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Timing of Stoma Closure in Neonates in England and Wales: 2014-2019

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MAIN SPONSOR: Manchester University

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1 INTRODUCTION

1.1 Background

Some babies require emergency abdominal surgery in the first few months of life. This may be because they developed necrotising enterocolitis or were born with a congenital blockage of the bowel. As part of this surgery, the ends of the bowel may be brought to the skin surface (called a stoma) to divert stool into a bag. The stoma allows time for the bowel to rest and recover and is intended to be temporary. The best time to reverse or "close" the stoma is unknown and is an area of controversy and limited data. Current practice is based on surgeon's preference or local protocols but is not evidence based. Some clinicians prefer earlier closure because stomas may cause dehydration, poor growth and skin problems; whilst some clinicians advocate for later closure when an infant is bigger.

The ideal way to find out which approach is better, is to conduct a study in which babies are randomly assigned to 'early' or 'late' stoma closure, and then compare the outcomes. However, to design such a 'clinical trial' needs careful planning.

This study is part of an NIHR funded pilot study *Timing of Stoma Closure in Neonates (ToSCiN) Study* https://www.fundingawards.nihr.ac.uk/award/NIHR128617 to help determine whether such a trial would be feasible.

The aim of this component of the *Timing of Stoma Closure in Neonates (ToSCiN) Study* is to use data from an already established database, the UK National Neonatal Research Database (NNRD) to help understand current practices and factors associated with timing of stoma closure. This information will help determine feasibility and design of a trial.

1.2 STUDY OBJECTIVES

The aim is to describe the timing of stoma closure in babies and investigate factors associated with timing of stoma closure in England and Wales, 2014-2019

We will:

i) Determine the number of babies who had a stoma and were cared for on a neonatal unit

ii) Describe the following, in a population of babies who had a stoma formed and were cared for on a neonatal unit:
   a. Background characteristics (e.g. gestation, gender, weight)
   b. Indication for stoma and other underlying diagnoses/comorbidities
   c. Postnatal age at formation of stoma
   d. Timing (days from operation) of stoma reversal (if occurred during neonatal stay) or whether discharged with stoma.

iii) Determine overall clinical status (e.g. respiratory support, inotropes, infection, enteral feeding, parenteral nutrition), growth parameters at the time of stoma formation

iv) Describe the outcomes of babies at the point of discharge from neonatal care (whether with stoma or reversed)

v) Identify clinical factors (e.g. respiratory support, inotropes, infection, enteral feeding, parenteral nutrition) and growth parameters associated with timing of stoma closure

This information above will help inform the design of a future trial by:

i) Identify current practice in relation to “early” and “later” time periods for stoma closure
ii) Estimate the number of eligible infants looked after on neonatal units
iii) Identify factors associated with an early or late closure
iv) Calculate the incidence of outcomes likely to be important for a future trial to inform sample size
v) Determine the feasibility of using national databases to gather require information for a potential trial

2 STUDY DESIGN

This is a retrospective study using data from the National Neonatal Research Database (NNRD). We will extract pseudo-anonymised data for babies born and admitted to neonatal units in England and Wales over a six year period between 2014 and 2019 inclusive. Data for babies with a stoma will be verified with host centres.

2.1 STUDY OUTCOME MEASURES

The primary outcome of the study is time to stoma closure defined as days from initial stoma formation.

A baby will be identified as having a stoma if one or more daily data indicate a stoma is present, and other diagnoses and daily data are consistent.

For the babies with a stoma, we will determine the following outcomes:

- Survival
- Length of hospital stay
- Duration of parenteral nutrition (PN)
- Time to full enteral feeds (defined as not receiving parenteral nutrition or IV fluid for 3 consecutive days)
- Growth
- Complications of surgery
- Days of invasive ventilation post-operatively
- Sepsis
- Necrotising enterocolitis
- Chronic lung disease/bronchopulmonary dysplasia (preterm only)
- Brain injury on imaging
- Retinopathy of prematurity (preterm only)

2.2 Data source

The NNRD holds data from all babies admitted to National Health Service (NHS) neonatal units in England, Scotland and Wales (approximately 80,000 babies annually; 8,000 less than 32 weeks gestation); all NHS neonatal units in England and Wales have been contributing data to the NNRD since 2012.

Contributing neonatal units are known as the UK Neonatal Collaborative (UKNC). Data are extracted from point-of-care neonatal electronic health records completed by health professionals during routine clinical care. A defined data extract, the Neonatal Dataset of approximately 450 data items (1), is transmitted quarterly to the Neonatal Data Analysis Unit at Imperial College London and Chelsea and Westminster NHS Foundation Trust where patient episodes across different hospitals are linked and data are cleaned (queries about discrepancies and implausible data configurations are fed back to health professionals and rectified) (2). Data items include demographic and admission items (e.g. maternal conditions, gestation, birth weight), daily items (e.g. respiratory support, medication, surgery, feeding information), discharge items (e.g. feeding and weight at discharge) and ad hoc items (entered if and when they occur, e.g. suspected infection, ultrasound scan findings, abdominal x-ray findings.

3 PARTICIPANT ENTRY

3.1 INCLUSION CRITERIA

Eligible babies of any gestational age within the NNRD who are recorded as having a stoma during neonatal care in England and Wales

3.2 EXCLUSION CRITERIA

Infants with anorectal malformations and Hirschsprung's will be excluded because stoma closures in these infants are usually part of a planned treatment pathway

Data from Scotland will be excluded.

4 STATISTICS AND DATA ANALYSIS

4.1 Analysis plan

Descriptive results will be presented using medians (interquartile ranges) and proportions for continuous and categorical variables, respectively. Chi-squared test will be used to compare categorical data. For continuous variables, the t-test is applied with normally distributed data, and the Wilcoxon test otherwise. Methods to explore factors associated with timing of stoma closure will be developed in this study.

4.2 Missing data

We expect missing data from babies that are transferred to surgical centres not co-located within a neonatal unit as they do not submit data to NNRD. These include Great Ormond Street Hospital, Sheffield Children's Hospital, Birmingham Children's Hospital, Alderhey Children's Hospital. However, we expect that the majority of babies should be repatriated back to neonatal units for post-surgical management. For these babies, if they have more than one stoma day recorded following their return from such a site, they will be identified as having a stoma. We will validate a subset of all identified cases with neonatal units and will validate any cases with unclear data.

5 Regulatory issues

5.1 ETHICS APPROVAL

No patient identifiable information will be used in this study and only existing anonymised data held in the NNRD will be used. The Neonatal Data Analysis Unit (NDAU) holds UK Research Ethics Committee approval, 16/LO/1093, and Confidential Advisory Group (CAG) approval, ECC 8-05(f/2010), to form the NNRD.

This study has been approved by the London-Dulwich Research Ethics Committee (REC) REC Ref number 20/LO/1227. The study has Health Research Authority (HRA) and Health and Care Research Wales (HCRW) approval IRAS 278331.

5.2 CONSENT

Not applicable

5.3 SPONSOR AND INDEMNITY

The sponsor is Manchester University; insurance policies are held that apply to this study.

5.4 FUNDING

This is part of an NIHR funded pilot study *Timing of Stoma Closure in Neonates (ToSCiN) Study no. 128617* https://www.fundingawards.nihr.ac.uk/award/NIHR128617

5.5 AUDITS AND INSPECTIONS

The study may be subject to inspection and audit by Manchester University 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.

6 STUDY MANAGEMENT

The database to be used in this study is the NNRD; researchers, clinicians, managers, commissioners, and others are welcome and encouraged to utilise the NNRD. More details are available here: https://www.imperial.ac.uk/neonatal-data-analysis-unit/neonatal-data-analysis-unit/

7 PUBLICATION POLICY

The results will be published in an academic journal and presented at conferences. The UK Neonatal Collaborative will be named collaborators and will be acknowledged in all academic publications.

8 CONFIDENTIALITY

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

9 REFERENCES

1. Digital N. National Neonatal Data Set. In: Dictionary ND, editor. 3 ed. https://datadictionary.nhs.uk/data_sets/clinical_data_sets/national_neonatal_data_set/national_neonatal_data_set_-_episodic_and_daily_care.html

2. Spencer A, Modi N. National neonatal data to support specialist care and improve infant outcomes. Archives of Disease in Childhood - Fetal and Neonatal Edition. 2012.