**The ROMANS Study**

Rates Of Morbidity and Mortality Associated with Neonatal Stomas

**ANZSCRAFT** (Australian and New Zealand Surgery in Children Registrars’ Association for Trials): A Trainee-led research collaboration based in Australia and New Zealand

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Abbreviations

ANZSCRAFT: Australian and New Zealand Surgery in Children Registrars’ Association for Trials

NEC: Necrotising enterocolitis

ARM: Anorectal malformation

NICU: Neonatal Intensive Care Unit

PICU: Paediatric Intensive Care Unit

## Contents

Abstract………………………………………………………………………………………………………………………………. 3

Introduction…..…..…..…..…..…..…..…..…..…..…..…..…..…..…..…..…..…..…..…..…..…..…..…..…..…..… 4

Materials & Methods…..…..…..…..…..…..…..…..…..…..…..…..…..…..…..…..…..…..…..…..…..…..…..… 6

Data Management & Sharing…..…..…..…..…..…..…..…..…..…..…..…..…..…..…..…..…..…..…..………. 8

Appendix…………………………………………………………………………………………………………………………… 12

## Abstract

### Background

Stoma formation in the neonatal period is necessary in many surgical conditions. There remains debate surrounding a number of factors (such as indications, type, timing of closure) and a paucity of quality literature to inform these decisions.

### Aim

To assess the rates of morbidity and mortality associated with neonatal stomas in Australia and New Zealand.

### Methodology

The ANZSCRAFT network will be used to recruit patients from centres across Australia and New Zealand, allowing for a prospective multi-centre observational study. All collaborators will be co-authors of resulting presentations and publications.

De-identified data will be collected on all neonatal patients undergoing stoma formation for a minimum 3-month period August-October 2022, with a 3-month follow-up period November 2022 – January 2023. This will include patent demographics, clinical status, procedure performed and outcomes. The data will be recorded on REDCap, a secure, online data collection tool.

Primary outcomes will be the occurrence of complications. Secondary outcomes will be timing of stoma closure.

Multivariate logistic regression analysis will be conducted to identify patient and procedure factors affecting outcomes with adjustment for confounding factors. P<0.05 will be taken as significant.

National study approval will be sought through the relevant Health Research Council Ethics Committee in Australia and the relevant Health and Disability Ethics Committee in New Zealand in addition to site approval from the relevant authorities for all participating centres.

### Dissemination

The results will first be shared at the Royal Australasian College of Surgeons Annual Scientific Congress, to be held 1-5 May 2023 in Adelaide, Australia.

Subsequent to this it is intended that the findings be published in a peer-reviewed journal.

### Outcome

The study aims to give an accurate reflection of practice and outcomes in Australia and New Zealand. Results will be used to aid and improve decision-making for this vulnerable group of patients.

## Introduction

Formation of a gastrointestinal stoma (into stomach, small or large bowel) in the neonatal period (</= 30 days corrected gestational age [CGA]) is a common paediatric surgical procedure.

### Indications

Indications for stoma formation vary widely but may include immediately life-threatening conditions, such as spontaneous intestinal perforation (SIP), necrotising enterocolitis (NEC) and midgut malrotation volvulus with bowel ischaemia. Other indications include small or large bowel obstruction associated with an anorectal malformation (ARM), meconium ileus or Hirschsprung disease.

Primary bowel anastomosis (joining of the bowel at the time of the initial surgery), rather than stoma formation, has been suggested as an alternative to enterostomy for over 20 years1, but debate surrounding which strategy should be employed continues2-5. Primary anastomosis has been shown to be safe in extremely premature and low birthweight neonates6-8.

However, despite this debate, there are many institutions (and indeed indications) where stoma formation would still be considered standard of care.9

### Morbidity

It is, therefore, important to be able to accurately describe outcomes associated with the formation of neonatal stomas. Reported complication rates of stoma formation vary widely, from 27 to 80%1,10-15. These include mechanical complications, such as stenosis, prolapse, retraction and parastomal hernia formation. There may be peristomal skin irritation, infection and dehiscence. The stoma itself may become ischaemic, may ulcerate and/or bleed and fistulate. Finally, stomas may lead to physiological disturbances from high output losses/electrolyte derangements, and malnutrition/malabsorption leading to poor weight gain.

### Timing of closure

Timing of closure is influenced by patient factors (e.g. prematurity, weight, ventilatory status and cardiovascular support) and disease factors (e.g. previous peritonitis, stoma complications). The data regarding timing of stoma closure remain inconclusive, with one published systematic review reporting closure <8 weeks from formation could be just as safe as closure >8 weeks from formation16.

## Study aims

The majority of literature published on this subject consists of retrospective series. Given this, and the low patient numbers generally encountered in single-centre paediatric surgical series, our intention is to benefit from the multi-institution framework of our trainee-led research study collaborative, the Australian and New Zealand Surgery in Children Registrars’ Association for Trials (ANZSCRAFT).

The ANZSCRAFT network provides the mechanism for performing a prospective, multi-centre observational study to give accurate and up-to-date information.

The intention is to prospectively audit patients’ outcomes. Patients will be audited over a minimum 3-month period, with a 3-month follow up period for each patient, collecting data from centres in Australia and New Zealand. Ethics and site-specific approvals will be sought at each site.

## Study objectives

1. To describe the mortality in patients after stoma formation
2. To describe post-operative complications after stoma formation
3. To identify factors affecting outcomes which may be modifiable
4. To describe current practice across Australia and New Zealand with respect to stoma formation and timing of closure in different conditions

## Materials & Methods

### Study design

This is a bi-national, multi-centre, prospective observational study. It will involve data collection from paediatric surgical centres in Australia and New Zealand.

### Collaborator recruitment

Trainees from each centre were identified during the annual registrar training seminar.

### Authorship

All collaborators will be recognised according to the ANZSCRAFT collaborative authorship model (see Appendix). The eventual publishing journal will be asked to make all collaborators PubMed citable co-authors. The authorship of the article on the title page will read ‘ANZSCRAFT’, with all collaborators names and roles listed in the supplementary material.

### Inclusion criteria

* All new neonatal gastrointestinal stomas (gastrostomies, small bowel enterostomies, colostomies) undertaken during the minimum 3-month recruitment period
* </=30 days CGA at time of operation

### Exclusion criteria

* >30 days CGA at time of operation

### Time period

Data collection may start as soon as ethics approval for each centre is granted, but is intended to be from August – October 2022 (initial cohort) and November 2022 – January 2023 (3 month follow-up period for this cohort).

Participation requires submission of data from at least a 3-month period with 3-month follow-up, but collaborators may submit more data.

Each month of data collection must start on the 1st day of the month and finish on the last day of the month.

### Data collection

#### Patient factors

* Birth weight (grams), weight at time of operation(s)
* Gestational age (weeks + days), age at time of stoma formation
* Sex (male, female, indeterminate)
* Ethnicity (Aboriginal, Asian, Australian South Sea Islander, Maori, Middle Eastern/Latin American/African, Pacific peoples, Torres Straight Islander, Other)
* Cardiorespiratory support at time of operation (whether intubated, ventilation settings, whether getting pressor support and if so, which ones)

#### Surgical disease factors

* Indication for laparotomy + stoma formation
  + Causes associated with ischaemia +/- sepsis
    - NEC
    - SIP
    - Volvulus
  + Causes associated with luminal pathology
    - Meconium ileus
    - Milk curd obstruction
  + Causes associated with obstruction
    - Duodenal atresia
    - Jejunal atresia
    - Ileal atresia
    - Colonic or rectal atresia
    - ARM
    - Hirschsprung disease
  + Other (please specify)
* Antenatal diagnosis of underlying disease Y/N

#### Operation factors

* Urgency of operation (timing of decision to operate)
  + Emergency (within 12 hours)
  + Urgent (within 72 hours)
  + Semi-elective (>72 hours)
* Location of operation
  + NICU
  + PICU
  + Operating theatres
* Time from diagnosis to operation (minutes, hours or days)
* Location of stoma (bowel)
  + Gastrostomy
  + Small bowel, distance from DJ flexure (cm)
    - Jejunostomy
    - Ileostomy
  + Large bowel
    - Location
* Location of stoma (abdominal wall)
  + In wound (medial edge, lateral edge, or middle)
  + Separate from wound (where)
* Type of stoma
  + Divided
  + Loop
  + Mucous fistula
  + End stoma (no fistula)
  + Chimney type stoma
  + Multiple
* Presence of contamination at time of operation
  + Y/N
* Bowel resection
  + Y/N

* How much residual bowel left in situ (cm small bowel and cm colon)
* ICV retained?
  + Y/N

#### Complications

* Immediate
  + Ischaemia
  + Stomal bleeding
* Early
  + Wound infection
  + Wound dehiscence
    - Skin
    - Fascia
  + Ischaemia
  + Stomal bleeding or ulceration
  + High output (>20ml/kg/24 hours OR limiting feeds)
    - Sodium supplementation
  + Need for revision
* Medium
  + Parastomal hernia
  + Prolapse
  + Retraction
  + Stenosis
  + Peristomal excoriation and/or cellulitis requiring antibiotic
  + Stomal bleeding or ulceration
  + High output (>20ml/kg/24 hours OR limiting feeds)
    - Poor weight gain/failure to thrive
    - Sodium supplementation
  + Need for revision
* Late
  + Parastomal hernia
  + Prolapse
  + Retraction
  + Stenosis
  + Peristomal excoriation and/or cellulitis requiring antibiotic
  + Stomal bleeding or ulceration
  + High output (>20ml/kg/24 hours OR limiting feeds)
    - Poor weight gain/failure to thrive
    - Sodium supplementation
  + Intussusception
  + Small bowel obstruction
  + Need for revision
* Enteral re-feeding Y/N

#### Closure

* Closed/unclosed 3 months from date of formation
  + Weight and age at closure
  + Discharged prior to closure (Y/N)
  + Was closure earlier than intended due to complications of stoma? (Y/N)
  + Wound infection post closure (Y/N)
  + Anastomotic leak post closure (Y/N)
  + Small bowel obstruction or ileus post closure (Y/N)

#### Mortality

* Death within 3 month follow up period

### Data collection tool

We will use REDCap, a secure, web-based data collection tool. Data can be uploaded directly, or collated by collaborators and uploaded at a later date. This may be done through a computer or mobile phone using the app. Patient identifying information, including National Health Identifiers (New Zealand) or hospital record numbers MUST NOT be entered into REDCap to comply with likely restrictions on data transfer.

A unique REDCap ID will be created for each patient. Collaborators will keep a secure list of patients on hospital hardware so that later validation could be undertaken if necessary (e.g. password-protected spreadsheet). This will be held according to local data protection protocols.

Access to REDCap will only be granted to collaborators once the study coordinators have received evidence of ethics approval for each centre.

A guide for registering with REDCap and subsequent data entry will be sent to all collaborators upon receipt of ethics approval.

### Data analysis plan

Data will be analysed using Prism (GraphPad Software, San Diego, CA; USA). Data will be screened for duplicates and these removed. Missing data for co-variates will be dealt with by running a) complete case analysis and b) using multiple imputation to allow inclusion of cases with missing data.

A formal power calculation was not performed for this observational study due to the rates of complications and practice in Australia and New Zealand being unknown and the goal of characterising practice and outcomes here. Based on published case series and the number of centres involved, the expected cohort would total approximately 50 infants.

Summary statistics for the demographic data will be calculated, i.e. median and interquartile range for birthweight, weight at operation, gestational age, corrected age at operation, type of stoma for each indication, median longevity of stomas closed during the study period).

Significant differences in complications between indications will not be calculated as this would likely represent an oversimplification – any differences could well be explained by confounders such as gestational age and birthweight (e.g., NEC patients likely to have lower gestational age and weight compared with those with Hirschsprung disease).

Multivariate logistic regression will therefore be performed between each complication and the covariates listed under patient factors, surgical disease factors and operation factors. Coefficients with a p-value of <0.05 will be considered significant, but all will be tabulated.

No comparisons will be made between individual hospitals, states or countries due to small numbers expected at some centres.

## Data management and sharing

* Each centre will have access to its own data, but not that of other centres
* The principal investigators will have access to the full, anonymised dataset through REDCap. Additional study team members may be granted access to the full dataset as required, for example for a statistician to assist with data analysis. Additional coordinating team members may be given access in order to contact collaborators to complete missing data
* The full dataset will be stored securely for at least 10 years
* Data will be backed up on password protected hardware at the hospitals of the principal investigators at least on a weekly basis
* Open access of the full de-identified anonymous dataset will not be made available
* Separate data management plans will be drawn up according to local requirements

## Appendix - ANZSCRAFT Authorship Policy v2.2 June 2020

1

Contributors

Ela Hyland, Damir Ljuhar, Jessica Rayner

1. Purpose

1.1 This authorship policy should be applied to all ANZSCRAFT publications, presentations,

and posters.

2. Aim of authorship model

2.1 Recognition of ANZSCRAFT collaborative as a trainee led and run network.

2.2 Appropriate recognition of an individual’s contribution to projects.

2.3 Act as supporting documentation in satisfying 3.6.1 and/or 3.6.4 of Research

Requirement as stipulated in the Board of Paediatric Surgery Training Regulations.

2.4 Encourage involvement in ANZSCRAFT at multiple levels ensuring sustainability of trials

network.

3. Principles of authorship

3.1 The ANZSCRAFT collaborative is to be listed as a PubMed citable author (see 6.1 for

example) in the top by-line unless otherwise approved by Trainee Lead(s).

3.2 All authors are to have a PubMed citable reference.

3.3 Where large number of authors are involved the degree and type of contribution should

be stipulated. This has the added benefit of supporting completion of research

requirement.

3.4 Authors will be listed in alphabetical order for all first authors and then followed by all

co-authors. If authorship categories used, this will be stipulated as an appendix on the

paper with authors listed under appropriate categories.

3.5 The authorship model should be agreed by the study Steering Group at the outset of the

study and should be included in the study protocol. This should include an outline of

authorship categories and pre-defined criteria that individuals must fulfil to be included

in each category.

3.6 The authorship model should be submitted to the Trainee Lead(s) for approval prior to

the study protocol being finalised. Written agreement from the Trainee Leads should be

obtained prior to a finalised protocol being circulated to collaborators. This ensures that

both the steering committees and study collaborators’ expectations are aligned.

3.7 If it becomes necessary to change the authorship rules whilst the study is ongoing, this

should first be agreed in writing with the Trainee Lead(s) and should then be promptly

communicated to study collaborators.

3.8 Prior to submission, all abstracts and manuscripts attributable to ANZSCRAFT must have

written approval by the Trainee Lead(s).

4. Requirements for authorship

4.1 As per the International Committee of Medical Journal Editors (ICMJE), an individual

should meet all four of the following criteria to be an author:

4.1.1 Substantial contributions to the conception or design of the work; and/or

the acquisition, analysis, or interpretation of data for the work

4.1.2 Drafting the work or revising it critically for important intellectual content

4.1.3 Final approval of the version to be published. Final draft to be circulated to

all co-authors at least 1 week prior to submission

4.1.4 Agreement to be accountable for all aspects of the work in ensuring that

questions related to the accuracy or integrity of any part of the work are

appropriately investigated and resolved.

5. Authorship categories

5.1 Not all projects will require authorship categories.

5.2 Authorship categories are encouraged for projects with large number of authors, or

where contribution of authors differs significantly. A list of recommended authorship

categories are listed below

5.3 Writing group

5.3.1 Individuals who have lead the drafting, writing, and editing of manuscript or

poster

5.3.2 Individuals are responsible for submission to journal/conference and

subsequent edits

5.4 Steering committee

5.4.1 Individuals who lead protocol development, disseminating study, design

and management of data collection system and/or co-ordination of data

collection

5.5 Statistical analysis

5.5.1 Individuals responsible for completion of statistical analyses.

5.6 Site leads

5.6.1 Individuals who represent and coordinate data collation and management

at their hospitals or institutions. This may be more than one per institution

if the study runs over multiple rotations

5.7 Collaborators

5.7.1 Individuals responsible for appropriate data collation and management at

individual sites

5.7.2 Miscellaneous. This includes individuals who have roles not otherwise

specified.

5.8 First author

5.8.1 Can have multiple first authors

5.8.2 Criteria for first authorship should be documented

5.9 Corresponding author

5.9.1 To be determined at the outset of authorship clarification

6. How the article is cited

6.1 In a reference list in another manuscript

ANZSCRAFT Collaborative. Rate of surgical site infection in patients undergoing major

gastrointestinal surgery. Journal of Pediatric Surgery. 2020 Jul 27;2(6):400-410.

6.2 In a collaborators CV

Smith J (state role), ANZSCRAFT Collaborative. Rate of surgical site infection in patients

undergoing major gastrointestinal surgery. Journal of Pediatric Surgery. 2020 Jul

27;2(6):400-410.

This policy was adapted from the Clinical Trials Network Australia and New Zealand (CTANZ)

network authorship policy draft.

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