Cape Peninsula University of Technology

A description of sedation and analgesia practices at a South African aeromedical service: A retrospective review

By

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DECLARATION

I Stephen Colman declare that the contents of this dissertation/thesis represent my own unaided work, and that the dissertation/thesis has not previously been submitted for academic examination towards any qualification. Furthermore, it represents my own opinions and not necessarily those of the Cape Peninsula University of Technology.

Signed

07/03/2026

Date

DEDICATION

For my partner, Brad.

I wish to dedicate this thesis to Brad. Thank you for always supporting me to further my academic and professional career, and for the sacrifices you made to do so. I promise not to miss another adventure because of my studies – at least for a while.

ABSTRACT

Background

Sedation and analgesia practices vary and are not described in the South African aeromedical setting. Rescue sedation has been identified as a sedation practice in the aeromedical setting but has not been defined in this context before. Previous literature has shown that validated sedation and analgesia monitoring tools are rarely used, and deep sedation is common.

Early deep sedation in the prehospital setting could result in negative patient outcomes associated with fewer ventilator-free days, increased hospital length of stay, and mortality. Under sedation has been associated with negative patient outcomes relating to awareness during paralysis and may result in severe psychological and physical implications for affected patients.

It is important to establish the proportion of patients who receive rescue sedation during transfer to determine how common this practice is. As sedation and analgesia affect patient outcomes during the early phase of patient care, a description of contemporary sedation and analgesia practices in the aeromedical setting is important. These insights may determine further research priorities in the South African aeromedical setting, which may influence guideline development and quality improvement.

Aim

The aim of this research is to describe sedation and analgesia practices in the aeromedical setting and determine the proportion of patients who received rescue sedation.

Methods

A descriptive cross-sectional design using retrospective chart review of patient care records (PCRs) was chosen to determine the proportion of patients in the sample who received rescue sedation and describe sedation and analgesia practices during aeromedical transfer. Inclusion and exclusion criteria were applied to sampled PCRs. A sampling technique of simple random sampling was used during the study period, and a predetermined sample size was calculated to determine the proportion of patients who received rescue sedation.

Findings

This research found that the proportion of patients who received rescue sedation was 13.9% (95% CI 9.2 - 20). The most common rescue sedative administered was ketamine.

In most cases, combinations of ketamine and midazolam (62.7%) were used to provide continuous sedation and analgesia during transfer. These medications were administered by syringe driver, as a continuous infusion, in 89.2% of cases. Mean doses of the ketamine-midazolam combination infusion were 2.3mg/kg/hr (SD = 0.9) of ketamine and 0.05mg/kg/hr (SD = 0.03) of midazolam. Multimodal analgesia was rarely used (13.9%). Sedation and pain assessment scores were not documented during transfer at the participating service. The adverse event rate was 32.3%, and the most common AEs were hypotension (21.5%) and hypoxia (12%).

Conclusion

Rescue sedation is used occasionally at the research site. The rationale for this practice is unknown and needs to be investigated further. Recommendations have been made to include routine documentation of sedation depth and pain assessments to establish how common deep sedation is, and whether current sedation doses -as described in this research- are accomplishing adequate sedation and analgesia during transfer. Adverse events require further research to establish potential causative factors with more certainty. Sedation and analgesia practices represent modifiable risk factors affecting patient outcomes. As such, they represent areas for further research and quality improvement.

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LIST OF ABBREVIATIONS

AE – Adverse Event

AEA – Ambulance Emergency Assistant

ALS – Advanced Life Support

AMS – Air Mercy Service

ANT – Paramedic

BPS – Behavioural Pain Scale

CCR – Critical Care Retrieval

CCRS – Critical Care Retrieval Service

CDST – Clinical Decision Support Tool

CPG – Clinical Practice Guideline

CVA – Cerebral Vascular Accident

ECP – Emergency Care Practitioner

ECT – Emergency Care Technician

EMS – Emergency Medical Services

ETT – Endotracheal Tube

FW – Fixed Wing

HEMS – Helicopter Emergency Medical Services

HPCSA – Health Professions Council of South Africa

ICU – Intensive Care Unit

IHT – Interhospital Transfer

ILS – Intermediate Life Support

MO – Medical Officer

PBEC – Professional Board of Emergency Care

RASS – Richmond Agitation Sedation Scale

RFDS – Royal Flying Doctor Service

RW – Rotor Wing

SOP – Standard Operating Procedure

SSA – Sub-Saharan Africa

TBI – Traumatic Brain Injury

TERMS AND DEFINITIONS

Advanced Life Support: This refers to an advanced level of emergency care that may be delivered in the prehospital environment, by those registered with the Health Professions Council of South Africa (HPCSA) at the level of Emergency Care Practitioner, Emergency Care Technician, or Paramedic. These individuals may perform skills and administer medications as outlined by the scope of practice determined by the HPCSA.

Adverse Event: An unfavourable or potentially harmful clinical event during patient care (MacDonald et al., 2008).

Analgesia: Absence of pain in response to stimulation which would normally be painful (IASP, 2021).

Behavioural Pain Scale (BPS): The BPS is a validated observational pain scale for unconscious mechanically ventilated patients and is based on the sum score concerning the following 3 behavioural items: facial expression, movements of the upper limbs, and compliance with ventilation. Each item is scored from 1 (no response) to 4 (full response). The total BPS score ranges from 3 (no pain) to 12 (maximal pain) (Rijkenberg et al., 2015). Refer to Annexure C.

Continuous sedation and analgesia: Provision of sedative and analgesic medications by continuous infusion, using an infusion pump or syringe driver. This may include bolus dose administration of sedatives and analgesics provided that these medications are continuously administered at set intervals.

Emergency Care Practitioner: A prehospital care provider registered with the Health Professions Council, holding a four-year bachelor’s degree in emergency medical care. These practitioners can administer medications and perform interventions in accordance with the ECP scope of practice outlined by the Health Professions Council of South Africa (HPCSA). ECPs deliver the highest level of prehospital care in South Africa.

Emergency Care Technician: A prehospital care provider registered with the Health Professions Council, holding a two-year national certificate or diploma in emergency medical care. These providers can administer advanced life support interventions as stipulated by the HPCSA.

Pain: An unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage (IASP, 2021).

Postintubation Sedation and Analgesia: Sedation and analgesia administered by either bolus or continuous infusion following intubation, varying definitions exist, with some using a fixed time from intubation, while others using a variable time based on the duration of action of the sedative given for intubation (Baumgartner et al., 2026)

Rescue Sedation: The administration of bolus dose sedation in addition to a continuous sedation infusion, usually due to inadequate sedation achieved by the initial infusion. Rescue sedation can also be administered for unsafe patient care situations.

Richmond Agitation Sedation Scale (RASS): The RASS is a 10-point scale, with four levels for anxiety and agitation (+1 to +4), one level to denote a calm and alert state (0), and five levels of sedation (-1 to -5), culminating in unarousable (-5). The RASS is a validated scale to measure a patients depth of sedation or wakefulness (Sessler et al., 2002). Refer to Annexure B.

Sedation: Sedation is a drug-induced depression of consciousness, with a continuum varying from minimal sedation/anxiolysis, moderate sedation and analgesia, dissociative sedation, to deep sedation, and finally general anaesthesia (Roelofse & Jansen van Rensburg, 2020).

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CHAPTER 1: INTRODUCTION

1.1. Background

Sedation and analgesia are common interventions and core components of critical care among mechanically ventilated patients as they reduce patients' pain and discomfort, while facilitating ventilator synchrony (Minhas et al., 2015). There are a limited number of intensive care unit beds in peri-urban and rural areas in South Africa, which necessitates critical care retrieval to urban tertiary facilities (Venter et al., 2021). Helicopter emergency medical services (HEMS), play a vital role in critical care transfers in South Africa (Vlok et al., 2023).

In South Africa, Emergency Care Practitioners (ECPs)[1] and Paramedics (ANT)[2] may perform critical care transfers of mechanically ventilated patients in both the aeromedical and road transfer setting (HPCSA, 2018). Further, ECPs may perform rapid sequence intubation (RSI), necessitating postintubation analgesia and sedation.

There are various methods of sedation and analgesia, and no study in South Africa has described these practices in the aeromedical setting. Recently, a Clinical Decision Support Tool (CDST) has been published by the PBEC[3] of the Health Professions Council of South Africa (HPCSA) for use by prehospital emergency care providers (HPCSA-PBEC, 2024). The CDST contains recommendations for continuous sedation and analgesia however, there remains a paucity of research pertaining to out-of-hospital sedation and analgesia practices for mechanically ventilated patients in South Africa.

Most research has been conducted in ground EMS (GEMS), for primary scene calls[4] as opposed to interhospital transfers (IHTs). Research regarding continuous sedation and analgesia in the aeromedical setting is limited but has the potential to provide valuable insights into these practices due to the high volume of critical care transfers that are serviced.

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[1] Emergency Care Practitioners are independent practitioners registered with the Professional Board of Emergency Care (PBEC). They can provide advanced life support interventions such as rapid sequence intubation, and mechanical ventilation, and are the highest qualified prehospital emergency care providers in South Africa. They must hold a bachelor's degree.

[2] Paramedics (ANT) are independent practitioners who have completed either vocational training encompassing up to nine months, or formal tertiary training to a diplomate level. Paramedics may perform interhospital transfers of mechanically ventilated patients, but they may not perform intubation.

[3] PBEC – Professional Board for Emergency Care

[4] Primary scene calls are attended by emergency medical services in the out-of-hospital setting, representing the first point of contact between the patient and the healthcare system immediately following an emergency.

This research aimed to describe contemporary sedation and analgesia practices and determine the proportion of mechanically ventilated patients who receive rescue dose sedation and analgesia during aeromedical transport. For this research, rescue sedation is defined as the administration of bolus dose sedation in addition to a continuous sedation infusion, usually due to inadequate sedation achieved by the initial infusion. Rescue sedation can also be administered for unsafe patient care situations. Unsafe patient care situations include attempts to remove the endotracheal tube, ventilator dyssynchrony, or any situation that the practitioner views as a threat to the patient's safety.

1.1.1. Critical Care Retrieval in South Africa

There are a limited number of intensive care unit beds in the rural and peri-urban areas of South Africa. In the Western Cape Province there is a public sector bed: population ratio of less than 1:20,000 (Scribante & Bhagwanjee, 2007). At least 10% of public hospitals without intensive care facilities were more than 300km away from the nearest hospital with an Intensive Care Unit (ICU) (Scribante & Bhagwanjee, 2007). Due to these factors, the transfer of critically ill and injured patients over moderate to long distances is inevitable and occurs frequently. The distances involved favour aeromedical transport by either rotor wing[5] or fixed wing[6] to save time and provide the most appropriate level of care for the duration of transfer.

Critical care retrieval is the stabilisation and transport of a critically ill or injured patient from a location where the patient's healthcare requirements outweigh the diagnostic or treatment abilities, and/or expertise available, to an appropriate facility where these are available (Venter et al., 2021). CCR should be performed by dedicated crew with specialised training in critical care, retrieve patients using dedicated specialised equipment, and transport (Venter et al., 2021). These transport modalities include ambulance, rotor wing, or fixed wing transport.

The role of aeromedical transport has not been extensively researched in South Africa. A single centre study showed that the majority (77.8%) of HEMS missions were for interhospital transfers, and over half of these patients were intubated and mechanically ventilated (Vlok, Wylie and Stassen, 2023). This study also showed that 45% of patients transported by HEMS for IFT received sedation, and 28.6% received analgesia (Vlok et al., 2023). However, no description of sedation and analgesia practices is discussed. This study shows that the use of HEMS for IFT of mechanically ventilated patients is common, as is the use of sedation and analgesia.

[5] Rotor wing refers to a helicopter.
[6] Fixed wing refers to an aeroplane.

A study of private sector ground EMS CCRS showed that sedatives and analgesics were the most administered medications among patients undergoing transfer (Venter & Stassen, 2023). These medication types were described, but no differentiation was made between how they were administered, nor were the doses described.

It is established that IFT of patients requiring ICU facilities is common in South Africa due to limited resources in the public sector (Scribante & Bhagwanjee, 2007a). Vast distances from ICU facilities necessitate the use of aeromedical transport with CCR capabilities. Core practices of critical care retrieval have been identified as mechanical ventilation, sedation, and analgesia in various studies locally. However, these practices have not been described in the literature.

1.1.2. Overview of CCR teams in South Africa

In South Africa, EMS are responsible for all interfacility transfers and CCRs regardless of patient acuity (Venter & Stassen, 2023). Interfacility transport of mechanically ventilated patients may be undertaken by Emergency Care Practitioners (ECP) and Paramedics (ANT). These prehospital emergency care providers can provide mechanical ventilation and sedation and analgesia. In the aeromedical setting, the primary clinician is either an ECP or Paramedic, with an Ambulance Emergency Assistant (AEA)[7] or Emergency Care Technician (ECT)[8] partner. Physicians do not routinely attend complex CCRs as part of a dedicated team due to the severe shortage of physicians in South Africa (Venter & Stassen, 2023). The prehospital emergency care providers undertaking CCR are not able to specialise in this field, and feel poorly prepared and lack confidence in CCR (Venter & Stassen, 2023).

In South Africa, CCR may take place using a dedicated ICU Ambulance or by air transport. Aeromedical services offer CCR by either rotor or fixed wing transport, and these platforms are crewed by various compositions of the qualifications discussed. As a minimum, these platforms are crewed with either an ECP or Paramedic.

1.1.3. Sedation and analgesia practices in the South African aeromedical setting

The published literature has not yet described sedation and analgesia practices in the South African aeromedical transfer environment. Guidelines for sedation and analgesia in this setting originate from standard operating procedures (SOP) and protocols such as the Air Mercy

[7] Ambulance emergency assistants have undergone vocational training for up to six months and may practice intermediate life support interventions. They are registered with the Health Professions Council.

[8] Emergency care technicians have completed a two-year National Certificate which allows them to practice advanced life support interventions, with consultation required for certain medications and skills. They are registered with the Health Professions Council.

Service Drug Infusion Protocol, which has not been updated in recent years (Roos et al., 2012). This protocol is still used in the Western Cape Province of South Africa, at the Air Mercy Service (AMS). AMS are responsible for providing aeromedical services to the Western Cape Department of Health and Wellness, and as such, attend CCRs throughout the province. At this service, the primary provider on the aircraft must either be a registered ECP or ANT.

The Clinical Practice Guidelines (CPG) make no specific reference to postintubation sedation and analgesia (PISA), except for patients who are mechanically ventilated with sepsis or septic shock (HPCSA, 2018). In this recommendation, the CPG recommends minimising continuous or intermittent bolus dosing of sedatives in mechanically ventilated sepsis patients, and suggests targeting specific titration endpoints (HPCSA, 2018). Remaining references made in the CPG pertain to sedation prior to intubation, or procedural sedation and analgesia (PSA).

A Clinical Decision Support Tool (CDST) published by the Professional Board of Emergency Care (PBEC) makes specific recommendations for postintubation sedation and analgesia. The CDST is endorsed by the PBEC and the HPCSA and therefore emergency care providers are encouraged to use these guidelines nationally (HPCSA-PBEC, 2024).

1.1.4. Sedation and analgesia management practices

ECPs and Paramedics may administer ketamine, midazolam, etomidate, morphine, Entonox, methoxyflurane, paracetamol, diazepam, and lorazepam to provide sedation or analgesia to patients (HPCSA, 2018). ECPs may also use rocuronium or vecuronium for ongoing paralysis if it is deemed necessary by the practitioner (HPCSA, 2018). Succinylcholine is the second paralytic medication within the ECP capabilities list for neuromuscular blockade during rapid sequence intubation (RSI) (HPCSA, 2018). When accompanied by a physician, additional sedatives such as propofol and dexmedetomidine can be administered during CCR. Under consultation, fentanyl may also be administered by an ECP for analgesia in these settings (HPCSA, 2018).

Previous studies into HEMS showed that sedation and analgesia were the most common interventions during IFT by HEMS (Vlok et al., 2023). International studies have described these practices with reference to medication types, doses used, and sedation depth (Roginski et al., 2023) (Moy et al., 2021). Important findings of these studies included that patients were often deeply sedated, and that the use of benzodiazepines was still common (Roginski et al., 2023). These findings are important, as literature from the intensive care unit and Emergency Centre (EC) settings have demonstrated that early deep sedation may result in prolonged hospital stay, increased mortality, increased duration of mechanical ventilation, and delirium (Roginski et al., 2023).

Until recently, there were no comprehensive HPCSA/PBEC guidelines for the provision of continuous sedation and analgesia in the prehospital setting (HPCSA, 2018). A Clinical Decision Support Tool (CDST) has been published and contains recommendations for continuous sedation and analgesia (HPCSA-PBEC, 2024). However, this tool was published after the data collection period for this research and would not have an impact on sedation and analgesia practices described in this research. It is unknown whether the sedation and analgesia doses recommended in the CDST will be appropriate for the aeromedical setting.

Sedation and analgesia in the aeromedical setting may have been guided by institutional SOPs and Protocols, as well as the referring facility's regime on handover to the air crew. However, until sedation and analgesia practices in the South African aeromedical setting are described, it is difficult to further update or develop guidelines and make recommendations that are fit for purpose.

1.1.5. Rescue sedation

Bolus dose sedation and analgesia is used in the out-of-hospital setting, and has been described in the period immediately following rapid sequence intubation as 'postintubation sedation and analgesia (PISA)' (de Kock et al., 2022). In the aeromedical transfer setting, this modality of administering sedation and analgesia is less appropriate due to the duration of most transfers. Anecdotally, sedation and analgesia are administered by continuous infusion during aeromedical transfers of longer duration. The practice of administering bolus sedation in addition to a continuous infusion has not been described by the term 'rescue sedation' in the published literature before. Rescue sedation is usually necessitated due to unsafe patient care situations that arise due to inadequate sedation achieved by the continuous infusion (Roginski et al., 2023).

1.1.6. Sedation and analgesia monitoring practices

Sedation and analgesia infusions are administered according to dose ranges originating from various guidelines. A tendency for deep sedation has been noted in the out-of-hospital and aeromedical transport setting (Roginski et al., 2023) (Moy et al., 2021). Deep sedation has been implicated in increased risk of mortality and morbidity among mechanically ventilated patients in the ICU (Moy et al., 2021). During aeromedical transfer, moderate and deep sedation was associated with an increased hospital length of stay by 59% (aRR: 1.59; 95% CI: 1.40–1.81) and 24% (aRR: 1.24; 95% CI: 1.10–1.40), respectively (George et al., 2020).

Sedation depth and pain is routinely assessed in both the ICU, and increasingly, in Emergency Centres internationally (Varndell et al., 2015). Performing routine sedation depth assessments enables healthcare providers to titrate sedatives to a desired effect, or sedation depth, rather than to a prescribed dose range. It may be beneficial to individualise sedation requirements on a patient-to-patient basis, rather than administering recommended doses as stipulated by guidelines to all patients, irrespective of pathology.

Use of sedation depth scores, like the Richmond Agitation Sedation Scale (RASS)[9], during aeromedical transfer have been discussed internationally (Moy et al., 2021). Findings from these studies showed that validated sedation scores were not routinely documented, and instead were substituted with the GCS, which is commonly measured out-of-hospital. GCS is not validated for assessing sedation depth, and is traditionally used as a prognostic indicator for patients who have suffered from traumatic brain injury (Varndell et al., 2015). However, a GCS (≤9) was regarded as deep sedation and GCS 3 was equated with coma (Moy et al., 2021). Deep sedation was common in the aeromedical retrieval of mechanically ventilated patients (Moy et al., 2021; Roginski et al., 2023).

Prior to this study, there were no studies in the South African aeromedical setting have described sedation and analgesia monitoring practices, or how sedation and analgesia infusions are titrated. Implementation of sedation depth scoring and routine pain assessment for mechanically ventilated patients may influence the incidence and recognition of deep sedation, or under-sedation, both of which pose harm to patients (Varndell et al., 2015). Further, the use of sedation depth monitoring may assist in the development of sedation guidelines where doses are titrated to achieve a desired depth of sedation. This may avoid incidences of deep sedation or under-sedation potentially related to prehospital practitioner adherence to dose ranges originating from the in-hospital setting.

Sedation practices during aeromedical transfer are associated with potentially deleterious clinical outcomes, and further investigation into sedation monitoring and management practices is needed in South Africa.

1.1.7. Adverse events

An adverse event (AE) is classified as an unfavourable or potentially harmful occurrence during patient care from the time the air crew arrives at the referring facility until the patient is handed over at the receiving facility (MacDonald et al., 2008). Critically ill and injured patients are at higher risk of adverse events (Jeyaraju et al., 2021).International literature has shown that in the aeromedical transfer environment, medical adverse events occur in up to 11% of cases (95% CI: 7.5%-16%) (Jeyaraju et al., 2021). Adverse event rates in this setting are largely undocumented and have not been described in South African literature.

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[9] The Richmond Agitation Sedation Scale (RASS) is a 10-level scale examining consciousness and agitation and is validated for use among mechanically ventilated patients (Sessler et al., 2002). See Annexure E.

AEs described in the literature include medical events related to oxygenation, ventilation, haemodynamic status, cardiac rhythm, pain, level of consciousness (including seizures), and cardiac arrest (Jeyaraju et al., 2021). Factors thought to be associated with the occurrence of adverse events include the use of vasopressors, distance of transfer, and the patient's baseline condition – patients in critical condition are at a higher risk of adverse events occurring.

Knowledge of these factors may assist in further training, and AE reporting, hopefully culminating in improved patient safety. The underlying consensus however, is that critically ill patients are at greater risk of adverse events due to the nature of their condition (Jeyaraju et al., 2021). Patients included in this study were all receiving mechanical ventilation and were all critically ill or injured, and therefore all at risk of AEs.

1.2. Problem Statement

Despite evidence to suggest that aeromedical services play an important role in critical care retrieval in South Africa, there is limited research surrounding sedation and analgesia practices in this setting.

Sedation and analgesia are core components in the critical care of mechanically ventilated patients. Sedation practices during aeromedical transfers abroad have shown tendencies for deep sedation and the use of benzodiazepines (Moy et al., 2021; Roginski et al., 2023).

Deep sedation and benzodiazepine use are linked to deleterious effects such as prolonged length of hospital stay, increased days of mechanical ventilation, and increased risk of death (Moy et al., 2021). Early deep sedation during the first 48 hours of ICU care has been independently associated with higher mortality (Moy et al., 2021). Similarly, early deep sedation among patients with respiratory failure has been associated with worse clinical outcomes in the Emergency Centre (Moy et al., 2021). The prevalence of deep sedation in the South African aeromedical transfer setting is unknown, and due to these concerns, further research into sedation and analgesia practices is necessary.

Benzodiazepines are still widely used for ongoing sedation in South Africa, as evidenced by guidelines such as the Clinical Decision Support Tool (CDST) published by the PBEC (HPCSA-PBEC, 2024), and the National Drug Infusion Protocol for Air Mercy Service (Roos et al., 2012). Ketamine is another sedative medication that is available for use in the aeromedical transfer setting. It is unknown which medications are favoured or used more frequently for sedation and analgesia during aeromedical transfer in South Africa.

Describing contemporary practices in the aeromedical setting will help to prioritise future research to inform evidence-based sedation and analgesia practices and monitoring. This is important as literature shows that these practices, even in the early stages of a patient's care have downstream implications for clinical outcomes. Moy et al (2021) showed that the use of sedation depth scores was rare, and that deep sedation was common. As sedation depth was not routinely assessed, it is likely that instances of deep sedation or under sedation are under-recognised in the aeromedical transfer of these patients. These authors also showed that benzodiazepines were frequently used for continuous sedation and analgesia among mechanically ventilated patients (Moy et al., 2021).

A lack of routine pain assessment was found in this cohort of mechanically ventilated patients (Moy et al., 2021; Zia et al., 2019). Zia et al (2019) stated that – at the time - there were no published guidelines for the assessment and management of pain among adult mechanically ventilated patients undergoing interhospital transfer. These findings are concerning and may pose a risk to patient safety and comfort. The most recent literature describing the use of sedation depth scores and pain assessments during transfer pertains to paediatric patients (Lyons et al., 2024). In keeping with adult literature on the subject, prior to the article by Lyons et al (2024), no specific tools for monitoring sedation depth among mechanically ventilated paediatric patients during transfer could be found. Whether this represents a risk to instances of unrecognised under sedation, deep sedation, or pain is unknown and necessitates further investigation due to the implications that these practices have for this patient cohort.

Under sedation, pain, and awareness during paralysis have serious implications for intubated patients (Pappal et al., 2021). Practices resulting in under sedation, pain, and awareness are associated with the development of PTSD, anxiety, and depression (Pappal et al., 2021). Under sedation can result in patient agitation, which has been associated with unplanned extubation in select patient cohorts (Lyons et al., 2024). Protocolised sedation and analgesia assessment and guidelines have been proposed to empower clinicians to respond appropriately to assessments.

Describing sedation and analgesia practices in the South African aeromedical setting may establish whether these issues are present locally. By describing sedation and analgesia practices in the South African aeromedical transfer setting, further research can prioritise sedation and analgesia guideline development with immediate improvements to monitoring and management practices.

1.3. Research Aim

To describe current sedation and analgesia practices and determine the proportion of mechanically ventilated patients who receive rescue dose sedation and analgesia during aeromedical transport.

1.4. Significance of the Study

In achieving this aim, the research may inform policy makers, researchers, and aeromedical service providers, and emergency care providers on important actions that should be taken to improve sedation and analgesia monitoring and management practices. This study might guide prospective research and inform guideline development. These actions could standardise and improve our approach to provision of safe and effective sedation and analgesia during aeromedical transfer of mechanically ventilated adult patients.

1.5. Research Questions

- What is the proportion of mechanically ventilated patients undergoing aeromedical IHT receive rescue sedation?
- Were sedation and analgesia scales/assessment tools used to monitor mechanically ventilated patients during aeromedical IHT?
- What types of medications, doses, and methods of administration are used to provide sedation and analgesia to mechanically ventilated patients during aeromedical IHT?
- What was the adverse event rate during aeromedical IHT of mechanically ventilated patients?

1.6. Research Objectives

The primary objective was to determine the proportion of patients who required rescue sedation during aeromedical transfer. Secondary objectives of this research were:

1.6.1. Describe sedation and analgesia monitoring practices[10] and sedation and analgesia management practices[11].

1.6.1.1. Describe the use of sedation depth monitoring tools.

1.6.1.2. Describe the use of pain assessment tools.

1.6.1.3. Describe the administration of medications used for sedation and analgesia.

1.6.2. Describe adverse events associated with rescue sedation and analgesia.

1.7. Chapter One Summary

Chapter one provides background information to support and contextualise this research. Critical care retrieval is defined and discussed with regards to the South African critical care

[10] Sedation and analgesia monitoring practices refer to the use of validated sedation and analgesia assessment tools to assess and document a patient's depth of sedation, or pain.

[11] Sedation and analgesia management practices refer to the type of medications administered, the doses used, and modes of administration (syringe driver, bolus, infusion pump).

context. The need for aeromedical critical care retrieval is justified by discussing how few ICU beds are available to the public and this is emphasised by the vast distances between referring facilities and those with ICU capabilities in South Africa.

The chapter discusses the composition of CCR teams in South Africa, which shows that these retrievals are led by independent Emergency Care Practitioners (ECP) or Paramedics (ANT), which may be due to a severe shortage of physicians (Venter et al., 2021). Despite teams comprising of prehospital emergency care providers in the majority of CCRs, there is no specialist training available to them.

These providers may refer to various guidelines originating from different settings when providing sedation and analgesia to mechanically ventilated patients during aeromedical transfer. The chapter discussed what medications are available to ECPs and Paramedics for sedation and analgesia, noting that options are limited to ketamine, midazolam, morphine, methoxyflurane, Entonox, lorazepam, diazepam, and fentanyl in most cases. The practice of administering rescue sedation was defined in the context of aeromedical transfer. Rescue sedation in this setting has not been defined previously, and therefore this research aims to determine the proportion of patients who receive rescue sedation. Further study may be indicated to determine why rescue sedation is administered to these patients.

Sedation and analgesia monitoring practices refer to the use of validated tools to assess sedation depth and pain severity among mechanically ventilated patients during aeromedical transfer. International research has shown that these tools are rarely used or documented, and in most cases a GCS is used as a surrogate for sedation depth. This research aims to determine how sedation depth and pain are assessed and monitored among mechanically ventilated patients in the aeromedical setting. Without the use of such tools, deep sedation or undersedation and pain may go unrecognised, which may confer harm according to various sources (Moy et al., 2021; Pappal et al., 2021).

Finally, the chapter discusses how AEs were identified and screened by the researcher in this study. AE rates in similar settings internationally are relatively low, but no data exist in the South African aeromedical transfer environment to determine whether this finding is applicable locally.

In conclusion, sedation and analgesia management and monitoring practices among mechanically ventilated patients are undocumented in the South African aeromedical transfer setting. The primary clinicians are predominantly prehospital care providers, with no specialist training in CCR. No consensus exists for continuous sedation and analgesia guidelines for mechanically ventilated patients undergoing aeromedical transfer, and available standard operating procedures and guidelines may be outdated or not fit for purpose. AEs have not been extensively studied in the aeromedical transfer setting, which poses a risk to patient safety and quality improvement.

CHAPTER 2: LITERATURE REVIEW

2.1. Objectives

The objectives of this literature review were to determine known sedation and analgesia practices and methods of assessing sedation depth and pain in mechanically ventilated patients undergoing aeromedical transfer. Previous definitions of ‘rescue sedation’ were described.

The literature review aimed to describe postintubation sedation and analgesia in South Africa and internationally, describe the use of protocol-directed sedation and analgesia and the medications used for sedation and analgesia among mechanically ventilated patients undergoing aeromedical transfer. AE rates and types of AE were also discussed in the literature review.

2.2. Search strategies

The following major databases were searched through the EBSCOhost Research Database:

- Medline
- CINAHL
- PubMed

Google Scholar was also searched for relevant journal articles.

The following limiters were used during the search:

- English Language
- Adults >18 years of age
- Human
- 2000-2025

Duplicates were removed using Mendeley reference manager.

<u>Search strings and Boolean operators:</u>

- ‘aeromedical’ OR ‘air medical’ OR ‘HEMS’ AND ‘sedation’ OR ‘analgesia’ AND ‘mechanical ventilation’
- ‘rescue sedation’ AND ‘emergency department’ OR ‘emergency centre’

Keywords: Aeromedical, sedation, analgesia, rescue sedation, mechanical ventilation, prehospital, interhospital transfer/transport, helicopter emergency medical service (HEMS).

2.3. Aeromedical transport in the Western Cape Province of South Africa

The South African Air Mercy Service (AMS) operates from the Western Cape, Eastern Cape, and Kwa-Zulu Natal (KZN) provinces of South Africa.

This research focused on the Western Cape, where AMS complements ground transport of critically ill or injured patients from rural areas of the province (Egger et al., 2025). AMS operates two aeroplanes (Pilatus PC-12) and two helicopters (Agusta Westland 119 Koala) in the Western Cape. These aircraft are staffed predominantly by paramedics providing advanced and intermediate life support capabilities (Egger et al., 2025).

Intensive care resources are limited in the public health sector in South Africa, and most are limited to the urban areas of the country (Venter et al., 2021). This implies that critical care retrieval and transport of patients from rural or resource-limited settings must occur to enable access to specialist care (Venter & Stassen, 2023; Venter et al., 2021). AMS performs critical care retrieval of patients from rural areas in the Western Cape to the metropole, where specialist and intensive care resources are located (Egger et al., 2025).

2.4. Sedation and analgesia practices

Sedation and analgesia are regularly administered during critical care transport (Wilcox et al., 2015). In the aeromedical retrieval setting, sedation and analgesia of mechanically ventilated patients is common practice (Moy et al., 2021). However, there is limited data pertaining to rescue dose sedation and analgesia during aeromedical transfer. Rescue sedation is currently defined in the context of chemical restraint used for psychotic, combative patients (Klein et al., 2019). However, there is scope for rescue sedation to be defined in terms of critical care and continuous sedation in the aeromedical setting.

2.4.1. Sedation Depth and Pain Scoring Tools

The literature advised that sedation be administered in a patient-centric manner, with a pre-determined depth of sedation as the objective (De Jonghe et al., 2010). This cannot be achieved unless the depth of sedation is measured and monitored. Therefore, practitioners providing sedation to mechanically ventilated patients require a tool to monitor the effectiveness of the sedation they are administering (De Jonghe et al., 2010).

Nursing staff experienced improved confidence and sedation practices when using sedation-scoring instruments for mechanically ventilated patients (Varndell et al., 2015). Currently, many prehospital practitioners use the Glasgow Coma Scale (GCS) to assess a patient's depth of sedation. The GCS was developed to quantify the prognosis of brain-injured patients, but has been used in previous literature to assess patients' sedation depth (Carraway et al., 2021). As the GCS is a coma scale that was previously extrapolated to sedation depth assessment, it does not measure agitation adequately and for this reason may be difficult to compare to conventional sedation depth assessment tools (Nassar et al., 2008).

There are various tools that can be used to measure or quantify a patient's depth of sedation. However, only five tools were assessed for applicability or 'ease of use'; the Richmond Agitation Sedation Score (RASS), Motor Activity Assessment Scale (MAAS), Sedation Agitation Score (SAS), Ramsey Sedation Scale (RSS), and the Nursing Instrument for the Communication of Sedation (NICS) (Varndell et al., 2015). Of these tools, the RASS, SAS, and NICS were found to be the most reliable sedation depth tools (Varndell et al., 2015).

Communication between staff, and the ability to provide target-specific sedation improved with the use of the RASS (Mirski et al., 2010). The RASS has a high interrater reliability, and demonstrated high levels of reliance and ease of use when compared to the RSS, MAAS, and SAS (Varndell et al., 2015). There is an abundance of literature examining the use of the RASS, and this tool has been shown to be acceptable, valid, and reliable when used for sedation depth monitoring (Wang et al., 2021). The RASS improved communication of sedation depth in the ICU setting (Mirski et al., 2010).

Wang et al (2021) described various sedation assessment tools and compared them in terms of their advantages and disadvantages, as well as describing their origins. The Ramsey Sedation Scale (RSS) is the earliest and most widely used scale to date (Peck & Down, 2010). It is a single-item tool to measure consciousness across three levels in critical patients who are deemed to be asleep, and those deemed to be awake (Wang et al., 2021).

The Sedation Agitation Scale (SAS) was developed to assess for agitation and sedation among patients in ICU (Riker et al., 1999). The SAS is a single-item seven point scale which has been shown to be reliable and valid for use in the ICU (Wang et al., 2021). The SAS has previously shown the best correlation and interprofessional agreement when compared to alternative sedation depth assessment tools (Nassar et al., 2008). Additionally, the SAS can provide an assessment of sedation tolerance, and has demonstrable longitudinal validity (Wang et al., 2021).

The Nursing Instrument for the Communication of Sedation (NICS) is reportedly easy to use and simpler than other available sedation tools (Wang et al., 2021). It is favoured by nurses when communicating about sedation and has been ranked highest in nursing preference for use in the ICU (Wang et al., 2021). A limitation of the NICS is that it is subjective however, it is still a valid and reliable sedation scoring tool and can be applied to a mixed population of ICU patients (Wang et al., 2021). The Motor Activity Assessment Scale (MAAS) was developed to assess sedation depth in the surgical ICU setting (Wang et al., 2021). According to the literature, the MAAS is a reliable and valid sedation scoring tool for use in surgical ICU, but evidence to support its use in the Emergency Centre is insufficient (Wang et al., 2021).

In literature describing the use of sedation monitoring tools in the aeromedical setting, the RASS was the most commonly used (Roginski et al., 2023) (Moy et al., 2021). However, in some studies a RASS or alternative sedation score was rarely recorded in patient care reports (PCRs) (Zia et al., 2019). This may indicate that there is a lack of standardisation of sedation depth monitoring in the aeromedical setting (Moy et al., 2021).

Pain assessment tools such as the Behavioural Pain Scale (BPS) and the Critical Care Pain Observation Tool (CPOT) are used to assess pain in nonverbal critically ill patients (Zia et al., 2019). Despite the use of these tools by aeromedical services, they have not been validated for use in the aeromedical environment (Zia et al., 2019). Both the BPS and CPOT have been reported as reliable, valid, and sensitive for detecting pain in mechanically ventilated patients in the intensive care unit (Al Darwish et al., 2016). The sensitivity of the BPS was determined by a significant increase in pain score during suctioning and turning of mechanically ventilated patients ($p<0.001$) (Al Darwish et al., 2016). The CPOT was also proven to be highly sensitive to increases in pain ($p<0.001$) (Al Darwish et al., 2016). This study concluded that the BPS was most valid and reliable in the assessment of pain for nonverbal patients(Al Darwish et al., 2016).

In an aeromedical study, monitoring patients with either the Ramsey Sedation Scale (RSS) or the RASS was independently associated with lower odds of deep sedation (Moy et al., 2021). Prehospital use of validated scales may be effective in achieving on-target sedation scales, avoiding unnecessary deep sedation (Moy et al., 2021). Despite these findings, routine monitoring with the RASS or similar sedation scales is rare in the aeromedical environment (Moy et al., 2021; Zia et al., 2019). In an international survey to evaluate the mechanical ventilation infrastructure in HEMS, a reported limitation was that authors were unable to provide information on whether sedatives and analgesics were administered on the basis of scoring systems like the RASS or BPS (Hilbert-Carius et al., 2020).

2.4.2. Sedation and Analgesia Practices in the Aeromedical Setting

Early studies indicated that up to 91.3% of paralysed mechanically ventilated patients undergoing aeromedical transfer were receiving some form of sedation (Frakes & Lord, 2006). Patients commonly received benzodiazepines alone (70.2%), omitting analgesia (Frakes & Lord, 2006). Only 23.4% of patients received benzodiazepines and an opioid, while the remainder either received an opioid alone (5.3%) or propofol (1.1%) (Frakes & Lord, 2006). In patients where sedation was omitted, 'haemodynamic instability' was the documented reason for withholding sedation or analgesia (Frakes & Lord, 2006). This research demonstrated earlier sedation and analgesia practices in the HEMS setting. It also demonstrated a risk of awareness[12] during paralysis for these patients, and encouraged further research and practice development in the area (Frakes & Lord, 2006).

A survey of U.S Aeromedical Programs was conducted to gather information pertaining to Emergency Airway Management Techniques. Included in this survey, was information regarding postintubation sedation and analgesia, and paralysis. Most programs continuously administer fentanyl for analgesia post intubation (James et al., 2009). All programs use sedation post intubation, with 94% favouring midazolam over other non-benzodiazepine options (James et al., 2009). There was some indication from respondents that ongoing paralysis was administered following rapid sequence intubation (RSI), and concerningly 25% administer long-acting NMBAs in response to hypertension and tachycardia (James et al., 2009).

A retrospective study sought to determine the incidence of haemodynamic deterioration after administration of sedatives and analgesics during critical care transport (CCT). The study included fixed wing and rotor wing transports only and took place in Canada. Fentanyl (44.8%) and midazolam (37.5%) were the most administered analgesics and sedatives (Singh et al., 2015). Propofol was the most administered sedative infusion (61.5%) (Singh et al., 2015).

In a review of therapeutic agents used by a HEMS service in Australia, medications used for sedation and analgesia for intubated patients were; morphine, fentanyl, propofol, and midazolam (Hayward et al., 2016). The authors reasoned that these medications were used due to their fast onset and offset times, which they stated as favourable in the critical care

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[12] Awareness with recall of paralysis is the recollection of sensory perceptions while under the influence of a neuromuscular blocking agent (Pappal et al., 2021).

setting (Hayward et al., 2016). A mixed aeromedical-ground CCT study described patterns of medication administration during transport. They found that the most commonly administered medications used for sedation and analgesia were fentanyl, propofol, and midazolam (Wilcox et al., 2015). Sedatives and hypnotics were administered most frequently, accounting for 26.1% of prescription medications (Wilcox et al., 2015).

A study examining sedation practices among mechanically ventilated patients undergoing aeromedical transfer and its effects on clinical outcomes reported that the majority of patients received sedation during transport (79.2%) (George et al., 2020). Deep sedation[13] occurred in 41% of patients with a RASS score of -4 documented (George et al., 2020). Over half of patients received benzodiazepines for sedation (58.3%) (George et al., 2020). Both moderate and deep sedation were associated with a longer hospital stays - 59% (aRR: 1.59; 95% CI: 1.40–1.81) and 24% (aRR: 1.24; 95% CI: 1.10–1.40) (George et al., 2020).

A descriptive analysis of patients with coronavirus requiring air medical evacuation discussed when and why certain sedatives and analgesics were necessary. Half of patients in this study were receiving mechanical ventilation (50%) during flight (Davis et al., 2022). A quarter of patients receiving mechanical ventilation required paralytics (25%) (Davis et al., 2022). All of these patients received continuous fentanyl and propofol infusions for analgesia and sedation, with 25% concurrently receiving ketamine infusions (Davis et al., 2022). Many patients experienced patient-ventilator asynchrony (PVA) (63%), which was resolved with bolus doses of ketamine in four out of five patients (Davis et al., 2022). One patient required a continuous paralytic infusion to manage PVA (Davis et al., 2022).

Studies have stated that deep levels of sedation, defined as a Richmond Agitation Sedation Score (RASS) of -3 to -5, have been implicated in increased length of hospital stay, fewer ventilator-free days, and higher mortality rates (Roginski et al., 2023). Most patients in this mixed aeromedical-ground CCT study were deeply sedated (91.7%), with fentanyl boluses (86.9%) and propofol infusions (66.1%) being the most frequent sedatives/analgesics administered during transport (Roginski et al., 2023).

Up to four boluses of different medications were administered throughout the transfers sampled, with ketamine being administered infrequently as a bolus (Roginski et al., 2023). The study also documented when bolus sedation was administered for unsafe situations like

[13] Deep sedation was defined as a Richmond Agitation Sedation Score of -3 to -5, or a Glasgow Coma Score of ≤9 (Moy et al., 2021).

extubation, and ventilator dyssynchrony. Interestingly, it reported that despite initial sedation depth, patients received the same quantity of sedation throughout the transfer (Roginski et al., 2023). Patients only received additional sedation and analgesia in thirteen cases, three (0.7%) for an unsafe patient care situation, and ten (2.2%) for ventilator dyssynchrony (Roginski et al., 2023).

The AIR-SED (A Multicenter Cohort Study of SEDation Practices, Deep Sedation, and Coma Among Mechanically Ventilated AIR Transport Patients) study showed that most patients received bolus sedation and analgesia (Moy et al., 2021). Commonly used agents were fentanyl (50.8%), midazolam (38.8%), ketamine (38.6%), and propofol (13.0%); all of which were delivered via bolus dosing. In addition to these medications, 63% of patients received neuromuscular blockers such as rocuronium, succinylcholine, and vecuronium. This study showed that bolus dosing is standard practice at these organisations. Additional doses of sedation and analgesia were administered most commonly for ventilator dyssynchrony (2.2%) and unsafe patient care situations (0.7%) (Roginski et al., 2023).

A study based in Canada identified the most common analgesic administered during aeromedical transfer as fentanyl (Zia et al., 2019). The authors found that 73% of mechanically ventilated patients received analgesia during aeromedical transfer, with longer transfer times resulting in repeat doses being administered (Zia et al., 2019). Clinicians used the Critical Care Pain Observation Tool (CPOT) to assess their patients for pain. Repeat doses were administered in 97% of cases, usually when transport times exceeded 180 minutes. It is unclear what prompted the re-administration of analgesics however, a CPOT score of 0-1 was documented after the administration of analgesics (Zia et al., 2019). It is likely that clinicians re-administered analgesics to maintain the CPOT score between 0 and 1. There was no reference made to the use of rescue sedation or analgesia in the study.

A retrospective chart review was conducted to evaluate analgesia practices among non-intubated patients during critical care transport. Most patients in this study were transported by rotor wing. The primary outcome was to determine the proportion of patients who became over sedated (RASS of -3), and secondary outcomes sought to characterise the different analgesia techniques used in this chart review. The study found that 2.9% of patients became over sedated during transport (Esteves *et al.*, 2023). Fentanyl was the most used analgesic medication and was usually administered as a monotherapy at a mean dose of 1.5 +/- 1.1mcg/kg (Esteves *et al.*, 2023). Ketamine was administered to 4.3% of patients, at a median dose of 0.4mg/kg (IQR: 0.3 – 0.7). Patients who received a benzodiazepine in addition to their analgesic had higher odds of oversedation (OR = 5.75; 95% CI, 1.60-20.7) (Esteves *et al.*, 2023).

There is a reported paucity of data pertaining to patient-oriented outcomes regarding ketamine use for mechanically ventilated patients (Moy et al., 2021). This is noteworthy, as one of the infusions commonly used in parts of the South African critical care retrieval setting is a combination of ketamine and midazolam (Roos et al., 2012). There is recent literature examining the effectiveness of ketamine for analgesia and sedation in the intensive care setting however, this does not extend to the aeromedical setting.

A retrospective chart review examined ketamine sedation for acute behavioural disturbance during aeromedical retrieval. This review also included patients who required intubation due to resistance to ketamine sedation culminating in continued agitation despite high doses of ketamine, or due to loss of airway protection reflexes. This study showed that among patients who received ketamine for sedation, non-intubated patients received a mean dose of 1.2mg/kg/hr and intubated patients received a mean dose of 2.8mg/kg/hr (Gangathimmaiah et al., 2017).

Rescue sedation refers to administration of an additional sedative or analgesic agent, as the initial medication achieved inadequate sedation (Klein et al., 2019). In the intensive care unit, rescue analgesia and sedation are administered for incidental and procedural pain (Travers, 2010). During aeromedical transfer, patients will be exposed to increased movement, noise, and vibration. This may increase their analgesia and sedation requirements to maintain a safe and comfortable depth of sedation for transport.

Neuromuscular blocking agents (NMBAs) are occasionally administered in conjunction with continuous sedation and analgesia and therefore form part of sedation practices. There are various indications for NMBA administration beyond intubation. Additional indications include ventilator dyssynchrony, acute respiratory distress syndrome (ARDS), refractory elevated intracranial pressure (ICP), shivering associated with therapeutic hypothermia, and severe intra-abdominal compartment syndrome (Esteves et al., 2024).

Due to these additional indications, continuous infusions or maintenance of NMBAs with bolus doses is often used in CCT (Esteves et al., 2024). A cohort study showed that NMBAs were administered due to ventilator dyssynchrony in 56.4% of cases, and rocuronium was used in 89.7% of cases where ongoing NMB was maintained (Esteves et al., 2024). Mean RASS score prior to administering NMBAs was -3.7 +/- 2.4, indicating that not all patients were deeply sedated prior to NMB (Esteves et al., 2024). However, authors state that in most cases (79.4%), sedation strategy was changed post continuous NMB and included additional boluses of sedation and analgesia (70.6%), increased infusion rates (4%), or new agents added (4.8%) (Esteves et al., 2024).

2.4.3. Administration Strategies for Sedation and Analgesia

Sedation practices vary in the literature, with most aeromedical data describing bolus dose sedation as opposed to continuous infusions. Bolus medications pose a risk of error, due to the frequency with which they are administered, and the different means of delivery (Wilcox et al., 2015). The use of continuous infusions poses different challenges, such as the need for infusion pumps or syringe drivers, and dedicated intravenous lines (Wilcox et al., 2015). A study conducted at Ornge, in Canada, described the use of bolus dose analgesics for mechanically ventilated patients undergoing aeromedical transfer (Zia et al., 2019).

A Critical Care Transport study aimed to describe the patterns of medication administration by providers (Wilcox et al., 2015). The study cohort consisted of patients suffering from hypoxic respiratory failure. The CCT team often continued infusions of sedatives, but did not initiate any sedation and analgesia infusions independently (Wilcox et al., 2015). However, teams often stopped sedative infusions and elected to administer bolus dose sedation instead (Wilcox et al., 2015). The practice of stopping sedation infusions in favour of bolus doses was deemed to reflect local practice patterns (Wilcox et al., 2015).

A study of aeromedical critical care transports showed that sedatives and analgesics were routinely administered as bolus doses (86.5%) and less frequently via infusions (13.5%) (Singh et al., 2015). Midazolam was commonly administered as a bolus (84.2%) sedative, with propofol boluses being less frequently administered (38.5%) (Singh et al., 2015). Bolus dose sedation and analgesia may result in haemodynamic sequelae in patients with reduced cardiovascular reserve, as it results in rapid peak concentration of the drug (Singh et al., 2009). Hypotension following bolus dosing has been reported, being independently associated with the frequency of bolus doses administered during aeromedical transfer (Singh et al., 2009). The number of sedation bolus doses was independently associated with new in-transit hypotension (OR 1.08; p=0.04) (Singh et al., 2009).

A more recent publication showed that post-medication hypotension was rare, and only occurred in 0.6% of the study cohort (Singh et al., 2015). This study also stated that there was no association between bolus administration and the development of hypotension (Singh et al., 2015). Adverse events related to bolus analgesia seem rare (1.8%), and most commonly result in new hypotension (MAP <65mmHg) (Zia et al., 2019).

Patterns of medication administration vary in CCT, and may be due to the patient population, and the health care system they are operating in (Wilcox et al., 2015). In a study among patients with acute behavioural disturbance, patients received ketamine for sedation prior to aeromedical retrieval (Gangathimmaiah et al., 2017). Patients in this study received continuous sedation with ketamine, whether they were intubated or non-intubated patients. Among those who were intubated, all patients received ketamine by continuous infusion or by bolus and continuous infusion (Gangathimmaiah et al., 2017). This study sample was drawn from an Australian aeromedical retrieval service.

2.4.4. Medications used for continuous sedation and analgesia

In South Africa, there are various sedatives and analgesics available to Emergency Care Practitioners administering continuous sedation and analgesia. Drugs such as ketamine, morphine, and midazolam are within the ECP and Paramedic scope of practice (HPCSA-PBEC, 2020). Fentanyl is in the ECP scope of practice, provided the practitioner consults with a medical officer prior to its administration. Propofol is not within the scope of practice for any prehospital care providers but anecdotally, it is commonly encountered in the aeromedical critical care retrieval setting and is worth discussing.

Common infusion combinations in the South African critical care retrieval setting are ketamine and midazolam, and midazolam and morphine. The Air Mercy Service (AMS) is an aeromedical service providing critical care retrieval to outlying hospitals in the Western Cape, Eastern Cape, and Kwa-Zulu Natal. AMS have adapted a sedation protocol from the Royal Flying Doctor Service (RFDS), whereby these infusion combinations are used routinely during transfer of mechanically ventilated patients (Roos et al., 2012).

2.4.4.1. Ketamine

Ketamine is used in continuous infusions for analgosedation[14], despite only being listed as an induction agent by the Adult Hospital Level (AHL) South African National Treatment Guidelines

[14] Analgosedation foresees early analgesia or pain management and then, if necessary, administration of additional sedation. This practice favours an 'analgesia-first' response to signs of patient discomfort or agitation in during mechanical ventilation (Lia et al., 2023).

and Essential Medicines List (STG EML)[15] (National Department of Health, 2024). The use of ketamine for PISA was reviewed to determine whether it is effective in mechanically ventilated trauma patients (Hendrikse et al., 2023). The authors concluded that ketamine was effective for analgosedation of mechanically ventilated trauma patients when used as monotherapy or as an adjuvant medication (Hendrikse et al., 2023). The use of ketamine for postintubation sedation was shown to have a morphine-sparing effect (Hendrikse et al., 2023).

Ketamine's pharmacokinetic and pharmacodynamic properties, reasonable risk profile, and favourable haemodynamic effects make it an attractive agent for PISA (Amer et al., 2021). Ketamine has a rapid onset and recovery, with limited bioaccumulation (Hendrikse et al., 2023). Contrary to previous beliefs, ketamine does not increase intracranial pressure and is appropriate for use among patients with traumatic brain injury (TBI) (Hendrikse et al., 2023). It may promote bronchodilation and confer anti-inflammatory effects in patients with reactive airway disease (Hendrikse et al., 2023). Ketamine can result in psychomimetic adverse effects, and at high doses may result in hypertension, tachycardia, and arrhythmias (Chan et al., 2022).

Ketamine has been evaluated for its effectiveness as the primary agent in analgosedation. The vast majority of patients achieved their pain management goals with low doses of ketamine, and opioids as needed (Peters et al., 2024). Most (88%) patients did not require concomitant opioid infusions while receiving ketamine for analgosedation (Peters et al., 2024). This finding displayed an opioid-sparing effect, which is in keeping with previous studies (Peters et al., 2024). Another study demonstrated that after 24 hours of initiating ketamine, 63% of patients' concomitant sedatives were discontinued or reduced (Groetzinger et al., 2018). Perceived toxicity was reported in 7% of cases, which is similar to other studies which documented adverse clinical reactions at 7.7% (Peters et al., 2024; Groetzinger et al., 2018).

When ketamine is used in conjunction with an additional analgesic or sedative agent, it resulted in sedative-sparing and increased time at the desired level of sedation for mechanically ventilated patients (Garber et al., 2019). Ketamine use has also been shown to achieve goal RASS scores at 24 and 48 hours post initiating ketamine analgosedation compared to other sedative agents (Amer et al., 2021). However, ketamine adjunctive therapy does not seem to have an effect on the duration of mechanical ventilation (Chan et al., 2022; Manasco et al., 2020). With very low certainty evidence, some studies reported that ketamine

[15] The STG EML for primary health care (PHC) and Adult Hospital Level (AHL) have been developed to enable equitable access to effective, safe, and affordable essential medicines across South Africa.

adjunctive therapy reduced mortality (OR 0.88, 95 % CI 0.54 to 1.43, P = 0.60, very low certainty evidence, 5 RCTs, n = 307 patients) (Chan et al., 2022).

2.4.4.2. Propofol

Propofol is one of the most common sedatives used for induction of anaesthesia and for maintenance of sedation in ICU (Sahinovic et al., 2018). It has a rapid onset time, and a short duration of action which makes it beneficial for early recovery of consciousness after sedation (Garcia et al., 2021). A meta-analysis comparing midazolam to propofol showed that patients receiving propofol sedation had a significantly shorter duration of mechanical ventilation when compared to those receiving midazolam (Garcia et al., 2021). Critically-ill patients had a shorter time to extubation when compared to midazolam (Garcia et al., 2021). Acute surgical patients sedated with propofol had a shorter ICU stay when compared to patients who received sedation midazolam (Garcia et al., 2021).

Propofol is used for sedation in the aeromedical environment, although it seems to be used less frequently than medications such as midazolam and fentanyl (Moy et al., 2021). This could be due to the need for deep sedation during aeromedical transfer, which is one of the reasons for the continued use of midazolam in the ICU (Garcia et al., 2021). Propofol may also be avoided due to the risk of haemodynamic instability precipitated by reducing cardiac output and systemic vascular resistance (Chan et al., 2022; Hendrikse et al., 2023).

2.4.4.3. Fentanyl

Fentanyl infusions are frequently used for analgosedation in the ICU (Tedders et al., 2014). One potential reason for this is that they are associated with lower incidences of hypotension and bradycardia when compared to propofol (Tedders et al., 2014). In this study patients being mechanically ventilated in ICU either received fentanyl or propofol by continuous infusion. The study found that when compared, both groups had a similar median duration of stay in ICU and duration of mechanical ventilation (Tedders et al., 2014). However, patients in the propofol group required rescue opioids compared to patients in the fentanyl group (56% vs 34%, $p<0.04$) (Tedders et al., 2014). In two aeromedical studies, fentanyl was the most commonly used analgesic (73%) and sedative medication (50.8%) administered to patients undergoing aeromedical transport (Moy et al., 2021; Zia et al., 2019).

2.4.4.4. Midazolam

Midazolam is a lipophilic benzodiazepine which accumulates in the patient’s tissues, causing it to remain in the patient’s metabolism for longer. As midazolam needs to be broken down into its active form, it can accumulate in the kidneys; therefore its use in patients with kidney failure is not recommended (Garcia et al., 2021). Continuous infusions of midazolam can result in prolonged effects of the medication, and blur patient's neurological assessments (Garcia et al., 2021; Anton et al., 2024).

Aeromedical studies indicate that midazolam is still regularly used for sedation during transport of mechanically ventilated patients. One study showed that midazolam boluses were used in 38.8% of cases, to a cumulative dose of 5mg (Moy et al., 2021). Despite evidence against the routine use of benzodiazepines for sedation, there is still a role for their use in the ICU and during CCT (Garcia et al., 2021; Lia et al., 2023). The need for deep sedation is a reason for the continued use of benzodiazepines in ICU (Garcia et al., 2021). Due to the air medical environment exposing patients to loud noise, vibrations, and frequent movement, the use of deep sedation may be indicated for patient comfort and crew safety (Moy et al., 2021; Anton et al., 2024). Midazolam is associated with depression of the respiratory system, delirium, oversedation, delayed extubation, and longer time to discharge (Garcia et al., 2021; Lia et al., 2023; Wang et al., 2019).

2.4.4.5. Morphine

Morphine is commonly used as a continuous analgesic infusion for mechanically ventilated patients in the ICU (Casamento et al., 2021). Morphine is rapidly metabolised to glucuronides, however renal impairment can result in accumulation and prolonged effects (Casamento et al., 2021). Patients who received morphine had less ventilator-free days compared to those who received fentanyl (Casamento et al., 2021). The RASS scores were similar between the morphine and fentanyl groups; however, the fentanyl group required a slightly higher hourly propofol dose compared to the morphine cohort (Casamento et al., 2021). Aeromedical studies have shown that morphine (1.2%) may be used less frequently than fentanyl (97.9%) for analgesia in mechanically ventilated patients (Zia et al., 2019).

2.4.5. Post intubation sedation and analgesia practices in South Africa

A South African retrospective study examined postintubation sedation and analgesia practices at a private ambulance service. It was emphasised that both over and undersedation of patients is undesirable, and that undersedation could lead to increased catecholamine release; with sequelae such as self-extubation, aspiration, hypoxia, and death (de Kock, Buma and Stassen, 2022). Of those sampled, 69% received postintubation sedation and analgesia (PISA) (de Kock, Buma and Stassen, 2022). Sedation and analgesia were delivered using boluses of various sedatives and analgesics, with morphine and midazolam being the most common PISA administered (de Kock, Buma and Stassen, 2022). There were significant differences in the time until a second dose of PISA was administered between the groups who received rocuronium and succinylcholine.

Those who were paralysed with succinylcholine received a second dose of PISA earlier than those paralysed with rocuronium (de Kock et al., 2022). This may be due to succinylcholine's short duration of action as a paralytic, leading to patient movement in the absence of adequate sedation. Patient movement may have been used as a prompt for practitioners to administer subsequent bolus doses of sedation. This is a concern, as patients will not move for prolonged periods of time after the administration of rocuronium, placing them at risk of awake paralysis.

A descriptive analysis of endotracheal intubations at a HEMS service in South Africa stated that patients who were intubated received mechanical ventilation and sedation during transport to hospital (Stassen et al., 2018). Postintubation sedation was administered by bolus only. Ketamine and midazolam were most commonly administered for sedation, while morphine was added for analgesia (Stassen et al., 2018).

In the intensive care setting, analgosedation is aimed at keeping patients comfortable but easily rousable (Travers, 2010). Analgesia is comprised of mainly opiate based medications, administered as boluses or rescue doses for incidental and procedural pain (Travers, 2010). Sedation is maintained at light levels, using bolus dosing and infusions of various medications (Travers, 2010). Commonly used sedative agents include midazolam, propofol, and ketamine. Dexmedetomidine is less commonly used due to its relative expense (Travers, 2010).

2.4.6. Sedation Depth and related Sequalae

Both under and oversedation are potentially harmful to mechanically ventilated patients (Stephens et al., 2018; Stewart, 2018). Many guidelines focus on administering sedation and analgesia while prioritising rehabilitation and quick liberation from mechanical ventilation (Chanques et al., 2020). These recommendations were made by the Pain, Agitation/sedation, Delirium, Immobility, and Sleep disruption (PADIS) guidelines, which have since been updated (Lewis et al., 2025). These guidelines emphasise the importance of lighter sedation in the intensive care unit, with a focus on optimising analgesia and ventilator settings prior to administering more sedation where feasible (Lewis et al., 2025).

A study examining sedation and analgesia among patients with acute respiratory distress syndrome (ARDS) argues that light sedation is not always feasible due to the patient's underlying clinical requirements (Chanques et al., 2020). These authors argue that patients with ARDS often require neuromuscular blockade in the first 24 hours of admission, to facilitate lung protective ventilation and patient-ventilator synchrony (Chanques et al., 2020). However, they recognise the risk of awareness during paralysis and stipulate that when continuous NMB is required that patients receive adequate analgesia and deep sedation prior to its initiation. This study indicates that despite the risks associated with deep sedation, it is still unavoidable in certain clinical settings (Chanques et al., 2020).

Deep sedation was commonly used during aeromedical transfer of mechanically ventilated patients (Roginski et al., 2023). In a retrospective review of mechanically ventilated patients undergoing aeromedical transfer, 91.7% were deeply sedated (Roginski et al., 2023). The Air-SED study reported that 88% of patients were deeply sedated during aeromedical transfer, while coma occurred in 58.9% of patients (Moy et al., 2021). Light sedation with the use of non-benzodiazepines is currently recommended in ICU (Stollings et al., 2022). However, this may not be appropriate or safe in the aeromedical transport environment (Moy et al., 2021).

A quality improvement initiative by Anton et al (2024) sought to reduce deep sedation and benzodiazepine use among mechanically ventilated patients during critical care transport (CCT). The authors state that previous work showed that over 90% of patients were deeply sedated, and sought to decrease the incidence of nonindicated deep sedation (Anton et al., 2024). This study defined indications for deep sedation during CCT, and determined that 70% of patients who were deeply sedated had no indication for deep sedation (Anton et al., 2024).

The proportion of deep sedation decreased by 25% during the study period but remains common practice in the CCT setting. This study lent evidence to the safety of non-deep sedation during CCT despite the majority of patients still receiving deep sedation (63%) (Anton et al., 2024). Authors proposed that there is a culture of deep sedation in CCT due to perceived safety risks of light sedation during transport (Anton et al., 2024).

2.4.6.1. Under sedation

If unrecognised, under sedation could result in increased anxiety, agitation, unplanned extubation, or violence towards staff (Varndell et al., 2015). Anaesthetic awareness may occur in patients who are insufficiently sedated (Gibson & Flabouris, 2006; Pappal et al., 2021). Anaesthetic awareness is the spontaneous recall of events that occur while a patient is under anaesthesia (Gibson and Flabouris, 2006). There have been case reports detailing patient experiences of awareness during critical care retrieval despite the administration of continuous sedation and analgesia (Gibson & Flabouris, 2006).

Awareness during retrieval can manifest as post-traumatic stress disorder (PTSD) after the patient has recovered (Gibson and Flabouris, 2006). Risk factors specific to the aeromedical retrieval setting include staff ignorance to awareness, anaesthesia at high altitude, reliance on intravenous boluses of sedatives, and patient severity of illness (Gibson and Flabouris, 2006). Often patients are critically ill, presenting with haemodynamic instability. This may be a contributing factor to undersedation, as clinicians will administer lower doses of sedatives and analgesics due to the risk or exacerbating the patient's haemodynamic instability (Gibson and Flabouris, 2006).

A national audit of accidental awareness during general anaesthetic (AAGA), the 5th National Audit Process (NAP5)[16] received 300 reports of possible AAGA (Pandit et al., 2014). Out of the cases considered to be probable/certain (37%), neuromuscular blocking medications (NMBs) were administered in 97% of cases (Pandit et al., 2014). One third of accidental awareness events occurred during maintenance of anaesthesia (Pandit et al., 2014).

Awareness during paralysis placed patients at risk of psychological and physiological sequalae. The ED-Awareness study aimed to assess the prevalence of awareness during paralysis among mechanically ventilated patients in the emergency department (Pappal et al., 2021). The prevalence of awareness with paralysis was 2.6%, demonstrating that only a minority of mechanically ventilated patients experienced awareness while being paralysed (Pappal et al., 2021).

Despite the reported low prevalence, the consequences of awareness during paralysis are severe and may manifest as post-traumatic stress disorder (PTSD), complex phobias, and major depression. In this cohort, patients who experienced awareness during paralysis often experienced perceived threat, which is predictive of developing PTSD (Pappal et al., 2021). Most (70%) patients who experienced awareness during paralysis were exposed to longer-acting paralytics like rocuronium (Pappal et al., 2021).

A narrative review of sedation and analgesia related to the use of long-acting neuromuscular blockade stated that despite the benefits of using rocuronium for RSI, the deferred resumption of muscle activity may result in delayed administration of sedation and analgesia after intubation (Ender et al., 2025). This may result in awareness during paralysis among patients

[16] NAP5 of the Royal College of Anaesthetists and the Association of Anaesthetists of Great Britain and Ireland concerned accidental awareness during general anaesthesia (AAGA). It is the largest and most comprehensive study of AAGA.

who receive long-acting NMBAs like rocuronium (Ender et al., 2025). Authors stated that various retrospective reviews have indicated that patients who received rocuronium as opposed to succinylcholine had a longer mean time until receiving sedation and analgesia (Ender et al., 2025). In the CCT setting, patients receiving rocuronium were less likely to receive any sedation or analgesia (Ender et al., 2025). Despite these findings, light sedation is still advocated in the ICU setting, as patient outcomes appear to be favourable compared to when patients are deeply sedated (Ender et al., 2025).

Light sedation is recommended for mechanically ventilated patients in ICU (Stephens et al., 2018). Despite this recommendation, deep sedation is common and has been associated with increased mortality, delirium, and lengths of hospital-stay (Stephens et al., 2018). A comparison between deep sedation and light sedation has revealed that light sedation is associated with fewer ICU [mean difference -3.0; (95% CI, -5.4 to -0.6)] and mechanical ventilation days [mean difference -2.1; (95% CI,-3.6 to -0.5)] (Stephens et al., 2018).

2.4.6.2. Deep sedation

Deep sedation can result in the development of hypotension, hypoventilation, and hypothermia (Varndell et al., 2015). Early deep sedation has also been associated with increased risk of mortality (Varndell et al., 2015). This has been further supported as additional research states that deep sedation, even during the early stages of patient care, has been associated with increased mortality and length of hospital stay (Stephens et al., 2018).

Previous research demonstrated that early deep sedation, in the first 48-hours of ICU care was independently associated with increased risk of mortality (Shehabi et al., 2018). Pre-hospital deep sedation has been implicated in causing increased hospital length of stay and fewer ventilator-free days (Moy et al., 2021; George et al., 2020). There was a risk of therapeutic inertia related to deep sedation; patients who were deeply sedated in the emergency department (ED) resulted in an increased frequency of deep sedation in the intensive care unit (ICU) (Fuller et al., 2019). Early deep sedation of patients suffering respiratory failure was common in the ED, and has been implicated in worse outcomes for this cohort of patients (Moy et al., 2021; Fuller et al., 2019).

Deep sedation can result in burst suppression (Watson et al., 2008). Burst suppression was a pattern of brain activity characterised by an electroencephalographic (EEG) pattern of intermittent interruptions or low voltage (Hogan et al., 2020). Burst suppression was associated with increased mortality among mechanically ventilated patients receiving sedatives in the ICU (Watson et al., 2008). The risk of oversedation was that once a patient is unresponsive or comatose, it was not possible to determine whether their depth of sedation was deepening without the use of an EEG. This placed deeply sedated patients at risk of burst suppression due to unrecognised oversedation (Watson et al., 2008).

Burst suppression in mechanically ventilated ICU patients was associated with increased mortality (Hogan et al., 2020). Authors have concluded that burst suppression was more commonly a result of the patient's critical illness, but high cumulative doses of sedatives like propofol may have increased burst suppression burden, with the potential for indirect contribution to mortality (Hogan et al., 2020). However, it remained an important consideration as it demonstrated the risk that oversedation posed to mechanically ventilated patients.

2.5. Protocol versus non-protocol directed sedation

Early research indicated that protocol-directed sedation may result in decreased time on ventilation (Stollings et al., 2022). A Clinical Practice Guideline for the Sustained use of Sedatives and Analgesics in the Critically Ill Adult (SAG) placed emphasis on a daily sedation goal, such as sedation interruption, to promote decreased time on ventilation (Stollings et al., 2022). This guideline also recommended propofol if patients required rapid awakening for neurological assessments, and midazolam for short-term sedation (Stollings et al., 2022). These recommendations have evolved since SAG was published in 2002.

This guideline was followed by PADIS, which suggested light sedation and the use of propofol for cardiac patients, and either propofol or dexmedetomidine in medical or non-cardiac patients (Stollings et al., 2022). However, more recent trials have disputed these recommendations, showing that there was no difference between propofol, or usual care and dexmedetomidine in clinical outcome (Shehabi et al., 2019).

Sedation is recognised as an important component of critical care, playing a vital role in recovery and humane treatment of patients undergoing mechanical ventilation (Aitken et al., 2018). A systematic review aimed to compare protocol-directed sedation usual care on mortality outcomes in mechanically ventilated patients in the ICU (Aitken et al., 2018).

When compared, protocol-directed sedation versus usual care did not result in a reduction in mortality (RR 0.77, 95% CI 0.39-1.50) (Aitken et al., 2018). There was no difference in the length of time mechanical ventilation was required, nor was there a difference in the rate of extubation or the need for reintubation (Aitken et al., 2018). This research took place in the ICU environment, and therefore it may not be generalisable to the aeromedical setting.

In a small ICU-based study, the use of protocol-directed sedation had beneficial effects for mechanically ventilate patients (Green & Staffileno, 2021). The duration of mechanical ventilation, ICU stay, and continuous sedation was shorter after the implementation of protocol-directed sedation (Green & Staffileno, 2021). When protocol-directed sedation was used, it resulted in standardisation of care and promoted evidence-based practice in this study (Green & Staffileno, 2021).

Aeromedical services still utilise standard operating procedures for the provision of sedation and analgesia in mechanically ventilated patients (Roos et al., 2012). Research in the aeromedical setting has stated that protocol-driven, goal-oriented delivery of sedation and analgesia in conjunction with validated sedation scales will reduce medication requirements and may help to achieve targeted sedation, improving outcomes (Moy et al., 2021).

2.5.1. Prehospital sedation and analgesia protocols/guidelines

Various protocols and guidelines exist for prehospital sedation and analgesia post-intubation. In South Africa, the Clinical Decision Support Tool (CDST) was published in 2024 and provides guidance for medications and doses for the maintenance of sedation and analgesia in the post-intubation period (HPCSA-PBEC, 2024). The CDST was published by the Professional Board for Emergency Care (PBEC) and is endorsed by the regulatory body for prehospital care providers in the country. Within the CDST, recommendations are made pertaining to types of medications that can be used for continuous sedation and analgesia, and their doses.

According to the PBEC (2024), combinations of midazolam and morphine, or ketamine and midazolam are recommended. When ketamine was combined with midazolam, the recommended doses are Ketamine: 0.25-0.5mg/kg/hr and Midazolam: 0.06-0.24mg/kg/hr. When midazolam was combined with morphine, the recommended doses for Midazolam: 0.05-0.3mg/kg/hr and Morphine: 0.02-0.08mg/kg/hr (HPCSA-PBEC, 2024).

Further recommendations were made around haemodynamic considerations when selecting which combination to administer. In haemodynamically unstable patients, ketamine and midazolam were recommended while for haemodynamically stable patients, midazolam and morphine was recommended. The methodology describing how sedation doses were determined is not contained in the CDST (HPCSA-PBEC, 2024). Additionally, currently no sedation depth goal is recommended in the CDST (HPCSA-PBEC, 2024). The CDST recommends administering a paralytic after optimising/ensuring adequate sedation and analgesia if ventilator dyssynchrony persists (HPCSA-PBEC, 2024).

A document used in the South African aeromedical setting is the Air Mercy Service Drug Infusion Protocol developed by Roos et al (2012). This document provides guidance on various medications that may be administered during aeromedical transfer. The Drug Infusion Protocol lists sedation and analgesia combinations with recommended dosing. No recommendations are made pertaining to when to use a particular sedation regime, and discretion is left to the independent practitioner using the document. This guideline includes combinations of both ketamine and midazolam, and midazolam and morphine (Roos et al., 2012). It also includes guidelines on the use of propofol and various medication classes, such as vasopressors, inotropes, and anti-arrhythmic agents. The Drug Infusions Protocol states dose ranges of ketamine ranging from 2-4mg/kg/hr, midazolam at 60-240mcg/kg/hr, morphine at 20-80mcg/kg/hr, and propofol at 1-3mg/kg/hr (Roos et al., 2012).

2.6. Rescue sedation and analgesia

Rescue sedation and analgesia is often referred to in the literature with varying applications and is described in the next paragraphs. It has been described in more detail when used to treat acute agitation among patients experiencing psychiatric emergencies or psychosis.

A trial of rescue sedation when treating acute agitation defined it as the administration of additional sedation, when initial medication achieved inadequate sedation (Klein et al., 2019). A study examined the use of dexmedetomidine for sedation in the ICU by comparing continuous dexmedetomidine infusion to a placebo, with morphine and midazolam administered for rescue sedation when clinically indicated (Venn et al., 1999). Rescue sedation was also described as the administration of an additional sedative, which in this case was dexmedetomidine, in cases where patients failed to be sedated by other medications like midazolam or chloral hydrate (Zhang et al., 2017).

Rescue doses are referred to in analgesia literature for the management of breakthrough pain. Rescue dose morphine was used to manage breakthrough pain in patients receiving controlled-release morphine (Kraychete et al., 2023). Authors described using a rescue dose of morphine for patients who experienced greater nociceptive stimuli while receiving continuous morphine infusions (Kraychete et al., 2023).

In a quality improvement initiative, authors sought to reduce the proportion of patients who received nonindicated deep sedation for CCT (Anton et al., 2024). Sedation practices targeted light sedation (RASS -1 to -2). It was reported that sedation boluses were administered for one unsafe patient care situation, and for sixteen patients who experienced ventilator dyssynchrony (Anton et al., 2024). These instances of sedation boluses may represent the practice of administering ‘rescue sedation’ as defined by our study.

2.7. Adverse events

Critically-ill patients were at a higher risk of adverse events, largely due to the clinical course of their condition (Jeyaraju et al., 2021). MacDonald et al (2008) defined adverse events as follows: ‘An adverse event is an unfavourable and potentially harmful occurrence during or after the course of patient care. Adverse events are caused by circumstances that may or may not be preventable. An error is a preventable adverse event.’

Studies examining whether paramedics could safely lead interhospital transfer of critically ill patients showed that the frequency of adverse events ranged from 5-18% (Alabdali et al., 2017). Most literature reports the occurrence of in-transit adverse events, excluding events that occur at the referring or receiving facility (Alabdali et al., 2017).

A meta-analysis reported an AE rate of 11% during IHT (11%, 95% CI, 7.5%-16%) (Jeyaraju et al., 2021). The most common AE was hypotension (Jeyaraju et al., 2021). These authors concluded that the overall rate of AEs was low and linked to the patient’s disease severity. Jeyaraju et al (2021) found that conditions like respiratory failure due to coronavirus, the use of extracorporeal membrane oxygenation (ECMO), and stroke were associated with higher AE prevalence ($p<0.001$). Additionally, transport by nurses or physicians appeared to be associated with increased AE prevalence (Jeyaraju et al., 2021).

A retrospective cohort study examined adverse events occurring among mechanically ventilated patients during rotor wing transfer. In this study, adverse events were either considered major (death, arrest, pneumothorax, seizure) or minor physiologic events (requirement for additional sedation/paralysis, new arrythmia, physiological decompensation) (Seymour et al., 2008). The authors found that no major adverse events occurred, and the rate of minor adverse events was 22% (Seymour et al., 2008). Vasopressor administration prior to flight, and the total flight distance were associated with adverse events ($p<0.05$).

Overall, the literature suggested that the AE rate was low for aeromedical IHT. However, these studies had varying transfer team configurations, patient populations, and flight times. This made the results difficult to generalise to other populations, and has left a gap in the literature when considering the safety of paramedic-led IHT and the prevalence of AEs during aeromedical transfer of mechanically ventilated patients (Jeyaraju et al., 2021).

2.8. Summary and interpretation

There is a paucity of research pertaining to sedation and analgesia practices in the aeromedical setting. Most research conducted in the aeromedical setting has taken place in the USA or Canada. This data is not generalisable to South African critical care retrieval and transport, necessitating further local research.

Sedation practices in the aeromedical setting described that medications are predominantly administered by bolus, with very few documented infusions. This could be due to factors such as shorter flight times, practitioner familiarity/comfortability, and a lack of standard operating procedures. For shorter flights, practitioners may opt for bolus dose administration as it may be viewed as more convenient, requiring less equipment, and no complex dose, concentration, or rate calculations. In lieu of published SOPs dictating that practitioners use infusions, they are free to use their discretion, allowing for critical thinking and pragmatism. The caveat to bolus dosing, however, is that practitioners may forget to administer or omit repeat doses at appropriate intervals, resulting in under sedation and pain, or awareness during paralysis.

Ketamine was used far less frequently than expected, and this was likely in contrast to the South African setting. Benzodiazepines, and propofol were the most common sedatives used during transfer. Despite a wide range of sedation scales, sedation depth assessments were not routinely documented during transports; studies indicated that practitioners were more reliant on GCS to determine sedation depth. Most patients were deeply sedated by flight crews.

Monitoring sedation depth with validated sedation scales such as the RASS or the RSS is important because unrecognised under sedation and over-sedation have been associated with negative patient outcomes. Pain scales like the BPS or CPOT were reportedly rarely used or documented by flight crews in the literature, which may indicate a lack of standardised pain assessment methods in mechanically ventilated patients during aeromedical retrieval. Regular pain assessments should occur among these patients, as their pain can be difficult to assess through other means. The use of physiological parameters to assess sedation and analgesia adequacy were unreliable when used in isolation.

Analgesia was frequently administered by bolus during flights. Fentanyl was the most used analgesic medication, while morphine was rarely used. This may be due to the desirable haemodynamic and pharmakokinetic properties that fentanyl offered, making it an attractive choice for critical patients. Fentanyl may be used less frequently in the South African retrieval setting as ECPs must consult a medical officer (MO) prior to administering it, unless pre-existing standing orders have been issued by an MO. Due to the challenges of contacting an MO in flight, it is unlikely that fentanyl use will be common practice. It is likely that morphine will be commonly used for analgesia during flight, as well as sub-dissociative dose ketamine.

Sedation and analgesia protocols were used by most aeromedical providers in the literature. This is interesting, as the evidence shows that protocol-directed versus non-protocol-directed sedation made no difference to patient outcomes. However, this evidence originates from the ICU setting and may not be generalisable to aeromedical critical care retrieval. As these environments pose unique challenges, use of protocols may be favourable to reduce the cognitive burden of practitioners and to improve patient safety.

Rescue sedation and analgesia are described in the literature, but no explicit definition of these terms have been made in relation to the ICU or aeromedical retrieval setting. From the literature reviewed, a definition in the context of aeromedical retrieval can be posed. Rescue sedation was the administration of additional bolus dose sedatives to achieve a desirable sedation depth – a patient must have been receiving sedation already, either by infusion or bolus dose, for this definition to apply. Rescue analgesia was the administration of additional bolus dose analgesics to achieve a desirable pain score among patients who were already receiving continuous analgesics by infusion or regular bolus dosing.

The literature showed that sedation and analgesic practices vary broadly in the aeromedical setting. It is therefore important to describe local sedation and analgesia practices to assist in the development of local guidelines.

CHAPTER 3: METHODOLOGY

3.1. Introduction

In this chapter, the methodology used for data collection; sampling procedures; and analysis of the data is outlined. Assumptions of the research are also outlined, as well as limitations, and ethical considerations.

3.2. Study Design

The study followed a quantitative, descriptive cross-sectional design to describe analgesia and sedation practices and estimate the proportion of patients requiring rescue sedation during interhospital transfers in an aeromedical setting. A descriptive cross-sectional design was chosen for this research, as it enabled the researcher to explore sedation practices and examine associations between exposures and outcomes during a specified time period (Rezigalla, 2020). Data were obtained through retrospective chart review of patient care records (PCRs). This would allow the objectives of the research to be met.

An observational study design best aligned with the study objectives to describe sedation and analgesia practices among mechanically ventilated patients undergoing mechanical ventilation. Observational studies describe and examine the distributions of independent and dependent variables in a population, while allowing for analysis of associations between them (Capili, 2021).

A descriptive cross-sectional design was chosen to characterise the prevalence of rescue sedation in the sample of patients who were mechanically ventilated during aeromedical transfer. This was a cross-sectional design as data was collected from the same population during a specified period between June 2019 to June 2024 (Capili, 2021).

3.3. Study Setting

The study took place at an aeromedical service in the Western Cape Province, South Africa. The aeromedical service operates two helicopters (rotor wing - RW) and aeroplanes (fixed wing - FW) in the City of Cape Town, Western Cape, South Africa. An additional helicopter is based in a rural town of the Western Cape Province, approximately 400km outside of Cape Town. All data in the sample were collected from missions completed by these aircraft, no bases outside of the Western Cape Province of South Africa were included.

The fixed wing aircraft based in Cape Town operate throughout the Western Cape Province, which spans 129 462 square kilometres. The rotor wing flies to more hospitals than the fixed wing, many of which range from primary to secondary facilities and are within a 300-350km radius of Cape Town. In the Western Cape Province, tertiary healthcare facilities with specialist and intensive care resources are concentrated in the metropole (Egger et al., 2025). This necessitates frequent aeromedical transfer of critically ill or injured patients from rural areas to the City of Cape Town.

Patient care reports (PCRs) were sampled from patients undergoing interhospital transfer (IHT) only, no primary calls including those that involved rescue by winching, short haul[17], or from water were included in the sample.

3.4. Sampling

The study employed a probability sampling method in the form of simple random sampling (Crowe & Sheppard, 2012). The sampling frame included all patient records for the past 5 years currently catalogued on the research site's patient record database. This allowed the researcher to include possible seasonal variation in the sample. Based on known historical call volumes it was estimated that the number of patients possibly eligible for inclusion in the study to be approximately 800-1250 for the included period.

Sample size calculation was performed using the OpenEpi, Version 3, open-source calculator, using the sample size calculation for single proportion option (Sullivan et al., 2003). Considering that the potential population size could be estimated the calculation considered the finite population correction factor. The hypothesised proportion of rescue sedation was considered at between 10% and 50%. A confidence level of 95% (Margin of Error = 5%) was selected. Considering the potential variation in rescue sedation proportion point estimates, sample sizes were estimated between 125 to 295 to achieve a 95% confidence interval of the point estimate. The formula used in the calculation is shown below.

n = [DEFF*Np(1-p)]/ [(d2/Z21-α/2*(N-1) +p*(1-p)]

Where:

p = hypothesised proportion

N = population size

d = confidence limits

A pilot study was conducted at the beginning of the data collection phase to test the assumptions made in the abovementioned sample size calculation. A random sample was generated using a random number generator. Numbers were assigned to PCRs, and the

[17] Short haul refers to a helicopter rescue technique where a rescuer and/or patient are suspended beneath the helicopter on a long rope/fixed line, to reach areas where it is impossible to land.

random number generator was limited to a range between 0-50. PCRs with the assigned number selected by the random number generator were included in the total sample for the pilot study. A sample of n=50 patient care records was included, and the primary outcome point estimate was calculated. The results informed the final sample size calculation. This also informed the over sampling proportion which was estimated at 10 to 20%. The final sample size to calculate a statistically significant (CI=95%) proportion of patients requiring rescue sedation was n= 158.

3.4.1. Inclusion Criteria

- Adult patients ≥18 years of age.
- Intubated with an endotracheal tube.
- Mechanically ventilated.
- Receiving continuous sedation and analgesia.
- Undergoing interhospital transfer (IHT).
- Transfer by air, either rotor wing or fixed wing transport.

3.4.2. Exclusion Criteria

- Patients <18 years of age (paediatrics and neonates).
- Patients who were intubated during flight.
- Primary calls, including rescues[18].
- Patients transported by road ambulance.
- Patients who received manual ventilation.
- Researcher was involved in patient care.

3.5. Data Collection, Management, and Protection

Data was collected by the researcher at the participating service. The participating service has an electronic register which listed and tracked PCRs, and this was used to determine how many PCRs there were in total for the study period (the register did not contain any personal or detailed clinical data). The total number of PCRs for this period was 4609 (N), and of these PCRs, the database indicated that there were 829 (n) patients who received mechanical ventilation.

[18] 'Rescue' refers to any mission where the rotor wing aircraft was requested to conduct wilderness search and rescue, air-sea-rescue, winch extraction or insertion, and short-haul extraction.

Paper-based patient records were securely stored in the archives according to the year, month, and aircraft registration. Initially, PCRs for patients who were receiving mechanical ventilation (n=829) on the rotor wing and fixed wing aircrafts were collected by month and year for the sampling period of five years (June 2019-June 2024). These PCRs were allocated numbers in a spreadsheet database according to the order in which they were collected. The first PCR collected was allocated number 1, and this sequence continued chronologically. Subsequently, these PCRs were randomly selected using a random number generator (Urbaniak & Plous, 2013). For this study sample, there were n=829 PCRs collected where patients were receiving mechanical ventilation. Research Randomizer was a computer program that generated sets of random number sequences within a pre-specified range (Urbaniak & Plous, 2013). Forty-one sets of twenty numbers per set between a range of 1-829 were generated by Research Randomizer. PCRs were selected from the total of n=829 according to the random number sequence for screening.

The researcher screened the selected cases and where the patient was under 18-years-of-age, the researcher was involved in patient care, or the case was a primary call, these cases were excluded from the sample. Primary calls referred to any call where the aircraft was called to a scene of an accident or medical emergency, rather than to a healthcare facility. This included when the aircraft was called to a scene to provide any form of rescue, such as wilderness search and rescue, winching, short-haul, or air-sea-rescue. From this simple random sample cases were excluded with reasons recorded (n=196) and sampling continued until the calculated sample size of n=158 was reached. See Figure 1.

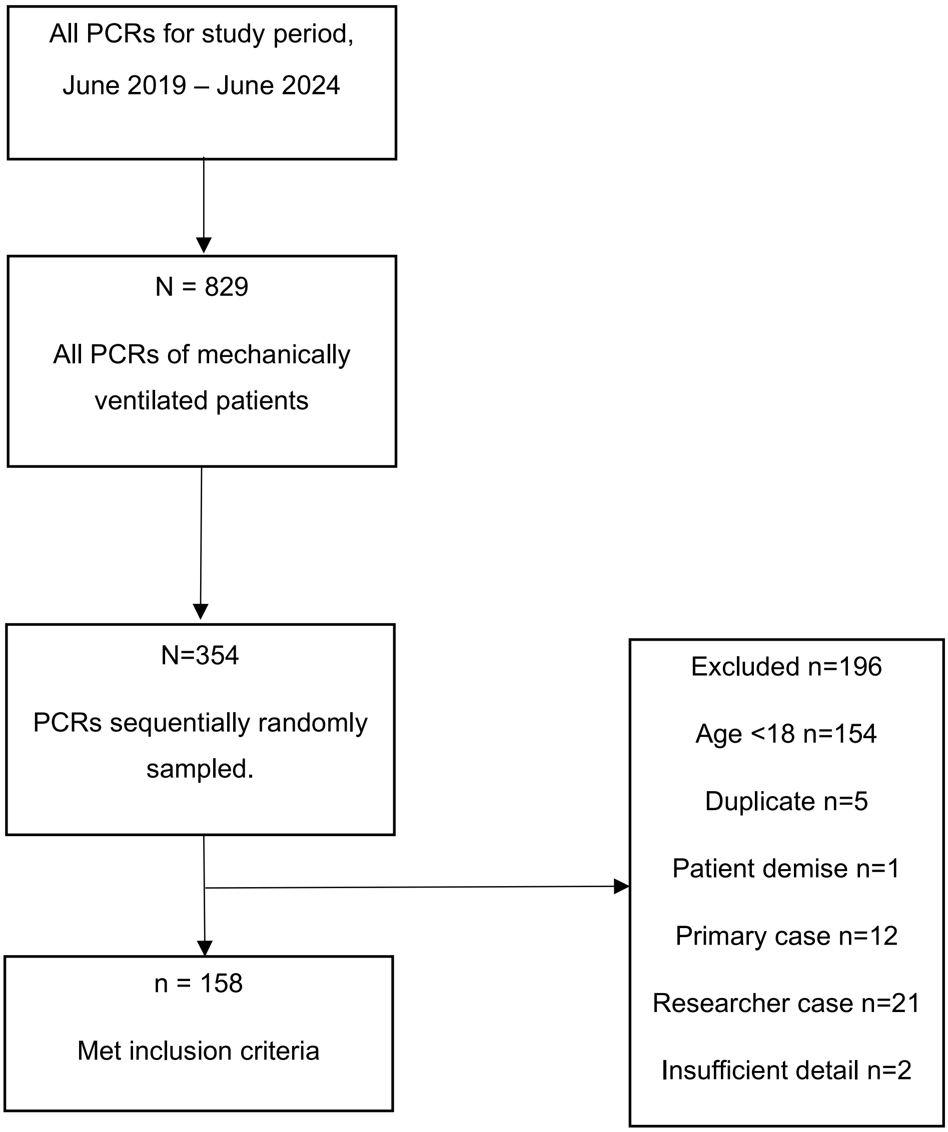

Figure 1: Flow diagram showing the sampling process

Data aligning to the variables under study were extracted from the paper PCRs. These variables were captured on a spreadsheet database which was stored on a password protected drive, on a password protected computer (Corporation, 2024). PCRs did not leave the research site premises, and PCRs were returned to a secure safe when not in the presence of the researcher. This was to ensure that the patient's private information was securely stored in accordance with the Protection of Private Information Act (POPIA) (RSA, 2013). Only the researcher and supervisors had access to these spreadsheets.

A separate password protected sheet which was an identifier log linked case numbers to unique research case numbers. The research case numbers were used in the database to ensure that patient identifiers were removed from the database prior to analysis. The data was analysed using SPSS® (IBM Corp, 2023), and this was conducted over approximately five days with the researcher present. Having the researcher present enhanced the analysis as specific questions and relationships could be analysed by the statistician upon request. Figure 2 shows the data collection and analysis process.

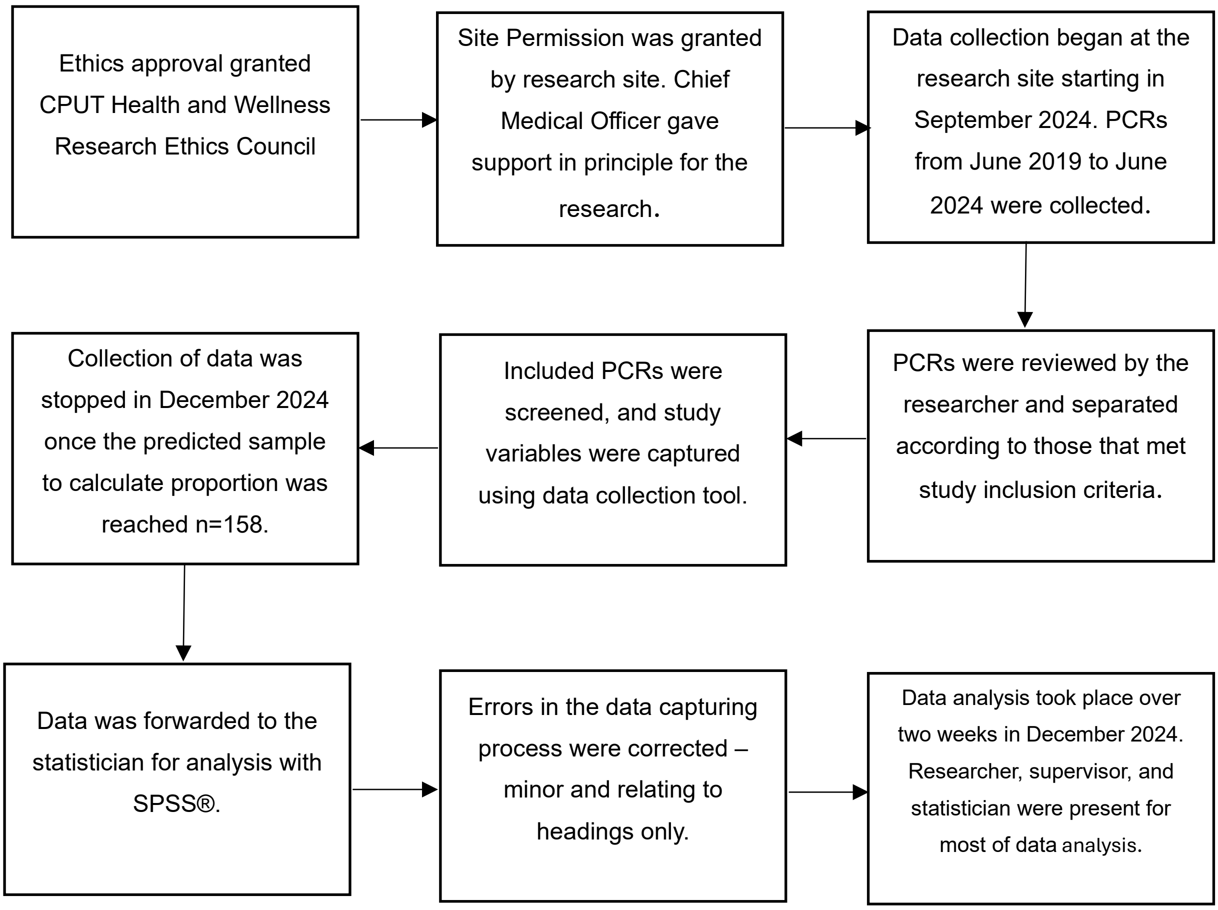

Figure 2: Flow chart outlining the data collection and analysis process

3.4. Variables

The variables studied were: aetiology of presentation, patient age, weight, sex, drug types (analgesics, sedatives, and miscellaneous drugs), drug doses (recorded in mg/kg/hr), adverse events, use of rescue sedatives (yes/no), mode of ventilation, and vital signs (blood pressure, mean arterial pressure, oxygen saturation, GCS, and end tidal carbon dioxide). Drug doses were also categorised according to whether they were appropriately dosed, underdosed, or overdosed. Variables extracted from PCRs are displayed in Table 2.

Rescue sedation was classified as the administration of *additional* sedative medications, such as ketamine or midazolam, to patients already receiving sedation and analgesia by continuous infusion. The term 'rescue sedation' did not include loading doses of sedatives or analgesics prior to the initiation of an infusion, nor did it include the technique of bolus dosing for sedation and analgesia where continuous infusions were not used. Instances where rescue sedation was administered were identified by the researcher through screening of the patient notes, and the 'drugs administration' section of the PCR. Sedative administration was rescue sedation if it was administered as a bolus, and the time of administration was after the initiation of the infusion.

An administration was also considered a dose of rescue sedation if the reason for administration was documented in the patient notes was indicative of rescue sedation. Key words used to identify and justify the administration of rescue sedation were, 'inadequate sedation', 'patient restless', 'patient fighting ventilator', or to 'maintain sedation.' Rescue sedation was not always discussed in the patient notes section and could only be identified by means of its time of administration in relation to the time that sedation infusions were initiated.

Drug doses were calculated according to the patient's recorded weight. Drug doses were in mg/kg/hr, and appropriate dose ranges were determined in accordance with the a national standard operating procedure that is widely used for sedation and analgesia (Roos et al., 2012). The doses in Table 1 were considered appropriate for sedation and analgesia in this research, and aligned with doses recommended by the National Drug Infusion Protocol (Roos et al., 2012). When ketamine was used as monotherapy, the same dose range listed in Table 1 was considered appropriate for sedation and analgesia.

Table 1: Standard doses of sedatives and analgesics contained in the National Drug Infusion Protocol

Ketamine & Midazolam	
Medication Type	**Standard Dose**
Ketamine	2 – 4mg/kg/hr
Midazolam	0.05 – 0.1mg/kg/hr
Midazolam & Morphine	
Midazolam	60 – 240mcg/kg/hr
Morphine	20 – 80mcg/kg/hr
Propofol	
Propofol	4 – 12mg/kg/hr

At the time the research was conducted, there was no alternative or relevant local standard operating procedure available to determine whether sedation and analgesia doses were appropriate.

Adverse events were classified as as an unfavourable or potentially harmful occurrence during patient care from the time the air crew arrived at the referring facility until the patient was handed over at the receiving facility. Adverse events were identified by the researcher, through screening patient care reports (PCRs). Adverse events were not classified according to severity, and no physiology or injury severity scores were used to classify how severely ill or injured patients were at the time of AE occurrence.

No distinction was made between preventable and non-preventable adverse events. Additionally, this study was not powered to calculate statistically significant associations or relationships between adverse events and other variables. No follow-up analysis was performed to establish whether adverse events affected patient outcomes. There was no predetermined list of adverse events (i.e. hypotension) when the researcher screened the patient report forms but, acceptable values were determined for various vital signs prior to screening. These values are described in the variables table below.

Aetiologies were used to categorise patients and were further described according to whether the aetiology was traumatic or non-traumatic. Categories were developed from the 'Differential

Diagnosis' section of the patient report form, i.e. where a practitioner stated the differential diagnosis as 'Traumatic Brain Injury (TBI)' or 'Cerebrovascular Accident (CVA)', this was used to categorise patients. Table 3 shows the categories according to aetiology and defines them.

The researcher did not define categories that were not identified in the PCR, and therefore some categories listed may include traumatic injuries such as fractures or thoracic trauma, i.e. 'Polytrauma' likely encompasses injuries such as fractures, thoracic injury, which is why these are not presented as their own categories. Further, if a practitioner recorded a differential diagnosis using a synonym of a variable, i.e. 'stroke', this would be categorised according to the more common and medically correct term, such as 'cerebrovascular accident'.

Table 2: Variables extracted from patient care reports

Type of drug (s) used for analgesia.	All analgesics administered from the time that crews arrive at the referring facility until handover.
Types of drug (s) used for sedation.	All sedatives administered from the time that crews arrive at the referring facility until handover.
Mode of administration (infusion or bolus).	Mode of administration during interhospital transfer (IFT) *1.
Proportion of rescue sedation administered.	All rescue sedation administered during the IFT.
RASS	Whether RASS was recorded during IFT.
RASS Scores	What RASS scores were documented and at what times.
CPOT	Whether CPOT scores were recorded during IFT.
CPOT Scores	What CPOT scores were recorded?
	What times were CPOT scores recorded?
BPS	Whether BPS was recorded or not.
BPS Scores	What BPS Scores were recorded?
	What times were BPS scores recorded?
Systolic Blood Pressure (SBP)	What is the SBP?
	What time was it measured?
Diastolic Blood Pressure (DBP)	What is the DBP?
	What time was it measured?

Mean Arterial Pressure (MAP)	What is the MAP?
	What time was it measured?
Heart Rate	On arrival at referring facility, during transfer, and on arrival at receiving facility.
Heart Rhythm	On arrival at referring facility, during transfer, and on arrival at receiving facility.
Oxygen Saturation	On arrival at referring facility, during transfer, and on arrival at receiving facility.
Glasgow Coma Score (GCS)	GCS on arrival at referring facility. GCS normally scored out of 15, however patients included in this research were intubated. This means no verbal score can be recorded – so GCS is out of 10. This is denoted with a 'T' after the score, indicating the patient is intubated (e.g. 2T).
Mode of ventilation	For duration of IFT.
Occurrence of adverse events: - Hypotension (SBP<90mmHg, MAP<60mmHg) - Hypertension (SBP>160mmHg, MAP >120mmHg). - Arrythmia - Hypercapnia (ETCO2 >50mmHg) - Hypocapnia (ETCO2<25mmHg) - Desaturation (SpO2<90%) - Ventilator dyssynchrony - Self-extubation - Seizure - Cardiac arrest	What adverse event occurred?
	What time did the adverse event occur?
	Did the adverse event occur after administration of a medication? (within five minutes of administration).
*1: *'During IFT'* refers to any time from when the air crew contacts the patient at the referring facility, to when they hand over at the receiving facility. This can be identified by the time that vital signs begin to be recorded, and when they stop being recorded.	

Table 3: Subcategories according to patient aetiology

Traumatic aetiology	
TBI	TBI is damage to the brain caused by an external force (Adegboyega et al., 2021).
TBI + polytrauma	TBI with concomitant trauma to multiple anatomical regions and organs of the body (van Wessem et al., 2022).
Polytrauma	Traumatic injury to two or more anatomical regions or organs of the body due to the same incident, which may be life threatening or life changing (Balogh, 2022).
Airway trauma	Injury to the airway due to blunt or penetrating injuries to the neck and /or chest (Sell & Patel, 2014)
Burns	Injury to the skin or other soft tissue after exposure to heat, either thermal, electrical, chemical, or radiation (Stritar & Mikša, 2023).
Burns + inhalation burns	Burns with concomitant burns to the airway and/or lungs, usually secondary to inhalation of superheated vapour, smoke, chemicals, or extreme heat (Dyson et al., 2021).
Spinal cord injury (SCI)	Injury to the spinal cord itself, or nerves surrounding the cord, resulting in temporary or permanent neurological impairment (Ding et al., 2022).
Poisoning	Harmful effects caused by exposure to a toxic substance, either intentionally or unintentionally (Ghannoum & Roberts, 2023).
Non-traumatic aetiology	
Cerebrovascular accident (CVA) / Stroke	Disruption to the brain's blood supply either due to a haemorrhage (haemorrhagic stroke) or thrombus (ischaemic stroke). Non-traumatic in origin (Burns et al., 2024).
Acute abdomen	Acute onset of severe abdominal pain, requiring prompt medical evaluation and surgical intervention. May also refer to peritonitis (Kopitnik et al., 2025).

Autoimmune disease	The presence of self-reactive adaptive immune components. Autoimmune diseases are considered autoimmunity with associated clinical pathology i.e. Guillain Barre Syndrome (Miller, 2023).
Cardiac/cardiovascular disease (CVD)	CVD is comprised of ischaemic heart disease and stroke (CVA) (Brunham et al., 2024). This research separated CVAs from this definition to show stroke prevalence independently of cardiac conditions. Therefore, illness classified as 'CVD' in this research does not include stroke (CVA).
Neurological	Diseases affecting the neurological system, excluding seizures, or CVA i.e. meningitis, tumour, abscess, hydrocephalus.
Obstetric Emergency	A life-threatening emergency arising during labour or pregnancy, or after delivery (Mashamba & Ramavhoya, 2021). These emergencies commonly comprise cases of bleeding, pregnancy-induced hypertension, cord prolapse, shoulder dystocia, poor progress, placenta abruptio, placenta praevia and amniotic fluid embolism (Mashamba & Ramavhoya, 2021).
Post return of spontaneous circulation (ROSC)	The period immediately following cardiac arrest, after successful re-establishment of a perfusing heart rhythm. Characterised by post-ROSC syndrome (Fasolino et al., 2022).
Renal failure	Kidney failure resulting in ineffective waste and fluid removal from the body (Rachel, 2011).
Respiratory	Any non-traumatic cause of breathing difficulty or respiratory failure i.e. pneumonia, asthma.
Seizures	Specifically, status epilepticus, recurrent tonic-clonic seizures that are refractory to conventional management (Williams et al., 2024).
Sepsis	Sepsis is a dysregulated host immune response to infection. This can culminate in septic shock, with end-organ dysfunction and hypoperfusion (Evans et al., 2021).

3.5. Statistical Analysis

Descriptive statistics were calculated and displayed using frequency tables, histograms, pie charts, and box and whisker plots. Frequency tables were used to display proportions for categorical variables where relevant, specifically for the primary outcome. Histograms and box and whisker plots were used to display how data was distributed.

A 95% confidence interval was calculated for proportions in the study. For certain categorical values, mean and medians were calculated depending on the distribution of the data. If data was normally distributed, a mean was displayed with the standard deviation (SD). If data was skewed or not normally distributed, the median was reported with the interquartile range (IQR).

Due to the potential for analytical measures of normal distribution to be less accurate in smaller sample sizes, quantile-quantile (Q-Q) graphs were primarily used to visually assess for normal tendencies of distribution. In conjunction with Q-Q graphs, histograms were also used to assess for normal distribution in the form of a bell curve.

Where necessary, distribution of the data was analysed using Kolmogorov-Smirnov and Shapiro-Wilk tests. Where the sample size was smaller than 50, a Shapiro-Wilk test was used to determine whether data was normally distributed. It is more appropriate to use Shapiro-Wilk tests for smaller sample sizes. In these cases, a p-value of less than 0.005 indicated that the data was not normally distributed. If the p-value was greater than 0.05, data was normally distributed. Where sample sizes were greater than 50, a Kolmogorov-Smirnov test was used to assess for normal distribution. Where $p>0.05$, data was normally distributed.

3.6. Ethical Considerations

Ethical clearance was sought from the Health and Wellness Sciences Research Ethics Committee (REC) and was granted with the approval number: CPUT/HWS-REC 2024/H15. Site permission was requested through the official gatekeeper portal and was granted by the participating service research site on 10/09/2024. As part of this process, a meeting was set up with the Chief Medical Officer for the participating service site, to explain the study and clarify any questions. The participating service research site approved access to records and collection of data. Only clinical data was extracted from the PCRs, and no identifying information was extracted (Sarkar and Seshadri, 2014).

The PCRs collected were anonymised, and no patient names or private information such as contact details, identification numbers, or addresses were recorded. PCRs were identified by the existing PCR number and were subsequently coded to remove the PCR number as a potential identifier. Prior to coding the PCR numbers, this data was be stored on a password-protected spreadsheet. Only the primary researcher had access to this spreadsheet. This upholds the ethical principle of confidentiality (Yousuf, London and Salman, 2014).

Patients could not consent to the research; however, this was mitigated by the fact that their details were anonymised. All data collected was stored on a password-protected data storage system. Only the researcher and supervisors had access to these documents, limiting access to only authorised researchers (Yousuf, London and Salman, 2014). The researcher was the only person with continuous access to the data, supervisors and data analysts had limited access, granted for short time periods only. No copies of the database were made.

The research site name was anonymised and would only appear in the research after explicit permission had been granted by the research site. No practitioner details were included in the research, and any private information was de-identified.

The POPI Act (RSA, 2013) was adhered to:

The identity of the participants was not revealed during the investigation and communication of findings; and no information of the participants was given to third parties without the written permission from the participants (RSA, 2013). All PCRs were de-identified to protect the privacy of patients.

At the time of the research and data collection phase, the primary investigator was employed by the research site as an operational Emergency Care Practitioner (ECP). All PCRs where the primary investigator was the treating clinician were excluded from the sample.

3.7. Delineation of the Research

This study did not include PCRs where patients were intubated and ventilated at a primary response call. Additionally, only patients who received mechanical ventilation were included in the analysis – those receiving non-invasive ventilation such as continuous positive airway pressure (CPAP) or high flow nasal oxygen (HFNO) were excluded. Only patients undergoing aeromedical transfer between facilities (IHT) who were intubated and ventilated were included in the sample. Therefore, the research did not analyse sedation and analgesia practices for any patients who were intubated and mechanically ventilated during primary response.

Only adults, categorised as patients over 18 years of age were included in the research. The participator service attends a high volume of neonatal retrievals comprising intubated and ventilated neonates. Sedation and analgesia practices are likely to vary greatly between adult, paediatric, and neonate populations, and for this reason only adult patients were included. Different sedation scales and pain measurement tools are also used for different age groups, increasing the variation too much to gain a meaningful insight into sedation and analgesia practices of specific populations.

Further, despite the research site having additional aircraft in Kwa-Zulu Natal (KZN) and the Eastern Cape, only PCRs from bases in the Western Cape were used as this is the only province using both fixed and rotor wing aircraft. The study did not analyse sedation practices at other aeromedical services operating in the Western Cape Province in South Africa and only included patients who were from the research site.

3.8. Limitations

Retrospective study designs have limitations owing to their design. These studies rely on the review of PCRs that were not designed to collect data for research and may have missing information (Talari & Goyal, 2020). These studies may be prone to selection and recall bias, which may affect the reporting of results (Talari & Goyal, 2020).

The research was reliant on practitioners documenting rescue doses of sedation and analgesia. Some practitioners may have opted to use the syringe driver ‘bolus’ function when delivering rescue sedation and analgesia and may have omitted this from their PCR.

The research objectives also sought to describe why practitioners were administering rescue sedation and analgesia, another finding that can only be made if they documented their reasoning behind administering rescue medications. If these details were omitted, the research may be limited in terms of its findings and their accuracy.

The research took place at one aeromedical service and only bases operating in the Western Cape were sampled from. This could have affected the generalisability of the research. No PCRs from primary response or rescue calls were included in the analysis, which may be a limitation as the findings of this research would not be generalisable to sedation and analgesia practices occurring outside of the interhospital transfer setting.

Drug doses were calculated according to the patient's recorded weight which represents a limitation as it is not known how this were determined. It was unknown whether patients were weighed routinely, and in most cases, this would not be possible if they were in critical condition on arrival of the aeromedical crew. This could have affected the accuracy of how drug doses were calculated and classified as being 'underdosed', 'overdosed', or 'appropriate dose'. There was a possibility that patient weight was either derived from a height-based calculation or simply estimated. However, the method by which the patients' weight was calculated is not clear in the PCRs sampled.

Sedation and analgesia doses were classified as 'appropriate', 'underdosed', 'overdosed', or 'none'. These classifications were determined in accordance with the recommended doses in the Air Mercy Service National Drug Infusion Protocol for sedation and analgesia, which was last updated in 2012 (Roos et al., 2012). However, through the literature reviews conducted, there did not appear to be an accepted, validated alternative dosing guideline that could be used for this purpose at the time of the research. This may be a limitation, as services in other regions may consider different doses to be appropriate or inappropriate.

Any medications administered or adverse events that occurred were recorded from the time that the air crew arrived at the referring facility. Therefore, some administrations of rescue sedation may have occurred at the referring hospital and not during aeromedical transport. This also applied to the occurrence of adverse events. The air crew attached monitoring from the time of arrival at the referring facility, and therefore any adverse events that occurred at these facilities would have been captured in the data. These adverse events may not be directly attributed to actions taken by the air crew, but rather the results of the referring hospital or the patient's condition when first assessed. This must be considered when interpreting the findings.

Data from the adverse events analysis was performed using a subgroup analysis. The study sample size was calculated to evaluate the primary objective of the study with sufficient power. However, the study sample was not calculated to perform subgroup analysis and is underpowered for this purpose. A major limitation to this subgroup analysis was multiplicity, which is the increased probability of making a false positive finding (Barraclough & Govindan, 2010). As more subgroup analyses occurred, there was a greater possibility of making a significant finding by chance alone, and this must be considered a major limitation when interpreting this data (Barraclough & Govindan, 2010).

3.9. Assumptions

It was assumed that to the best of their ability, practitioners would have completed their paperwork in an accurate manner, and the study variables were documented. A further assumption was that when rescue sedation was administered, the intentions were to provide additional sedation or analgesia.

3.10. Expected Outcomes and Contributions of the Research

This research was expected to describe sedation and analgesia practices among mechanically ventilated patients undergoing aeromedical transfer. It also aimed to determine the proportion of patients who received rescue sedation and/or analgesia. This was important, as these practices were largely undocumented in South African literature.

Sedation monitoring practices were also analysed, and an expected outcome was that sedation scores like the RASS would rarely be used. The same assumption was made for the use of behavioural pain scores like the BPS. A potential contribution of the research was to show that at the time of the research, sedation and analgesia practices were not being monitored. The participator service expressed interest in this specifically and responded by implementing sedation and analgesia scores (RASS and BPS) to the PCRs as part of standard practice.

The research aimed to determine the rate of adverse events in this setting, while also describing the types of common adverse events that occurred. These findings were helpful, as they may assist in the improvement of patient safety for future IHTs by defining when these adverse events occurred, what made them more likely to occur, and what types of events were most common. Through classification of these AEs, training can take place at the participating service to improve patient safety and incident reporting.

The findings of this study may assist with determining the need for further research in this field, with specific reference to sedation and analgesia practices among paediatric and neonatal populations. There may also be a need to describe sedation and analgesia practices after rapid sequence intubation at primary and rescue calls. Further prospective research after the implementation of sedation scoring and pain assessment tools would be appropriate, to determine how routine monitoring would affect sedation and analgesia practices, and whether it would reduce the need for rescue sedation.

The findings will be disseminated through publication in South African journals, and through presentations at relevant local and international conferences. Findings pertaining to sedation and analgesia practices were already presented at the Western Cape Government Health and Wellness Emergency Medical Services Research Day. A meeting with the Regional Manager at the participator service was organised to discuss the findings, with specific reference to adverse events and sedation monitoring practices. In this way, the research may have contributed by affecting change through implementation of further training to improve patient safety and patient monitoring during aeromedical transfer.

3.11. Chapter Summary

This chapter outlined the research methodology used for the study. A descriptive cross-sectional design, using a retrospective chart review of patient care records was chosen to describe sedation and analgesia practices. A simple random sampling technique was employed to reduce the risk of bias in the collection of data. Ethical clearance and site permissions were sought prior to any data collection, and all principles of patient confidentiality and protection of private information were followed. The research aimed to contribute to the participating service through informing future training and recommendations pertaining to sedation and analgesia, as well as patient safety.

CHAPTER 4: RESULTS

4.1. Introduction

This chapter presented the analysis and results of clinical data generated between June 2019 to June 2024 at an aeromedical service in the Western Cape Province of South Africa. A total of 354 PCRs were randomly sampled and 158 met inclusion criteria for the study. The sample size target was 158 to calculate statistical significance for the proportion of patients who received rescue sedation, and sampling stopped when this target was achieved.

The descriptive data analysis was presented in accordance with the research design and the *a priori* data analysis plan for the study. The main objectives of the study were to determine the proportion of mechanically ventilated patients requiring rescue sedation[19] during aeromedical transfer, and to describe sedation and analgesia monitoring and management practices in the aeromedical setting. Results are displayed using descriptive statistics, tables, graphs, and charts. Data was statistically analysed using SPSS® version 29.0.2.0.

4.2. Descriptive data and patient demographics

This section presented the descriptive data obtained from the research, relating to sedation management and monitoring practices, as well as the proportion of patients requiring rescue sedation. Demographic information included data describing the population's weight, sex, and age. Additional descriptive data separated patients into subcategories according to their aetiology of illness or injury, and according to the aircraft platform[20] in which they were transferred.

4.2.1. Patient Sex, Age, and Weight Characteristics

From the retrospectively sampled cases in the five-year-period, 70.3% (n=111/158) were male, and 29.7% (n=47/158) were female as shown in Figure 3 below.

[19] Rescue sedation refers to the administration of bolus dose sedation in addition to a continuous sedation infusion, usually due to inadequate sedation achieved by the initial infusion. Rescue sedation can also be administered for unsafe patient care situations.

[20] Aircraft platform refers to either fixed (aeroplane) or rotor wing (helicopter) aircraft.

Figure 3: Distribution of patient sex characteristics as a proportion

As depicted by the boxplot below (Figure 4), 50% of patients were aged between 30-50 years old. The median age was calculated as 35 (IQR: 22). The age range was between 18 - 83 years. There were no extreme outliers identified in the data analysis.

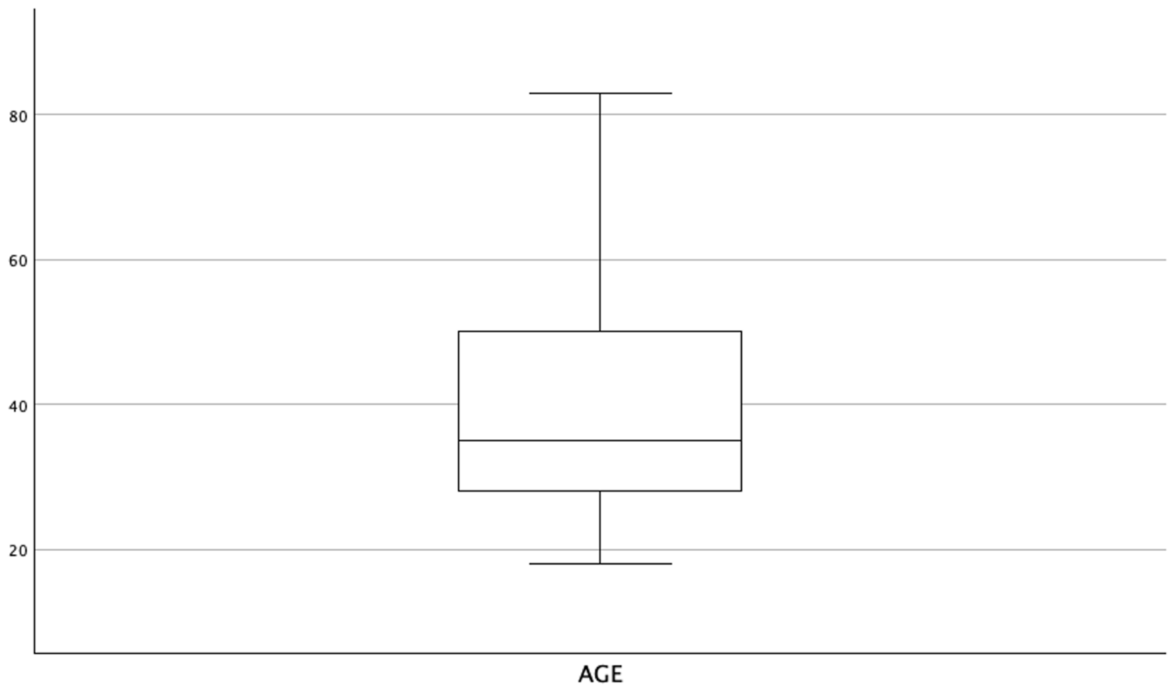

Figure 4: Patient age distribution (years)

The median patient weight is reported as 70kg (IQR:15). The histogram below (Figure 5) is normally distributed with clear outliers displayed in the distribution of the graph.

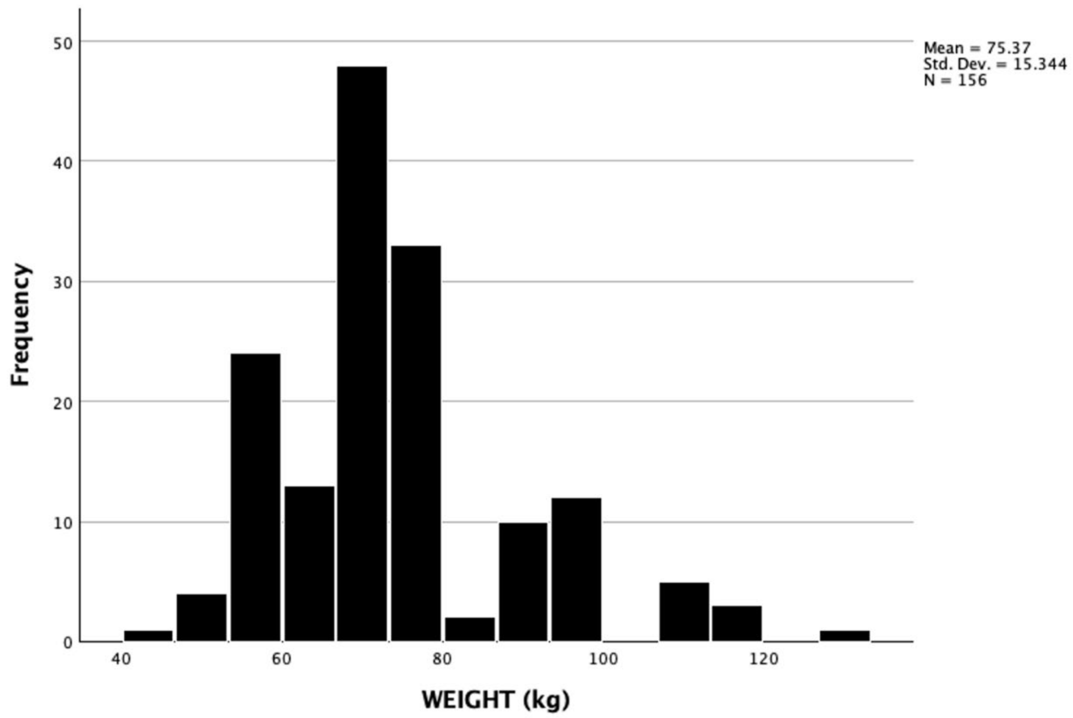

Figure 5: Distribution of patient weight

Patient weight ranged from 40kg to 130kg. There were many outliers in the dataset, with most outliers weighing over 100kg, and one outlier weighing 40kg.

4.2.2. The proportion of patients who received rescue sedation

From the 158 patient report forms sampled during the collection phase of the research, 13.9% (95% CI: 9.2 - 20) of patients received rescue sedation during transfer.

Table 4: Proportion of patients who received rescue sedation

		n (%)	95% CI
Rescue sedation	No	136 (86.1%)	80.0 - 90.8
	Yes	22 (13.9%)	9.2 – 20.0

4.2.3. Description of Case Characteristics

Over half, 56.3% (n=89/158), of patients in the sample sustained traumatic injuries. The remaining 43.7% (n=69/158) of patients had a non-traumatic clinical aetiology. Figure 6 shows the distribution of cases according to traumatic and non-traumatic aetiology.

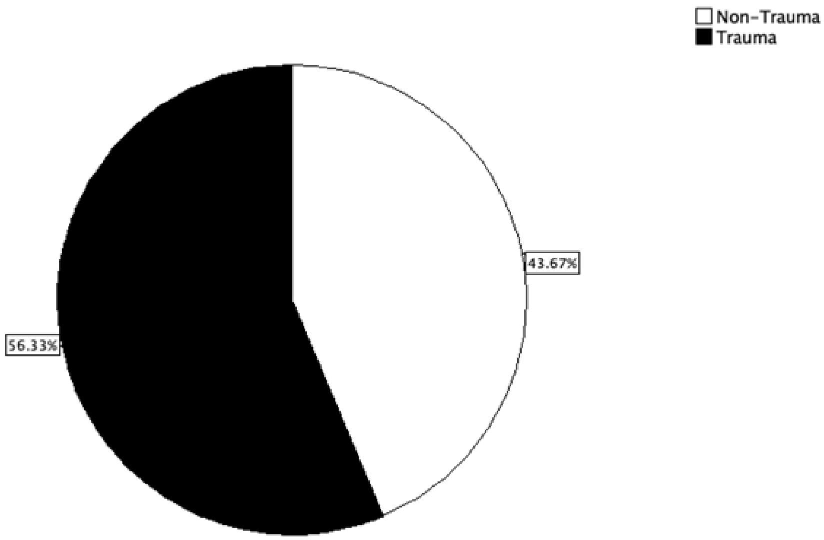

Figure 6: Cases according to category - Trauma[21] or non-trauma[22]

[21] 'Trauma' refers to a physical injury due to external force – such as a fall, or car accident.

[22] 'Non-trauma' refers to a disease process within the body that results in illness – such as cerebrovascular accident, myocardial infarction.

Cases were also described according to the platform that transported patients. Patients in this sample were either transported by rotor wing (helicopter) or fixed wing (aeroplane).

Most patients in the sample were transported by helicopter, 62.7% (n=99/158). The remaining 37.3% (n= 59/158) were transported by aeroplane, as shown in Figure 7.

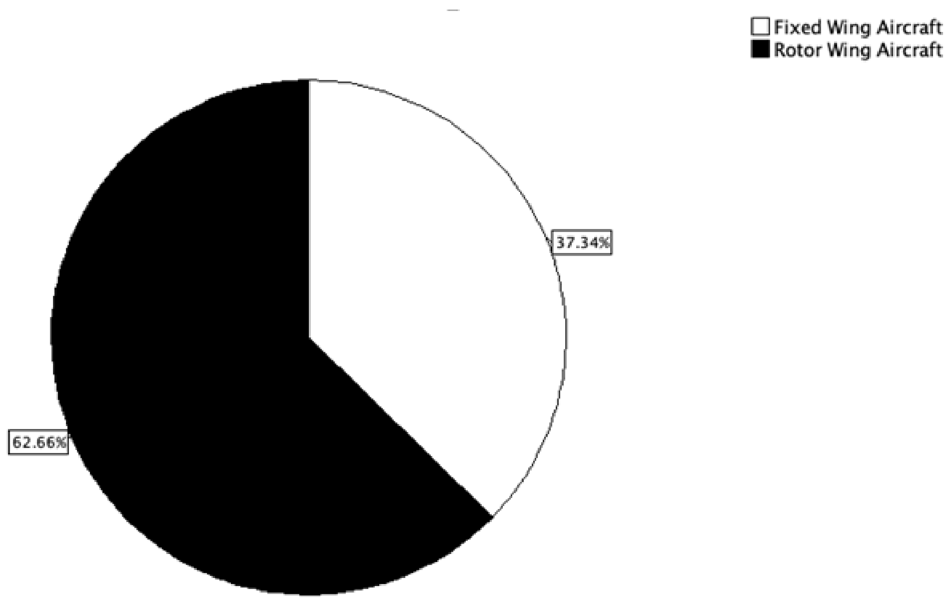

Figure 7: Rotor wing vs fixed wing transport

In terms of traumatic injuries, 29.7% (n=47/158) of patients sustained a traumatic brain injury (TBI). Cerebrovascular accident (CVA) accounted for 9.5% (n=15/158) of total cases in the sample. Polytrauma[23] alone accounted for 8.9% (n=14/158) of total cases, and when combined with 'polytrauma TBI[24]', together these cases accounted for 10.13% (n=16/158) of the population. This was followed by poisoning and respiratory aetiologies, with each accounting for 8.9% (n=14/158) of the sample. Burns[25] accounted for 7% (n=11/158) of cases and when combined with 'burns and inhalation burns[26]' these cases accounted for 9.5% (n=15/158). The remaining subcategories are displayed by Table 5 and Figure 8 below.

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[23] 'Polytrauma' refers to injuries involving multiple traumatic injuries involving more than one body system, and in this research, it does not include those patients with traumatic brain injury (TBI).

[24] 'Polytrauma-TBI' refers to a patient who has sustained polytrauma with a traumatic brain injury (TBI).

[25] 'Burns' refers to burn injuries to any area of the body except the airway.

[26] 'Burns and inhalation burns' encompasses burns to any area of the body in conjunction with confirmed airway burns.

Table 5: Subcategories describing patients' aetiology

Subcategories describing patients' aetiology	n (%)
Acute Abdomen	3 (1.9%)
Airway Trauma	4 (2.5%)
Autoimmune Disease	6 (3.8%)
Burns	11 (7%)
Burns and Inhalation Burns	4 (2.5%)
Cardiovascular	2 (1.3%)
CVA	15 (9.5%)
Neurological	3 (1.9%)
Obstetric	2 (1.3%)
Poisoning	14 (8.9%)
Polytrauma	14 (8.9%)
Polytrauma TBI	2 (1.3%)
Post ROSC	4 (2.5%)
Renal Failure	1 (0.6%)
Respiratory	14 (8.9%)
Seizures	4 (2.5%)
Sepsis	7 (4.4%)
Spinal Cord Injury	1 (0.6%)
TBI	47 (29.7%)

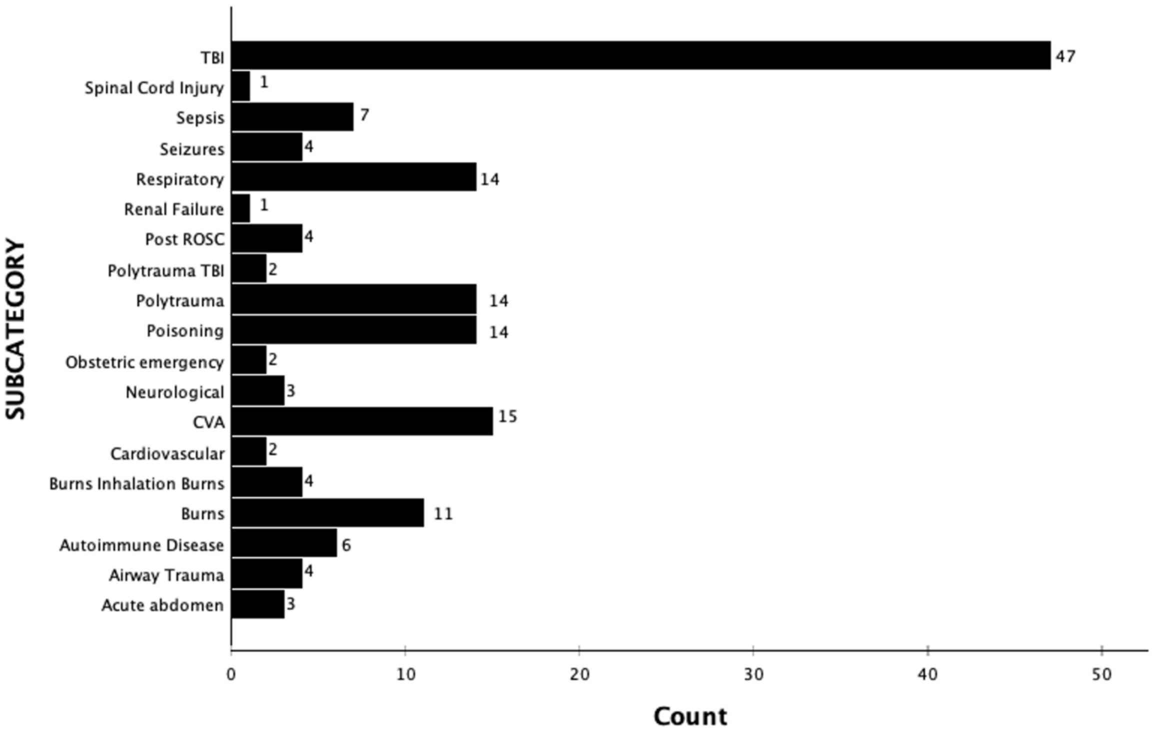

Figure 8: Subcategories describing patients' aetiology

4.2.4. Description of Case Characteristics by Rescue Sedation use Category

Table 6 illustrates the demographic characteristics by rescue sedation group. Among the subcategories of patient aetiologies, only those with airway trauma, burns, polytrauma, TBI, post ROSC, respiratory, seizures, and poisoning subcategories received rescue sedation in this sample. Table 8 shows that most patients who received rescue sedation were transferred by helicopter. Combinations of ketamine and midazolam were administered in most cases on both the helicopter and aeroplane platforms. Table 8 further illustrates that multimodal analgesia was rarely used across both platforms.

Table 6: Characteristics of participants by rescue sedation category

Category		Rescue Sedation	
		Yes (n%)	No (n%)
Aircraft platform	Rotor wing	16 (72.7%)	83 (63%)
	Fixed wing	6 (27.3%)	53 (39%)
Sedation and analgesia medications	Ketamine	0 (0%)	2 (1.5%)
	Ketamine + midazolam	13 (59.1%)	86 (63.2%)
	Midazolam	0 (0%)	3 (2.2%)
	Midazolam + morphine	8 (36.4%)	27 (19.9%)
	None	0 (0%)	17 (12.5%)
	Propofol	1 (4.5%)	0 (0%)
	Propofol + morphine	0 (0%)	1 (0.7%)
Multimodal analgesia	Yes	4 (18.2%)	3 (2.2%)
	No	18 (81.8%)	133 (97.8%)
Continuous analgesia dose	Appropriate	13 (59.1%)	79 (58.1%)
	Appropriate (bolus)	0 (0%)	1 (0.7%)
	Overdosed	5 (22.7%)	31 (22.8%)
	Underdosed (bolus)	0 (0%)	4 (2.9%)
	Underdosed	4 (18.2%)	21 (15.4%)
Continuous sedation dose	Appropriate	10 (45.5%)	66 (48.5%)
	Overdosed	5 (22.7%)	31 (22.8%)
	Underdosed (bolus)	0 (0%)	5 (3.7%)
	Underdosed	7 (31.8%)	34 (25%)
Paralytic administered	Yes	7 (31.8%)	15 (11%)
	No	15 (68.2%)	121 (89%)

Most - 72.7% (n=16/22) - patients who received rescue sedation were transported by helicopter, while the remaining 27.3% (n=6/22) were transported by aeroplane (Table 6).

To determine whether patients were receiving the ‘appropriate dose’, a weight-based dose was calculated using the patient’s weight as documented on the PCR, and the dose that the patient was receiving over an hour (mg/hr). This dose, represented in mg/kg/hr, was compared to the recommended dose in the Drug Infusions Protocol used by the research site to determine whether the dose was appropriate, underdosed, or overdosed (Roos et al., 2012).

Figure 10 shows whether dosing was appropriate for sedation and analgesia in groups of patients who received rescue sedation versus those who did not.

Figure 9 shows sedation and analgesia infusion medication regimes received by patients. Rescue sedation use was most common in infusion combinations with midazolam. Compared to the ketamine and midazolam (59.7%) group, patients in the morphine and midazolam (36.4%) group had a slightly lower count of patients requiring rescue sedation. However, in patients who received morphine and midazolam infusions (22.9%), the rate of rescue sedation was higher than in patients receiving ketamine and midazolam (13.1%). No patients receiving ketamine or midazolam monotherapy required rescue sedation. None of the patients who did not receive continuous sedation and analgesia received rescue sedation. Figure 9 also shows that some infusions were not combined with analgesia.

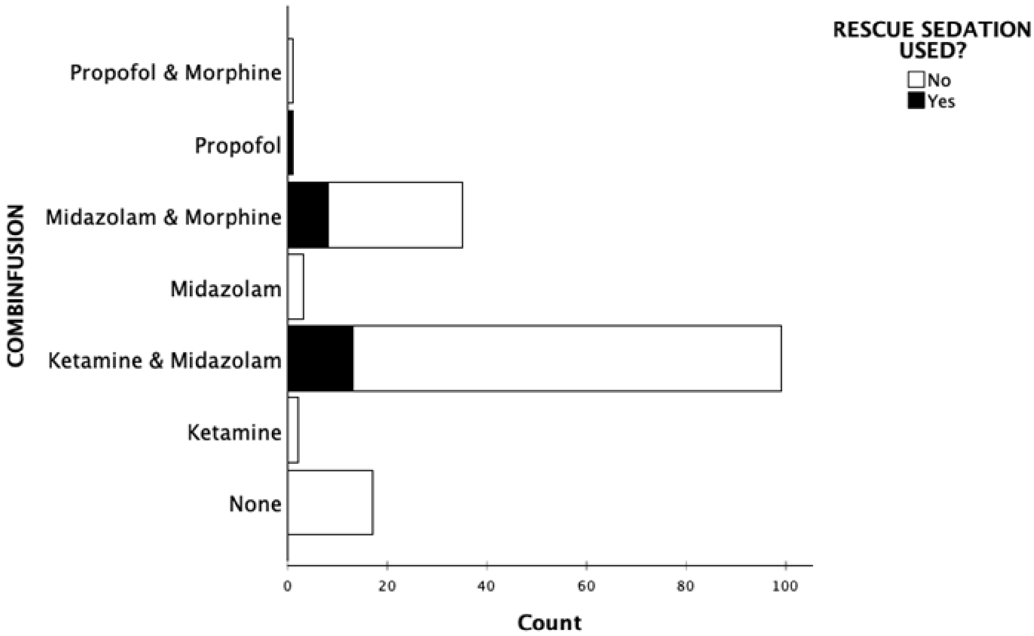

Figure 9: Sedation and analgesia medications used for continuous infusion

Figure 10 shows that most patients were receiving appropriate sedation doses. The graph further illustrates that in all sedation infusion dose groups (underdosed, appropriate dose, and underdosed) there were cases requiring rescue sedation. More patients receiving appropriate sedation doses required rescue sedation than in the underdosed and overdosed group. The patients who received overdosed sedation required the least rescue sedation.

Ketamine was the most used rescue sedative and was administered to 68.2% (n=15/22) of patients who required rescue sedation. Midazolam was administered to 22.7% (n=5/22) of patients, while propofol was administered to 2.1% (n=2/22). Figure 11 shows the different types of rescue sedation used according to aircraft platform.

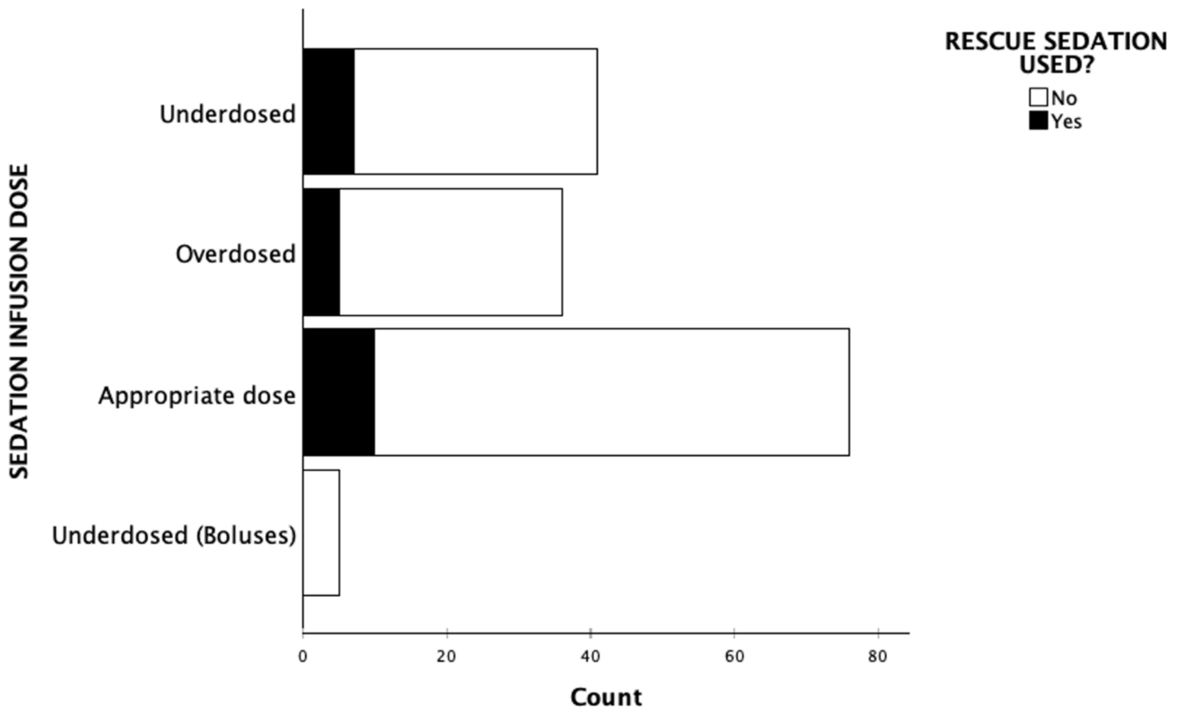

Figure 10: Sedation infusion doses

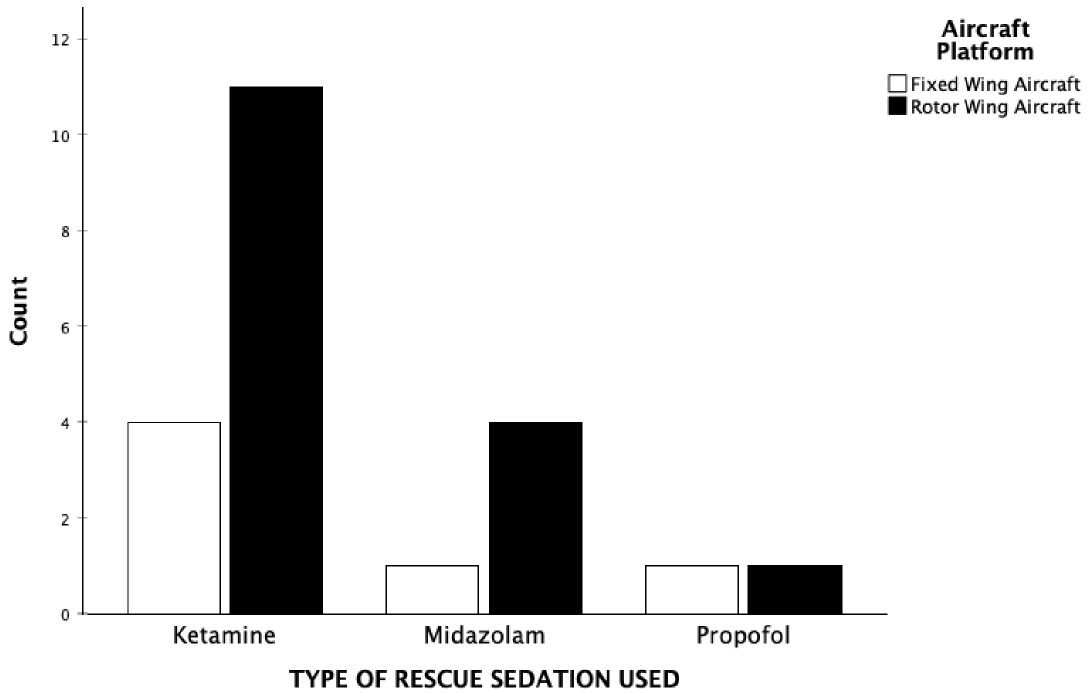

Figure 11: Type of rescue sedation used according to aircraft type (rotor wing or fixed wing)

Of the patients who received rescue sedation, 81.8% (n=18/22) did not receive multimodal analgesia, while 18.2% (n=4/22) of patients in this group did. Analgesia was initiated by aeromedical crews among both patient cohorts in the 83.5% (n=132/158) of cases. In most cases, sedation was mixed by the flight crew. In the rescue sedation group, 31.8% (n=7/22) of patients received a paralytic agent. Among patients who did not receive rescue sedation, 11% (n=15/136) received a paralytic agent.

Few patients in the rescue sedation group were receiving inotropes or vasopressors, 9.1% (n=2/22). Most patients in the rescue sedation group did not receive vasopressors or inotropes, 90.9% (n=20/22). Overall, 22.8% (n=36/158) of patients in the sample received vasopressors or inotropes. Among patients who received these medications, adrenaline was most administered in 21.5% (n=34/158) of patients, followed by 0.63% (n=1/158) on noradrenaline, and 0.63% (n=1/158) on a combination infusion of noradrenaline and dobutamine. Most patients, 77.2% (n=122/158), were not receiving any form of vasopressor or inotrope.

4.2.5. Sedation Monitoring Practices

As shown no patients in either group had evidence of sedation or analgesia monitoring recorded on the PCRs. This is evidenced by the fact that no validated measurements or assessments were documented. There were no other validated scales recorded.

4.3. Rescue Sedation Subgroup Analysis

A subgroup analysis of patients who received rescue sedation was performed and split into rotor wing (helicopter) and fixed wing (aeroplane) categories. Table 7 shows that a total of 22 patients received rescue sedation in the sample, 72.7% (n=16/22) of rescue sedation recipients were transported by rotor wing.

On both the fixed wing (FW) and rotor wing (RW) platforms, ketamine was most frequently used as rescue sedation. Ketamine was used for 66.7% (n=4/6) of fixed wing patients who required rescue sedation, and 68.8% (n=11/16) of patients on the rotor wing. Midazolam was used less often on both platforms, 16.7% (n=1/6) on the fixed wing and 25% (n=4/16) on the rotor wing. Propofol was used in a minority of cases, with one instance of propofol being administered on both the rotor and fixed wing platforms. This is depicted in Figure 11 above.

Rescue sedation was administered most often while crews were on scene or at hospital, during the initial stabilisation phase prior to transport (Figure 12). This accounted for 72.7% (n=16/22) of all rescue sedation administration. On the rotor wing, 81.3% (n=13/16) of rescue sedation administration occurred while crews were stabilising the patient on scene or at the referring facility. Half, 50% (n=3/6) of patients on the fixed wing aircraft received rescue sedation at the referring facility. During flight, 13.6% (n=3/22) of patients required rescue sedation.

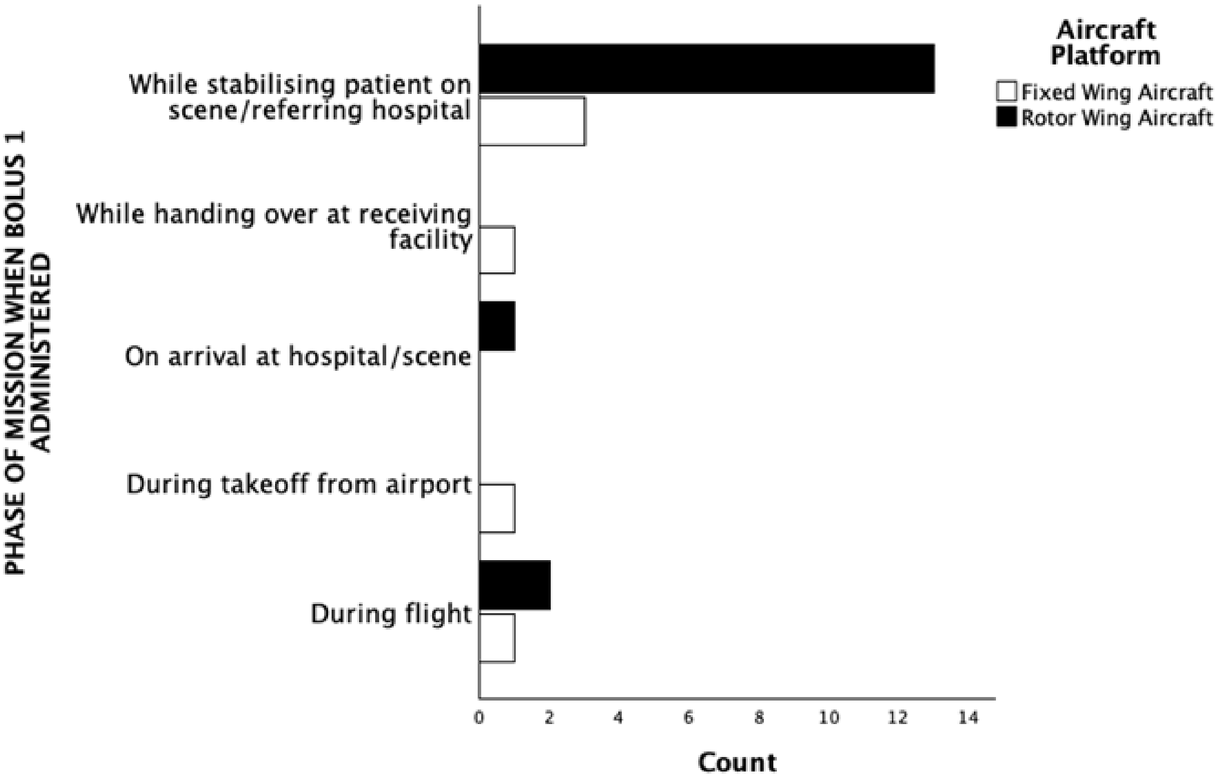

Figure 12: Phase of mission when rescue sedation was administered

Repeat boluses of rescue sedation were required in 50% (n=11/22) of cases. More patients on the rotor wing (56.3%) required repeat doses compared to the fixed wing (33.3%). Most patients required only one, or two doses of rescue sedation (47.6%). On the fixed wing, most patients received one dose of rescue sedation (66.7%), while more than half of patients on the rotor wing required at least two doses (53.3%). One patient on the rotor wing required four doses of rescue sedation, accounting for 4.8% (n=1/22) of cases in the rescue sedation group.

In the rescue sedation group, 90.9% (n=20/22) of cases did not receive vasopressors or inotropes during transfer. No patients who received rescue sedation on the fixed wing received vasopressors or inotropes. On the rotor wing, 12.5% (n=2/16) of cases received vasopressor or inotropic support.

Paralytics were administered in 31.8% (n=7/22) of cases, with 68.2% (n=15/22) of patients not receiving paralytics. All patients who received paralytics were given rocuronium. Rocuronium was administered to seven patients on the rotor wing (37.5%) and one on the fixed wing platform (16.7%).

Table 7: Rescue sedation subgroup analysis by RW/FW categories

		Aircraft Type (FW – aeroplane, RW – helicopter)		
		FW	RW	Total
		n (%)	n (%)	n (%)
Type of Rescue Sedation Used	Ketamine	4 (66.7%)	11 (68.8%)	15 (68.2%)
	Midazolam	1 (16.7%)	4 (25.0%)	5 (22.7%)
	Propofol	1 (16.7%)	1 (6.3%)	2 (9.1%)

4.4. Medication Subgroup Analysis

4.4.1. Types of medications used for infusion combinations and monotherapies

A medication subgroup analysis was undertaken to determine what types of medications were used, how they were administered, and what doses were used. Table 8 shows what medications were used during transfer of patients.

Ketamine and midazolam were used in 62.7% (n=99/159) of cases, while midazolam and morphine combinations were used in 22.2% (n=35/158) of cases. Ketamine was used as monotherapy in 1.3% (n=2/158) of cases. Midazolam was also used in isolation, without a concomitant analgesia infusion in 1.9% (n=3/158) of patients. A small number of patients, 10.8% (n=17/158), did not receive analgesia or sedation by infusion. One patient (0.6%) received propofol and one received propofol and morphine as a continuous infusion.

When bolus dose medications excluding *rescue* sedation or analgesia were administered, it was either the technique selected to maintain continuous sedation or analgesia, or a loading dose of analgesia or sedation prior to infusions being initiated.

Medications that were administered as boluses for sedation included ketamine, propofol, and midazolam. Analgesic medications administered as boluses were ketamine, fentanyl, and morphine.

Table 8: Infusion medication combinations and monotherapies

Medications used for continuous sedation and analgesia	n (%)
Ketamine	2 (1.3%)
Ketamine & Midazolam	99 (62.7%)
Midazolam	3 (1.9%)
Midazolam & Morphine	35 (22.2%)
No infusion	17 (10.8%)
Propofol	1 (0.6%)
Propofol & Morphine	1 (0.6%)

4.4.2. Methods of administrating sedation and analgesia

Sedation and analgesia were administered by means of syringe driver in 89.2% (n=141/158) of patients. A minority of patients received these medications by bolus[27], in 3.8% (n=6/158) of cases. In 7% (n=11/158) of patients, there was no recorded method of sedation or analgesia administration. This is shown in Table 9.

Table 9: Methods of administering sedation and analgesia

Method of Medication Administration	n (%)
Bolus	6 (3.8%)
Infusion	141 (89.2%)
None	11 (7%)

[27] A bolus is a single dose of a medication administered at once, either by using the 'bolus' function of a syringe driver or infusion pump, or by syringe.

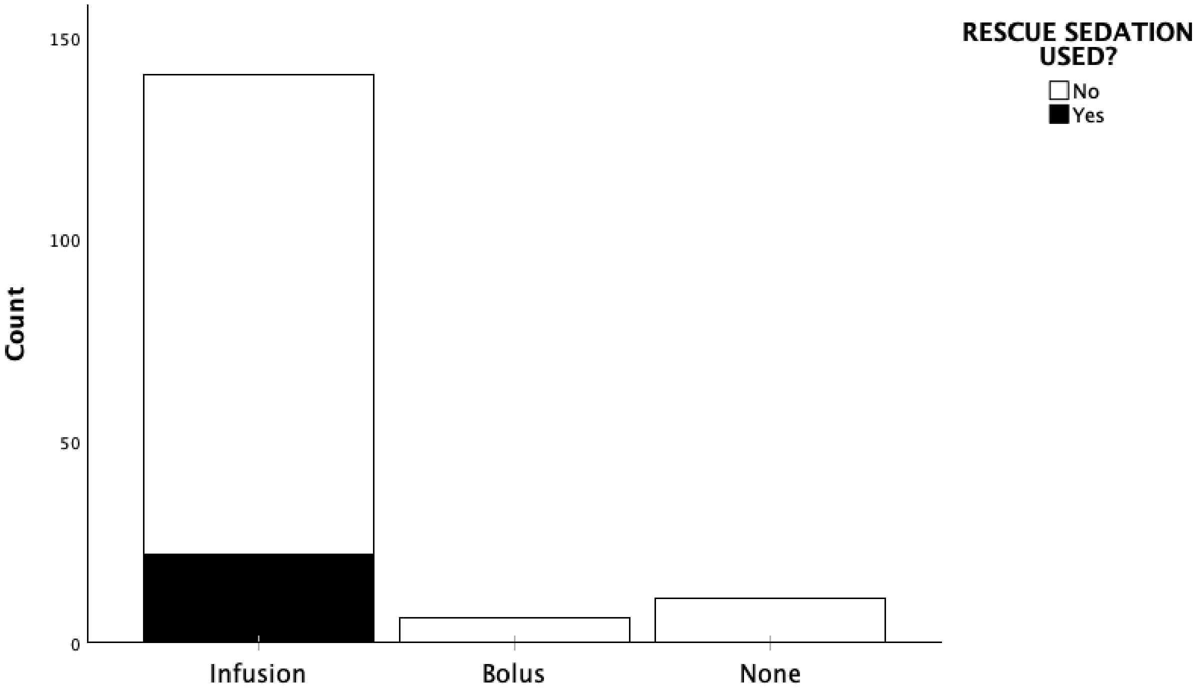

Figure 13: Methods of administering sedation and analgesia by rescue sedation category

Figure 13 shows that most patients received continuous sedation and analgesia by means of infusion.

4.4.3. Dosing of Sedative and Analgesic Infusions

The mean ketamine dose administered was 2.3mg/kg/hr (SD = 0.9). The lowest dose of ketamine used was 0.09mg/kg/hr, and the highest was 4.6mg/kg/hr.

The mean ketamine infusion dose of 2.3mg/kg/hr (SD = 0.9) was combined with midazolam in a combination infusion. Patients receiving the ketamine-midazolam combination infusion were receiving mean doses of 2.3mg/kg/hr of ketamine and 0.05mg/kg/hr of midazolam. The mean dose of midazolam was 0.05mg/kg/hr (SD = 0.03) when combined with ketamine. See Table 10.

In cases where midazolam and morphine were combined for infusion, the mean dose of midazolam was 0.05mg/kg/hr (SD = 0.03). The mean dose of morphine used in combination with midazolam was 0.05 (SD = 0.02).

When midazolam was used as a monotherapy for sedation, the mean dose was 0.09mg/kg/hr (SD = 0.03). This dose was higher than when midazolam was combined with morphine.

When ketamine was used as a monotherapy, the mean dose was 2.3mg/kg/hr (SD = 0.9). The mean propofol dose administered to patients was 0.09mg/kg/hr (SD = 0.01) when administered in isolation.

Table 10: Mean doses of analgesic and sedative medications administered by continuous infusion (mg/kg/hr)

Types of medications	Mean dose (SD)	95% CI
Ketamine and midazolam combined:		
Ketamine	2.3 (0.9)	2.2 - 2.5
Midazolam	0.05 (0.03)	0.04 - 0.06
Morphine and midazolam combined:		
Morphine	0.05 (0.02)	0.04 - 0.06
Midazolam	0.05 (0.03)	0.04 - 0.06
Monotherapies:		
Propofol	0.09 (0.01)	0.01 - 0.19
Midazolam	0.06 (0.02)	0.05 - 0.06
Ketamine	2.3 (0.9)	2.1 - 2.5

4.5. Ventilation Modes During Transfer

Ventilation was provided by the Hamilton T1 Ventilator (Hamilton Medical AG, Switzerland). Modes used in the patients sampled included Pressure Synchronised Intermittent Mandatory Ventilation (PSIMV), Synchronised Intermittent Mandatory Ventilation (SIMV), Adaptive Support Ventilation (ASV), Control Mode Ventilation (CMV+), Volume Control Ventilation (VCV), Pressure Control Ventilation (PCV+), and Spontaneous mode (Spont). In some cases, no ventilation mode was documented.

In the patients who received rescue sedation, SIMV was used 50% (n=11/22) of the time and PSIMV was used in 40.9% (n=9/22) of cases. CMV was used in one case (4.5%), and one case had no mode documented. ASV was not used for any cases in the rescue sedation group.

In patients who did not require rescue sedation, PSIMV was used in 52.9% (n=72/136) of cases and SIMV was used in 39.7% (n=54/136) of cases. ASV was used in 3.7% (n=5/136) of patients who did not require rescue sedation. Only one patient received PCV+, another received SPONT, and one patient was ventilated on VCV, accounting for 0.7% respectively. In two cases (2.5%) no ventilation mode was documented.

4.6. Vital Signs on Arrival at Referring Facility/Scene

Vital signs were recorded throughout transfer of patients in this sample. In some cases, vital signs were not recorded at each interval set out by the researcher. Intervals were described by phase of mission, i.e. on arrival at referring facility, during flight, etcetera. Vital signs recorded include systolic blood pressure, diastolic blood pressure, mean arterial pressure (MAP), end tidal carbon dioxide ($EtCO_2$), oxygen saturation (SpO_2), and Glasgow Coma Score (GCS). Heart rate was omitted, due to variability in accuracy as not all clinicians utilise electrocardiogram (ECG) to monitor heart rate and rhythm.

Quantile-quantile plots and histograms were used to graphically determine whether data was distributed normally. Analytical tests such as the Shapiro-Wilk and Kolmogorov-Smirnov tests were used to support graphical analysis of data distribution. If a $p>0.05$ was calculated by either test, data was considered normally distributed. Normally distributed data is reported with means and standard deviation (SD), while skewed data is reported with medians and interquartile ranges (IQR).

4.6.1. Systolic Blood Pressure (SBP) on arrival at referring facility/scene

The mean systolic blood pressure (SBP) was 120.4mmHg (SD = 24.1), with some extreme outliers present in the data. The minimum value in the dataset was 67mmHg, and the maximum value was 191mmHg, with a range of 124mmHg. The histogram (Figure 14) shows a normal distribution of the data with some outliers present. Quantile-quantile plots support that the SBP data is normally distributed.

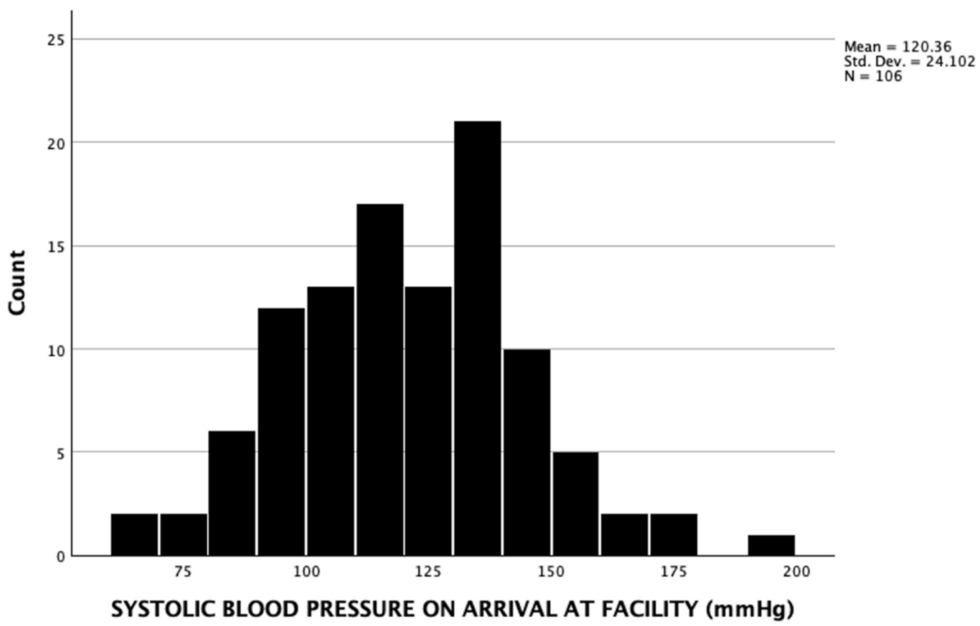

Figure 14: Histogram plotting the distribution of systolic blood pressure (SBP) in mmHg

In Figure 14, 50% of patients had an SBP between 100mmHg to 135mmHg according to the histogram's distribution of data. Most (90%) patients had an SBP between 60mmHg-176mmHg.

4.6.2. Diastolic Blood Pressure (DBP) on arrival at facility

The DBP measurements showed some extreme outliers in the dataset. For this reason, the median was reported as opposed to the mean. The median DBP for patients on arrival to the referring facility is 75mmHg (IQR: 21). The minimum DBP recorded was 35mmHg, and the maximum was 132mmHg, with a range of 92mmHg. The standard deviation is 16.68, which indicates that data was spread out over a large range of values, far from the mean. The histogram below (Figure 15) shows a unimodal, non-symmetrical distribution of data. There are extreme outliers shown in the histogram.

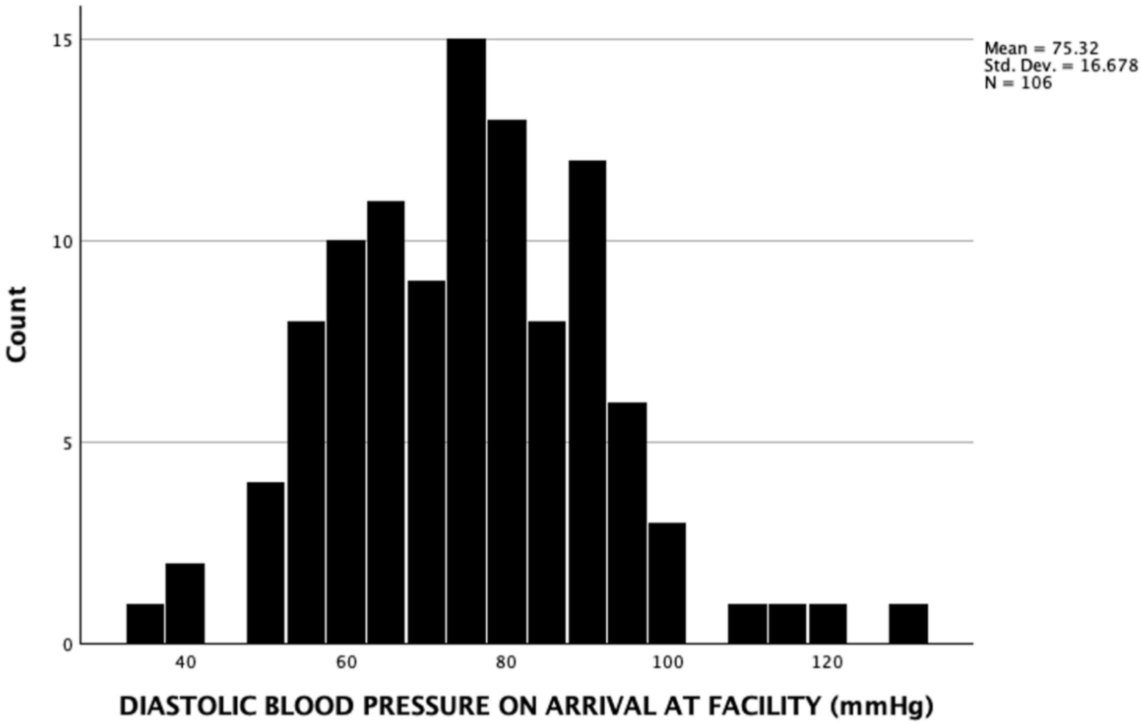

Figure 15: Histogram plotting the distribution of diastolic blood pressure (DBP) in mmHg

4.6.3. Mean Arterial Pressure (MAP) on arrival at referring facility

Mean arterial pressure (MAP) was recorded every time a blood pressure was measured. The mean MAP was 91.03 (SD = 17.7). The lowest MAP recorded at a referring facility was 46mmHg, and the highest was 147mmHg.

In Figure 16, the histogram shows a symmetrical distribution of the data. The histogram is unimodal, with some extreme outliers displayed by the graph. Most of the data was clustered around the mean. The histogram in figure 16 shows that 25% of patients had a MAP below 80mmHg on arrival at the referring facility. Half of patients (50%) had a MAP between 80-100mmHg within the data.

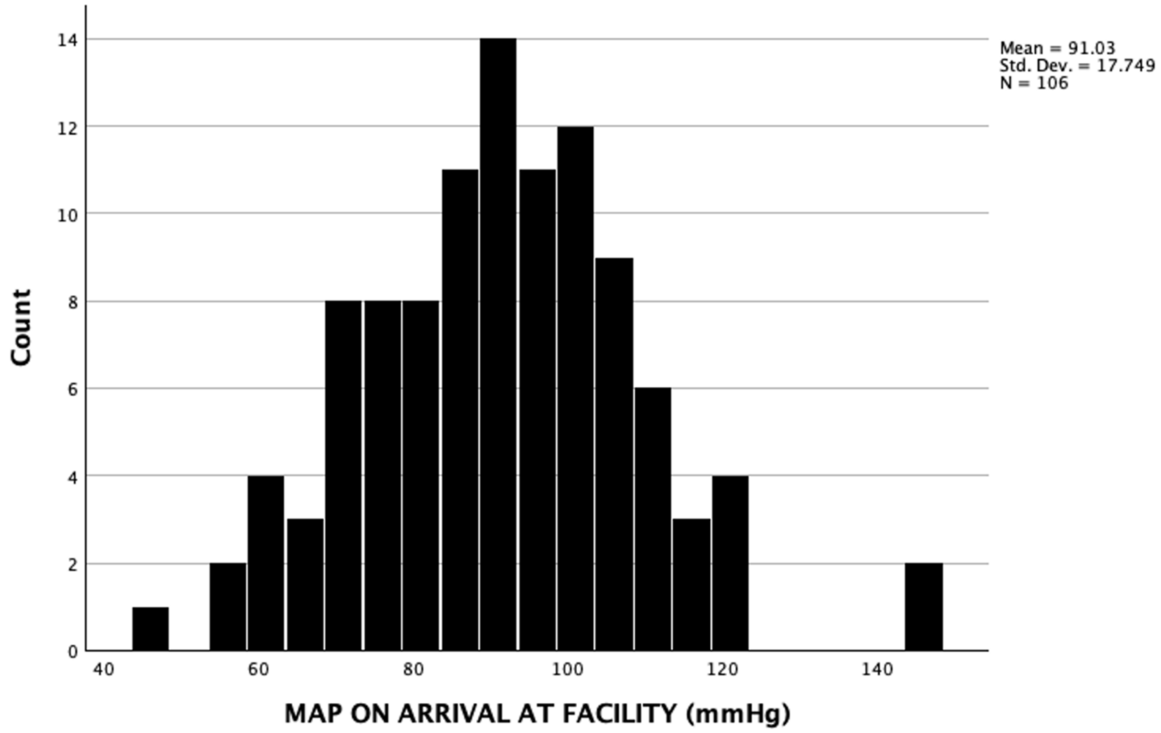

Figure 16: Histogram displaying the distribution of MAP on arrival at referring facility (mmHg)

Table 11 summarises all blood pressure values reported in this study.

Table 11: Blood pressure and mean arterial blood pressure on arrival at referring facility (mmHg)

Blood pressure components:	**Mean (SD)**	**95% CI**	**Median (IQR)**
Systolic blood pressure	120.4 (24.1)	115.7 – 125	
Diastolic blood pressure			75 (21)
Mean arterial blood pressure	91 (17.7)	87.6 – 94.5	

4.6.4. Oxygen saturation (SpO_2) on arrival at referring facility

The median SpO_2 is 99% (IQR: 3). The lowest SpO_2 value recorded on arrival was 88%, and the highest was 100%. There was a narrow range, of 12. The histogram (Figure 17) shows that data is skewed to the left (negatively skewed) showing that most of the values in this data set were near the higher end of the range. The data was not normally distributed according to Q-Q plots and Shapiro-Wilk tests ($p<0.001$), and median was reported.

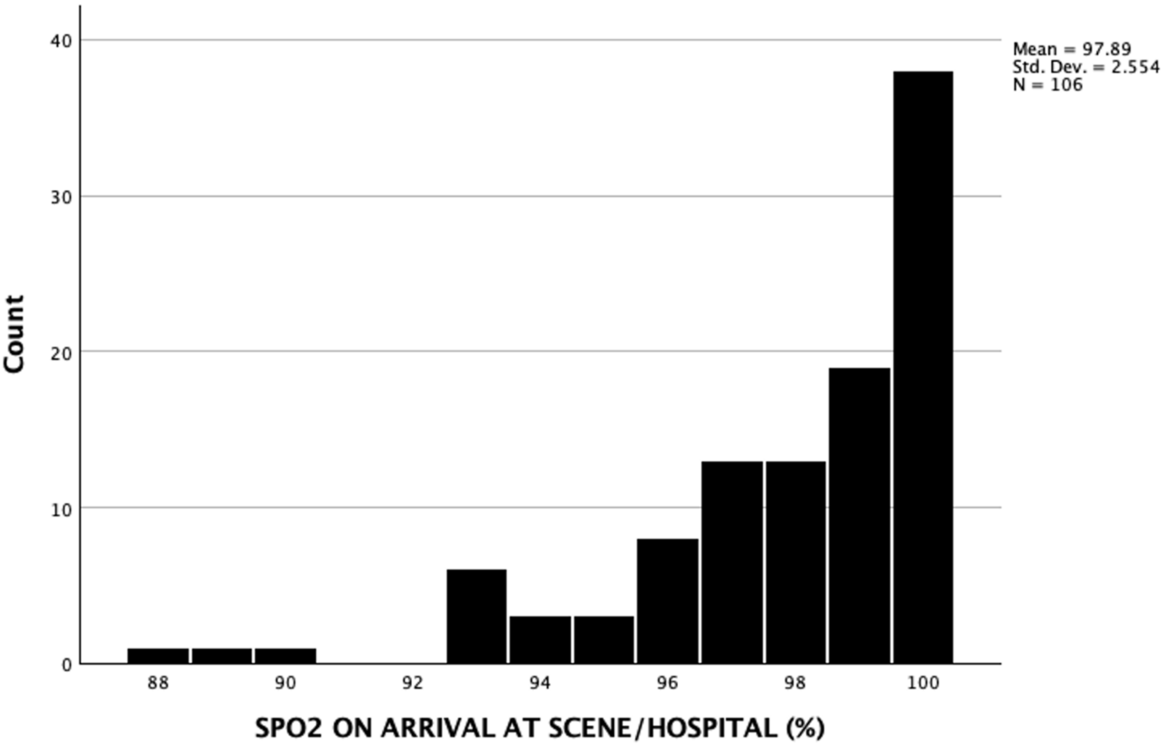

Figure 17: SpO2 on arrival at referring facility (%)

4.6.5. End Tidal Carbon Dioxide ($EtCO_2$) on arrival at referring facility

End tidal carbon dioxide was measured by the transport crew, as most referring facilities did not have the ability to do this. Therefore, the $EtCO_2$ on arrival represents the first measurement after the crew applied their monitoring to the patient. This could have resulted in some time delay before the first $EtCO_2$ measurement was documented.

End tidal carbon dioxide was not normally distributed. Q-Q plots and the Shapiro-Wilk test indicated that data was skewed ($p<0.001$). The median is 36mmHg (IQR: 11). There was a large range for $EtCO_2$ (87), and a minimum value of 11mmHg was recorded, with a maximum value of 98mmHg.

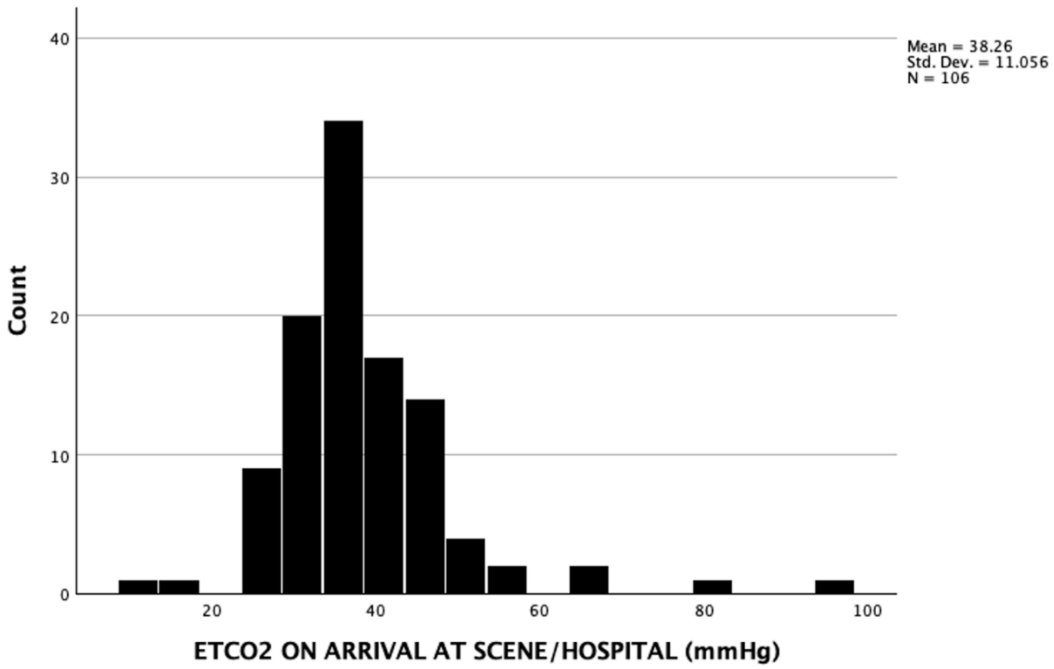

Figure 18: End tidal carbon dioxide at referring facility (mmHg)

Figure 18 (above) shows the distribution of the data as unimodal and skewed right. The data is asymmetrical, with extreme outliers depicted to the left and right of the graph. Most patients had $EtCO_2$ between 30-50mmHg.

4.6.6. Glasgow Coma Score (GCS) on arrival at referring facility

Table 12 (below) shows that most patients had a low GCS on arrival at the referring facility. A GCS of 2T[28] represented the lowest possible score and accounted for over half of the study sample (53.2%). Less common GC scores on arrival were 6T (12%), and 5T (8.9%). The remaining scores made up a minority of the scores on arrival at the referring facility. For seven patients (4.4%), no GCS was recorded.

Table 12: Glascow coma scale on arrival at referring facility

Glascow coma scale of patients on arrival to referring facility	
GCS on arrival to facility	**n (%)**
10T**	4 (2.5%)
2T	84 (53.2%)
3T	7 (4.4%)
4T	8 (5.1%)
5*	1 (0.6%)
5T	14 (8.9%)
6T	19 (12%)
7*	3 (1.9%)
7T	5 (3.2%)
8T	4 (2.5%)
9T	2 (1.3%)
Unrecorded	7 (4.4%)
*Where there is no ‘T’, patients were not yet intubated. **A ‘T’ represents the score for voice as patient is intubated.	

[28] Where ‘T’ is a component of the GCS score, it denotes that the patient is intubated and is therefore unable to receive a score for the verbal assessment of the GCS – a GCS 2T is comprised of E:1, V: T, M:1.

4.7. Adverse Events

4.7.1. Types of adverse events by rescue sedation category

The overall adverse event rate was 32.3% (n=51/158) for the entire sample. Adverse events were further separated according to whether patients received rescue sedation or not.

In the rescue sedation category, 50% (n=11/22) of patients had adverse events. Of these patients, just less than half experienced more than one adverse event during transfer (45.5%). 36.3% of patients experienced one adverse event, 45.5% had two adverse events, and 18.1% experienced three adverse events in the rescue sedation category.

In the category of patients who did not receive rescue sedation, 29.4% (n=40/136) had adverse events. Most only experienced one adverse event (65%), while 20% experienced two adverse events and 15% experienced three adverse events.

Fourteen different types of adverse events (AE) were recorded in this dataset. They were not classified according to whether they were preventable or non-preventable and cannot be attributed to practitioner error. An AE was considered as an unfavourable or potentially harmful occurrence during patient care from the time the air crew arrived at the referring facility until the patient was handed over at the receiving facility. Ventilator dyssynchrony was identified if the clinician stated it in their PCR. Most other AEs could be identified based on the patient's vital signs.

In the rescue sedation group, the most frequent type of AE was hypoxia (SpO_2<88%) occurring in 31.8% of cases. This was followed my hypotension, which occurred in 13.6% of patients in the rescue sedation group. Table 13 displays the less common adverse events that occurred in this group of patients.

In the group not requiring rescue sedation, hypotension was the most common adverse event, occurring in 22.8% of patients. Hypoxia occurred in 8.8% of patients, and the remaining adverse events were far less frequent as seen in Table 13.

Overall, in a subgroup analysis of adverse events, 32.2% (n=51/158) of patients experienced adverse events. The most common AE across the sample was hypotension, which occurred in 21.5% (n=34/158) of the entire sample. Hypoxia was the second most common event, to which 12% (n=19/158) of patients were exposed. Cardiac arrest only occurred in one patient (0.6%), in the rescue sedation group. Ventilator dyssynchrony was uncommon and was documented in two cases in the entire sample.

Most adverse events occurred while stabilising the patient at the referring facility (49%). The remaining adverse events occurred while loading the patient into the aircraft (20%), during flight (18%), at multiple points throughout the transfer (11%), and during handover at the receiving facility (2%).

Table 13: Adverse events according to rescue sedation category

		Rescue Sedation		Total
		Yes (n = 22)	**No (n = 136)**	**(n=158)**
		n (%)	**n (%)**	**n (%)**
Adverse event	No	11 (50%)	96 (71%)	107 (67.8%)
	Yes	11 (50%)	40 (29.4%)	51 (32.2%)
Number of adverse events	1	4 (36.3%)	26 (65%)	30 (19%)
	2	5 (45.4%)	8 (20%)	13 (8.2%)
	3	2 (18.1%)	6 (15%)	8 (5%)
Type of adverse events	Hypercapnia	1 (4.5%)	4 (2.9%)	5 (3.2%)
	Hypertension	2 (9.1%)	7 (5.2%)	9 (5.7%)
	Hypotension	3 (13.6%)	31 (22.8%)	34 (21.5)
	Hypoxia	7 (31.8%)	12 (8.8%)	19 (12%)
	Ventilator dyssynchrony	2 (9.1%)	0 (0%)	2 (1.3%)
	Tachycardia	1 (4.5%)	2 (1.5%)	3 (1.9%)
	Arrythmia	1 (4.5%)	0 (0%)	1 (0.6%)
	Attempted to self-extubate	0 (0%)	1 (0.7%)	1 (0.6%)
	Bradycardia	1 (4.5%)	1 (0.7%)	2 (1.3%)
	Cardiac arrest	1 (4.5%)	0 (0%)	1 (0.6%)
	Hypocapnia	1 (4.5%)	0 (0%)	1 (0.6%)
	Hypoventilation	0 (0%)	1 (0.7%)	1 (0.6%)
	Seizure	0 (0%)	1 (0.7%)	1 (0.6%)

Figure 19 (below) shows how adverse events were distributed between the rescue sedation and no rescue sedation groups. Hypotension and hypoxia were the most common events to occur in the sample.

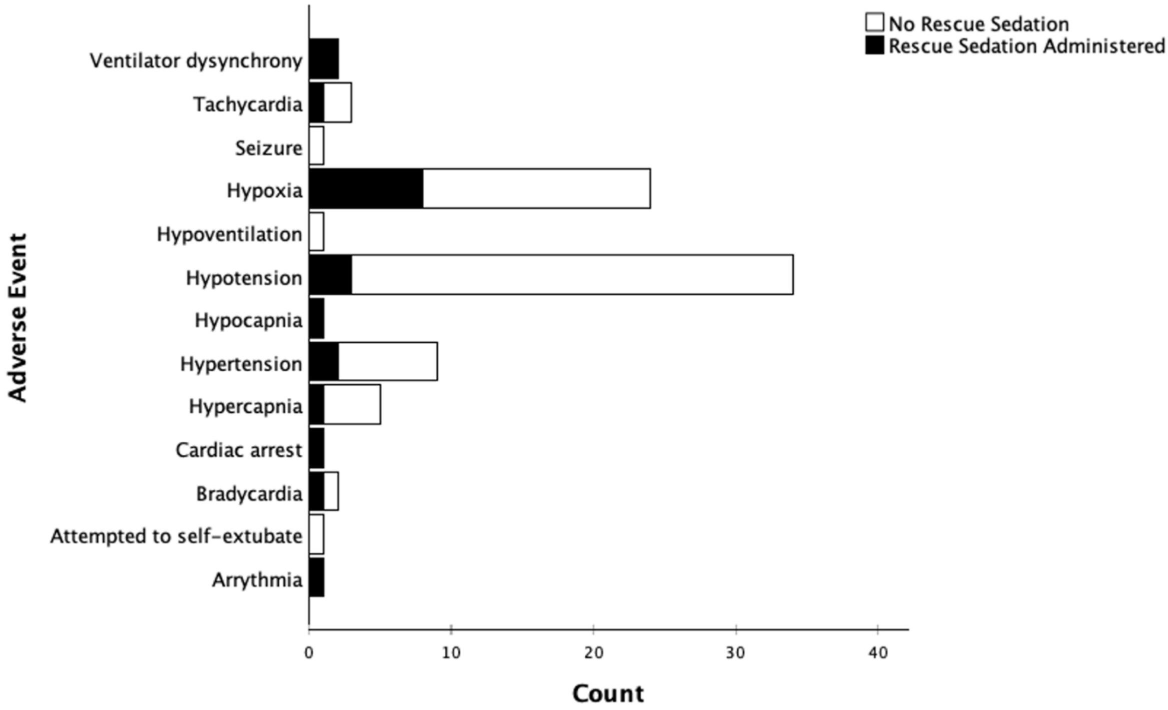

Figure 19: Graph illustrating types of adverse event by rescue sedation category

4.8. Results chapter summary

This chapter presented a descriptive analysis of the research findings. This chapter described demographic information of the study sample and presented descriptive data to address the study objectives. The proportion of patients who received rescue sedation was 13.9% (95% CI 9.2 – 20). Importantly, the results show that sedation and analgesia assessments are not being documented at the participating service. Ketamine is frequently used for both rescue sedation and continuous sedation and analgesia. The most common adverse events were hypotension and hypoxia, and most adverse events occurred while crews were stabilising patients at the referring facility. These results indicate potential areas for further research and training to improve sedation and analgesia practices in this setting.

CHAPTER 5: DISCUSSION

5.1. Introduction

This chapter contained a discussion of the findings presented in Chapter 4. The discussion chapter was written in accordance with the study objectives. It contextualised the findings in relation to the literature and any available evidence.

5.2. Sedation and Analgesia Practices

The study's primary objective was to describe sedation and analgesia practices among patients undergoing aeromedical transfer, and to determine the proportion of patients requiring rescue sedation. This study was one of the first in the Western Cape Province of South Africa to describe sedation and analgesia practices among mechanically ventilated patients undergoing transfer by air. Furthermore, the term 'rescue sedation' had not been used in the literature to describe the administration of additional sedatives or analgesics while patients are receiving continuous sedation and analgesia. To our knowledge, this is the first study in South Africa to determine the proportion of patients who required rescue sedation during transfer.

5.2.1. Patient Demographics and Case Characteristics

Most patients in the study sample were male (70.3%), and the median age was 35. The median weight of patients was 70kg. Over half of cases were traumatic in origin (56.3%), with the remaining 43.7% recorded as non-traumatic. In this study, over half of patients were traumatically injured and the majority were male. Male mortality rates due to all external causes in South Africa are significantly higher than for females (Matzopoulos et al., 2015). These findings are in keeping with previous literature, and accurately depict the trauma burden of low middle-income countries, and South Africa (Vlok et al., 2023).

Trauma accounts for 10% of all-cause mortality in South Africa (Dixon et al., 2024). The trauma death rate in South Africa is 157.8 per 100,000, and the Western Cape bears a large burden of South Africa's trauma epidemic (Dixon et al., 2024). This aligns with the study sample, the majority of which sustained traumatic injury. Polytrauma, burns, and traumatic brain injury comprised most traumatic aetiologies in this research. Patients with severe traumatic injuries require rapid conveyance to major trauma centres for definitive care, which potentially accounts for the sample representation of this research.

In the sample, 29.74% (n=47/158) of patients had sustained traumatic brain injury (TBI), which was the most common aetiology of critical injury in this research. These findings align with those described in a scoping review on the burden of TBI in Sub-Saharan Africa (SSA). The review showed that the incidence of TBI was 316 per 100,000 in South Africa, with most patients being males between 20-40 years of age (Adegboyega et al., 2021). To supplement this data, a study of preventable and non-preventable trauma deaths in the Western Cape showed that the most common cause of death due to catastrophic tissue destruction (CTD) was from brain injuries (70%) (Dixon et al., 2024).

Among those who were critically ill with a non-traumatic aetiology, cerebrovascular accident (CVA) and respiratory causes were the most common differential diagnoses recorded in PCRs. In this study, 9.5% (n=15/158) patients were transferred due to CVA. CVA is the leading cause of mortality second to HIV/AIDS in South Africa (Matizirofa & Chikobvu, 2021). The incidence of CVA in South Africa has been reported as 244 per 100,000 person-years in the literature (Matizirofa & Chikobvu, 2021). The high number of patients transferred with CVA may be due to resource limitations in rural areas of the Western Cape, specifically related to cerebral imaging and limited specialist care required to definitively manage CVA. Additionally, aeromedical transfer may be utilised for the potential timesaving offered by helicopter or aeroplane. Timesaving was potentially beneficial in patients with CVA, where early access to specialist care is crucial for optimal outcome following stroke (Vlok et al., 2023).

An estimate from the World Health Organisation (WHO) stated that the burden from non-communicable disease (NCD) in South Africa was up to three times higher than in developed countries (Nkhoma et al., 2023). This research showed that respiratory illness was a differential diagnosis for 8.9% (n=14/158) of mechanically ventilated patients undergoing transfer by air. According to data from the Western Cape Province, there is a high mortality rate among patients with cardiovascular and respiratory causes of illness (Nkhoma et al., 2023). Tuberculosis (TB) was also implicated in respiratory causes of illness, with South Africa contributing to 3% of cases globally (van der Walt & Moyo, 2018). These data indicated that respiratory causes of critical illness are common, which necessitates access to intensive care resources in the metropole – necessitating aeromedical transfer in select cases.

Interestingly, cardiac (1.3%) aetiologies including post-ROSC (2.5%), represented a low number of case types in the study sample. Previous research examining the utilisation of HEMS in South Africa showed that cardiac pathologies were under-represented (Vlok et al., 2023).

From this data, it is likely that the sample collected was representative of the population, which may improve this study's generalisability.

5.2.2. Rescue Sedation

Rescue sedation has previously been described in the literature for psychiatric indications. In these contexts, rescue sedation referred to the administration of additional sedative medications when initial medications achieved suboptimal sedation (Klein et al., 2019).

Anecdotally, it is a well-known practice to administer bolus dose sedation and analgesia in addition to continuous sedation and analgesia infusions prior to exposing patients to increased stimuli, or in response to signs of inadequate sedation and analgesia. Common signs that clinicians may use in lieu of using validated assessment tools include ventilator dyssynchrony, witnessing the patient attempt to remove an endotracheal tube, grimacing, rigidity, and resistance to passive movement (Asman et al., 2019). The practice of rescue sedation has not been discussed in this context previously, but as it is a known practice, this research aimed to describe it's use among mechanically ventilated patients during aeromedical transfer.

For this research, rescue sedation referred to the administration of bolus dose sedation in addition to a continuous sedation infusion due to inadequate sedation achieved by the initial infusion, or to prevent an unsafe patient care situation. An unsafe patient care situation referred to an action by the patient (usually unconscious in nature, or due to a pain response) that poses a risk to the air crew, or the patient themselves. Such events included attempts to remove the endotracheal tube (ETT), patient movement identified as under sedation, attempts to remove intravenous lines, biting of the ETT, or other unsafe situations identified by the researcher. Previous research has shown that additional sedation boluses were administered for cases of unsafe patient care situations, but did not refer to these boluses as 'rescue sedation' (Roginski et al., 2023). Literature also did not describe what comprised an 'unsafe patient care situation'. To differentiate between bolus doses administered for continuous sedation or as loading doses, this research chose to define rescue sedation as an entirely separate entity of bolus dosing.

The definition of rescue sedation in this context excludes any loading doses that were administered prior to initiating a continuous infusion. The proportion of patients who required rescue sedation in this study was 13.9%. This shows that the administration of rescue sedation is relatively common practice in this research, and further study would be indicated to describe the rationale behind this. Reasons for the use of rescue sedation were not routinely recorded in PCRs, which could mean that the actual proportion of patients who received rescue sedation is higher than reported in this study. This research did not aim to determine why rescue sedation was administered, but it seemed plausible that it would be administered in cases where deeper sedation was required to facilitate ventilator compliance, or to keep the patient safe and unaware for the duration of the transfer.

The literature reviewed showed that additional sedation boluses were rarely administered for unsafe patient care situations (Roginski et al., 2023). A study where lighter sedation was targeted during aeromedical transfer showed that additional bolus dose sedation was administered for one unsafe patient care situation, and in sixteen cases of ventilator dyssynchrony (Anton et al., 2024). However, neuromuscular blockade (NMB) administration was more common in these studies, which was in contrast to the findings of this research and is a potential reason for infrequent administration of rescue sedation.

More frequent administration of paralytics made it difficult to reliably assess patients' depth of sedation or whether they are adequately sedated (Esteves et al., 2024). While patients are paralysed, practitioners may not have the same visual cues to indicate when they are under sedated or in need of additional 'rescue sedation' compared to when patients are not receiving continuous NMB. In this research, patients received NMB infrequently and therefore visual cues were preserved and could assist practitioners to recognise signs of under sedation, prompting a response with administration of rescue sedation.

The literature showed that bolus dose sedation and analgesia are more commonly used than continuous infusions. Continuous infusions were the most frequently used method of sedation and analgesia administration in this research. Bolus doses of most sedative medications have a shorter duration of action as opposed to neuromuscular blocking agents (NMBA)[29] and pose the risk of patients being aware during paralysis, unable to express pain or distress because of longer-acting NMBAs. This necessitated careful timing of repeated boluses, to ensure that patients remained adequately sedated and pain-free while paralysed. The practice of administering NMBAs render sedation depth and pain assessment tools practically useless. It was recommended that deep sedation could be ensured by using tools like the RASS prior to administering continuous NMBAs to patients for critical care transport (CCT) (Esteves et al., 2024).

Infrequent NMBA use was a potential reason for the proportion of rescue sedation administered in this research, where the administration of NMBAs only occurred in 13.9% (n=22/158) of patients. The rationale for this is that if patients were under sedated or experiencing pain in this research, they would present with visual signs of distress that would otherwise be absent in a patient receiving continuous NMB. However, in a subgroup analysis of patients who received rescue sedation, 31.8% (n=7/22) received a paralytic. This finding somewhat contradicts the proposed rationale for increased administration of rescue sedation

[29] Neuromuscular blocking agents (NMBA) are medications that result in muscle relaxation and paralysis. They are also referred to as 'paralytics', and the term 'NMB' may be used to denote neuromuscular blockade.

in this research. It showed that among patients who received rescue sedation, paralytic administration was administered concurrently in most cases.

This may indicate a cohort of patients who were difficult to sedate using conventional methods, where additional boluses of rescue sedation were not sufficient to achieve adequate sedation without NMB. Alternatively, NMBAs may have been administered for different reasons, such as persistent ventilator dyssynchrony. This may have demonstrated that practitioners were mindful of awareness during paralysis and administered rescue sedation to prevent it.

This finding was supported by the literature, which demonstrated that post NMBA administration, the majority of patients received changes to their sedation strategy (Esteves et al., 2024). These changes included additional boluses of analgesia and sedation following NMBA administration (Esteves et al., 2024). The literature has long-stated that administration of neuromuscular blockade (NMB) has been associated with increased risk of awareness (Gibson & Flabouris, 2006). Therefore, another potential reason for concomitant rescue sedation and paralytic administration could be that practitioners are mindful that the potential for awareness during paralysis is increased by maintenance of NMB. However, the reasons for administration of rescue sedation in this cohort would need further investigation.

Ketamine was used for rescue sedation in most cases (68.2%). It was likely favoured by aeromedical crews due to its rapid onset, dual functionality as an analgesic and sedative, favourable haemodynamic effects, safety among patients with elevated intracranial pressure (ICP), and potential for neuroprotection (Peters et al., 2024; Ornowska et al., 2023; Zeiler et al., 2014). International literature does not discuss the use of rescue sedation in these contexts, but it does describe the use of intermittent bolus dosing in addition to continuous infusions of sedative. Despite ketamine being commonly used in this study, this was not the case in aeromedical services abroad, where ketamine boluses were used in as little as 38.6% of cases or described as being ‘infrequently used’ (Moy et al., 2021; Roginski et al., 2023). However, these trends may change in future, as the same authors have stated that ketamine use increased significantly over their study period, with midazolam use declining (Moy et al., 2021).

Midazolam was used less frequently for rescue sedation in this study - 22.7% of patients in the rescue sedation group received midazolam. Midazolam does not provide analgesia, and therefore it may have been used in cases where practitioners needed to deepen the patient’s level of sedation without additional analgesia. These results were similar to those documented internationally, where midazolam boluses were used in 29.8% and 38.8% of patients who were mechanically ventilated for aeromedical transfer respectively (Roginski et al., 2023; Moy et al., 2021).

Only 2.1% of patients received propofol for rescue sedation in this study. Propofol was not within the capabilities of ECPs in South Africa and could only be administered in the presence of a medical officer (MO). Propofol was not carried or stocked by the participating service. It was reasonable to assume that in these cases there was either a doctor present for the transfer, or propofol sedation was requested by the referring or receiving facility and prescribed by the respective doctors involved. Propofol administration was common according to similar studies, where in one cohort it was the most frequently used sedative, administered to 66.1% of patients (Roginski et al., 2023).

Fentanyl was not used as a rescue medication in any of the cases sampled for this study. It was used as a bolus analgesic in three cases, none of which were for rescue analgesia. Fentanyl was regularly bolused (86.9%) in addition to continuous infusions of propofol internationally (Roginski et al., 2023). A study in Canada showed that fentanyl was used in 97.9% of cases where analgesia was required during flight (Zia et al., 2019). The use of fentanyl appears to be more common internationally when compared to South African practice.

Fentanyl was introduced into the ECP and Paramedic scope of practice in 2020, and was subsequently removed from independent practice, with consultation becoming a requirement for its administration in 2022 (HPCSA, 2018). ECPs are the primary clinicians for the majority of IHTs in the study and it is uncommon for a doctor to accompany the retrieval team in this setting. Practitioners may instead have opted to use ketamine or alternative medications for these indications and may have used fentanyl in very select circumstances.

Despite appropriate continuous analgesia doses, patients in this group still required rescue sedation in over half of cases. Patients who were receiving appropriate doses of sedation in the rescue sedation group still required rescue sedation in 45.5% of cases.

In the group of patients who required rescue sedation, multimodal analgesia was only used in 18.2% of cases. Multimodal analgesia in this context refers to the use of analgesic medications with different mechanisms of action, which result in an additive or synergistic effect (de Souza et al., 2022). Multimodal analgesia has been shown to reduce opioid consumption, and some research suggested that it reduced the use of fentanyl in mechanically ventilated patients (de Souza et al., 2022). Multimodal analgesia could potentially affect how frequently rescue sedation and analgesia is administered and is worth investigating further.

Most rescue sedation was administered while crews were stabilising the patient at the referring hospital, accounting for 72.7% of administrations. This may be indicative of suboptimal sedation in the referring units, which has been described as common in emergency departments internationally (Freeman et al., 2020). Alternatively, it was possible that with patient movement and packaging, additional sedation was required to facilitate safe movement and transport to the aircraft. Only 13.6% of rescue sedation was administered during flight.

Repeat doses of rescue sedation were required in half of cases, with most of these repeat doses taking place during rotor wing transport compared to fixed wing transport. The rotor wing exposes patients to more vibration and noise in comparison to fixed wing transport and vibration has been documented to increase patients' sedation requirements (Stewart, 2018). These factors may influence why most repeat doses of rescue sedation were administered on the rotor wing.

5.2.3. Continuous Sedation and Analgesia Practices

Continuous sedation and analgesia refer to the administration of these medications over a specified period, either by infusion or repeated boluses. This is necessary for patients who are mechanically ventilated while undergoing aeromedical transport to facilitate ventilator compliance, and to provide effective analgesia (Moy et al., 2021). The study sought to describe these practices but did not examine the reasons why certain medications were chosen. It was likely that the participating service's Drug Infusion Protocol, as well as the Clinical Practice Guidelines (CPGs) informed or influenced these practices (Roos et al., 2012; HPCSA, 2018). The Clinical Decision Support Tool (CDST) also made recommendations pertaining to postintubation sedation and analgesia (PISA) (PBEC., 2024) However, the CDST was published recently (December 2024) and was not used to guide sedation or analgesia practices at the time that this study data was generated.

5.2.3.1. Medications used for continuous sedation and analgesia

The Clinical Decision Support Tool (CDST) developed by the Division of Emergency Medicine provides a quick reference guide for PISA (PBEC., 2024). It provides guidelines for the use of ketamine and midazolam or morphine and midazolam for PISA. The CDST further stipulates, that unless there are haemodynamic concerns, midazolam and morphine should be used for sedation and analgesia. However, in the presence of haemodynamic instability, practitioners should consider using ketamine and midazolam (HPCSA-PBEC, 2024). No such recommendations were made in the participating service's Drug Infusion Protocol, and the choice of sedative and analgesic medications is left to the discretion of the practitioner. This research found that the combinations of sedatives and analgesics recommended in the CDST were used routinely.

Use of these medications is outlined in the Air Mercy Service Drug Infusions Protocol (Roos et al., 2012). This protocol was available as a reference for practitioners at the participating service since its development. Despite the availability of guidelines and protocols, the decision to use a specific medication remained the responsibility of the treating practitioner. The factors influencing these decisions have not been documented in this study, as it is outside the scope of the research. However, it was likely that decisions would have been influenced by protocols that were available during the data collection period, practitioner scope of practice, and availability of select sedatives and analgesics.

Ketamine and midazolam were used in combination as sedation and analgesia for most patients in the study (62.7%). Ketamine and midazolam combinations have been described in South African ambulance operations for PISA prior to this study (de Kock et al., 2022). However, de Kock, Buma and Stassen (2022) stated that the consensus according to varying guidelines was to administer small boluses of benzodiazepines and opioids as needed, based on physiological indicators, while avoiding any negative haemodynamic effects (de Kock et al., 2022).

Bolus sedation may be appropriate for transporting patients over short distances but was not advisable for longer transport times in an aeromedical setting, where repeat boluses may be omitted due to increased difficulty associated with identifying early signs of under sedation – increased environmental noise, vibration, confined space. It was unreliable to use physiological indicators in isolation to assess for under sedation, as these could be attributed to the patient's underlying pathology or condition.

These factors necessitate the use of continuous infusions of ketamine or midazolam combinations to ensure maintenance of sedation and analgesia; thus, avoiding high doses of bolus opiates and benzodiazepines, potentially avoiding unrecognised early deep sedation and the risks associated with benzodiazepine use (Roginski et al., 2023).

A large proportion of patients in the study sample were being transported due to traumatic brain injury (TBI) and polytrauma. These patients may have been haemodynamically unstable, and the need for neuroprotection could have played a role in the choice of sedative used. Frequent use of ketamine and midazolam for sedation may be due to the haemodynamic stability that ketamine confers when compared to sedation with benzodiazepines or opiates alone (Manasco et al., 2020). Ketamine has the potential to reduce vasopressor requirements when compared to morphine-based analgesia and sedation infusions which can potentiate histamine-mediated vasodilation (Hendrikse et al., 2023).

Ketamine also has neuroprotective properties which may prove beneficial for patients with traumatic brain injury, and bronchodilatory effects which are beneficial for patients with obstructive respiratory pathologies (Manasco et al., 2020; Ornowska et al., 2023). Ketamine may be used as a neuroprotective agent due to its reduction in postinjury glutamate toxicity and inhibition of cortical sparing depressions (Peters et al., 2023). These neuroprotective features may play a role in the frequent use of ketamine and midazolam in this study, as many patients had sustained TBI (29.7%) or CVA (9.5%) in the study sample. However, there was no proven association between these aetiologies and the sedative medication used.

Ketamine was also used as a single sedative agent in a minority of cases in the study, which represents a deviation from the available guidelines. The addition of midazolam is recommended by guidelines and Drug Infusions Protocol to prevent emergence delirium (Roos et al., 2012). This side effect has been reported as a potential negative neuropsychiatric complication of ketamine infusions (Manasco et al., 2020). A potential rationale for use of ketamine alone would have been to avoid the negative haemodynamic effects of benzodiazepines in patients with critical injuries, but this was not investigated in the study. Additional unwanted effects of ketamine may influence how practitioners choose the primary sedative. Ketamine can result in increased bronchial secretions, and may elevate blood pressure in some cases (Manasco et al., 2020). In patients where these effects would be perceived as detrimental to their condition, practitioners may opt to use midazolam as the primary sedative.

International drug infusion manuals, such as the one developed by the Royal Flying Doctor Service (RFDS) in Western Australia, use ketamine as a monotherapy for sedation of mechanically ventilated patients and patients experiencing acute behavioural disturbances (RFDS, 2013). There was a report of using benzodiazepines in cases where emergence phenomenon arose, but no routine indication for combining ketamine and midazolam was described in the manual (RFDS, 2013).

International practices indicated that the use of propofol and fentanyl appear to be most common in the United States of America, and Canada (Roginski et al., 2023). In this research however, propofol was rarely used in isolation or as a combined infusion with morphine. Its use was only documented in one patient for the study sample. This is likely due to propofol being excluded from the Clinical Practice Guidelines and the ECP capabilities list, and therefore it can only be administered by a medical officer (HPCSA, 2018). It was not routine for an MO to be present for retrievals at the research site. Propofol is not included in the CDST, but it was included in the AMS infusion protocols when prescribed by a medical officer (Roos et al., 2012; HPCSA-PBEC, 2024).

Midazolam and morphine were used in combination for 22.2% of cases in this study. The CDST recommends the use of this combination for cases where the patient was haemodynamically stable (PBEC., 2024). In the AMS National Drug Infusions Protocol, no recommendations are made pertaining to the patient's haemodynamic status when considering which sedation and analgesia combinations to administer. Evidence over recent years have emphasised a preference toward non-benzodiazepine sedatives (Peters et al., 2024). This de-emphasis of benzodiazepine-based sedation emerged from research that suggested that when compared to propofol, sedation with midazolam resulted in a longer time to extubation, and longer duration of mechanical ventilation (Garcia et al., 2021). Despite this, Garcia et al (2021) stated that benzodiazepines may be necessary to achieve deeper sedation in select patients.

This finding was applicable to the aeromedical setting, where deeper sedation may be needed to facilitate safe transport of mechanically ventilated patients. According to international aeromedical practice, the use of benzodiazepines like midazolam had decreased over time, with ketamine and propofol used steadily increasing (Moy et al., 2021). However, some guidelines and drug manuals like the RFDS Drug Infusion Guidelines still advised for the use of midazolam and morphine when sedation for mechanically ventilated patients was needed. The reasons for this are not stated in the guideline but is important to note that the practice of using benzodiazepines for sedation still occurring internationally.

This research showed that morphine was still used regularly in conjunction with midazolam to provide continuous analgesia for mechanically ventilated patients. Morphine was used less often internationally, and has mostly been replaced by fentanyl for analgesia (Moy et al., 2021; Zia et al., 2019; Roginski et al., 2023). The reason for continued morphine use was not examined in this research, but it was possibly related to organisational preferences, cost, availability, and the fact that fentanyl required consultation prior to administration in the absence of a medical officer.

Propofol was administered by infusion for one case in this research. Despite propofol being used regularly in aeromedical services internationally, it was not within the capabilities list or medicines formulary for ECPs and paramedics at the research site, and either required that a doctor be present or prescribe its use for IFT under consultation (HPCSA, 2018). ECPs and paramedics may not be familiar with propofol for these reasons, and this may contribute to its infrequent use in this research.

There was a tendency for practitioners to use ketamine and midazolam rather than midazolam and morphine combinations in this research. The rationale behind choosing which sedatives and analgesics to use was not examined in this research however, these two combinations are the only choices available for sedation and analgesia in the current practice guidelines and capabilities list for ECPs and Paramedics (HPCSA, 2018). Further studies would be necessary to examine the reasons why particular combinations were used, but from this research it was apparent that sedative and analgesia choice was limited, and dependent on the practitioner’s discretion and scope of practice.

5.2.3.2. Methods of Medication Administration

The research found that most patients received sedatives and analgesics by syringe driver. A minority of patients received either bolus dose sedation and analgesia, or no method of administration was recorded. The use of syringe drivers to administer these medications ensured greater accuracy and reliability in terms of dose consistency and maintenance of sedation and analgesia.

Despite the common use of syringe drivers in this research, international studies have showed that bolus dosing is more common in the aeromedical setting (Roginski et al., 2023). All IHTs in this research ranged between 1.5 hours to 4.5 hours in duration and would have necessitated continuous infusions of sedation and analgesia by syringe driver. In a study by Moy *et al* (2021), transport times did not exceed 1.2 hours and hence, bolus dosing may have been more acceptable. This study did not examine the reasons why either method was used, and therefore the rationale behind these choices could not be proven.

Infusion pumps were not used at the aeromedical service in this study, and therefore practitioners would either use bolus dosing or syringe drivers. With limited options available for administration of these medications, it was likely that practitioners used their discretion to decide when either method should be used.

5.2.3.3. Sedation and Analgesia Dosing

Ketamine and midazolam were combined in the same syringe for cases where ketamine was administered as the primary sedative medication. Midazolam was added to ketamine for the perceived risk of emergence delirium and was therefore administered at a lower dose than when used as the primary sedative.

The mean dose of ketamine administered in this study was 2.3mg/kg/hr (95% CI 2.2 - 2.5). This dosing fell within the acceptable range according to the research site's Drug Infusion Protocol, which recommended using between 2-4mg/kg/hr (Roos et al., 2012). The recommended dosing for sedation is 2mg/kg/hr, and to maintain anaesthesia 4mg/kg/hr was advised (Roos et al., 2012). Slightly lower ketamine doses have been described in the literature, where a dose of 1mg/kg/hr was more commonly used (Roginski et al., 2023).

Compared to infusion manuals from the RFDS, the doses described in this research were far higher. The RFDS Infusion Manual (2018) recommended dosing between 0.25-1mg/kg/hr when ketamine was used in isolation for varying indications. A possible reason for this wide dose range with lower dosing recommended may be due to the additional indications listed in the RFDS manual. According to this manual, in addition to sedation for mechanical ventilation, ketamine was also indicated for ongoing conscious sedation, analgesia in conscious patients, and for acute sedation of patients experiencing behavioural disturbances (RFDS, 2013). These additional indications explain the inclusion of significantly reduced ketamine doses, as outlined in the RFDS manual.

Despite these additional indications, the maximum dose is 1mg/kg/hr, which is less than half the dose used in this study. It is unknown whether it is routine practice to administer ongoing NMBAs for mechanically ventilated patients at the RFDS. If NMBAs are used in conjunction with continuous sedation and analgesia, this may account for lower doses of ketamine administered to facilitate ventilation and safety during transport. Awareness during paralysis is a risk of using lower doses of sedation in conjunction with NMBAs (Pappal et al., 2021). Use of longer-acting NMBAs like rocuronium had been associated with delays in administering postintubation sedation, and lower initial sedation doses (Pappal et al., 2021).

Similarly, the CDST recommended lower doses of ketamine between 0.25-0.5mg/kg/hr (PBEC., 2024). Whether these doses had been validated for use in the out-of-hospital environment, be that ground or aeromedical, is unknown. The dose range of 0.25-0.5mg/kg/hr was intended for patients immediately following rapid sequence intubation (RSI). These patients received a large induction dose of sedative and NMBA to facilitate intubation. Induction and NMBA doses for emergent RSI were intended to anaesthetise and completely paralyse the patient to facilitate first pass success and minimise risk of awareness during the procedure. This may have reduced patients' PISA requirements immediately following RSI, which could account for the lower doses recommended in the CDST.

In the setting immediately post intubation, as described in the CDST, patients may not require doses of ketamine exceeding 0.5mg/kg/hr as they have recently received an induction dose of sedative and an emergency dose of NMBA. Induction doses of ketamine range from 1-2mg/kg, and emergency NMBA doses of rocuronium are 1-1.2mg/kg (Brown et al., 2018). At the dose described, rocuronium would render a patient paralysed for up to an hour, depending on the dose administered. It was difficult to assess sedation depth in these patients, and there was a higher risk of unrecognised under sedation and pain occurring during this period of NMB (Pappal et al., 2021). Practitioners have no reliable means of assessing adequacy of sedation and analgesia during the period of NMB following RSI and need to consider these factors when using lower doses of continuous sedation and analgesia. These factors could contribute to the lower doses recommended in the CDST, as patients should remain sufficiently sedated immediately post-intubation due to large loading doses of induction agent and NMBA.

However, in this study, only patients undergoing interhospital transfer (IHT) were sampled. Anecdotally, in most cases the air crew arrive hours after the patient had been intubated with RSI doses of sedative and NMBA. Patients were subsequently sedated with the hospital's dosing regime, which differed between facilities, and may have been appropriate for the in-hospital setting. However, at the point of IHT, patients would no longer be paralysed or deeply sedated from the induction doses they received during RSI. Additionally, aeromedical transport exposes patients to increased movement and auditory stimuli, factors which may necessitate higher doses of sedation and analgesia for safe transport while ensuring the patient is pain-free and comfortable (George et al., 2020).

This research showed that air crews routinely initiated sedation and analgesia after arriving at the referring facility, and that most rescue sedation was administered while stabilising the patient for transfer. These findings may indicate that patients were either too lightly sedated for transport or inadequately sedated at the referring facilities. This necessitated rescue sedation and higher doses of continuous sedation and analgesia for safe transport.

Initial light sedation and infrequency of continuous NMB by the referring facility may have been a reason for higher ketamine doses used in this research compared to guidelines and international studies where continued paralysis is common practice. However, it was not a research objective to determine why certain doses were used, and the theories in this discussion would need to be substantiated with further study.

When midazolam was used as the primary sedative, the mean dose was 50mcg/kg/hr (95% CI 0.04 - 0.06). Morphine was routinely combined with midazolam to provide analgesia in this study. The mean morphine dose was 50mcg/kg/hr (95% CI 0.04 - 0.06) when combined with midazolam. According to the research site Drug Infusion Protocol, the recommended midazolam and morphine doses range between 60-240mcg/kg/hr, and 20-80mcg/kg/hr respectively (Roos et al., 2012). This research found that midazolam doses were slightly lower than those recommended in the Drug Infusion Protocol, at 50mcg/kg/hr. Morphine was being administered at an appropriate dose according to this protocol.

When combined, these medications exert strong synergistic effects, which may account for less midazolam being required to achieve adequate sedation. The CDST recommended that between 50-200mcg/kg/hr is used to maintain sedation when midazolam was administered in conjunction with morphine 20-80mcg/kg/hr. The RFDS infusion manual recommended combining midazolam and morphine for sedation, and administering both medications at 20-80mcg/kg/hr. There appeared to be more consensus in various guidelines when this medication combination was used compared to other medication combinations that were used.

When propofol was used as an infusion in this research, the mean dose was 0.09mg/kg/hr (SD = 0.01). This was far lower than the dose range listed in the research site Drug Infusion Protocol, which stated a dose of 1-3mg/kg/hr was required to maintain continuous sedation in

ICU (Roos et al., 2012). This may reflect a lack of familiarity with propofol due to its infrequent use in the research. Such low doses may lead to sub-therapeutic effects and suboptimal sedation in patients who received propofol during transfer. In contrast to this research, propofol was used regularly in aeromedical services abroad, and higher doses were used with a median dose of 2.34mg/kg/hr being administered (Roginski et al., 2023). As propofol was infrequently used in this research, it may be appropriate to remove it from local guidelines like the Drug Infusion Protocol or to implement further training in its use to ensure that patients did not receive potentially harmful or suboptimal sedation during transfer.

The findings of this research aligned closely with practices described in local and international guidelines. Ketamine infusion doses were substantially higher in this research than those recommended by some local guidelines. Morphine and midazolam doses in this research were identical to those recommended in local and international guidelines. Propofol was infrequently used in this study, which was likely because it was not included in the ECP/Paramedic capabilities list and medicines formulary. In this research setting, practitioners only had access to ketamine, morphine, midazolam, and fentanyl (under consultation) within their capabilities list (HPCSA-PBEC, 2020). Therefore, their sedative and analgesia choices were limited, and this was reflected by the study's findings.

5.2.3.4. Sedation dosing

In this research, doses were categorised as being 'underdosed' in accordance with the guideline used at the research site, which recommended higher doses of ketamine (2-4mg/kg/hr) in comparison to newer guidelines (0.25-0.5mg/kg/hr) (Roos et al., 2012; HPCSA-PBEC, 2024). Therefore, a patient categorised as being 'underdosed', may have been receiving doses between 0.25-0.5mg/kg/hr, which would be deemed appropriate according to the CDST (HPCSA-PBEC, 2024).

When the finding was viewed in this context, it was unsurprising that using a dose range to determine whether a patient was 'underdosed' and under sedated or 'appropriately dosed' and sedated was not accurate due to a lack of consensus on what was considered an 'appropriate dose'. Future research should analyse this relationship using the patient's depth of sedation as an indicator of appropriate sedation. This was not possible in our research, as no sedation depth was assessed or documented.

5.2.4. Sedation Monitoring Practices

Sedation depth was not documented in any cases sampled for this study. Use of a validated sedation depth monitoring tool such as the Richmond Agitation Sedation Scale (RASS) was not documented in PCRs, and there were no alternative scores or methods of assessment documented. There were no documented pain assessments for patients in this research, such as the Behavioural Pain Scale (BPS). No alternative documentation was made in relation to pain assessments.

This was an important finding of the research and became apparent quite early during data collection. The finding in this study aligns with that of Moy et al (2021), who anticipated that crews would not routinely monitor sedation depth with a validated scale, as prehospital sedation has not received much attention in clinical research. In cases where no RASS was recorded, these authors used the GCS as a surrogate for sedation depth (Moy et al., 2021). Over half of patients (53%) had a GCS of 2T recorded throughout the transfer, which could be interpreted as deep sedation or a consequence of their underlying condition. Moy *et al* (2021) defined a GCS of 3 as equivalent to 'coma', and a GCS<9 as equivalent to 'deep sedation'. If the same assumption was applied to this research, 91.8% of patients had a GCS < 9 and were therefore deeply sedated. If this manner of categorising sedation depth was used in this study, the rate of deep sedation and coma would be exceedingly high (91.8%), which aligns with findings of research where the GCS was used as a surrogate for sedation scores.

Moy *et al* (2021) found that deep sedation occurred in 88% of cases, and coma occurred in 58.9% of patients transferred by air. However, the limitations of applying the GCS in this manner were not considered in this research, and this finding should be interpreted cautiously. The GCS was not validated as a sedation monitoring tool, and many patients in these studies received NMBAs or were being transported due to neurological pathologies. Both factors affect the final GCS calculated and confound any association between GCS and sedation depth. These factors were limitations to the research findings which appeared to indicate high rates of deep sedation.

Sedation monitoring and pain assessment were important as they could be used to guide sedative dosing and the need for additional analgesia. Some studies have shown that there was a tendency for deep sedation in the aeromedical setting, where it occurred in as many as 91.7% of cases (RASS -3.9 to -4.5) (Roginski et al., 2023). This tendency towards deep sedation may be due to a range of factors, from the patient's condition to the risks posed by the transport environment. Sedation depth of patients was unknown in this study, but based on the doses of continuous sedation administered, and the recorded GCS, it was likely that patients were at least moderately or deeply sedated.

The literature findings aligned with those of this research if applying the logic that GCS could serve as a surrogate for sedation scores. However, this was an association that should not be made without contextualising these findings with the inherent limitations of using GCS for this purpose. Therefore, this research drew no firm conclusions from the finding that most patients (91.8%) in the study had a GCS less than 9. Further prospective research would be valuable in this setting, using validated sedation depth scores and pain scales to properly assess the rate of deep sedation and adequacy of analgesia. Due to the infrequent maintenance of neuromuscular blockade (NMB) at this research site, prospective study using sedation depth scores and pain scales would elucidate more accurate results compared to sites where NMB was maintained during transfer.

Deep sedation had been associated with increased length of hospital stay, mortality, and decreased ventilator-free days (George et al., 2020). This finding held in cases where early deep sedation occurred, and was therefore relevant to the out-of-hospital setting (Moy et al., 2021). Light sedation and the use of shorter-acting non-benzodiazepines had been recommended for sedation of mechanically ventilated patients to avoid unnecessary deep sedation and related sequalae (Roginski et al., 2023). The true rate of deep sedation was unknown in this study and warrants further prospective study. However, benzodiazepines were still commonly used in this research and recommended in local guidelines like the CDST and the Drug Infusions Protocol (HPCSA-PBEC, 2024; Roos et al., 2012).

This study found that midazolam was routinely used in combination with ketamine and morphine for continuous sedation and analgesia. Routine use of midazolam may contribute to cases of deep sedation in this study, but it was difficult to determine with certainty, as no validated sedation assessments were performed. Prospective study on the rate of deep sedation in patients receiving morphine and midazolam versus those receiving ketamine and midazolam may be useful to determine how benzodiazepine use contributes to early deep sedation. Although, this research found that when midazolam was combined with ketamine, the mean dose of midazolam was equivalent to cases where midazolam was used as the primary sedative with morphine (0.05mg/kg/hr). This seems contradictory to recent research, which had suggested that concomitant administration of ketamine resulted in a reduction of opioid and other sedative requirements (Peters et al., 2024).

However, as these medications were usually mixed in the same syringe at the research site (i.e. 800mg ketamine + 20mg midazolam) titrating them individually was impossible in most cases, which may account for the persistently high doses of midazolam used in combination with ketamine. Mixing sedatives and analgesics in the same syringe was common practice and may occur due to a limited availability of syringe drivers in cases where patients required multiple infusions during transfer. Future studies should examine the feasibility of administering ketamine sedation as a monotherapy, or in combination with intermittent bolus dose midazolam as opposed to combining medications in the same syringe.

When assessing the risk versus benefits to sedation regimes, practitioners may consider the immediate risks of light sedation to outweigh the long-term effects of deep sedation in the transport setting. The perceived risks of light sedation in the transport setting are self-extubation, increased patient anxiety, risk to crew safety, patient awareness with paralysis, morbidity, mortality, and delirium (Roginski et al., 2023). Only one attempt at self-extubation was recorded in this study, and the rate of NMBA administration was low (13.9%) which may have prevented or reduced the risk of awareness with paralysis. These critical events (attempts to self-extubate, awareness during paralysis) may have occurred infrequently due to deep sedation of patients in this study.

However, sedation depth was not documented in this research, and there were no documented sedation depth targets in the data. Another risk posed by early deep sedation in the transfer setting is therapeutic inertia to the ICU or ED (Roginski et al., 2023). Deep sedation during the transfer of mechanically ventilated patients may be continued after handover to the receiving facility in ICU or the ED, increasing patients' duration of exposure to the risks associated with deep sedation. Absence of documented sedation scores and pain assessments in this research did not necessarily mean that practitioners were not performing these assessments in practice. However, it was important to document sedation and pain scores and to formalise them as part of routine assessment, which was not found in this research.

Early sedation and analgesia practices instituted in the aeromedical transfer setting have proven to contribute to patient outcomes (Pappal et al., 2021; Moy et al., 2021; Roginski et al., 2023). These outcomes underscore the importance of monitoring sedation depth and pain scores during transfer as these monitoring practices directly influence the doses of sedatives and analgesics administered, and the types of medications chosen for mechanically ventilated patients during transfer.

5.3. Mechanical Ventilation Practices

Mechanical ventilation was provided using the Hamilton T-1 ventilator. Some modes used in the study are unique to the Hamilton T-1 ventilator, such as Adaptive Support Ventilation (ASV). The most used modes of ventilation in this study were PSIMV and SIMV. When the patient initiates a breath, both modes of ventilation provide synchronised, pressure-supported breaths in addition to mandatory breaths set by the practitioner.

This was beneficial for patients who are spontaneously breathing, as it decreases their work of breathing and reduces patient-ventilator dyssynchrony (Shelledy et al., 1995). Patient-ventilator dyssynchrony was documented twice in this research (1.26%), making it a rare occurrence. Few patients received ongoing paralytics for the duration of their transfer (4.43%), allowing spontaneous patient-triggered breaths. Despite the infrequent practice of administering paralytics, patient-ventilator dyssynchrony was very rare. It was unlikely that dyssynchrony was under-recognised by practitioners as paralytics were not used routinely and signs of patient-ventilator dyssynchrony would have been easily identified.

In the rescue sedation group, 90% of patients were being ventilated with either SIMV or PSIMV. There was no statistically significant relationship between the mode of ventilation and the need for rescue sedation.

5.4. Adverse Events

In this research, adverse events were described as an unfavourable or potentially harmful occurrence during patient care from the time the air crew arrived at the referring facility until the patient was handed over at the receiving facility (MacDonald et al., 2008). There is no consensus regarding what defines an adverse event in the aeromedical setting. Previous research had used methods such as retrospective chart review at the discretion of a researcher to screen for and identify adverse events (Seymour et al., 2008). Some reviews classified adverse events into major or minor physiological events, while others did not (Seymour et al., 2008). Very few studies provided follow-up analysis of patients who suffered an AE during transfer, and therefore the impact on patient outcome was unknown (Alabdali et al., 2017).

This research was not designed to make statistically significant conclusions regarding adverse events and did not classify AEs according to their severity or preventability. Previous research had classified AEs into preventable and non-preventable events. Preventable adverse events were due to factors such as error (Alabdali et al., 2017). No physiological severity scores were calculated for patients in this sample, and their baseline condition was not quantified. However, as all patients in this sample were mechanically ventilated, their condition was presumed to be critical in most cases.

The research aimed to determine the adverse event rate at the research site and relate this to sedation and analgesia practices where possible, however limited the findings may be. The adverse event data was drawn from a subgroup analysis, and this study was not powered to make statistically significant findings regarding adverse events. Therefore, this data must be interpreted cautiously due to the inherent possibility of bias.

The adverse event rate among mechanically ventilated patients undergoing transfer in this study was 32.28%, which was slightly higher than rates documented in the literature (MacDonald et al., 2008). There was a paucity of research regarding AEs in the aeromedical setting. Internationally, AEs in interhospital transfers (IHT) occur in 11% of cases, which was far lower than the findings in this research (Jeyaraju et al., 2021). An important consideration relating to the higher AE rate found in this research was that adverse events were recorded from the time that the patient was first contacted in the referring facility. This may have resulted in a higher AE rate compared to the literature, as these studies only included adverse events that occurred during flight or in transit (Singh et al., 2009). This research did not aim to determine what factors influenced the adverse event rate.

The severity of patient condition had been cited as a risk factor for adverse events (Jeyaraju et al., 2021). All patients in this study were receiving mechanical ventilation and were critically ill or injured, which may predispose them to AEs. This may explain the relatively high AE rate in comparison to international literature, where all patients regardless of their illness or injury severity, were included in the analysis. The logistics of aeromedical transfer further predispose patients to AEs, as patients must undergo multiple movements during transfer.

AEs occurred in half of patients requiring rescue sedation, and in 29.4% of patients who did not require rescue sedation. In this study, AEs were more common in the group of patients who required rescue sedation. There were findings to indicate that the administration of bolus dose medications, including rescue sedation, may be associated with a higher risk of AEs. Patients who required rescue sedation may have been difficult to sedate, necessitating higher doses of sedatives and analgesics compared to patients who were easily sedated. Higher doses of sedative infusions and repeat boluses of rescue sedation may predispose patients to the hypotensive effects of these medications. This study was not powered to establish the reason for this association, and these were only hypothesised reasons for this relationship.

Hypoxia and hypotension were the most common AEs recorded for mechanically ventilated patients undergoing aeromedical transfer. Many patients in this study had sustained traumatic brain injury (TBI), or TBI with associated polytrauma. It was well known that any incidence of hypotension or hypoxia during the care of patients with TBI drastically increased mortality and disability. An incidence of hypotension, hypoxia, or hypocarbia in the prehospital setting had been shown to increase mortality and unfavourable outcomes for patients with TBI (Maiga et al., 2025). This study showed that hypoxia and hypotension occur often, which may pose a risk to this cohort of patients with TBI. Early detection and correction of hypotension and hypoxia to reduce secondary brain injury is the mainstay of AE prevention in this case (Maiga et al., 2025). Careful choice of correctly dosed sedatives with more stable haemodynamic properties and neuroprotective effects may assist in the prevention of hypotension and hypoxia, but further study would be required to confirm this. Ketamine has demonstrable neuroprotective effects, and favourable haemodynamic properties that make it a suitable choice for ongoing sedation and analgesia in patients with TBI (Peters et al., 2024).

It would seem logical to have vasopressors prepared for patients deemed to be at risk of hypotension during transfer. Retrospective data suggested that vasopressor use and flight distance were associated with an increased rate of adverse events (Seymour et al., 2008). However, this was likely due to the patient's preexisting haemodynamic instability, rather than the use of vasopressors themselves.

Adrenaline was the only medication used for this purpose in this study and may be a factor when considering why vasopressor use was associated with adverse events. High doses of adrenaline could result in arrythmias and severe tachycardia, as well as hypertension in some cases (Russell, 2019). These may have accounted for some of the AEs related to the use of vasopressors. It may be prudent to investigate the addition of alternative medications, such as noradrenaline, to the ECP capabilities list in the setting of critical care retrieval. However, noradrenaline was significantly more expensive than adrenaline and the differences in adverse effects may not be as significant as initially depicted in the literature (Leong et al., 2025). A recent systematic review of noradrenaline and adrenaline in the management of septic shock has stated that there was no difference in mortality between patients who received adrenaline or noradrenaline for septic shock, and no difference in the occurrence of arrhythmias (Leong et al., 2025).

Administration of NMBAs was infrequent in this study and anecdotally it was not routinely used unless patient-ventilator dyssynchrony persisted despite attempts to optimise ventilator settings or sedation strategies. The incidence of ventilator dyssynchrony was rare according to the PCRs that were examined (9.1%). Additional AEs where a paralytic may have been considered included 'attempts to self-extubate', and 'hypoventilation' or 'hypocapnia'. Due to its infrequent use, when NMBAs were administered, it could be assumed that it was for complex cases where ventilation and oxygenation was challenging despite other interventions.

These patients may have been predisposed to AEs relating to hypoxia or hypercapnia/hypocapnia due to their underlying condition, and NMBAs may have been used to manage these events. Therefore, rather than NMBAs being implicated in causing AEs related to hypoxia or hypoventilation, they may have been administered to manage them.

When compared to fixed wing transport, more AEs occurred on the rotor wing aircraft (helicopter) . Most fixed wing aircraft (aeroplane) IHTs of mechanically ventilated patients were from intensive care units (ICU) at district hospitals. These patients received intensive care prior to transport by fixed wing and may have been extensively stabilised for transfer prior to the air crew arriving. This contrasts with patients who were transported by rotor wing aircraft, mostly retrieved from rural emergency centres after the initial phase of resuscitation and stabilisation. Anecdotally, HEMS patients at this research site undergo transfer during the acute phase of their care. Therefore, it was likely that patients transported by rotor wing aircraft were unstable on arrival of air crews and required further interventions prior to transfer.

Many of the AEs recorded on the rotor wing platform occurred while stabilising the patient at the referring facility. These patients may have presented as critically ill or injured on arrival of the air crew, and these vital signs recorded would have been screened as adverse events. This was a major limitation of the data, as AEs could not be classified according to preventable and non-preventable events. Non-preventable events may account for many the AEs recorded in this research, as most were recorded at the referring facility and likely represented the patient's acute condition on arrival of the transporting crew. These adverse events were likely to reflect the patient's underlying instability and the acute phase of their care, as opposed to adverse events resulting from practitioner error or the hazards posed by transfer. This was supported by authors of a meta-analysis, who stated that adverse events are more likely to occur among critically ill patients, as a result of their underlying condition (Jeyaraju et al., 2021).

Extensive patient movement was involved in both rotor and fixed wing transport. However, the rotor wing was more confined than the fixed wing and exposes the patient to loud noise and vibration. These factors made it more challenging for rotor wing crews to recognise audible cues provided by the monitor and ventilator, and the confined space hinders select advanced interventions. The environment complexity and task burden associated with rotor wing operations and critical care transport are factors to consider when contextualising this finding (Roginski et al., 2023). Rotor wing aircraft were associated with increased AEs likely due to the high acuity of patients being retrieved, and the added environmental complexities of working in a confined space, with loud noise and vibration (Roginski et al., 2023; Jeyaraju et al., 2021).

This finding should serve as a motivation to ensure that dedicated, appropriately trained, and experienced air crew are utilised for rotor wing operations while recognising that the rotor wing poses a unique environment complicated by task complexity and high acuity patient cohorts. Due to increased AE prevalence on the rotor wing, it may be prudent to introduce an adverse event or near miss reporting tool to guide further training and to improve patient safety while ensuring more accurate capturing of adverse events.

Most AEs took place at the referring facility, while the air crew was stabilising the patient for transport. Just less than half (49%) of the total adverse events took place at the referring facility. Far fewer occurred during flight (17%), and while loading patients into the aircraft (19.6%). The reasons for AEs occurring during certain phases of the transfer were not studied in this research. However, it was important to identify where AEs are most likely to occur, as this may assist practitioners to recognise phases of the transfer where increased risk of AEs is present.

A potential reason for why most AEs occur at the referring facility is because most interventions are performed during this stage of the transfer, prior to loading the patient for flight. Most interventions occur during this phase of care as it was easier to access and assess the patient, and often additional interventions are required to prepare the patient for transfer. This was the phase of transfer when sedation strategies and medications were initiated by the air crew, and where additional stabilisation such as initiating vasopressors or intubation may occur. Therefore, it was logical that the most AEs would occur at this point, as the most interventions were performed during this phase.

Importantly, adverse events occurring during this phase of the transfer cannot be attributed directly to the air crew or the process of aeromedical transfer in isolation. Typically, the referring facility staff were involved in this phase of the transfer and the condition in which the patient was found by the air crew was dependent on what interventions had been initiated by the referring facility. Therefore the condition of the patient may determine their predisposition to AEs (Jeyaraju et al., 2021), and patient condition during this phase of transfer was dependent on the interventions that were provided by the often rural and under-resourced referring facility.

Although the initial adverse event rate appeared high when compared to the literature, most studies only account for AEs that occurred 'in-transit' (Alabdali et al., 2017). In contrast, this research included adverse events that occurred from the time the air crew arrived at the referring facility until the patient was handed over. If the AEs that occurred while stabilising the patient at the referring facility and on handover are disregarded, the adverse event rate was 15.8% (n=25/158). This adverse event rate was comparable to the literature.

5.5. Vital Signs

Mechanically ventilated patients undergoing aeromedical transfer required continuous monitoring of the following vital signs: blood pressure and mean arterial pressure, oxygen saturation, heart rate, end tidal carbon dioxide with waveform, and Glasgow Coma Score (CGS). Heart rate was recorded by practitioners in this study, but the researchers chose to omit it due different measurement techniques that are used to measure HR and the concern for accuracy and reliability of the recorded data.

Vital signs were recorded throughout the transfer, from the time of arrival at the referring facility until handover at the receiving facility. However, in this study, only the vital signs at the referring facility were reported to establish the patients' baseline condition upon arrival of the flight crews.

In this study, patients were reported to have a median systolic blood pressure of 120mmHg and a diastolic of 75mmHg. These values represent a normal physiological blood pressure for healthy adults (Sapra et al., 2023). The mean MAP reported was 91mmHg, which was also indicative of a haemodynamically stable patient. However, there were extreme outliers in the data, and extremely low and high blood pressures and MAPs were still recorded in the research. Just over 20% of patients in the sample required vasopressors, which indicates that haemodynamic instability affected a significant number of mechanically ventilated patients undergoing transfer. These blood pressure and MAP values may indicate that instances of haemodynamic instability were addressed by the referring facility prior to the air crew's arrival.

Oxygen saturation was recorded at a median of 99%, with the lowest oxygen saturation recorded at 88%. This showed that there were few instances of acute hypoxia on initial arrival at the referring facility. An oxygen saturation of 88% is acceptable in patients suffering from chronic obstructive pulmonary disorder (COPD) (Echevarria et al., 2021).

End tidal carbon dioxide was an invaluable vital sign when transporting patients who are intubated and receiving mechanical ventilation as it confirms endotracheal tube placement in the trachea and guides ventilation (HPCSA, 2018). The mean $EtCO_2$ in this study was 36mmHg, which is physiological (Sapra et al., 2023). Unfortunately, there were no descriptions of the waveform available, which could be a useful addition to PCRs for future research.

These vital signs indicated that in most cases, patients were vitally stable on first contact with the air crew. However, a limitation in interpreting these vital signs was that in cases where the air crew arrived to find the patient in critical condition, they may have delayed attaching their vital signs monitor while stabilising the patient. Typically, vital signs recorded from the PCR would be from the air crew's monitoring and the trends that it can print. However, the crew may elect to defer attaching their monitor in favour of stabilising the patient and this could lead to omission of vital signs being recorded on *actual* 'first contact' with the patient. This seemed a likely hypothesis, as most adverse events were reported during the initial phases of the transfer while stabilising the patient at the referring facility/scene, which made these vital signs questionable.

Additionally, vital signs were manually recorded on the PCR, and the accuracy thereof was dependent on how the practitioner completed the paperwork. If practitioners completed their PCR retrospectively or during flight, then vital signs were drawn from the trends available on the air crew's monitoring. The phase of the transfer when the monitoring was attached may vary from case to case, and therefore the first set of vitals recorded could be just prior to the departure from the referring facility to the helipad or airport, or they could in fact be on first contact with the patient. This variation could account for why patients appeared more stable than expected during this phase. An additional argument in favour of this hypothesis was that referring facilities do not have $EtCO_2$ monitoring equipment, and so if an $EtCO_2$ measurement was listed in the PCR, it was taken from the air crew's monitoring after the crew had attached their ventilator to the patient. This argues that most of the vital signs recorded 'during initial stabilisation at the referring facility' could have been recorded any time after contacting the patient and not just upon immediate contact.

5.6. Chapter Five Summary

This chapter discussed the results of the study. This was the first study to describe rescue sedation in the context of mechanically ventilated patients undergoing aeromedical transfer. Rescue sedation occurred relatively frequently, and the reasons for this should be researched further.

The research shows that ketamine was frequently used for both continuous sedation and analgesia, and as a rescue sedative. Midazolam was still used often, although less so than ketamine which showed that practitioners were less inclined to use benzodiazepines for continuous sedation. Multimodal analgesia was not commonly used in this research, which indicated a potential area for further training.

Currently no validated sedation scores or pain assessment tools were being documented during aeromedical transfer, and recommendations have been made to change this practice. The RASS and BPS have been recommended for use at the research site, and training had been delivered to facilitate the implementation of these tools. Further prospective research to determine the rate of deep sedation is necessary to establish whether the current doses of sedation and analgesia are appropriate.

Adverse events occurred most frequently while patients were being stabilised at the referring facility, but the rate of adverse events during flight was quite low. The most common adverse events were hypotension and hypoxia. This knowledge may assist practitioners to anticipate and prevent AEs through risk mitigation.

CHAPTER 6: CONCLUSION AND RECOMMENDATIONS

6.1. Introduction

The final chapter of this thesis made conclusions and recommendations relating to the findings of the research, in accordance with the research objectives. Recommendations were made for future research, and for future sedation and analgesia practices. These recommendations included training and guideline development for aeromedical services conducting transfers of mechanically ventilated patients.

6.2. Objective 1:

To determine the proportion of mechanically ventilated patients requiring rescue sedation and analgesia during aeromedical transport.

6.2.1. Research outcome and conclusion

Rescue sedation was defined as the administration of bolus dose sedation in addition to a continuous sedation infusion, due to inadequate sedation achieved by the initial infusion, or to prevent an unsafe patient care situation. The research found that rescue sedation was administered to 13.9% (n=22/158) of patients in the study.

Ketamine was used in most instances where rescue sedation was required, and midazolam was used less frequently. Rescue sedation was administered predominantly at the referring facility, during initial stabilisation of the patient.

Patients received rescue sedation irrespective of whether sedation and analgesia doses were ‘appropriate, under dosed, or overdosed’.

6.2.2. Recommendations

Practitioners should document rescue sedation with reasons for administration included in the PCR. If a dose of sedation was explicitly classified as ‘rescue sedation’ this will assist in future data collection. The research site could consider adding fields to the PCR specifically for rescue sedation and the reasons for its administration. This too will assist with future research pertaining to rescue sedation. Further research should be undertaken to determine why rescue sedation is being administered, and whether the proportion of patients receiving rescue sedation differs to what was reported in this study. This could inform future practice in terms of sedation dosing, and the use of non-pharmacological methods to reduce the need for rescue sedation.

Prospective study should be undertaken to determine what factors influenced administration of rescue sedation, such as the patient's initial sedation depth, continuous sedation strategy (type of medication, dose), and type of aircraft used for transfer (rotor wing versus fixed wing). Future studies should also include an analysis of sedation requirements according to the underlying condition of the patient, as certain pathologies may require higher doses of sedation than others. To achieve this, implementation of routine sedation depth scoring is essential to conduct prospective quantitative research assessing sedation depth during aeromedical transfer at the research site. Further qualitative research could be conducted using either surveys or focus groups to discuss the reasons for administering rescue sedation with the practitioners at the research site.

The sedation and analgesia regime handed over at the referring facility should be documented by the air crew to better understand the doses that these facilities are administering to patients prior to transfer. This data could be used to understand why rescue sedation is administered predominantly at the referring facility. If significantly lower doses of sedation and analgesia were being administered at the referring facility compared to those administered by the air crew, this may be a reason for the high proportion of patients who receive rescue sedation during the initial phase of transfer. A potential way to research this would be to review hospital handover notes to determine the doses of sedation and analgesia being administered on arrival of the air crew. This type of research could be achieved through a retrospective chart review, or crews could begin capturing this data at handover for future research.

6.3. Objective 2:

To describe sedation and analgesia monitoring practices and management practices. Sedation monitoring practices refers to the use of validated sedation depth monitoring tools. Pain monitoring practices describes the use of validated pain assessment tools. Sedation management practices refer to the types of medications administered for sedation and analgesia, the doses used, and how they are administered.

6.3.1. Research outcome and conclusion

Validated sedation and pain assessments were not documented, and it was unknown whether these assessments are being performed. Ketamine and midazolam were the most common sedation infusions administered, and the mean dose of ketamine used aligns with the current National Drug Infusion Protocol but is higher than doses recommended in the literature, and those recommended in the CDST (PBEC., 2024; Moy et al., 2021). Propofol was rarely used but underdosed on average. Syringe drivers were the most common means of administering sedation and analgesia during transfer.

6.3.2. Recommendations

Implementation of mandatory sedation depth assessments using a validated tool would be recommended for aeromedical transfers of mechanically ventilated patients. This recommendation was made early during the research process as it is the most logical way to avoid routine deep sedation or unrecognised under sedation by allowing practitioners to titrate sedation doses to desired effect (e.g. RASS -3) rather than according to dose ranges (e.g. ketamine 2-4mg/kg/hr). Pain assessments would be included in this recommendation, as they differ for patients who are mechanically ventilated.

Based on the recommendations made in accordance with these research findings, it is proposed that the RASS and BPS be included as vital signs on updated PCRs at the research site. Education pertaining to the RASS and BPS should be provided to staff at the research site, and additional training has been proposed in the future. Prospective study should occur when these sedation and analgesia monitoring practices have been formally initiated. Future prospective studies should aim to determine the depth of sedation of mechanically ventilated patients during aeromedical transfer and examine the doses of sedation associated with differing levels of sedation.

Future studies can implement quantitative methods, such as a prospective cohort study to determine whether patients receiving continuous sedation and analgesia in this setting are experiencing deep sedation, or undersedation and determine whether this affects clinical outcomes. This proposed study could aim to determine whether deep sedation is associated with increased hospital stay, or duration of mechanical ventilation – outcomes which have been assessed in similar research internationally. Additionally, it may be useful to determine whether certain dose ranges are associated with deep sedation to guide future dosing regimens in the aeromedical setting.

Based on this research, it is hypothesised that the current sedation doses being administered may be associated with deep sedation, or coma. Dose ranges associated with moderate to deep sedation may be considered 'appropriate' in the aeromedical setting. The aeromedical setting may necessitate deep sedation due to repetitive movements and additional external stimuli that patients are exposed to. After the proposed prospective research, appropriate sedation doses may be recommended and implemented in guidelines for aeromedical transfer in this region.

This research found that multimodal analgesia was rarely used. Multimodal analgesia has been recommended for patients undergoing aeromedical transfer at this research site. Prospective study should examine whether there is an association between multimodal analgesia and reduced sedation doses to further strengthen the stance that patients receive adequate analgesia prior to additional sedation or paralysis.

Further investigation into how different sedative and analgesic agents affect the patient's depth of sedation during transfer should occur. This may assist in de-emphasising routine use of benzodiazepines, which have been associated with deep sedation in this setting (Moy et al., 2021).

6.4. Objective 3

To determine the adverse event rate and describe adverse events associated with rescue sedation, continuous sedation, and analgesia.

Research outcome and conclusion

The overall adverse event rate was 32.3% for the entire sample (n=158). The most common AEs were hypotension and hypoxia. Most adverse events occurred while stabilising the patient at the referring facility.

6.4.1. Recommendations

These findings showed that most AEs occur prior to transfer, while crews were at the referring facility. In-transit AEs accounted for 18% of adverse events in this research, which appeared comparable to AE rates reported in the literature but requires further study to confirm. To mitigate AEs, a dedicated system should be developed for reporting near miss and/or adverse events. A set of standardised definitions for AEs should be created to assist practitioners with recognition and reporting AE occurrence (Jeyaraju et al., 2021). Developing a standardised method for identifying AEs is a complex task likely influenced by the setting and patient cohort, requiring a nuanced approach that may be specific to the research site.

Adverse events should be reviewed by a clinical governance team, and suitable actions taken to prevent them from occurring in future. In some cases, this may involve clinical education to improve recognition of high-risk periods during transfer and ways to mitigate against AE occurrence. High-risk periods have been identified as the time when crews are stabilising the patient at the referring facility, during loading of the patient into the aircraft, and to a lesser extent during flight (in-transit).

Future research should include injury severity scores and disease severity scores to determine whether the severity of a patient's condition is related to increased odds of adverse events occurring. Future research should also categorise AEs according to the patient's underlying condition, as explained by Jeyaraju et al (2021), patients receiving mechanical ventilation for respiratory disease may experience hypoxia that is nonpreventable due to their disease state.

Future research could be conducted by prospective observational study after developing a dedicated adverse event reporting system at the research site. Ideally, the reporting system would record the type of AE, phase of transfer when it occurred, the platform (helicopter or aeroplane) and whether it was associated with an intervention or procedure. Any AE recorded on the reporting system could be linked to the original PCR according to the PCR number, allowing the researcher to review the PCR if necessary.

AE research could establish the rate of AEs occurring in-transit and while stabilising patients at the referring facility. Future research should determine whether associations exist between the number or type of interventions performed and the occurrence of AEs. Another potential research aim would be to assess whether there is an association between the patient's physiology score and the occurrence of adverse events. AE research could be more impactful if there was longitudinal follow-up of patient mortality following adverse events, and as such determining whether AEs affect patient mortality outcome could be assessed through collection of patient care records from the receiving hospital.

6.5. Summary

Rescue sedation refers to the administration of bolus dose sedation in addition to a continuous sedation infusion, usually due to inadequate sedation achieved by the initial infusion. Rescue sedation can also be administered for unsafe patient care situations. This research determined that the proportion of patients who received rescue sedation was 13.9%. Patients who received NMBAs such as rocuronium frequently received rescue sedation. These patients may have been difficult to sedate using conventional methods, or this may represent practitioner mitigation against awareness during paralysis. Prospective study may show that this proportion is higher if practitioners document this practice in future, as it was not always possible to identify rescue sedation in this research.

Ketamine was the most frequently used rescue sedative and seems a logical choice due to its rapid onset and potent analgesic effects. Ketamine and midazolam were combined to provide continuous sedation and analgesia in most cases. The mean ketamine doses used in this infusion seem comparatively higher than those found in similar published guidelines and protocols available locally and internationally. Despite literature reporting the potential deleterious effects of benzodiazepine-based sedation regimes, combinations of midazolam and morphine are still regularly used at the research site and are still recommended in local guidelines.

Neither sedation depth nor pain assessment scores were documented in this research. As sedation depth has been associated with patient outcomes, this represents an important finding. Implementation of mandatory sedation depth monitoring and pain assessment has been recommended for future practice at this research site. Prospective study to describe sedation depth and pain scores during transfer is recommended to assist in sedation and analgesia guideline development for future practice. Deep sedation has been associated with mortality, increased duration of ICU length of stay and fewer ventilator-free days and therefore represents a potentially modifiable factor in patient outcomes. Continuous sedation depth monitoring during aeromedical transfer may assist in preventing unnecessary deep sedation or inadvertent under sedation and requires further research in the South African IHT setting.

Fourteen different adverse events were identified in this research, with hypotension and hypoxia accounting for the most frequently occurring AEs. Unlike previous published research, this study also accounted for AEs that occurred while not in-transit. Due to the way AEs were defined and screened in this research, many could represent the patient's initial condition on arrival of the air crew, rather than clinical error or patient safety issues.

6.6. Conclusion

This thesis examined sedation and analgesia practices among patients undergoing aeromedical transfer and determined the proportion of patients who received rescue sedation through retrospective chart review. Ketamine is frequently used for both continuous sedation and analgesia and for rescue sedation.

Importantly, the research identified an absence of documented sedation and analgesia monitoring practices. Another distinctive finding was that almost half of adverse events occur at the referring facility – necessitating further investigation to determine the reasons for this.

These findings suggested that sedation and analgesia practices in the South African aeromedical setting may differ to those described in international literature and in local ground EMS. The reasons for this are unclear and necessitate further research. However, this research does inform contemporary sedation and analgesia practices in the aeromedical setting and offers areas for future improvement. There is a need for improved sedation and analgesia monitoring, a practice which can provide insights into sedation depth during aeromedical transfer. Sedation depth monitoring could inform recommendations pertaining to sedation doses and potentially improve recognition of deep sedation or conversely, under sedation – mitigating against the risk of awareness during paralysis and the deleterious effects of deep sedation. Sedation and analgesia practices represent modifiable risk factors affecting patient outcomes. As such, they represent areas for further research and quality improvement.

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ANNEXURES

Annexure A: Ethics Clearance Certificate by the Faculty of Health and Wellness Sciences Research Ethics Committee – Cape Peninsula University of Technology

Cape Peninsula
University of Technology

HEALTH AND WELLNESS SCIENCES RESEARCH ETHICS COMMITTEE (HWS-REC)
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9 September 2024
HWS-REC Approval Reference No: CPUT/HWS-REC 2024/H15

Faculty of Health and Wellness Sciences

Dear Mr. S Colman (217021247)

Re: APPLICATION TO THE CPUT HWS-REC FOR ETHICS CLEARANCE

Approval was granted by the Health and Wellness Sciences-REC to **Mr. S Colman** for ethical clearance. This approval is for research activities related to research for **Mr. S Colman** at Cape Peninsula University of Technology.

TITLE: Sedation and analgesia practices of mechanically ventilated patients during aeromedical transfer

Supervisor: Mr. R Matthews and Prof. K Najaar

Comment:
Approval will not extend beyond 10 September 2025. An extension should be applied for 6 weeks before this expiry date should data collection and use/analysis of data, information and/or samples for this study continue beyond this date.

The investigator(s) should understand the ethical conditions under which they are authorized to carry out this study and they should be compliant to these conditions. It is required that the investigator(s) complete an **annual progress report** that should be submitted to the CPUT HWS-REC in December of that particular year, for the CPUT HWS-REC to be kept informed of the progress and of any problems you may have encountered.

Kind Regards

Ms. Carolynn Lackay
Chairperson – Research Ethics Committee
Faculty of Health and Wellness Sciences

Annexure B: Sedation Depth Assessment Tools

Sedation Tool	Description	Score Components
Richmond agitation sedation score (RASS)	Single-item scale with ten levels of response. Five levels of response for patients who are not conscious, and four for those that are conscious.	+4 – Combative (overtly combative, danger to staff and self) +3 – Very agitated (pulls/removes tubes or catheters) +2 – Agitated (frequent non-purposeful movement, PVA*) +1 – Restless (anxious, but movements are not aggressive) 0 – Calm -1 – Drowsy (eye opening to voice lasting >10s) -2 – Light sedation (briefly awakens with eye contact to voice lasting <10s) -3 – Moderate sedation (movement or eye opening to voice, but no eye contact) -4 – Deep sedation (no response to voice, movement or eye opening to physical stimulation) -5 – Unarousable sedation (no response to physical or verbal stimuli)
Ramsey sedation scale (RSS)	Single-item scale which measures three levels of response for patients deemed to be awake and three levels of response for those deemed to be asleep.	1 – Awake, agitated, or both. 2 – Awake, orientated, and tranquil. 3 – Awake but responds to commands only. 4 – Asleep; brisk response to light glabellar tap or loud auditory stimulus. 5 – Asleep; sluggish response to light glabellar tap or loud auditory stimulus. 6 – Asleep; no response to glabellar tap or loud auditory stimulus.
Sedation agitation scale (SAS)	A single-item seven-point scale.	7 – Dangerous agitation (tries to remove monitors, tosses and turns, lashes out at staff. 6 – Very agitated (remains restless despite verbal reassurance, bites ETT, requires restraints). 5 – Agitated (anxious or restless, attempts to move, calms down with reassurance). 4 – Calm and cooperative (calm, easy to arouse, able to follow instructions). 3 – Sedated (difficult to awaken, responds to verbal prompts or gentle shaking but drifts off again).

		2 – Very sedated (incommunicative, responds to physical stimuli but not verbal instructions, may move spontaneously). 1 – Unarousable (incommunicative, little or no response to verbal stimuli).
Nursing instrument for the communication of sedation (NICS)	A seven-point scale ranging from 3 to +3 with positive scores denoting the depth of sedation and negative scales measuring the patient's agitation.	-3 – Dangerously agitated (physical risk to patient and others, attempting to pull/pulling on invasive devices, fighting restraints. -2 – Agitated (frequent or constant motor activity requiring restraints, not controlled with verbal reminders). -1 – Anxious (fidgety, calms with reassurance). 0 – Awake, calm, and cooperative. 1 – Lethargic (arouses easily to voice or gentle tactile stimulation, attentive purposeful motor assessment, eyes closed when not stimulated). 2 – Deeply sedated (requires loud voice or deep stimulation to arouse, will follow commands briefly only when stimulated, rapidly returns to deep sedated level, purposeful movements during stimulation). 3 – Unresponsive to deep stimulation (no command following or purposeful motor movements)
Motor activity assessment scale (MAAS)	A single-item tool with seven response-defined categories of behaviour. Developed from the SAS and shares similarities with this tool.	0 – Unresponsive (does not respond to noxious stimuli) 1 – Responsive to noxious stimuli only (opens eyes, or raises eyebrows, moves head toward noxious stimulus or moves limb with noxious stimulus. 2 – Responsive to touch or name (opens eyes or moves head toward stimulus or moves limb toward stimulus or when name is spoken loudly). 3 – Calm and cooperative (no external stimulus is required to elicit movement, and patient is adjusting sheets or clothing purposefully and follows commands). 4 – Restless and cooperative (patient is picking at sheets or tubes or uncovering self.
*PVA – Patient-ventilator asynchrony		

Annexure C: Table of Pain Assessment Tools

Behavioural Pain Scale (BPS)		
Components of assessment	Criteria	Score
Facial Expression	Relaxed	+1
	Partially tightened	+2
	Fully tightened	+3
	Grimacing	+4
Upper Limbs	No movement	+1
	Partially bent	+2
	Fully bent with finger flexion	+3
	Permanently retracted	+4
Compliance with mechanical ventilator	Tolerating movement	+1
	Coughing but tolerating ventilation for most of the time	+2
	Fighting ventilator	+3
	Unable to control ventilation	+4
Explanation of scores	Scores ≤3 indicate no pain. Scores 4-5 indicate mild pain. Scores 6-11 indicate an unacceptable amount of pain. Scores ≥12 indicate maximum pain. Scores ≥6 warrant sedation and analgesia	

Critical Pain Observation Tool (CPOT)			
Components of assessment	Criteria	Score	Description
Facial Expression	Relaxed, neutral	0	No muscular tension observed
	Tense	1	Presence of frowning, brow lowering, orbit tightening
	Grimacing	2	All the above facial movements plus eyelids tightly closed
Body Movements	Absence of movements	0	Does not move at all (does not necessarily mean absence of pain)

	Protection	1	Slow cautious movements, touching or rubbing the pain site, seeking attention through movements
	Restlessness	2	Pulling tube, attempting to sit up, moving limbs/thrashing, not following commands
Muscle Tension	Relaxed	0	No resistance to passive movements
	Tense, rigid	1	Resistance to passive movements
	Very tense, rigid	2	Strong resistance to passive movements; inability to complete them
Ventilator Compliance	Tolerating ventilator, or movement	0	Alarms not activated, easy ventilation
	Coughing, but tolerating.	1	Alarms stop spontaneously
	Fighting ventilator	2	Asynchrony: blocking ventilation, alarms frequently activated
Explanation of scores	For those patients with a CPOT score of ≤ 2: • There is likely minimal to no pain present. Consider re-evaluation in the future. For those patients with a CPOT score of >2: • There is an unacceptable level of pain. Consider further or alternative analgesia and sedation.		