Place of Birth of Extremely Premature Babies in the Thames Valley Network Area – an update

Oxford AHSN Maternity Network
July 2016

Oxford Academic Health Science Network
MATERNITY

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- Share clinical evidence and benchmarking
- Scale innovation adoption
- Learn from each other – clinical standards, models of care, commercial models
- Enable data sharing, operational, patients and research to improve outcomes
- Share evaluation knowledge
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Executive Summary

Since the first report published in April 2015, and the implementation of the Oxford AHSN Maternity Network Place of Birth project, the percentage of extremely premature babies being born in a Level 3 unit has increased significantly; from 50% to 77%.

Health Economics analysis indicates that this improvement is likely to be saving the lives of around 4 of these vulnerable babies in the Oxford AHSN region per year (appendix 1).

The project included establishing an improved referral pathway for arranging in utero transfers of women at risk of preterm birth, the development, agreement and implementation of a set of network wide guidelines and an ongoing audit of cases where babies were born outside of a unit with a Level 3 NICU.

This report summarises the findings of the ongoing audit, April 2015 to March 2016.

During this audit period, only 3 cases occurred in which the place of birth could have been different.

The administration of antenatal steroids remained high, and the use of magnesium sulphate for neuroprotection was significantly improved.

Challenges remain with referrals from primary care to maternity services.

Continued recommendations and actions arising from this audit include: continued monitoring of cases, a programme of teaching and disseminating the changes to include new staff and continued collaboration with the Thames Valley and Wessex Neonatal Network (appendix 2).

Introduction

Preterm birth remains a major contributor to neonatal mortality and long term disability. Extremely preterm babies born in a Level 3 neonatal unit are less likely to die than those born into a Level 2 (or less) setting. Because of this, neonatal networks recommend delivery of extremely preterm babies in a L3 unit. This is not always possible because of the unpredictable nature of preterm delivery, but high antenatal transfer rates can be achieved where there is consistency and cooperation among maternity units.

Preterm birth precedes the development of cerebral palsy in almost 50% of cases, and is a major cause of neonatal death. The risk is strongly related to the gestation at delivery, with babies born before 27 weeks at highest risk. The incidence in the UK remains unchanged, with preterm birth being possibly the greatest challenge for maternity services.
Marlow et al (2014), using the EPICure 2 data, considered the effect of place of birth and perinatal transfer on survival and neonatal morbidity within a prospective cohort of births of extremely preterm babies in England. Within this cohort of babies (born with a gestation between 22 and 26 weeks), the study found a significantly reduced mortality for those born within a Level 3 neonatal unit when compared with birth in a 'Level 2 or less' setting (AOR 0.73, 95% CI 0.59-0.90). This was attributed to both a reduction in fetal deaths and a reduction in deaths in the first week of life and may therefore be related to both obstetric and neonatal care.

Since the Oxford AHSN Maternity Network Place of Birth audit and report published in April 2015, and the concurrent improvement project, the Oxford AHSN area has shown a significant improvement in the proportion of extremely premature babies being born in a Level 3 unit, from 50% up to 77%.

This report serves to provide an update on the project and improvements made, including a health economics review, alongside further detail of the ongoing audit of cases where babies were born outside of the Level 3 unit.

Summary of Key Findings of the previous Place of Birth Report (April 2015)

During the audit period (April 2012 to March 2014), of 146 neonates meeting the antenatal transfer criteria in the Thames Valley region, 67 (46%) were delivered outside a L3 unit. In > 90% of cases, the baby/babies were transferred from the place of birth to a Level 3 unit after birth.

In utero transfer (IUT – transfer by ambulance of the pregnant woman) was attempted in 6 (13%) of these cases; in each case the referral pathway to the L3 unit impeded this. In total, in 41% of cases (18 cases, 21 babies) an IUT could reasonably have been attempted.

No issues were identified with the ambulance services that impeded IUT.

Management of threatened preterm labour was inconsistent and evidence-based diagnostic aids were seldom used. Although the use of steroids for lung maturation (83%) was good, magnesium sulphate for neuroprotection was infrequently used.

Key actions of the Oxford AHSN Maternity Network Place of Birth project since 2015

- A revised referral pathway to improve urgent in utero transfer rate to the John Radcliffe Hospital was developed and implemented.

- Common network guidelines and pathways were developed and implemented throughout the network for management of threatened preterm labour and in utero transfer, including the appropriate uses of fibronectin testing and the use of magnesium sulphate for neuroprotection (appendix 2).
- Common network guidelines and pathways were developed and implemented throughout the network regarding management of premature small for gestational age pregnancies (appendix 2).
- Audit report sent to key stakeholders and findings presented at maternity and neonatal network events and meetings

The Area

The Thames Valley area has an average birth rate of over 27,000 per year, and includes The John Radcliffe and Horton Hospitals (Oxford University Hospitals NHS Trust), Milton Keynes Hospital (Milton Keynes University Hospital NHS Foundation Trust), Wexham Park Hospital in Slough (now part of Frimley Health NHS Foundation Trust) and Stoke Mandeville Hospital (Buckinghamshire Healthcare NHS Trust). There is one Level 3 Neonatal Intensive Care Unit (NICU) situated in Oxford, and 4 LNUs and 1 SCU.

NICUs are sited alongside (usually, and in this region) tertiary referral fetal and maternal medicine services. They provide the whole range of medical neonatal care for their local population. Medical staff in a NICU have no clinical responsibilities outside the neonatal and maternity services. Local Neonatal Units (LNUs) provide neonatal care for their own catchment population, except for the sickest babies. They provide all categories of neonatal care, but they are required to transfer babies who require complex or longer-term intensive care to a NICU. Special Care Units (SCUs) provide special care for their own local population. In addition, SCUs provide a stabilisation facility for babies who need to be transferred to a NICU for intensive or high dependency care.

In this region, due to various issues including capacity constraints, some hospitals were historically commissioned to provide care to babies that would normally be cared for at a NICU (Level 3 Unit). This was changed on the 1st April 2012, where upon the John Radcliffe Hospital became the sole provider of these services in the region. The units in the region committed to the Thames Valley Neonatal Network policy on transfer of infants to a Neonatal Intensive Care Unit (updated in 2014), which includes the requirement to transfer babies under 27/40 or under 28/40 multiples, or an estimated birthweight of under 800g.

Hospital	Type
John Radcliffe Hospital, Oxford	NICU (Level 3)
Royal Berkshire Hospital, Reading	LNU
Wexham Park Hospital, Slough	LNU
Stoke Mandeville Hospital, Aylesbury	LNU
Milton Keynes General Hospital, Milton Keynes	LNU
Horton General Hospital, Banbury	SCU

Methods

Each unit was provided audit forms (appendix 3). A nominated clinical representative, usually a consultant obstetrician, was requested to fill the information required within 3 months of the delivery being identified by the Thames Valley Neonatal Network.

Criteria for delivery in a L3 NICU Unit as defined by Thames Valley and Neonatal Network includes:

Gestation under 27 weeks (singleton)
Gestation under 28 weeks (multiples)
Birthweight under 800g

It should be noted that the manner in which the data is collected means that only babies that had an admission to a special care unit were able to be identified. The audit therefore excludes those that died very shortly after birth, including those in which the parents requested no active resuscitation.

Each case was graded by a Consultant Obstetrician and a senior Midwife. Cases were graded as to whether the place of birth could have been different and whether aspects of clinical care may have prevented an IUT. Grading also took into account any organisational factors that may also have prevented an IUT.

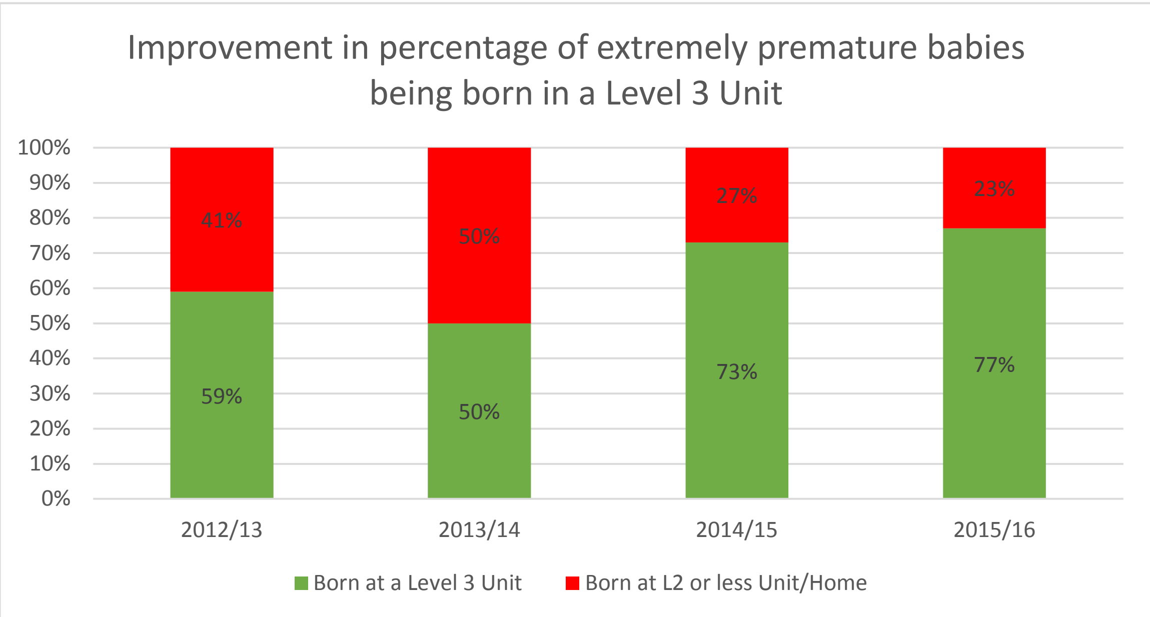
Criteria for preventable lack of in utero transfer were:

- Elective delivery for fetal or maternal wellbeing when the patient was stable enough for a transfer to occur
- Labour that could have reasonably been predicted, such as patients presenting with signs of pre-term labour that were missed, or where diagnostic tests were not used when clinically indicated
- Transfer prevented by problems with units accepting referral, delay in ambulance services or other organisational factors

Summary of previous audit period compared to current audit period

In the last year of the previous audit (April 2013 to March 2014), 76 pregnancies met criteria for delivery in the region's Level 3 unit. Of these pregnancies, 38 were delivered at the John Radcliffe Hospital while the remaining 38 pregnancies were delivered in other settings across the region.

During the current audit period of April 2015 to March 2016 there were 50 cases meeting the criteria born at the John Radcliffe Hospital, and a further 15 cases born in other settings in the region. In percentages, 77% of babies meeting criteria were born in a local Level 3 unit, a significant increase from 50% in 2013/14.



In the previous audit it was estimated that around 40% of the cases of babies being born outside of a Level 3 unit there were factors in their care that, if different, could have changed where they delivered. In the current audit period (April 2015 to March 2016) only 3 cases had factors in there care which had potential to change where the delivery took place - 20% of the total.

Attempted in utero transfers

In the previous report, a failed attempted to arrange an in utero transfer occurred in 14% of cases. In each of these cases, the John Radcliffe Hospital, as the first choice for referrals, either refused the transfer, delayed the transfer, or took such a long time to accept the transfer that the woman was no longer suitable or had already delivered. In addition, this represented a considerable amount of clinical time spent on this rather than on caring for patients, and may contribute to parental distress at an already difficult time.

During this audit period there were no cases of a unit attempting to arrange an in utero transfer that was not successful. This was following the implementation of a revised referral pathway to the John Radcliffe Hospital by the Oxford AHSN Maternity Network.

Transfer not attempted – why?

In the cases where an IUT was not considered we looked at the reasons why this was the case.

In 12 of the cases it was because the women were in established labour, delivered precipitously at home, or too unwell, and as such, unsuitable to transfer.

In 2 cases there were factors in their clinical care which may have impacted potential transfer.

In 1 case there were organisation factors that may have impacted potential transfer – this was a delay in initial assessment after admission due to the department being very busy.

It is noted that there were 4 cases where the gestation was very close to the cut off for transfer of 27 weeks – this was a trend also seen in the previous report. It could be reasoned that clinicians may be less likely to prioritize transfer when the pregnancy is 1-2 days from the gestation where transfer would not be required.

Use of Steroids and Magnesium Sulphate

The incidence of administration of antenatal steroids for lung maturation and magnesium sulphate for neuroprotection was analysed. The use of antenatal

Case Study: a missed opportunity

A woman who was 26 weeks pregnant with an uncomplicated pregnancy visited her GP complaining of tightenings.

The GP documented that the cause was a probable UTI and she was not referred to any maternity services. At this point it would have been likely that using a fibronectin (or equivalent) test which is available at the local maternity unit, would have indicated that she was in the early stages of premature labour.

24 hours later she presented to hospital in established labour, too late for a transfer to a Level 3 unit, and quickly delivered her baby.

steroids was excellent, administered in all cases where it was appropriate and possible.

In the previous report, the administration of magnesium sulphate for neuroprotection was limited, with only 20% of cases who were admitted to a unit more than 2 hours before delivery receiving the treatment. These were mainly isolated to the use of it by one unit.

This audit showed a significant increase in the administration of magnesium sulphate. In cases where there was opportunity and it was appropriate to administer, 8 cases (72%) received magnesium sulphate and only 3 cases did not.

The appropriate use of magnesium sulphate and steroids was included in the network wide guidelines which were agreed and implemented in the middle of 2015 (appendix 2).

Conclusion, Actions and Recommendations

This report shows the significant improvement in the region's ability to ensure most babies who are born extremely prematurely are delivered in a unit in which they are more likely to survive, has been sustained. Only 3 cases in the 12 month period had potential factors in their care that if different, an in utero transfer may have been possible.

There remain a number of challenges to maintain this improvement and address the factors in those cases in which the optimum care could have potentially changed the place of birth.

The Network therefore advises the following -

Action 1: Continued audit

The benefits of auditing cases of babies born outside of a Level 3 are two-fold. It allows the network to be able to see any causal factors that need be addressed, and the attention of each individual Trust on each case that occurs. For these reasons, it is proposed that the audit will continue in its current format.

The Thames Valley and Wessex Neonatal Network are now adding the birth of extremely premature babies outside of a Level 3 unit to their Neonatal Dashboard which is sent to Trusts within the region. This will further assist with monitoring.

Action 2: Regular information disseminated to staff

The network proposes a consistent regime of reminders and regular updates regarding the referral pathway and network wide guidelines. This is to maintain awareness of the issue, and to make sure as new staff come into post in each unit, they are aware. This will also be assisted by HETV continuing to use the guidelines as part of the teaching of rotating junior doctors.

Communication between sites and medical/midwifery/neonatal staff is key to the continued success of the project, and we will continue to facilitate this.

Action 3: Review of issues

Timely and appropriate referral of women to maternity services from primary care remained a challenge, having been a factor in both audits. The Network will review how to address this issues.

Action 4: Continued communication and collaboration with the Thames Valley and Neonatal Network

It is important that the established collaboration with the Thames Valley Neonatal Network continues in order to maintain effective relationships with neonatal staff and as another mechanism for monitoring and awareness of any upcoming issues which may affect the system – such as the impact of staffing in units.

Future Challenges

Continuation of the success of this project relies heavily on various aspects of hospital organisation factors; predominantly around capacity of the units involved.

Capacity at the Neonatal Unit at the John Radcliffe Hospital, Oxford, may be adversely affected by caps on agency payment. This will reduce their capability to staff the neonatal unit and potentially prevent transfer of pregnancies which meet criteria.

In addition, there is the impact of a possible forthcoming reduction in capacity at the Horton General Hospital. If this reduction in capacity goes ahead, there may be an overall reduction in SCBU beds available across the Trust.

The Network will monitor these issues and potential effects on transfer rates.

Health Economics Report

The Oxford AHSN commissioned the Office of Health Economics and RAND Europe to conduct a Health Economics Report to determine the tangible value that the Oxford AHSN was adding locally. The report focused on four cases which played a crucial role in improving patient care and exemplified the Oxford AHSN's work in the region.

The report included an analysis of the work conducted in the Place of Birth Project. It was found that the work done to improve the referral pathway for premature babies had led to an improvement in the likelihood of survival of 5.2% percentage points in comparison to the survival rates before the project began). This translates to an increase of approximately 4 additional babies surviving per annum. It outlined how the new pathway represents good value for money when compared to conventional thresholds at which healthcare interventions are typically considered cost-effective.

As this represents improved patient outcomes, it is likely that there are additional, wider benefits that have not been captured.

The Maternity Clinical Network section of this report can be found in the following pages.

Appendicies

Appendix 1: The following pages are an extract of a report commissioned by the Oxford AHSN to look in detail at the health economics effect of the project.

Maternity Clinical Network: Improving referral pathways for premature babies – a health economics assessment

Extracted from 'Exploring the Added Value of Oxford AHSN', Office of Health Economics & RAND Europe, April 2016, written by Grace Marsdena, Adam Martinb, Bernarda Zamoraa, Jo Exleyb, Jon Sussexb and Adrian Towsea,

3.2 Maternity Clinical Network: Improving referral pathways for premature babies

3.2.1 Introduction

The aim of this case study was to assess the value of the Oxford AHSN in terms of their contribution to an improvement in the number of extremely premature babies being transferred in-utero to Level 3 (L3) maternity units that occurred in the Oxford AHSN maternity clinical network during 2015. This followed evidence that maternity units in the network area had much lower rates of in-utero transfer than comparable areas in England, and that this was likely having adverse consequences for survival and wellbeing.

This section includes a brief overview of the main issues, including definitions of key terms, and a description of the maternity clinical network. The case study then proceeds with Methods, Results and Discussion.

3.2.1.1 Neonatal networks in England

Since 2003, neonatal services across England have been organised into managed clinical networks (renamed 'Operational Delivery Neonatal Network' in 2013) (Marlow and Gill, 2007; NHS England, 2016). The Networks were introduced, in part, in response to the British Association of Perinatal Medicine's recommendation that hospitals should work together to ensure that the care of the smallest and sickest babies is concentrated in specialised hospitals, and because of safety concerns related to the unplanned transfer of pregnant women and neonates (Marlow and Gill, 2007). Within each network, care pathways have been developed to ensure that mothers and babies are treated and cared for in the most appropriate hospital unit (see Box 2).

Box 2: Designation of hospital unit with neonatal networks (Laing, 2012)

Hospitals units are designated according to the intensity of care provided:

Level 1 (L1) units provide special care but do not aim to provide continuing high dependency or intensive care;

Level 2 (L2) units provide high dependency care and some short-term intensive care; and

Level 3 (L3) units provide the whole range of medical and neonatal care, also referred to as a neonatal intensive care unit (NICU).

In order to minimise risk and reduce the number of babies that needed to be transferred within the first 24 hours post-birth, it is recommended that all high risk deliveries – including both premature and very low birthweight infants (see Box 3) – be conducted in a L3 unit (Phibbs, 2012; Gale et al., 2012).

Box 3: Definition of premature babies and low birthweight babies

PREMATURE BABIES: In England, all babies born before 37 weeks of pregnancy are classified as premature (NHS Choices, 2015), and those born before 27 weeks of pregnancy are classified as extremely premature (EPICure, 2011).[19]

LOW BIRTHWEIGHT BABIES: Low birth weight-babies are defined as those weighing less than 2,500 grams at birth. This can be further subdivided into very low birth weight babies (<1,500g) and extremely low birth weight babies (<1000g).

3.2.1.2 The Oxford AHSN maternity clinical network

The Oxford AHSN area is served by six maternity units which form a maternity clinical network (British Association of Perinatal Medicine, 2016). On average, there are 27,000 births in the area per annum.

The policy of the maternity clinical network is that extremely premature babies (<27 weeks gestation)[20] and extremely low birth weight babies weighing less than 800g should be delivered in a L3 unit (see Box 4). In 2013/14 (the most recent available annual data), 76 babies met these criteria (Oxford AHSN, 2015).

The Oxford AHSN area is currently served by one L3 maternity unit at the John Radcliffe Hospital, Oxford (Oxford University Hospitals NHS Foundation Trust), and five further maternity units which do not provide L3 services:

- Stoke Mandeville Hospital, Aylesbury (Buckinghamshire Healthcare NHS Trust)
- Wexham Park Hospital, Slough (Frimley Health NHS Foundation Trust)
- Milton Keynes General Hospital, Milton Keynes (Milton Keynes University Hospital NHS Foundation Trust)
- Royal Berkshire Hospital, Reading (Royal Berkshire NHS Foundation Trust)
- Horton General Hospital, Banbury (Oxford University Hospitals NHS Foundation Trust).

An audit of the area for the 24-month period April 2012 to March 2014 was completed by the Oxford AHSN in April 2015 (Oxford AHSN, 2015). The audit revealed that babies were not accessing L3 maternity services as appropriate. Of 146 babies that met the criteria for birth in a L3 unit, 67 (46%) were born in one of the five maternity units without L3 facilities. In these cases, in-utero transfer was attempted in only 14% of pregnancies, none of which resulted in an actual transfer. This was due to inefficiencies in the referral pathway. Nevertheless, in line with the current policy of units in the maternity clinical network, these babies[21] were all subsequently transferred to the L3 maternity unit at the John Radcliffe Hospital after birth (Oxford AHSN, 2015).

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[19] Throughout this document, we use the English definitions to classify premature babies. However, international definitions for premature birth vary. For example, the World Health Organisation (WHO) defines "preterm" as babies born alive before 37 weeks of pregnancy and further distinguishes between extremely preterm infants born alive at less than28 weeks of gestation, very preterm infants born alive between 28 and 32 weeks of gestation, and moderate to late preterm infants born alive between 32 and 37 weeks of gestation.
[20] Or babies with less than 28 weeks gestation in the case of multiple pregnancies
[21] Excluding those which did not survive at least 12 hours after birth (4%) and a small number of special cases (7%) for whom delivery in a L2 unit was deemed suitable despite meeting the published criteria for delivery in a L3 unit.

Box 4: Criteria for delivery in a Level 3 Unit in the Oxford AHSN area

-Extremely premature baby (i.e. under 27 weeks gestation) Or -Under 28 weeks gestation in the case of a multiple pregnancy And/or -An extremely low birth weight of less than 800g (regardless of gestation)

In light of the Oxford AHSN audit, and the national landscape presented in 3.2.1.1, it was clear that improvements could be made to the referral pathway ('policy change') for the delivery of premature or extremely low weight babies in the maternity clinical network. These changes could be expected to lead to an improvement in survival rates, as well as other aspects of the health and wellbeing of mothers and their babies, whilst also potentially reducing the cost of post-birth transfers to L3 units.

3.2.1.3 The added value of the Oxford AHSN

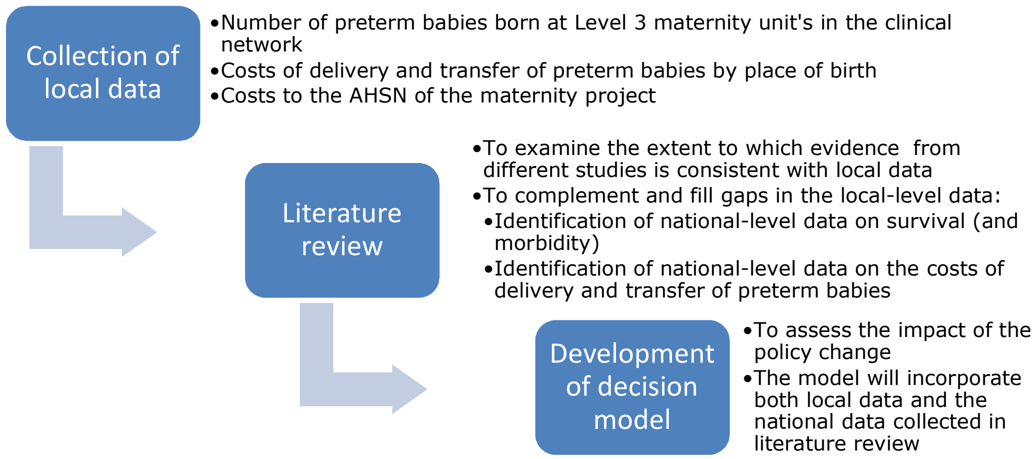
Following changes in early 2015 to the referral pathway and development of new guidelines for the Oxford AHSN maternity clinical network, it was agreed at the Oxford AHSN/OHE workshop in November 2015 that an assessment would be made of the added value of the Oxford AHSN given the effectiveness of those improvements in terms of additional live births, and the total cost (from the perspective of the NHS) of achieving them.

A before-and-after study design would be used to assess the numbers and proportion of preterm babies born at L3 maternity units within the maternity clinical network since April 2015 when compared to the data gathered for the Oxford AHSN audit during a 24-month period prior to the policy changes. This would be supplemented by a literature review which would identify national-level data to provide estimates of the likely impact on levels of mortality and, if possible, morbidity. An assessment would also be made of the changes in costs that occurred within the units of the maternity clinical network, and the project-related costs incurred by the Oxford AHSN.

3.2.2 Methods

The assessment of the policy change (i.e. changes to the referral pathway and development of new guidelines) in terms of changes in survival ('effectiveness') and costs comprised three stages (see Figure 7) which are described in turn in the rest of this section: collection of local data, literature review, and development of an Excel-based decision tree model (including model inputs, assumptions and proposed sensitivity analysis).

Figure 7: Overview of methods used in study on improving referral pathways for preterm babies



3.2.2.1 Collection of local data

Local data was collected in relation to both the effectiveness and costs of the policy change.

Effectiveness data:
Local data were collected from the existing Oxford AHSN audit for a 24-month period prior to the changes ('before') on:

- The number of live births at all six maternity hospitals within the maternity clinical network and related information (e.g. weeks of gestation at birth)
- The number of antenatal and neonatal transfers to the L3 unit at the John Radcliffe Hospital, subsequent early neonatal death rates, and other related information (e.g. the number of proposed transfers which were refused)

More recent data collected during 2015 ('after') was also sought through telephone and email contact with Katherine Edwards (Oxford AHSN Maternity Clinical Network Manager).

Cost data:
Recent data on the local cost of delivering preterm babies in L3 units when compared to L2 units, and the costs of transferring preterm babies between units (e.g. ambulance costs) in the maternity clinical network was sought through telephone and email contact with Katherine Edwards and Dr Eleri Adams (Clinical Lead for the network).

We also sought information from the Oxford AHSN on the costs, including staff time and overhead costs, of their contribution to the project.

3.2.2.2 Literature review

We undertook a 'best evidence review' of literature relevant to England. We sought to identify studies which had examined differences in rates of survival (and morbidity) and costs at L3 versus L2 units.

Specifically, the aim of the review was to identify:

- Data on survival (and morbidity) rates amongst premature babies born in L3 units when compared to L2 units.

- Studies which compared the cost (or resource use) related to delivery of premature babies in a L3 units compared to L2 units.

Effectiveness data:
A snowballing technique (Wohlin, 2014) was used, beginning with a paper published as part of the EPICure 2 study (EPICure, 2012). This paper reported on perinatal outcomes for extremely premature babies born between 22 and 26 weeks gestation and was based on data from all 182 maternity units in England (Marlow et al., 2014). This study was identified by maternity specialists at Oxford AHSN and the maternity clinical network and was cited in the Oxford AHSN audit as being highly relevant to the context (Oxford AHSN, 2015). We undertook forward and backwards citation searching: the reference list of included papers were screened for potentially relevant studies and citation searching was conducted in Google Scholar[22] to identify potentially relevant papers that had cited the included study. The search was restricted to post-2008 publications; this cut-off point was chosen based on the identification of a review and meta-analysis of relevant data by Lasswell et al. (2010) which had included literature published between 1976 and 2008 (Lasswell et al., 2010). This literature included studies published in Europe, North America and Australasia which had compared outcomes for premature babies (<32 weeks gestation in this case) and very low birthweight infants (i.e. <1,500 grams).

In addition we manually searched relevant websites: EPICure, the confidentiality enquiry into maternal and child health (CEMAH); and the Royal College of Paediatrics and Child Health using the terms ‘audit’ and ‘preterm’ and ‘NHS’.

Cost data:
A snowballing technique was used beginning with a recent review of both the peer-reviewed literature and additional sources for information on the economic consequences of premature birth by Petrou et al. (2012). Forward and backwards citation searching for studies published post-2012 was performed.

3.2.2.3 Development of an Excel model

An Excel-based model was developed to analyse the impact of Oxford AHSN’s maternity project in terms of (i) effectiveness (survival rates and, where possible, survival without morbidity) and (ii) associated costs.

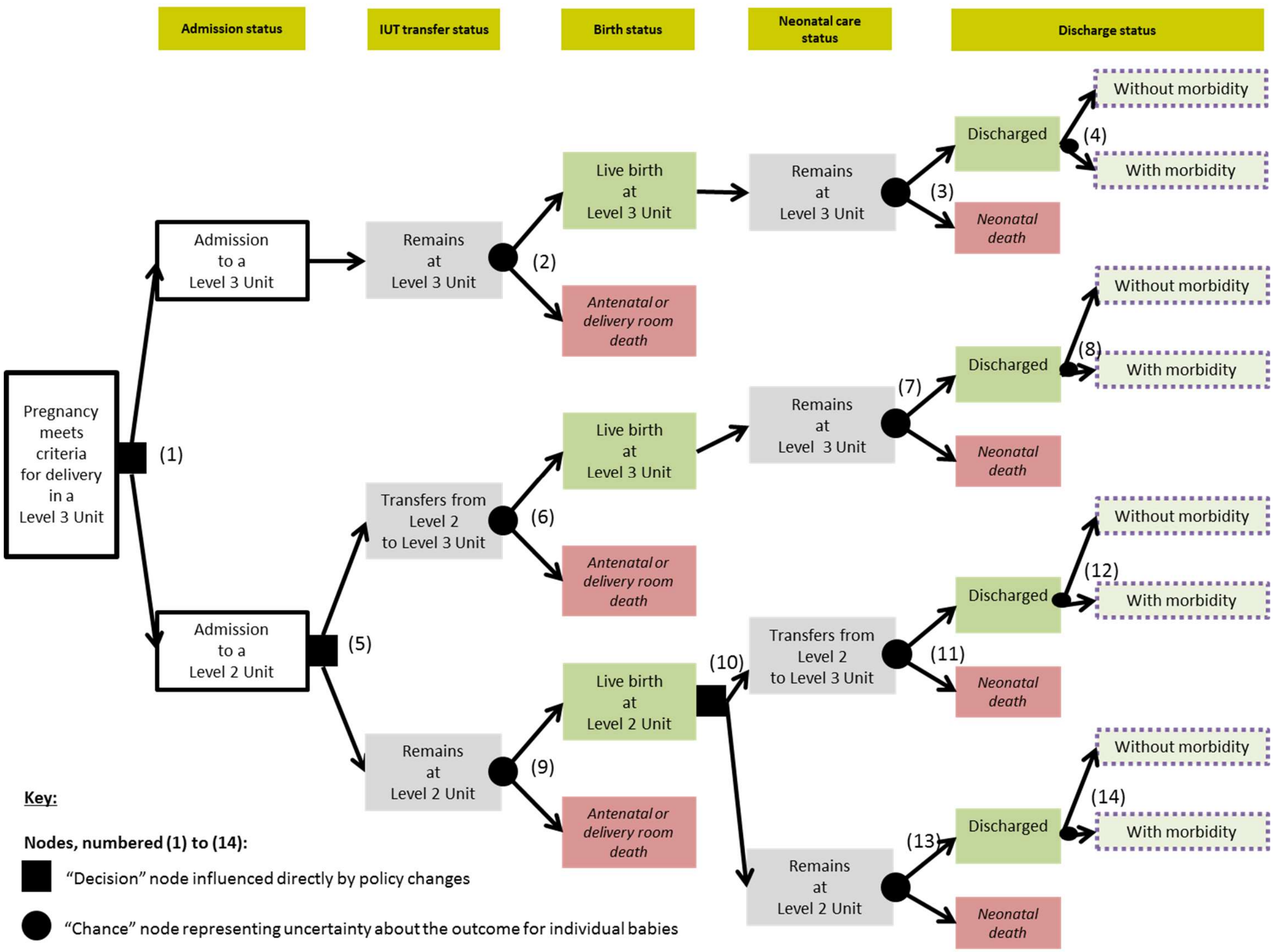
Model structure:
The structure of the model is shown in Figure 8 (a screen shot from the Excel is also provided in Appendix 1). It takes the form of a decision tree which is a widely used, if simplest form of decision modelling used in health economic evaluation (Drummond, 2005). The decision tree is designed to represent the full range of potential pathways for a pregnancy and subsequent birth that meets the criteria for delivery in a L3 unit in the maternity clinical network (see Box 4).

[22] Google Scholar, http://scholar.google.co.uk

The key features of the model are:

- Arrows which indicate pathways through the model (or routes through the tree) from admission to a L2 or L3 unit on the left, through to discharge with(out) morbidity on the right.
- Three 'decision' nodes at various stages, indicating a decision point between two alternative options concerning whether or not a L3 or L2 unit is chosen. For each baby, these decisions are expected to be influenced by the maternity clinical network's 'policy change' (i.e. a change in the referral pathway or relevant clinical guidelines).
- Multiple 'chance' nodes, which represent the uncertainty for each baby about what the outcome (successful discharge or neonatal death, for instance) will be.
- Boxes which indicate the various 'events' that can occur as the baby moves through the model. They represent admission status (to a L3 or L2 unit), in-utero transfer (IUT) status (remaining in the hospital of first admission, or transfer from a L2 unit to a L3 unit), birth status by place of birth (live birth, or antenatal or delivery room death), neonatal care status (remaining in the hospital of birth, or transfer from a L2 unit to a L3 unit), or discharge status (successfully discharged with or without morbidity, or neonatal death).
- Probabilities (ranging from 0% to 100%) are assigned to the arrows emanating from the 'decision' or 'chance' nodes, such that for each node, all probabilities sum to 100%. Moving from left to right in the model, the probability of admission to a L2 and L3 unit is represented by the first decision node. Subsequent probabilities in the model are conditional probabilities in that the likelihood of a given event (or outcomes) occurring are dependent on an earlier event (or outcome) having (or not having) occurred. Thus, in order to calculate the probability (known as 'joint probability') of any complete pathway in the model it is necessary to multiply the probabilities at each node on the pathway.

Figure 8: Overview of the decision model



Model inputs:
Required inputs to the model are:

- Probabilities at each 'decision' or 'chance' node
- The number of live births reported at L3 and L2 units
- Costs associated with delivery of babies at L3 and L2 units
- Cost associated with the transfer of babies between units

Where data were identified in literature published in earlier years, costs (or prices) have been adjusted for inflation using the 'composite price index' published by the Office for National Statistics and reported in £2016.

Model outputs:
There will be three iterations of the model:

(1) Using the national-level data from 182 maternity hospitals in England in 2006 reported in Marlow et al (2014)

(2) Using the local-level data from the 6 maternity hospitals in the clinical network reported in the Oxford AHSN audit ('before')

(3) Using the local-level data from 6 maternity hospitals in the clinical network collected for this study ('after')

Where there are gaps in data for the second and third model iterations, assumptions were made based on the national-level data used in the first model iteration (as shown in Table A, Appendix 1). A sensitivity analysis was used to alter some of the assumptions made in third iteration, where there was a particular shortage of data (typically this sensitivity analysis would involve altering the assumptions so that they matched the second iteration, rather than the first iteration; these are discussed in further detail in the Results section below). Limitations associated with this approach are assessed in the Discussion section below.

For each of the three model iterations, the primary output of interest is the probability of survival 'after' the policy change (i.e. the third model iteration) compared to the probability of survival 'before' the policy change (i.e. the second model iteration). Other secondary model outputs are explored below in the Results section.

3.2.3 Results

In this section, we first report on the data which was identified through local contacts and the literature review. We then provide the outputs of the model.

3.2.3.1 Collection of local data

Effectiveness data:
Table 12 to Table 14 show the data which was collected from the Oxford AHSN and maternity clinical network.

Table 12 shows the number of babies meeting antenatal transfer criteria (as reported in Box 3) who were delivered in L2 and L3 units in the clinical network for the 24-month period 01/04/2012-31/03/2014 ('before') and a ten-month period 01/04/2015-31/12/2015 ('after'). These numbers were annualised (e.g. number of babies born during a six-month period would be doubled, whereas number of babies born in a two-year period would be halved) to support a comparison between periods.

The annualised figures showed that, whilst there were estimated to be fewer total births per annum meeting antenatal transfer criteria overall (n=73 'before' and n=60 'after'), there had been an increase in the proportion of those babies being delivered at the L3 unit (John Radcliffe Hospital) from 54% to 78% (as well as in absolute terms - n=39.5 'before' and n=46.8 'after').

The magnitude of change that occurred 'before' and 'after' the policy change was much greater than the changes that were observed when comparing the first 12 months to the second 12 months of the 24-month 'before' period. For example, the proportion of babies meeting the criteria who were born in a L3 unit fell by seven percentage points between 2012/13 and 2013/14 (from 57% to 50%).

Table 12: Number of infants meeting transfer criteria who were delivered in Level 2 and Level 3 units 'Before' and 'After' the policy change

	'Before'				**'After'**	
	2012/13 (12 months)	2013/14 (12 months)	2012-2014 (24 months)*	Annualised	2015 (10 months)	Annualised
Total births	70	76	146	73	50	60
Level 3 births	41 (59%)	38 (50%)	79 (54%)	39.5 (54%)	39 (78%)	46.8 (78%)
Level 2 births	29 (41%)	38 (50%)	67 (46%)	33.5 (46%)	11 (22%)	13.2 (22%)
Source	Oxford AHSN audit				Personal communication	

*this column sums data from the previous two columns

Table 13 provides a summary of the available data from the Oxford AHSN audit on the transfer status of the babies born in L2 units during the 24-month period 'before' the policy change. Whilst none of the potentially eligible babies were transferred from L2 to L3 units prior to birth, an attempted transfer was made in 13.6% of cases (however in all these cases, the transfer request was refused). A post-hoc review of case notes completed for the Oxford AHSN audit indicated that, in a further 40.9% of cases, a transfer could have been feasible (whereas in the remaining cases a transfer would have been unworkable due to the mother being in established labour, for example) (Oxford AHSN, 2015).

Table 13: Transfer status of infants meeting transfer criteria who were born in Level 2 units 2012-14

	Of 44 pregnancies[1]	Of 57 babies born[1]	Proportion of babies or pregnancies[1]
In-utero transfer			
Attempted but refused	6	n/a	13.6%
Did not occur	38	n/a	86.4%
Could have been attempted	*18*	*n/a*	*40.9%*
Neo natal transfer			
Occurred	n/a	51 [2]	89.5%
Did not occur	n/a	6 [3]	10.5%

Source: Oxford AHSN audit, 2015

[1]The Oxford AHSN audit reviewed the notes of 57 babies (of 67 babies born) associated with 44 (of 54 pregnancies). Thus data was missing for 18.5% of all pregnancies and 7.5% of babies born

[2] Of the 51 babies were neo-natal transfer occurred, 60% survived and 40% died

[3] Of the 6 babies where neo-natal transfer did not occur, 2 died within 12 hours of birth, and 4 were twins which were deemed suitable for birth in a L2 unit despite meeting the criteria for birth in a L3 unit

Cost data:

Our discussion with a representative of the maternity clinical network (on 26th February 2016) confirmed the finding from our own initial inspection of NHS Reference Cost data that had revealed no relevant information on differences in the cost of delivering preterm babies at L3 and L2 units.

In the view of our representative, the most significant change in cost which had arisen as a result of the policy change was a reduction in neonatal ambulance transfers which, per transfer, were reported through the personal communications of our representative to be £1,101.

It was argued that any additional costs of delivering infants at the John Radcliffe L3 unit which would otherwise have been delivered at a L2 unit were insignificant. This was because it was reported that the John Radcliffe Hospital had spare capacity sufficient to manage the observed rise in cases (which amounted to an additional 7.3 babies per annum, a rise of 18.4%, according to the calculations in this study - see Table 1).

Costs to the Oxford AHSN:

Table 14 provides an estimate of the costs to the Oxford AHSN which were approximated based on the amount of staff input time the Oxford AHSN reported as having contributed to the maternity project.

We proxied the costs of staff time using the costs of wages and overheads; these costs are included to represent the opportunity cost of staff time. We were informed by Oxford AHSN that the total time charged to this project was equivalent to 75% of a full-time equivalent at NHS band 8a over a 12 month period. Thus the total cost of this was estimated to be £70,825.

Table 14: Oxford AHSN staff costs for the maternity project

Component	Value
Salary[±]	£45,081
Salary oncosts[1,†]	£11,701
Overheads[2,†]	£36,202
Capital overheads[3,†]	£4,370
Annual total (A)	**£97,354**
Non-London Multiplier (B)	0.97
Working time dedicated to the maternity project (C)	75%
Total staff cost to Oxford AHSN (A x B x C)	**£70,825**

Reference: Curtis and Burns, 2015
[1]Essential associated costs, for example the employer's national insurance contributions
[2]Management and other non-care staff overheads include administration and estates staff
[3]Includes costs for office, travel/transport and telephone, education and training, supplies and services (clinical and general), as well as utilities such as water, gas and electricity
[±]Mean annual basic pay per FTE by Agenda for Change band 8a
[†]Approximated by values for Band 8a scientific and professional staff

3.2.3.2 Literature review

Effectiveness data:
In total we identified 11 studies which reported on differences in mortality and morbidity for premature or very low birthweight babies by place of birth (Gale et al., 2012; Lasswell et al., 2010; Binder et al., 2011; Boland et al., 2015; Chung et al., 2011; Jensen and Lorch, 2015; Lapcharoensap et al., 2015; Lorch et al., 2012; Marlow et al., 2014; Watson et al., 2014; Zeitlin et al., 2010). In addition to comparing outcomes by place of birth, three studies also looked at difference based on level of hospital activity. Half of the studies were conducted in the US (n=5), three were conducted in the UK, one in Australia and one in France. A meta-analysis by Laswell et al. (2010) included 41 studies published between 1976 and 2008; the vast majority were conducted in North America.

In the text below we summarise findings related to extremely premature babies (i.e. <27 weeks gestation) and/or extremely low birthweight (i.e. <1,000 grams), as defined in Box 2. A complete report of the literature review is provided in Table B, Appendix 1.

Two studies found an improvement in mortality outcomes following the reorganisation of neonatal services to increase regionalisation (Gale et al., 2012; Zeitlin et al., 2010). Zeitlin et al. (2010) found that the greatest gains in in-hospital mortality were made for extremely premature babies (24 to 27 weeks gestation). In both studies, there are challenges in distinguishing the reorganisation from underlying temporal trends.

In terms of direct comparisons between L3 and L2, for extremely premature and/or extremely low birthweight there was evidence that the odds of mortality increased for babies born in a L2 compared to L3 unit (Lasswell et al., 2010; Binder et al., 2011; Boland et al., 2015; Marlow et al., 2014; Watson et al., 2014), but with a more mixed-picture for morbidity (Binder et al., 2011; Lapcharoensap et al., 2015; Marlow et al., 2014; Watson et al., 2014).

Three out of four studies that examined in-hospital mortality (from birth to discharge) found a significant improvement in mortality for babies born in a L3 unit (Lasswell et al., 2010; Binder et al., 2011; Marlow et al., 2014). The meta-analysis by Lasswell et al.

(2010) found an 80% increase in the odds of pre-discharge mortality for extremely low birth weight (i.e. <1,000 grams) infants born in a non-L3 hospital compared with those born in L3 (OR 1.80 [95%CI 1.31, 2.46]).[23] The UK study by Marlow et al. (2014) found that births of extremely premature babies in a L3 unit were associated with a 27% reduction in overall mortality (aOR 0.73 [95%CI 0.59, 0.90]);[24] this was the result of significant reductions in mortality around the time of delivery (aOR 0.53 [95%CI 0.37, 0.77]) and during the first week of life (aOR 0.69 [95%CI 0.51, 0.94]). Likewise, the second UK study (Watson et al., 2010) found a significant reduction in odds of mortality for extremely premature babies (<27 weeks gestation) during the neonatal period (first 28 days of life) associated with being born in a L3 unit (OR 0.65 [95%CI 0.46, 0.91]), but found no difference in-hospital (deaths before discharge) between units (OR 0.78 [95%CI 0.57, 1.06]).

Finally one study conducted in Australia (Boland et al., 2015) found increased odds of mortality within the first year of life for extremely premature babies born in a non-tertiary hospital compared to a tertiary hospital (OR 3.16 [95%CI 2.52, 3.96]).

The two studies conducted in the UK (Marlow et al., 2014; Watson et al., 2014) also reported a significant association between mortality and hospital activity, in both cases a reduction in odds was observed in higher activity units. Watson et al. (2014) found a significant reduction for extremely premature babies in both neonatal mortality (OR 0.62 [95%CI 0.44, 0.87]) and in-hospital mortality (OR 0.71 [95%CI 0.52, 0.97]). While Marlow et al. found no evidence for differences in time-specific mortality, overall in-hospital mortality was lower in higher activity L3 units (aOR 0.68 [95%CI 0.52, 0.89]). This finding was supported by two studies from the US (Chung et al., 2011; Jensen and Lorch, 2015) that looked at very low birth weight (500g-1,500g) infants. Chung et al. (2011) found no difference in the odds of mortality during the first year by place of birth but found that increasing volume of activity was associated with progressive reductions in the odds of mortality, with those units caring for less than 10 very low birth weight babies per annum having an 80% higher odds of mortality compared to units caring for more than 100 babies (aOR 1.79 [95%CI 1.38, 2.13]). Jensen and Lorch (2015) assessed the impact of a hospital's activity and NICU level and found that the annual volume of deliveries of very low birthweight infants had a greater effect on mortality within the first 24 hours of life than NICU level; among hospitals that deliver fewer than 50 very low birthweight or very premature infants per year the odds of death was 25% to 64% higher after controlling for NICU level.

Marlow et al. (2014) found that morbidity (defined as having one or more of: retinopathy of prematurity requiring retinal surgery; moderate or severe bronchopulmonary dysplasia; a severe brain injury; or necrotising enterocolitis managed by laparotomy) did not vary by place of birth and that improved survival was not associated with significantly increased morbidity (aOR 1.27 [95%CI 0.93, 1.73]). Conversely one study in the US (Binder et al., 2011) found increased odds of morbidity in L2 compared to L3 units for babies with extremely low birthweight of 500g to 900g for all four outcomes measured (bronchopulmonary dysplasia or death; intracranial haemorrhage or death; retinopathy of prematurity or death; and necrotising enterocolitis or death). A second US study (Lapcharoensap et al., 2015), which looked only at bronchopulmonary dysplasia,

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[23] OR: Odds ratio

[24] aOR: Adjusted odds ratio

reported an increased odds at 36 weeks for premature babies (22 to 29 weeks gestation) born in L2 units compared to L4[25] (OR 1.23 [95%CI 1.02, 1.49]). Finally, one further UK study found that extremely premature babies (<27 weeks gestation) born at a L3 unit were at increased odds of developing bronchopulmonary dysplasia compared to babies born in a L2 unit (OR 1.50 [95%CI 1.11, 2.01]), but found no difference in the odds of developing either necrotising enterocolitis or retinopathy of prematurity by place of birth.

Only one of the studies identified had considered the impact of being transferred between units (Marlow et al., 2014). Marlow et al. (2014) found that extremely premature babies who were born in a L2 unit were at 44% increased odds of mortality compared to those babies which were transferred to a L3 unit prior to birth (aOR 1.44 [95%CI 1.09, 1.90]). Transfer after birth was found not to improve mortality outcomes compared to babies who remained in n L2 unit (aoR 1.08 [95%CI 0.83, 1.41]), and babies transferred from a L2 to a L3 unit after birth were less likely to survive without morbidity than babies born at a L3 unit (aOR 0.72 [95%CI 0.48, 1.08]).

Cost data:
The review on the economic consequences of premature birth by Petrou et al. (2012) revealed three studies that had used UK data. These were categorised as follows: studies of the costs associated with the initial hospitalisation, studies of the costs following the initial hospital discharge, and economic models of the economic costs throughout childhood. However, none of these had included any estimate of the difference in costs associated with delivery in different units.

A further study which was identified by Mistry et al. (2009) drew comparisons on the average cost of care for babies with extremely low birth weight (i.e. <1,000g) being cared for in L2 and L3 units. Whilst the study concluded that costs were greater for care in L3 units when compared to L2 units (e.g. the cost was £26,815 (s.d. £19,558) at L3 and £13,431 (s.d. £16,777) at L2),[26] this was due to the sickest babies being quickly transferred out of L2 units and differences in case mix (i.e. the sickest babies may have been more likely to be admitted to L3 units before birth). The study did not assess the total cost of care for babies born in a L2 unit (including their care after transfer in a L3 unit) when compared to babies born in a L3 unit.

Implications of the literature review for the decision model:
Overall there is evidence to suggest that being born in a L3 unit is associated with increased survival but the impact on morbidity is less clear. While the majority of evidence comes from outside the UK, in their meta-analysis, Lasswell et al. (2010) suggested that although there is the possibility of variation between health systems, they found no significant between-group difference for studies conducted in different settings. The lack of clarity on the impact on morbidity was suggested to be a result of higher mortality in non-L3 units, limiting the ability to determine the impact of hospitals factors on morbidity (Jensen and Lorch, 2015). Where morbidity was higher in a L3 unit this was suggested to be as a result of a survival bias.

There is some evidence to suggest that the level of hospital activity might be a more important determinant of mortality than the hospital level. This finding is supported by

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[25] Level of care was defined according to the Committee on Fetus and Newborn of the American Academy of Pediatrics policy statement. Neonatal levels of care are currently classified as well newborn nursery (L1), special care nursery (L2), NICU (L3), and regional NICU (L4).
[26] S.d.: Standard deviation

Poets et al (2004), which recommended that neonatal units need to be caring for at least 36 to 50 very low birth weight infants to achieve best outcomes.

For the purpose of building the decision model, the data available on costs was very limited since no study provided an estimate of the total cost of delivery of a baby in a L3 unit (necessary for our 'after' scenario) when compared the total cost in a case where the infant is born in a L2 unit but later transferred to a L3 unit (necessary for our 'before' scenario).

Considering the evidence on effectiveness and cost together, this review thus identified only one study which assessed the impact of being transferred between units. The remaining studies reported outcomes only by place of birth and did not consider the impact of any subsequent transfers between hospital units. The study by Marlow et al suggested that a transfer to a L3 unit should occur prior to birth in order to improve mortality outcomes. Given that the model aimed to determine the costs associated with the entire care pathway i.e. based on babies discharge status, we considered that only this study by Marlow et al. provided relevant information which could be used directly in the decision model.

3.2.3.3 Decision model

Model inputs and running the model:
Data on the number and proportion of births at L2 and L3 units were derived from the Marlow et al study (iteration 1), data in the Oxford AHSN audit ('before'; iteration 2; see Table 12), and data released by Oxford AHSN for this study ('after'; iteration 3; see Table 12).

In the case of the study by Marlow et al., this data was sufficient to assign probabilities to each of the 14 'decision' and 'chance' nodes used for the first iteration of the model (these are reported in Table A, Appendix 1).

Where probability data was missing in either the second or third iterations of the model, the probabilities from the study by Marlow et al. (i.e. the first iteration) were used instead.

A sensitivity analysis was also completed for the third iteration of the model (the 'after' scenario). This analysis used probabilities that were available in the 'before' but not the 'after' data. These probabilities were substituted in the sensitivity analysis for the Marlow et al. probabilities that had been used in the main analysis (See Table A, Appendix 1). For example, we have assumed in the main analysis that the proportion of babies meeting the maternity clinical network's criteria who were transferred to L3 after birth in a L2 unit (chance node 11, Figure 8) would fall from 89.5% ('before') to 56.3% ('after', based on the national-level data in the study by Marlow et al.). This may be realistic because babies that were previously transferred after birth are now more likely to be antenatal transfers, thus a smaller proportion of L2 babies would be expected to be transferred after birth. Nevertheless, the sensitivity analysis assumes that the proportion remains unchanged at 89.5%. In this respect, the sensitivity analysis would thus be expected to provide a larger expected impact on survival rates since more preterm babies are receiving care in the L3 unit than in the main analysis.

Model outputs:
The model outputs for the three iterations of the model and the sensitivity analysis are shown in Table 15. The primary model output shows that, for babies who met the

maternity clinical network's transfer criteria, the probability of survival increased from 40.7% prior to the policy change to 45.9% after the policy change. This is similar in magnitude to what would be expected should the Oxford AHSN area be consistent with the national picture reported in Marlow et al (2014) where the overall likelihood of survival was 45.2%.

The sensitivity analysis which had substituted data from the Marlow study in the 'after' scenario for data in the 'before' scenario, suggested that the improvement was slightly smaller: the probability of survival increased from 40.7% to 43.4%. However, this was mainly due to a smaller proportion of babies being transferred from a L2 to a L3 unit prior to birth. Thus the sensitivity analysis provided a conservative estimate of the impact of the policy change.

Other results from the model indicated that the likelihood of antenatal death fell from 34% to 29% and the likelihood of being discharged without morbidity increased from 6% to 9%.

Cost implications:
In the model, there was an estimated reduction in the number of post-natal ambulance transfers required per annum from 30.0 to 7.4 (from 89.5% to 56.0% of annual births in a L2 unit). Thus, based on the local data provided by Oxford AHSN on the cost of neonatal ambulance transfers, we estimated that there would be potential annual cost reductions of £24,883 (=£1,101*(30.0 - 7.4)).

Whilst it was clear from our discussion with the Oxford AHSN that there could be very low short run marginal costs associated with the increased number of births at the L3 unit (due to spare capacity), we nonetheless cannot presume that the spare capacity would be available indefinitely. Furthermore, if not immediate financial costs, then there are clearly opportunity costs associated with the use of the L3 facilities (since these resources could have been reallocated to other uses, including premature babies born after 28 weeks, for example). Thus we used the data from the study by Mistry et al. to calculate the annual cost of the additional births (= 46.8-39.5 = 7.3 births; see Table 14) which occurred at the L3 unit after the policy changes as amounting to £263,654 (where the unit cost was £36,117, after adjustment for 2016 prices). Also using the data reported in the study by Mistry et al., we calculated the corresponding annual cost reductions at the L2 units as amounting to £139,167 (where the unit cost was £19,064).

Overall, when combined with the cost to the Oxford AHSN reported in Table 14, these estimates suggest that there could have been an increase in costs attributable to the policy of £170,429 per annum in the first year (falling to £99,604 in later years; see Table 16). However, we emphasise that this should be considered a 'worst case' cost scenario. In reality, the cost is likely to be much lower since the costs we have used for birth in a L3 unit are not directly comparable to the estimates of a birth in a L2 unit due to limitations in the data available to us (as discussed in 3.2.3.2 above; no other suitable cost data was identified). In a 'best case' cost scenario, where the assumption suggested in conversations with the maternity clinical network that the transfer of births from L2 units to L3 units did not result in an increase in costs, the cost to the Oxford AHSN of the policy change (£70,825, Table 13) is roughly equivalent to the savings that would be achieved from reductions in neonatal ambulance transfers over a three year period (which amount to £24,883 per annum). We suggest that the most likely cost scenario falls between these two extremes.

Table 15: Outputs for three iterations of the model

Probability of survival at discharge		Secondary outcomes											
		Baby meets antenatal criteria (see Box 2)	Total live births	Live birth at Level 3 unit		Live birth at Level 2 unit		Antenatal death		Neonatal death		Discharged without morbidity	
	%	N	N	N	%	n	%	n	%	n	%	n	%
Model iteration 1: Real data reported in the Marlow study (for comparison)													
	45.2%	2216	1543	1031	47%	512	23%	673.0	30%	540.8	24%	189.4	9%
Model iteration 2: 'Before' the policy change													
	40.7%	110.4	73	39.5	36%	33.5	30%	37.4	34%	28.1	25%	6.7	6%
Model iteration 3: 'After' the policy change													
Main analysis	**45.9%**	84.3	60	46.8	55%	13.2	16%	24.3	29%	21.3	25%	8.0	9%
Sensitivity analysis*	43.4%	85.9	60	46.8	55%	13.2	16%	22.7	30%	22.7	26%	7.3	8%

% refers to the proportion of all babies meeting antenatal criteria (i.e. joint probabilities calculated once a complete pathway from the left hand side through to the right hand side has been competed)

* In the main analysis, gaps in the local data were filled with national-level data from the study by Marlow et al. The sensitivity analysis instead uses some of the local data available in the 'Before' period (iteration 2; see Table A, Appendix 1 for details)

Table 16: Estimated change in annual costs which could be attributed to the policy changes

	'Worst-case' scenario	'Best case' scenario
Increased costs		
Cost to the Oxford AHSN	£70,825*	£70,825*
Increased number of L3 births	£263,654	£0
Cost savings		
Decreased number of L2 births	£139,167	£0
Decreased number of neonatal transfers	£24,883	£24,883
Total change in cost		
Total	£170,429 increase	£45,942 increase
Excluding costs to the Oxford AHSN*	£99,604 increase	£24,883 saving

* Costs to the Oxford AHSN are reported in Table 14. Note that these would arise only in the first year.

3.2.4 Discussion

Main findings:

The main finding of this analysis has been the estimated improvement in the likelihood of survival after the policy change of 5.2% percentage points (as shown in column 1, Table 14), rising from 40.7% prior to the policy change to 45.9% after the policy change. Based on our estimate of 84.3 babies meeting the maternity clinical network's criteria for transfer to a L3 unit per annum, this translates into an increase of approximately 4 babies surviving per annum than would have been the case prior to the policy change (our more conservative estimate provided in the sensitivity analysis suggests an increase of approximately 2 survivals). These improvements in survival are set against our estimates of changes in cost in Table 17. Given the improvement in survival that is identified in our model (and supported by the wider literature), we suggest that the policy change (and Oxford AHSN's contribution to the policy change) does represent good value for money.

The literature review identified some evidence that, in addition to the improvement in survival which is likely to be attributable to a transfer of extremely premature babies from L2 to L3 units, there is also likely to be an improvement in survival attributable to the transfer of extremely premature babies from low-volume units to high-volume units. Further exploration of this point was beyond the scope of this study. However, given the very small numbers of babies meeting the transfer criteria which were previously being born each year in L2 units (e.g. for the Oxford AHSN area, n<8 was reported in all 5 of the L2 units in at least one of the two years for which we have data, including n<4 in 2 of those units in 2012-13), this could be a further significant factor supporting the policy change which has occurred.

Table 17: Summary of main findings

	'Worst-case'*	'Best case'*
Change in survival		
Increase in live births per annum	2.3	4.4
Change in cost		
Total cost per annum	£170,429 increase	£45,942 increase
Excluding costs to the Oxford AHSN**	£99,604 increase	£24,883 saving

*The 'worst case' reports costs at the higher end of our estimates, and additional live births that occurred in the sensitivity analysis used in our model. The 'best-case' reports costs at the lower end of our estimates, and additional live births that occurred in the main outputs of our model.

**Note that costs to the Oxford AHSN would arise only in the first year.

Limitations:

Our findings are based on the best available evidence and, to the extent that it was possible to alter some of the assumptions made in the main analysis, our sensitivity analysis also showed an improvement (albeit smaller) in survival rates based on more conservative assumptions. Nevertheless, all the reported findings in this study are subject to significant caveats arising from limitations in the data and methodology used.

Related to the effectiveness data:

- As shown in Table A (Appendix 1), local data was not available for many of the 'decision' and 'choice' nodes. Hence it was necessary to make assumptions which were based on national data. We recommend that the maternity clinical network continue to collect data over a longer period of time related to each of the pathways in the decision model (Figure 8) so that a more complete assessment of the improvement in survival can be made in the future.
- Even with complete data, the sample sizes used in this analysis remain very small, due not only to the short period of follow-up since the policy change, but also because of the relatively small number of babies who meet the criteria for transfer to L3 units. As a result it is not possible to conclude whether or not the results reported in our analysis were statistically significant. This is a substantial limitation. Hence in this study we included evidence from the literature review to support our findings wherever possible. In particular we suggest that the reported findings on survival with/without morbidity be treated with caution since these are based on very small sample sizes and the evidence from the literature on differences in morbidity between places of birth have mixed results. Nevertheless, the evidence from the literature on survival overall when comparing L3 to L2 units is stronger, and thus supports the results reported here from the decision model.
- The primary outcome measure used in the decision model was survival at discharge. This is a relatively crude measure, considering the other health and wellbeing benefits that could have arisen as a result of the policy change for mother and baby. Furthermore we have not considered the longer term impact on the health and life chances of the baby (although some studies have attempted to assess this using economic modelling (Petrou and Khan, 2012). Based on our reading of this literature, we suggest that inclusion of these additional measures

would increase (rather than decrease) the likelihood that the policy change represented good value for money.

Related to the cost data:

- There was a significant shortage of data (at the local and national levels) on the cost of care for premature babies in L3 units when compared to preterm delivery of babies in L2 units and their subsequent transfer to L3. Nevertheless, whilst we provided two extreme scenarios ('best case' and 'worst case'), set against the improvement in survival we do not consider that the choice of scenario would have a significant impact on assessing whether or not the policy change represented good value for money.

Insights from the literature review:

- The study by Marlow et al. was used extensively throughout this study. Whilst this analysis is supported by a large sample size (all maternity units in the UK), it is nonetheless based on data which is ten years old and from a single source. Ideally we would have been able to use more recent data and data from a wider range of sources. Unfortunately the study by Marlow et al. was the only study to provide detailed information on all of the potential pathways in the decision model (Figure 8). Despite having identified some other sources of evidence which support the main findings of the study by Marlow et al. (although as stated above we are aware that the evidence on morbidity particularly is quite mixed), it is the more specific evidence related to particular pathways in the model which is missing from other studies.

Appendix 2: Place of Birth of Extremely Premature babies Oxford AHSN Network Wide Guidelines.

- Simplified patient pathway and management algorithm for Prelabour Preterm SROM
- Simplified patient pathway and management algorithm for presentation with threatened extreme premature labour
- Management of preterm singleton/DC twin intrauterine growth restriction (IUGR)
- Magnesium Sulphate – Loading Dose for severe pre-eclampsia/eclampsia and neuroprotective dose for severe preterm delivery
- Network PTL transfer policy change - Urgent in utero transfer to the John Radcliffe Hospital

Simplified patient pathway and management algorithm for Prelabour Preterm SROM: Version 1, 21/04/15

Authors: Mr Lawrence Impey/ Oxford AHSN Maternity Network Steering Group. Ratified 22/4/15

Suspected Prelabour Preterm SROM at >/=22+5[1] weeks , <34+0

Severe maternal sepsis[2] or

Acute fetal compromise/ abruption major PV bleeding

Stabilise[8]

Deliver

No 'severe' sepsis/fetal compromise

Contracting +/-minor bleed

Steroids
Mg[4] if <30+0
EFW[5] if poss
IV antibiotics[6]
VE

> minor PV bleed not contracting

Steroids
Consider Mg if <30+0 [4]
EFW[5] if poss
No antibiotics/ erythromycin po

Not contracting/ minor PVB, but likely SROM/AP[3] +ve

Steroids
No Mg
EFW[5] if poss
No antibiotics/ erythromycin po

Likely not SROM/ AP[3] –ve

Consider no steroids
No Mg
Non-urgent USS
No antibiotics

Consider discharge

Gestation is<27+0 (singleton) or <28+0 weeks (multiple) or EFW <800g[7] (incl if <25+0 weeks or EFW <600g IF parents want active management)[9]

Request IUT[10] if del not imminent

Consider tocolysis[11] for IUT only

No tocolysis

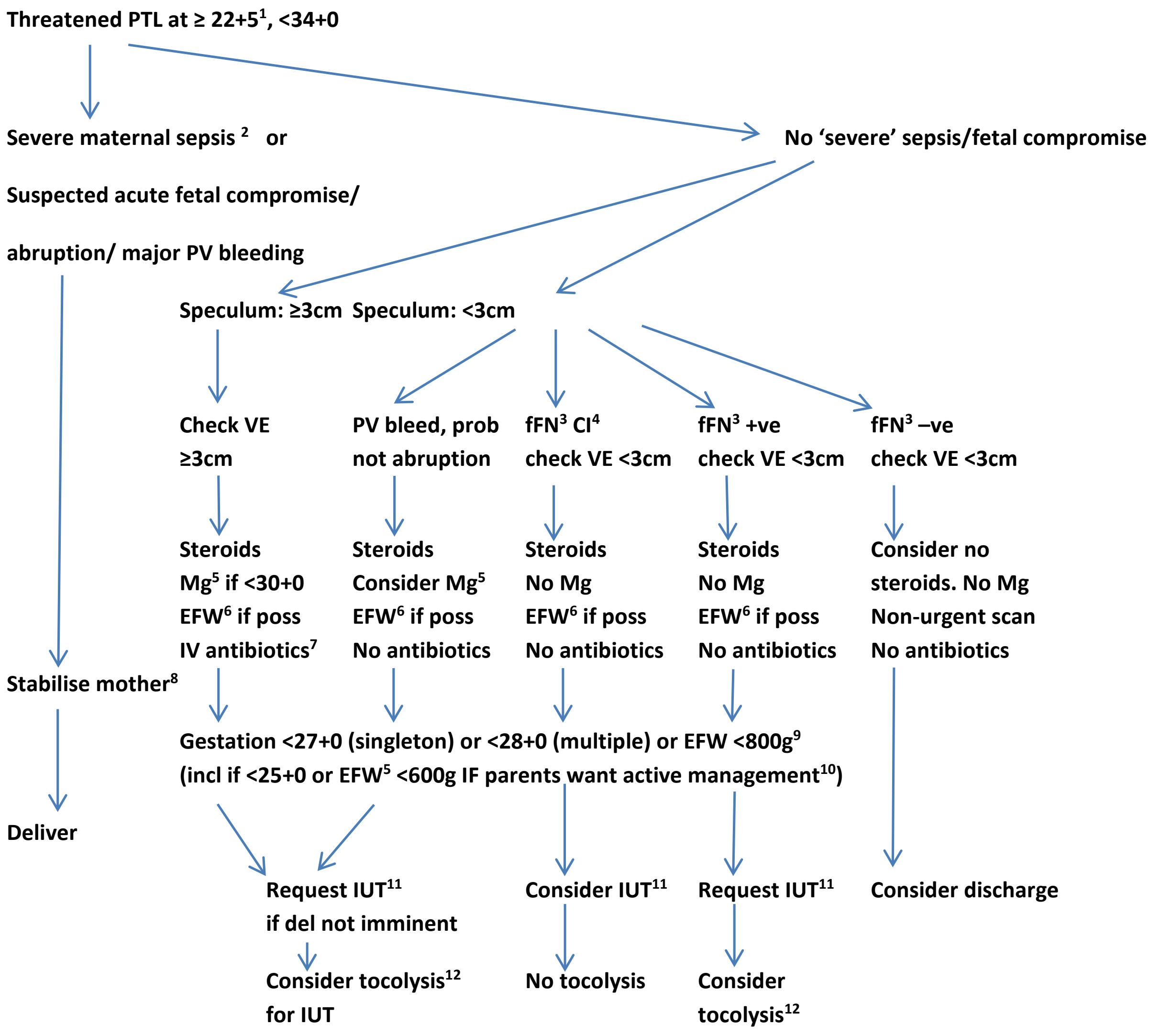
Request IUT[10]

No tocolysis

1. Note active resuscitation for neonates <23+0 will not usually be performed. The management pathway should not be followed prior to 22+5 the 3 day difference allowing for steroids etc. Dates according to CRL excl in IVF pregnancies.
2. Sepsis meeting criteria for local severe sepsis bundle
3. AP: Actim PROM, or equivalent. Only use if available. Obvious SROM overrides Actim PROM-ve.
4. Mg: Magnesium bolus 4g (16mmol) Magnesium Sulphate as 20mls of 20% magnesium sulphate IV over 5 – 10 minutes
5. EFW: estimated fetal weight +/-15% if possible
6. IV antibiotics. Follow unit antibiotic guideline; avoid co-amoxiclav
7. Stabilisation of acutely unwell mother beyond scope of this.
8. Criteria for delivery in Level 3 Neonatal Unit
9. If time, offer discussion with paediatrician. Document any discussion regarding IUT with parents. Consider providing Thames Valley Neonatal Network patient information leaflets if available.
10. IUT: in utero transfer, try OUH first. 8-5pm call Delivery Suite (01865 221988/7), and specifically request to speak to the consultant obstetrician on Delivery Ward. From 5pm to 8am, hospital switchboard (01865 741166), with the request to speak to the obstetric consultant on call. DO NOT call neonatal unit or delivery ward manager first.
11. Tocolysis. Follow unit tocolysis guideline. Do not use nifedipine if magnesium given or to be given

<u>Simplified patient pathway and management algorithm for presentation with threatened extreme preterm labour: Version 1, 21/04/15.</u>

Authors: Mr Lawrence Impey/ Oxford AHSN Maternity Network Steering Group. Ratified 22/4/15



1. Note active resuscitation for neonates <23+0 will not usually be performed. The management pathway should not be followed prior to 22+5 the 3 day difference allowing for steroids etc. Dates according to CRL excl in IVF pregnancies.
2. Sepsis meeting criteria for local severe sepsis bundle
3. fFN: fibronectin or equivalent to assess likelihood of preterm delivery more accurately than history and examination
4. CI: contraindicated/ not recommended. Consider fFN usage if postcoital as false negatives unlikely
5. Mg: Magnesium bolus 4g (16mmol) Magnesium Sulphate as 20mls of 20% magnesium sulphate IV over 5 – 10 minutes
6. EFW: estimated fetal weight +/-15% if possible
7. IV antibiotics. Follow unit antibiotic guideline; avoid co-amoxiclav
8. Stabilisation of acutely unwell mother beyond scope of this document
9. Criteria for delivery in Level 3 Neonatal Unit
10. If time, offer discussion with paediatrician. Document any discussion regarding IUT with parents. Consider providing Thames Valley Neonatal Network patient information leaflets if available.
11. IUT: in utero transfer, try OUH first. 8-5pm call Delivery Suite (01865 221988/7), and specifically request to speak to the consultant obstetrician on Delivery Suite. From 5pm to 8am, hospital switchboard (01865 741166), with the request to speak to the obstetric consultant on call. DO NOT call neonatal unit or delivery ward manager first.
12. Tocolysis. Follow unit tocolysis guideline. Do not use nifedipine if magnesium has been given or is to be given

Management of preterm singleton/ DC twin Intrauterine Growth restriction (IUGR): Version 1, 24/04/2015

Authors: Mr Lawrence Impey/Oxford AHSN Maternity Network Steering Group. Ratified 22/4/15

Section 1: Management of severe preterm singleton/ DC twin IUGR without absent end –diastolic flow

EFW[1] or AC[2] <10th centile[3] with UmbA[4] RI/PI[5]>95th centile at <34+0 weeks

Repeat anomaly scan

Check maternal CMV and toxoplasmosis (IgM) status

Consider uterine arteries, karyotype, middle cerebral artery Doppler

Likely placental origin

Likely fetal origin → **manage appropriately, consider IUT[10]**

Gestation >24+0w and EFW[1]>500g

Gestation <24w+0 or EFW[1]<500g

See 1-2 weeks

UmbA[4] RI/PI >95th c

Repeat UmbA[4] 2-3/ week

Monitor mother (BP[8] and urinalysis)

UmbA[4] AEDF[6]

<32+0 w

>/=32+0 w

See page 2

deliver by CS[7]

Section 2: Management of severe preterm singleton/ DC twin IUGR: with AEDF

UmbA[4] AEDF[6] detected (note significant growth now unlikely)

↓

Steroids (may get temporary improvement)

Daily fetal assessment.

Monitor mother BP[8] and urinalysis

If:

Gestation: <26+0w	26+0w to 29+6w		30+0w-31+6w		>/=32+0w
If active Rx requested[9]:	<27+0w[15] or <800g EFW[1]	>/=27+0w[15] or >800g EFW[1]	<800g EFW[1]	>/=800g EFW[1]	
IUT[10]	IUT[10]	consider IUT[10]	IUT[10]	consider IUT[10]	
UmbA[4]: no action	UmbA[4]: no Rx (alone)		UmbA[4]: del if REDF[12]		UmbA[4]: del if AEDF[4]
CTG[11]: don't do	CTG[11]: del if STV[12] <3.0		CTG[11]: del if STV[11] <3.0		CTG[11]: del if STV <3.0
DV[13]: del if rev[14] a wave	DV[13]: del if absent[14]		DV[13]: del if PIV>95th centile		

NB: pre eclampsia often increases rate of deterioration and may necessitate delivery

1. 1: EFW: estimated fetal weight
2. AC: abdominal circumference
3. Centile. Use current Trust standard, accepting variation, ultimately aim to move to international chart. Avoid customised chart as ethnicity likely independent risk factor (see Intergrowth results)
4. UmbA: umbilical artery
5. RI/PI: resistance index/ pulsatility index. Follow current Trust practice as to which.
6. AEDF: absent end-diastolic flow
7. CS: caesarean section
8. BP: blood pressure
9. If active treatment requested: Following paediatric consultation. Document any discussion regarding IUT with parents. Consider providing Thames Valley Neonatal Network patient information leaflets if available.
10. IUT: in utero transfer. Where neonatal guidelines require IUT this is designated 'IUT'. Where fetal medicine guidelines advise IUT this is designated 'consider IUT'. This is because it is recognised that within the Thames Valley area many units have fetal medicine expertise. However, IUT may be discussed with any pregnancies at any stage on this guideline according to individual units' or consultants' preference. Non urgent IUT to the OUH for IUGR is normally arranged by calling fetal medicine office (01865 221716) or the fetal medicine consultant (07810 376679)
11. CTG: computerised cardiotocograph. Evidence based tool in severe IUGR
12. STV: short term variability on computerised cardiotocograph
13. DV: ductus venosus
14. 14: Absent/ reversed a wave of ductus venosus. From 26+0w, computerised CTG as effective
15. 15: Note this threshold is <28+0 if DC twin pregnancy

This document takes account of national neonatal guidelines and national fetal medicine guidelines (RCOG Greentop and Specialised Commissioning CRG service Specifications)

<u>Magnesium sulphate: Loading dose for severe pre-eclampsia[1]/ eclampsia AND neuroprotective[2] dose for severe preterm delivery guideline: Version 1, 20/01/15</u>

Authors: Mr Lawrence Impey/ Oxford AHSN Maternity Network Steering Group. Ratified 22/4/15

- Take ONE 20 ml syringe and fill with contents of one pre-prepared 20 ml Vial of 20% Magnesium Sulphate[3]. This contains 4g (16mmol) of Magnesium Sulphate.
- Give the 4g (16mmol) Magnesium Sulphate by slow IV bolus
- Administer this over 5-10 minutes manually.

1. Criteria for use in severe pre-eclampsia may differ
2. Criteria for neuroprotective usage may differ
3. Pre-prepared vials can be supplied by the Oxford University Hospital Trust Pharmacy, if local pharmacy unable to provide

Oxford Academic Health Science Network
Maternity

Network PTL transfer policy change v2 15/12/2014

Urgent in utero transfer to the John Radcliffe Hospital

Where there is a risk of extreme preterm delivery, either iatrogenic or spontaneous, in utero transfer to a neonatal unit is advised by BAPM: extreme preterm birth is associated with a decrease in neonatal mortality and morbidity if it occurs in a level 3 neonatal unit (Marlow et al 2014). Currently, in the Thames Valley network, over 50% of extremely preterm babies are born outside the level 3 centre. This issue is currently the subject of much scrutiny and is likely to be assessed as an important measure of the quality of a maternity unit's performance at some stage in the near future.

An audit by the Maternity Network of the AHSN has identified, perhaps not surprisingly, that in utero transfer within the Thames Valley to the John Radcliffe Hospital as the local Level 3 neonatal unit can be difficult to achieve, and the John Radcliffe Hospital's refusal to take in utero transfers has been a reason why delivery has taken place outside a Level 3 neonatal unit. It is also recognised that capacity alters rapidly over a short time frame and that delivery may occur days later than transfer and therefore neonatal capacity at the exact time of referral may be irrelevant.

In response to this we have agreed the following policy change:

Requests for urgent in utero transfer to the John Radcliffe Hospital should initially be directed to the **Consultant Obstetrician on call**, rather than the neonatal unit.

From 8am-5pm this call should be made to the Delivery Suite (01865 221988/7), with the specific request to speak to the Consultant Obstetrician on Delivery Suite.

From 5pm to 8am, the call should be to the hospital switchboard (01865 741166), with the request to speak to the Consultant Obstetrician on call.

Only in exceptional circumstances (such as imminent delivery and neonatal unit red alert) will transfer be declined. If transfer is declined by either the neonatal unit or the Delivery Ward, without speaking to the consultant on call, then please request specifically to speak to the consultant on obstetrician on call.

We very much hope that this will make IUT easier and therefore increase patient safety in these extreme circumstances. If however, the John Radcliffe Hospital is unable to accept delivery, every effort should be made to move the mother to an alternative level 3 unit. We would be grateful if this information is disseminated locally.

Signed

Dr Eleri Adams, Consultant Neonatologist; Clinical Director Neonatal Services, OUH

Miss Veronica Miller, Consultant Obstetrician; Clinical Director, Women's Services, OUH

Mr Lawrence Impey, Consultant Obstetrician, OUH; Maternity Network Lead.

Appendix 3: Place of Birth audit form provided to units involved in project.

Extremely pre-term delivery audit

Inclusion- <27/40 Singleton or <28/40 multiple, or birthweight <800g delivered outside of a hospital with a Level 3 neonatal unit

Previous medical history

Hospital	
Audit number	
Gestation at delivery	
Date of delivery	
EDD	
Parity	
No of babies this pregnancy	
Maternal age at delivery	
BMI at booking	
Gestation at booking	
Ethnicity	

Risk factors present? If yes, indicate whether they were recognised by clinicians at the time

Risk factor present?	**Y**	**N**	**If Yes, recognised by clinicians?**	**Y**	**N**
Prev pre-term delivery	☐	☐			
PET	☐	☐		☐	☐
APH	☐	☐		☐	☐
Signs of infection	☐	☐		☐	☐
PSROM	☐	☐		☐	☐
Shortened cervix on scan	☐	☐			
Prev cervical treatment	☐	☐			
Fetal abnormality	☐	☐		☐	☐
Placenta Praevia	☐	☐		☐	☐
IVF pregnancy	☐	☐			
Smoker?	☐	☐			

Preterm delivery care

	Y	**N**	**N/A**		**Y**	**N**
Fibronectin (or equiv.) test used?	☐	☐	☐	Magnesium Sulphate given?	☐	☐
1st dose of steroids given?	☐	☐		Rescue Cerclage performed?	☐	☐
2nd dose of steroids given?	☐	☐		Antibiotics given?	☐	☐

Delivery Details

Start of labour	Date: Time: Spontaneous ☐ IOL ☐ No labour ☐
Rupture of membranes	Date: Time: SROM ☐ ARM ☐ No ROM ☐
Delivery – Baby 1	Date: Time: Type SVD ☐ Vaginal Breech ☐ Ventouse☐ Forceps☐ ELCS☐ EMCS☐ If CS, for what indication?: Livebirth? Y☐N☐ Sex F☐M☐ Weight: Apgar at 1 min: Apgar at 5 mins: Blood gases:
Delivery – Baby 2 (if applicable)	Date: Time: Type SVD ☐ Vaginal Breech ☐ Ventouse☐ Forceps☐ ELCS☐ EMCS☐ If CS, for what indication?: Livebirth? Y☐N☐ Sex F☐M☐ Weight: Apgar at 1 min: Apgar at 5 mins: Blood gases:
Was an in utero transfer attempted?	Y☐N☐ If yes, please supply details of why it was not successful
Why did the delivery occur outside of a Level 3 unit?	

Were there any contributing factors that if different could have allowed delivery in a Level 3 unit?	
Baby/babies transferred postnatally?	Y☐ N☐ If yes – Date Time: Where:

Completed by (name, role):
Date:

Thank you for completing this form. The information will be used by the Oxford AHSN Maternity Network and the Thames Valley and Wessex Neonatal Network to help ensure that as a region we are providing the best possible care for extremely premature babies and reduce any barriers to timely in utero transfers between hospitals.

Audit and report written and compiled by Katherine Edwards, Oxford AHSN Maternity Network Manager/Lead Midwife and Mr Lawrence Impey, Oxford AHSN Maternity Network Clinical Lead.

Health Economics report extracted from 'Exploring the Added Value of Oxford AHSN', Office of Health Economics & RAND Europe, April 2016, written by Grace Marsdena, Adam Martinb, Bernarda Zamoraa, Jo Exleyb, Jon Sussexb and Adrian Towsea,

Thank you to the Thames Valley and Wessex Operational Delivery Network for their contribution to, and support of the audit and all clinical staff from each unit contributing to data collection and the members of the Oxford AHSN Steering Group for their contributions and work on the Place of Birth project.

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Thames Valley & Wessex Operational Delivery Networks
Thames Valley & Wessex Neonatal Operational Delivery Network
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References

Costeloe et al.(2012). “Short term outcomes after extreme preterm birth in England: comparison of two birth cohorts in 1995 and 2006 (the EPICure studies)”. BMJ 2012;345:e7976

Marlow, N., et al. (2014). "Perinatal outcomes for extremely preterm babies in relation to place of birth in England: the EPICure 2 study." Archives of Disease in Childhood - Fetal and Neonatal Edition **99**(3): F181-F188.

Stock, S. J., et al. (2014). "Variation in management of women with threatened preterm labour." Archives of Disease in Childhood - Fetal and Neonatal Edition.

Thames Valley & Wessex Operational Delivery Networks (2014), “Policy for transfer of infants to a Neonatal Intensive Care Unit/Local Neonatal Unit**”,** www.networks.nhs.uk/nhs-networks/thames-valley-wessex-neonatal-network/documents/network-policies

Vogel, J. P., et al.(2014) "Use of antenatal corticosteroids and tocolytic drugs in preterm births in 29 countries: an analysis of the WHO Multicountry Survey on Maternal and Newborn Health." The Lancet **384**(9957): 1869-1877.