Re-Growth

Reassessing the growth of infants born below 32 weeks' gestation in the UK, 2014-2018

Version 5 DATE- 14/1/2020

SPONSOR: University Hospital Southampton NHS Foundation Trust

COORDINATING CENTRE: University Hospital Southampton NHS Foundation Trust- Neonatal Unit

Sponsor's protocol number
Ethics reference no:

Protocol authorised by Chief Investigator:

Name: Mark Johnson **Role:**

Signature: **Date:**

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PROJECT COORDINATION CENTRE

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STUDY SITES

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SPONSOR

University Hospital Southampton NHS Foundation Trust is the research sponsor for this project. For further information regarding sponsorship conditions, please contact the Director of Research and Development at:

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SGH - Level E, Laboratory & Pathology Block,
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NURSING CONTACT DETAILS:
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FUNDER
NIHR BIOMEDICAL RESEARCH CENTRE SOUTHAMPTON, NUTRITION THEME
(DETAILS AS ABOVE)

Protocol Information
This protocol describes the above project and provides information about procedures for obtaining and analysing data. Corrections or amendments may be necessary. These will be circulated to investigators in the project, but please contact the NIHR Southampton Biomedical Research Centre clinical project coordinator to confirm you have the most recent version.

Compliance
This project will adhere to the principles outlined in the International Conference on Harmonisation Good Clinical Practice (ICH GCP) guidelines. It is subject to research ethics committee approvals and will be conducted in compliance with the protocol, the Data Protection Act and all other regulatory requirements, as appropriate.

TABLE OF CONTENTS

LIST OF ABBREVIATIONS

A list of the abbreviations, and lists and definitions of specialized or unusual terms or measurement units used in the report should be provided. Abbreviated terms should be spelled out and the abbreviation indicated in parentheses at first appearance in the text

BRC	Biomedical Research Centre
CGA	Corrected Gestational Age
GA	Gestational Age
LNU	Local Neonatal Unit
NICU	Neonatal Intensive Care Unit
NNRD	National Neonatal Research Database
NDAU	Neonatal Data Analysis Unit
NHS	National Health Service
NHSFT	National Health Service Foundation Trust
NIHR	National Institute for Health Research
RCPCH	Royal College of Paediatrics and Child Health
REC	Research Ethics Committee
SCBU	Special Care Baby Unit
SITAR	SuperImposition by Translation and Rotation

Keywords-

Preterm, Growth, Weight, Head circumference, Length, Nutrition

PROJECT SYNOPSIS

A brief synopsis (usually limited to three pages) that summarises the study should be provided. The synopsis should include numerical data to illustrate results, not just text or p-values.

Full title:	Reassessing the growth of infants born below 32 weeks' gestation in the UK, 2014-2018
Sponsor:	University Hospital Southampton NHSFT
Sponsor Ref No:	CHI1013
Chief Investigator	Mark Johnson
Study phase if not mentioned in title	
Funder:	NIHR BRC Southampton
Eudract No:	N/A
REC No:	Awaited
Project Type:	Study limited to working with data (as defined by IRAS)
Primary Objective:	To reassess the early growth pattern of very preterm infants born in the UK.
Rationale:	1. Early growth of infants born below 32 weeks' gestation has been previously described and has demonstrated that preterm infants routinely lose weight during their first week of life and do not regain their birth centile (or z-score) by the time they reach term corrected age [1]. 2. Recent data suggests that the pattern of growth described in this study is not inevitable and that improved growth can be achieved [2]. 3. A dataset of all preterm births in the UK is recorded on the National Neonatal Research Database (NNRD) held by the Neonatal Data Analysis Unit (NDAU) (managed by Imperial College London for the Royal Society of Paediatrics and Child Health)[3]. This database records data covering many aspects of neonatal care, including a comprehensive record of patient demographics/characteristics, growth, nutritional inputs and longer term outcomes 4. This study will use the NNRD to describe the current pattern of early growth of very preterm infants on a national level using similar methods to those described by *Cole et al.*[1] It will look at variations in growth at a regional level and in relation to the level of care offered by neonatal units. 5. This study will also integrate data regarding nutritional care from the NNRD to assess associations between nutrition and growth, and two-year follow-up data to assess associations between early growth and subsequent growth and development.
Project Design:	Database review project
Inclusion Criteria:	1. Infant born in England below 32^{+0} weeks gestational age.

	2. Infant admitted to a neonatal unit in England reporting to the National Neonatal Research Database.
Exclusion Criteria:	1. Consent for inclusion not obtained from reporting neonatal unit.
Total No. of Sites:	1
Study Duration	12 months
Data collection	Data to be supplied by NDAU according to their application processes. Application supplied as Appendix 2.
Biological samples	None
Number of Participants	
Primary endpoint	Data analysis completed.
Secondary endpoint	Publication of data in a peer-reviewed journal.
Statistical Methods:	Core data to be analysed using the superimposition by translation and rotation (SITAR) model and LMS methods as previously described[4]. Additional data analysis will be performed using linear regression with mixed modelling.

1. INTRODUCTION

1.1. BACKGROUND INFORMATION

Preterm infants, particularly those born below 32 weeks gestation, are at risk of early growth failure[5]. This is important because there is evidence that patterns of growth in early life have an impact on the risk of non-communicable disease in later life[6 7], and also some evidence that growth in the neonatal period influences subsequent development in childhood[8]. Their growth pattern has been characterised by significant weight loss within the first week of life, followed by weight gain which fails to result in growth sufficient for them to attain the weight, head circumference and length upon reaching term corrected gestational age (CGA) that they would have achieved if they had continued to follow the growth trajectory on which they were on at the time of their premature birth. This means that, when potted on a UK-Newborn Infant Close Monitoring (NICM) growth chart, they fall down several marked centile lines and then follow a pattern that is slightly divergent from that of the marked centiles lines. Mathematically this is represented by a fall in their standard deviation score (SDS, also called a z-score) for weight, length and head circumference between birth and term CGA compared to reference population data. This pattern was described in a seminal paper more than five years ago[1]. This group used SITAR, a novel statistical method, to assess and describe growth curves which they had developed[4].

There is however continuing uncertainty about the optimal growth pattern of infants born very preterm as it relates to this later growth and development. Since 2011 (the latest year included in Cole's study) there has been ongoing interest in increasing the quality and quantity of nutrition which is received by very preterm infants. Recent work has shown that the previously described fall in weight z-score is not inevitable, using data from one neonatal unit[2]. It is not known whether this is due to specific nutritional practices in that particular neonatal unit, or whether this is the result of more widespread changes in nutritional care and the resulting growth patterns of very preterm infants across the country since Cole's study. Therefore, it is not known whether this change will be confirmed in other settings

The National Neonatal Research Database (NNRD) comprises a large dataset concerning all infants admitted to neonatal units in the UK. It is held by the Neonatal Data Analysis Unit (NDAU) (part of Imperial College London) on behalf of the Royal College of Paediatrics and Child Health (RCPCH)[3]. This database is approved by a REC and is an approved NHS Information Standard (ISB1575). Access to the data for research purposes requires specific REC approval and consent from each contributing neonatal unit. Among its data fields[9], the NNRD contains data defining the baseline characteristics of infants (e.g. gestation, weight and head circumference at birth) along with longitudinal data describing their stay on the neonatal unit (e.g. weight, length and head circumference measured throughout their admission). It also records data describing their nutritional intake during each day of their admission and their weight and development at two years CGA.

1.2. STUDY SCHEDULE

MONTHS	0-6	6-9	9-12
Ethical approval, approval from all NDAU sites, acquiring data from NNRD	X		
Data Analysis		X	X
Writing Up			X

2. STUDY OBJECTIVES AND PURPOSE

2.1. AIM

1. To characterise the growth patterns of very preterm and extremely preterm infants born in the UK between 2014 and 2018, and to look at variations in growth at a regional level and in relation to the level of care offered by neonatal units(NICU/SCU/LNU[10])
2. To assess the association between nutritional practices unit and growth and in the neonatal period.
3. To assess for associations between neonatal growth and subsequent growth and development as measured at a CGA of two years.

2.2. STUDY DESIGN

- A required dataset has been drawn up using the list (data dictionary) of all NNRD data fields [11] and is included as Appendix 1. In summary, this will provide anonymised data describing the infant's baseline characteristics, markers of comorbidities, the type of neonatal unit providing care, the region of the country, growth, nutritional intake and growth and developmental status at two years CGA. The National Neonatal Research Database is a Clinical Dataset (The National Neonatal Data Set) within the NHS Data Dictionary. Details of all data items are searchable at the following webpage: http://www.datadictionary.nhs.uk/data_dictionary/messages/clinical_data_sets/data_sets/national_neonatal_data_set/national_neonatal_data_set_-_episodic_and_daily_care_fr.asp?shownav=1"
- A request for this information will be submitted to NDAU using their application form (Appendix 2).
- Local REC approval is required.
- Each contributing neonatal unit will need to consent to our using their data and this will be facilitated by NDAU (as per item 5 in [12]).

Primary Data

- The primary data analysis will be a description of the growth pattern of very preterm and extremely preterm infants using the SITAR method. This will require baseline characteristics of sex and GA at birth, and longitudinal measurements of weight during the neonatal care episode. Longitudinal growth curves for each gestational age group (by weeks of completed gestation age at birth) will be generated and overlaid on the existing NICM chart for comparison. These analyses will be carried out at both a national level and by regional level (neonatal networks) and in relation to the type of neonatal unit and level of care offered (SCBU/LNU/NICU).

Secondary Data

- Regression analysis will be performed to explore associations between nutritional care, type of neonatal unit and growth pattern.
- Regression analysis will be performed to assess for associations between neonatal growth and later growth and development as measured at two years CGA.

2.3. DEFINITION OF END OF PROJECT

The primary data collection will be complete when statistical analysis has been completed.

3. SELECTION AND WITHDRAWAL OF PARTICIPANTS

SUBJECT SELECTION

Subjects will consist of all infants delivered below 32 weeks GA and cared for on a neonatal unit in England in the period 2014-2018 (inclusive, 5 years total). Subjects will be excluded if the relevant neonatal unit does not consent to their inclusion. We anticipate approximately 5000 subjects.

3. STATISTICS AND DATA

- The SITAR method has been previously described[4] and used in this context[1]. It will be used to describe the growth patterns of infants stratified by GA at birth. This analysis is carried out in the R programming language. LMS methods may also be used[1].
- Standard mixed linear regression models will be applied to assess for associations (either using R or the Stata statistical analysis package).

4. SAFETY ASSESSMENTS

This study will use anonymised retrospective descriptive data and will not pose a safety risk to subjects.

5. STOPPING / DISCONTINUATION RULES

It is not anticipated that stopping or discontinuation will be required for this descriptive study which uses historical prospectively-collected data.

6. STUDY GOVERNANCE

6.1. ETHICAL CONSIDERATION

This study will not include any intervention. It uses anonymised prospectively collected descriptive data. NDAU will supply data from the NNRD in an anonymised form. Electronic patient data recorded

at participating neonatal units that collectively form the United Kingdom Neonatal Collaborative (UKNC) are transmitted to the NDAU to form the NNRD. In order to assess the type of neonatal unit providing care to the infant, we will be supplied with data which identifies the neonatal unit (NNRD/NDAU does not collect this information directly but it can be derived by cross-referencing with other sources). Data will be analysed stratified by type of neonatal unit and region but not by individual neonatal unit and individual units will not be identified in publications arising from this study. None of the information supplied will constitute patient-identifiable information as defined by the Caldicott Report[13].

The Chief Investigator will submit a final report at conclusion of the trial to the REC within the timelines defined in the Regulations.

6.2. INSURANCE AND INDEMNITY

The sponsor of the project is University Hospital Southampton NHS Foundation Trust (UHS). For NHS sponsored research HSG (96) 48 reference no.2 refers. If there is negligent harm during the clinical project when the NHS body owes a duty of care to the person harmed, NHS Indemnity covers NHS staff, medical academic staff with honorary contracts, and those conducting the project. NHS Indemnity does not offer no-fault compensation and is unable to agree in advance to pay compensation for non-negligent harm. Ex-gratia payments may be considered in the case of a claim.

6.3. SPONSOR

University Hospital Southampton NHS Foundation Trust is acting as Sponsor for this project. We will ensure that the study is compliant with submissions to regulatory authorities and GCP. Other delegated duties will be assigned to the NHS Trusts or others taking part in this project by means of the site clinical project agreement where appropriate.

6.4. FUNDING

No dedicated source of funding is sought for this project. Aneurin Young is funded as a research fellow by NIHR Southampton BRC.

6.5. MONITORING, AUDITS AND INSPECTIONS

This study will be monitored and may be participant to inspection and audit by UHS, under their remit as sponsor, the BRU as the Sponsor's delegate and other regulatory bodies to ensure adherence to ICH GCP, Research Governance Framework for Health and Social Care, applicable contracts/agreements and national regulations. All study related documents will be made available on request for monitoring and audit by UHS, the relevant REC or other licensing bodies.

7. DATA HANDLING AND RECORD KEEPING

Study documents (paper and electronic) will be collected and retained in accordance with the Data Protection Act 1998 in a secure location during and after the trial has finished. All essential documents will be retained for a minimum period of 5 years following the end of the study.

8. PUBLICATION POLICY

8.1. BACKGROUND

When submitting items for publication it is important for authors to acknowledge the organisations involved in the research. This acknowledgement assists with building the reputation of organisations making it more attractive to external bodies that are in a position to place future business and research funding with departments and individuals within Southampton.

The policy is provided to ensure authors identify the University of Southampton and University Hospital Southampton NHS Foundation Trust in a way that will increase the ability of search engines, routinely used by funders of research (e.g. by the RAND association and National Institute of Health Research), to identify publications from the Southampton partnership.

Specifically, this project will be performed in collaboration with the Neonatal Data Analysis Unit (NDAU) (Imperial College London and Chelsea and Westminster NHSN Foundation Trust) and with Professor Tim Cole (UCL GOS Institute of Child Health, University College London). These collaborators will be acknowledged as authors in resulting publications.

8.2. SCOPE

The policy applies to all staff and students whose research outputs from pre-clinical and clinical research derive from their employment by the University and/or Trust, from research grants awarded to the University and/or Trust or otherwise from the use of University and/or Trust resources and facilities. The policy applies to all authors of publications, and not simply to principal authors or reprint authors. Citing both organisations on all papers covered by this policy acknowledges the success of each organisation resulting from working in partnership.

8.3. POLICY

When submitting items for publication the Trust and University of Southampton require that affiliations and acknowledgements are included in the formats provided below.

Where any author has a substantive or honorary contract with the University of Southampton and/or the University Hospital Southampton NHS Foundation Trust both organisations must appear as affiliations in ALL submissions for publication.

8.4. REQUIRED FORMAT FOR AFFLIATIONS

8.4.1. AUTHOR'S AFFILIATION

National Institute for Health Research Biomedical Research Centre Southampton, University Hospital Southampton NHS Foundation Trust and University of Southampton

8.4.2. ADDITIONAL AFFILIATIONS

The University Faculty should be listed as the second affiliation where appropriate. Further affiliations of all authors should be listed using the appropriate form of words as given below:

- University of Southampton Faculty of Medicine (change Faculty as appropriate)
- Southampton Centre for Biomedical Research (SCBR)

8.4.3. ACKNOWLEDGMENTS

We will ensure acknowledgement of:

- Any sponsorship you have received for the research you are publishing. For grants, include the grant number and source.
- Names of individual staff that have supported the project that led to the publication as well as the relevant department using an appropriate title.
- The Neonatal Data Analysis Unit, together with all the families that agreed to the inclusion of their baby's data in the NNRD, and the health professionals who recorded data and the NDAU team.
- Professor Tim Cole (University College London)

8.5. OPEN ACCESS

The Department of Health and National Institute for Health Research has an Open Access Policy which affects all researchers who are funded (partly or wholly) by them. Resulting research papers that have been accepted for publication in a peer-reviewed journal should be deposited to UK PubMed Central (UKPMC) within six months.

For projects that are funded by DH/NIHR, Open Access costs should be budgeted for by the researcher. The Wellcome Trust, however, provides grant holders with additional funding to cover open access charges.

9. SUPPLEMENTS

Appendix 1 – Required items from the NNRD

Appendix 2 – Request form for NDAU for access to NNRD data

10. PROJECT MANAGEMENT

Dr M Johnson and Dr A Young are responsible for the day to day running and progress of this study. Prof RM Beattie will oversee progress and will act as the medical expert.

11. REFERENCES

1. Cole TJ, Statnikov Y, Santhakumaran S, et al. Birth weight and longitudinal growth in infants born below 32 weeks' gestation: a UK population study. Arch Dis Child Fetal Neonatal Ed 2014;99(1):F34-40.
2. Andrews ET, Ashton JJ, Pearson F, et al. Early postnatal growth failure in preterm infants is not inevitable. Arch Dis Child Fetal Neonatal Ed 2018.
3. Neonatal Data Analysis Unit. Neonatal Data Analysis Unit. Secondary Neonatal Data Analysis Unit 2019. https://www.imperial.ac.uk/neonatal-data-analysis-unit/about-us/.
4. Cole TJ, Donaldson MD, Ben-Shlomo Y. SITAR--a useful instrument for growth curve analysis. Int J Epidemiol 2010;39(6):1558-66.
5. Lee SM, Kim N, Namgung R, et al. Prediction of Postnatal Growth Failure among Very Low Birth Weight Infants. Sci Rep 2018;8(1):3729.
6. Barker DJ. The malnourished baby and infant. British medical bulletin 2001;60:69-88.
7. Barker DJ, Osmond C. Infant mortality, childhood nutrition, and ischaemic heart disease in England and Wales. Lancet (London, England) 1986;1(8489):1077-81.
8. Shah PS, Wong KY, Merko S, et al. Postnatal growth failure in preterm infants: ascertainment and relation to long-term outcome. J Perinat Med 2006;34(6):484-9.
9. Neonatal Data Analysis Unit. National Neonatal Dataset. In: London IC, ed. London, 2018.
10. Department of Health. Toolkit for High-Quality Neonatal Services, Section 3.8. London: Department of Health, 2009.
11. Utilising the NNRD. 2018. https://www.datadictionary.nhs.uk/data_dictionary/messages/clinical_data_sets/data_sets/national_neonatal_data_set/national_neonatal_data_set_-_episodic_and_daily_care_fr.asp?shownav=0 (accessed December 19).
12. Neonatal Data Analysis Unit. Utilising the NNRD. 2019.
13. The Caldicott Committee. Report on the Review of Patient-Identifiable Information London: Department of Health, 1997:149.

Appendix 1: Required Data from the NNRD

Selected Data Items

EPISODIC/BASELINE

AnonPatientID
DateTimeofBirthMonth
DateTimeofBirthYear
PlaceofBirthNHSCode
Birthweight
Birthlength
BirthHeadCircumference
GestationWeeks
GestationDays
SexPhenotype
SexGenotype
CriticalCareIdentifier
ProviderNHSCode
DischDateTimeAnonDate
DateofDeathAnonDate
ActiveDateAnonDate

DAILY GROWTH

DayProviderNHSCode
DayWorkingWeight
DayHeadCirc
DayLength

NUTRITION

ParenteralNutrition
GlucoseElectrolytes
DayEnteralFeed
DayFormulaType
Totalvolume

TWO-YEAR FOLLOW-UP

TwoYearAssessmentAnonDate
TwoYearDeathDateAnon
GrowthWeight
GrowthWeightDateAnon
GrowthLength
GrowthLengthDateAnon
GrowthHeadCirc
GrowthHeadCircDateAnon
DevelopmentNormal
DevelopmentMildDelay
DevelopmentModerateDelay
DevelopmentSevereDelay

ADDITIONAL DATA

PostCodeMotherLSOA
FetusTotal
apgar_1min
apgar_5min
apgar_10min
SurgicalProcedure
RespiratorySupport
ModeofRespiratorySupport
PulmonaryVasodilator
OygenPerc
Inotropesgiven
SurgeryforPDA
DayNEC
LinesIn

Appendix 2: Request form for NDAU for access to NNRD data

[See next page]

NNRD data extraction request form

The purpose of this form is to allow the Neonatal Data Analysis Unit (NDAU) to better understand the data you require; please enter as much information as you can

Applicant information:

NNRD reference number (if known)	
Applicant name	Aneurin Young
Applicant job title	Neonatal Nutrition Research Fellow
Email address	a.young@soton.ac.uk
Applicant telephone	07828065831
Affiliated organisation	University Hospital Southampton NHSFT University of Southampton

Chief Investigator information (required if different from applicant):

Chief Investigator name	Mark Johnson
Chief Investigator job title	Neonatal Consultant, Honorary Senior Clinical Lecturer
Chief Investigator Email address	m.johnson@soton.ac.uk
Chief Investigator telephone	023 8120 4643
Chief Investigator organisation	University Hospital Southampton NHSFT University of Southampton

General information

Project title	Reassessing growth in infants born below 32 weeks' gestation in the UK, 2014-2018
Date of application	1st August 2019
Is this a commercial or industry project?	YES ☐ NO ☒
Is this project	Research ☒ Quality improvement ☐ Service evaluation ☐ Other ☐ Audit ☐
What is your research question? **(no more than 5 lines)** Research projects please use PICOT format if appropriate	In preterm infants born <32 weeks gestation and cared for in neonatal units in England, how have advances in neonatal medicine and nutritonal care in the 5-year period since 2014 affected growth (weight, length and head circumference) between birth and discharge, and growth and neurodevelopment at 2 years.

P: patient I: Intervention C: comparator O: outcome T: timescale	
REC number (if available)	

Analysis

Brief purpose of analysis for which you need NNRD data	Postnatal growth of infants born below 32 weeks' gestation in England has been previously described (*Cole, Statnikov et al. 2014*) using NNRD data, showing a pattern of poor growth, with infants falling two marked centile lines on a UK NICM growth chart in the first two weeks of life. Recent work published by our unit has demonstrated that the pattern of growth failure previously demonstrated is not inevitable, and that growth similar to that seen in utero can be achieved. However, it is not clear whether this is due to specific practices within our neonatal unit, or in fact the result of more widespread changes in neonatal medicine and nutritional care that have occurred since *Cole et al*'s original study. This study will assess the distribution of birthweights and the patterns of weight gain using routinely-gathered data in infants born below 32 weeks' gestation in the 5 year period since 2014. Professor Tim Cole (UCL) will act as a collaborator. In particular, we are interested in regional variations in patterns of growth, and those due to the level of care offered by neonatal units. We will also assess the associated changes in length and head circumference. Feeding data will be used to assess associations with the type of neonatal unit and the mode of feeding and related variables on growth. Additionally, we will use two-year follow-up data to assess associations between growth in the neonatal period and subsequent growth and development. This study will provide important information about the current impact of neonatal care on growth and subsequent outcomes. It will also help identify practices that are associated with improved growth. In addition, if it demonstrates the improved growth seen in our unit over the past 5 years is due to specific practices, we can share these more widely to help other units achieve similar growth.

Patient cohort: Please describe the infants that you would like data extracted for

Cohort Please describe the cohort that you are	All infants admitted to a neonatal unit in England following birth below 32 weeks' gestation.

interested in in no more than 5 lines	
Time period: Please state the start and end date for your cohort and whether these dates refer to admissions, discharges or other	Start date: 01/01/14 End date: 31/12/18 Infants admitted for neonatal care ☒ Infants discharged from neonatal care ☐ Other ☐ (please provide more detail below)
Geographic criteria: Please indicate which geographic areas you would like to receive data from, you can choose a whole nation or individual Operational Delivery Networks ** For Scottish Data an application must be made prior to data sharing to the PBPP	Whole NNRD ☐ National regions: England ☒ Wales* ☐ Scotland **☐ **Welsh data has been collected since 2012* ***Scottish data has been collected since 2015* If you only require data from individual networks within England then please choose from the list below: East of England ☐ Thames Valley & Wessex ☐ South East Coast ☐ South West ☐ Northern ☐ North West ☐ Trent ☐ Yorkshire ☐ SW Midlands ☐ Staffordshire/Shropshire/Black Country ☐ North East & Central London ☐ South London ☐ North West London ☐
Inclusion criteria: *e.g. Infants born at < 27 weeks; infants with a birthweight >1500g; infants with a diagnosis of Hirschprungs disease*	All infants born at <32 weeks' gestation
Exclusion criteria: *e.g. Infants who were admitted to Transitional care; infants with a congenital anomaly (you will need to define this); infants with missing gestational age at birth data*	None

NNRD data items & data format:

Data format: Please select if you will require your dataset to be at a patient level or if you require aggregated data	*If you are requesting patient level data for research, neonatal units will need to be contacted.* *Aggregated data refers to higher level grouped data where the counts or rates have already been calculated for you, usually presented in a table format.* Patient level ☒ Aggregated data ☐
Patient level data items: If you require patient level data please indicate which NNRD data items you will need in your dataset. ALL data items held in the NNRD are found here ALL diagnostic, procedural and treatment codes used in the NNRD are found here	AnonPatientID, DateTimeofBirthMonth, DateTimeofBirthYear, PlaceofBirthNHSCode, Birthweight , Birthlength , BirthHeadCircumference, GestationWeeks, GestationDays, SexPhenotype, SexGenotype, CriticalCareIdentifier, ProviderNHSCode, DischDateTimeAnonDate, DateofDeathAnonDate, ActiveDateAnonDate, DayProviderNHSCode, DayWorkingWeight, DayHeadCirc, DayLength, ParenteralNutrition, GlucoseElectrolytes, DayEnteralFeed, DayFormulaType, Totalvolume, TwoYearAssessmentAnonDate, TwoYearDeathDateAnon, GrowthWeight, GrowthWeightDateAnon, GrowthLength, GrowthLengthDateAnon, GrowthHeadCirc, GrowthHeadCircDateAnon, DevelopmentNormal, DevelopmentMildDelay, DevelopmentModerateDelay, DevelopmentSevereDelay, PostCodeMotherLSOA, FetusTotal, apgar_1min, apgar_5min, apgar_10min, SurgicalProcedure, RespiratorySupport, ModeofRespiratorySupport, PulmonaryVasodilator, OygenPerc, Inotropesgiven, SurgeryforPDA, DayNEC, LinesIn
Patient level derived data items: If you require additional data items to be derived please list and describe them here	None
Aggregated data items: If you require aggregated data please describe the features of the data set you would like describe	None
Method of aggregation: Please indicate how you would like the data aggregated (i.e. by geographical area)	

Denominator data: Do you need denominator data to describe you cohort within a wider context? E.g. total number of neonatal unit admissions over the same period

Denominator data required We cannot provide data on total number of live births, this is available from ONS	None ☒ Total neonatal unit admissions ☐ Total neonatal unit admissions by gestation ☐ • Gestation range: Total neonatal unit admissions by birth weight ☐ • Birthweight range: Other ☐ • Describe:
Descriptive variables for denominator data These will be provided as standard summary measures (e.g. means and standard deviation)	Gestation at birth ☐ Birthweight ☐ Other

Dissemination: Please specify how you will disseminate the outcome of your project after analysis is complete	The intention is to publish in a peer-reviewed journal and/or present at appropriate conferences

How did you hear about the NNRD?	A colleague/collaborator ☒ Another research article ☐ A talk or presentation ☐ Social media ☐ NNRD website ☐ Other (please describe):