parent interviews, are detailed in *Report Supplementary Material 8*.

Presentation of data

Our findings are divided into two main sections. In *Section 1: Deciding and enacting place of care*, we show how decisions about place of care are made and operationalised. We focus on perspectives of neonatal staff who make and enact decisions about 'best place of care' for babies, because, while decisions may take account of parents' individual situations, parents were not usually directly involved in decision-making. We show how staff make decisions about place of care in practice, incorporating managerial concerns about financial sustainability of the unit and resources available, in addition to clinical considerations. We highlight the extensive organisation and negotiation involved in transferring babies, as well

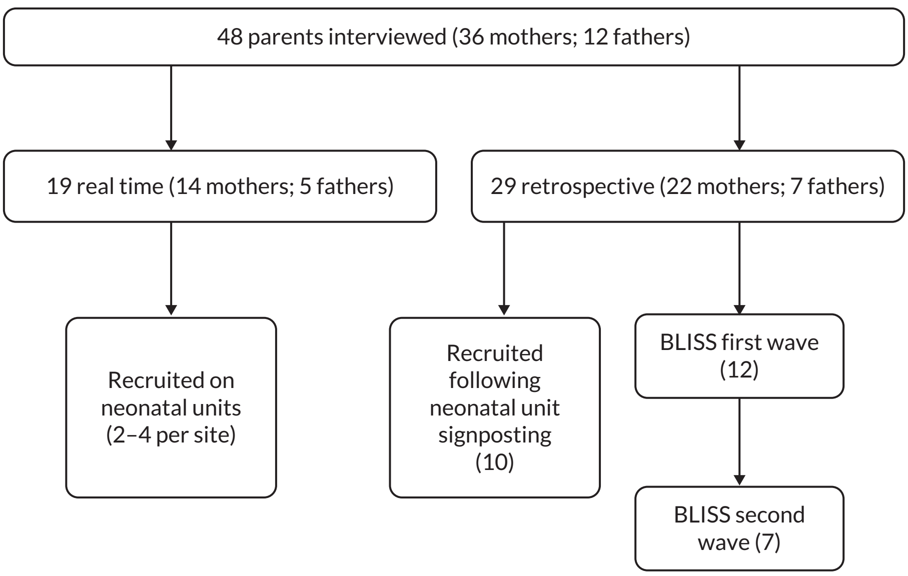

FIGURE 10 Recruitment routes for parents interviewed (both real time and retrospective).

as the practicalities of transfer. In *Section 2: Parent perspectives on place of care*, we discuss the perspectives of parents, and how place of care decisions impact on them and their baby. We demonstrate how transfers disrupt their ability to create continuity for their baby, with potentially far-reaching consequences. Finally, we reflect on the current organisation of neonatal care, and how parents may best be supported in this context. We illustrate our findings with data excerpts, labelled using 'Doctor' or 'Nurse' to identify the broad staff group, and 'Mother' or 'Father' to identify the parent. These categories are followed by their participant number. The site number is identified only when labelling observational field notes, to protect participants' anonymity.

Section 1: Deciding and enacting place of care

Contextualising decisions about place of care

Clinicians emphasised the variation in the needs of babies who are born (or likely to be born) in this gestational age group; their needs are influenced by a range of factors such as number of weeks gestation, number of babies, complications in pregnancy, baby's size. Although some of these factors may be known prior to delivery (and an informed guess made about their subsequent needs), babies in this group are unpredictable:

> *These are [a] very notorious group because they can behave like an extreme premature or they can just need a bit of support .... It's very difficult to predict these babies.*
>
> *Doctor12, LNU*

The difficulties of co-ordinating preterm delivery have been noted by Edwards and Impey[129] who found that only 50% of extremely preterm babies (< 27 weeks) are born in a specialist unit, despite this being the recommendation. For the OPTI-PREM group, there is no existing recommendation. When mothers seek medical help at 27–31 weeks gestation, they may telephone their booked hospital, and the advice given often hinges on the physical capacity of the unit (cots available):

> *[The nurse said:] Sometimes [LNU site] is full and [they] tell people to rock up [here] without checking [we] can take the pressure.*
>
> *Observation, Site 5, LNU*

Advice about the suitable place of care is orientated to the 'capacity' of the specific unit to which the mother presents – in this case over the phone rather than in person. The nurse highlights that hospital neonatal units, although linked as part of a network, are managed relatively self-sufficiently; here, staff at the booked hospital lack overview knowledge and/or interest in the capacity of other nearby sites.

Mothers often present in person (and often in labour) at the unit which is local or convenient to them. When time allows, neonatal and obstetric staff look to 'in-house rules' to guide decisions about which babies it is 'safe' for them to care for. Such local protocols dictate, for instance, the minimum gestational age at which it is appropriate to care for a baby in a LNU based on nationally recommended frameworks of practice.[3]

> *Majority of the time, it's quite a simple decision, for example guidelines we can't deliver, or we shouldn't manage anyone less than 27 weeks here ... And [we] have clear guidelines of how many nurses we need to run an ITU, how much space you need and all that ...*
>
> *Doctor12, LNU*

Such protocols are based on biomedical characteristics of the mother and baby (e.g. clinical conditions triggering early delivery) and the suitability of the unit to which the mother presents in terms of resources.

For mothers presenting at LNU, it is often considered 'optimal' for them to be transferred to a NICU, in recognition of the uncertainties surrounding the baby's likely condition:

> *We can scan but we don't have the expertise to confidently say there's no bleeds going on or the head's normal. So just small things that add up to not having good care or optimal care for the extreme premature baby just because we are not*

funded, we've not got the personnel or the skills because we don't deal with that so often. So I think even mums would say they want to be in the place where their baby's going to get the optimal care.

Doctor12, LNU

Units often must handle an imminent delivery regardless of whether they are equipped to care for that baby according to recognised standards and guidelines for neonatal care. Even mothers classified in advance as being 'high risk' (and therefore booked at a NICU hospital) often present in labour at their local hospital, where the unit is obliged to manage the delivery:

Triplets were booked for Site 1 but were born at Site 5. Consultant said this happens a lot; that high-risk pregnancies are booked at Site 1 but then mum presents at Site 5 too far along to be moved.

Observation, Site 5, LNU

This situation is problematic as mother and baby may subsequently become separated, as the babies are transferred to a more specialist unit. One nurse predicted that the system would need to change:

In years to come, you'll ring in, 'I'm in labour, I'm 25 weeks', [and a central co-ordinator will say] 'yes, that's fine ... the ambulance is on its way that will take you straight to [Hospital X]. When things have settled down you'll be transferred to [Hospital Y], your booking hospital'. That's how it would happen in years to come but at the minute people just turn up to the booking hospitals.

Nurse18, LNU

This nurse argues that a centralised system would allow a better view across the system and remove work for staff in LNU units tasked with delivering babies for which they are not equipped and/or arranging urgent transfers.

Our findings highlighted that decisions about the 'best' place of care are highly contextualised within the unit to which the mother presents. In many cases, the delivery takes place there despite staff considering it as non-ideal, and further decisions about the best place of care are made from that starting point:

If the birth is imminent then we just go for it. Personally I've dealt with babies who are twenty-three-and-a-half weeks onwards [at another unit]. So personally speaking I'm comfortable and I'm pretty sure my nursing colleagues are pretty comfortable. So we deal with them, but as soon as the baby comes out, one of my colleagues starts looking around, hunting for a bed [elsewhere].

Doctor20, LNU

In such situations, staff must cope with whatever happens and prepare to transfer the baby after delivery.

Sometimes a suboptimal delivery at a LNU is due to delays in identifying an alternative site or arranging an in utero transfer. Such delays concerned some staff who felt that the care of the baby was potentially compromised:

Fair enough if they come in overnight and they just deliver, then obviously no one can complain – we have to deliver that baby – but when they come in and we have 5/6 hours to sort out transfer, that's where, you know, I have issues.

Doctor12, LNU

Staff also draw on their local and dynamic knowledge about the current unit's capacity, the capacity of other nearby units, and an assessment of risk in relation to in utero transfer. The following example highlights that local guidelines may be 'bent' to avoid a transfer that is considered unnecessary:

On a December cold, wintery night and a mum came in utero [with triplets] and there was possibly a small window for her to go elsewhere, but I carefully calculated the risk and said 'your twenty-nine-weekers have very good growth for all those babies and, because it's winter and there is a chance that things might happen en route'. And at the time I had a very experienced registrar with me and I did have another member of the team who could definitely come back [into work after

> *leaving shift], and this mum had had steroids as well in the last week. So looking at all those calculations I actually did look after them and they [have] all grown well and [been] discharged with very brief ventilatory support. They all went home safely, never had to go to a tertiary unit.*
>
> *Doctor30, LNU*

Staff employ nuanced knowledge of capacity issues such as staffing experience on the unit at the time, and other variable factors such as the vagaries of the weather and transport infrastructure to weigh up the potential (but uncertain) benefits and risks of transferring the baby in utero.

After delivery, decisions about whether the baby is in the 'right' place continue to relate not only to the physical needs of the baby (requirement for ventilation, tube feeding, surgery, etc.), but also to local protocols, and the wider management of the neonatal network. In some cases, decisions are relatively simple, as the baby has particular needs that require equipment that is not available in a LNU:

> *It depends on their condition when they were born. There are some preterm babies who are born healthy so they will go directly to high dependency [equivalent to LNU in a NICU unit], but then there are some babies who are really in poor condition and need to be ventilated or need to be in an intensive care.*
>
> *Nurse10, NICU*

In other cases, staff balanced multiple formal and informal protocols, some of which were applied rigidly, and some treated more like 'rules of thumb' that could be varied:

> *For any particular baby that's in front of me, we also have some background, in-house rules … If they are very small babies, although they are twenty-seven plus, [then] we have a magic number of eight hundred grams or less. Then we do speak to the [NICU] to say 'er, it's better for the baby to be looked after elsewhere' … If it says singleton baby, and if it's say good growth for that twenty-seven to thirty-two weeks, I would rather be happy to look after the baby.*
>
> *Doctor30, LNU*

Often staff have to take account of multiple factors that are contributing to the overall 'capacity' of the unit at that particular moment in time. 'Capacity' includes many different elements – including staff numbers, qualifications, experience and the various types of equipment available, as well as number of cots:

> *So in our Unit [LNU], it's twenty-eight weeks and above, and then we look at ourselves. How are we? Is there enough nursing staff? Are there enough doctors? And then we look at bed capacity, and [intensive care capacity], whether there's enough space. For example, if there's only one space we'll be reluctant, because if there's an emergency, that baby doesn't care that [there's now] a [new] emergency baby [to take its spot]. … We basically look at the baby's condition, whether the baby has any specific needs, if there's any congenital anomaly. If yes, then we become reluctant. And rightfully so. We're reluctant for the sake of the baby's health and the mother's. Babies like that go to a tertiary centre. So that is the few things we look at. And weight as well.*
>
> *Doctor20, LNU*

Integrating 'managerial thinking' into decisions about transfers

Staff spoke of their 'network responsibility' to try to accommodate babies – a responsibility linked to national tariffs for different categories of care and locally negotiated contracts and payments.[130–132] Both LNU and NICU staff knew that they needed to 'think managerially' about capacity and resources – and this included considerations about income generation:

> *And then we like to think managerially as well. If [a Level 1] has a twenty-eight week [baby] and they ask whether you would like to accept, we are more than happy because not only it's good for our practice that we keep on getting prem babies, second, it brings money to the [hospital]. So that's the other way of looking at it. So we are always looking for kids.*
>
> *Doctor20, LNU*

Units were paid for their 'activity' (number of babies), so accepting new babies was important for income generation as well as to maintain the unit's status (also linked to the category of babies they are allowed to accept):

> *You have to accept, because we are a LNU, we cannot afford our activity to go down. Because [then] we'll be relegated to a Level 1 unit. So we won't want to be seen as refusing … I mean it's good to be hands-on. It's good to have activity. We can get deskilled if we don't have activity. … And the more activity we do, the more funds we get [so] that'll improve [the] financial situation as well. So it's a win-win situation. … Our network's constantly looking to activity. So you don't want to be showing that activity is going down.*
>
> *Doctor26, LNU*

LNU therefore tried to retrieve babies who had been transferred to NICU care, as soon as they were clinically ready for repatriation:

> *There is a baby here from an out-of-network hospital. [The hospital] has been ringing to see if it can come back.*
>
> *Observation, Site 1, NICU*

In addition, the tariff that each baby was believed to attract, according to the category of care that was required, was felt to be an important consideration:

> *While waiting, [another hospital] has rung up with an ex utero transfer (twins). 'We must be the only place with beds!' Everyone is excited to take the babies as it is an ITU transfer and that brings in a lot of money. [Staff member] singing 'one thousand and twenty-one pounds. Thank you!'*
>
> *Observation, Site 3, LNU*

Similarly, NICU needed to maximise income from babies attracting greater levels of funding – as they were equipped to provide care for this group. However, this was sometimes in tension with providing a broad spectrum of neonatal delivery for the local population – who happened to live near a NICU, and whose babies might therefore be transferred out to a distant LNU if they did not require 'high-end' intensive care support:

> *So it's finding a divide between running a hospital, just purely thinking about the service and how much activity you can churn through at the high end of intensive care, versus running a service that makes sure you provide the right service for the families of your local population.*
>
> *Doctor06, NICU*

Staff decision-making about place of care integrated managerial thinking with considerations of the baby's medical needs. Although sometimes obvious, more often it formed the backdrop for discussions about clinical needs and resources available. Sometimes a focus on managerial concerns created tensions within units, as in the following excerpt between medical and nursing staff:

> *Consultants want to have a better way of recording why babies can't be accepted. They want specifics, so they were saying things like 'why have you said we're busy? What is it about the category of babies in today that means we can't take another one? Are any of those eligible to go to an LNU or a Level 1?' Nurses said 'it's not that simple because staff shortage takes management nurses on to the ward and they can't properly identify the dependency and so it's hard to know exactly why a baby is refused admission other than "busy"'.*
>
> *Observation, Site 1, NICU*

Here, management priorities require that various staff align to focus on maximising income to the unit, and this work comes into tension with the everyday work of nursing. Nursing staff often wanted to 'operate at gold standard', while the resources available across a network, and the pressure for units to maintain income, together ensured that this was not feasible:

The doctor was also complaining about how there is no standardised practice for closing the unit because it depends on the person who is on that day. That the nurses always want to operate at a gold standard, but it is impossible to operate at that level because the unit is always falling short due to staff shortages.

Observation, Site 1, NICU

The following conversation between the researcher and two transport nurses highlights how high tariffs for particular categories of baby were believed to encourage units to be flexible about accepting babies when they were close to capacity (to exercise their 'network responsibility'), but also precipitated a need to 'jiggle' or 'shuffle' babies from one unit to another in order to make space.

TN05A: The units are very good, if it is a really sick baby that's got a specific problem then they're very good at trying to make beds, so often we'll move other babies out so that they can have a space for that baby, so we do jiggling around quite a lot as well. ... I think the NICU, especially the surgical ones, always really try and move babies to the wards [off the unit] and do whatever they can to accommodate.
TN05B: Because they get more money for the surgical ones! [laughs]

Researcher: Do you think that's part of the motivation?

[Short silence]

TN05A: I wouldn't want to comment.

TN05B: And also the interesting cases. Sometimes if they're really interesting ... and well, maybe there's a bit more [funding].

TN05A: Yeah, I think they're probably more likely to make space for a surgical baby than they would be for a non-surgical – because it's something a bit more interesting. ... And also, like you say, those sort of babies don't want to be travelling, you don't want to be going hours with them either, do you? They try and shuffle to make them fit in don't they?

TN05B: Sometimes we have been known to take babies from out of our catchment area for surgery when generally they should be going to another hospital that's in their catchment area, but if they call us then we will generally accept because ... our unit thinks 'yeah, why would we not take a surgical baby?'

Transport Nurse05A/05B

It is important to note that recognising this managerial thinking in decisions about place of care created some discomfort for staff, such as one of the nurse's initial responses in the extract above that they 'wouldn't want to comment' on this. It is also the case that we did not explicitly seek to verify the factual accuracy of funding flows within particular units.

The practical art of 'shuffling'

When a need for either in utero or postnatal transfer was identified, it had to be agreed with the receiving unit. For in utero transfers, the decision about whether to accept a baby was not only for the neonatal unit but also for the maternity service; a 'yes' was needed from both to proceed.

31 week in-utero transfer from Site Z [SCBU], NNU have said yes, but Delivery [ward] hasn't decided yet. 'They'll say no. That's what happens. We say yes, and they say no' (Charge Nurse)

Observation Notes, Site 3, LNU

Receiving units employed their own in-house 'rules' for negotiating transfer requests (like those described above); these helped staff determine whether they had adequate capacity to safely accept a new baby:

> *They have a white board in the sister's office that has two tick boxes to indicate open or closed to in-utero transfers. Then under is a list that says: 'Twins over 27+6 weeks, singleton over 26+6 weeks, babies over 800 grams'. Ward clerk has given me their external cot request book to see accepts/refusals. Majority of requests all the way back to Dec 2017 are in utero transfer requests, and the main reasons for refusing the request are capacity in labour [wards] or NNU.*
>
> *Observation, Site 6, LNU*

Arrangements for moving babies took considerable time and energy and were organised differently depending on the network arrangements for transport. In one network, a system was in place in which:

> *… transport do so much of the work, so if we've got a baby that we need to transfer out, we call transport, the doctor will give transport the handover and say: 'This is the baby it needs to go to a NICU unit for A, B, and C [reason]' then the transport team will find a NICU unit for us and then call us back.*
>
> *Nurse32, LNU*

In the other network, clinicians took on more of the work:

> *It takes time going through switchboards and asking people around, it can take 15/20 minutes easily to call one hospital. … Out of hours I'll just have one registrar and myself [consultant] and an SHO. It's a bit unfair for me to ask the SHO to phone and discuss these high-risk and complex cases, so it usually ends up with the registrar doing the lines and the procedures and I'm on the phone, so yeah it can be a bit stressful, it doesn't need a doctor to find out where the beds are available.*
>
> *Doctor12, LNU*

'Shuffling' babies around was a constant occupation in some units:

> *For the first time during ward round there has also been no discussion of moving babies out. This is normally an ongoing discussion on ward rounds. With 12 available beds patient flow is not a priority or need [today].*
>
> *Observation, Site 1, NICU*

> *Site 3 keep track of the babies they transfer out in their handover notes. 'We need to hassle on a daily basis'. Consultant is telling nurses to get beds for a new transfer on to the unit.*
>
> *Observation, Site 3, LNU*

When multiple units in a network were close to capacity, one baby's need for transfer precipitated another:

> *It can be quite frustrating for everybody … sometimes we'll need beds so we tend to ring [NICU hospital]. Sometimes we'll do a swap, so we'll have a baby [and] they can take one of our vented babies.*
>
> *Nurse17, LNU*

Decisions to move a baby took hours or days and could remain live for hours, days and even weeks. Even once a transfer was confirmed, the time for transfer was often unknown until an hour before the team arrived, necessitating babies to be 'transfer ready' at a moment's notice. As a result, treatments (e.g. ventilation, antibiotics) were often delayed to maintain a baby's status as 'ready' for transport; staff feared that starting these treatments could result in the baby no longer being eligible for transfer, and missing the small window of opportunity they had organised for the baby to move:

> *The consultant has recommended not intubating (if possible) the transfer babies as that complicates things and might set the transfer back.*
>
> *Observation, Site 3, LNU*

Transfers themselves were labour-intensive for staff:

Doctors keep changing out with the transfer team on the phone. The focus is on stabilising the baby medically (serious work though, three doctors, all in scrubs, one ANNP and two nurses all working to ventilate and put lines in). Also prepping all the paperwork, electronic system etc. for transfer and ticking the boxes for transfer out ASAP.

Observation, Site 2, NICU

This was exacerbated when the transport team itself was operating near capacity and there was considerable delay:

So, it's just waiting for the transportation to come. … if [the baby's] not on the priority list then you need to wait for like twelve hours for the next shift before [transport] comes. So really there the stress comes in waiting for the transporting to come.

Nurse10, NICU

It's quite hard on the units, … It can really change the entire day for the whole unit.

TransportNurse05

A lack of consistency of protocols and technologies created additional work and stress related to transfer:

Everyone agrees that a lot of time and equipment is lost because of a lack of consistency of equipment between hospitals. Can end up being very wasteful if sending hospital has a different policy from transport team, who have a different policy from receiving hospital. Three opportunities for wastage (milk, drugs, equipment) all get binned if they don't comply … This also means that there are often interventions to 'correct' between the different standards and baby can be poked and prodded three times just so that leads or drugs comply with new standards. Donor milk is not consistent across sites either.

Observation, Site 6, LNU

Chasing up reports, test results, and even verifying care received between the hospitals was difficult for staff, who had to rely on: a verbal handover from the transfer team; a verbal, over the phone report from the sending hospital; and patient notes that were often not in the same format as the receiving hospital used. Scan results were very difficult for receiving hospitals to access, necessitating new scans and interventions by the receiving hospital.

A baby transferred from Site X had no records. Medical staff were aware of baby and had discussed him during handover, but on electronic system there was nothing …

Observation, Site 1, NICU

As we will go on to highlight in *Section 2: Parent perspectives on place of care*, transfers were also very stressful for parents, and staff were caught up in managing these parents' concerns:

Nurse prepping the transfer was double-checking the 'Transport Information Systems Checks' sheet quite a lot. Even just transport through the hospital is very stressful and emotional for these parents and they are crying at the thought.

Observation, Site 1, NICU

Section 2: Parent perspectives on place of care

Parents' priorities in relation to place of care centred on the medical needs of their baby – having access to the 'correct care'. Being an obvious concern, this rationale was often used by staff to prepare and/or convince parents that transfer was in the best interests of the child:

The way it's explained is 'at the end of the day, your baby needs to be in the right place at the right time having the correct care' … I've even had mums say, you know, 'if you've got to send my baby to London, I don't care where you send it, as long as the baby's looked after properly'.

Doctor12, LNU

Parents generally deferred to clinicians' knowledge about the 'best place of care', but were also concerned about the practical consequences of a decision that would involve care at a distance:

> *Obviously I would have done whatever they told me, but in the end it was fine, they managed to find a space for him and he stayed close to home the whole time.*
>
> *Mother72A*

Being able to care for your own baby

As discussed in the Methods, most of the parents included in this study had experienced a 'positive outcome' (a healthy baby). Their descriptions of positive experiences are relevant to our discussion about place of care because, as highlighted, they may be more difficult to achieve when the baby is moved or receives care a long way from home.

In particular, it was important to parents that they were central to their baby's care – knowing what was going on and doing as much as they could to care for their own baby. This necessitated developing continuity with staff – that they were able to 'get to know' them:

> *I was there all day, twenty-four seven really so I just got to know all the staff. … they're just brilliant aren't they? I just couldn't fault them in any way.*
>
> *Mother16*

This also allowed them to be confident that the staff were paying attention to the baby's needs:

> *When they were looking after [baby], it all felt, it really was personal. It wasn't just like doing their job, it felt like they wanted to look after her, not just because they were being paid to.*
>
> *Mother25*

This relational continuity with staff was not seen as peripheral or 'soft', but as enabling parents to oversee the care of their own baby. Consistent staffing enabled them to access reliable information and exercise vigilance in their baby's care:

> *We saw probably two consultants and it was consistent. So it wasn't somebody different every day, and you soon get used to learning what they're doing with the hourly obs and stuff. That was explained and you could just sit with them, and you can help them, and they encourage you to get involved.*
>
> *Mother23*

It was very important to parents that they knew that they would be kept informed of what was going to happen next, particularly when staff became concerned or there was likely to be some change in the baby's care:

> *We knew from the very beginning what the process was going to be, and they kept us in the loop, they always told us what's coming next.*
>
> *Father72*

Being able to get to know, and trust, staff enabled parents to better balance their need to be with their baby with their own well-being and other domestic arrangements:

> *I stayed with my twins a lot, and I was moving house at the same time. And [staff at the unit] were really nice. I think I'd been there for about three or four days and the nurse came in, and she was like, 'Look, you know, we're not trying to get rid of you, but maybe just go and grab a coffee. Just take a little bit of time, go outside, see somebody'. They'd just do nice things like that, or 'the twins are settled, why don't you go and have a bath, and if something happens, we can always come and get you'.*
>
> *Mother77*

Parents valued the way in which staff recognised their practical needs and difficulties – for example, providing support with food and accommodation when they were unable to commute to the hospital. This enabled them to remain centrally involved in their baby's care, for example by supporting breastfeeding, or enabling them to travel backwards and forwards to the hospital:

> *They sorted out, they went through everything with where we were staying and the keys and told us what was what and they arranged food for us because I was breastfeeding. ... They knew we didn't have any facilities.*
>
> *Mother22*

> *The food is quite dear at the hospital anyway, but then petrol too because it's about a 15- to 20-minute drive from here. Luckily Family Funds did help us out a lot. So we was able to get a weekly ticket for the parking instead of buying it daily when we were there.*
>
> *Mother36*

Transfers disrupting parental care

As highlighted in *Section 1: Deciding and enacting place of care*, decisions about place of care were made in a context of limited capacity – staff, cots, equipment or other resources – across neonatal networks. This meant that, although babies' medical needs were at the forefront of decision-making, staff also had to incorporate 'managerial thinking' into transfer decisions – 'shuffling' babies in relation to the resources needed and available and paying attention to the financial sustainability of their own unit. As we highlighted, capacity was constantly changing in the different units across a network, as were parents' and babies' needs. This created a dynamic situation in which clinical staff were involved in ongoing preparation and negotiations with other units over transfer.

Stresses of transfer

The uncertainties of transfer generated considerable work and stress for parents as well as staff:

> *So yes, it's just basically not knowing. Can't plan anything, it's play it hour-by-hour, day-by-day.*
>
> *Mother14*

Everything was put on hold:

> *We needed both the bed and the transport to be available at the same time. So, the amount of times they'd say 'oh, there's a bed available, we can move tomorrow, we're just going to go and sort transport'. And then they'd go and sort Transport but, by the time Transport got back to them, the bed had gone.*
>
> *Mother65*

Parents often had to react and adapt very quickly, and this was stressful when the mother was still an inpatient:

> *It all happened really quickly – I was absolutely terrified, and didn't really know what was happening ... There was nothing I could do. They transferred [baby] up to [NICU hospital] and I was like adamant that they needed to transfer me up there as well [as an inpatient].*
>
> *Mother31*

In the following case, the mother rushes to get herself discharged while the baby is being prepared for immediate transfer:

> *[My husband] phoned me from special care [at Hospital A] and said 'they're moving her to [Hospital B]'. I said, 'what do you mean ..., when?' He said 'Now, the transport team are on their way, you've got about an hour'. So he stayed there talking to them while I hobbled over [following complications with delivery and C-section]. It was down one corridor and across another, so it was probably about a two-minute walk, maximum. It took me twenty minutes, I think. But I got myself over there, hoping I was going to talk them out of it. But they explained the situation ... So I went back, just in time for my midwives and they were 'How you feeling?' And they said, 'Oh, we can try and arrange a transfer to [Hospital B], but you know how long discharges take in hospitals'. And I thought, 'Well, if they keep me in any longer, I'm going to be separated*

from her'. So I just said 'No, I'm doing really, really well, yeah, I think I'm ready to go now', so that they'd discharge me, basically.

Mother75

Alongside the baby's transfer, parents had to organise their lives around the new location – and the new routines and arrangements that would be necessary, and possible. As highlighted below, these often involved complex arrangements in relation to the father's employment and/or the care of other children.

Parents generally accepted that their baby might have to move in response to medical concerns, but moves related to capacity issues were more difficult:

It didn't help [that baby had to move to (distant LNU hospital)]. It really didn't help but they had literally no room [in local LNU hospital]. They said, 'If we had room, we would keep her here because we know you're from [local place]'. … [But Distant LNU hospital] were brilliant. Every day, probably three or four times a day, they were ringing to see if there was a place [in local hospital].

Mother36

These kinds of moves were not to benefit the baby, and might have detrimental consequences:

I think the hardest conversation is the move out for capacity reasons. So making a decision to impact significantly on a family potentially, when they might not want to, for the care of a different baby who they don't have nothing to do with can be quite difficult sometimes.

Doctor09, NICU

It was not always the parents' priority to be transferred closer to home, if they were concerned that this would disrupt the baby's care:

I did worry actually when they transferred [baby]. Because [NICU hospital] was so different – it's a different world in [NICU hospital] to [LNU hospital (where they had previously had a bad experience of care)]. Even the size of it, and the capability. And when the consultants and the surgeons are speaking to you, you know, they speak to you so that you understand [in a NICU]. … I remember chatting to a guy saying 'Are you sure that she's alright to go?' but of course they'd got more ill babies, they needed to move her of course. She was alright but the confidence [a parent can have in a NICU hospital] is different I think [to what they can have in a LNU hospital].

Mother25

Parents did not always feel that they could trust that decisions were being made in the best interests of their baby, and some questioned whether there might be managerial motivations for moving the baby:

And then it came – the worry – because he was doing so well by day eight, they wanted to get him out of there [NICU hospital (80 miles away)]. Because they needed the beds for the more ill children, and also because we weren't booked there, they kept pushing to get us back to [local Level 1 hospital]. … [I was worried that] [local Level 1 hospital] had said to me they aren't able to look after him, that made me queasy … And then I was upset that [NICU hospital] didn't know that [Level 1 hospital] weren't able to take babies until they were thirty-two weeks'.… They push you because it's all about finance. Because [local Level 1 hospital] are paying them all the time, so [NICU hospital] know that [local Level 1 hospital] are going to start phoning them to say 'When can I have the baby back?'

Mother71

Transfers disrupted the baby's medical care and parents were often concerned they made babies sicker in the short term:

And then the bit that I was scared of was the move as well. So as soon as he moved, he needed to go back on to oxygen which he wasn't on before. And all that happened with the move. And they didn't have any of his x-rays or anything so they had to start all over again.

Mother71

Getting to know and trust a new unit

Parents arriving in a new unit had to be inducted into the new setting and their responsibilities, requiring considerable assimilation of new knowledge, often under stressful and exhausting conditions:

> *'This is the milk kitchen, this is the linen store, this is this, this is that'. And we were going round and I'm thinking, 'I really just want to sit down' [laughs]. And then it was, 'Oh, you need to hire one of our pumps, so we need a deposit for the pump, can you get (…)' Okay, fine sure, I'll book that out somehow, and after all this, eventually, they just let me sit next to her incubator again.*
>
> *Mother75*

However, parents were often most concerned about the disruption to their relationships with staff, and the shared knowledge that had been built up:

> *I think for me it's the ongoing care [that's important], because you know as soon as you move hospitals you're going to have to start again. And you've worked so hard: you know the routine, you know the staff, they know [baby].*
>
> *Mother71*

Not only did staff at a new unit need to 'get to know' the baby in a technical sense (e.g. investigations such as X-rays documented on the notes), but they also needed to 'get to know' the baby's individual characteristics that were not covered by the notes, and the parents' circumstances and capacity to be involved.

Continuity of relationships with staff was important to parents, to support management of their baby's care. Parents felt the need to oversee the care their baby was receiving, bearing in mind that staff in the new unit would not 'know' their baby:

> *I wanted to see, I didn't know the nurses there and I wanted to see how they were. And then after those first two nights I was like 'okay, I'm happy now to leave her because now I know'.*
>
> *Mother64*

Getting to know staff was especially important when trying to understand significant differences in unit management or their approach to tasks in which the parents had been involved:

> *So it was a bit weird to begin with because they had a completely different routine to how they did things with like even just the breast pump and where you put your milk and all that sort of thing.*
>
> *Mother22*

> *Every single hospital, there were different pumps, different sterilising. How the milk worked – some hospitals you took charge of the milk, other hospitals they did. They are all very good at showing us how to do it, it was fine [but] it did astound me that every single hospital was different.*
>
> *Mother73*

For parents, the different approaches across different units caused a lot of uncertainty. They also made it difficult for them to know if their baby was being well cared for, as procedures they used to benchmark care in the old hospital were often completely different in the new hospital. As a result, many parents said they found the change between hospitals difficult to cope with as they were never sure if they were caring for their child properly in the new unit, and were scared they would do something to affect the outcome of their child's prognosis:

> *Different hospitals have different procedures, it was like, 'Oh, what's that?' And she was like, 'Oh, it's something we do for all our babies, don't worry'. And you're like, 'But I want to worry'. Not that I [really] want to worry, but I want to know what's … happening.*
>
> *Mother77*

Shift patterns and other unit policies also tended to disrupt continuity:

> *I thought it would have been a lot better if we had a specific nurse dealing with babies because then they, not so much bond with them, but get to know the baby a bit better to understand its needs. When you keep swapping and swapping and swapping, you're only going to know from what the paperwork tells you.*
>
> *Mother36*

Some staff (and units more generally) were more enthusiastic about allowing parents to be involved than others, and this created uncertainty and stress for parents.

> *[Hospital A] teach their parents to tube feed their prem babies whereas, when I went to [Hospital B], the sister was like 'No, we don't do that here, the nurses will do that for you'. And I didn't want them to, I wanted to do that myself. And I wasn't allowed. And then, I wasn't allowed to hold them and I said, 'I feel like it's just taking them away from me'.*
>
> *Mother77*

In relation to this mother, nursing staff insisted that differences between units were inevitable and that parents should accept this:

> *All she kept saying to me was like, 'You've just got to adapt'. And it was like, 'I don't want to adapt'. And I struggled because I had to commute and get the train every day, leaving them on a night, and I said to the nurse, 'Please don't let them cry, they're not used to crying'. ... There was a baby in another room, and the mum couldn't be there as much, because, like me, she didn't live near the area. And her baby was crying for about twenty minutes and I had to go and get the nurse one day, and I was like, 'He's really unsettled' and, she was like, 'Well, he's been fed and changed. Sometimes, you've just got to let babies cry'. And I said 'Well I don't want my baby to cry and I'm pretty sure she doesn't want her baby to cry either'.*
>
> *Mother77*

Staff insisted that some jobs were better carried out by staff, but mothers were often keen to take on as much care as they could handle. Continuing with the same example:

> *At [Hospital A], they leave their patient notes at the end of the bed and they encourage you to read what the nurse has wrote, so they're like '[Baby] had a really good night, but her heart rate dropped around two am' and they'd say, 'Have you had a chance to look through?' And I'd say 'Yeah, what happened at two o'clock?' and she was like, 'I don't know. She could have just had a sneezing fit, and her heart rate dropped'. Whereas in [Hospital B], it was very much, 'Oh, you can't read those, those are the medical records'.*
>
> *[The nurse said] 'You really need to let us do our job, we know what we're doing'. ... and she was just like, 'We do this all the time, even when you go home'. And it was like, 'Yeah, but I've never left them'. If there was ever a problem, I'd always [be there], like get up in the night and feed them, because, to me, that's part of my job.*
>
> *Mother77*

Tensions between neonatal staff and parents over their involvement were only mentioned by a few parents. Their accounts suggested that this was more likely when the mother had less prior knowledge of health care, had fewer resources at their disposal, and/or a (perceived) lack of deference to the authority of staff:

> *There are plenty of mums that would also go to do things with their baby and then be told, 'Oh no, we can't do that now', I know that that wasn't just me. Some mums would cause absolute havoc in there and be like, 'No, that's my baby, I don't care what you say. If he gets poorly, you can look after him because he's in the place to be looked after, but I'm doing it my way because that's my child'.*
>
> *Mother78*

Impact of being far from home

Where the transfer took the baby a significant distance from home, this created particular issues for parents who were trying to care for their new baby as well as balance other priorities:

> *We couldn't really stay as often as we'd have liked [at distant hospital], but we did try as much as we could. … You can't just say, 'Well I'm just going to go to see the baby for a couple of hours', because there's that much you have to sort out just to go to see the baby, you know, feeding the kids, travelling, money costs as well.*
>
> *Mother36*

Many parents found this extremely stressful:

> *It's very stressful – trying to balance home life and hospital life. Obviously you want your baby to be with you 24/7 but it's not possible. I've got a five-year-old to look after and my husband's at home – it's very stressful trying to balance being between the two places.*
>
> *Mother28 (with triplets)*

Some parents were able to cope easily with a transfer away from home, but others with fewer resources (e.g. financial, family, employment flexibility) on which to draw, found it particularly difficult:

> *[My time in the neonatal unit was] a bit all over the place, like, my daughter was only fourteen months, so my boyfriend quit his job to help with childcare and visits. And we would go in the daytime for about an hour or two hours, sometimes with our daughter, sometimes without. And then I would spend the majority of my day with my daughter at home, and I'd get her to bed about seven o'clock in the evening, then I'd go straight back to hospital until three or four in the morning. I'd come back for a few hours to sleep and then get up with my daughter again, so it was very all over the place. I felt torn between the two. … But that's the only way I could be at peace with myself.*
>
> *Mother78*

It caused extensive disruption that sometimes required drastic action such as quitting a job (see above excerpt). Extended family were brought in where possible but parents were often exhausted:

> *Literally everything was turned upside down. We had to, we've got two dogs so who's going to sort out a little thing like that? Who's gonna? What are we going to do about the house? Who's going to look after the dogs? Luckily my dad moved in for a bit and then my husband's sister moved in for a bit. Because my husband cut down to four days at work so he could literally spend one whole day with her mid-week, so he could take a break in between. When he went back [to work] after a month, he'd go for one night in the week and then he'd stay over in the weekend for two nights. And then he would come over every night for two hours after work, he'd drive straight over and stay six till eight to see her every night in [NICU hospital]. So, he was knackered because that's all he was doing was driving over every night after work after having a full day and then not eating and then grabbing some fast food on the way home or a toast or something. He was exhausted. I was just emotionally drained and exhausted because I'd sit with her and then sometimes I'd just go back to the unit after I'd eaten or I wouldn't even eat, I'd just stay there until ten o'clock at night because I was on my own so, I'd rather stay there. … it was kind of very isolating.*
>
> *Mother64*

Logistical issues for parents were not just inconveniences; they had potential to significantly affect the baby's health and development. A particular problem of caring for a baby at a distance from home was establishing and maintaining the mother's milk production, and getting this to the baby at the right time. If a baby was transferred away from the mother while she was still an inpatient, this created a clear physical barrier:

> *When I'd had the twins, on day three after having my C-section, the maternity ward were ready to discharge me to go home. And we didn't know whether or not I could stay on the unit at [Hospital A]. If not, I'd have to travel. Which to me, was just the worst, I just cried, because it was just the thought of just leaving them.*
>
> *Mother77*

Commuting long distances also created serious difficulties for mothers trying to provide breast milk for their babies:

> *I was commuting an hour and a half each way. Every day, just to try and, you know, be with her. Obviously, I was expressing off milk for her so, I needed to take that to her every day.*
>
> *Mother65*

Travelling back and forth, and being away from the baby, created difficulties producing and expressing milk:

> *I'd seen it as my duty, you know, I needed to [express] milk for her [but] expressing off every three hours, not having the baby with you, was really, really hard.*
>
> *Mother65*

The management of milk was often an overwhelming task in these circumstances:

> *I'm trying to express as much as I can but it's awkward with travelling here and going back and I don't really – I haven't kept up with it at all. … you've got to wash all the stuff and sterilise it and then when you've finished go and do it all again … leaving the house and forgetting the milk, I've done that a few times, so then I've had to go back and get it. It's stressful.*
>
> *Mother24*

Mothers described that stress and exhaustion had made their milk 'dry up':

> *I expressed in [Hospital A] and did really, really well. The twins were exclusively on breast milk for the first seven weeks. But in [Hospital B, where there was no room to stay, and she felt excluded from the babies' care], I just couldn't, the stress of it, my milk dried up within about three days.*
>
> *Mother77*

Although mothers valued support for expressing/breastfeeding (e.g. with techniques for expressing), those with fewer resources on which to draw noted that staff sometimes failed to adapt advice to their broader circumstances – leaving mothers feeling alienated and deflated:

> *And then my milk would dry up for a few days and I'd have like a slower flow, and then I'd have to ask for help to get my milk, like, back in. And you'd have to speak, you wouldn't speak to like a normal nurse, you'd speak to the breastfeeding nurse. And that almost felt like judgement, 'you're not doing it properly, you're not doing it enough', and there was no like, 'Okay, let's talk about your family, let's talk about where you are at home, and then how you come in, and let's try and work around your life'. … I was always on the go, and I couldn't keep my milk for very long.*
>
> *Mother78*

Accessing practical and emotional support

Staff (particularly nurses) took on the role of co-ordinating practical and emotional support for parents. This included discussions about whether accommodation or hardship funds could be made available, along with induction to the unit that would help parents to be actively involved in their baby's care. As highlighted above, parents were often very grateful for the support received:

> *It was a bit of a nightmare getting backwards and forwards to [LNU hospital, 27 miles away]. We did have [help] didn't we? They got us there. They gave us money for coach fare or whatever it was then – we didn't have the car at the time. That hospital was amazing.*
>
> *Mother36*

However, nursing staff were usually working around limited accommodation, which they allocated to the most deserving cases:

> *The sister in charge of their ward was like, 'Yeah, it's absolutely fine [for you to stay in hospital accommodation] but, obviously, if another parent comes in and they do need that room, you will have to give it up. It comes on like a priority basis'.*
>
> *Mother77*

Parents had radically varying experiences of the support that was provided to them – depending on the unit involved:

> *I think they sort of didn't understand that it's a lot of, it's a lot of pressure to have two babies in the hospital, be by yourself, and try and find, figure out where the nearest supermarket is [and then walk to it for nappies].*
>
> *Mother77*

It was obviously challenging for parents if their baby was moved to a unit that was not so supportive:

> *Medically [the care] was fine at [Hospital A]. I don't think they emotionally gave the support though. As soon as I got to [Hospital B], they were amazing, I had a counsellor with me within minutes. There was somebody … there getting everything, filling in forms for if we were potentially going to be there long-term, to try and find us accommodation.*
>
> *Mother73*

Several parents wanted to emphasise a need for greater emotional support from staff:

> *I just think they should have someone to go out and reach out to every mum on the unit, and support them with their wellbeing and to try and boost them into caring for their baby. I don't, I don't feel that that was there. And if it was, then maybe I wouldn't have felt so out of control, and other parents wouldn't feel so out of control. … Any parent that has a baby on NICU needs emotional support, because it is very traumatic. And there probably was plenty of emotional support if I looked for it. But you don't, you're not in the right headspace to look for it at that time. Your only focus is on going to see your baby, doing the housework when you get home and go back to see your baby. … They could help you build your confidence up, and nurture you into caring for your baby in that environment rather than at home.*

This need for someone to 'reach out' to them, and help them maintain practical and emotional control of their situation when under immense pressure, was the main area that parents highlighted for improvement:

> *That's the one thing that I could honestly say throughout the whole of our neonatal journey was that I feel that the mental health support for parents is quite poor. … Someone just to be there to say, 'if you need to talk to anybody, this is who you can go and talk to' because I just felt that that was something that was so lacking*
>
> *Mother65*

Discussion

Findings in context

This workstream highlighted that staff make decisions about place of care within an unstandardised, uncertain and rapidly evolving context. Decisions involve attention to the individual needs of babies, but also to management concerns relating to demand, capacity and income generation in individual neonatal units and across the wider network. The funding systems to which staff are orientated are an important consideration in discussions about best place of care, as they govern the practical management of neonatal units and the 'juggling' of babies between and within units. In a resource-constrained context, these systems are likely to take precedence over more abstract ideas about 'best place of care', or aspirations to, for example, involve parents, or communicate more effectively.

The 'organising work' undertaken by staff to plan, and practically implement transfers is extremely resource intensive. 'Juggling' babies takes considerable time and effort for both staff and parents. Highlighting this work may open discussions about how resources are employed in neonatal units to both improve efficiency and, importantly, improve the experience of babies and families.

Our study found that parents typically did not consider the category of unit (NICU/LNU) to be meaningful or particularly important. Rather, they were concerned to ensure that their baby had the care that was needed to maximise their development and homecoming. Beyond the survival of their baby, and technical quality of care, parents placed a high priority on continuity of care. Care far from home, transfers and inconsistent procedures across units (e.g. equipment, access to medical notes, milk management and feeding) disrupted continuity for the baby, with disruption mediated by difficulties in maintaining practical parenting and overseeing clinical intervention. Parents valued support for both practical parenting (e.g. feeding, holding, hygiene) and also understanding (and feeling some control over) clinical intervention.

Our findings suggest that continuity should be more central in discussions about best place of care – a finding supported by other evidence from neonatal and other services.[133,134] Continuity has been recognised as a casualty of a modern focus on 'value' and 'efficiency',[135] which we see in policy-making design and delivery of neonatal services. Although stakeholders are rightly concerned to ensure value and efficiency, other ways of knowing about what constitutes 'good care' should be kept in view alongside the managerial goals of an increasingly industrial healthcare system, such as family integrated care.[136–138] As our findings highlight, parents undertake much of the work to maintain continuity for their babies and want to do this as much as possible. This form of parental involvement is an invaluable resource, with the potential to support efficiency and value by relieving pressure on clinical staff. However, place of care discussions should include assessment of the burden placed on parents of various socioeconomic backgrounds and their consequent ability to maintain continuity work in the face of disruptions. Work to support continuity for parents is not only a vital element in improving parents' subjective experience of neonatal services, but there is also strong evidence suggesting that continuity reduces stress on baby and both short- and long-term developmental outcomes.[136,138]

Diversity

During the study period, we encouraged staff and parent participation. While we acknowledge that not routinely collecting demographic data about our participants may be considered a limitation, we attempted to make our study population as inclusive and representative as possible. We sought participation of individuals from a range of socioeconomic backgrounds and from ethic minority groups. We sought to ensure that participants reflected the diversity of experiences of neonatal care. Our aim was to include a broader group of parents than might often choose to participate in research. We wished to capture diversity of experiences and/or perceptions of neonatal care to strengthen the research findings and increase the generalisability of the results of the study.

Limitations

The verbatim quotes reported in the text reflect perceptions within the cohort of 15 doctors/nurses and 48 parents studied. Fieldwork further to explore their perspectives on management, and additionally interviewing managers around funding and flow, and validating these observations, was not possible, nor the purpose of the OPTI-PREM project. This could potentially be an area of future study.

Summary points from OPTI-PREM qualitative ethnographic study, workstream 4

What was already known prior to this study

- Parents' perspective on the care of the babies has been under-represented in clinical decision-making on place of birth and care.

What this study adds

- Staff: make decisions in an unstandardised, rapidly evolving and uncertain way.
- Organisation of work and finding capacity for babies is labour-intensive.
- For parents, continuity of care is most important, together with steps to maximise development and homecoming.
- Parents want more involvement in care and in understanding the decisions made around their baby.
- Support for parents' emotional and physical well-being was important.

How this study may affect policy

- Discussions and reviews on how resources are employed in neonatal units to both improve the efficiency of staff working and improve the experience of babies and families is required.

Chapter 9 Stakeholder engagement

Introduction

In this workstream, we describe OPTI-PREM engagement with relevant stakeholders throughout the project. This was to reassure LNU and NICU teams regarding the intent of the project, and to ensure that the questions, ideas and concerns by stakeholders (clinicians, decision-makers, managers, researchers, parents, members of the public) could be utilised to enhance the analysis and interpretation of the data. The potential implications of our findings are discussed. Dissemination of information around the findings of OPTI-PREM is in progress.

Aim

To engage with stakeholders regarding OPTI-PREM.

Objectives

Collaboration with stakeholders to

i. review with neonatal teams the study design and plan
ii. share preliminary results for face validity
iii. incorporate stakeholder comments into study analysis and interpretation of findings
iv. identify potential implications of the study findings, and future work needed to fine-tune this
v. promote dissemination of study results.

Methods

We held multiple discussions and workshops with key stakeholders.

i. Early engagement with a national LNU working group: this included BLISS Parent Advisory Panel participation.

Rationale: The study team was careful to include representatives from the national organisation supporting perinatal medical and nursing care in England, the BAPM. This was to allay anxieties that the work could be targeted towards a NICU outcome, based on the predominant NICU representation of clinicians who were driving the project. As a result, a call-out was made to BAPM for a LNU working group to review the project design and advise of any shortcomings that could disadvantage LNU in the analyses.

ii. Review of results stage: we engaged with stakeholders involved in neonatal service decision-making from LNU and NICU units, operational delivery networks and national government bodies involved in neonatal and maternity health care, together with parent panel and BLISS support at two time points:

    a. when the first results were available, and
    b. after near completion of all workstream results.

Transcripts from the stakeholder meetings were analysed and themes manually extracted. These were either included in the analysis and reporting of the study or justified, if the study team perspectives were different, in the discussion in this NIHR report.

iii. Presentation of project and findings at national, international and regional forums and submission of main findings to high-impact peer-reviewed medical journals.

Results

National stakeholder engagement with OPTI-PREM

Early engagement with British Association of Perinatal Medicine local neonatal unit working group

A 1-day meeting was as a round-table workshop on 4 October 2019. There was representation from four different LNU from the East Midlands Operational Delivery Network (ODN), South West Neonatal ODN (two representatives, from different LNU) and West Midlands ODN. All LNU consultants attending were BAPM members. Each workstream lead presented their plans, with preliminary data where available.

The outcome from the meeting was positive, and the LNU members attending supportive of the work, its design and intent. There were no concerns regarding the project direction. Ideas regarding dealing with confounding factors such as congenital anomalies, multiple pregnancies, maternal illness, analysis, and interpretation of preliminary data were discussed. These have been assimilated into the project report where appropriate.

National stakeholder engagement with preliminary results

Two meetings were held in April 2022: a national parent stakeholder meeting on 11 April 2022, followed by combined (parent and professional) national stakeholder meeting on 25 April 2022. The national stakeholder meetings were virtual, using an MS Teams® (Microsoft Corporation, Redmond, WA, USA) platform. Both meetings were chaired by the chairman of OPTI-PREM study steering committee.

11 April 2022: Four parents responded to a BLISS advert for the meeting, and participated in discussions around the preliminary findings, together with the parent panel lead, a BLISS representative. The perspectives of parents and members of the public were collated and represented at the meeting on 25 April 2022, by the parent panel lead.

25 April 2022: A further 76 individuals across England, Northern Ireland, Scotland and Wales participated in the national stakeholder meeting on this day. These included:

i. Maternity ODN: managers, clinical leads, their representatives and interested clinicians and midwives
ii. Neonatal ODN: managers, clinical leads, their representatives and interested clinicians
iii. Royal College of Paediatrics and Child Health National Neonatal Audit Programme Lead
iv. Representation from NHS England, Public Health Scotland, Northern Ireland and Wales
v. Parents and members of the public (n = 7, responding to a second national call-out through BLISS)
vi. the senior engagement officer at BLISS.

We elected first to engage with colleagues and managers, clinicians and researchers in neonatal and maternity care and members of the public. We anticipated that detailed discussions with the Royal College of Midwifery, Neonatal Nursing Association and the Royal College of Obstetrics and Gynaecology would begin after submission of the NIHR project report and peer review of this work. Ideas shared, expressed and explained were assimilated and are included in this NIHR report (see *Report Supplementary Material 10*).

Presentation at conferences and regional meetings

i. *NNAP-NDAU National Collaborators meeting, Leeds, 18 March 2019*: oral presentation to parents, multidisciplinary neonatal unit staff members and neonatal network representatives.
ii. *Health Systems Research UK Conference, Manchester, 2–3 June 2019*: oral presentation to NHS research audience.
iii. *5th Annual Preterm Births Conference, Birmingham UK, 30 September 2019*: oral presentation to obstetricians (UK and internationally), with an interest in reducing preterm births. Further regional presentations to ODNs that requested further information were conducted.
iv. *Evidence and Excellence joint BAPM EBNeo conference, Newcastle, UK, 11–13 September 2019*: our systematic checks in data and the lessons learnt from using large-scale routinely collected national data were presented as a poster titled 'Using routinely recorded operational clinical data from electronic patient records for clinical research: The

challenges and messages from OPTI-PREM, a national study evaluating best place of care for babies born at 27–31 weeks gestation', Yang M, *et al.*

v. *BAPM Annual Conference 'Addressing Inequalities in Perinatal Care', Sheffield, UK on 5 October 2021*: oral presentation to a national audience. The stakeholders were neonatal consultants, neonatal nurses, and those interested in perinatal care, decision-makers at neonatal unit and regional level.
vi. *UK Neonatal Society Meeting on 10 March 2023, London, UK:* oral presentation of morbidity outcomes data, to an international audience, with interest in neonatal research. The audience included neonatal consultants and researchers involved in neonatal basic science and clinical research, and clinicians who had decision-making responsibility for their units and regions.
vii. *UK Neonatal Society Meeting on 4 March 2021 and Perinatal Conference UK 2020, London, UK* . There was a general acceptance of the findings, and questions were similar to those described in *Report Supplementary Material 10*.
viii. *HSR UK conference on 5–7 July 2022 in Sheffield, UK*: the overall OPTI-PREM project was presented (short oral) as 'Place of care for babies born at 27–31 weeks in England: a qualitative study of staff decision-making perspectives and practices'. There were no concerns raised and there wasgeneral acceptance of the methodologies utilised. Workstream 4 was also presented at the conference.
ix. *British Sociological Association Medical Sociology Conference 11–13 September 2019, York, UK*: workstream 4 results were presented at this meeting.
x. *Royal College of Obstetrics and Gynaecology World Congress, London 12–14 June 2023:* workstream 1 findings were presented orally at this international congress.
xi. *BAPM autumn meeting September 11–12, 2023, Sheffield, UK:* workstream 1 findings were presented orally at this national congress for neonatologists and perinatal teams.

List of published papers from OPTI-PREM

i. Pillay T, Modi N, Rivero-Arias O, Manktelow B, Seaton SE, Armstrong N, *et al.* Optimising neonatal service provision for preterm babies born between 27 and 31 weeks gestation in England (OPTI-PREM), using national data, qualitative research and economic analysis: a study protocol. *BMJ Open* 2019;**9**:e029421. https://doi.org/10.1136/bmjopen-2019-029421
ii. Ismail AQT, Boyle EM, Pillay T, Boyle EM, Modi N, Rivero-Arias O, *et al.* Clinical outcomes for babies born between 27–31 weeks of gestation: should they be regarded as a single cohort? *J Neonatal Nurs* 2022;**29**:27–32. https://doi.org/10.1016/j.jnn.2022.04.003
iii. Ismail AQT, Boyle EM, Pillay T; OPTI-PREM Study Group. The impact of level of neonatal care provision on outcomes for preterm babies born between 27 and 31 weeks of gestation, or with a birth weight between 1000 and 1500 g: a review of the literature. *BMJ Paediatr Open* 2020;**4**:e000583. https://doi.org/10.1136/bmjpo-2019-000583. eCollection 2020
iv. Ismail AT, Boyle EM, Oddie S, Pillay T. Exploring variation in quality of care and clinical outcomes between neonatal units: a novel use for the UK National Neonatal Audit Programme (NNAP). *BMJ Open Qual* 2022;**11**:e002017. https://doi.org/10.1136/bmjoq-2022-002017
v. Yang M, Campbell H, Pillay T, Boyle EM, Modi N, Rivero-Arias O. Neonatal health care costs of very preterm babies in England: a retrospective analysis of a national birth cohort. *BMJ Paediatr Open* 2023;**7**. https://doi.org/10.1136/bmjpo-2022-001818
vi. Cupit C, Paton A, Boyle E, Pillay T, Armstrong N; OPTI-PREM Study Group. Managerial thinking in neonatal care: a qualitative study of place of care decision-making for preterm babies born at 27–31 weeks gestation in England. *BMJ Open* 2022;**12**:e059428. https://doi.org/10.1136/bmjopen-2021-059428
vii. Paton A, Cupit C, Armstrong N. Organising work in neonatal transfer: Optimising place of care for babies born moderately preterm. *Sociol Health Illn* 2023;**45**:1634–51. https://doi.org/10.1111/1467-9566.13656
viii. Cupit C, Paton A, Boyle E, Pillay T, Anderson J, Armstrong N. Parenting through place-of-care disruptions: a qualitative study of parents' experiences of neonatal care. *Health Expectations*. 2023;**1**. https://doi.org/10.1111/hex.13933

Doctor of Philosophy

Ismail AQT. Exploring the relationship between care provided and outcomes for preterm babies born between 27 and 31 weeks gestation in England. PhD successfully defended July 2023, University of Leicester

Presentation of near-final results to key stakeholders

A presentation of OPTI-PREM findings was held on 23 March 2023. Participants were the leads for

- the Neonatal Clinical Reference Group
- the National Neonatal Critical Care Transformation Programme
- BAPM
- GIRFT Neonatology
- National Clinical Director for Maternity Review and Women's Health
- National Programme of Care Manager for Women and Children NHS England
- RCPCH NNAP
- research engagement in BLISS, the national charity for parents of babies born premature or sick.

The purpose of the meeting was to briefly share the findings from OPTI-PREM and to get a steer on the implications of our observations.

Points of discussion in stakeholder meeting

Our scientific observations are that for England, based on current practice:

i. The clinically safe threshold for care for babies born at 27–31 weeks gestation in either NICU or LNU is 28 weeks. For babies born at 27 weeks gestation, care in LNU is associated with a higher rate of SBI. This appears to also be related to postnatal transfers.
This suggests that antenatal triage to maternity services colocated with NICU is advantageous for expectant preterm births at 27 weeks gestation.
This finding was accepted, and the strength of significance at 99% CI was acknowledged. However, it was noted that capacity in NICU was the determining factor. A discussion on high-volume and low-volume LNU was raised at the meeting, as, if high-volume LNU were functioning as effectively as NICU in relation to SBIs then, recommending only low-volume LNU plans for in utero transfers would limit the capacity burden currently facing NICU. On further analysis our work supports that the benefits of reduced SBI apply for NICU over *all* LNU. The justification for this is as follows:
Justification: the definition of high-volume and low-volume used in the OPTI-PREM project was based on previous scientific study,[11] and the experience of teams looking after babies born at < 32 weeks gestation.
We analysed this (using the IV approach and adjusting for confounders) for high versus low volume using two definitions of high versus low volume:
    1. the single uppermost quartile (high volume) versus the lower three quartiles (low volume) on the number of IC days provided to babies born at < 32 weeks gestation in the unit; or
    2. the upper three quartiles (high volume) versus the single lowermost quartile (low volume) on the number of IC days provided to babies born at < 32 weeks gestation in the unit.

   We observed that the difference in SBI was significant for high-volume versus low-volume units when the single uppermost quartile was used to define high/low volume (threshold 1614 days/year of providing IC to babies born at < 32 weeks gestation), but not when the single lowermost quartile was used to define high/low volume (threshold 440 days/year of providing IC to babies born at < 32 weeks gestation).
Current service specification low-volume units are defined as those providing < 1000 IC and HD days for all babies in the neonatal unit, and there are 26 of these identified in the UK. We were unable to run our analysis comparing these 26 units against the rest, as the data for OPTI-PREM were pseudonymised, and we did not have unit permissions to explore this. All low-volume neonatal units provided between < 268 IC days per year overall in 2019 [GIRFT data, with permission, E Adams (Getting It Right First Time; NHS England)].[15]
Loss of significant differences in SBI using the OPTI-PREM definitions at a low-volume threshold of 440 days IC days (for babies born at < 32 weeks gestation) while noting differences at a threshold of 1614 IC days (for babies born at < 32 weeks gestation) suggests that further subdivision to service specification thresholds for low-volume (< 268 IC days for all babies) are unlikely to yield significant differences for SBI. Our initial scientific observation that expectant births at 27 weeks gestation in maternity services colocated with NICU versus LNU therefore remains.

TABLE 30 Comparison of SBI analysis using different thresholds to define high- vs. low-volume neonatal units, and NICU vs. LNU

	OPTI-PREM	*p* = for difference in SBI
High volume (highest quartile for IC days) Low volume (lower 3 quartiles for IC days)	> 1614 days per year ≤ 1614 days per year	0.003 This was driven by babies born at 27 weeks gestation. This lost significance when babies born at 27 weeks gestation were excluded ($p = 0.019$) and on excluding postnatal transfers in the first 72 hours of life. Here the NNT was 4 (95% CI 2 to 29)
NICU LNU	> 1000 IC days per year[a] < 1000 IC days per year[a]	0.007 This was driven by babies born at 27 weeks gestation. This lost significance when babies born at 27 weeks gestation were excluded ($p = 0.037$) and on excluding postnatal transfers in the first 72 hours of life ($p = 0.554$). Here the NNT was 25 (99% CI 10 to 59)
High volume (top three quartiles for IC days) Low volume (lowest quartile for IC days)	> 440 days per year < 440 days per year	0.115 (not significant)

a All NICU provided > 1000 IC days in the 2019 GIRFT report, and all LNU < 1000 IC days.[15]

Note
Comparison of definitions for high vs. low volume in OPTI-PREM and significant differences in SBI.

There may be future work required to refine NICU care, as high-volume units using the upper quartile for IC days incorporated NICU only, and here we found statistically significant differences for SBI.

i. Our data suggest that capacity transfers at 27 weeks gestation offer no advantage for SBI and should cease; there were no objections to this.
ii. A discussion on the difficulties of distinguishing between uplifts for clinical care compared with uplifts for protocol-driven reasons was noted.
The suggestion that clinical teams risk-assess the need for clinical transfer at 27 weeks gestation is dependent on clinical team capabilities, and an assessment of the degree of illness in the baby. We do not wish to make any recommendation that could worsen outcomes for babies born at 27 weeks gestation who are retained at LNU.
iii. It was noted that outcomes were no different between NICU and LNU for babies born at 28–31 weeks gestation. Here again, stakeholders were cautious of recommending transfers to make capacity, as this would take families further away from home. The issue of redirecting the burden of SBI to babies of higher gestational age was noted as a theoretical possibility, as transfers in this age group could potentially increase, to make capacity for those at 27 weeks gestation in NICU.

The remaining points were noted and accepted:

1. High-quality care, measured by the culture of units in adhering to evidence-based or consensus-based early preterm care, is associated with a shortened length of neonatal stay.
2. The costs of care in LNU and NICU amount to ~0.26 billion pounds a year and are driven by daily care costs, not by specialised medications costed separately.
3. Cost-effectiveness of care: data on this was not presented at this meeting, and will be presented, in the dissemination phase of this work.
(For the purposes of this report, there was no difference in cost of care between NICU and LNU for births between 27 and 29 weeks gestation. This suggests that the recommendation of antenatal transfer to maternity services colocated with a NICU will be cost neutral per baby. The cost savings to the NHS of preventing SBI has not been calculated in this project. However, it can be assumed that this will represent a cost saving to the NHS and to society.)

4. Parents value optimising their baby's development and getting baby home. They place emphasis on continuity of care, integration of families in care of their baby, and support for their physical and mental well-being.

Discussion

In all the stakeholder meetings, the OPTI-PREM project protocol was accepted, participants understood the nature of the project and there were no areas of dissent. At the obstetrics preterm birth meeting, it was noted that care needed to be taken to ensure that unmeasured confounders due to degree of maternal illness were adequately addressed. The aspects discussed in *Report Supplementary Material 10* with national stakeholders overlapped with ideas expressed at these meetings and so are not repeated. When presented to our stakeholder discussion on 23 March 2023, multiple points were reviewed regarding the implication of OPTI-PREM findings. These, together with OPTI-PREM study team review, are discussed in the next section. They provide context to potential considerations for policy-making in neonatal service delivery once the scientific findings from OPTI-PREM are published.

Chapter 10 Discussion and conclusion

Principal findings

Impact of place of birth on mortality and key neonatal morbidities

In workstream 1, we found no difference in mortality up to the first year of life between birth and early care in a NICU (tertiary) compared with LNU (non-tertiary) setting. There was a significant risk of SBI in those born in LNU; the highest proportion of this was in babies born at 27 weeks, who were transferred out of LNU in the first 72 hours of life. When we removed babies transferred out in the first 72 hours of life, and then babies born at 27 weeks, from the analysis, our data lost significance.

We calculated that for babies born at 27 weeks gestation, birth in maternity services colocated with NICU reduced the risk of SBI from 11.9% to 7.7%, a reduction of 4.2%, with a NNT of 25. This means that 25 babies would need to be delivered in a NICU, rather than LNU, to prevent one SBI for babies born at 27 weeks gestation.

When we examined the association of SBI in more detail, analysing high- versus low-volume units (based on quartiles for IC days) we found that there was additional benefit for reduced SBI in high-volume units where the threshold for separation of high- versus low-volume units was 1614 IC days per year (upper quartile of IC days; NNT of 4). This was lost when the threshold for high- versus low-volume days was 440 IC days per year (lowest quartile of IC days).

Overall, 1 in 3 babies were transferred between units in this cohort, and 1 in 2 at 27 weeks gestation.

Does quality of care, independent of designation as neonatal intensive care unit or local neonatal unit, matter?

In workstream 2, we identified a positive association between units that comply with selected evidence- or consensus-based clinical practice, and a reduction in LOS. Units in high areas of social deprivation, and those with less staff, were less likely to meet best practice. These findings may have significant implications for cot capacity in neonatal units, parent and family engagement and taking baby home earlier, allocation of resources, and an overall cost saving for the NHS.

Cost-effectiveness of care in local neonatal unit compared with neonatal intensive care unit

In workstream 3, we found that the NHS costs for babies born at 27–31 weeks gestation was ~0.26 billion GBP annually, and that the largest contribution to this was the costs of daily care in neonatal units. These costs were highest for those born at 27 weeks gestation as they utilised the greatest number of neonatal bed-days. Within our cohort, their costs were more than three times those for babies born at 31 weeks gestation in England. In our cost-effectiveness analysis, we found that the cost of care was similar for babies born at 27, 28 and 29 weeks gestation in NICU and LNU, but that it was significantly lower in NICU for babies born at 30 and 31 weeks gestation. This was driven by the differences in the durations of the different levels of care provided in NIC compared with LNU, with more ICU/HDU days in LNU and more special care days in NICU.

Parent and staff perspectives on place of care

Our findings in workstream 4 suggest that for parents, continuity of care mattered most. Place of care discussions should include assessment of the burden placed on parents of various socioeconomic backgrounds and their consequent ability to maintain continuity in the face of disruptions. Supporting continuity[133,134] is not only a vital element in improving parents' subjective experience of neonatal services, but there is also strong evidence suggesting that continuity reduces stress on babies and improves both short- and long-term developmental outcomes.[138]

Engagement with stakeholders

In workstream 5, we demonstrate that there is an appetite to understand this better, to contribute ideas, and hopefully drive changes in decision-making that improve outcomes for very preterm babies, their families and the NHS.

Potential implications for health service delivery, families and society

The 'safe' threshold at which care can be delivered close to home is 28 weeks gestation

Care in either LNU and NICU for these babies is safe, based on current practice, and using OPTI-PREM outcome measures. Our data indicates no difference in outcomes between the babies born in NICU compared with LNU, even when early postnatal transfers were excluded, and after robustly adjusting for unmeasured confounders.

A higher severe brain injury rate occurs in preterm babies born at 27 weeks gestation in local neonatal unit

We cannot assign causality to postnatal transfers although it was an associated observation. This is because there may be other factors that have caused a baby to have a SBI, such as degree of illness in the baby and/or mother, and the finer details of care provided initially. However, to reduce the risk of SBI for babies born at 27 weeks gestation, antenatal triage of expected preterm births at this gestation, to maternity services colocated with NICU for care, would be indicated. This is because we would not always be able to predict which baby born at 27 weeks in LNU would be sick enough and/or need postnatal transfer for support in NICU.

Practically, a review of neonatal unit capacity may be required to safely implement this triage. This is because against current resources NICU teams do not have capacity to deal with existing caseloads and pathways of care. We studied 777 preterm babies born at 27 weeks gestation in LNU, and 18,847/29,842 (63.5%) of the cohort born in the 5-year period. Estimating from this, 1220 births (777 × 100/63.5) over the 5-year period means that approximately 240 additional preterm births per year in LNU would need to be antenatally triaged to NICU settings. To optimise care for preterm babies born at 27 weeks gestation, capacity to accommodate these babies in NICU as defined by OPTI-PREM findings is required. This capacity would need to include a review of training and rotation of staff to ensure skills are maintained especially to cater for the unexpected ill very preterm birth in LNU, or to provide support for existing LNU especially if geographically distant.

It would also require later review of care for babies born at 28 weeks gestation in LNU, to assess whether outcomes for these babies would be the same if born and cared for in either LNU or NICU setting, if LNU were not caring for babies born at 27 weeks gestation.

Our findings could guide individual ODNs to redirect obstetric, emergency care and ambulance services so that a mother with an expected preterm birth at 27 and at 28–31 weeks gestation has her baby delivered and cared for at a hospital with the most appropriate facilities for neonatal care for baby, while at the same time supporting parents and families better. Redirecting a mother to the correct maternity facility would be cost-effective, as opposed to transporting a preterm baby after birth to the most appropriate neonatal unit. Our work highlights the importance of joint working between maternity and neonatal service providers, rather than as separate ODNs.

Risk assessment of postnatal transfers of inadvertent births in local neonatal unit is required

For inadvertent births at 27 weeks in LNU, clinical judgement, balancing the benefits of clinical uplift against risk of SBI should be made, in determining need for early postnatal transfers to NICU neonatal units for ongoing care.

It is accepted that there will always be inadvertent births in LNU settings due to the unpredictability of preterm birth, and where mothers are too ill or too advanced in labour to facilitate safe in utero transfer. Optimal health service delivery might mean retaining care of babies born at 27 weeks gestation who are stable in LNU/low-volume neonatal units, to prevent any unnecessary potential SBI associated with postnatal transfer. However, this cannot be determined in advance. Clinical assessment is required, weighing risks of SBI associated with postnatal transfer to NICU for uplift care against risks of retaining care of the preterm baby and considering the expertise and resources to manage this need. Where care is retained, support for local teams (such as telemedicine, staff rotation, NICU oversight) need to be in place so that care and outcomes for very preterm babies are not compromised.

Capacity transfers in babies born inadvertently in local neonatal unit, at 27 weeks gestation, should be approached cautiously

OPTI-PREM was not designed to differentiate between reasons for postnatal transfer at 27 weeks. These could have been transfers for (a) 'capacity' reasons or for (b) protocol-driven reasons of stable preterm babies born at 27 weeks gestation or (c) based on clinical need. In most cases in LNU the distinction between a baby being transferred for either protocol (i.e. stable and ventilated at 48 hours) or progressive deterioration may be difficult to make. Clinical teams would need to judge this. Limiting capacity transfers in stable babies at 27 weeks gestation inadvertently born in maternity units colocated with LNU is the most practical and immediate intervention.

Capacity transfers at 28–31 weeks gestation should be approached cautiously

As care is equitable for babies born at 28–31 weeks gestation in NICU and LNU, one temptation may therefore be to recommend triage of care for these mothers and babies to LNU, so that NICU can care for the babies born at ≤ 27 weeks gestation. However, moving these babies postnatally or in utero as capacity transfers would constitute major disruptions for families and parents' mental health. Factors around obstetric resources, the options for antenatal triage, and considering patient and family experiences by delivering care closer to home may need to be factored into the decision-making. We believe that caution needs to be adopted here. The OPTI-PREM study was not designed to distinguish between SBI that may be primarily related directly to the process of postnatal transfer and, alternatively, SBI associated with transfers primarily related to the degree of illness of the baby. To shift postnatal transfers from 27 weeks to 28–31 weeks gestation for capacity reasons may shift the burden of SBI to these gestational ages.

Costs of care

The costs of care for these babies, at each gestational age in weeks and overall, provides for the NHS a framework to facilitate adequate allocation of resources for very preterm babies.

That cost of care is lower at higher gestations in NICU, driven by fewer ICU days for babies born at 30 and 31 weeks, and potentially implies that efforts towards streamlining efficient care packages between NICU and LNU are required, rather than a review of place of birth for these babies.

That there is no difference in costs of care for babies born at 27 weeks gestation in LNU compared with NICU supports that recommending in utero transfer of all anticipated births at 27 weeks will not have a significant impact on the cost of care per baby while in neonatal care. However, the health economic cost of reducing a SBI for each baby, for short- and long-term outcomes, for their families, the NHS and society is likely to be substantial.

Evidence from workstream 2 (see *Chapter 5*), and our observations regarding TPN and surfactant use (see *Chapter 7*), supports future work examining costs and effects of care by quality of care provided. These will provide valuable insights that could be used in future efforts to optimise neonatal service delivery.

OPTI-PREM provides an analytic framework for future cost and effects analysis for key morbidities in very preterm babies. This scientific data could drive redistribution and allocation of resources for cost-effective interventions, that are evidence- and consensus-based. For example, if we understood the cost of disease in England, as is emerging from Canada,[139] and the cost effects of evidence- and consensus-based practices such as 1 : 1 nurse provision, early BMF, and optimised delivery room non-invasive ventilatory support, we may be more effectively able to channel resources for cost-effective neonatal health care in England.

Implications for further research around making postnatal transfers safe

More scientific research is required around how better to optimise the process of postnatal transfers in the longer term, as these are unlikely to be prevented entirely. One in three babies born at 27–31 weeks were transferred between units in the postnatal period. This is accepted as a key area in which research needs to be optimised.

In addition, work on how better to optimise stabilisation and ongoing clinical care in a LNU setting for both mother and baby may be required. As we cannot completely exclude babies being transferred being more likely to be ill and at greater risk for SBI, research on how/whether resources should be directed (additionally) to optimising clinical training and support for teams in LNU *as opposed to, or in support of*, safer postnatal transfer is also required. This could include a review of thinking around provision of rotational medical and nursing care between LNU and NICU to limit deskilling of teams and the impact of postnatal transfers.

Implications for neonatal clinical teams and service provision

OPTI-PREM evidence supports adherence to national prespecified targets and aiming for the top end of performance in benchmarking exercises and accepted best practice. These, if resources are allocated appropriately (units that were understaffed and in areas of high indices of social deprivation were less likely to be higher performing), could have beneficial effects for families, babies, staff and the NHS in relation to reduced number of days in hospital. However, conceptualising what is realistic and achievable for units in areas of high indices of deprivation, and those not adhering to best practice models as defined within OPTI-PREM, is complex. It may require more than just a redistribution of funds and staffing. For example, an in-depth qualitative review of how better to recruit, retain, train and upskill staff may be required. This may include developing innovative models of rotation of staff between units of differing designations and possibly performance, to learn, export and maintain the skills necessary for optimal service delivery, even in impoverished settings where maternal morbidity, and therefore neonatal morbidity, is generally higher.

The observations in workstream 4 (see *Chapter 8*) highlight the importance of decision-makers and managers providing appropriate support for neonatal teams on the ground managing capacity and undertaking clinical care. Institutional processes and systems around capacity management and demand often drive internal conflict in clinical teams dealing with babies and families. More effort should be channelled into providing a layer of administrative support to clinical teams on the ground, allowing them to focus on delivering excellence in clinical care, with as little moral distress as possible, in trying to manage the needs of the individual baby versus available resources in units and networks.

Implications for babies

SBI may be associated with neurological findings ranging from mild developmental delay to severe cerebral palsy.[140,141] From the EPICure studies, we understand better the educational and behavioural phenotype of preterm babies, and the cost to society is being increasingly reported in the literature .[80,84,142–144] If we can prevent one preterm baby born at 27 weeks gestation having SBI, the cost savings to the NHS and society would be substantial, considering the lifetime healthcare costs of cerebral palsy,[85,86] independent of the costs of other associations with prematurity.[139] Supporting and including parents and families during their baby's time in neonatal care will likely contribute to their better bonding with their preterm baby.

Implications for parents and families

Identifying that continuity of care has the most agency for parents is an important finding which should promote streamlining of services across neonatal units. Keeping families close to home will reduce stress and anxiety and support the mental and physical well-being of families. For those where transfer is necessary, strategies to better support parents social, economic and mental well-being need to be pursued. Working in partnership with parents will allow them to feel included, and to understand and accept the care pathways most appropriate for their baby.

Conclusion

Advances in neonatal care and improvements in outcomes, especially for the very preterm baby,[145] has necessitated in England meta-management of neonatal health service delivery. Managed clinical networks comprising a mix of non-tertiary and tertiary services in different regions of the country, have evolved over the past 20 years,[146–149] its philosophy being the provision of maternity (and neonatal) care close to home. However, with this came uncertainties of what this would mean for postnatal transfers, NHS resources and capacity, for very preterm babies, their families and society. Here we show evidence that place of birth matters, in all these aspects. We show that there is an appetite to understand this better, to contribute ideas, and hopefully drive changes that optimise outcomes for very preterm babies, their families and the NHS.

We found that the safe gestational age cut-off for babies to be born between 27^{+0} and 31^{+6} weeks and early care at either location was 28 weeks. We found no effect on mortality while in neonatal care or in infancy, including after sensitivity analyses. We found a significantly greater proportion of babies in LNU had SBI which appeared to be driven by those born at 27 weeks gestation, and those transferred in the first 72 hours. We identified that 25 babies at 27 weeks would have to be delivered in a NICU to prevent one SBI.

When we explored this difference in SBI between units further, we found that the significance remained in high-volume units providing the upper quartile of neonatal IC days (i.e. there was a significantly lower risk of SBI for babies cared for in high-volume neonatal units, which were all NICU), but not for low-volume units providing the lowest quartile of IC days (which included LNU). These observations support refinement of neonatal and maternity health service delivery for very preterm births in England.

Capacity for expectant mothers at maternity centres colocated with NICU is a major issue in England at present, so, simply suggesting to emergency teams, GP practices and obstetric teams that in utero transfers of all anticipated very preterm births at 27 weeks gestation should be redirected to these services, without addressing the wider capacity issues, will not succeed. At present there are neonatal operational delivery networks that co-ordinate provision of care and movement of newborn babies between units, and separate, less-developed maternity operational delivery networks, for mothers. To effect change based on our findings, obstetric and neonatal services need to co-configure or superimpose on each other, and effectively function as joint ‘perinatal’ networks. This is because capacity implications for one impact on the other. At the same time, there should be adequate information sharing to empower parents and expectant parents regarding decision-making on presentation to a maternity service colocated with a NICU for birth and early care, should they be expecting a birth at or before 27 weeks gestation[6,7,14,132] in the UK.

Our study provides in-depth understanding of the costs of care, and the implications for services in caring for babies at these gestational ages. The inverse relationship between cost of care and degree of prematurity, and the risks of complications such as SBI, argue for more efforts to promote prevention of preterm births. That the burden of care is cost neutral within the neonatal period for the most immature of this cohort should argue towards NICU triage for anticipated births at 27 weeks gestation, coupled with the potential health economic benefits of preventing SBI. We have detailed information on the pressures and priorities harboured by staff and parents, and what potential avenues to pursue in working towards optimising delivery and quality of care of very preterm babies in England. Altogether, the findings from OPTI-PREM provide evidence supporting optimising health service delivery for very preterm babies in England through multiple avenues.

Chapter 11 Future research

Developmental outcomes, transfers and severe brain injury

At the time of protocol writing, we considered that the 2-year follow-up recorded in the routinely collected EPRs was inadequate for robust unbiased assessment. There were no other reliably collated retrospective records for later developmental assessment into school years and beyond, for our cohort.

Now that we have identified that one in three babies born very preterm in the OPTI-PREM cohort are transferred at some stage of their neonatal stay, it becomes important to understand the impact of the transfers overall on the development and outcomes of very preterm babies, and their impact on families. SBI may represent only one extreme of the spectrum; the developmental aspects associated with early transfers in very preterm babies are unexplored.

Cost analysis

Societal costs of care

The societal cost of care to babies, families and society, for babies born very preterm between 27 and 31 weeks gestation, is unclear. We need to research this so that adequate resources and avenues for support for families can be set aside. These will contribute to optimising the delivery of care for these vulnerable babies, and families.

Cost savings of preventing severe brain injury

Having defined the impact of postnatal transfers at 27 weeks gestation, on SBI, the cost savings for the NHS of preventing these with antenatal triage should be calculated. This is important to define, to inform costs of reorganisation of services for support for maternity centres colocated with NICU, and their NICU, for anticipated preterm births at 27 weeks gestation.

The costs and effects of care using outcomes of key morbidities as opposed to mortality may guide optimisation of services, together with and evaluation of the impact of serious morbidities such as SBI on long-term quality of life for families and individuals born very preterm at 27–31 weeks gestation.

Costs of care for high-performing units compared with lower-performing units

OPTI-PREM has begun to uncover potential health economic cost benefits of caring for these very preterm babies in higher-performing units (shorter duration of hospital stay, hence lower NHS hospital cost). This should be explored in conjunction with further research on quality of care for very preterm babies.

Cost-effectiveness of evidence- and consensus-based interventions to reduce key morbidities in very preterm neonatal care

We have the framework in place for future cost and effects analysis for key morbidities in very preterm babies. Understanding the cost of neonatal complications in very preterm babies in England, and the cost effects of current practices will provide the scientific evidence to more effectively be able to channel resources for cost-effective neonatal health care in England.

Quality of care research

The quality of care observations in OPTI-PREM could drive further research into consolidating these using national benchmarks and targets, and with the NNAP. We believe that such research on quality of care should be conducted against robust outcome measures, partly addressed in OPTI-PREM. Except for OPTI-PREM, and earlier work supporting OPTI-PREM observations,[11] this has not been described in very preterm babies.

Basic science and clinical studies of risks of postnatal transfer

The high rate (one in three) of postnatal transfers in this cohort supports that we should be proactive in optimising the transport process itself, to limit any known and as yet undefined dangers posed by the transport of very preterm babies pose. We are unlikely to be able to avoid transporting babies between units completely, due to the nature of babies being born early, their illness, capacity, and need for specialised services that only a few centres can provide etc. Optimising transport processes is a key element of optimising health service delivery for very preterm babies.

Chapter 12 Equality, diversity and inclusion

Participant representation

Workstreams 1, 2, and 3: equality, diversity and inclusion in OPTI-PREM was optimised as the OPTI-PREM data set of 29,842 was extracted from neonatal units across England. Within this national cohort we expect a representation of wide geographic, ethnic, socioeconomic, and clinical variation in presentation. This cohort would also have included parents whose first language was not English.

Workstream 4: staff and parent participation as study subjects was as inclusive and as representative as possible. Parents (both mothers and fathers) from a geographic range across England, a wide range of socioeconomic backgrounds and from ethic minority groups, were included in the interviews. Recruiting parents via social media enhanced the diversity in obtaining perspectives from across the country. We included parents who had experienced neonatal care across all gestational ages between 27^{+0} and 31^{+6} weeks gestation, and across a variety of neonatal units across England. The unit ethnography was undertaken in the East and West Midlands Operational Delivery Network, which has a wide representation of urban-rural, geographic, socioeconomic and ethnic diversity in staff, parents and babies admitted.

Due to the nature of the ethnography, the interviews were conducted and observed in English. We did not have interpreters assigned to the project, although the option of Language Line (telephone interpreting services) was available as part of the routine NHS service. This was an identified gap. Future qualitative studies should explore how best to capture the nuances and perspectives of parents and families in whom English is not the main language.

Workstream 5: stakeholders from a diverse ethnic, geographic and neonatal service background, including maternity, neonatal, management, policy- and decision-making participated in workstream 5. This included parents.

Project representation

The patient and public involvement panel

The parent panel comprised parents from across England, both mothers and fathers, and of a wide ethnic background. It also included a parent who had experienced the death of their very preterm baby. Parents contributed to the development of parent information leaflets, interview of the social scientist employed for the study, and contributed photographs (with permission) for use on posters. We believe that this was done in a manner not to be discouraging to under-represented groups.

A second gap identified, was in the use of social media to recruit parents from across the country for interview, and in stakeholder meetings. We recognise that this produced a bias towards technologically capable parents and excluded those with no ability or resources to access the internet or mobile data to be recruited and be aware of projects such as OPTI-PREM and make themselves available for participation. Further work on how best to be more inclusive to families is necessary.

The research team

The project team was ethnically diverse, had a mix of genders, and members were diverse in their professional expertise. They were geographically spread across England (London, Oxford, Leicester, Wolverhampton, Staffordshire) and included a data analyst and social scientist working internationally and then recruited into English institutions to conduct specific aspects of the OPTI-PREM work. The parent panel lead, and representation from BLISS, were part of the research design, protocol application stages, and maintained participation throughout all stages of the project.

The study steering committee included representation from a wide geographic distribution (Bristol, Birmingham, Bradford, Oxford, Warwick, Wolverhampton, London, Cambridge), of academics with diverse areas of expertise (health economics, academic neonatology, statistical expertise, social science expertise, parent group involvement, and sponsor trust guardianship). The project team supported growth and development of multiple members of the team. For example, career progression and the flexibility to undertake a Master of Science (Data Science, with distinction) for our data analyst, and a PhD (supported by NIHR funding as part of OPTI-PREM) for a paediatric doctor in specialist training.

OPTI-PREM aligns closely with the NIHR-INCLUDE road map[56] at the stages of

a. Research priority setting.
b. Research investigator questions, protocol development and funding application.
c. Conduct of the research study.
d. Analysis and interpretation of results.
e. Implications of findings.
f. And will be key participants in dissemination of results once peer reviewed through the NIHR report and published outputs.

Additional information

CRediT contribution statement

Thillagavathie Pillay (https://orcid.org/0000-0002-4159-3282): Project conceptualisation (lead), Funding acquisition (lead), Methodology (equal), Project administration (lead), Supervision (equal), Visualisation (lead), Writing – original draft (lead), Writing – reviewing and editing (lead).

Oliver Rivero-Arias (https://orcid.org/0000-0003-2233-6544): Conceptualisation (lead for WS3), Methodology (lead for WS3 and equal for WS1), Investigation (lead for WS3, equal for WS1), Supervision (lead for WS3 and equal for WS1), Writing – original draft (lead for WS3), Analysis (equal WS1, lead WS3), Writing – editing and reviewing (supporting for overall project), Data curation (equal WS1 and WS3, and equal for linkage to NHS Digital).

Natalie Armstrong (https://orcid.org/0000-0003-4046-0119): Conceptualisation (lead for WS4), Methodology (lead for WS4), Supervision (lead for WS4), Investigation (equal), Analysis (equal), Writing – original draft (lead for WS4), Data curation (lead WS4).

Sarah E Seaton (https://orcid.org/0000-0001-8711-4817): Conceptualisation (supporting WS1), Methodology (equal for WS1), Investigation (equal WS1), Analysis (equal for WS1), Writing – original draft (equal WS1), Writing – editing and reviewing (supporting overall project), Data curation (equal WS1).

Miaoqing Yang (https://orcid.org/0000-0001-7975-374X): Data curation WS1 (equal) and WS3 (lead), Investigation (supporting WS1 and WS3), Analysis (supporting WS1 and WS3), Writing – editing and reviewing supporting for WS1 and WS3 overall project.

Victor L Banda (https://orcid.org/0009-0000-5251-5055): Data curation (lead for data extraction, curation at NDAU and lead for travel time computation for the instrumental variable analysis) and Linkage to NHS Digital (equal).

Kelvin Dawson (https://orcid.org/0009-0002-0080-9283): Supervision (supporting), Validation of WS4 (supporting), Writing – editing and reviewing (supporting).

Abdul QT Ismail (https://orcid.org/0000-0003-4125-8684): Methodology (supporting WS2), Investigation (lead WS2), Analysis (lead WS2), Writing (lead WS2).

Vasiliki Bountziouka (https://orcid.org/0000-0003-2522-1582): Data curation (equal WS1), Investigation (supporting WS1), Analysis (supporting WS1), Writing (equal WS1), Writing – editing and reviewing (supporting WS1).

Alexis Paton (https://orcid.org/0000-0003-4310-6983): Investigation (supporting), Analysis (supporting), Writing – editing and reviewing (supporting WS4), Data curation (supporting).

Caroline Cupit (https://orcid.org/0000-0002-3377-8471): Investigation (supporting), Analysis (supporting), Writing – editing and reviewing (supporting WS4), Data curation (supporting).

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Elizabeth S Draper (https://orcid.org/0000-0001-9340-8176): Conceptualisation (supporting), Methodology (supporting), Writing – editing and reviewing (supporting).

Neena Modi (https://orcid.org/0000-0002-2093-0681): Conceptualisation (supporting), Methodology (supporting), Supervision (equal), Writing – editing and reviewing (supporting).

Helen E Campbell (https://orcid.org/0000-0003-2070-7794): Analysis (supporting WS3 and WS1), Writing (supporting WS1 and WS3).

Elaine M Boyle (https://orcid.org/0000-0002-5038-3148): Conceptualisation (supporting), Methodology (equal), Supervision (equal), Writing – editing and reviewing (supporting).

Mohammed Riaz: Data analysis (supporting WS1).

The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted. All authors reviewed and contributed to the final version.

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Parents, babies and the OPTI-PREM parent panel (patient and public involvement)

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The OPTI-PREM parent panel was led by initially by M Greenaway-Crissold (MG-C), then K Dawson. Initially MG-C, then KD participated in all study steering committee and OPTI-PREM collaborator meetings. K Dawson, M Irfan, M Patel, N Khabbah, A Ferris, C Shepard, M Anderson, L Alexander, J Jeffreys, R Murray, I Marie, L Flanagan, K Hodge, L Hamilton, M West, J Monoghan, K Lund, L Barker, K Micallef, A Eggington, S Marlow, G Lynch, M Greenaway-Crissold. These parents volunteered their time either face to face or virtually at different stages of the project.

Participating neonatal units, and stakeholders

We wish to thank all participating neonatal units, and their research and clinical staff for their contribution to OPTI-PREM. The participating neonatal units and their representative leads at the time of recruitment into OPTI-PREM are noted in *Report Supplementary Material 9*. We wish to thank all stakeholders for their time spent on reviewing our findings and their critical comments offered.

Specifically, we wish to thank BAPM, for supporting this work, through stakeholder engagement (Eleri Adams), and in the LNU representation that guided the initial discussions (Wendy Tyler, Sarah Bates, Steve Jones, John McIntyre).

Study steering committee

This was led by Andrew Ewer (Emeritus Professor, Neonatology) and included Stavros Petrou (Professor, Health Economics), Lisa Hinton (Dr, senior social scientist), Mehali Patel, then Josie Anderson (Ms, senior engagement officer, BLISS), David Laughton (Professor, Chief Executive, sponsor trust), Karen Luyt (Professor Neonatal Medicine), Gillian Santorelli (Dr, principal statistician).

Sponsor trust and research and development directorate

We wish to thank the sponsor trust, The Royal Wolverhampton NHS Trust, and its Research and Development Directorate: Professor James Cotton, Lorraine Jacques, Sarah Glover and Amy Bennett.

East Midlands and Birmingham RDS teams

We wish to thank these RDS for supporting the development of the project protocol.

The UK Neonatal Collaborative

We wish to thank all the neonatal units and their operational delivery networks, for participating in the study. The details of the participating UK Neonatal Collaborative are listed in *Report Supplementary Material 9*.

Patient data statement

This work uses data provided by patients and collected by the NHS as part of their care and support. Using patient data is vital to improve health and care for everyone. There is huge potential to make better use of information from people's patient records, to understand more about disease, develop new treatments, monitor safety, and plan NHS services. Patient data should be kept safe and secure, to protect everyone's privacy, and it's important that there are safeguards to make sure that they are stored and used responsibly. Everyone should be able to find out about how patient data are used. #datasaveslives You can find out more about the background to this citation here: https://understandingpatientdata.org.uk/data-citation

Data-sharing statement

The National Neonatal Research Database can be accessed by making a request to the Neonatal Data Analysis Unit at Imperial College London, through the Health Data Research UK Gateway website. All requests for qualitative research data should be sent to the corresponding author.

Ethics statement

Patient consent for publication is not required. Research ethics approval for the OPTI-PREM programme of work was obtained through the national IRAS reference number 212304 and REC reference number 17/NE/0800; North East – Tyne and Wear South.

Dates of approvals were as follows:

i. REC approval (17/NE/0080): 17 March 2017.

ii. Confidentiality Advisory Group (CAG) (19/CAG/0104) approval: 07 November 2019.

iii. Data Access Request Service (NHS Digital, DARS) (DARS-NIC-125031-Z3D7S-v0.13) Data-sharing framework contract signed 23 December 2020.

Information governance statement

The Royal Wolverhampton NHS Trust is committed to handling all personal information in line with the UK Data Protection Act (2018) and the General Data Protection Regulation (EU GDPR) 2016/679. The NNRD privacy notice, providing information to parents of babies admitted to NHS neonatal units can be found online[150] and is General Data Protection Regulation compliant (National Neonatal Research Database/National Research Ethics Service Reference16/LO/1093/Privacy Notice/050618). Under the Data Protection legislation, The Royal Wolverhampton NHS Trust is the Data Controller, and you can find out more about how we handle personal data, including how to exercise your individual rights and the contact details for our Data Protection Officer here www.royalwolverhampton.nhs.uk/privacy-notice/our-services/trust-privacy-notice.html.

Disclosure of interests

Full disclosure of interests: Completed ICMJE forms for all authors, including all related interests, are available in the toolkit on the NIHR Journals Library report publication page at https://doi.org/10.3310/JYWC6538.

Primary conflicts of interest: Thillagavthie Pillay declared funding from the Leicester, Leicestershire and Rutland Clinical Commissioning Group for qualitative work on reducing risks for infant mortality, from Leicester Local Maternity and Neonatal Systems for qualitative research on perinatal dashboards in health inequalities, from De Montford University as visiting lecturer. She was a steering committee member Children's HIV Association, and its national audit lead (2020–3).

Oliver Rivero-Arias is a member of the Fetal, Maternal and Child Health Reference Group, National Screening Committee.

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Victor L Banda declared funding through Imperial College for attendances at OPTI-PREM related and HQIP (Healthcare Quality Improvement Partnership) meetings. He has been subcontracted for work with the University of Oxford, HQIP and University of Leeds.

Neena Modi is Director of the UK National Neonatal Research Database.

Protocol versions and major changes from original protocol

These are described in *Report Supplementary Material 11*.

Publication

Pillay T, Seaton SE, Yang M, Bountziouka V, Banda V, Campbell H, *et al*. Improving outcomes for very preterm babies in England: does place of birth matter? Findings from OPTI-PREM, a national cohort study. *Arch Dis Child Fetal Neonatal Ed* 2025:fetalneonatal-2024-327474. https://doi.org/10.1136/archdischild-2024-327474

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Appendix 1

TABLE 31 List of major congenital anomalies

Atresia and stenosis of small intestine
Atresia of bile ducts
Atresia of oesophagus with tracheo-oesophageal fistula
Atresia of oesophagus without fistula
Atresia of urethra
Atrioventricular septal defect (AVSD)
Coarctation of aorta
Coarctation of the aorta
Congenital absence, atresia and stricture of auditory canal (external)
Congenital absence, atresia/stenosis of anus with/without fistula
Congenital absence, atresia/stenosis of rectum with/without fistula
Congenital cardiac disease – acyanotic
Congenital cardiac disease – non-cyanotic
Congenital malformations of aortic and mitral valves
Congenital malformations of cardiac chambers and connections
Congenital malformations of pulmonary and tricuspid valves
Down syndrome (translocation)
Down syndrome (trisomy 21)
Edwards syndrome (trisomy 18)
Encephalocele
Encephalocele (unknown or unspecified cause)
Eventration of diaphragmatic hernia
Eventration of the diaphragm
Exomphalos
Exomphalos (major)
Exomphalos (minor)
Exomphalos malrotation
Extropy of urinary bladder
Gastroschisis
Hypoplasia of aortic arch
Malformation of aorta
Oesophageal atresia

TABLE 31 List of major congenital anomalies (*continued*)

Oesophageal atresia with distal tracheal fistula
Oesophageal atresia with tracheoesophageal fistula
Oesophageal atresia without distal fistula
Other congenital malformations of aortic arch
Polycystic kidney
Polycystic kidney (unknown or unspecified cause)
Potter's syndrome
Spina bifida
Spina bifida (unspecified)
Stenosis of aorta (AS)
Stenosis of pulmonary artery (PS)
Tetralogy of Fallot
Total anomalous pulmonary venous connection
Total anomalous pulmonary venous drainage
Transposition great arteries (TGA)
Trisomy 18

Appendix 2

TABLE 32 A comparison of cohort excluded due to missing data, for workstream 1

Characteristic	Included cohort (*n* = 18,847)	Missing cohort (*n* = 7438)
Place of birth, n (%)		
Unit attached to LNU	8468 (44.9)	3368 (45.3)
Unit attached to NICU	10,379 (55.1)	4070 (54.7)
Gestational age, n (%)		
27 weeks	2284 (12.1)	912 (12.3)
28 weeks	3031 (16.1)	1128 (15.2)
29 weeks	3412 (18.1)	1339 (18.0)
30 weeks	4379 (23.2)	1789 (24.1)
31 weeks	5741 (30.5)	2249 (30.2)
Missing/inconsistent	–	21 (0.3)
Died in neonatal care, *n* (%)	574 (3.1)	210 (2.8)
Died in 1 year, *n* (%)	695 (3.7)	264 (3.6)

Note
The denominator is 18,847 based on *Figure 1* and after exclusions of born outside NICU/LNU and excluding congenital anomalies.

Appendix 3

TABLE 33 A comparison of gestational age at birth between very preterm births in the study cohort and those identified from national live birth statistics in England for 2016, 2017 and 2018

Year	Weeks gestation	Study cohort (%)	National data for England from Office for National Statistics (ONS) (%)	*p*-value[a]
2016				
	27	704 (12.6)	768 (12.6)	0.977
	28	883 (15.8)	950 (15.5)	
	29	1015 (18.2)	1101 (18.0)	
	30	1282 (23.0)	1412 (23.1)	
	31	1689 (30.3)	1881 (30.8)	
2017				
	27	638 (11.7)	690 (11.6)	0.987
	28	860 (15.7)	949 (16.0)	
	29	991 (18.1)	1078 (18.2)	
	30	1305 (23.9)	1427 (24.1)	
	31	1670 (30.6)	1787 (30.1)	
2018				
	27	476 (11.0)	696 (12.0)	0.151
	28	620 (14.3)	888 (15.3)	
	29	760 (17.5)	1039 (17.9)	
	30	1035 (23.8)	1358 (23.4)	
	31	1448 (33.3)	1835 (31.6)	

a Chi-squared test of proportions.

Note

Office for National Statistics;[17] births extracted from a data set containing birth registrations. 2016 and 2017 figures exclude births where mothers' usual residence was outside of England. 2018 figures include births where mothers' usual residence was in England and Wales. All figures were based on babies born in the calendar year.

Appendix 4

We described our patient population using the above demographic and unit details. After categorising units by measures of quality of care, the demographic/unit profiles of comparator groups were compared to look for significant differences that could act as confounding factors when conducting analyses to look for associations with outcomes.

- Number of units and their designation.
- Number of babies, average number of babies born per unit, and number of babies by each gestational week of birth.
- Birthweight, gender, multiplicity, presence of major congenital anomalies.
- Condition of baby at birth (cord base excess, Apgar score at 5 minutes of age, number of babies requiring resuscitation involving cardiac massage or adrenaline, worst base excess in first 24 hours of life).
- Socioeconomic factors (ethnic group and the Index of Multiple Deprivation – IMD_Q).
- Health status of mother (pre-pregnancy, during pregnancy, and drug and alcohol use).

To understand whether the differences observed between the patient populations were significant, statistical tests were carried out. For unit designation, gestational week, gender, the IMD_Q, and resuscitation involving cardiac massage or adrenaline, the chi-squared test was used. For comparing distribution of surgical versus non-surgical NICU the Fisher's exact test was used. For birthweight, the weighted two sample *t*-test was used.[151] Missing data were variable. Any parameter with above the threshold level of missing data (10%) was excluded from statistical testing. This included Apgar score at 5 minutes (10.7%), cord base excess (60.5%), worst base excess in first 24 hours of life (100%), ethnic group (18.7%) and maternal health (38.8%).

One hundred and thirty-seven babies had major congenital anomalies and were also excluded. When we conducted analyses for LOS, we excluded 166 babies who died pre-discharge. For analyses involving the binary outcome variable, mortality, we used logistic regression, and for the continuous outcome variable, we used LOS, linear regression.

For logistic regression, our data met the assumptions for large sample size, binary response variable, independent observations, lack of multicollinearity among explanatory variables, and removal of extreme outliers. A Box Tidwell plot showed birthweight had a non-linear relationship with mortality and so this was changed from a continuous variable to

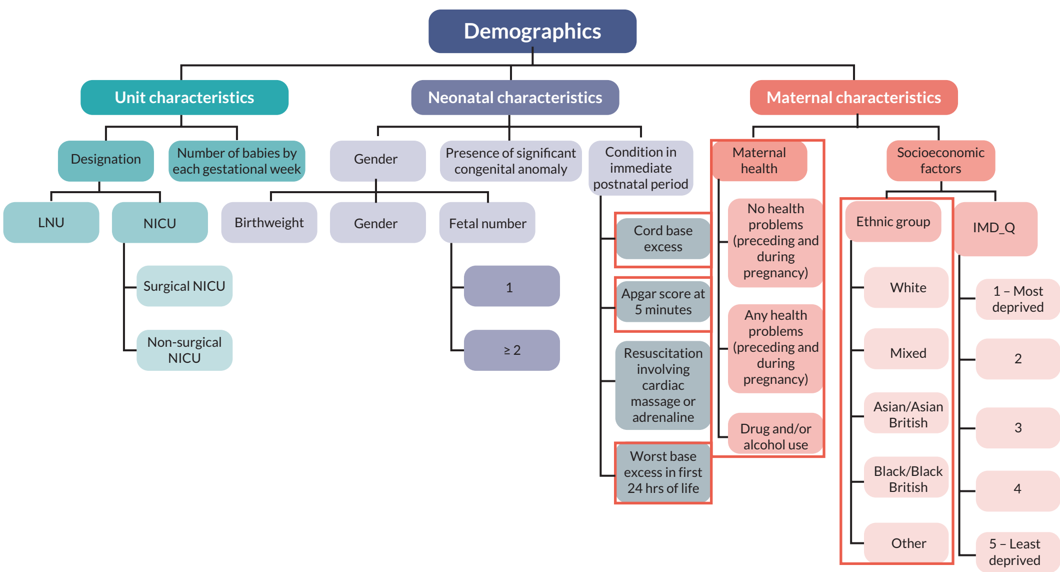

FIGURE 11 Schematic showing demographic parameters chosen for inclusion in workstream 2 analysis. Note: Parameters in red outline had > 10% missing data and were excluded from statistical analyses.

categorical variable using internationally accepted classification of normal BW (> 2500 g), LBW (1500–2499 g), VLBW (1000–1499 g) and ELBW (≤ 999 g).

For linear regression, our data met the assumptions for linear relationship between outcome and confounding variables and lack of multicollinearity. However, examining a graph of regression standardised residuals against regression standardised predicted values showed heteroscedasticity, and a histogram showed the data skewed to the left. For this reason, LOS data were transformed using natural log. To analyse the results, a reverse log calculation was applied to the unstandardised coefficient and CIs.

Appendix 5

TABLE 34 Unit costs (expressed in 2018–9 Great British pounds) used within the cost analysis

Resource use item	Unit cost 2018–9 UK £	Source
Neonatal unit inpatient bed-days		
Intensive care level	£1531	National Cost Collection Data Publication. National Schedule of NHS Costs 2018–2019. HRG code XA01Z[27]
High-dependency care level	£1007	National Cost Collection Data Publication. National Schedule of NHS Costs 2018–2019. HRG code XA02Z[27]
Special care level (carer not resident alongside baby)	£661	National Cost Collection Data Publication. National Schedule of NHS Costs 2018–2019. HRG code XA03Z[27]
Special care level (carer resident at cot-side and caring for baby)	£493	National Cost Collection Data Publication. National Schedule of NHS Costs 2018–2019. HRG code XA04Z[27]
Normal care level	£514	National Cost Collection Data Publication. National Schedule of NHS Costs 2018–2019. HRG code XA05Z[27]
Neonatal critical care, transportation	£1257	National Cost Collection Data Publication. National Schedule of NHS Costs 2018–2019. HRG code XA06Z[27]
Inhaled nitric oxide (iNO) (per day)	£266.52	European iNO Registry for Liverpool Women's NHS Foundation Trust
Surfactant replacement – poractant alfa (per day, by birthweight)[a]		
Birthweight ≤ 0.6 kg (1 bottle 1.5 ml)	£281.61	British National Formulary online: NHS indicative price[105]
0.7 kg ≤ birthweight ≤ 1.2 kg (1 bottle 3 ml)	£547.40	
1.3 kg ≤ birthweight ≤ 1.8 kg (1 bottle 3 ml and 1 bottle 1.5 ml)	£829.01	
1.9 kg ≤ birthweight ≤ 2.4 kg (2 bottles 3 ml)	£1094.8	
2.5 kg ≤ birthweight ≤ 3 kg (2 bottles 3 ml and 1 bottle 1.5 ml)	£1376.41	
3.1 kg ≤ birthweight ≤ 3.6 kg (3 bottles 3 ml)	£1642.2	
3.7 kg ≤ birthweight ≤ 4.2 kg (3 bottles 3 ml and 1 bottle 1.5 ml)	£1923.81	
Total parental nutrition (per day, over 14 days of use)[b]	£48.15	Inflated to 2018–9 prices[106]
Palivizumab (per day at 15 ml/kg birthweight)	£435	British National Formulary online: NHS indicative price[105]
ROP surgery	£1731	National Cost Collection Data Publication. National Schedule of NHS Costs 2018–9. HRG code BZ86C, elective care[27]
Neonatal surgery[c]	Various	HRG4 + 2017–8[107] inflated to 2018–9 prices

a Surfactant use was reported from three separate fields from the data sets: surfactant given today, drugs given today and surfactant given at resuscitation. The first two variables were recorded at the daily level, while the third variable was recorded at the episode level and therefore we defined its use for the first daily record of this episode.
b The use of total parental nutrition (TPN) was reported from two separate fields from the data sets: TPN given today and drugs given today.
c Different types of neonatal surgery were identified from OPCS and ICD-10 codes using the HRG4 + 2017–8 Reference Costs Grouper Software.

Appendix 6

TABLE 35 Baseline characteristics of babies, without missing NNRD data on daily records or level of care provided

	Babies with missing daily records or level of care data (n = 1669)	Babies with complete information (n = 28,173)	
	n (%)	n (%)	p[a]
Gestational age at birth			
27 weeks	284 (17.0)	3296 (11.7)	p < 0.001
28 weeks	304 (18.2)	4370 (15.5)	
29 weeks	289 (17.3)	5036 (17.9)	
30 weeks	354 (21.2)	6625 (23.5)	
31 weeks	435 (26.1)	8827 (31.3)	
Missing	*3 (0.2)*	*19 (0.1)*	
Gender of baby			
Male	961 (57.6)	15,363 (54.5)	0.046
Female	704 (42.2)	12,755 (45.3)	
Missing	*4 (0.2)*	*55 (0.2)*	
Number of fetus			
Singleton birth	1229 (73.6)	20,555 (73.0)	0.632
Multiple birth	438 (26.2)	7598 (27.0)	
Missing	*2 (0.1)*	*20 (0.1)*	
Birthweight (g) – mean (SD)	1282.6 (358.2)	1330.2 (332.2)	p < 0.001
Missing	*8 (0.5)*	*82 (0.3)*	
Apgar score at 5 minutes – mean (SD)	8.1 (1.7)	8.1 (1.8)	0.030
Missing	*156 (9.4)*	*2877 (10.2)*	
Died in neonatal care	22 (1.3)	985 (3.5)	p < 0.001
Missing	*1 (0.1)*	*0 (0.0)*	

a Continuous variables were tested by independent t-test, categorical variables by chi-squared test.

Note
Data are frequencies unless otherwise stated.

Appendix 7

TABLE 36 Unadjusted estimates of days spent receiving each level of care by neonatal unit type

Resource item	Mean (SE) days per baby		Mean resource use difference (99% CI)
	NICU (n = 10,241)	LNU (n = 8371)	
Levels of daily care			
Intensive care days	9.08 (0.121)	7.73 (0.104)	1.35 (0.93 to 1.77)[a]
High-dependency days	12.81 (0.172)	10.69 (0.153)	2.12 (1.51 to 2.72)[a]
Special care (no carer) days	29.87 (0.141)	28.64 (0.143)	1.23 (0.71 to 1.75)[a]
Special care (carer) days	1.48 (0.025)	1.74 (0.033)	−0.26 (−0.37 to −0.15)[a]
Normal ward days	0.00 (0.000)	0.00 (0.000)	0.00 (0.00 to 0.00)

a Statistically significant at $p < 0.01$.

Appendix 8

TABLE 37 Estimates of days spent receiving each level of care by neonatal unit – adjustments made for measured confounders only[a]

Resource item	Mean (SE) days per baby NICU (n = 10,241)	Mean (SE) days per baby LNU (n = 8371)	Mean resource use difference (99% CI)
Levels of daily care			
Intensive care days	8.49 (0.098)	8.45 (0.095)	0.04 (−0.31 to 0.39)
High-dependency days	12.00 (0.142)	11.67 (0.139)	0.33 (−0.18 to 0.84)
Special care (no carer) days	29.53 (0.133)	29.05 (0.143)	0.48 (−0.02 to 0.98)
Special care (carer) days	1.50 (0.026)	1.72 (0.033)	−0.22 (−0.33 to −0.11)[b]
Normal ward days	0.00 (0.000)	0.00 (0.000)	0.00 (−0.00 to 0.00)

a Adjusted for gestational age; sex; birthweight z-score; multiplicity; mode of delivery; maternal ethnicity; maternal age and IMD score.
b Statistically significant at $p < 0.01$.

Appendix 9

TABLE 38 Estimates of days spent receiving each level of care by neonatal unit and weeks gestation at birth – adjustments made for measured and unmeasured confounders (using IV)[a]

Resource item	Mean (SE) days per baby		Mean difference (99% CI)
	NICU	LNU	
Overall (n = 18,612)			
Intensive care days	7.94 (0.128)	9.13 (0.145)	−1.19 (−1.80 to −0.59)[b]
High-dependency days	11.42 (0.187)	12.38 (0.235)	−0.96 (−1.91 to −0.00)[b]
Special care (no carer) days	30.02 (0.182)	28.46 (0.219)	1.56 (0.66 to 2.46)[b]
Special care (carer) days	1.38 (0.040)	1.87 (0.053)	−0.49 (−0.70 to −0.28)[b]
Normal ward days	0.00 (0.001)	0.00 (0.000)	0.00 (−0.00 to 0.00)
27 weeks (n = 2243)			
Intensive care days	18.13 (0.513)	18.94 (0.867)	−0.80 (−3.93 to 2.33)
High-dependency days	27.14 (0.868)	28.06 (1.586)	−0.92 (−6.72 to 4.88)
Special care (no carer) days	31.62 (0.642)	28.08 (1.123)	3.54 (−0.54 to 7.63)
Special care (carer) days	1.33 (0.092)	1.75 (0.180)	−0.42 (−1.06 to 0.22)
Normal ward days	–	–	–
28 weeks (n = 2985)			
Intensive care days	13.44 (0.425)	14.85 (0.504)	−1.41 (−3.46 to 0.64)
High-dependency days	19.51 (0.623)	19.24 (0.865)	0.27 (−3.15 to 3.69)
Special care (no carer) days	32.64 (0.545)	31.59 (0.743)	1.04 (−1.89 to 3.98)
Special care (carer) days	1.50 (0.107)	1.85 (0.161)	−0.36 (−0.99 to 0.27)
Normal ward days	0.00 (0.002)	0.00 (0.000)	0.00 (−0.004 to 0.010)
29 weeks (n = 3372)			
Intensive care days	8.81 (0.255)	10.53 (0.305)	−1.72 (−2.93 to −0.50)[b]
High-dependency days	11.08 (0.440)	12.06 (0.519)	−0.98 (−3.13 to 1.16)
Special care (no carer) days	33.65 (0.461)	31.54 (0.544)	2.11 (−0.17 to 4.40)
Special care (carer) days	1.39 (0.096)	1.96 (0.128)	−0.57 (−1.09 to −0.05)[b]
Normal ward days	–	–	–
30 weeks (n = 4327)			
Intensive care days	5.03 (0.159)	5.98 (0.199)	−0.95 (−1.74 to −0.16)[b]
High-dependency days	7.17 (0.264)	8.45 (0.339)	−1.28 (−2.59 to 0.03)
Special care (no carer) days	30.61 (0.317)	29.67 (0.383)	0.94 (−0.61 to 2.50)
Special care (carer) days	1.46 (0.083)	1.87 (0.101)	−0.41 (−0.83 to 0.01)
Normal ward days	0.00 (0.001)	0.00 (0.000)	0.00 (−0.001 to 0.002)

TABLE 38 Estimates of days spent receiving each level of care by neonatal unit and weeks gestation at birth – adjustments made for measured and unmeasured confounders (using IV)[a] (*continued*)

Resource item	Mean (SE) days per baby		Mean difference (99% CI)
	NICU	LNU	
31 weeks (n = 5685)			
Intensive care days	2.82 (0.210)	3.71 (0.170)	−0.90 (−1.79 to −0.00)[b]
High-dependency days	4.42 (0.161)	5.66 (0.195)	−1.24 (−2.02 to −0.45)[b]
Special care (no carer) days	25.29 (0.241)	24.11 (0.244)	1.18 (0.12 to 2.25)[b]
Special care (carer) days	1.27 (0.071)	1.86 (0.084)	−0.59 (−0.95 to −0.23)[b]
Normal ward days	–	–	–

a Adjusted for gestational age; sex; birthweight z-score; multiplicity; mode of delivery; maternal ethnicity; maternal age and IMD score in the IV model.
b Statistically significant at $p < 0.01$.

Appendix 10

TABLE 39 Association between care setting and overall and gestational age-specific mortality while in neonatal care using IV only (without adjustment for measured confounders)

	Number of deaths	Cohort size	NICU setting	LNU setting	Mean difference (99% CI)
Mortality					
Overall	784	25,352	0.03 (0.002)	0.03 (0.003)	0.000 (−0.011 to 0.011)
27 weeks	231	3086	0.06 (0.008)	0.10 (0.016)	−0.039 (−0.097 to 0.019)
28 weeks	226	4023	0.05 (0.007)	0.06 (0.009)	−0.008 (−0.046 to 0.029)
29 weeks	118	4578	0.03 (0.005)	0.02 (0.006)	0.001 (−0.023 to 0.025)
30 weeks	97	5936	0.02 (0.004)	0.01 (0.004)	0.006 (−0.011 to 0.022)
31 weeks	112	7709	0.02 (0.003)	0.01 (0.003)	0.009 (−0.004 to 0.023)
Total costs					
Overall		25,046	£45,832 (£359)	£47,979 (£112)	−£2118 (−£3884 to −£352)[a]
27 weeks		3029	£78,318 (£1225)	£83,655 (£2445)	−£5336 (−£14,076 to £3403)
28 weeks		3963	£64,825 (£953)	£67,142 (£1239)	−£2320 (−£7239 to £2598)
29 weeks		4525	£49,652 (£656)	£51,765 (£766)	−£2113 (−£5236 to £1010)
30 weeks		5867	£37,428 (£417)	£39,384 (£518)	−£1956 (−£4001 to £90)
31 weeks		7642	£27,007 (£333)	£29,073 (£331)	−£2066 (−£3533 to −£599)[a]

a Statistically significant at $p < 0.01$.

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