Protocol for non-CTIMPs

**Clinical Management and Short-Term Outcomes of Neonates Born at 22 Weeks in UK Neonatal Intensive Care Units**

(IRAS Short title – The 22 Week Study)

v1.0

21st October 2025

MAIN SPONSOR: Imperial College London

FUNDERS: Chelsea and Westminster NHS Trust

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IRAS Project ID: 346626

REC reference: 25/PR/0089

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Sponsor

Imperial College London is the main research Sponsor for this study.

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Funder

This study is supported by Chelsea and Westminster NHS Trust.

REDCap payment will be from the NIHR Advance Fellowship awarded to Dr Cheryl Battersby.

No participant payments or funding.

This protocol describes the Clinical Management and Short-Term Outcomes of Neonates Born at 22 Weeks in UK Neonatal Intensive Care Units study and provides information about procedures for entering participants. Every care was taken in its drafting, but corrections or amendments may be necessary. These will be circulated to investigators in the study. Problems relating to this study should be referred, in the first instance, to the Chief Investigator.

This study will adhere to the principles outlined in the UK Policy Frame Work for Health and Social Care Research. It will be conducted in compliance with the protocol, the Data Protection Act and other regulatory requirements as appropriate.

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**GLOSSARY OF ABBREVIATIONS**

| | |
|---|---|
| BAPM | British Association for Perinatal Medicine |
| CI | Chief Investigator |
| CLD | Chronic lung disease |
| CO2 | Carbon dioxide |
| CRF | Case report form |
| CRUSS | Cranial ultrasound |
| ECG | Electrocardiography |
| GCP | Good Clinical Practice |
| GDPR | General Data Protection Regulations |
| GI | Gastrointestinal |
| ICMJE | International committee of medical journal editors |
| IVH | Intraventricular Haemorrhage |
| LNU | Local Neonatal Unit |
| NEC | Necrotising enterocolitis |
| NHS | National Health Service |
| NICU | Neonatal Intensive Care Unit |
| NI | Northern Ireland |
| NNRD | National Neonatal Research Database |
| PDA | Patent Ductus Arteriosus |
| PN | Parenteral nutrition (also TPN – total parenteral nutrition) |
| PHVD | Post Haemorrhagic Ventricular Dilatation |
| PVL | Periventricular leucomalacia |
| REDCap | Research Electronic Data Capture |
| ROP | Retinopathy of prematurity |
| SCU | Special Care Unit |
| SIP | Spontaneous intestinal perforation |
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**KEYWORDS**

Extreme preterm, Low birth weight, Tiny baby, 22 weeks, limits of viability, Survival, Intraventricular, Haemorrhage (IVH), periventricular leukomalacia, Necrotising enterocolitis (NEC), Chronic lung disease (CLD), Retinopathy of prematurity (ROP), Sepsis

**STUDY SUMMARY**

| | |
|---|---|
| TITLE | Clinical Management and Short-Term Outcomes of Neonates Born at 22 Weeks in UK Neonatal Intensive Care Units |
| DESIGN | Multi-centre prospective observational cohort study in tertiary UK neonatal intensive care units |
| AIMS | In this study, we aim to conduct a national prospective study to describe the clinical care and outcomes up to neonatal discharge or death for babies born at 22 weeks over a one-year period. We hypothesise that we will find variations in clinical practice and decision making. By describing these at a population level, we will begin to learn more about this new population and consider ways to optimise clinical care. |
| OUTCOME MEASURES | Primary objectives<br><br>1.To determine whether neonatal admissions align with BAPM recommendations based on risk stratification<br><br>2.To report the proportion of infants receiving interventions in the following areas of clinical care at a baby and network level (see appendix 1):<br>Delivery room stabilisation<br>Respiratory & cardiovascular<br>Neurological<br>Gastroenterological & Surgical<br>Renal<br>Haematology<br>Infection<br>Skin, thermal management, monitoring<br><br>3.To report the short-term outcomes (survival or death) following neonatal care. Additional outcomes to be reported: length of stay, Chronic Lung Disease at 36 weeks, Patent Ductus Arteriosus closure (medication, device or ligation), Necrotising enterocolitis requiring surgery, Retinopathy of prematurity requiring laser or injection, severe brain injury including periventricular leukomalacia (PVL), grade 3-4 IVH post haemorrhagic ventricular dilatation (PHVD), culture-positive sepsis.<br><br>To analyse outcomes by sub-group of:<br><br>Region/Network<br>Individual BAPM risk factors |

| | |
|---|---|
| | 4.For those babies that die, to report the timing, cause of death, whether reorientation to comfort care took place and influencing factors or indications for redirection |
| | Secondary objectives<br><br>To explore associations between baby and clinical care factors and outcomes. To generate hypotheses, inform the design of future studies, support proof of concept and feasibility for a larger scale study or registry for 22-week babies in the UK.<br><br>To conduct a national survey across the NICUs and report<br>i) the proportion of units and networks which have protocols for the care of babies born at 22 weeks.<br>ii) Report similarities and differences in clinical care approaches.<br>iii) Report common challenges faced by teams caring for babies born at 22 weeks |
| POPULATION | All babies born at 22+0-22+6 weeks gestation at tertiary level neonatal intensive care units in the United Kingdom within the study period. Estimated sample size 200 infants. |
| ELIGIBILITY | Born at 22+0-22+6 gestation within 12-month study period at Neonatal Intensive Care Units (NICU) in UK, with neonatal team in attendance. |
| DURATION | Inclusion time period – birth within 12 month period. Data capture will continue from birth until the end of neonatal journey for every baby included (discharge from neonatal unit or death). |

REFERENCE DIAGRAM

N/a

# 1. INTRODUCTION

## 1.1. BACKGROUND

Extremely premature babies born at the earliest point in pregnancy where survival is considered possible (22-24 weeks gestation) are at high risk of death or survival with long term medical conditions and disability, impacting the child, their family and society. Parent and professional discussions and decision-making antenatally around whether to provide 'survival-focused care' with stabilisation and neonatal intensive care after birth, or 'comfort-focused care', where the baby's comfort is the main priority in palliation, are extremely challenging for all involved.

In 2019, the British Association for Perinatal Medicine (BAPM) changed their national guidance[1] and recommended that, in certain circumstances, some babies born at 22 weeks gestation could be offered survival focused care, lowering the recommendation from 23 weeks gestation. Prior to this, babies born this early were only offered comfort-focused care.

Research using the UK National Neonatal Research Database to evaluate the impact of the change in guidance showed [2] a threefold increase in babies born at 22 weeks gestation receiving survival-focused care and being admitted to neonatal units in the UK. Out of 183 babies receiving survival focused care in 2020-2021, only 21% survived to discharge. Survival was lower at 12% when all babies born alive were included.[2] These findings have implications for service provision and palliative care needs. For comparison, in 2020-2021, 528 babies born at 23 weeks received survival focused care and survival to discharge was higher (42%) for this group; 39% for live births.[2]

International studies from mainly single-centre sites in United States (US), Japan and Scandinavia, include recently published comparisons of clinical management in each centre.[3-5] These centres have higher survival rates (39% in Sweden[6], 60% in Japan of live births[3]), but widely different approaches to treatment and management, different populations and health care systems.

## 1.2. RATIONALE FOR CURRENT STUDY

Rationale for 22 weekers

Neonatal teams in the UK are providing survival focused care to a new population of 22-week gestation babies with a lack of research to inform optimal care. The current evidence base used for clinical decision-making has not included babies of this gestation in studies and centres abroad currently publishing their experience are unlikely to be reflective of the healthcare system or population of the UK as a whole. There is no information on how UK centres are currently managing these babies. As patient numbers are small, individual clinicians or centres are unlikely to have significant amounts of experience, and it would be helpful to share clinical challenges, dilemmas and successes or good practice. The study findings may support discussions and decision-making with families in the antenatal and postnatal settings. It may also allow identification of key factors leading to timely reorientation to palliative care to avoid prolonged suffering of babies and families.

Information on differing survival rates across the country and common themes may allow the creation of a framework of what is considered good practice (in the absence of robust evidence).

Rationale for UK-Wide Study

As numbers will be small at each centre per year (likely single figure), it is vital that the study is on a large national scale to be meaningful. In addition, using data collected from across the UK within the National Health Service will allow an in-depth look across geographical locations and include ethnically and socio-economically diverse patient populations, making the results more relevant to and realistic of the UK experience. Although numbers will be small, we may find differences in clinical care between units with higher versus lower survival which could generate hypotheses that can be tested in future studies.

Rationale for inclusion of NICU births and Neonatal Attendance only

National guidance is for all babies born at less than 28 weeks gestation to be cared for in a neonatal intensive care unit (NICU). Therefore, data from NICUs should include those born in local neonatal units (LNU)/special care units (SCU) and transferred postnatally.

Many parent(s) are counselled by neonatal teams between 21+5 and 22+6 weeks, but do not go on to give birth within the 22 week window. In order to limit screening of data and identify babies where neonatal care was involved, the entry point into the study will be for any baby born at 22-22+6 where the neonatal team attended delivery. This may include babies given comfort care only, where stabilisation of the baby was unsuccessful and those stabilised and admitted to neonatal intensive care units. The antenatal counselling of these babies will then be reviewed for data collection.

The study will therefore exclude

i) babies who received comfort care at a NICU without any neonatal team in attendance
ii) babies who received comfort care at an LNU or SCU centre or died following attempted resuscitation or neonatal admission in an LNU or SCU. The number of babies this will apply to will be small (<10% of total) and with around 125 LNU and SCU sites it is likely that in trying to collect this data, it would potentially be incomplete due to rarity of the event, without providing significantly more insight into the aims of this project.

Some of these data are captured at a population level through the annual MBRRACE-UK report.[7]

Aim

In this study, we aim to conduct a national prospective study to describe the clinical care and outcomes up to neonatal discharge for babies born at 22 weeks over a one-year period. We hypothesise that we will find variations in clinical practice and decision making. By describing these at a population level, we will begin to learn more about this new population and consider ways to optimise clinical care.

## 2. STUDY OBJECTIVES

Primary objectives

1. To determine whether management of infants born at 22 weeks align with BAPM recommendations based on risk stratification

2. To report the proportion of infants receiving interventions in the following areas of clinical care at a baby and network level (see appendix 1a):
    a. Delivery room stabilisation
    b. Respiratory & cardiovascular
    c. Neurological
    d. Gastroenterological & Surgical
    e. Renal
    f. Haematology
    g. Infection
    h. Skin, thermal management, monitoring

3. To report the short-term outcomes (survival or death). Additional outcomes to be reported: length of stay, Chronic Lung Disease at 36 weeks, Patent Ductus Arteriosus closure (medication, device or ligation), Necrotising enterocolitis requiring surgery, Retinopathy of prematurity requiring laser or injection, severe brain injury including periventricular leucomalacia, grade 3-4 IVH, PVHD, culture-positive sepsis
    a. To analyse outcomes by sub-group of:
    b. Region/Network
    c. Individual BAPM risk factors

4. For those babies that die, to report the timing, cause of death, whether reorientation to comfort care took place and influencing factors or indications for redirection

Secondary objectives

To explore associations between baby and clinical care factors and outcomes. To generate hypotheses and inform the design of future studies UK which may include linkage to existing national data on longer term outcomes. This study will support proof of concept and feasibility for a larger scale study or registry for 22-week babies.

To conduct a national survey across the NICUs and report

i) the proportion of units and networks which have protocols for the care of babies born at 22 weeks.
ii)Report similarities and differences in clinical care approaches.

iii)Report common challenges faced by teams caring for babies born at 22 weeks

## 3. STUDY DESIGN

Design (see appendix 1b)

Prospective multi-centre observational cohort study with each unit using a standardised data collection tool using the REDCap tool (Imperial).

Data will be collected daily for the first week, then weekly until 44 weeks corrected gestational age and then outcomes at discharge from neonatal care or death.

Proposed Study Sites (see appendix 2)

53 NHS Trust Organisations in total comprising: 52 tertiary level NICUs (51 NHS Trusts) and 4 neonatal surgical centres (2 additional NHS Trusts).

NICU centres: 43 (+4 surgical centres) England, 3 Wales, 5 Scotland, 1 Northern Ireland (NI)

Sample Size

Estimated sample size is 200 patients.

This is based on a recent published review of England and Wales Badgernet National Neonatal Research Database (NNRD) data from 2020-2021[2] where 134 babies born at 22+0-22+6 were admitted alive to a neonatal unit. MBRRACE 2016 data showed there were 290 live births in England and Wales in one year (prior to change in guidelines). Including Scotland and NI but not attending all live births gives this estimate.

Rationale for study design

Whilst the National Neonatal Research Database[8] (in which variables are derived from the patient's electronic patient record), provides key daily levels of support example respiratory support, feeding, and key outcomes, it does not hold granular data such as details of antenatal counselling, the amount of humidity in the incubator, skin integrity, how much oxygen the baby is in, and how decisions around redirection of care were made. Recent (unpublished) UK data show that most of the babies who do not survive their admission, die within the first 7 days of life, which is why the first week of life will be the main focus with daily data collection. Those who survive beyond this will have data collected on a weekly basis to death or discharge (or at 44 weeks CGA).

The data categories to be collected have been drawn from reviewing the international literature,[3-6, 9-12] standardised neonatal reporting outcomes and experience of the steering group.

The study is not powered to detect any statistically significant differences, particularly with the likelihood of small numbers within the survival to discharge group.

**3.1.** STUDY OUTCOME MEASURES

See primary and secondary objectives with outcome measures above also.

End of study for each participant is either death or discharge.

Data Collection. Data points to be collected – see Appendix 3

Data to be collected:

1. Demographic categories: gestational age at birth, birth weight, sex, plurality (single, twin, triplet), ethnic group, geographical region, time period of birth (day/night/week/weekend), inborn/ outborn (where), if transferred after birth.
2. Counselling – was counselling completed, location, joint with obstetrics, any remote counselling, grade of counsellor, gestational age at counselling, fetal information available when counselled (in relation to the BAPM guidance risk factors), antenatal decision for survival focused or comfort care, any palliative or bereavement care team involved.
3. Pregnancy and perinatal optimisation: antenatal steroid course and when given, magnesium sulphate, antibiotics, delayed cord clamping at delivery, any pregnancy or maternal health issues, rupture of membranes, indication for delivery, mode of delivery.
4. Delivery stabilisation:
    a. Primary management provided (survival focused care, comfort care) of team at delivery, if consultant present
    b. Airway - non-invasive ventilation and pressures, attempts at intubation, size and brand of endotracheal tube (ETT), experience of intubator (as per BAPM airway guidance)[13]
    c. Respiratory – dose of surfactant, if given pre or post chest xray for position check, access to volume ventilation, any pneumothorax, needle thoracocentesis or chest drain required
    d. Cardiovascular – chest compressions given, central access on delivery suite, any emergency drugs given, any emergency blood given
    e. Thermoregulation - thermal control on delivery suite
    f. Family – delivery room cuddles and summary of parental discussion
    g. Outcome – admitted to NICU, unsuccessful resuscitation or comfort care
5. First 24 hours:
    a. Airway – ETT fixation, any unplanned or planned extubation, ETT change, videolaryngoscope use, any barriers or difficulties.
    b. Respiratory – dose of any surfactant, ventilation mode, maximum oxygen requirement, pneumothorax, chest drain, inhaled nitric oxide, steroid dosing and reason, suction catheter use.
    c. Cardiovascular – fluid bolus, inotropes, reason, echocardiogram findings, patent ductus arteriosus (PDA) treatment.
    d. Neurological – cranial ultrasound (CRUSS), results, any sedation or relaxant, nursed in midline, nest.
    e. Fluids –total fluid commenced, PN, time to start PN, hypoglycaemia, any insulin, any bicarbonate (how), flushes (type of fluid and if recorded), maximum sodium level, if weight performed daily, size of Nasogastric tube

f. Nutrition/ GI –probiotics, any milk (type), time to enteral feeding, increase protocol, bowels open, glycerine chip given, any fortifier added
g. Surgical – surgical consultation or any operation, diagnosis, management
h. Renal - urine output over 24 hours, maximum creatinine level, any hyperkalaemia management
i. Venous Access/ Lines – peripheral line, central line(s), sizes, mechanism of position checking, skin preparation, difficulties
j. Infection – antibiotics, anti-fungal prophylaxis, anti-fungal treatment, any positive blood culture (organisms), colonisation
k. Haematology – clotting checked, any clotting products, packed red cell transfusion, platelets and results/ reason
l. Skin and Thermal Management – incubator or open with radiant heater, level of incubator humidity, any skin concerns and management, site, any precipitant.
m. Monitoring – saturations, ECG leads, transcutaneous CO2, end tidal CO2, arterial line blood pressure, non-invasive blood pressure cuff, temperature probe
n. Family – seen baby, any skin to skin, any discussion about reorientation or parallel planning.
o. Other - comments

6. The main same data categories plus growth parameters will then be collected on a daily basis until day 7 of life or death, whichever is earlier
7. Following this, data will be collected on a weekly basis until death, discharge or 44 weeks, whichever is sooner. Additional data includes any specialist review input or tests.
8. An outcome form at discharge from neonatal care or death will include:
    a. Length of stay
    b. Discharge – death, transfer to other hospital, home
    c. Corrected gestational age in completed weeks
    d. If survival co-morbidities
        i. Chronic lung disease at 36 weeks, nasal cannula oxygen amount, non-invasive ventilation, ventilated, tracheostomy
        ii. Retinopathy of prematurity, laser treatment, intravitreal injection
        iii. Brain abnormalities – periventricular leucomalacia (PVL), intraventricular haemorrhage (IVH) grade 3/4, PHVD any reservoir or ventriculoperitoneal shunt for hydrocephalus
        iv. Necrotising enterocolitis or SIP requiring surgery, stoma closed or open, on PN
        v. Patient ductus arteriosus, surgical ligation
        vi. Late-onset sepsis (organism)
9. If baby dies, outcome questions include:
    a. Cause of death
    b. If care re-orientated prior to death and reason
    c. If active acute resuscitation was undertaken/ unsuccessful prior to death

Unit Questionnaire

There will also be a unit questionnaire (Appendix 4) completed once at the beginning of the study to ascertain unit protocols, any guidance available, equipment availability and challenges and set up of the department including staffing.

Some units may voluntarily review routinely recorded data in terms of number of live births and admissions at 22 weeks gestation in the timeframe they run the study to review their own patterns of practice. The overall numbers may be shared with the study investigators to review numbers of babies eligible but missed by recruitment and the proportions of babies admitted. This can be accessed by individual units through their maternity records but only aggregate numbers will be required. This will be uploaded onto REDCap. The proportions admitted will help to reflect variation in counselling and patterns of practice in terms of providing survival focused or comfort care. It will support primary objective 1 and exploration of practice variation.

## 4. PARTICIPANT ENTRY

### 4.1. PRE-REGISTRATION EVALUATIONS

Participant Identification

Babies born at 22+0-22+6 will be identified through clinical team recording attendance and informing the data collection members of the team. Hospital electronic patient systems should also be checked 1-2 times per week for admissions.

Once patient is identified, data will be then collected daily from Patient Records (electronic or paper) contemporaneously by a member of the local study team and entered into the REDCap system under the patient's study number.

### 4.2. INCLUSION CRITERIA

Inclusion criteria

- Born at 22+0-22+6 gestation at site with Neonatal Intensive Care Units (NICU) with neonatal team in attendance
- Born at 22+0-22+6 gestation and admitted alive to a NICU centre (outborn)
- Born in 12-month period from the study start date

### 4.3. EXCLUSION CRITERIA

Exclusion criteria

- Babies ≥23+0
- 22+0-22+6 who died in LNU/ SCBU prior to transfer to NICU
- 22+0-22+6 without neonatal team in attendance at NICU
- Babies with congenital anomalies

### 4.4. WITHDRAWAL CRITERIA

Parents have the right to withdraw from the study by contacting their direct care local NICU team or research team.

## 5. ASSESSMENT AND FOLLOW-UP

Final outcome data will be input at death or discharge from neonatal care.

## 6. STATISTICS AND DATA ANALYSIS

Data and all appropriate documentation will be stored for a minimum of 10 years after the completion of the study.

Data Analysis

Data will be analysed from the de-identified pooled data in REDCap, using Microsoft Excel. Categorical data will be analysed using standard statistical methods using proportions and percentages of the total. Continuous data will be analysed using mean, median, range and interquartile ranges. Tests of difference (t-test, chi squared) may be utilised. A funnel plot will be used for regional differences in survival.

Collection Tool

REDCap tool (Imperial)

Once eligibility has been confirmed, de-identified data will be entered directly onto the study database in REDCap by 2-3 study collaborators at participating NHS hospital sites. REDCap is a password-protected, secure, web-based software platform designed to support data capture of single and multi-site studies.

A local lead will keep a record of patient identifiable information and maintain it within the hospital trust. Each data entry will receive a unique ID number specific to the study in REDCap, available to the local team. Each participating hospital will have access only to its own patients from the database, allowing validation of the correct patient and extra information to be added to a patient record if becomes available. REDCap will only contain the de-identified information and no protected information will be shared outside of the hospital trust.

If a patient moves between NHS trusts for clinical care reasons, the transferring team can make the REDCap data manager aware using the REDCap ID number and inputting access can be changed to the current treating team. If a patient is transferred outside of the participating hospitals, then it will be the responsibility of the team at the transferring NICU to record any follow up or final form(s).

The online database has been designed to allow sites to securely access an individual patient's data for all the Case Record Forms (CRFs) throughout the study period. This means that any missing or erroneous data can be altered by the local investigators whilst the data collection period is ongoing. In order to maximise data completion and emphasise its importance to collaborators participating centres with >5% missing data in mandatory fields (i.e. <95% data completeness) will be excluded from the study.

Imperial administrators will oversee password allocation and data manager with oversee access limitations to those on the study teams (local and national).

The main study team will have access to the REDCap pooled data for analysis.

Data Security

Data management and data security will abide by the requirements of the General Data Protection Regulations (GDPR) and any subsequent amendments. The study will be conducted at collaborating sites in accordance with the country-specific data protection requirements. Data will be acquired and stored on the REDCap platform. Access to the data will be restricted, each individual collaborator entering data for the study will have their own username and password. Each participant will be allocated a unique study number at entry. All communication will use this as the identifier. All data will be analysed and reported in summary format.

No identifiable patient information will be held.

Any local participant information should be kept on a password-protected NHS computer server. Any downloaded summary data will be held on NHS computers and password protected where applicable. Data will be maintained at Imperial in and kept in line with data standards for 10 years.

## 7. REGULATORY ISSUES

### 7.1. ETHICS APPROVAL

The Study Coordination Centre has obtained approval from the 25/PR/0089 Research Ethics Committee (REC) and Health Research Authority (HRA). The study must also receive confirmation of capacity and capability from each participating NHS Trust before accepting participants into the study or any research activity is carried out. The study will be conducted in accordance with the recommendations for physicians involved in research on human subjects adopted by the 18th World Medical Assembly, Helsinki 1964 and later revisions.

### 7.2. CONSENT

This is a prospective study using pseudonymised, routinely recorded, clinical data. There will be no direct contact with patients. and therefore, no consent is required. No changes to management will occur as a result of the study. No extra data other than what is within clinical records will be needed.

However, to aid understanding, a patient information leaflet will be available for parents to outline why and how their baby's clinical data is being analysed, and will be given by the team looking after the family.

The patient information leaflet can be found in Appendix 5 and has been reviewed by a parent of an extreme preterm baby.

### 7.3. CONFIDENTIALITY

The Chief Investigator will preserve the confidentiality of participants taking part in the study and is registered under the Data Protection Act.

Data will be pseudonymised. Data will be inputted to REDCap and managed by study team.

Where data set numbers are small or contain unusual detail that may identify an individual, data will be pooled to report e.g. in regions or reported as below the number able to report.

**7.4.** INDEMNITY

Imperial College London holds negligent harm and non-negligent harm insurance policies which apply to this study.

**7.5.** SPONSOR

Imperial College London will act as the main Sponsor for this study. Delegated responsibilities will be assigned to the NHS trusts taking part in this study.

**7.6.** FUNDING

This study is supported by Chelsea and Westminster NHS Trust.

REDCap payment will be from the NIHR Advance Fellowship awarded to Dr Cheryl Battersby. Funding for staff role is from Chelsea and Westminster NHS Trust.

**7.7.** AUDITS

The study may be subject to audit by Imperial College London/ Imperial College Healthcare NHS Trust under their remit as sponsor and other regulatory bodies to ensure adherence to GCP and the UK Policy Frame Work for Health and Social Care Research.

## 8. STUDY MANAGEMENT

The day-to-day management of the study will be co-ordinated through the CI and study group.

The Chief investigator will be responsible for producing all relevant reports/documents required and submit them to relevant bodies.

For any amendment to the study, the Chief Investigator or designee, in agreement with the sponsor will submit information to the appropriate body for them to issue approval for the amendment.

Research & Development (R&D)/ Research and Innovation (R&I)

All participating sites should give confirmation of capacity and capability.

Protocol compliance

The following arrangements for monitoring and auditing the conduct of the research will be in place:

1. Regular meetings will be organised between the CI, study co-ordinator and the study investigators

2. REDCap will be reviewed regularly to ensure data being collected is sufficient and does not contain extraneous information

## 9. PUBLICATION POLICY

Once complete, a final study report will be prepared.

Results of the study will be reported and disseminated through

- Publication in peer-reviewed journal
- Conference presentations
- Other educational presentations and talks
- Any other publication

Authorship

Authorship will correspond to the guidelines set out by ICMJE.

All investigators involved in the study will be acknowledged in any publication with roles clearly described. All will have the opportunity to review and revise any report or publication prior to submission. Any conflicts of interest must be declared.

## 10. REFERENCES

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**APPENDICES**

Appendix 1

Clinical outcome reporting plan

Appendix 2

Neonatal Intensive Care Units and Geographical Region

Appendix 3

Data collection points

Appendix 4

Unit questionnaire

Appendix 5

Parent information leaflet

**Appendix 1a - Clinical area outcomes to be reported**
**Overall outcomes**
**Sub-groups by baby characteristics and by network**

**Delivery Room**
**Proportion of infants receiving:**

- Delayed cord clamping
  - Length of time (median, range)
- Cardiac compressions
- Drugs
- Delivery room cuddles

**Time (median) to:**

- Time to intubation – to first attempt and to successful attempt
- Time to first dose of surfactant

Number of intubation attempts and size for each (2mm or 2.5mm endotracheal tube)

- Grade of intubator (airway BAPM guidance) for each
- Proportion using video or direct laryngoscopy

**Respiratory**
Proportion of infants with any unplanned extubations
Median time to first planned extubation attempt
Median number of doses of surfactant given, median and ranges of age of administration
Proportion of infants commenced on different modes of ventilation (HFOV +/-VG, conventional with VG, pressure ventilation), levels of PEEP
Maximum fractional inspired oxygen
Proportion receiving any inhaled nitric oxide
Proportion of infants experiencing a pneumothorax, having chest drain inserted
Proportion of infants receiving postnatal steroids, which most frequently used, clinical reason (hypotension, respiratory rescue, CLD prophylaxis)

**Cardiovascular**
Proportion of infants receiving fluid bolus and types
Proportion of infants receiving inotropic support – which inotrope, reasons for starting
Proportion of infants having had echo, timing of echo and proportion influencing management
Proportion of infants receiving treatment for PDA, which medication (paracetamol, ibuprofen)

**Neurological**
Proportion of infants with abnormalities on cranial ultrasound (initial acute phase)
Proportion of infants receiving any sedation, relaxant, sub-divide into routine sedation and reasons for starting (pain, ventilatory requirements)
Proportion nursed in midline for first 72 hours

**Fluids and Feeds**
Median volume of fluid commenced on
Median age (in hours) when parenteral nutrition (PN) started
Median age when enteral feeding commenced including colostrum

Median age when enteral feeds began to increase
Proportions of types of milk used (MEBM, DEBM, formula)
Proportion of infants receiving fortifier
Proportion of infants receiving probiotics
Proportion of infants receiving insulin
Proportion of infants receiving 0.9% sodium chloride or 0.45% sodium chloride flushes
Proportion receiving bicarbonate and types of administration (routine, UAC, half or full correction) and indications
Median time to first spontaneous bowel opening
Proportions receiving glycerine suppositories and frequencies, median time to GS

**Surgical**
Proportion of infants requiring surgical consultation
Proportion of infants receiving surgical intervention
Frequency of causes and interventions
Median age and weight when surgical intervention occurred

**Renal**
Median urine output daily over first week
Maximum creatinine levels daily over first week
Proportion requiring hyperkalaemia management

**Lines/Access**
Proportion of infants having IV cannula before central access gained
Proportion of umbilical line attempt success
Proportion with long lines inserted
Frequency of sizes and type of UVC (single or double lumen) or long line

**Infection**
Proportion of infants receiving antibiotics in first week then frequency of courses throughout stay
Proportion of infants receiving routine anti-fungal prophylaxis or treatment
Proportion of infants with any positive colonisation results (and organisms)
Proportion of infants with any positive cultures (blood, CSF, urine)

**Haematology**
Proportion of infants with clotting checked routinely within first 24 hours
Proportion of infants receiving clotting products, frequency of indications
Proportion of infants receiving packed red cells, indications
Proportion of infants receiving platelet transfusion, indications

**Skin Integrity and Thermal Management**
Proportion of infants nursed in incubator
Median level of humidity in incubator
Proportion with compromised skin integrity and median timing first noted
Frequency of site affected, types of skin management and any precipitant

**Monitoring**
Proportion of infants with saturation monitor on
Proportion of infants with temperature probe on

Proportion of infants with transcutaneous CO2 monitors on
Proportion of infants with ECG leads on
For all, if not at admission, median age at which monitoring started

**Family**
Proportion on infants receiving skin-to-skin in each week of life, median time to first skin-to-skin
Proportion and timing of conversations of re-orientation of care or parallel planning

(Where median reported, range will also be reported)

**Weekly Data – additional outcomes**
Median number of postnatal steroid courses
Median length of time ventilated
Median time to full enteral feeds
Median time to removal of initial central lines
Frequency of other healthcare professional specialist input and types
Proportion of infants requiring surgical vascular access
Measurement of growth parameters

**Outcomes if Baby Dies**

1. Median age at death (day of life)
2. Frequencies of causes of death
3. Proportion where care was re-orientated prior to death?
   Reason/detail
4. Proportion where there was acute active resuscitation that was unsuccessful at time of death?
   Reason/detail

**Outcomes if Baby Survives**

1. Proportion discharged to home, other hospital, still in NICU at 44 weeks
2. Proportions of infants with chronic lung disease at 36 weeks, ROP requiring treatment, NEC requiring surgery, IVH grade 3 or 4 or PVL, hydrocephalus requiring shunt or reservoir, PDA requiring ligation, late onset sepsis
3. Proportions requiring PN and enteral feeding types at discharge

All – median length of stay

Appendix 2
Neonatal Intensive Care Units and Geographical Region

| Location | Contact |
|---|---|
| **Scotland** | |
| Aberdeen Maternity Hospital, Aberdeen | |
| Simpson Centre for Reproductive Health, Edinburgh | |
| Royal Hospital for Children, Queen Elizabeth University Hospital, Glasgow | |
| Ninewells Hospital, Dundee | |
| University Hospital Wishaw, NHS Lanarkshire | |
| **Northern Ireland** | |
| Royal Maternity Hospital, Belfast | |
| **Wales** | |
| Singleton Hospital, Swansea | |
| University Hospital of Wales, Cardiff | |
| Grange University Hospital, Wales (Aneurin Bevan) | |
| **England** | |
| North-East | |
| Royal Victoria Infirmary, Newcastle | |
| Sunderland Royal Hospital, Sunderland | |
| James Cook University Hospital, Teeside | |
| Yorkshire | |
| Hull Royal Infirmary | |
| Leeds Neonatal Service | |
| Bradford Royal Infirmary | |
| The Jessop Wing, Sheffield | |
| North West | |
| Royal Preston Hospital (Lancashire Teaching Hospitals NHS Trust) | |
| Lancashire Women & Newborn Centre, Burnley | |

| | |
|---|---|
| (East Lancashire NHS Trust) | |
| Royal Bolton Hospital | |
| Royal Oldham Hospital<br>(Northern Care Alliance NHS Foundation Trust) | |
| St Mary's Hospital, Manchester<br>(Manchester University NHS Trust) | |
| Liverpool Women's Hospital | |
| Arrowe Park Hospital, Upton | |
| West Midlands | |
| Royal Stoke University Hospital, UHNM | |
| New Cross Hospital, Wolverhampton | |
| Birmingham Women's Hospital, BWC | |
| Birmingham Heartlands Hospital, UHB | |
| University Hospitals of Coventry & Warwickshire | |
| East Midlands | |
| Leicester Royal Hospital | |
| QMC, University Hospital Nottingham<br>(Nottingham University Hospitals Trust) | |
| Nottingham City Hospital<br>(Nottingham University Hospitals Trust) | |
| East of England | |
| Norfolk & Norwich University Hospitals | |
| Rosie Maternity Hospital Addenbrookes, Cambridge | |
| Luton & Dunstable Hospital<br>(Bedfordshire NHS Trust) | |
| Thames Valley & Wessex | |
| John Radcliffe Hospital, Oxford | |
| Princess Anne Hospital, Southampton | |
| Queen Alexandra Hospital, Portsmouth | |
| South-West | |
| Southmead, North Bristol NHS Trust | |

| | |
|---|---|
| St Michael's Hospital, Bristol, UHBW | |
| Derriford Hospital, Plymouth | |
| Kent, Surrey, Sussex | |
| Royal Sussex County Hospital, Brighton | |
| William Harvey Hospital, East Kent Hospitals University NHS Foundation Trust | |
| Medway Maritime Hospital, Gillingham | |
| Ashford & St Peter's Hospital, Chertsey | |
| London | |
| St George's University Hospital | |
| King's College Hospital | |
| Chelsea & Westminster Hospital | |
| Queen Charlotte and Chelsea Hospital | |
| Guy's & St Thomas' Hospital | |
| University College Hospital | |
| Royal London Hospital, Barts Health NHS Trust | |
| Homerton Hospital | |

Stand-alone neonatal surgical centres (without co-existing NICU)

- Alder Hey (Alder Hey NHS Trust)
- Birmingham Children's Hospital (Birmingham Women's and Children's NHS Trust)
- Sheffield Children's Hospital (Sheffield Children's Hospital NHS Trust)
- Great Ormond Street Children's Hospital (GOSH NHS Trust)