# Anaesthesia-Related Adverse Events in Patients with Gastroschisis Presenting to Red Cross Children's Hospital from 2012 to 2021

Written By

**Dr Andrew Heald**

*MBChB(UCT), DiPPEC(SA), DA(SA), FCA(SA)*

**Student Number: HLDAND006**

SUBMITTED TO THE UNIVERSITY OF CAPE TOWN

In fulfilment of the requirements for the degree:

**Master of Medicine in Anaesthesiology**

Faculty of Health Sciences
UNIVERSITY OF CAPE TOWN

*Date of submission:* 09 June 2024

*Format:* Journal submission ready
*Word count:*

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## Acknowledgements

To Hayli Geffen for her help with the biostatistical component of the dissertation.
To Ms Simone Adams for her help with file retrieval and administration.
Finally, and most importantly, to Dr Rebecca Gray and Dr Heidi Meyer for their unwavering support in this project, which was met with its fair share of challenges.

## Authors:

Andrew Heald, Heidi M. Meyer[1], Marion Arnold[2], Rebecca Gray[1]

### *Corresponding Author*

Dr. A. Heald

ORCID ID: 0009-0006-3202-1369

Department of Anaesthesia and Perioperative Medicine, Division of Paediatric Anaesthesia, Red Cross War Memorial Children's Hospital, Cnr Klipfontein and Milner Road, Rondebosch, Cape Town, South Africa, 7700

Email: drandyheald@icloud.com

*Affiliations:*

[1]Department of Anaesthesia and Perioperative Medicine, Division of Paediatric Anaesthesia, Faculty of Health Sciences, University of Cape Town, South Africa

[2]Red Cross War Memorial Children's Hospital, Division of Paediatric Surgery, Faculty of Health Sciences, University of Cape Town, South Africa

## List of Abbreviations

| | |
|---|---|
| ARAE | Anaesthesia-related adverse event |
| CVC | Central venous catheter |
| CVS | Cardiovascular |
| GA | General Anaesthesia |
| GAE | General anaesthetic exposure |
| GS | Gastroschisis |
| HIC | High income country |
| HREC | Human research ethics committee |
| ICC | Intraclass correlation co-efficient |
| ICU | Intensive care unit |
| IQR | Interquartile Range |
| LMIC | Low- and middle-income country |
| RCWMCH | Red Cross War Memorial Children's Hospital |
| SARCI | Serious anaesthesia related critical incidents |
| STROBE | Strengthening the Reporting of Observational Studies in Epidemiology |
| TPN | Total Parenteral Nutrition |
| UCT | University of Cape Town |

## Abstract

**Introduction:** Patients with gastroschisis (GS) are a vulnerable population who present to the operating theatre for pathology or central venous access related indications. Little is known about anaesthesia-related adverse events (ARAEs) in children from low- and middle-income countries (LMICs).

**Methods:** We performed a single-centre retrospective observational study at Red Cross War Memorial Children's Hospital (RCWMCH), in Cape Town, South Africa. Data was collected from patient folders from the hospital's GS database. Each general anaesthetic exposure (GAE) was treated as an independent event and a binary logistic regression analysis was performed to assess the association between indication for GAE and the odds of an ARAE. A mixed-effects logistic regression model was used to analyse the association between adverse complications and key predictor variables in paediatric anaesthesia.

**Results:** Seventy folders were collected between 2012 and 2021. The median gestational age was 36 weeks and median birthweight 2270g. 56 (80%) patients survived to full enteral feeds and the median duration of TPN was 18 days (IQR 12-29). There were 196 GAEs, of which pathology-related indications comprised 59%. There was a total of 94 ARAEs. At least one ARAE occurred in 79 (40%) of the 196 GAEs. Cardiovascular instability was the most common ARAE, comprising 76% of the total ARAEs. Respiratory events comprised 18% of the ARAEs, with reintubation predominating. Patients presenting for pathology related indications were associated with an unadjusted 6-fold odds increase (95% CI = 3.10, 12.27) in the odds of ARAEs compared to patients with CVC-related indications ($p<0.001$), however at least one ARAE occurred in 18% of CVC related GAEs. No statistically significant association with ARAE was found for gestational age, birth weight or sex.

**Conclusion:** At RCWMCH, many patients with GS experience a complicated clinical course, requiring multiple general anaesthetic exposures. They have a high prevalence of anaesthetic related adverse events, particularly instances of CVS instability and reintubation. Establishing a multidisciplinary management protocol for these patients may decrease intervention frequency and improve outcomes.

## Introduction

Neonates and preterm infants represent one of the most vulnerable patient groups encountered in clinical practice due to their limited physiological reserve and immature organ systems, placing them at a higher risk for perioperative adverse events, morbidity, and mortality. Data from high income countries (HICs) have reported the incidence of anaesthesia related adverse events (ARAEs) in the neonatal population to be more than double that of the general paediatric population (12.1% vs. 5.2%)(1, 2). Research on ARAEs in these patients in low- or middle-income countries (LMIC) is scarce, however published data from South Africa reported 4-fold increased odds of a serious anaesthesia-related critical incidents (SARCIs) occurring within neonates compared with older children(3). Concerns also exist within this patient group regarding anaesthesia neurotoxicity and the effect of repeated and prolonged anaesthesia exposures on the developing human brain(4-7).

Patients with gastroschisis (GS), an abdominal wall defect affecting approximately 1 in 4000 live births(8), represent a challenging subpopulation of neonates and young infants at risk of multiple surgeries and anaesthetic exposures, with pathology specific risks including abdominal compartment syndrome(9). Despite interventions aimed at minimising anaesthesia exposure, including the utilisation of a preformed silo or implementing a suture-less closure technique(10, 11), these patients frequently require multiple anaesthesia exposures depending on the complexity of the lesion, the occurrence of surgical complications, and the requirement for central venous access for prolonged total parenteral nutrition (TPN) secondary to temporary intestinal failure. At our institution, Red Cross War Memorial Children's Hospital (RCWMCH), the majority of CVC insertions are done in theatre. General anaesthetic

exposures (GAEs) can be reduced by inserting longer lasting tunnelled central venous catheters (CVCs), or peripherally inserted central catheters (PICCs), but the former are expensive and these options are not always available in LMICs(12, 13).

Compared to HICs, outcomes in patients with GS in many LMICs have been shown to be poor. While survival rates with GS in HICs exceed 90%, studies from Sub-Saharan African countries report mortality rates ranging from 58.1% to 100%(14-16). Even within the HIC context, morbidity in these patients is significant(13), however, data on intraoperative adverse events and the impact on outcomes in these patients are few. A single study from a HIC setting reported on the adverse impact excessive fluid volumes has on prolonged ventilation, duration of hospital stay, length of TPN, and bacteraemic episodes(17). To the best of our knowledge there are no published data on the incidence and nature of ARAEs in these patients specific to a LMIC setting.

The primary objectives of our study were twofold: to explore the frequency and indications for general anaesthesia exposure (GAE) among patients with GS at RCWMCH, and to investigate the nature and incidence of ARAEs in these patients. We specifically sought to understand how frequently anaesthesia exposure was solely for central venous access and whether these events were associated with ARAEs, recognising that developing a central venous access protocol might reduce the number of anaesthetic exposures in these vulnerable patients.

Our secondary objectives were to establish survival to full enteral feeds, duration of TPN and the number of CVCs these patients require until establishment of full enteral feeds.

## Material and Methods

This was a single-center retrospective observational study of all consecutive patients with GS admitted to the RCWMCH, a large quaternary referral center in Cape Town, South Africa, and entered into the surgical database from January 2012 to December 2021. The commencement date (1 January 2012) coincided with the introduction of a comprehensive anaesthetic chart, which allowed for more reliable data capture.

Ethical approval for the study was granted by the Human Research Ethics Committee (HREC) of the Faculty of Health Sciences, University of Cape Town (UCT) (HREC REF: 381/2021). Local hospital approval was given by the Research Review Committee.

A password protected excel spreadsheet was used to capture data and data were captured by the corresponding author alone.

### *Data collection and Variables*

Relevant data were collected from the corresponding patient folders, which included paper anaesthetic records, patient progress notes, surgical notes, and dietician reviews.

Patient demographics included age, birth weight, sex, and gestational age. General anaesthesia (GA) related data included total number of GAEs until abdominal wall closure, indication for GA and total number and type of ARAEs. TPN related data included total cumulative days on TPN, total number of CVCs and survival to full enteral feeds.

Indication for GA were categorised into pathology or CVC-related. Pathology-related indications encompassed any surgical procedure associated with closure of the GS defect or its complications, while CVC-related indications encompassed any GA for insertion of a non-tunnelled CVC or insertion or removal of a tunnelled CVC.

ARAEs were defined as events occurring from the induction of anaesthesia until discharge from the post anaesthesia care unit (PACU), or within 1 hour of handover to the intensive care unit (ICU). ARAEs, including cardiovascular (CVS), respiratory, neurological, and drug-related events, were defined based on the criteria used in the APRICOT and NECTARINE studies (Table 1). Surgical complications such as unexpected bleeding or iatrogenic bowel injury were excluded.

Table 1: Definitions of Anaesthesia-Related Adverse Events

| System: | Event: | Included if: |
|---|---|---|
| **Respiratory** | Laryngospasm | Named in the Anaesthetic chart |
| | Bronchospasm | Named |
| | | Beta agonist use |
| | Post-operative stridor | Named |
| | Pulmonary aspiration | Named |
| | Need for reintubation | Named |
| **Cardiovascular** | Cardiac arrest | Named (e.g. Cardio-pulmonary Resuscitation/chest compressions/defibrillation) |
| | CVS instability | Bolus of more than 20 ml/kg crystalloid fluid (also 2 x 10 ml/kg) above routine maintenance infusion. |
| | | Bolus of 10 ml/kg or more of albumin and/or colloids (including blood products). |
| | | Any inotrope/vasopressor |
| | | Named dysrhythmia/ECG change |
| **Neurological** | Seizure | Named |
| **Drug** | Anaphylaxis | Named |
| | Drug Error | Named |

Study reporting was in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement(18).

### *Statistical Analysis:*

Categorical variables are reported as number and percentage. Normal distribution of continuous variables was determined by Shapiro-Wilk testing and summarised appropriately as means ± standard deviation or as medians ± interquartile range (IQR). The intraclass correlation coefficient (ICC) was used to assess the hierarchical nature of the data. Since the ICC was 0.004, each GAE was included in the analysis as an independent event.

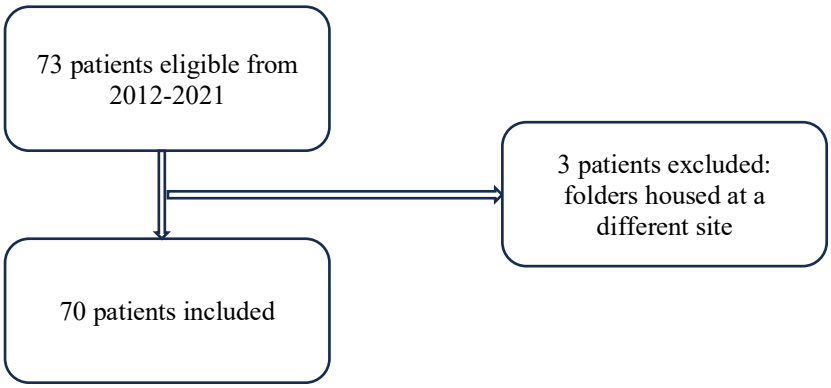
A binary logistic regression analysis was performed to assess the association between indication for GAE, pathology-related or CVC-related, and the odds of an ARAE occurring. A mixed-effects logistic regression model was used to analyse the association between adverse complications and key predictor variables in paediatric anaesthesia. The binary outcome variable was the occurrence of any adverse complication. Predictor variables included gestational age at birth (weeks), birth weight (grams), sex, and indication (surgical vs. CVC-related). Indication was treated as a time-varying variable since it differed across anaesthetic events for the same patient. To account for repeated measures, a random intercept for patient ID was included, allowing for multiple anaesthetic events per patient. The coefficients from the logistic regression model were exponentiated to obtain odds ratios (ORs).

For all statistical tests, statistical significance was defined as $\alpha \leq 0.05$. Data analysis was performed using R Statistical Software(19).

## Results:

The database contained 73 consecutive patients from 2012 to 2021. 3 patients were excluded due to unavailability of medical records with 70 (95.9%) patients being included in the final analysis. (Figure 1).

Figure 1: Flowchart depicting how the 70 patients were included in the study and reasons for exclusion.




### *Patient Demographics*

70/73 (95.9%) patients were included in the final analysis (Table 2). 55% of patients were born prematurely and 69% had a birth weight less than 2500g, of these 8% had a very low birth weight (<1500g).

Table 2: Patient demographics and clinical characteristics

| Variable | All patients N = 70 |
|---|---|
| **Gestational age (weeks), median (IQR)** | 36 (35, 37) |
| **Birth weight (grams), median (IQR)** | 2270 (1985, 2608) |
| **Sex (female), n (%)** | 35 (50%) |
| **Survived to full enteral feeds, n (%)** | 56 (80%) |
| **Number of general anaesthetic exposures, n (%)** | |
| 0 | 5 (7%) |
| 1 | 19 (27%) |
| 2 | 17 (24%) |
| 3 | 13 (19%) |
| 4 | 8 (11%) |
| >= 5 | 8 (11%) |
| **Number of anaesthesia-related adverse events, n (%)** | |
| 0 | 19 (27%) |
| 1 | 28 (40%) |
| 2 | 13 (19%) |
| >=3 | 10 (14%) |
| **Started on TPN, n (%)** | 64 (91%) |
| **Duration on TPN (days), median (IQR)** | 18 (12, 29) |
| **TPN > 7 days, n (%)** | 59 (92%) |
| **Number of CVCs, n (%)** | |
| 0 | 5 (7%) |
| 1 | 14 (20%) |
| 2 | 23 (33%) |
| 3 | 12 (17%) |
| >= 4 | 16 (23%) |

Sixty-five of seventy (93%) patients underwent a total of 196 GAE. Of the patients that did not have a GAE, two were managed with sutureless closure and PICC

insertion for TPN outside of theatre and the other three were palliated. The most frequent indications for general anaesthesia were pathology-related (59%), while the remainder were for CVC insertion or removal (table 3). The median number of GAs per patient was two (IQR 1-3) and 46 (70%) patients underwent two or more GAEs, with three patients undergoing 10 or more GAEs during their admission. Sixteen (25%) patients required four or more GAEs solely related to central venous access.

Table 3: Indication for General Anaesthetic and Anaesthesia-Related Adverse Events.

| **Indication for GA** | **(N = 196)** | **Presence of at least one ARAE (n = 79)** | **No ARAE (n = 117)** | **Unadjusted odds ratio (95% CI)** | **p-value** |
|---|---|---|---|---|---|
| **CVC related, n (%)** | 80 (41%) | 14 (18%) | 66 (56%) | Reference | |
| **Pathology related, n (%)** | 116 (59%) | 65 (82%) | 51 (44%) | 6 (3.1,12.3) | <0.001 |

Of the 64/70 (91.4%) patients that were started on TPN, 59 required TPN for longer than seven days and the median duration of TPN was 18 days. The six patients that were not started on TPN were palliated and only one of these had a CVC inserted. Fourteen (20%) patients did not survive to full enteral feeds.

### *Anaesthesia-related adverse events*

Of the 65 patients that had GAEs, 51 (80%) suffered at least one ARAE (Table 3). In total, there were 94 ARAEs and these occurred during 79/196 (40%) of GAEs.

Table 4: Anaesthesia-Related Adverse Events

| Variable | N = 94 |
|---|---|
| **Respiratory events, n (%)** | **16 (18%)** |
| Bronchospasm | 2 (2%) |
| Post-op stridor | 2 (2%) |
| Reintubation | 8 (9%) |
| Pulmonary aspiration | 4 (4%) |
| **Cardiovascular events, n (%)** | **75 (79%)** |
| Cardiac arrest | 1 (1%) |
| CVS instability | 71 (76%) |
| Inotrope requirement | 2 (2%) |
| Dysrhythmia | 1 (1%) |
| **Other events, n (%)** | **3 (2%)** |
| Seizure | 1 (1%) |
| Drug error | 2 (2%) |

The median number of intraoperative complications per anaesthetic was 1.0 (IQR, 1.0-2.0). Cardiovascular instability was the most frequent adverse event occurring in 36% of GAE, although inotropes were only used on two occasions. There was one intraoperative cardiac arrest, but no intraoperative deaths.

Respiratory adverse events comprised nearly 20% of the total ARAEs and 8/16 (50%) of these were reintubations. Two indications for reintubation included respiratory failure in ICU following primary closure and an inadvertent extubation in ICU upon transfer. One patient was reintubated twice, in the first instance the

indication was unclear and the patient had a subsequent failed controlled extubation in theatre after CVC insertion, the other instances are unknown (n=4).

Drug errors occurred in two patients. Bupivacaine was inadvertently flushed through a newly sited CVC without any adverse outcome in one patient, while the other patient received an incorrect dose of the reversal agent. The first patient survived to full enteral feeds, while the second patient subsequently died, it is unlikely that this outcome was due to the dosing error.

The mixed-effects logistic regression model analysed the predictors of ARAEs. Pathology-related indications had 6.5 times higher odds of experiencing an ARAE compared with CVC related indications (OR = 6.55, 95% CI: 3.03 to 14.32, p < 0.001). (Table 5)

Table 5: Logistic Regression Results for Anaesthesia Related Adverse Events

| Variable | Coefficient (β) (95% CI) | Standard Error | Z-value | P-value |
|---|---|---|---|---|
| Intercept | -8.1603 (-15.066, -1.255) | 3.523 | -2.316 | 0.021 |
| Sex (Male) | 0.0264 (-0.648, 0.701) | 0.344 | 0.077 | 0.939 |
| Indication (Surgical) | 1.8833 (1.106, 2.661) | 0.397 | 4.746 | <0.001 |
| Gestational Age (Weeks) | 0.1739 (-0.049, 0.397) | 0.114 | 1.53 | 0.126 |
| Birth Weight (grams) | -0.00006175 (-0.001, 0.001) | 0 | -0.138 | 0.891 |

No statistically significant associations were found for gestational age (OR = 1.19, 95% CI: 0.95 to 1.49, p = 0.13), birth weight (OR = 1.00, 95% CI: 0.99 to 1.00, p = 0.89), or sex (OR = 1.03, 95% CI: 0.52 to 2.02, p = 0.94). The model had a pseudo R-squared of 0.1225.

## Discussion

Patients with GS admitted to RCWMCH frequently undergo a complicated surgical course, often requiring multiple anaesthetic exposures. The principal finding of this study is that ARAEs are common, occurring in 40% of general anaesthetic exposures (GAEs). Although patients undergoing procedures related to abdominal pathology had six-fold increased odds of experiencing an ARAE compared to those undergoing CVC-related procedures, ARAEs still occurred frequently during CVC-related procedures. While ARAEs were primarily cardiovascular, affecting over a third of patients, respiratory adverse events were also common. There was one intraoperative cardiac arrest, but no intraoperative deaths.

Data on the incidence and nature of ARAEs in neonates are largely limited to HIC. In 2017, the landmark APRICOT study was published, aiming to provide a benchmark for the occurrence of complications requiring immediate intervention and potentially leading to major disability or death in children up to 16 years of age undergoing anaesthesia for surgical and non-surgical procedures(2). This prospective observational multicentre cohort study included 361 (1·2%) neonates and 2912 (9·4%) infants. The authors reported a significantly higher incidence of cardiovascular and respiratory critical events in neonates and infants compared with older children, and specifically noted that neonates had the highest rate of cardiovascular complications (12·1%, 95% CI 8·9–15·9; p<0·0001). Similarly, a secondary analysis of the South African Paediatric Surgical Outcomes Study cohort reported a 4-fold increased odds for serious anaesthesia related critical incidents (SARCIs) in neonates and a 3-fold increased odds of SARCIs in infants, with an actual incidence of SARCIs ranging from 26.0% in infants to 34.5% in neonates(3).

Data from the subsequent NECTARINE study, a prospective study involving 165 participating centers in Europe, focused on infants up to 60 weeks post-menstrual age undergoing anaesthesia exposures for surgical and non-surgical procedures(1). It reported a similar overall incidence of critical events requiring intervention (35.3%) compared to the secondary analysis of the SAPSOS cohort and the 40% incidence of pre-defined anaesthesia-related adverse events (ARAEs) in our patient cohort. The NECTARINE study revealed that episodes of cardiovascular instability prompted 60.7% of all interventions, with hypotension being the most common cause, accounting for nearly 50%. Although the findings of these studies appear to be similar to our study, it is important to recognise that, direct comparisons remain challenging, due to the heterogeneity of procedures, patients and definitions used in the NECTARINE and APRICOT study. For pragmatic reasons we limited the definition of cardiovascular instability to the administration of fluid boluses, use of inotropes or vasopressors, arrythmias, and cardiac arrest, as it was not possible to retrospectively identify the baseline blood pressure within our patient cohort, or to accurately identify the blood pressure thresholds at which fluid boluses were administered. It is also important to highlight the potential harm related to the administration of liberal intravenous fluids in patients with GS. It is possible that earlier consideration of inotropic support may facilitate a more restrictive approach to fluid management while still maintaining adequate end-organ perfusion. However, whether this will translate to improved outcomes, such as earlier abdominal wall closure, reduced incidence of raised intra-abdominal compartment syndrome, and earlier extubation, remains unknown.

Respiratory ARAEs were also common, constituting 18% of the events in our patient cohort. A history of prematurity has previously been identified as a significant factor associated with a nearly 2-fold increase in the occurrence of severe respiratory critical events, which is relevant to our patient cohort, among whom 55% were preterm neonates and infants(2). While some of our respiratory findings echoed those of the APRICOT study (bronchospasm and post-op stridor), we found no documented incidences of laryngospasm and had a higher incidence of pulmonary aspiration (4% vs. 0.1%). We suspect this is likely due to the pathology, in comparison with the APRICOT cohort who underwent a variety of surgical and non-surgical procedures. Additionally, our patients had a notably higher incidence of reintubation (9% of ARAEs). For comparison, of the 976 cases that suffered a respiratory complication in the APRICOT study, only 33 (3%) required intubation for management. Factors contributing to the decision to avoid extubation or causing failed extubation in these patients include high intra-abdominal pressures after closure, particularly if associated with significant fluid administration. While drawing conclusions from this data is challenging, it is prudent to be mindful of the risk of failed extubation.

Given the high incidence of ARAEs in these patients, developing pathways and protocols to reduce the number of GAEs required may offer an opportunity to minimise harm in these patients, particularly when considering the necessity of central venous access for TPN in cases of intestinal failure. The majority of patients required prolonged TPN (>7 days), with 41.5% of indications for general anaesthesia being CVC-related. Additionally, approximately one quarter of patients required four or more anaesthetics for CVC insertion and/or removal. Only two patients achieved

full enteral feeds without a GAE, suggesting that non-operative closure and insertion of a PICC until establishment of full enteral feeds is rare in GS patients at RCWMCH. While earlier consideration of tunnelled central venous access could potentially reduce the need for repeat GAEs for central venous access, further comment on the type of central venous access is limited since the indication for the type of CVC was not included, and factors influencing the choice of CVC, such as ongoing sepsis, were not recorded.

Given the retrospective nature of the study, drug errors were probably underreported, despite being equivalent to the incidence of the APRICOT study (1% vs 0.9%).

The adoption of a multidisciplinary management bundle that includes prenatal diagnosis and aims to secure longer-term venous access from presentation, with the goal of avoiding unnecessary GAE should be strongly considered in these patients.

### *Limitations:*

This study has several major limitations. Given the small size and retrospective nature, generalisability and implications from this study should be interpreted with caution. The sample size was also further limited due to unavailable patient folders and availability of anaesthetic charts.

Due to the retrospective nature of these data, the true incidence of ARAEs may have been either under- or over-estimated. The small study size also limited the ability to detect any significant risk factors associated with ARAEs. Further larger prospective studies are needed to better quantify perioperative ARAEs and associated risk factors.

The lack of universal definitions for anaesthesia-related adverse events (ARAEs) in this population, along with the use of differing definitions, even when considering studies such as APRICOT and NECTARINE, makes drawing comparisons between studies challenging. Due to the retrospective nature of the study and for pragmatic reasons certain ARAEs, including hypotension and hypoxia, were excluded due to the challenge of accurately documenting every episode of low blood pressure and desaturation in a paper-based record system. Hypoglycaemia is a common ARAE in these patients but glucose measurements are not documented routinely intra-operatively, especially during CVC insertion/removal. Episodes of hypothermia would have been useful to interrogate.

Whilst the incidence and nature of ARAEs is important, this study did not explore the relationship between these events and adverse outcomes. Recording anaesthesia duration would have been useful, as longer duration may be associated with risk or ARAEs and even neurotoxicity.

Important information, including the indication for central venous access (such as difficult peripheral access, intravenous antibiotics, or total parenteral nutrition), was not recorded. Additionally, it was not possible to ascertain whether the CVC was percutaneously inserted or if a tunneled line was used, nor the factors influencing

this decision, such as the availability of tunneled CVC or the presence of sepsis. Understanding the expected duration of different types of CVCs in these patients would also provide important information when deciding on the appropriate type of CVC to use, whilst aiming to minimise the need for repeated GAE for insertion of CVCs.

Further studies are needed to obtain this vital information, which will be critical for informing decisions regarding the development of central venous access protocols or guidelines for patients with gastroschisis.

### *Conclusion:*

At RCWMCH, patients with GS undergo a complicated clinical course, especially until closure of the defect and while requiring TPN. They require frequent abdominal and CVC related interventions and have a high prevalence of ARAEs, particularly instances of CVS instability and potential for requiring reintubation. Establishing an institution specific, multidisciplinary management protocol for these patients may decrease the frequency of these interventions and improve outcomes.

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## Appendix 1: Data collection tool

| | |
|---|---|
| **General data** | |
| Gestational age | weeks |
| Date of Birth | Dd/mm/yyyy |
| Sex | m/f |
| Birth weight | grams |
| Date of admission | |
| | |
| **Anaesthetic and complication related data** | |
| Number of general anaesthetics | n |
| Number of anaesthesia-related adverse events (total) | n |
| Total respiratory complications | n |
| Total cardiovascular complications | n |
| Total "other" complications (see below) | n |
| | |
| **For each general anaesthetic exposure** | |
| Indication for general anaesthetic | pathology or central venous catheter related |
| Respiratory complications for each exposure | n |
| - Laryngospasm | yes/no |
| - Bronchospasm | yes/no |
| - Postoperative stridor | yes/no |
| - Reintubation | yes/no |
| - Pulmonary aspiration | yes/no |
| Cardiovascular complications for each exposure | n |
| - Cardiac arrest | yes/no |
| - Intraoperative hypotension* | yes/no |
| - Dysrhythmia | yes/no |
| - Inotrope requirement | yes/no |
| Other complications for each exposure | n |
| - Anaphylaxis | yes/no |
| - Drug error | yes/no |
| - Seizure | yes/no |
| | |
| **Central venous catheter (CVC) and total parenteral nutrition (TPN) related data** | |
| - Started on TPN | yes/no |
| - Date of commencing TPN | dd/mm/yyyy |
| - Date of stopping TPN/ establishment of full enteral feeds | dd/mm/yyyy |
| - Number of CVC | n |
| | |
| **Survival related data** | |
| - Survived to full enteral feeds | yes/no |
| - Survived more than seven days? | yes/no |
| | |

*See main body for how this was defined.

The above variables were captured in a password protected excel spreadsheet.

## Appendix 2: Human Research Ethics Approval, Progress Report and Amendment Approval

**UNIVERSITY OF CAPE TOWN**
**Faculty of Health Sciences**
**Human Research Ethics Committee**

**Room G50- Old Main Building**
**Groote Schuur Hospital**
**Observatory 7925**
**Telephone** [021] 406 6492
**Email:** hrec-submissions@uct.ac.za
**Website**: www.health.uct.ac.za/fhs/research/humanethics/forms

18 June 2021

**HREC REF: 381/2021**

**Dr R Gray**
Division of Anaesthesia & Perioperative Medicine
Ward D 23 NGSH
Email: Rebecca.gray@uct.ac.za
Student: drandyheald@icloud.com

Dear Dr Gray

**PROJECT TITLE: AUDIT OF DURATION OF TOTAL PARENTERAL NUTRITION IN GASTROSCHISIS (TPNINGS)-MMED CANDIDATE-DR ANDREW HEALD**

Thank you for submitting your study to the Faculty of Health Sciences Human Research Ethics Committee (HREC) for review.

It is a pleasure to inform you that the HREC has **formally approved** the above-mentioned study.

- Please provide the Form A for this study.

**This approval is subject to strict adherence to the HREC recommendations regarding research involving human participants during COVID -19, dated 17 March 2020 & 06 July 2020.**

**Approval is granted for one year until the 30 June 2022.**

Please submit a progress form, using the standardised Annual Report Form if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.
(Forms can be found on our website: www.health.uct.ac.za/fhs/research/humanethics/forms)

***The HREC acknowledge that the student: Dr Andrew Heald will also be involved in this study.***

**Please quote the HREC REF 381/2021 in all your correspondence.**

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please note that for all studies approved by the HREC, the principal investigator **must** obtain appropriate institutional approval, where necessary, before the research may occur.

UNIVERSITY OF CAPE TOWN

FACULTY OF HEALTH SCIENCES
Human Research Ethics Committee

# FHS017: Annual Progress Report / Renewal

## Record Reviews/Audits/Collection of Biological Specimens/Repositories/Databases/Registries

| HREC office use only (FWA00001637; IRB00001938) | | | |
|---|---|---|---|
| This serves as notification of annual approval, including any documentation described below. | | | |
| ☑ Approved | Annual progress report | Approved until/next renewal date | 30.11.2024 |
| ☐ Not approved | See attached comments | | |
| Signature Chairperson of the HREC/ Designee | | Date Signed | 4/12/2023 |

**Note:** Please note that incomplete submissions will not be reviewed.
Please email this form and supporting documents (if applicable) in a combined pdf file to hrec-enquiries@uct.ac.za.

HUMAN RESEARCH ETHICS COMMITTEE
- 4 DEC 2023
HEALTH SCIENCES FACULTY
UNIVERSITY OF CAPE TOWN

Please clarify your plan for research-related activities during COVID-19 lockdown

## Principal Investigator to complete the following:

### 1. Protocol information

| | | | |
|---|---|---|---|
| Date (when submitting this form) | 01/12/2023 | | |
| HREC REF Number | 381/2021 | Current Ethics Approval was granted until | 30/06/2023 |
| Protocol title | Audit of Total Parenteral Nutrition in Gastroschisis | | |
| Principal Investigator | Rebecca Gray | | |
| Department / Office Internal Mail Address | Department of Anaesthesia, Red Cross Hospital rebecca.gray@uct.ac.za | | |
| 1.1 Does this protocol receive US Federal funding? | | ☐ Yes | x No |

### 2. Protocol status (tick ✓)

| | |
|---|---|
| ✓ | Research-related activities are ongoing |
| ☐ | Data collection is complete, data analysis only |

Please indicate (in the block below) the titles and HREC reference numbers of any projects currently making use of the Database/registry/repository.

### 3. Protocol summary

| | | |
|---|---|---|
| Total number of records or specimens collected, reviewed or stored since the original approval | | 54 |
| Total number of records or specimens collected, reviewed or stored since last progress report | | 23 |
| Have any research-related outputs (e.g. publications, abstracts, conference presentations) resulted from this research? If yes, please list and attach with this report. | ☐ Yes | ✓ No |

### 4. Signature

| | | | |
|---|---|---|---|
| Signature of PI | | Date | 01/12/2023 |

Form FHS006: Protocol Amendment

| HREC office use only (FWA00001637; IRB00001938) | | |
|---|---|---|
| ☑ Approved | ☐ Type of review: Expedited | ☐ Full committee |
| This serves as notification that all changes and documentation described below are approved. | | |
| Signature HREC Chairperson / Designee | | Date: 11/10/2021 |

**Note:** All **Major** amendments must include a **Cover Letter** and a local PI **Synopsis** justifying the changes for the amendment. Please note that incomplete amendment submissions will not be reviewed.

Please email this form and supporting documents (if applicable) in a combined pdf-file to hrec-enquiries@uct.ac.za with subject line: FHS006 + (HREC Reference number).

The latest forms are found on our website.

http://www.health.uct.ac.za/fhs/research/humanethics/forms

Please also clarify your plan for research-related activities during COVID-19 lockdown.

| Comments from the HREC to the Principal Investigator: |
|---|
| |
| **Note:** The approval of this protocol amendment does not grant annual approval. Please complete the FHS016 / FHS017 form for annual approval at least one month before study expiration. |

**Principal Investigator to complete the following:**

**1. Protocol Information**

| | | | |
|---|---|---|---|
| Date (when submitting this form) | 08/10/2021 | | |
| HREC REF Number | 381/2021 | | |
| Protocol Title | Audit of Duration of Total Parenteral Nutrition in Gastroschisis | | |
| Protocol Number (if applicable) | | | |
| Principal Investigator | Dr Rebecca Gray | | |
| Department / Office Internal Mail Address | Paediatric Anaesthesia, Red Cross Hospital. | | |
| 1.1 Is this a major or a minor amendment? (see FHS006hlp) Major (tick box) Minor (tick box) | | ☐ Major | x Minor |
| 1.2 Does this protocol receive US Federal funding? | | ☐ Yes | x No |

# Appendix 3: Institutional Approval

Western Cape Government
Health

**DR T KERBELKER**
**Acting Manager: Medical Services**
**Red Cross War Memorial Children's Hospital**
Email: Tamara.Kerbelker@westerncape.gov.za
Tel: +27 21 658 5383 Fax: +27 21 658 5006/5166

**08 July 2021**

Dr A Heald
Department of Anaesthesia

Dear Dr Heald,

**RESEARCH: RXH: RCC 284 / WC_202106_054**

**PROJECT TITLE: AUDIT OF DURATION OF TOTAL PARENTERAL NUTRITION IN GASTROSCHISIS (TPNINGS)**

It is a pleasure to inform you that the hospital Research Review Committee has approved your application to conduct above-mentioned study at Red Cross War Memorial Children's Hospital.

Kindly note that this approval is subject to strict adherence to the HREC recommendations regarding research involving participants during COVID-19, dated 17 March 2020 (UCT HREC notice attached).

Yours sincerely,

**DR T KERBELKER**
**ACTING MANAGER: MEDICAL SERVICES**

## Appendix 4: Author Guidelines for Paediatric Anaesthesia Journal

Research reports describe systematic original scientific investigations. The text body must include an introduction, materials and methods, results and discussion. All research reports must adhere to the journal minimal reporting standards. Reports that do not adhere to these standards cannot be considered for publication.

Word Limit: 3500 words

Maximum figures and tables – 6

Maximum references – 25

Abstract/Summary: Structured abstract up to 300 words Background; Aims; Methods; Results; Conclusions.

Other Requirements

In Clinical Implications, add 1-2 sentences answering:

a. What is already known about the topic

b. What new information this study adds (indicate the salient research results)

https://onlinelibrary.wiley.com/page/journal/14609592/homepage/forauthors.html#manuscript