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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

Abdul Qader Tahir Ismail ,[1,2] Elaine M Boyle,[1] Thillagavathie Pillay,[2,3] On behalf of The OptiPrem Study Group

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For numbered affiliations see end of article.

Correspondence to
Dr Abdul Qader Tahir Ismail; aqt.ismail@bnc.oxon.org

ABSTRACT

Objective There is evidence that birth and care in a maternity service associated with a neonatal intensive care unit (NICU) is associated with improved survival in preterm babies born at ≤27 weeks of gestation. We conducted a systematic review to address whether similar gains manifested in babies born between 27+0 and 31+6 weeks (hereafter 27 and 31 weeks) of gestation, or in those with a birth weight between 1000 and 1500 g.

Methods We searched Embase, Medline and CINAHL databases for studies comparing outcomes for babies born between 27 and 31 weeks or between 1000 and 1500 g birth weight, based on designation of the neonatal unit where the baby was born or subsequently cared for (NICU vs non-NICU setting). A modified QUIPS (QUality In Prognostic Studies) tool was used to assess quality.

Results Nine studies compared outcomes for babies born between 27 and 31 weeks of gestation and 11 studies compared outcomes for babies born between 1000 and 1500 g birth weight. Heterogeneity in comparator groups, birth locations, gestational age ranges, timescale for mortality reporting, and description of morbidities facilitated a narrative review as opposed to a meta-analysis.

Conclusion Due to paucity of evidence, significant heterogeneity and potential for bias, we were not able to answer our question—does place of birth or care affect outcomes for babies born between 27 and 31 weeks? This supports the need for large-scale research to investigate place of birth and care for babies born in this gestational age range.

What is known about the subject?

- Babies born at <27 weeks of gestation in maternity services linked to neonatal intensive care units (NICU), compared with local neonatal units (LNUs) have improved outcomes.
- Babies born between 27 and 31 weeks of gestation form a considerably larger patient group, and, in the UK are cared for in both NICU and LNU settings.

What this study adds?

- In nine studies addressing place of care for babies born between 27 and 31 weeks of gestation, there was significant heterogeneity in study design and outcomes, and potential for bias.
- Systematic review of the published literature reveals a lack of evidence about place of birth for babies born between 27 and 31 weeks of gestation.
- Large-scale research studies are needed to determine the effect of place of birth on outcomes for babies between 27 and 31 weeks of gestation.

INTRODUCTION

The concept of regionalisation was introduced into neonatal care in the 1970s, with the aim of improving outcomes while reducing associated costs.[1–8] Worldwide, especially in resource richer settings, this system has been implemented through clinical networks. Perinatal centres (comprising fetomaternal and neonatal units) of different levels work together to care for mothers and their babies in a unit which is close to home and can provide the appropriate level of care.

In the USA, Australia and New Zealand, and in many parts of Europe, care is centralised and all babies born at <32 weeks of gestation and/or of very low birth weight (VLBW; <1500 g) are provided with tertiary level care in neonatal intensive care units (NICUs) (table 1). In the UK, due to concerns regarding the time and travel burden this would impose on families, and unit capacity and staffing, a more regionalised system was implemented, consisting of three-tiers

Table 1 International summary of organisation of neonatal care services, extracted from national guidelines and relevant reviews

	Level 1	Level 2	Level 3
USA[51]	▶ Care for babies born ≥35 weeks	▶ Care for babies born ≥32 weeks and weight ≥1500 g ▶ Stabilise babies born <32 weeks or <1500 g, and brief periods of mechanical ventilation, before transfer to a NICU	▶ Level 3 NICU care for babies of all gestational ages and birth weight ▶ Level 4 regional NICU have level 3 capabilities and are located within an institution with surgical and paediatric medical capabilities
Canada[52]	▶ Tier 1a care for babies ≥37 weeks and ≥2500 g ▶ Tier 1b care for babies ≥35 weeks and ≥1800 g	▶ Tier 2a care for babies ≥32 weeks and ≥1500 g ▶ Tier 2b care for babies ≥30 weeks and ≥1200 g	▶ Tier 3 care for babies of all gestational ages and birth weight with non-life-threatening conditions ▶ Tier 4 provide tier 3 services to babies of all gestational ages and birth weight, including those with life-threatening conditions and requiring paediatric subspecialty input
Australia[53–56]	▶ Previously labelled level one now includes level 1, 2 and 3 ▶ Level 1 and 2 do not provide routine neonatal care ▶ Level 3 care for babies >36/≥37 weeks (>2000 g/≥2500 g)	▶ Previously labelled level 2a and 2b now includes level 4 and 5 ▶ Level 4 care for babies >32/≥34 weeks (>1500/>1700 g) ▶ Level 5 care for babies >31/≥32 weeks (>1250/>1350 g)	▶ Previously labelled level 3 now includes level 6 ▶ Care for babies of all gestational ages and birth weight, including surgery and congenital and metabolic diseases ▶ May be split into 6a and 6b, with only the latter providing surgical and specialty services
New Zealand[57]	▶ Care for babies >36 weeks	▶ Care for babies >32 weeks ▶ Some units (level 2+) care for babies >28 weeks	▶ Care for babies of all gestational ages and birth weight
Finland[58]	▶ Smaller, non-university hospitals provide care to babies >32 weeks and >1500 g		▶ University hospitals care for babies of all gestational ages and birth weight
Sweden[59]	▶ Smaller, non-regional centres provide care to babies >28 weeks		▶ Regional centres care for babies of all gestational ages and birth weight
France[60]	▶ No neonatal ward ▶ Not required to have a paediatrician on-site	▶ Care for babies >32 weeks ▶ Paediatrician must be present during the day, can be on-call at nights and weekends	▶ Care for babies of all gestational ages and birth weight ▶ Neonatologist must always be present

NICU, neonatal intensive care unit.

(NICU, local neonatal unit (LNU) and special care unit (SCU)), with both NICU and LNU caring for babies born at <32 weeks of gestation (table 2).[9]

There is evidence supporting both models of neonatal care provision. EPICure 2 and similar international studies show that, for preterm births at <27 weeks of

Table 2 Summary of differences between three levels of neonatal care within the UK, adapted from British Association of Perinatal Medicine[61 62]

Level 1 (special care unit—SCU)	Level 2 (local neonatal unit—LNU)	Level 3 (neonatal intensive care unit—NICU)
▶ Care for babies born ≥34 weeks (or ≥32 weeks depending on local network policy). ▶ Provide special care and may provide some high dependency care. ▶ Stabilise babies who need to be transferred to an LNU or NICU. ▶ Receive transfers from units within their network for continuing special care. ▶ Doctors and nursing staff are on a shared rota with paediatric services. ▶ Consultants are general paediatricians.	▶ Care for babies born ≥27 weeks of gestation (or ≥28 weeks depending on local network policy). ▶ Provide all categories of care for their local population (including short periods of intensive care), but transfer babies requiring complex or longer-term intensive care to a NICU. ▶ Depending on size and level of activity, doctors and nursing staff may be on a shared or separate rota with paediatric services. ▶ Some consultants have neonatal expertise, while others are general paediatricians.	▶ Care for babies of all gestational ages (>22/23 weeks). ▶ Sited alongside specialist obstetric and fetomaternal services. ▶ Provide all categories of neonatal care (including non-conventional modes of ventilation, inhaled nitric oxide, and therapeutic hypothermia). ▶ May be colocated with surgery and other specialised services. ▶ Consulted for advice and receive transfers from other units within their network. ▶ Doctors and nursing staff are not on a shared rota with paediatric services. ▶ All consultants have neonatal expertise.

gestation, birth in a maternity service with a NICU, as opposed to an LNU, is associated with significantly better rates of survival to discharge.[10–13] Similarly, a meta-analysis by Laswell *et al* and more recent studies have shown improved outcomes when all babies born <32 weeks of gestation and/or of VLBW are cared for in NICU.[14–18]

Therefore, in babies born <27 weeks there is a similar care pathway internationally; they are cared for in NICU. This is not true for babies born between 27+0 and 31+6 weeks (hereafter 27 and 31 weeks) of gestation. Specifically, within the UK these babies may be born and cared for in a centre with either a NICU or LNU, depending on maternal choice at booking, presentation to the nearest hospital, and neonatal unit cot availability and staff capacity at the time of delivery.

Babies born between 27 and 31 weeks account for around fourfold more throughput in neonatal units compared with those born at <27 weeks, and make up 12% of all preterm babies born in England. In 2014, they used twice as many neonatal bed days per year compared with the <27 weeks group.[19 20] Therefore, we wanted to investigate whether birth or care in a NICU as opposed to an LNU affects outcomes for these babies as it does for their more preterm counterparts. To answer this question, we conducted a systematic review.

METHODS

Criteria for considering studies

Our aim was to identify studies comparing outcomes for babies born between 27 and 31 weeks of gestation by the designation of neonatal unit linked to the maternity services where the baby was born or subsequently cared for (NICU vs non-NICU setting). To ensure we were not excluding evidence from studies published before the 1980s[5 21 22] and from countries which categorised babies by birth weight as opposed to gestational age,[17 23 24] we also included studies comparing outcomes for babies with a birth weight between 1000 and 1500 g. Of the commonly used birth weight stratifications, this weight range best aligned with the 50th centile for weight for preterm babies born between 27 and 31 weeks of gestation (see online supplementary figure S1).

Literature search

We conducted a search in Embase, Medline and CINAHL databases (1977–2018), using terms related to our patient group (including 'newborn, neonate, premature, preterm, infant, low birth weight'), intervention (including 'regionalisation, centralisation, level of care, size, volume, maternal/neonatal transfer, inborn, outborn') and outcomes (including 'mortality, morbidity, death, survival'). We did not specify specific morbidities within our search strategy (for the full search strategy, see online supplementary figure S2). Articles were analysed by AQTI and TP, with EMB arbitrating any differences of opinion as to suitability for inclusion. Study authors were contacted for further information if the gestational age range contained or overlapped with, but was not exactly 27 to 31 weeks, or outcome data were in a non-numerical format. The reference lists of articles retrieved from the search, and three systematic reviews on this topic were analysed,[14 25 26] as well as a search for relevant 'grey' literature (including research and industry reports, conference proceedings, theses, preprints, etc) in OpenGrey, Scopus, Embase and Web of Science databases (1977–2018). All searches were limited to the English language.

Analysis

To determine the feasibility of meta-analysis, we assessed articles included in the systematic review for uniformity of study characteristics, patient populations, and outcome measures. We assessed risk of bias in included studies using a modified version of the QUIPS (QUality In Prognostic Studies) tool.[27]

RESULTS

Of the 5043 articles identified (figure 1), 9 studies were eligible for inclusion based on reporting outcomes for babies born between 27 and 31 weeks of gestation by designation of hospital of birth or care.[13 28–35] A further 11 studies were identified based on birth weight categorisation (1000 to 1500 g).[1 18 36–44] In these, it was not possible to extract information about those born between 27 and 31 weeks to allow comparison with the nine other studies. There was heterogeneity in multiple areas—comparator groups, gestational age comparisons, timeframe for reporting mortality and description of morbidities (table 3). Therefore, a meta-analysis was deemed inappropriate and a narrative review was conducted.

The studies were all of cohort design but could be divided into three groups based on the following comparators (table 3): (group 1) *in utero* versus *ex utero* transfer to a NICU for continued care; (group 2) birth at a maternity service linked to a NICU versus non-NICU irrespective of subsequent main place of care; (group 3) main place of care in a NICU versus non-NICU, irrespective of the place of birth. Here, place of care referred to either the entirety of care (peripartum and postnatal) or the level of unit of care after the baby was transferred *ex utero*.

Mortality, based on location of birth/care

Group 1 (*in utero* versus *ex utero* transfer to a NICU):

We identified five studies that categorised babies by gestational age. Two found significant differences in survival to discharge[28] and infant mortality,[13] respectively, although Lamont *et al* found this only for babies born between 28 and 29 weeks of gestation. The other three studies did not find a significant difference.[31–33] Of the four birth weight studies investigating this outcome, three found a significant difference (in neonatal mortality,[44] predischarge mortality[38] and survival up to 2 years of age[42]).

Group 2 (birth at a maternity service linked to a NICU vs non-NICU):

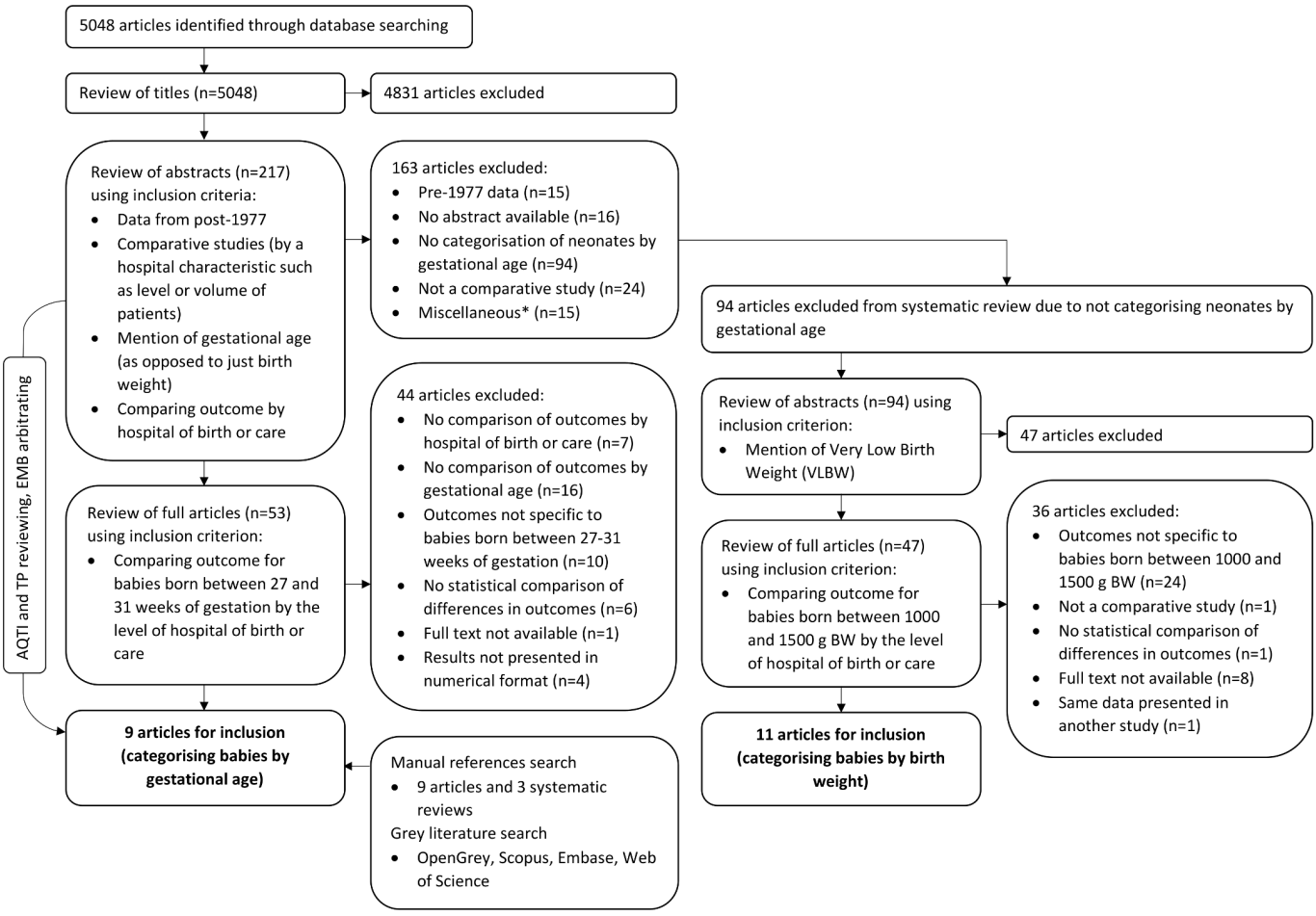

Figure 1 Flow diagram showing results from systematic review search strategy for studies categorising neonates by gestational age and birth weight. *Miscellaneous include studies excluded due to comparing outcomes in NICU versus NICU/a geographical area/paediatric hospitals/neonatal care in a non-regionalised healthcare system; studies investigating degree of regionalisation/incidence and avoidability of *ex utero* transfers; and studies comparing birth asphyxia in term infants/success of using early nasal CPAP. BW, birth weight; CPAP, continuous positive airway pressure; NICU, neonatal intensive care unit.

Of the two gestational age studies, neither found a significant difference in mortality.[29 34] Of six studies categorising babies by birth weight, three studies[1 36 43] found a significant difference in neonatal and infant mortality and three did not.[18 37 41]

Group 3 (main place of care in a NICU vs non-NICU):

Of the two gestational age studies in the third group. Jonas *et al* found a significant reduction in neonatal mortality,[35] but Field *et al* did not (undefined timeframe).[30]

Morbidity, based on location of birth/care

Group 1 (*in utero* vs *ex utero* transfer to a NICU):

Of the five studies that categorised babies by gestational age, there were conflicting results for incidence of intraventricular haemorrhage (IVH)[28 33] and respiratory distress syndrome (RDS).[32 33] A significant reduction was found in the incidence of chronic lung disease in babies born between 27 and 29 weeks (but not between 30 and 31 weeks),[33] and no significant difference found for necrotising enterocolitis (NEC) and retinopathy of prematurity (ROP).[33] Two birth weight studies also provided conflicting results for incidence of IVH.[39 40]

Group 2 (birth at a maternity service linked to a NICU vs non-NICU):

Two studies looked at morbidity outcomes. The gestational age study found an insignificant difference in the incidence of asphyxia (not strictly an outcome, but reported as such in this study).[34] The birth weight study found significant reduction in composite outcomes of bronchopulmonary dysplasia or death, IVH (grade III or IV) or death, ROP or death, but not NEC (Bell stage II or III) or death.[18]

None of the identified studies specifically investigated babies born between 27 and 31 weeks of gestation; data presented here was within the context of larger gestational age ranges. We did not identify any gestation-specific data (ie, by week of gestational age).

Quality assessment

Results of quality assessment of the nine studies that categorised babies by gestational age are summarised in table 4. Further details for these, and the 11 studies categorising babies by birth weight are provided as online supplementary tables S1 and S2.

Table 3 Study characteristics and outcomes for studies characterising neonates by gestational age and birth weight

Categorisation method	Type of study (comparator groups)	Study	Country of study	Total number of babies	Population (gestation (weeks $^{+days}$)/birth weight (g))	Outcomes reported by included studies								
						Mortality timeframe				Survival timeframe				
						Undefined	Perinatal	Neonatal	Discharge	Infant	2 years	Discharge	2 years	Morbidity
Gestational age	*In utero* versus ex *utero* transfer to NICU	Lamont *et al*[28]	UK	206	28^{+0}–29^{+6}							↑		Non-significant difference in incidence of IVH.
					30^{+0}–31^{+6}							NS		Significant reduction in incidence of IVH.
		Truffert *et al*[31]	France	157	27^{+0}–30^{+6}						NS			Non-significant difference in incidence of survival (up to 2 years of age) without disability.*
		Hauspy *et al*[32]	Belgium	315	28^{+0}–29^{+6}			NS						Non-significant difference in incidence of RDS.
					30^{+0}–31^{+6}			NS						
		Lee *et al*[33]	Canada	2148	27^{+0}–29^{+6}				NS					Non-significant difference in incidence of IVH, NEC and ROP. Significant reduction in incidence of RDS and CLD.
					30^{+0}–31^{+6}				NS					Non-significant difference in incidence of IVH, NEC, ROP and CLD. Significant reduction in incidence of RDS.
		Boland *et al*[13]	Australia	250	28^{+0}–31^{+6}					↓				No other outcomes measured.
	Level of unit of birth (NICU vs non-NICU)	Holmgren and Högberg [34]	Sweden	394	28^{+0}–31^{+6}		NS	NS		NS				Non-significant difference in incidence of asphyxiat†
		Johansson *et al*[29]	Sweden	1636	28^{+0}–31^{+6}					NS				No other outcomes measured.
	Level of unit of care (NICU vs non-NICU)	Field *et al*[30]	UK	171	29^{+0}–30^{+6}	NS								No other outcomes measured.
		Jonas and Lumley[35]	Australia	3331	28^{+0}–31^{+6}			↓						No other outcomes measured.

Continued

Table 3 Continued

Categorisation method	Type of study (comparator groups)	Study	Country of study	Total number of babies	Population (gestation (weeks $^{+days}$)/birth weight (g))	Outcomes reported by included studies								
						Mortality timeframe						Survival timeframe		
						Undefined	Perinatal	Neonatal	Discharge	Infant	2 years	Discharge	2 years	Morbidity
Birth weight	*In utero* versus *ex utero* transfer to NICU	Miller *et al*[38]	USA	94	1000–1500				↓					No other outcomes measured.
		Watkinson and McIntosh[44]	UK	154	1001–1500			↓						No other outcomes measured.
		Powell and Pharoah[42]	UK	390	1000–1500								↑	No other outcomes measured.
		Obladen *et al*[40]	Germany	220	1000–1249							**NS**		Non-significant difference in incidence of IVH.
					1250–1499							**NS**		No other outcomes measured.
		Mohamed and Aly[39]	USA	36 493	1000–1500									Significant reduction in incidence of IVH.
	Level of unit of birth (NICU vs non-NICU)	Gortmaker *et al*[36]	USA	4874	1000–1500			↓		↓				No other outcomes measured.
		Powell *et al*[41]	USA	947	1000–1500					**NS**				No other outcomes measured.
		Yeast *et al*[1]	USA	2852	1000–1500			↓						No other outcomes measured.
		Sanderson *et al*[43]	USA	1345	1000–1249			↓						No other outcomes measured.
					1250–1499			**NS**						No other outcomes measured.
		Gould *et al*[37]	USA	undefined (<4405)	1000–1500			**NS**						No other outcomes measured.
		Warner *et al*[18]	USA	474	1000–1500				**NS**					Non-significant difference in incidence of NEC (Bell stage II or III) or death. Significant reduction in incidence of BPD or death, IVH (grade III or IV) or death, ROP or death.

↑denotes direction of significant difference found between comparator groups (first comparator vs second comparator), and **NS** denotes lack of significant difference between comparator groups). For example, Jonas 1997 showed a significantly lower (arrow in downward direction) neonatal mortality for those babies born between 28^{+0} and 31^{+6} in a NICU (first comparator) versus a non-NICU (second comparator).
*Disability is a composite outcome measure consisting of cerebral palsy, deafness, Brunet-Lézine developmental score <80.[63]
†Asphyxia refers to Apgar score <5 at 10 min of age.
BPD, bronchopulmonary dysplasia; CLD, chronic lung disease; IVH, intraventricular haemorrhage; NEC, necrotising enterocolitis; NICU, neonatal intensive care unit; RDS, respiratory distress syndrome; ROP, retinopathy of prematurity.

Table 4 Assessment of study quality (categorising babies by gestational age) using modified QUIPS tool (for in-depth analysis, see online supplementary tables S1 and S2)

		Criteria of modified QUIPS tool				
Type of study (comparator groups)	**Study**	**Study participation (population, exclusion criteria, comparison of baseline characteristics between comparator groups)**	**Study attrition (prospective or retrospective, data source, completeness of data on demographic/confounding factors, proportion of babies outcome analysis carried out on)**	**Prognostic factor measurement (definition of birth location, explanation of facilities available at different level units)**	**Outcome measurement (definition)**	**Study confounding (adjustment for confounding factors, which variables used)**
In utero versus *ex utero* transfer to NICU	Lamont *et al*[28]	x	✓	x	x	x
	Truffert *et al*[31]	x	✓	x	x	x
	Hauspy *et al*[32]	x	✓	x	x	x
	Lee *et al*[33]	x	✓	x	✓	✓
	Boland *et al*[13]	✓	✓	x	✓	x
Level of unit of birth (NICU vs non-NICU)	Holmgren and Högberg[34]	x	✓	✓	✓	x
	Johansson *et al*[29]	x	✓	✓	✓	✓
Level of unit of care (NICU vs non-NICU)	Field *et al*[30]	x	x	x	x	x
	Jonas and Lumley[35]	x	✓	x	✓	✓

✓ denotes adequate quality, and **x** indicates inadequate quality.
NICU, neonatal intensive care unit; QUIPS, QUality In Prognostic Studies.

Of the nine studies, none were of reasonable quality across all five domains of our modified QUIPS tool. One study was of reasonable quality across three domains,[29] four studies across two domains[13 33–35] and four studies across zero domains.[28 30–32] Most significant sources of potential bias included inclusion of babies with life-threatening congenital anomalies, lack of definition of non-NICU birth locations, inclusion of birth settings in which an inadequate level of care would be provided (ie, home, or hospitals without obstetric or paediatric units) and lack of adjustment for confounding factors.

DISCUSSION

This is the first review to investigate outcomes of preterm babies born between 27 and 31 weeks of gestation by the level of neonatal unit of birth and/or care. Overall, the evidence identified in our review was limited, conflicting and prone to bias. The literature was heterogeneous with respect to gestational ages studied, study design and outcomes.

Strengths of our review include the use of a comprehensive search strategy and inclusion of studies based on birth weight between 1000 and 1500 g to avoid exclusion of relevant data. A limitation is the exclusion of non-English studies. A narrative review was undertaken since a meta-analysis was not appropriate, reflecting the quality of available literature.

There have been two previous similar systematic reviews. In the 1980s, Ozminkowski *et al*[25] carried out a meta-analysis investigating neonatal mortality for babies with birth weight <1500 g by hospital of birth. They identified 19 articles (1972–1984), a meta-analysis of which showed that odds of neonatal mortality for inborn babies was 62% of that for outborn (OR 0.62, 95% CI 0.55 to 0.69), but with a significant degree of heterogeneity. Subgroup analysis of the eight studies which provided data on babies with a birth weight between 1001 and 1500 g (n=3180) revealed consistent, statistically significant OR in favour of inborn status (0.53, 95% CI 0.36 to 0.79). The type of studies included (inborn vs outborn) is similar to the five we identified comparing *in utero* and *ex utero* transfers.[38–40 44] However, Ozminkowski *et al* did not provide information on level of unit or birth location from which outborn babies were being transferred to NICU.

Considering the overall group of preterm babies born at <32 weeks, Lasswell *et al*[14] conducted a meta-analysis of studies from 1976 to 2010, in which neonatal or predischarge mortality data were provided for births in level 3 units compared with lower level units. Forty-one studies met their inclusion criteria, from the USA, Canada, Europe, Australia, Israel and Ghana. Studies were classified as of insufficient quality if they provided 'no hospital information or lack of clear description of the distinction between hospital levels'. Even when excluding these studies, their meta-analysis showed increased odds of mortality for birth in non-level 3 units for VLBW (36% vs 21%; adjusted OR (aOR) 1.60, 95% CI 1.33 to 1.92) and very preterm (12% vs 7%; aOR 1.42, 95% CI 1.06 to 1.88) babies. Subgroup analyses were only performed for babies with birth weight of <1000 g.

Watson *et al*[45] advanced this analysis, by identifying that within this cohort of babies, it was predominantly those born at ≤27 weeks of gestation for whom place of birth had a major impact. They showed that care in a high volume (within the top quartile) or tertiary neonatal unit (NICU) was associated with significantly lower mortality to discharge for babies born at ≤27 weeks, but not for those born between 27 and 32 weeks of gestation.

However, this analysis could be taken a step further, by exploring outcomes by week of gestation for babies born between 27 and 31 weeks. This population represents a heterogeneous group; at the lower end of this gestational age range they often require significant intensive care interventions, whereas lower dependency care may be appropriate for the more mature babies. Across the whole spectrum of gestational age, the risk of adverse neurological and physical outcomes and the need for long-term health, social and educational care increases with increasing prematurity.[10 46–49] If the more immature babies within this population have similar outcomes as those born at <27 weeks (regarding place of birth/care), then caring for them in LNU may be associated with worse outcomes and long-term costs. Conversely, perhaps more mature babies would do better in LNU, through the avoidance of overmedicalisation. Watson *et al*[45] found that babies born between 27 and 32 weeks of gestation and cared for in NICU were more likely to receive ROP treatment than those born in non-NICU, although this might reflect differences in severity of illness of babies born and cared for in NICU. Even if outcomes are comparable, keeping mothers and their babies in local units could avoid unnecessary transfers and improve family-centred care. The cost to the UK NHS (National Health Service) of providing the same level of care in NICU versus LNU has not been quantified but may also be different. Therefore, grouping babies born between 27 and 31 weeks together might obscure benefits of birth/care in one type of unit over the other.

CONCLUSION

There is currently a paucity of evidence and data to guide the management of preterm babies born between 27 and 31 weeks of gestation with respect to place of birth or care and further research is therefore required.

Future perspective

The OptiPrem project, funded by the National Institute for Health Research - Health Systems and Delivery Research (NIHR HS&DR) Stream,[50] has been designed to address the question posed by our systematic review. OptiPrem will use data from the National Neonatal Research Database, linked to Hospital Episode Statistics and national mortality statistics through NHS digital

services. The project will evaluate associations between place of birth/care for babies born between 27 and 31 weeks of gestation, neonatal and infant mortality, and key neonatal morbidities, by week of gestation. Parent and staff perspectives, and costs of care will also be explored as these would be important drivers for health service change if infant health outcomes are not directly influenced by place of care.

Author affiliations
[1]Department of Health Sciences, College of Life Sciences, University of Leicester, Leicester, UK
[2]Royal Wolverhampton Hospitals NHS Trust, Wolverhampton, UK
[3]School of Medicine and Clinical Practice, Faculty of Science and Engineering, University of Wolverhampton, Wolverhampton, UK

Collaborators The OptiPrem Study Group include Elaine M Boyle, Neena Modi, Oliver Rivero-Arias, Brad Manktelow, Sarah E Seaton, Natalie Armstrong, Miaoqing Yang, Abdul Qader Tahir Ismail, Vasiliki Bountziouka, Caroline S Cupit, Alexis Paton, Victor L Banda, Elizabeth S Draper, Kelvin Dawson and Thillagavathie Pillay (Chief Investigator).

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ORCID iD
Abdul Qader Tahir Ismail http://orcid.org/0000-0003-4125-8684

REFERENCES

1 Yeast JD, Poskin M, Stockbauer JW, *et al*. Changing patterns in regionalization of perinatal care and the impact on neonatal mortality. *Am J Obstet Gynecol* 1998;178:131–5.
2 Peddle LJ, Brown H, Buckley J, *et al*. Voluntary regionalization and associated trends in perinatal care: the nova Scotia reproductive care program. *Am J Obstet Gynecol* 1983;145:170–6.
3 Committee on Reproductive Care. *Reproductive care: towards the 1990s: second report of the Advisory Committee on reproductive care*. Toronto, Ontario, 1988.
4 Papiernik E, Keith LG. The regionalization of perinatal care in France--description of a missing policy. *Eur J Obstet Gynecol Reprod Biol* 1995;61:99–103.
5 Viisainen K, Gissler M, Hemminki E. Birth outcomes by level of obstetric care in Finland: a catchment area based analysis. *J Epidemiol Community Health* 1994;48:400–5.
6 National Health and Medical Research Council. Statements adopted at 85th session, Adelaide. *Med J Aust* 1978;2: :1–4.
7 Lumley J. Better perinatal health. Australia. *Lancet* 1980;1:79–81.
8 Rosenblatt RA, Reinken J, Shoemack P. Is obstetrics safe in small hospitals? Evidence from New Zealand's regionalised perinatal system. *Lancet* 1985;2:429–32.
9 British Association of Perinatal Medicine (BAPM). *Standards for Hospitals Providing Neonatal Intensive and High Dependency Care*. 2nd edn. London, 2001.
10 Marlow N, Bennett C, Draper ES, *et al*. Perinatal outcomes for extremely preterm babies in relation to place of birth in England: the EPICure 2 study. *Arch Dis Child Fetal Neonatal Ed* 2014;99:F181–8.
11 , Fellman V, Hellström-Westas L, *et al*, EXPRESS Group. One-Year survival of extremely preterm infants after active perinatal care in Sweden. *JAMA* 2009;301:2225–33.
12 Anderson JG, Baer RJ, Partridge JC, *et al*. Survival and major morbidity of extremely preterm infants: a population-based study. *Pediatrics* 2016;138. doi:10.1542/peds.2015-4434. [Epub ahead of print: 14 Jun 2016].
13 Boland RA, Dawson JA, Davis PG, *et al*. Why birthplace still matters for infants born before 32 weeks: Infant mortality associated with birth at 22-31 weeks' gestation in non-tertiary hospitals in Victoria over two decades. *Aust N Z J Obstet Gynaecol* 2015;55:163–9.
14 Lasswell SM, Barfield WD, Rochat RW, *et al*. Perinatal regionalization for very low-birth-weight and very preterm infants: a meta-analysis. *JAMA* 2010;304:992–1000.
15 Rautava L, Lehtonen L, Peltola M, *et al*. The effect of birth in secondary- or tertiary-level hospitals in Finland on mortality in very preterm infants: a birth-register study. *Pediatrics* 2007;119:e257–63.
16 Bolisetty S, Legge N, Bajuk B, *et al*. Preterm infant outcomes in New South Wales and the Australian Capital Territory. *J Paediatr Child Health* 2015;51:713–21.
17 Phibbs CS, Baker LC, Caughey AB, *et al*. Level and volume of neonatal intensive care and mortality in very-low-birth-weight infants. *N Engl J Med* 2007;356:2165–75.
18 Warner B, Musial MJ, Chenier T, *et al*. The effect of birth hospital type on the outcome of very low birth weight infants. *Pediatrics* 2004;113:35–41.
19 Neonatal data analysis unit, NDAU 2014 report 2014.
20 Operational delivery networks, 2019. Available: https://www.england.nhs.uk/ourwork/part-rel/odn/
21 Improvement of outcome for infants of birth weight under 1000 G. the Victorian infant collaborative Study Group. *Arch Dis Child* 1991;66:765–9.
22 Lumley J. The safety of small maternity hospitals in Victoria 1982-84. *Community Health Stud* 1988;12:386–93.
23 Chung JH, Phibbs CS, Boscardin WJ, *et al*. Examining the effect of hospital-level factors on mortality of very low birth weight infants using multilevel modeling. *J Perinatol* 2011;31:770–5.
24 Goodman DC, Fisher ES, Little GA, *et al*. The relation between the availability of neonatal intensive care and neonatal mortality. *N Engl J Med* 2002;346:1538–44.
25 Ozminkowski RJ, Wortman PM, Roloff DW. Inborn/outborn status and neonatal survival: a meta-analysis of non-randomized studies. *Stat Med* 1988;7:1207–21.
26 Rashidian A, Omidvari AH, Vali Y, *et al*. The effectiveness of regionalization of perinatal care services--a systematic review. *Public Health* 2014;128:872–85.
27 Hayden JA, van der Windt DA, Cartwright JL, *et al*. Assessing bias in studies of prognostic factors. *Ann Intern Med* 2013;158:280–6.
28 Lamont RF, Dunlop PDM, Crowley P, *et al*. Comparative mortality and morbidity of infants transferred in utero or postnatally. *J Perinat Med* 1983;11:200–3.
29 Johansson S, Montgomery SM, Ekbom A, *et al*. Preterm delivery, level of care, and infant death in Sweden: a population-based study. *Pediatrics* 2004;113:1230–5.
30 Field D, Hodges S, Mason E, *et al*. Survival and place of treatment after premature delivery. *Arch Dis Child* 1991;66:408–11.
31 Truffert P, Goujard J, Dehan M, *et al*. Outborn status with a medical neonatal transport service and survival without disability at two years. A population-based cohort survey of newborns of less than 33 weeks of gestation. *Eur J Obstet Gynecol Reprod Biol* 1998;79:13–18.
32 Hauspy J, Jacquemyn Y, Van Reempts P, *et al*. Intrauterine versus postnatal transport of the preterm infant: a short-distance experience. *Early Hum Dev* 2001;63:1–7.
33 Lee SK, McMillan DD, Ohlsson A, *et al*. The benefit of preterm birth at tertiary care centers is related to gestational age. *Am J Obstet Gynecol* 2003;188:617–22.
34 HolmgrenPA, Högberg U. The very preterm infant - a population-based study. *Acta Obstet Gynecol Scand* 2001;80:525–31.
35 Jonas HA, Lumley J. Trends in stillbirths and neonatal deaths for very pre-term infants. *Aust N Z J Obstet Gynaecol* 1997;37:59–66.
36 Gortmaker S, Sobol A, Clark C, *et al*. The survival of very low-birth weight infants by level of hospital of birth: a population study of perinatal systems in four states. *Am J Obstet Gynecol* 1985;152:517–24.
37 Gould JB, Marks AR, Chavez G. Expansion of community-based perinatal care in California. *J Perinatol* 2002;22:630–40.

38 Miller TC, Densberger M, Krogman J. Maternal transport and the perinatal denominator. *Am J Obstet Gynecol* 1983;147:19–24.
39 Mohamed MA, Aly H. Transport of premature infants is associated with increased risk for intraventricular haemorrhage. *Arch Dis Child Fetal Neonatal Ed* 2010;95:F403–7.
40 Obladen M, Luttkus A, Rey M, *et al*. Differences in morbidity and mortality according to type of referral of very low birthweight infants. *J Perinat Med* 1994;22:53–64.
41 Powell SL, Holt VL, Hickok DE, *et al*. Recent changes in delivery site of low-birth-weight infants in Washington: impact on birth weight-specific mortality. *Am J Obstet Gynecol* 1995;173:1585–92.
42 Powell TG, Pharoah PO. Regional neonatal intensive care: bias and benefit. *Br Med J* 1987;295:690–2.
43 Sanderson M, Sappenfield WM, Jespersen KM, *et al*. Association between level of delivery hospital and neonatal outcomes among South Carolina Medicaid recipients. *Am J Obstet Gynecol* 2000;183:1504–11.
44 Watkinson M, McIntosh N. Outcome of neonatal intensive care: obstetric implications for a regional service. *Br J Obstet Gynaecol* 1986;93:711–6.
45 Watson SI, Arulampalam W, Petrou S, *et al*. The effects of designation and volume of neonatal care on mortality and morbidity outcomes of very preterm infants in England: retrospective population-based cohort study. *BMJ Open* 2014;4:e004856.
46 Petrou S. Economic consequences of preterm birth and low birthweight. *BJOG* 2003;110:17–23.
47 Mangham LJ, Petrou S, Doyle LW, *et al*. The cost of preterm birth throughout childhood in England and Wales. *Pediatrics* 2009;123:e312–27.
48 Johnston KM, Gooch K, Korol E, *et al*. The economic burden of prematurity in Canada. *BMC Pediatr* 2014;14:93.
49 Boyle EM, Poulsen G, Field DJ, *et al*. Effects of gestational age at birth on health outcomes at 3 and 5 years of age: population based cohort study. *BMJ* 2012;344:e896.
50 UK Clinical Trials Gateway. OPTI-Prem: Optimising Neonatal Service Provision for Preterm Babies Born Between 27 and 31 Weeks of Gestation in England, 2017. Available: https://ukctg.nihr.ac.uk/trials/trial-details/trial-details?trialNumber=NCT02994849
51 Shaffer ER. *State Policies and Regional Neonatal Care: Progress and Challenges 25 Years After TIOP*. White Plains, NY: March of Dimes.
52 Perinatal Services BC. *Perinatal Tiers of service module*, 2016.
53 State of Victoria. *Defining levels of care for Victorian newborn services*. Department of Health and Human Services, 2015.
54 Office of Kids and Families. *Nsw maternity and neonatal service capability framework*. Nsw Ministry of Health, 2016.
55 Department of Health Western Australia,. *Framework for the care of neonates in Western Australia*, 2009.
56 South Australia. *Dept. for Health and Aging, Standards for Maternal and Neonatal Services in South Australia*, 2015.
57 Ministry of Health New Zealand. *A review of neonatal intensive care provision in New Zealand*, 2004.
58 Finnish Medical Society Duodecim and the Finnish Gynecologist Association,. *Premature birth*, 2018.
59 Swedish Neonatal Quality Register. *Årsrapport SNQ 2016*, 2016.
60 Parant O, Maillard F, Tsatsaris V, *et al*. Management of threatened preterm delivery in France: a national practice survey (the EVAPRIMA study). *BJOG* 2008;115:1538–46.
61 British Association of Perinatal Medicine (BAPM). *Service Standards For Hospitals Providing Neonatal Care*. 3rd edn, 2010.
62 NHS and Department of Health (DH). *Toolkit for high-quality neonatal services*. London, 2009.
63 Brunet O, Lézine I. Le développement psychologique de la première enfance 1951.