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The Maintenance of Anaesthesia following Pre-hospital Induction of Emergency Anaesthesia in the United Kingdom (UK)

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‘Yr wyf drwy hyn yn datgan mai canlyniad fy ymchwil fy hun yw’r thesis hwn, ac eithrio lle nodir yn wahanol. Caiff ffynonellau eraill eu cydnabod gan droednodiadau yn rhoi cyfeiriadau eglur. Nid yw sylwedd y gwaith hwn wedi cael ei dderbyn o’r blaen ar gyfer unrhyw radd, ac nid yw’n cael ei gyflwyno ar yr un pryd mewn ymgeisiaeth am unrhyw radd oni bai ei fod, fel y cytunwyd gan y Brifysgol, am gymwysterau deuol cymeradwy.’

Rwy’n cadarnhau fy mod yn cyflwyno’r gwaith gyda chytundeb fy Ngrichwyliwr (Goruchwylwyr)’

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I confirm that I am submitting the work with the agreement of my Supervisor(s)’

Bangor University

Masters by Research (MRes)

The Maintenance of Anaesthesia following Pre-hospital Induction of Emergency Anaesthesia in the United Kingdom (UK)

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MBChB with Honours, BMedSci (Hons)

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Thesis Abstract

Background: Pre-hospital emergency anaesthesia (PHEA) is an advanced clinical intervention delivered by expert pre-hospital care services, operating on a regional basis, throughout the UK. Historically PHEA has been a controversial issue, but it is now widely accepted that PHEA is indicated for a small but significant number of patients. In the UK the most common indication for PHEA is trauma caused by road traffic collisions. PHEA consists of the initial induction of anaesthesia and intubation with subsequent maintenance of anaesthesia. PHEA is always delivered by the intravenous route (total intravenous anaesthesia - TIVA). The conduct and delivery of PHEA is not without risk. Current guidelines are available to reduce risk and optimise patient safety and outcome. They make recommendations for how PHEA should be conducted and consistently state that PHEA should be delivered to the same standard as in the hospital setting with equipment and monitoring also meeting stringent hospital standards. No research has been conducted which investigates how PHEA is currently maintained following pre-hospital induction and intubation nor how closely this reflects published guidelines.

Objectives: The aim of this study was to build a picture of how emergency anaesthesia is maintained following pre-hospital induction by services across the UK, and to identify to what extent current practice reflects guidelines for PHEA.

Methods: This has been investigated by conducting a scoping review and performing an analysis of secondary data. The initial scoping review was split into two separate streams of evidence. The first research strand sought to identify literature which describes the way in which PHEA is maintained in the UK. The second research strand sought to collate recommendations guiding the maintenance of PHEA. Secondary data analysis was then performed upon a dataset collected by senior clinical researchers from EMRTS, Cymru (a UK pre-hospital care service). The nationally representative and up-to-date dataset contained variables further describing the maintenance of PHEA in the UK.

Results: Most pre-hospital care services operating in the UK can provide PHEA (n=32, 78%). Of these, 87.5% (n=28) can provide PHEA during road or air transport. PHEA is most commonly maintained using bolus administration of anaesthetic agents (n=24, 75%). Most UK pre-hospital teams have a range of anaesthetic agents available, but midazolam and morphine are together the combination of drugs used most frequently for the purpose of maintaining PHEA (n=16, 50%). Free text responses indicate that if the patient were haemodynamically unstable, boluses of ketamine would be preferred. The reported average compliance with safety recommendations for TIVA was 17%.

Conclusions: UK practice conforms well with national PHEA guidelines. The findings illustrate a variation in practice, which is likely to be appropriate and is supported by major professional bodies. The results do however suggest poor compliance with some of the published recommendations for TIVA. Questions remain regarding the relevance and applicability of the TIVA guidelines to the field of pre-hospital emergency medicine.

Recommendations: Further research is required to further analyse the practice of PHEA in the UK and to build the evidence base surrounding pre-hospital emergency medicine, and PHEA in particular, with a view to establishing the subspecialties own comprehensive yet specific standards of practice.

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Chapter One

The Maintenance of Anaesthesia following Pre-hospital Induction of Emergency Anaesthesia in the UK: Introduction, Background and Context

1. Introduction

Pre-hospital emergency medicine

Pre-hospital emergency medicine (PHEM) constitutes emergency medical care given to seriously ill or injured patients prior to arrival and treatment in hospital or other fixed healthcare setting (Boylan & Nutbeam, 2013; Mackenzie, 2018; Wilson et al., 2015). In the UK this has traditionally involved a broad spectrum of care from bystander CPR to emergency treatment and transfer by regional ambulance services, supplemented by a small number of other agencies (including the Red Cross, Mountain Rescue and The British Association for Immediate Care Schemes (BASICS)), and clinicians often working on a voluntary, or altruistic basis (Boylan & Nutbeam, 2013; Mackenzie, 2018).

More recently, Pre-Hospital Emergency Medicine (PHEM) has become a General Medical Council approved subspecialty of Anaesthesia, Acute Medicine, Intensive Care Medicine and Emergency Medicine, with its own recognised training programme (Mackenzie, 2018; IBTPHEM, 2020). The formal development of this subspecialty has resulted in the establishment of a greater number of recognised roles for pre-hospital emergency medicine specialists and consequently an increase in the range of advanced clinical interventions that can be performed in the pre-hospital setting (Wilson et al., 2015).

In this paper the terms “pre-hospital (emergency) services” and “pre-hospital (emergency) teams” are used to refer to (the more recently developed) physician-led pre-hospital teams that are capable of providing a range of *advanced* on-scene and in-transit critical care interventions, including pre-hospital emergency anaesthesia (PHEA). In the UK, advanced pre-hospital care is largely delivered by regional Helicopter Emergency Medical Services (HEMS)/Air Ambulance services (AA) and BASICS organisations (Burgess et al., 2018). Whilst most areas in the UK are covered by a team capable of providing advanced pre-hospital care, PHEA is not available 24 hours a day across the country (Burgess et al., 2018). The actual geo-temporal provision of PHEA is largely unknown. Factors such as staff availability, the weather, the day of the week and the time of day all affect the provision of

PHEA. A recent observational study published by Bourn et al., (2020) found that only 10% to 56% of the UK population would be able to receive PHEA from a HEMS/AA team within 45 minutes of a major traumatic injury - a key NICE recommendation (NICE, 2016; NICE, 2018). Actual nationwide provision may be higher, as advanced pre-hospital care is also provided by 35 BASICS and three emergency department based teams (Burgess et al., 2018), in addition to the HEMS/AA teams included in the observational study (Bourn et al., 2020). Further research is necessary to elucidate the geo-temporal provision of advanced pre-hospital care.

The doctors working for HEMS/AA and BASICS organisations usually have a professional background in anaesthetics, intensive care medicine, emergency medicine, or occasionally general practice (Harris & Lockey, 2011). Together these regional pre-hospital care services carry out over 1600 PHEAs annually (Burgess et al., 2018). With more pre-hospital services having access to physicians capable of providing PHEA, an established subspecialty training programme in Pre-hospital Emergency Medicine (IBTPHEM, 2020) and an increasing number of pre-hospital critical care services expanding their operational hours (Mackenzie, 2018; McQueen et al., 2015), the number of cases of PHEA is likely to further increase.

Traditional ambulance services led by paramedics or emergency medical technicians have a complementary set of skills and a scope of practice that does not include PHEA. The role of advanced pre-hospital teams is to augment the existing pre-hospital response, rather than to replace it (Boylan & Nutbeam, 2013). Where a patient is receiving advanced on scene anaesthetic intervention, the paramedics or emergency medicine technicians will retain input into the ongoing care of the patient, for example by applying cricoid pressure to facilitate endotracheal intubation.

The care given by pre-hospital teams involves the provision of immediate life-saving treatment, in the context of a resource limited and environmentally challenging setting, under a high degree of time pressure (IBTPHEM, 2020). This is undoubtedly a challenging subspecialist area of medical practice.

Pre-hospital emergency anaesthesia (PHEA)

Pre-hospital emergency anaesthesia (PHEA) is a term used to describe the administration of drugs to a patient in the pre-hospital setting to attain a state of controlled unconsciousness, akin to general anaesthesia, and facilitate tracheal intubation (Hooper & Lockey, 2013).

Evidence demonstrates that a considerable proportion of morbidity and mortality can be prevented by good quality, timely pre-hospital care (Chiara et al., 2002; Kleber et al., 2010). The early

establishment of a patent, definitive airway is a critical priority (Hickman, 2006), as airway compromise is one of the most important causes of poor outcome and preventable death (Lockey et al., 2015; Stocchetti et al., 1996; Timmerman et al., 2006). Unless a patent airway is maintained all other interventions are likely to fail (Hickman, 2006).

Difficult to manage airways are present in a large proportion of this patient population and many severely injured patients require advanced airway interventions (Lockey et al., 2015; Timmerman et al., 2006). Tracheal intubation is considered the gold standard for securing a definitive airway and protecting the airway from aspiration of vomit or blood (Hooper & Lockey, 2013). Unless patients are in cardiac arrest or deeply unconscious with minimal or absent airway reflexes, drugs need to be administered to achieve general anaesthesia and facilitate tracheal intubation.

General anaesthesia is the triad of unconsciousness, analgesia and muscle relaxation. Accordingly, an induction agent (i.e., a sedative), an analgesic and a neuromuscular blocking drug are usually given to induce anaesthesia, however slight variations in practice are well recognised (Lyon et al., 2015). Anaesthesia comprises three phases: induction - putting a patient into a state of controlled unconsciousness, maintenance -subsequently keeping the patient asleep and finally emergence – waking the patient up. The maintenance of anaesthesia is the focus of this thesis.

Definitions

Terminology used in this field is variable and other terms closely related to PHEA include drug assisted intubation and rapid sequence induction (RSI). PHEA is normally used to describe the sequential processes of induction and maintenance of anaesthesia (as described above). Drug assisted intubation refers to the induction of anaesthesia using anaesthetic agents and also endotracheal intubation, but not the subsequent maintenance of anaesthesia. RSI is a specific way of inducing anaesthesia, commonly used for emergency patients and others at risk of aspiration of gastric contents into the lungs (Sinclair, 2005). It involves the use of a sedative (+/- analgesic) and a neuromuscular blocking drug to rapidly achieve a state of unconsciousness and flaccid paralysis (Sakles et al., 1998; Tayal at al., 1999). Endotracheal intubation is then performed whilst cricoid pressure is applied (Sinclair, 2005). Notably face mask ventilation is not used for RSI (Sakles et al., 1998; Tayal at al., 1999). In reality RSI (or a variation thereof) is almost always used for the pre-hospital induction of anaesthesia. Whilst these terms are sometimes used interchangeably in the literature, they refer to slightly different procedures/practices.

Of note, the term PHEA does not encompass pharmacologically assisted laryngeal mask insertion (a supraglottic airway device), nor post cardiac arrest interventions, where drug administration is not

necessary (Sandberg et al., 2013).

PHEA is almost always maintained using total intravenous anaesthesia (TIVA). TIVA describes the induction and maintenance of general anaesthesia with intravenous agents, without *inhaled* hypnotics. Any combination of intravenous hypnotics/sedatives (with or without analgesics) can be used to achieve this endpoint (Al-Rifai & Mulvey, 2016). Bolus dosing, fixed rate infusions, or a target-controlled infusion (TCI) pump may all be used for PHEA. Manual bolus dosing is easier and quicker to administer and allows real-time adjustment of dose based on patient physiology. Infusions may be more challenging and time consuming to set up, but should in theory guarantee the delivery of a continuous supply of anaesthetic agent. TCI pumps rely upon the clinician entering key patient characteristics (e.g., age and weight) and a desired target concentration to be achieved in the patient's plasma or brain. A computer algorithm then calculates and administers an initial intravenous bolus and a subsequent intravenous infusion to achieve this target concentration.

Indications for PHEA

Historically, conflicting reports have been written regarding the benefit of PHEA, however, it is now widely accepted that the provision of pre-hospital emergency anaesthesia (PHEA) can improve survival and functional outcome (Bernard et al., 2010; Eich et al., 2009; Klemen & Grmec, 2006).

The indications for pre-hospital emergency anaesthesia and intubation closely resemble those applicable in the hospital setting (Hickman, 2006; St Bartholomew's and The Royal London Hospital Department of A&E Medicine and Prehospital Care, 2005). They are: 1) actual or impending airway compromise, 2) ventilatory failure, 3) unconsciousness, 4) severe head injury, or head injury associated with unmanageable agitation 5) humanitarian indications, including severe pain and 6) anticipated clinical course (Hooper & Lockey, 2013). Further relative indications applicable in the pre-hospital setting include long transport time to hospital, the availability of robust equipment and airway management tools and appropriate environmental conditions, e.g. lighting, weather, terrain etc (Braun et al., 2010).

In the UK, PHEA is most frequently delivered in the context of trauma (Boylan et al., 2019; Burgess et al., 2018), where all the aforementioned indications for PHEA may easily arise. The 2007 National Confidential Enquiry into Peri-Operative Deaths (NCEPOD) 'Trauma: Who cares' report (National Confidential Enquiry into Patient Outcome and Death, 2007) found that approximately 10% of injured trauma patients had an inadequate airway or ventilation status on arrival to hospital. Current National Institute for Health and Care Excellence (NICE) guidelines specifically recommend that pre-hospital emergency anaesthesia (PHEA) and drug-assisted intubation should be performed within 45

min of the incident for trauma patients who cannot maintain their airway and/or ventilation (NICE, 2016; NICE, 2018).

Unfortunately, there is evidence that the delivery of PHEA carries risk of harm, particularly if performed sub optimally (Burgess, et al., 2018; Cowan et al., 2012; Davis et al., 2003; Davis et al., 2004). Potential adverse effects include the risk of iatrogenic harm to the patient because of complications associated with the drugs administered and/or intervention to the airway. Possible serious complications include haemodynamic instability and secondary changes in intracranial pressure (Hickman, 2006). The combination of drugs administered may also make it more difficult to monitor changes in the patient's physiology (Hickman, 2006). Additional difficulties arise from the lack of patient information, adverse environmental conditions, transport and logistical considerations, limited availability of equipment and drugs, and challenges for the practitioner in maintaining competency and confidence in the application of a rarely used skill set (Hickman, 2006).

The evidence base

Compared to interventions undertaken by well-established hospital specialties, for example bronchoscopy performed by respiratory physicians, there is a lack of high-quality evidence guiding pre-hospital clinical management. The evidence base surrounding PHEA is no exception (Hooper & Lockey, 2013). This has meant that hospital-based evidence, practice and standards have been extrapolated to the pre-hospital setting without the support of a robust evidence base.

Difficulties in interpreting the paucity of PHEA research lie in the fact that the patient case mix is highly heterogeneous (in terms of baseline physiology and medical history, as well as injury/illness sustained), various professional groups and skill levels have been included in research and drug assisted, and non-drug assisted intubations have often been conflated. Additional confounding variables include the lack of monitoring data, the challenging environmental conditions, and the retrospective nature of the studies (Braun et al., 2010; Hooper & Lockey, 2013; Tentillier et al., 2008; Timmermann et al., 2007).

PHEA guidelines

Despite the relative weakness of the evidence base, the provision of pre-hospital emergency anaesthesia (PHEA) is a national recommendation for a small but significant number of patients requiring medical attention in the pre-hospital setting (Hooper & Lockey, 2013; NICE, 2016; NICE, 2018).

Guidelines and recommendations have been published to regulate PHEA, reduce risk and enhance patient safety. Some published guidelines refer directly to PHEA (Lockey, 2017; NICE, 2016; NICE 2019) and others relate more generally to the use of TIVA (Nimmo et al., 2019; Safe Anaesthesia Liaison Group, 2009).

The TIVA guidelines include The Association of Anaesthetists of Great Britain and Ireland (AAGBI) and The Society for Intravenous Anaesthesia (SIVA) guidelines for the Safe Practice of Total Intravenous Anaesthesia (TIVA) (Nimmo et al., 2019). These guidelines recommend specific equipment for intravenous infusion and patient monitoring and build on recommendations previously published by the Safe Anaesthesia Liaison Group (SALG) in 2009 (Safe Anaesthesia Liaison Group, 2009). The TIVA guidelines are perhaps more directly relevant to routine hospital practice, but should arguably also be applied in the pre-hospital setting (Checketts et al., 2015; NICE, 2016; Nimmo, 2019; Safe Anaesthesia Liaison Group, 2009).

Key recommendations

The guidelines consistently state that PHEA should be performed to the same standard as in-hospital anaesthesia, with equipment and monitoring also meeting hospital standards (Lockey, 2017). PHEA should only be performed by highly trained and competent senior clinicians. This high-risk practice should not be performed in professional isolation; a trained assistant should be present and high-level direction and supervision is required. Robust clinical governance policies and practices should be in place (Hooper & Lockey, 2013).

Clinical practice guidelines

Clinical practice guidelines (CPGs) are systematically developed documents, which aim to assimilate evidence into recommendations to standardise care, optimise patient outcomes, facilitate shared decision making and inform public health policy regarding resource allocation (Tetreault et al., 2019; Woolf, 1999). Rigorous studies have demonstrated an improvement in the quality of patient care associated with the use of CPGs (Grimshaw & Russell, 1993; Woolf et al., 1999) and additional benefits for healthcare professionals, health services and funding bodies have been well described (Grimshaw & Russell, 1993; Rao & Tandon, 2017; Tetreault et al., 2019; Woolf et al., 1999). CPGs have thus been upheld as an essential part of quality medical practice for several decades (Kredo et al., 2016) and they remain a key component in the teaching and practice of medicine for a wide spectrum of clinical scenarios.

Over recent decades, the number of available CPGs has grown enormously, and increased emphasis

has been placed on the development and implementation of high-quality guidelines (Kredo et al., 2016; Tetreault, 2019). Historically guidelines consisted of consensus-based statements and expert opinion, but as evidence-based medicine has gained traction there have been significant changes to the guideline development process (Kredo et al., 2016). Current methodology is both more explicit and rigorous (Tetreault et al., 2019; Woolf, 1999), and the international consensus definition has been updated to reflect this: "Clinical guidelines are statements that include recommendations intended to optimize patient care that are informed by a systematic review of evidence and an assessment of the benefits and harms of alternative care options" (Steinberg et al., 2011).

Limitations of clinical practice guidelines

There is a growing awareness of the harms potentially associated with the content, quality, and application of CPGs. The most significant limitation is that their recommendations may be false (Woolf et al., 1999). There may be a relative lack of evidence, the evidence may not be examined closely enough, or design flaws in contributing studies may mean that their conclusions are misleading (Woolf et al., 1999, Tetreault et al., 2019). The construct of guidelines is also subject to the opinions, experience, and subconscious bias of the guideline development group (Rao & Tandon, 2017; Woolf et al., 1999). Guidelines that are not routinely reviewed and updated may perpetuate outdated and possibly harmful practices and policies (Woolf et al., 1999).

Patients are rarely the sole factor considered when developing CPGs. Social and economic factors are also considered, and sub-optimal treatments may ultimately be recommended to balance conflicting interests and control costs (Woolf et al., 1999). NICE recommendations, for example, are based upon systematic review of best available evidence and explicit consideration of cost effectiveness (Corbett et al., 2021).

A fundamental weakness of guidelines is that they may not support the most appropriate treatment for the individual patient i.e., what is best for patients overall, may not be best for any given individual (Rao & Tandon, 2017; Woolf et al., 1999). Algorithms which reduce the art and science of medicine to a series of binary decisions leave insufficient room for clinicians to adapt care to meet patients' personal circumstances (Rao & Tandon, 2017; Woolf et al., 1999).

CPGs can adversely affect public health policy. A negative (or even neutral) recommendation may prompt healthcare providers to reduce availability of and access to certain services, whilst imprudent recommendations for costly services may consume limited resources that are better allocated to interventions of a greater value to a greater number of patients (Rao & Tandon, 2017; Woolf et al., 1999).

Even when correct, clinicians describe some guidelines as inconvenient and a poor use of limited time (Rao & Tandon, 2017; Woolf et al., 1999). When multiple professional bodies/organisations publish guidelines concerning the same clinical problem, conflicting recommendations may arise. This can be a source of both confusion and frustration for practitioners (Woolf et al., 1999).

Guidelines may cause professional harm to clinicians (Woolf et al., 1999). They are used to judge the standards of clinical practice and when these guidelines are weak, or improperly developed, this may be unfair (Woolf et al., 1999). Furthermore, a theoretical concern is that instead of using guidelines to enhance patient care they may be used to castigate or sue clinicians who do not follow them (Rao & Tandon, 2017; Woolf et al., 1999).

CPGs may detrimentally impact upon scientific progress if further research is inappropriately discouraged (Woolf et al., 1999). For example, guidelines that conclude that a procedure or treatment lacks evidence of benefit may be misinterpreted by funding bodies as grounds for not investing in further research or development in that field (Woolf et al., 1999).

Though studies have demonstrated an improvement in quality of care associated with the application of CPGs, whether this effect is replicated in every day practice is less clear (Field & Lohr, 1990). Furthermore, this is likely to depend on the specific CPG, and CPGs are infrequently evaluated as comprehensively as we would desire (Grol et al., 2003; Rao & Tandon, 2017).

The development and implementation of CPGs is one way in which organisations seek to improve patient care and outcome. However, they are often associated with flawed aspirations of what they can and will achieve (Woolf et al., 1999). Clinical guidelines serve to enhance practitioner knowledge when they are uncertain about the best course of action and when scientific evidence can assist the decision-making process. They are a poor solution in many other circumstances (Woolf et al., 1999). Opponents argue that too frequently guidelines are seen as a “magic bullet” for a wide spectrum of health, social and political issues that ignore more effective, but more complex solutions (Woolf et al., 1999).

Finally, the ultimate challenge associated with CPGs, is that they may do little to effect behavioural change. When clinicians are already aware of the evidence and the recommendations, policy makers should instead focus their attention on identifying the barriers, beyond knowledge, that stand in the way of behavioural change.

The development of clinical practice guidelines

In recent years there has been an attempt to standardise CPG development (Kredo et al., 2016; Tetreault et al., 2019). Detailed protocols have been published by major international bodies including the World Health Organisation, (World Health Organisation, 2014), the Scottish Intercollegiate Guidelines Network (SIGN), (Scottish Intercollegiate Guidelines Network, 2019) and NICE, (NICE, 2020). Whilst many protocols are available, they bear a high degree of similarity (Field, 1995; Graham et al., 2011; Kredo et al., 2016; Tetreault et al., 2019; NICE, 2020; Scottish Intercollegiate Guidelines Network, 2019). The main steps involved in the development process are:

1) Defining the problem

The clinical topic must be "high-priority" and highly feasible. High priority in this context means that there is a genuine clinical need for the guideline, whether that be a considerable disease burden, or associated economic cost and that there is uncertainty regarding best practice and potential to improve patient outcome. There must be an adequate evidence base available to permit systematic review of relevant studies in order to inform the development process (Field, 1995; Graham et al., 2011; Tetreault et al., 2019).

The disease and/or intervention of interest must be clearly defined and key stakeholders, potential clinical implications and the implementation process must be considered (Field, 1995; Graham et al., 2011; Tetreault et al., 2019).

2) Assembling a multidisciplinary guideline development group and systematic review team

CPGs must be developed by a knowledgeable multidisciplinary group of 10-20 people that comprises physicians (experts and non-specialists), patients and policy makers. This should include a small number of experts in systematic review methodology (Burgers et al., 2003; Graham at al., 2011; Tetreault et al., 2019).

3) Conducting a systematic review of the literature

Recommendations must be informed by rigorous systematic review of the existing evidence with reference to the minimum steps reported by the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement (Moher et al., 2009). Systematic review methodology has been described in detail elsewhere (Moher et al., 2009).

1) Translating the evidence to recommendations

Each guideline statement must be accompanied by a rating of the quality of evidence and the

strength of the recommendation (Graham et al., 2011; Tetreault et al., 2019). Several tools may be used to guide this stage of the development process. They include the Conference on Guideline Standardisation (COGS) checklist for reporting CPGs, the AGREE (Appraisal of Guidelines for Research and Evaluation) tool, the ADAPTE framework, the GRADE (Grading of Recommendations, Assessment, Development and Evaluations) guideline development tool and the evidence to recommendation framework (The ADAPTE Collaboration; 2009; Andrews et al., 2013; Brouwers et al., 2010; Fervers et al., 2011; Guyatt et al., 2008; Guyatt et al., 2011; Shiffman et al., 2003; Shiffman & Michel, 2004).

The GRADE framework is the most widely used tool (Guyatt et al., 2008; Guyatt et al., 2011; Siemieniuk & Guyatt, n.d.) and it has been endorsed by over 100 organisations worldwide including the World Health Organization, BMJ Clinical Evidence and the Agency for Health Research and Quality (AHRQ) (Guyatt GH et al., 2011; Tetreault et al., 2019).

According to the GRADE framework translating the evidence into recommendations begins with critically analysing the systematic review data. An initial assessment of the quality of evidence is made based on the study type and then upgraded or downgraded depending on methodological factors. The quality of the evidence is thereby defined on a spectrum from very low to high (Tetreault et al., 2019). Evidence-based recommendations are then made. The development process ends with the determination of the strength of each recommendation. Four factors are considered when defining the strength of the recommendation: The balance between desirable and undesirable outcomes, the confidence in effect size, the degree of confidence in values and preferences of key stakeholders and resource implications (Andrews et al., 2013; Guyatt et al., 2008; Tetreault et al., 2019). A strong recommendation implies that (a) most patients would want to receive the intervention and only a small proportion would not, (b) most patients should receive the intervention and (c) the recommendation can be adapted as policy in most situations and be used as a performance indicator (Andrews et al., 2013; Guyatt et al., 2008; Tetreault et al., 2019). In contrast, weak recommendations will likely necessitate considerable debate before they are implemented into routine practice (Tetreault et al., 2019).

4) Critically appraising the clinical practice guideline

CPGs play a significant role in guiding daily clinical practice. Occasionally several inconsistent, and sometimes contradictory, guidelines are available for the same clinical problem, making clinical decisions more challenging instead of more straightforward.

CPGs should be externally reviewed by a multidisciplinary group prior to their publication. The

multidisciplinary group should include experts in the relevant field and key stakeholders.

Before using a CPG, healthcare professionals should be able to evaluate and identify those that have been developed using robust methodology (Tetreault et al., 2019). The Appraisal of Guidelines for Research and Evaluation (AGREE) II framework can be used by both clinicians and policy makers to evaluate CPGs and decide which guidelines should inform clinical practice and policy making (Brouwers et al., 2010; Tetreault et al., 2019).

5) Implementing the guideline

The final step in developing a clinical practice guideline is to implement it. However, guidelines have had limited success in changing clinical practice even when they are widely promulgated. Barriers to implementation can be categorized into personal, guideline-related, and external factors (Cabana et al., 1999; Fischer et al., 2016).

Personal factors include those related to both clinician knowledge and attitude. Clinicians need to be both aware of and familiar with the guidelines (Cabana et al., 1999; Fischer et al., 2016). Attitudes or beliefs such as lack of self-efficacy (lack of confidence in own ability to perform a practice), lack of outcome expectancy (where the clinician does not believe that a given practice will bring about a desired outcome), inertia of previous practice (lack of readiness or motivation for change) and lack of agreement with guidelines in general or with the specific guideline will all impact the effectiveness and application of a CPG (Cabana et al., 1999; Fischer et al., 2016).

Guideline-related factors include the complexity, layout, and accessibility of the guideline as well as ease of use and time considerations. Lack of clear objectives and lack of cited evidence may also detrimentally impact implementation (Cabana et al., 1999; Fischer et al., 2016).

External factors are also important, especially in the pre-hospital setting. Organisational constraints, resource availability, time pressure, environmental factors and lack of professional support can all pose barriers (Cabana et al., 1999; Fischer et al., 2016). Patient factors should also be considered. These include those related to the patient's injury or illness, physiological state, background medical history and previously expressed wishes (Cabana et al., 1999; Fischer et al., 2016).

Notably, the barriers that exist in one setting are unlikely to be generalisable. Little is known about the specific factors guiding adherence with CPGs in the relatively new and emerging field of pre-hospital emergency medicine. Specific strategies will need to be developed with the aim of identifying any relevant barriers to implementation in this unique field.

2. Research question and rationale

PHEA should be provided in specific pre-hospital emergency scenarios. Guidelines have been published to optimise the quality of care, and the safety and efficacy of the procedure and associated practices. (The Association of Anaesthetists of Great Britain and Ireland, 2008; Checketts et al., 2016; Denning & Barley, 2015; Lockey et al., 2007; Lockey et al., 2017; Nimmo et al., 2019). Evidence suggests that concordance with CPGs can improve patient outcome (Grimshaw & Russell, 1993; Woolf et al., 1999). The CPGs state that PHEA should be performed to an equivalent standard to that achieved during in-hospital anaesthetic practice.

An online search in EMBASE and MEDLINE using the keywords “UK” AND “pre-hospital anaesthesia” (OR “PHEA” OR “sedation”, OR “pre-hospital” “RSI”) AND “maintenance” (OR “TIVA”) produced no results. No research has been published, which describes how PHEA is currently maintained in the UK following pre-hospital induction of anaesthesia and intubation, nor how closely this reflects current guidelines.

The aim of this study was to build a picture of how emergency anaesthesia is maintained following pre-hospital induction by services across the UK, and to identify the extent to which current practice reflects guidelines for PHEA. This has been investigated as follows: Chapter 1 – Introduction, Chapter 2 – Scoping Review, Chapter 3 – Secondary Data Analysis and Chapter 4 – Discussion.

Chapter Two

The Maintenance of Anaesthesia following Pre-hospital Induction of Emergency Anaesthesia in the UK: Scoping Review

1. Introduction

The purpose of this scoping review was to provide an overview of the available research describing the current practices for the maintenance of anaesthesia in the pre-hospital environment and the clinical practice guidelines which steer pre-hospital practice. I aimed to do this by identifying and mapping the relevant literature. Conducting a scoping review enabled the elucidation of the type(s) of data available and any gaps in the literature, the clarification of key concepts, and the identification of relevant stakeholders (Munn et al., 2018). Ultimately, I sought to use the results from the scoping review to assess how closely current UK PHEA practice reflects the guidelines.

Only UK literature was used in this scoping review, primarily due to the fact that the aim of this study was to examine *UK* practice against *UK* guidelines. There are several reasons for this. As previously discussed, the field of pre-hospital emergency medicine is a relatively new and rapidly developing field, within which PHEA is a specialist area. Given the consequent paucity of relevant literature this national study will serve as a useful starting point against which international comparisons may be drawn and suggestions for quality improvement may be made. The fact that this study is based in the UK does not limit its relevance to physicians and clinical directors working in other parts of the world. In contrast, the conclusions are still likely to be of interest to those working in services with advanced pre-hospital teams staffed by expert physicians with anaesthetic competencies. Furthermore, the secondary data used in Chapter Three was gathered only from UK providers of advanced pre-hospital care. Analysis and comparison between the two sets of data would have been somewhat limited or less direct if literature from a wider region was used in the scoping review but not in secondary data analysis. Finally, and perhaps most importantly the organisation of pre-hospital healthcare systems varies considerably across the world, even between developed countries (Lindskou et al., 2019). Several studies have been published which describe the key distinctions between systems across the globe (Kruger et al, 2010; Lindskou et al., 2019; Pozner, 2004; Tanigawaw & Tanaka, 2006; Thomson, 2005; Vaitkaitis 2008; Van Gelder et al., 2005). Countries with established pre-hospital emergency services can be broadly categorised as being based upon Franco-German or Anglo-American models (Al-Shaqsi, 2010). The latter model is often

described as 'scoop and run' and delivered by paramedics and emergency medical technicians. Senior emergency medical physicians and anaesthetists are rarely involved prior to arrival in the emergency department. Literature from these countries would not be relevant to the research question. Even in countries with operational similarities to the UK, differences in structure, funding and resource availability can significantly impact clinical practice. Consider for example that the method of patient transfer (i.e. road or air) and average/expected transfer times can dictate the most appropriate method of delivering and maintaining PHEA.

2. Study Design

A pilot literature search indicated that a relatively small number of heterogeneous articles had been published which specifically described the *maintenance* of pre-hospital emergency anaesthesia in the UK.

This study was based upon scoping review methodology, which offered several advantages compared to the more traditional 'systematic review' process (Arksey & O'Malley, 2005; Munn et al., 2018; Pham et al., 2014; Tricco et al., 2016). This approach was well suited to conducting an exploratory analysis which sought to assess and map the scope of the literature, determine the breadth and depth of its coverage, and identify any gaps in the research (Arksey & O'Malley, 2005; Munn et al., 2018). The scoping review was useful as the field of pre-hospital emergency medicine and pre-hospital emergency anaesthesia is a relatively new and emerging subspecialist area and it was initially unclear whether other, more specific questions could or should be addressed by a systematic review (Armstrong et al., 2011; Munn et al., 2018).

The pilot literature search had suggested that the published data may be heterogeneous in format. By conducting a scoping review, I was able to ascertain how research had been conducted in the field of PHEM and correspondingly what type of evidence was available (Munn et al., 2018.). In contrast to systematic reviews, the scoping review did not limit eligibility for inclusion in the review by study type or design (Moher et al., 2015).

Whilst scoping reviews may be more flexible than systematic reviews in some respects, their conduct still requires rigorous and transparent methodology (Munn et al., 2018). The design of this scoping review was based upon widely upheld methodological guidance (Arksey & O'Malley 2005; Joanna Briggs Institute, 2015; Levac et al., 2010; Munn et al; 2018).

The aim of the scoping review was to find and assimilate evidence to answer the research question: 'What are the current practices for the maintenance of anaesthesia in the UK pre-hospital environment and are these practices aligned with the published guidance? The research question comprised two key strands:

A. The maintenance of anaesthesia following pre-hospital induction of emergency anaesthesia in the UK.
B. Guidelines for the maintenance of pre-hospital emergency anaesthesia

The two strands were dealt with separately in the design and conduct of the review, with the respective data gathered, charted, and analysed in distinct parts. At the final stage of analysis data from the two strands was assimilated and analysed together (Figure 1).

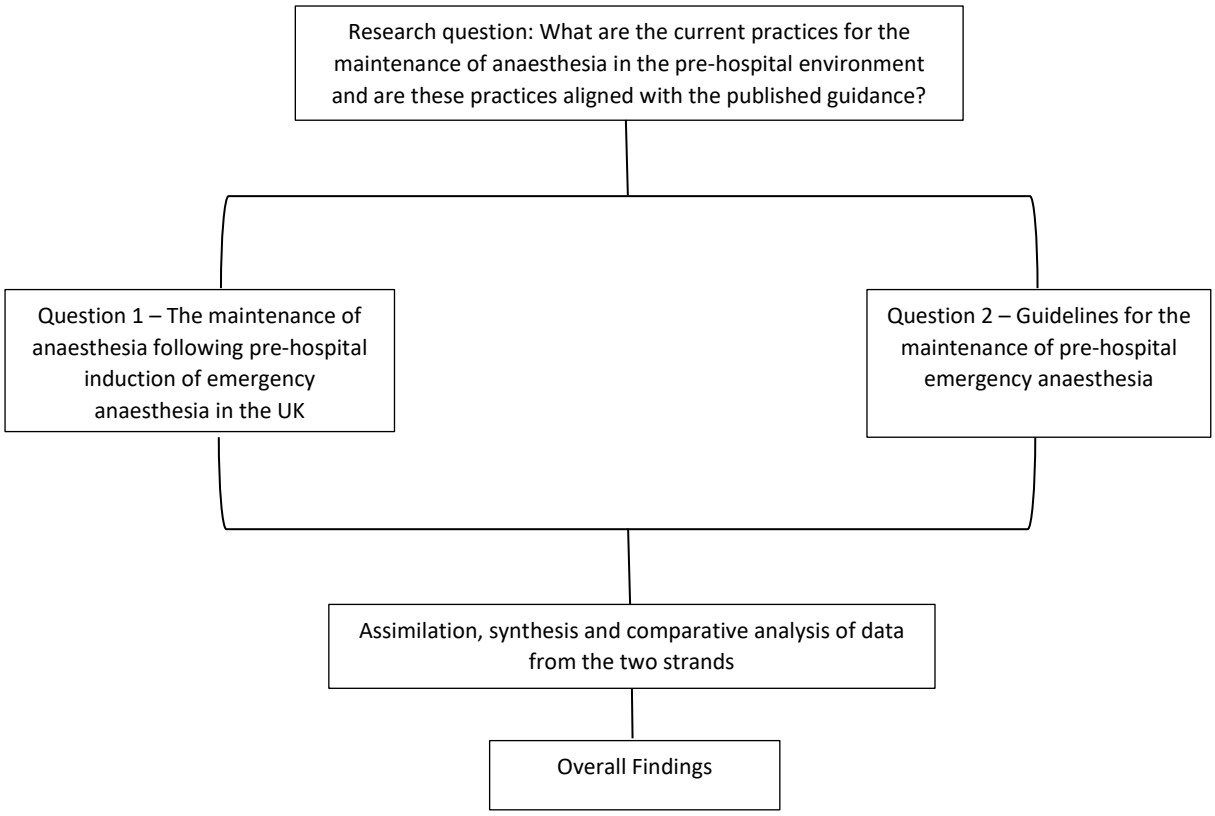


Figure 1. Study design: Exploring two streams of evidence.

A. Research strand 1 – The maintenance of anaesthesia following pre-hospital induction of emergency anaesthesia in the UK

1. Methodology

Eligibility criteria

Firstly, I considered eligibility criteria for inclusion in the scoping review, acknowledging that there would be a compromise between breadth and comprehensiveness vs relevance and feasibility (Levac et al., 2010). Results from an initial literature search suggested that there was a relative paucity of articles relating to this question, so relatively broad, lenient criteria were used. As the research question specifically related to UK practice, "UK" was included as a keyword. The search was not limited by study type nor design, as this was not believed to be correlated with the value of the paper. Papers published in the English language in the last ten years (2009 onwards) were eligible for inclusion. A criterion of 10 years was chosen, as articles published within this timeframe would likely still be highly relevant today. Given that this field has developed and evolved so significantly within the last two decades, it was felt that articles published over ten years ago may not be representative of today's pre-hospital operational structure and clinical practice.

Information sources and search strategy

Comprehensive literature searches were conducted using the online resource Ovid, in EMBASE and MEDLINE electronic databases. Search content and format were peer-reviewed by an expert in healthcare research at Betsi Cadwaladr University Health Board using the Peer Review of Electronic Search Strategies checklist (Sampson et al., 2009). The grey literature was searched using the Canadian Agency for Drugs and Technologies in Health approach (Canadian Agency for Drugs and Technologies in Health, 2015). The reference lists of articles identified by the electronic searches were also screened.

Search strategies
1) Ovid - EMBASE. Search performed on 12/11/19
1. anaesthesia/
2. emergency care/ or pre-hospital.mp. or emergency health service/
3. current practice.mp. or clinical practice/
4. United Kingdom/
5. 1 and 2 and 3 and 4

6 results 5 remained after language and date limits applied 1 duplicate excluded Repeating the search in MEDLINE returned no further results 4 articles for screening
2) Ovid - EMBASE. Search performed on 12/11/19 1. pre-hospital.mp. 2. anaesthesia/ 3. United Kingdom/ 4. 1 and 2 and 3 11 results 8 remained after language and date limits applied 2 studies removed as identified in previous search Repeating the search in MEDLINE returned no further results 6 articles for screening
3) Ovid - EMBASE. Search performed on 12/11/19 1. emergency health service/ or pre-hospital.mp. or emergency care/ 2. anaesthetic.mp. or anaesthetic agent/ 3. United Kingdom/ 4. 1 and 2 and 3 5. from 4 keep 1-37 54 results 37 remained after language and date limits applied 1 study removed as identified in previous search Repeating the search in MEDLINE returned no further results 36 articles for screening

Table 1. Search strategies used for research strand 1 - Maintenance of Anaesthesia following Pre-hospital Induction of Emergency Anaesthesia in the UK

Study selection

Articles returned from each of the three searches on Ovid were downloaded for screening. The papers were screened in a two-stage process during which the eligibility criteria were immediately available. In total 46 articles were screened by review of title and abstract (Stage 1) and 11 articles progressed to full text assessment (Stage 2). The review process was repeated by SW (Sion Williams, academic supervisor) to ensure the quality and reliability of study selection. Inter-rater agreement of 100% was achieved. In the case of discrepancies, the articles would have been forwarded to JG (Dr John Glen, academic supervisor) for a final decision. Three articles passed full text review and were selected for inclusion in the scoping review.

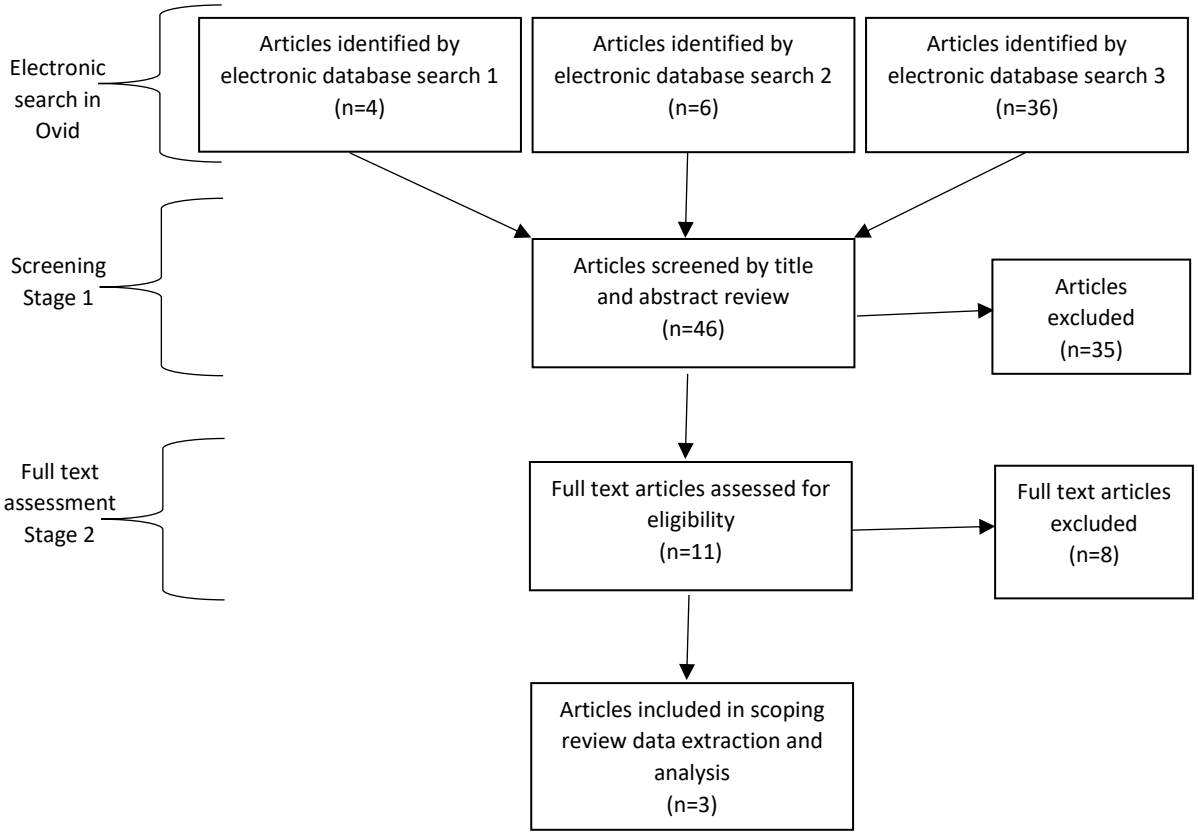


Figure 2. Research strand 1 - RISMA diagram depicting the number of articles identified, assessed for eligibility, and included or excluded

Data extraction and charting

Data were extracted from the articles and charted in a table using Microsoft Word software. The following data were charted: Author/Ref/URL; Literature type; Aims/Purpose; Study population, sample size (if applicable) and location; Methodology; Primary outcomes; Secondary outcomes relevant to the scoping review. The table was reviewed and refined during data extraction. The study reference, literature type, aims/purpose, population, sample size and methodology were always summarised and documented. Primary and secondary outcomes were only documented if they were highly relevant to the research question.

Reference	Literature type	Aims/Purpose	Study population, sample size (if applicable) and location	Methodology	Primary outcomes	Secondary outcomes relevant to the scoping review
Burgess, M. R., Crewdson, K., Lockey, D. J., & Perkins, Z. B. (2018). Pre-hospital emergency anaesthesia: an updated survey of UK practice with emphasis on the role of standardisation and checklists. *Emergency Medicine Journal*, *35*(9), 532-537.	Journal article – original research.	To describe the current practice of PHEA in the UK, in terms of incidence and conduct. To determine the use of checklists for PHEA. To describe the content, format and layout of any such checklists currently used in the UK.	UK pre-hospital care teams.	An online survey of UK pre-hospital teams was conducted with questions relating to both incidence and characteristics of PHEA. Results were grouped into teams delivering a high volume (>50) of PHEA per year and low volume (≤50). Checklists for use in standard and emergency practice were reviewed.	59 UK pre-hospital services were identified (19 HEMS, 35 BASICS and 3 ED-based services). 43 of these services participated in the study, thereby achieving a response rate of 74%. 30 of the 43 services that responded (70%) were able to provide PHEA. PHEA was not available 24 hours a day across the entire country. PHEA was performed on an average of 11% of callouts. The most common indication for PHEA was trauma (80.6% of cases for high volume services and 78.6% of cases for low volume services). Services variably used checklists to ensure availability of monitoring equipment (5-100%). 32% of services used a checklist to ensure maintenance of anaesthesia post induction of PHEA.	A small number (n=10) of 'high volume' services delivered 84% of cases of PHEA. A greater proportion of patients assessed and treated by high volume services underwent PHEA compared with those seen by low volume services. All services used training to improve familiarity with standard operating procedures and checklists.

Cowan, G. M., Burton, F., & Newton, A. (2012). Pre-hospital anaesthesia: a survey of current practice in the UK. *Emergency Medicine Journal*, *29*(2), 136-140.	Journal article – original research.	To establish the national picture of pre-hospital anaesthesia in the UK. To identify all pre-hospital services practicing in the UK. To ascertain which healthcare professionals perform pre-hospital anaesthesia. To elucidate the processes and equipment being used. To reference practice against the Association of Anaesthetists of	UK pre-hospital care teams.	The databases of BASICS providers and Air Ambulance services were searched. Lead clinicians from all pre-hospital services in the UK were invited to complete a detailed online survey (via Survey Monkey), which was both anonymous and confidential. Data were gathered regarding the incidence of PHEA, the team structure, the process for pre-hospital anaesthesia, drugs and equipment used, training and clinical governance arrangements.	66 pre-hospital services in the UK were identified. Survey invitations were sent to 63 of the 66 services identified. A response rate of 87.3% (n=55) was achieved. Data were successfully collated from 71% of the 66 services that were identified (n=47). 31 of the 47 services (70%) performed PHEA. 10 services had the capability of performing PHEA throughout their operational hours. 15 (48%) of the services undertaking pre-hospital anaesthesia responded only by road, 3 (10%) responded by air and 13 (42%) responded by both road and air. PHEA was always performed by a doctor, usually from a background of anaesthesia or emergency medicine. A doctor was not always present on pre-hospital callouts. Only 58% of teams always had a trained assistant. Twenty-five services (80.6%) used written guidelines for the process of pre-hospital anaesthesia and 22 (71%)	90% of teams maintained a database of cases of PHEA. 55% performed less than 20 cases of PHEA annually. 74% had a designated lead clinician. 84% of services had a requirement for a minimum level of anaesthetic experience prior to undertaking pre-hospital anaesthesia. 61% teams had mandatory continual training requirements.

		Great Britain and Ireland safety guideline on pre-hospital anaesthesia and to assess the degree of compliance with these recommendations .			used specific written indications for pre-hospital anaesthesia. Most services used a combination of midazolam and opioid for the maintenance of anaesthesia. Other drugs/combinations used for the maintenance of anaesthesia were midazolam (58%), ketamine (56%), propofol (42%), ketamine and opioid (32%), propofol and opioid (29%). 74% prepared the drugs at the scene prior to PHEA. 26% prepared the drugs at the start of each shift. All services used ECG, SpO2 and non-invasive blood pressure monitoring. The majority of services monitored end-tidal CO2 both during (83.9%) and after (96.8%) induction of anaesthesia. There were high rates of compliance with the recommendation for minimal monitoring. 58% routinely used a colorific CO2 detector device. 74% of services utilised a mechanical transport ventilator after intubation.	

McQueen, C., Crombie, N., Hulme, J., Cormack, S., Hussain, N., Ludwig, F., & Wheaton, S. (2015). Pre-hospital anaesthesia performed by physician/critical care paramedic teams in a major trauma network in the UK: a 12-month review of practice. *Emergency Medicine Journal*, *32*(1), 65-69.	Journal article – case study.	To describe the first 12 months of pre-hospital emergency anaesthesia performed by a 24hr Medical Emergency Response Incident Team (MERIT).	A single pre-hospital service (MERIT), based in West Midlands, UK.	Retrospective review of the service's database for the first 12 months of practice. Data were collected regarding the incidence of RSI, the indication, the number of intubation attempts, the grade of laryngoscopy view and the specialty/grade of the intubator.	Boluses of morphine and midazolam were used for the maintenance of anaesthesia, and rocuronium was used for neuromuscular blockade. PHEA was performed at 14% of scene attendances. PHEA was performed in a greater number of trauma cases than medical emergencies (n=130 (92%) and n=12 (8%) respectively). Road traffic collisions were the most common mechanism of injury in trauma cases requiring RSI (68% of trauma cases requiring RSI). The clinical indications for RSI were: unconsciousness (75%); actual or impending airway obstruction (10%); anticipated clinical course/ transport considerations (8%); severe haemorrhagic shock (4%) and oxygenation/ventilation failure (3%). The average on-scene time for patients requiring RSI was 43 minutes (range 17-110 minutes).	Registrar, consultants and CCPs were proficient in performing laryngoscopy and intubation. It was argued that the system employed by pre-hospital teams (high degree of exposure, comprehensive and robust training and clinical governance) is more important than the background or grade of the operator.

Table 2. Charted data for research strand 1 - Maintenance of Anaesthesia following Pre-hospital Induction of Emergency Anaesthesia in the UK

Data analysis

The information extracted and charted consisted of both qualitative and quantitative data and was therefore not easily amenable to high quality thematic analysis (Braun & Clark, 2006; Braun & Hayfield, 2015). Instead, a multi-stage domain summary approach was taken, based on methodology described by Braun & Clarke(2006; 2019).

1. Familiarisation with the data
2. Generating initial codes
3. Searching for themes
4. Reviewing potential codes and themes
5. Linking codes and themes
6. Data analysis

Familiarisation with the data

The first stage involved reading the charted data (Table 2) multiple times to understand and become more familiar with the information and to start to identify notable elements or results and interesting patterns.

Generating initial codes

Codes were initially developed by reading sections of the data and labelling them with a word or clause that best represented or described the data. This word or clause corresponded to a code (Table 3). Some sections of data were most appropriately labelled with more than one code.

Searching for themes

Similar or related codes were grouped into broader themes. Together these themes demonstrated the multi-faceted nature and complexity of the topic of pre-hospital anaesthesia.

Reviewing potential codes and themes

The development of the coding system was an iterative process; the codes and themes were continually reviewed and updated during this stage of the scoping review. Final codes and themes can be seen in Table 3.

The maintenance of anaesthesia following pre-hospital induction of emergency anaesthesia in the UK	
Codes	Themes

1.1		Study methodology
1.1.1	Recruitment	
1.2		Provision of PHEA
1.2.1	Pre-hospital care services	
1.2.2	Service capability/provision of PHEA	
1.2.3	Frequency of PHEA	
1.2.4	Temporal coverage	
1.3		Indication for PHEA
1.3.1	Clinical indications	
1.4		Conduct of pre-hospital callouts and PHEA
1.4.1	Standard operating procedures/protocols/ written guidance	
1.4.2	Transport	
1.4.3	Clinician/healthcare professional providing PHEA	
1.4.4	Assistant support	
1.4.5	Drugs	
1.4.6	Preparation for PHEA	
1.4.7	Monitoring	
1.4.8	Equipment used	
1.4.9	Scene time	
1.5		Resources
1.5.1	Human resources	
1.5.2	Equipment	
1.6		Professional guidelines
1.6.1	Guidelines	
1.6.2	Compliance with guidelines	
1.7		Training/Audit/Clinical governance
1.7.1	Training	
1.7.2	Clinical governance	

Table 3. Codes and themes used to facilitate data analysis for research strand 1 -The maintenance of anaesthesia following pre-hospital induction of emergency anaesthesia in the UK.

Linking codes and themes

As some sections of data were labelled with more than one code, they were likely to be relevant to multiple themes. Whilst the themes represent separate elements of the research question, meaningful in their own right, there are many conceptual and practical links (Figure 3).

Data analysis

The first stage of data analysis involved assessing the relative weighting of each theme by calculating the frequency with which each theme arose in the charted data. Figure 3 represents the results graphically, whilst also detailing thematic links.

The "'Conduct of pre-hospital callouts and PHEA" was the theme that occurred most frequently in the articles. This is a 'high order' theme and is a topic that drives the primary outcomes of the included articles. It is also a key element of my research question, suggesting that the search strategy was successful and that the included articles were appropriate. The "Provision of PHEA" theme also arose frequently, and this is both conceptually interesting and relevant to the research topic. The articles also discussed study methodology, indications for PHEA, resource considerations, professional guidelines, as well as training and clinical governance. These themes occurred less frequently and were of lesser importance.

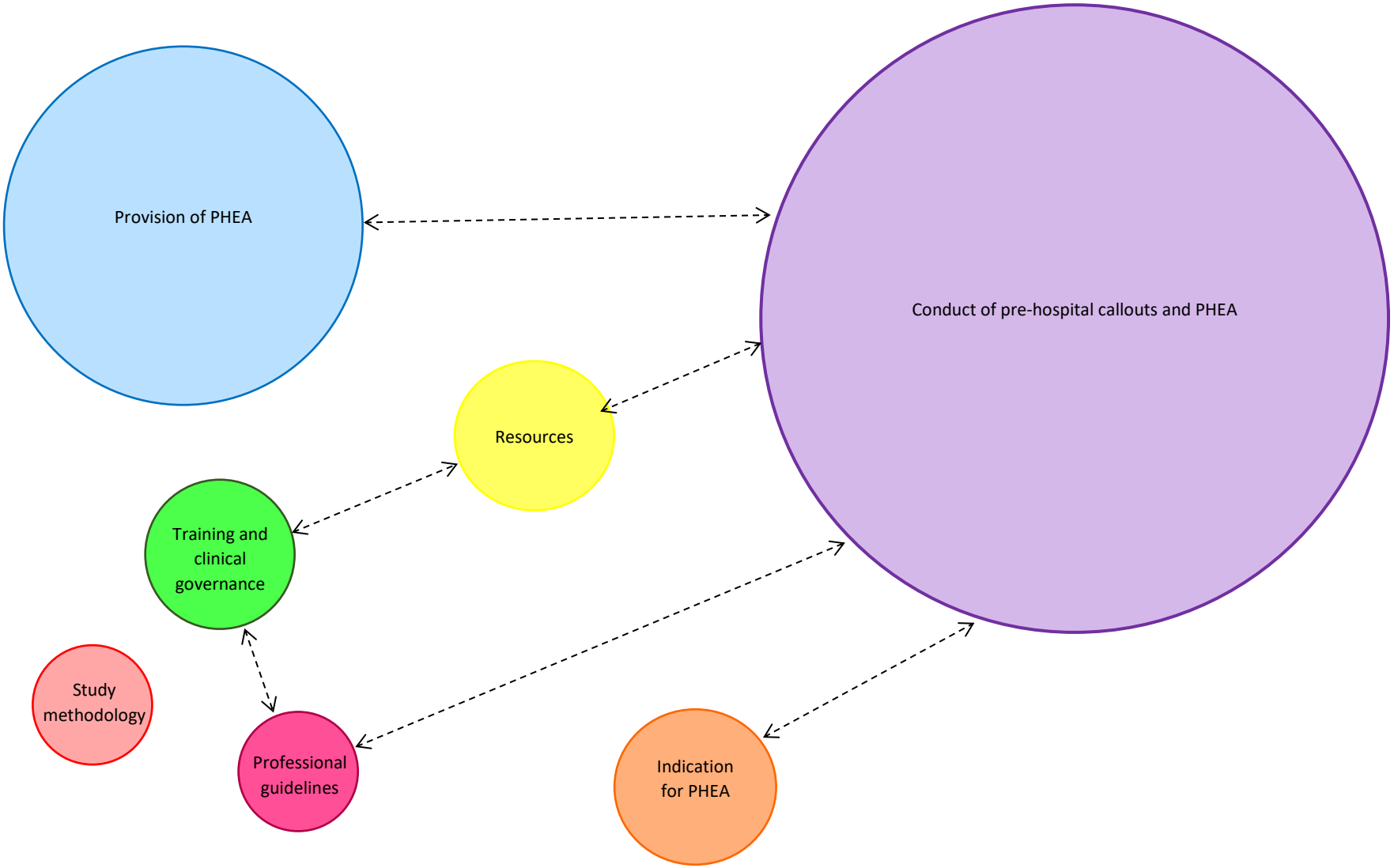


Figure 3. Research strand 1 - Graphical representation of thematic weighting, and inter-thematic links

2. Results

Overview

The main findings from this stream (Research strand 1 - The maintenance of anaesthesia following pre-hospital induction of emergency anaesthesia in the UK) have been summarised below.

Three articles met the criteria for inclusion in the scoping review (Burgess et al., 2018; Cowan et al., 2012; McQueen et al., 2015). Two were original research articles (Burgess et al., 2018; Cowan et al., 2012) and one was a case study (McQueen et al., 2015). The two original research articles had some similarities in that their principal objective was to conduct a survey of UK pre-hospital emergency anaesthetic practice and they intended to include all pre-hospital services in the UK in their study population (Burgess et al., 2018; Cowan et al., 2012). Both used an online survey for data collection and relied upon services voluntarily responding and participating in the study. They achieved an average response rate of 71-74% (Burgess et al., 2018; Cowan et al., 2012). A proportion, but not all, of the variables that they collected were the same. McQueen et al., (2015) focussed on one UK pre-hospital care team – the MERIT team based in the West Midlands – and undertook a retrospective 12-month analysis of their practice of pre-hospital emergency anaesthesia. They reported some of the same variables of interest as Burgess et al., (2018) and Cowan et al., (2012) including the frequency of and indications for PHEA, as well as the drugs used. They additionally reported information less relevant to the research question including intubation view and success rates. In summary, all three papers positively contributed to the scoping review (Burgess et al., 2018; Cowan et al., 2012; McQueen et al., 2015), two of which were similar in study type and design and perhaps most relevant (Burgess et al., 2018; Cowan et al., 2012). The data that the articles reported was largely consistent.

Provision of PHEA

Estimates of the number of UK pre-hospital care services varied from 59 (Burgess et al., 2018) to 66 (Cowan et al., 2012). Of all pre-hospital medical services identified, 70% could provide pre-hospital emergency anaesthesia (Burgess et al., 2018; Cowan et al., 2012) but only 10 could perform PHEA throughout their own operational hours (which were not reported) (Cowan et al., 2012). PHEA was not available 24 hours a day (Burgess et al., 2018). The pre-hospital services included in the survey worked on a regional basis, however the cumulative geographical coverage that they achieved was not clear (Burgess et al., 2018; Cowan et al., 2012).

A small number (10) of 'high volume' services deliver the vast majority of PHEAs and a greater proportion of patients seen by these 'high volume' services undergo pre-hospital emergency anaesthesia. Over half the services could be classed as 'low volume' services (with respect to PHEA) and provide PHEA less than twice per month (Burgess et al., 2018). Overall PHEA is performed on 11-14% of pre-hospital callouts (Burgess et al., 2018; McQueen et al., 2015).

Indication for PHEA

Trauma was by far the most common reason for PHEA (80-92% of cases) (Burgess et al., 2018; McQueen et al 2015), with medical emergencies only constituting a very small group of cases (~8%) (McQueen et al., 2015). Of the trauma cases, road traffic collisions were the most common mechanism of injury (68% of trauma cases requiring PHEA) and unconsciousness was the most common clinical indication (75% of cases) for pre-hospital emergency anaesthesia (McQueen et al., 2015).

Conduct of pre-hospital callouts and PHEA

The conduct of pre-hospital callouts and PHEA is not widely known and there are several factors that may affect logistics and clinical practice including the healthcare professionals present, equipment and monitoring available, the choice of drugs and clinical guidelines as well as local protocols (Burgess et al., 2018; Cowan et al., 2012; McQueen et al., 2015).

Clinicians performing PHEA

In many areas pre-hospital emergency anaesthesia is only performed by doctors (Burgess et al., 2018; Cowan et al., 2012; McQueen et al., 2015) and most pre-hospital services (84%) require the doctors to have a minimum level of anaesthetic experience and competence (Cowan et al., 2012). Consequently, most doctors routinely performing PHEA have a background in anaesthetics or emergency medicine (Cowan et al., 2012). Doctors are not however always present on pre-hospital callouts (Cowan et al., 2012).

Interestingly, McQueen et al., (2015) investigated the competence of both doctors and Critical Care Practitioners (CCPs) in performing emergency pre-hospital laryngoscopy and intubation. They concluded that registrars, consultants and CCPs were proficient and that the system employed by pre-hospital teams (with a high degree of exposure, comprehensive and robust training, and clinical governance) was more important than the background or grade of the operator (McQueen et al., 2015). My research question specifically sought to investigate practices surrounding the

maintenance of anaesthesia (after rapid sequence induction of anaesthesia and intubation) and it was unclear whether all practitioners included in this study also administered drugs to maintain anaesthesia (McQueen et al., 2015).

Only 58% of teams always had a trained assistant present, despite AAGBI guidelines stating this to be a requirement during PHEA (Cowan et al., 2012).

Standard operating procedures and guidelines

Pre-hospital medical services used written guidance for PHEA. Most (71%) referred to the documented indications for PHEA (Cowan et al., 2012) and some services used checklists to ensure the availability of monitoring equipment and/or to ensure the maintenance of anaesthesia after emergency induction (Burgess et al., 2018).

Drugs

Boluses of midazolam and opioid (usually morphine) were together the most common drugs given to maintain anaesthesia (Cowan et al., 2012; McQueen et al., 2015). Other drugs used alone or in combination included: midazolam (58%), ketamine (56%), propofol (42%), ketamine and opioid (32%) and propofol and opioid (29%) (Cowan et al., 2012). Rocuronium was the preferred choice when neuromuscular blockade was required (McQueen et al., 2015).

75% of services prepared the drugs at the scene prior to PHEA and the remainder prepared the drugs at the start of each shift (Cowan et al., 2012).

Monitoring

Pre-hospital medical services demonstrated high rates of compliance with the AAGBI recommendations for minimal monitoring (Burgess et al., 2018; Cowan et al., 2012). All services used ECG, SpO2 and non-invasive blood pressure monitoring, and most services monitored end-tidal CO2 both during (83.9%) and after (96.8%) the induction of anaesthesia (Cowan et al., 2012). 58% additionally used a colorific CO2 detector device (Cowan et al., 2012). The reasons why services variably chose to use these pieces of monitoring equipment have not been elucidated.

Logistical considerations

Average on-scene time for patients requiring PHEA was reported as 43 minutes (range 17-110minutes) (McQueen et al., 2015).

48% of teams responded only by road, 42% responded by both road and air and 10% responded by air only (Cowan et al., 2012)

Training and clinical governance

Training and clinical governance are essential for sustaining and continually improving upon high quality standards of care. McQueen et al., (2015) argued that the system employed by pre-hospital teams, with respect to training and clinical governance, is more important than the background or grade of the operator in optimising clinical outcome. Most pre-hospital medical services surveyed had an established clinical governance system and mandatory ongoing training requirements for healthcare professionals involved in PHEA (Burgess et al., 2018; Cowan et al., 2012). 90% of teams maintained a database of cases of PHEA and 74% had a designated lead clinician responsible for overseeing practice (Cowan et al., 2012).

B. Research strand 2 – Guidelines for the maintenance of pre-hospital emergency anaesthesia

1. Methodology

Eligibility criteria

Results from a pilot literature search and articles made available by early personal communication indicated that there was an abundance of literature relevant to this stream of the research question and it was therefore possible to impose more stringent eligibility criteria than for Research strand 1. This increased the relevance and utility of the articles returned and limited unnecessary workload.

It was important that the included articles reflected recent developments in the field, so the search was limited to those published in the last 15 years. Whilst the 15-year time period remained a lenient criterium, it permitted analysis of the development and progress of guidelines in this relatively new and emerging field. The search was not limited by article type; it included papers that were composed of guidelines and/or recommendations themselves and also those that evaluated or commented on relevant guidelines. Only papers published in English were eligible for inclusion.

Information sources and search strategy

Comprehensive literature searches were simultaneously conducted in the EMBASE and Medline electronic databases using the online tool Ovid. Search content and format were peer-reviewed by

an expert healthcare researcher at Ysbyty Glan Clwyd Hospital using the Peer Review of Electronic Search Strategies checklist (Sampson et al., 2009). Several additional papers were made available to me by professional communication. The grey literature was searched using the approach documented by the Canadian Agency for Drugs and Technologies in Health (Canadian Agency for Drugs and Technologies in Health, 2015). References of all reviewed papers were screened for further literature meeting the aforementioned eligibility criteria.

Search strategies
1) Ovid - MEDLINE & EMBASE. Search performed on 12/11/19 1. Pre-hospital 2. Anaesthesia 3. Guidelines 4. 1 and 2 and 3 5. 4 and 2005- 2019 17 results 2 excluded due to language 5 duplicates excluded 10 articles for screening
2) Ovid – MEDLINE & EMBASE. Search performed on 03/12/19 1. Pre-hospital 2. Emergency 3. Anaesthesia 4. TIVA 5. Guidelines 6. 1 and 2 and 3 and 4 and 5 0 articles returned
3) Ovid – MEDLINE & EMBASE. Search performed on 03/12/19 1. Pre-hospital 2. Emergency 3. Anaesthesia 4. TIVA 5. Guidelines 6. 1 or 2 7. 3 and 4 and 5 and 6 1 article for screening
4) Ovid – MEDLINE & EMBASE. Search performed on 03/12/19 1. Pre-hospital 2. Emergency 3. Anaesthesia 4. Depth of anaesthesia monitoring

5. Guidelines 6. 1 or 2 7. 7 8. 3 and 4 and 5 and 6 1 article for screening
5) Ovid – MEDLINE & EMBASE. Search performed on 03/12/19 1. Pre-hospital 2. Emergency 3. Anaesthesia 4. Depth of anaesthesia monitoring 5. Guidelines 6. 1 or 2 7. 7 8. 3 and 4 and 5 and 6 1 article for screening
6) Ovid – MEDLINE & EMBASE. Search performed on 03/12/19 1. Pre-hospital 2. Anaesthesia 3. Bolus 4. Infusion 5. Drugs 6. Guidelines 7. 3 or 4 or 5 8. 1 and 2 and 6 and 7 6 results 2 duplicates removed 4 articles for screening
7) Ovid – MEDLINE & EMBASE. Search performed on 03/12/19 1. Pre-hospital 2. Anaesthesia 3. Safety 4. Guidelines 2 articles found in preceding searches 0 articles for screening

Table 4. Search strategies used for research strand 2 - Guidelines for the maintenance of pre-hospital emergency anaesthesia

Study selection

In total 17 articles were found on Ovid and downloaded for screening. A further 12 articles were received by professional communication (of which four were ultimately included in the scoping review) . As for Research strand 1, a two-stage screening process was then conducted during which

the eligibility criteria were immediately available. 29 articles underwent title and abstract screening. 13 were excluded and 16 progressed to full text eligibility assessment. 14 studies were ultimately selected for inclusion. The review process was repeated by SW (Sion Williams, academic supervisor) to ensure quality and reliability of study selection. Inter-rater agreement of 100% was achieved. In the case of discrepancies, the articles would have been forwarded to JG (Dr John Glen, academic supervisor) for final decision.

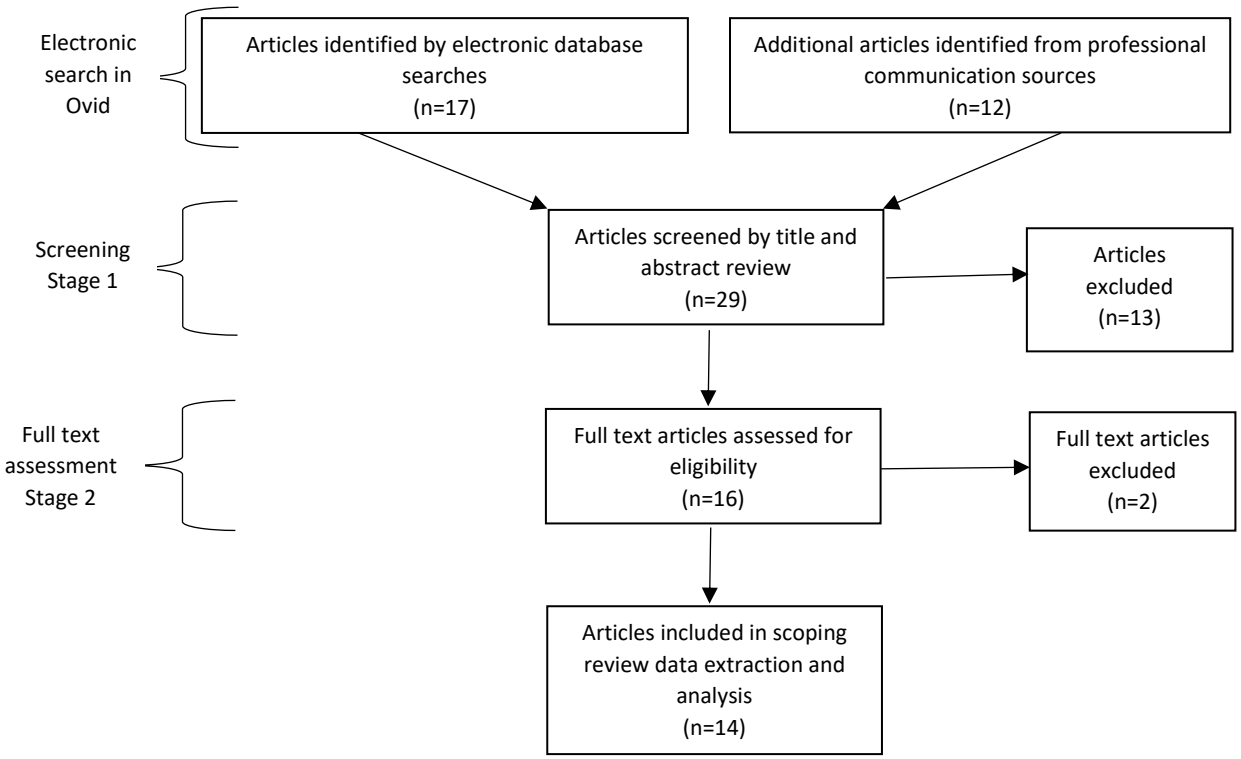


Figure 4. Research strand 2 - PRISMA diagram depicting the number of articles identified, assessed for eligibility, and included or excluded

Data extraction and charting

Relevant data were extracted from the articles and charted in a table using Microsoft Word software. The following data were charted: reference; literature type; aims/purpose; primary outcomes/recommendations; secondary outcomes and other comments relevant to the scoping review. Primary outcomes were directly related to the process and conduct of pre-hospital emergency anaesthesia. Secondary outcomes were defined as important recommendations or issues surrounding the concept of pre-hospital emergency anaesthesia but not specifically recommendations for practice. The table content and format were continually reviewed and refined in an iterative process.

Reference	Literature type	Aims/Purpose	Primary outcomes/Recommendations	Secondary outcomes	Comments relevant to the scoping review
The Association of Anaesthetists of Great Britain and Ireland. (2008). *Pre-hospital Anaesthesia*. London: The Association of Anaesthetists of Great Britain and Ireland.	Report: Clinical practice guidelines.	To disseminate concise, evidence-based guidelines to assist practitioner decisions regarding anaesthesia in the pre-hospital setting in order to improve the quality and process of pre-hospital emergency anaesthesia and thus optimise patient outcomes.	Standards of practice and monitoring should be similar to those for in-hospital emergency anaesthesia. Where possible rapid sequence induction (RSI) with oral intubation and maintenance of sedation is the technique of choice. PHEA should be performed only by appropriately trained practitioners. Anaesthesia should only be conducted in the presence of an appropriately trained assistant. Standards of care including adequate sedation, analgesia and, if necessary, neuromuscular blockade must be maintained throughout. Small doses of a hypnotic drug are usually necessary for the maintenance of anaesthesia. No particular drug nor route of administration is recommended. The choice of hypnotic drug depends on the physiological state of the patient and the operator's familiarity with the drug. Small, frequent doses minimise haemodynamic side effects and should be titrated against physiological variables.	The National Confidential Enquiry into Patient Outcome and Death (NCEPOD) emphasised the need for pre-hospital anaesthesia (NCEPOD, 2007). PHEA is carried out by a small number of skilled doctors; most current UK pre-hospital practitioners cannot and should not practise pre-hospital anaesthesia. PHEA is mostly predictable but can be more difficult than in hospital. All pre-hospital organisations must have written guidelines for the treatment of children. Anaesthesia in this group should only be considered after a careful risk-benefit analysis. Every pre-hospital service should have a robust clinical governance structure. The transport process should be carefully considered (availability and type of vehicle, distance and time to definitive	Relatively old (2008) paper.

			Infusions may be preferable, although infusion pumps are bulky, heavy and make transfer more complex. Accidental awareness is a possibility when neuromuscular blocking drugs are used and is more likely in patients with higher pre-induction Glasgow coma scores. All anticipated practical procedures should be performed before transport. Equipment should be appropriate, functional, and maintained to the same standard as hospital equipment. Equipment must also be portable, robust and weather-resistant, and be effective in different lighting conditions. Electrical equipment must have an appropriate battery capability. Alarms should be loud enough to be heard in the noisy pre-hospital environment. There is no role for nerve stimulation devices in pre-hospital anaesthesia. Minimum standards of monitoring should be the same as for hospital anaesthesia. Clinical assessment and non-invasive monitoring of vital signs must be made and recorded at least every three minutes.	care, journey, and terrain) before undertaking pre-hospital anaesthesia.	

			In all cases every effort must be made to keep 'scene time' to a minimum. Transport must be supervised by a clinician skilled in managing an anaesthetised patient.		
Checketts, M. R., Alladi, R., Ferguson, K., Gemmell, L., Handy, J. M., Klein, A. A., Love, N.J., Misra, U., Morris, C., Nathanson, M.H. and Rodney, G.E. (2016). Recommendations for standards of monitoring during anaesthesia and recovery 2015:	Journal article: Clinical practice guidelines.	To provide guidance on the minimum standards for physiological monitoring of any patient undergoing anaesthesia or sedation under the care of an anaesthetist.	Minimum monitoring standards must be met when a patient is anaesthetised, regardless of duration, location, or method of anaesthesia. All anaesthetic equipment must be checked before use and it is the responsibility of the anaesthetist to oversee this. Alarm limits must be set and enabled appropriately. Monitoring devices must be attached before induction and continued until after recovery from anaesthesia. They should also be used during transfer. Minimum monitoring data must be recorded at least every five minutes (and more frequently if the patient is unstable). The patient's physiological state and adequacy of anaesthesia need continual assessment. Monitoring devices supplement clinical observation in this respect. Minimal monitoring requirements:		Seminal paper for standards of monitoring during anaesthesia and recovery. Updates and replaces the 4th edition of the AAGBI Standards of Monitoring published in 2007. Whilst "locations outside the operating suite" are included in the guidance, no direct reference is made to the pre-hospital setting.

Association of Anaesthetists of Great Britain and Ireland. *Anaesthesia, 71*(1), 85-93.			○ Pulse oximetry ○ NIBP ○ ECG ○ Inspired and expired oxygen, carbon dioxide, nitrous oxide and volatile anaesthetic agent if used ○ Airway pressure ○ Peripheral nerve stimulator if neuromuscular blocking drugs used ○ Temperature for any procedure > 30 min duration. Monitoring data should be recorded on the anaesthetic record. Automated electronic anaesthetic record systems are recommended. Capnography monitoring is always essential in patients with endotracheal tubes, supraglottic airway devices and those who are deeply sedated. A peripheral nerve stimulator must be used whenever neuromuscular blocking drugs are given. A quantitative peripheral nerve stimulator is recommended. Infusion devices must be checked before use. Ideally, they should be powered from the mains supply. Alarm settings must be verified and set before commencing anaesthesia. The intravenous cannula should be visible throughout the procedure. If this is not practical, increased vigilance is necessary.		

			When using a total intravenous anaesthesia technique with neuromuscular blockade, a depth of anaesthesia monitor is required. Care should be taken to configure an appropriate monitoring display setup.		
Checketts, M. R. (2016). AAGBI recommendations for standards of monitoring during anaesthesia and recovery 2015 [Correspondence]. *Anaesthesia, 71*,(1) 470-471	Editorial.	To clarify concerns and misunderstandings arising from the AAGBI publication of 'Recommendations for standards of monitoring during anaesthesia and recovery 2015' as published by Lumb & McClure (2016).	The guideline document was designed to describe the standards that the AAGBI consider to be the current minimum monitoring requirements. Whilst some guidelines for monitoring requirements may initially be difficult to meet, they are deemed to be gold standard aspirational standards that anaesthetic departments should work towards. The previous publication raises awareness of the new, higher standards of patient monitoring and the need to procure appropriate equipment. The resource and economic implications are acknowledged.	Continuous core temperature monitoring is recommended during longer and more complex surgical procedures.	Not specific for PHEA

Checketts, M. R., Jenkins, B., & Pandit, J. (2017). Implications of the 2015 AAGBI recommendations for standards of monitoring during anaesthesia and recovery. *Anaesthesia, 72* (S1), 3-6.	Editorial.	To highlight the main updates from the 2015 AAGBI recommendations for standards of monitoring during anaesthesia and recovery and introduce supplementary material.	Monitoring of neuromuscular blocking drugs has become mandatory from induction to recovery. Quantitative monitoring is ideal (consistent with evidence of its superiority), whilst qualitative neuromuscular monitoring is the minimum standard. Capnography is now mandatory in any patient with a tracheal tube or supraglottic airway device or those who are deeply sedated. The AAGBI permit anaesthetists to use Depth of Anaesthesia monitoring when they see fit but recommend that it is necessary when total intravenous anaesthetic (TIVA) is used with NMB. The use of depth of anaesthesia monitoring with volatile gaseous anaesthesia is controversial and thus could not be mandated. AAGBI recommend the use of cuff manometers. All minimal monitoring should be continued during transfer from the operating theatre to the recovery room. The period without monitoring should be kept to a minimum. The use of electronic anaesthetic records is encouraged.	Quantitative monitors for neuromuscular blockade are likely to become the minimum standard in the near future, but the extra cost and training required limits their rapid and comprehensive uptake.	
Denning, S., & Barley, M. (2015). Guaranteeing drug delivery in	Editorial.	To discuss the ideal setup for TIVA TCI infusion pump systems.	Expert disagreement regarding the need for clamps on the drug administration line used for TCI pumps.		This paper highlights that there is still lack of expert consensus regarding the optimal

total intravenous anaesthesia. *An aesthesia*, *70*(3), 361-361.			There is an increased risk of accidental interruption to drug delivery, (thereby increasing the risk of accidental awareness under GA) when additional clamp applied. Authors argued that it is counterintuitive to add an additional layer of complexity and source of error.		setup for TCI TIVA infusion pumps.
The Faculty of Intensive Care Medicine. (2019). *Guidance On: The Transfer of The Critically Ill Adult.* London: Intensive Care Society.	Report: Clinical practice guidelines.	To disseminate evidence-based clinical guidance regarding the transfer of the critically ill. To promote high standards of care during the transfer of critically ill patients.	Patients should be stabilised prior to transfer to reduce the risk of later deterioration. Minimum standards of monitoring must always be met. Monitoring should be continuous. All monitors, including ventilator displays and syringe drivers should be visible. A documented record of observations and events must be maintained. Reassurance, sedation, analgesia and anti-emetics should be provided as required.	All equipment must be suitable for transfer and mounted according to regulations. Equipment must be maintained and checked to reduce the risks of failure during transfer. Standardised equipment offers practical and safety advantages. Prior to transfer a risk assessment must be undertaken to determine the competencies of the staff required for transfer. Checklists should be used at each stage.	More relevant to inter-hospital transfer, but some of the principles are applicable to pre-hospital care.

				Patients should be securely strapped to the transfer trolley by means of a 5-point harness. Portable equipment must be securely stowed. Staff must always remain seated and restrained during transfer. Only staff with appropriate training and competencies should undertake aero-medical transfers.	
Lockey, D. & Porter, K. (2007). Pre-hospital anaesthesia in the UK: position statement. *Eme rgency Medicine Journal*, *24*(6), 437-438.	Journal article.	To consider the issues of pre-hospital anaesthesia To issue a position statement on behalf of the Faculty of Pre-hospital care.	Most pre-hospital practitioners cannot and should not perform pre-hospital anaesthesia. Pre-hospital practitioners should have the same level of training and competence that would enable them to perform RSI unsupervised in the emergency department. PHEA should not be performed in professional isolation. Anaesthesia in the pre-hospital setting should only be conducted in the presence of an appropriately trained assistant.	A robust clinical governance structure must be in place. Pre-hospital organisations should ensure that there is a named responsible lead clinician who ensures competency-based practice and regular review and appraisal of practitioners.	

			Practitioners should perform rapid sequence induction sufficiently frequently to maintain competence. Equipment should be adequate for the purpose and maintained to the same standard as hospital equipment. Minimum standards of monitoring should be the same as for in-hospital anaesthesia.		
Lockey, D. J., Crewdson, K., Davies, G., Jenkins, B., Klein, J., Laird, C., Mahoney, P.F., Nolan, J., Pountney, A., Shinde, S. and Tighe, S. (2017). AAGBI: Safer pre-hospital anaesthesia 2017: Association of Anaesthetists of	Journal article: Clinical practice guidelines.	To update the existing AAGBI pre-hospital guidelines To outline safety considerations in the key areas of pre-hospital anaesthetic practice: conduct of PHEA, monitoring, minimal data collection, environmental considerations, training and clinical	The standard of PHEA should be equivalent to in-hospital emergency anaesthesia. Monitoring and equipment should be of the same standard as that used in-hospital. Equipment must be portable, robust, effective under varying light conditions, weather-resistant and have adequate battery power. The choice of equipment for very adverse conditions must be carefully considered. The patient's condition should be monitored from intubation, throughout anaesthesia and the transfer phase using both clinical assessment and monitoring devices.	There are both local and national guidelines available for PHEA and airway management. PHEA carries more risk than emergency anaesthesia in-hospital, due to environmental and patient factors, as well as the fact that skilled anaesthetic assistance is not always available. PHEA should only be conducted in the context of robust clinical governance arrangements. Practitioners carrying out PHEA should be skilled in emergency anaesthesia and	Specific to pre-hospital anaesthesia.

Great Britain and Ireland. *Anaesthesia*, *72*(3), 379-390.		governance and incident reporting.	Recording can be performed manually or electronically, though manual recording may be challenging in this environment. Clinical monitoring should include: o Pulse, location and rate o Respiratory rate o Pupil size and reactivity o Lacrimation o Muscular activity and limb movement Non-invasive monitoring should include: o Heart rate o Blood pressure o Oxygen saturation o Continuous waveform capnography o Electrocardiography. Equipment for PHEA: o Monitoring equipment o Oxygen and reserve o Adequate labelled drug supply for induction and maintenance of anaesthesia o Intubation equipment o Suction o Ventilation equipment o Mechanical ventilators o Rescue airway equipment	intubation and able to work safely in the pre-hospital environment. Procedural steps should be simple, reproducible and aided by checklists. The quality of the evidence base for PHEA and pre-hospital care in general is still relatively poor. In 2007, the 'Trauma: who cares?' National Confidential Enquiry into Patient Outcome and Death (NCEPOD, 2007) report found poor pre-hospital airway management. In patients with cardiac arrest, tracheal intubation has not been shown to improve outcome and drugs are not usually required to facilitate intubation in this group. Pre-hospital services must have clear guidelines for paediatric cases; the threshold for PHEA should be high.	

			○ Vascular access equipment ○ Lighting ○ Procedural checklists Vital signs should be measured and recorded at least every 3 mins. Anaesthetic gas monitoring is rarely indicated in the pre-hospital environment. Nerve stimulation devices are rarely used in the pre-hospital environment. With the above exceptions anaesthetic monitoring in the pre-hospital environment should meet the current AAGBI guidelines. Quantitative capnography is required. Temperature monitoring should be considered. Audio-visual alarms should be enabled to permit detection in the noisy pre-hospital environment. Monitoring may need to be suspended during extrication. The most commonly used anaesthetic drugs can be used in PHEA with appropriate consideration. Drug choice depends upon the physiology of the patient and operator familiarity.	Accidental awareness is more likely when neuromuscular blockers are used, particularly in patients with a near normal pre-induction GCS. The transport process should be carefully considered before undertaking PHEA. The transport vehicle must be suitable for the safe transfer of the anaesthetised patient and attending team. All equipment should be secured. The team should remain seated and restrained.	

			Every effort must be made to keep pre-hospital time to a minimum. Practical procedures should be completed prior to patient transfer. Intravenous cannulae and oxygen supplies should be made easily available prior to transfer. Most patients will require a hypnotic drug to maintain sedation during transfer. The haemodynamic side effects of sedatives may be minimised by using small, frequent doses. Infusions may be preferable for longer transfers, but infusion pumps may increase the complexity of the transfer. Standards of care must be continued during transport: o Continuous monitoring of vital signs – ECG, blood pressure, pulse oximetry and waveform capnography o Maintenance of anaesthesia – adequate sedation, analgesia and, if necessary, neuromuscular blockade o Appropriate provision of supporting equipment – airway suction, intubation equipment, intravenous fluids o Contemporaneous written or automatically generated records of vital signs and treatment interventions.		

Luck, H., & Morgan, P. (2019). *Anaesthesia tutorial of the week 398 - Pre-hospital Emergency Anaesthesia: Considerations, Pitfalls, and Controversies*. Luck, H., & Morgan, P. https://pdfs.semanticscholar.org/53cf/4194d45fd7466730d60c1566706f18fde25b.pdf?_ga=2.131933066.440286952.1578498516-967612014.1578498516	Online journal article.	To discuss the process of PHEA and relevant issues surrounding its practice.	Various drugs and combinations can be used for the maintenance of anaesthesia, including boluses of ketamine, midazolam, and opiate or propofol +/- opiate infusions. The choice of drug should be based on patient and operator factors. Extra care must be taken to ensure maintenance infusions are not obstructed. Repeat doses of a long-acting nondepolarizing muscle relaxant should be used.	Practitioners should be aware that induction is merely the start of the anaesthetic. The time from PHEA to scene departure should be <15 minutes.	Whilst this document is not written by a large professional body, the authors are experts in the field of pre-hospital emergency anaesthesia.

Lumb, A. B., & McLure, H. A. (2016). AAGBI recommendations for standards of monitoring during anaesthesia and recovery 2015-a further example of aggregation of marginal gains'. *Anaesthesia, 71*(1), 3.	Editorial.	To reflect upon and discuss recent updates to the AAGBI 'Recommendations for standards of monitoring during anaesthesia and recovery'.	The authors discussed reservations regarding the role of the AAGBI recommendations. They argued that the AAGBI recommendations cannot be applied to all clinical scenarios, they allow room for departments to choose to not adhere to the standards and they do not reflect gold-standard clinical care. Temperature monitoring is recommended to form part of the minimal monitoring throughout anaesthesia and recovery in all circumstances. However, in certain patient groups, intra-operative temperature monitoring is rarely performed. In patients receiving neuromuscular blocking drugs nerve stimulator monitoring is mandatory and quantitative methods are preferable. The authors believed that this represented a significant change, but an appropriate recommendation. The recommendation to monitor cuff pressures in tracheal tubes and supraglottic airway devices is new. Monitoring end-tidal capnography is recommended when sedation is used. This is already a common practice; however, it is not an indicator of the adequacy of ventilation and can only be used as an indicator of apnoea.	The utility of blanket clinical recommendations was questioned Other foreign, national bodies have produced guidelines for monitoring during anaesthesia, but in general, they lack detail. Adherence to the updated monitoring guidelines will infer substantial cost in the context of limited funds. The updated guidelines may however be used to help secure funding.	

National Institute for Clinical Excellence (NICE). (2012). *Depth of anaesthesia monitors—Bispectral index (BIS), E-Entropy and Narcotrend Compact M. NICE Diagnostics Guidance 6.* National Institute for Clinical Excellence (NICE). www.nice.org.uk/dg6. (Accessed 15 January 2020)	Report: Clinical practice guidelines.	To disseminate evidence-based recommendations on electroencephalography (EEG)-based depth of anaesthesia monitors (Bispectral Index (BIS), E-Entropy and Narcotrend-Compact M).	Depth of anaesthesia monitoring is most likely to be cost effective and of clinical benefit in the following contexts: o For high-risk patients, including patients at increased risk of awareness and those at risk of excessively deep anaesthesia. ▪ The Bispectral Index (BIS) depth of anaesthesia monitor is a recommended option in these patients o In all patients receiving TIVA. ▪ The Bispectral Index (BIS) depth of anaesthesia monitor is a recommended option in these patients Whilst there is less certainty of clinical benefit for the E-Entropy and Narcotrend-Compact M depth of anaesthesia monitors than for the BIS monitor, the E-Entropy and Narcotrend-Compact M monitors are broadly equivalent to BIS. These monitors are therefore recommended as options during any type of GA in high-risk patients. The E-Entropy and Narcotrend-Compact M monitors are also recommended as options in patients receiving total intravenous anaesthesia.	Anaesthetists using EEG-based depth of anaesthesia monitors should have appropriate training and experience with these monitors and understand the potential limitations of their use in clinical practice. The BIS system uses a disposable 4-electrode sensor on the patient's forehead to measure electrical activity in the brain before determining an index value between 0 (absence of brain electrical activity) and 100 (wide awake), representing the patient's response to anaesthetic drugs. The target range of BIS values during general anaesthesia is 40–60; this range indicates a low probability of awareness with recall. E-Entropy and Narcotrend-Compact M are different monitoring devices, that produce different outputs. Values must be interpreted with specific reference to the type of depth of anaesthesia monitor used.	

				NICE did not make any recommendations for further research prior to clinical use, because despite a high degree of uncertainty surrounding many aspects of its use, they felt that the current evidence suggests that depth of anaesthesia monitoring offers clinical benefits and they wished to avoid a delay in its uptake.	
Nimmo, A.F., Absalom, A.R., Bagshaw, O., Biswas, A., Cook, T.M., Costello, A., Grimes, S., Mulvey, D., Shinde, S., Whitehouse, T. and Wiles, M.D. (2019). Guidelines for the safe practice of total intravenous	Journal article: Clinical practice guidelines.	To serve as a guideline for the safe practice of TIVA.	When general anaesthesia is maintained with propofol, use of a target-controlled infusion (TCI) is recommended. The initial target concentration should be determined considering patient, pharmacological and clinical factors. Remifentanil and propofol should each be available in only one concentration. Programming should only be input after the drug-filled syringe has been placed in the pump. During programming of TCI pump the options should be restricted to those commonly used locally.		

anaesthesia (TIVA) Joint Guidelines from the Association of Anaesthetists and the Society for Intravenous Anaesthesia. *Anaesthesia, 74*(2), 211-224.			A consistent stacking of pumps will reduce the risk of incorrectly programming a pump to administer a different drug. TIVA should be administered to the same standards of practice and monitoring outside the hospital, as in the operating theatre. The infusion device used should have: o a Luer-lock connector at each end. o an antisyphon valve on the drug delivery line. o anti-reflux valves on all lines where more than one infusion is being given. Drug and fluid lines should join as close to the patient as possible to minimise the space in which anaesthetic agents may accumulate. The infusion lines should have as few sites for leakage as possible. The IV cannula or central venous cannula used for anaesthetic infusion should ideally be visible throughout anaesthesia. Where constant view of the intravenous cannula is not possible the anaesthetist should have a higher index of suspicion for problems, should regularly inspect the cannula site and should have a low threshold for using processed electroencephalography (pEEG). The use of EEG and electromyography is likely to aid monitoring.		

			A processed EEG monitor is recommended when a neuromuscular blocking drug is used with TIVA. This may reduce the risk of awareness. pEEG monitoring should be initiated before administration of the neuromuscular blocking drug and continued until after full recovery from the neuromuscular blockade has been confirmed. pEEG monitor displays may variably include the index value, EEG waveform, EEG signal quality, EMG activity and degree of burst suppression. Data should be used in addition to clinical observations and experience. If portable pEEG is not available, the pEEG monitoring in the period leading up to the transfer may assist with the determination of the appropriate target concentration and infusion rate. Anaesthesia may be maintained using manual dosing, or a TCI pump. Clinical calibration of the patient's response to anaesthetic is recommended. No effect-site concentration will be appropriate for all patients.		

			The administration of other drugs commonly used in the peri-anaesthetic period can markedly alter the brain propofol concentration required to produce general anaesthesia, as can the degree of "*surgical*" stimulus. The dose of propofol will need to be adjusted accordingly. Target propofol concentration and opioid infusion should be adjusted based on clinical assessment Pumps for both TCI and fixed rate infusions should have audible alarms enabled. Pumps should be charged before use and, if possible, mains powered during use. Syringes should be labelled with drug name and concentration. The drugs to be administered, the programming of the pump, the infusion set and the intravenous cannula should be checked before starting TIVA. Visual check of IV infusion rates be performed periodically during induction and maintenance of ongoing anaesthesia. When TCI is used additional boluses are not usually required and will result in an inaccurate drug concentration being displayed.		

			If a pump shuts down during TCI it is not appropriate to restart the pump, instead manual mode should be used to reset an infusion rate similar to that delivered at the time of failure. At the end of the procedure all vascular access devices should be flushed with at least twice the dead space volume of the device. Monitoring should be performed in accordance with the AAGBI recommendations for standards of monitoring during anaesthesia and recovery. Consideration must be given to the method of induction of anaesthesia and its effect on the pump accuracy of the effect-site concentration. If induction of anaesthesia is conducted using a TCI propofol infusion, the bolus dose is given more slowly than with manual infusions. If induction of anaesthesia is achieved using a manual propofol bolus then the TCI pump concentration will initially be inaccurate. The use of alternative induction drugs may avoid these issues. Ketamine may cause a paradoxical increase in pEEG value.		

Paal, P., Herff, H., Mitterlechner, T., von Goedecke, A., Brugger, H., Lindner, K. H., & Wenzel, V. (2010). Anaesthesia in pre-hospital emergencies and in the emergency room. *Resuscitation, 81*(2), 148-154.	Journal article	To review anaesthesia in pre-hospital emergencies and in the emergency room. To discuss guidelines for PHEA. To discuss other issues surrounding PHEA.	Ventilation should be monitored continuously with capnography. Anaesthesia should be maintained until definitive treatment. Long-acting drugs with almost inert haemodynamic properties (e.g., midazolam 0.1–0.4 mg/kg and fentanyl 2–5g/kg as anaesthetic/analgesic combination) should be chosen for transport. For maintenance of anaesthesia midazolam is recommended. Continuous monitoring with ECG, automated blood pressure measurement, pulse-oximetry and capnography should be performed during transport of the anaesthetised patient. Only experienced clinicians should induce/maintain pre-hospital anaesthesia and intubate.		
Safe Anaesthesia Liaison Group. (2009). Guaranteeing Drug Delivery in Total Intravenous	Report.	To review current practice and policy for TIVA in both adults and children.	The authors could not find any firm published guidelines on how TIVA should be administered. When administering TIVA a one-way valve should be used on the intravenous fluid line. Anti-siphon valves are recommended to reduce the risk of inadvertent free flow of drugs.	At an organisation level preference should be given to clearly labelled intravenous connectors and valves.	Written in 2008. Various more up to date documents exist. Not specific to pre-hospital setting. Data from the Reporting and

Anaesthesia. By personal communication			Sites of intravenous infusions should always be visible for monitoring throughout. It is essential that clinical staff know the applications and limitations of equipment that they are using. After reviewing data from the national Reporting and Learning System the following issues associated with the use of TIVA were identified: o Unavailability of appropriate pumps o Problems with pumps during TIVA o Syringe 'switched' to an incorrect one o Intravenous line pulled out in error o Cannula site had 'tissued' o Anaesthetist not familiar with the technique o Cases of potential awareness without problem with TIVA being identified. o Problems with the intravenous line, related to either Y connectors or 3-way taps. o Kinking/blocking of lines o Leaks from lines o Valves in lines becoming disconnected. o Problems associated with the use of multi-lumen connectors and other infusion devices.		Learning System is likely to be both incomplete and subject to considerable reporting and temporal bias.

Table 5. Charted data for Research strand 2 - Guidelines for the maintenance of pre-hospital emergency anaesthesia.

Data analysis

This relatively large set of descriptive data was analysed using a multi-stage domain summary approach based on methodology described by Braun & Clarke (2006; 2012; 2019). It comprised the following steps:

1. Familiarisation with the data
2. Generating initial codes
3. Searching for themes
4. Reviewing potential codes and themes
5. Linking codes and themes
6. Data analysis

Familiarisation with the data

During this first stage I read and reread the text with the aim of becoming "intimately familiar" with it (Braun & Clarke, 2012). As I read the charted data, I made notes. The note taking process helped me to explore and make sense of the information in my own mind and gain a deeper understanding of each individual article and how they fitted together as a whole (Braun & Clarke, 2012).

Generating initial codes

This stage was fundamentally important, as the codes generated served as the foundation upon which my analysis was based. Initially I identified and labelled all sections of data that were potentially relevant to the research question. I aimed to update and reorganise the codes in an iterative process. Each article was coded in its entirety before I proceeded to code the next. Some sections of data were coded in large chunks, some in smaller chunks depending on the relative volume of information charted.

The codes used summarised or provided a brief description of the data. Due to the nature of the data a limited number of interpretative codes were applied. As this stage progressed initial codes were amended, and additional ones made. Occasionally some sections were labelled with an additional code (Braun & Clarke, 2012).

Searching for themes

I then sought to identify broader issues, or topics around which similar codes clustered and termed these themes (Braun & Clarke, 2012). Each theme represented an important and meaningful

element of the research question. Several codes were relevant to more than one theme demonstrating that some concepts cut across themes. Through this active process I was able to map and summarise the comprehensive set of data with specific reference to my research question (Figure 5).

Reviewing potential themes

Themes were reviewed in a circular, looping process. Each theme was reviewed individually and then together as a framework. The themes were checked for relevance and importance to both the subserving codes and the overarching research question. Themes were amended or discarded if they did not represent an important element of the research question or topic or if there was not enough data to support their status as a theme. Finalised codes and themes are documented in Table 6.

Guidelines for the maintenance of pre-hospital emergency anaesthesia		
Codes		Themes
2.1		Standards
2.1.1	Equivalence to in-hospital standards	
2.1.2	Standards of practice	
2.2		Monitoring
2.2.1	Monitoring standards	
2.2.2	Data recording	
2.2.3	Evaluation of monitoring standards	
2.3		Human resources
2.3.1	Practitioners performing PHEA	
2.3.2	Practitioners present	
2.4		Pharmacology
2.4.1	Drug (class) required	
2.4.2	Drug choice	
2.4.3	Drug dosage/ dosing regimen	
2.4.4	Method of administration	
2.4.5	TIVA	
2.4.6	TCI	
2.4.7	Drug safety	
2.5		Risks associated with PHEA
2.5.1	Accidental awareness	
2.5.2	Drug side effects	
2.6		Transport considerations
2.6.1	Practical procedures	
2.6.2	Scene and transfer time	

2.6.3	Supervision of transport	
2.6.4	Implications of transport on practise	
2.7		Equipment
2.7.1	Requirements of the equipment	
2.7.2	Alarms	
2.7.3	Equipment required	
2.7.4	Equipment safety	
2.7.5	Challenges associated with equipment use	
2.7.6	Human factors associated with equipment use and safety	
2.8		Resources, other
2.8.1	Resource and economic implications	

Table 6. Codes and themes used to facilitate data analysis for research strand 2 - Guidelines for the maintenance of pre-hospital emergency anaesthesia.

Linking codes and themes

As previously mentioned, several codes were relevant to more than one theme. These links served as a basis for further exploring possible inter-thematic conceptual and practical links. These links have been illustrated in Figure 5.

Data analysis

The preliminary stage of data analysis involved weighting the themes by relative amount of data collated. This facilitated the conduct of further analyses focussed on the most salient issues in relation to the research question. The relative weighting of themes is illustrated in Figure 6.

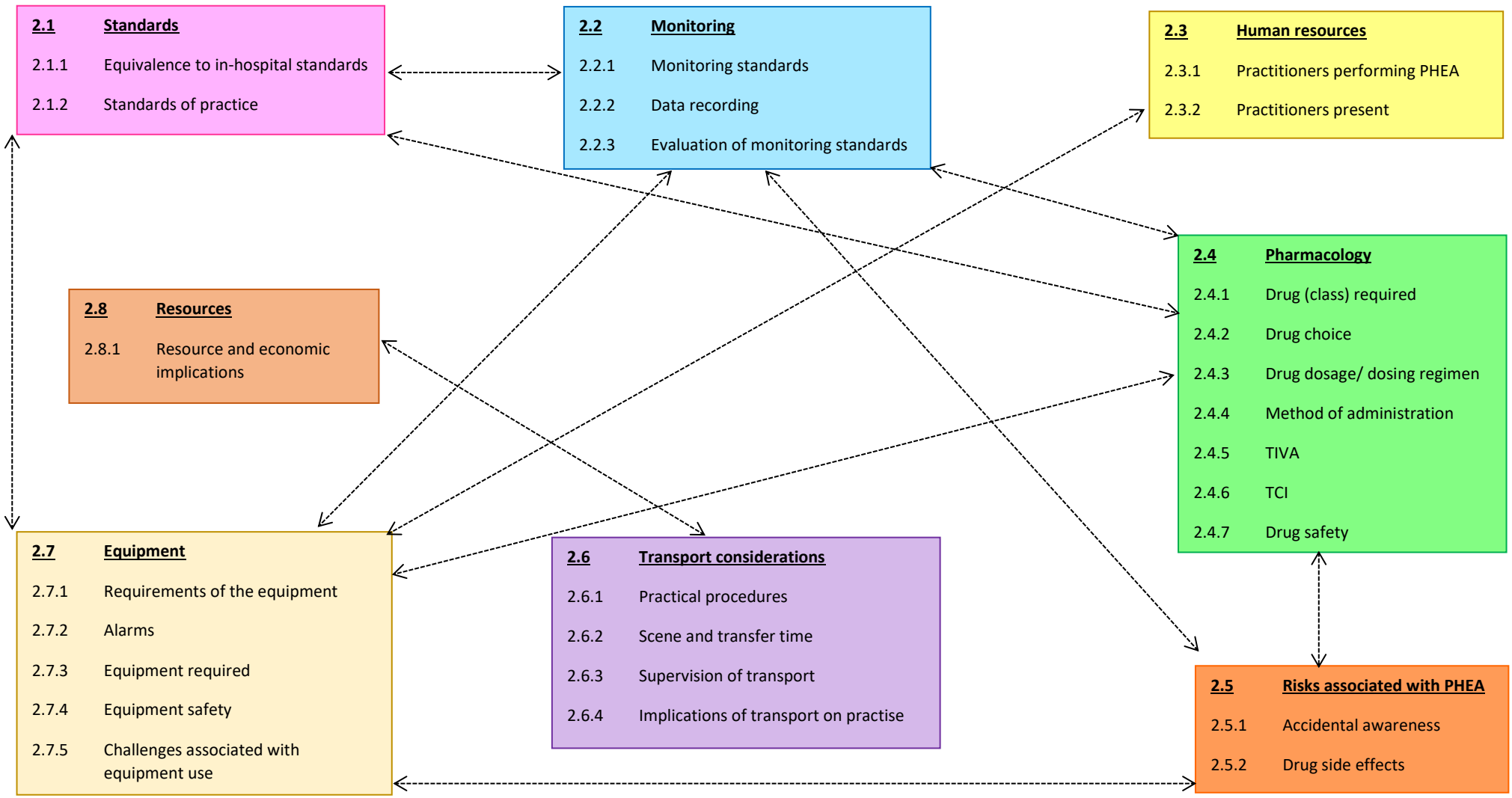
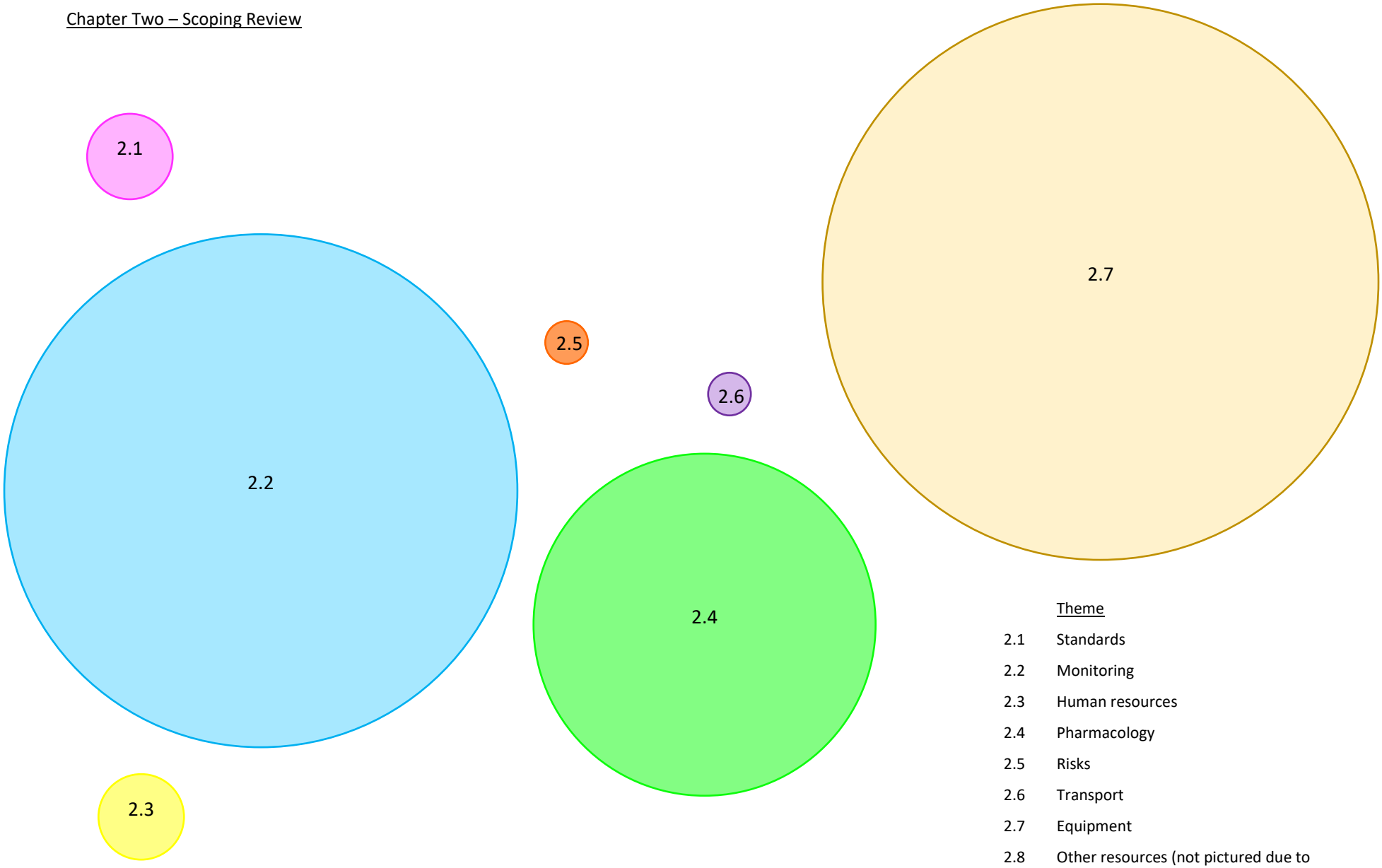


Figure 5. Research strand 2 - Coding guide depicting the multiple inter-thematic links and conceptual framework



	Theme
2.1	Standards
2.2	Monitoring
2.3	Human resources
2.4	Pharmacology
2.5	Risks
2.6	Transport
2.7	Equipment
2.8	Other resources (not pictured due to negligible weighting)

Figure 6. Research strand 2 - Graphic representation of thematic weighting, and inter-thematic links

2. Results

Overview

The main findings from this strand - "Guidelines for the maintenance of pre-hospital emergency anaesthesia" - are summarised below.

Fourteen articles met the criteria for inclusion in the scoping review. In terms of article type they were variable. Some included articles were themselves guidelines, written by major professional bodies such as the Association of Anaesthetists of Great Britain and Ireland (AAGBI) and the Faculty of Intensive Care Medicine (FICM) (AAGBI, 2008; FICM, 2019), or experts in the field (Lockey et al., 2017; Nimmo et al., 2019). Others were editorials, which discussed the strengths, limitations, and implications of the relevant guidelines (Checketts, 2017; Lumb & McLure, 2016). All included articles made direct reference to guidelines that were potentially important in relation to pre-hospital emergency anaesthesia in the UK.

The included articles were published between the years of 2008 and 2019. The more recent articles are arguably of more relevance as they provide a more up to date insight into pre-hospital anaesthetic practice which take into account recent changes in infrastructure and clinical practice.

Some of the included guidelines relate specifically to pre-hospital anaesthesia (Lockey et al., 2017) and others refer to general standards of anaesthetic practice theoretically applicable in any setting (Checketts et al., 2016). A small number of articles refer to concepts or methods of practice, such as TIVA (total intravenous anaesthesia) that are important in the pre-hospital environment (Nimmo et al., 2019).

There was a reasonable degree of consistency in the guidelines recommended in the included articles (AAGBI, 2008; Checketts et al., 2016; Checketts et al., 2017; FICM, 2019; Lockey & Porter, 2007; Lockey et al., 2017; Nimmo et al., 2019; Paal et al., 2010). There was however some disagreement between experts regarding the utility and feasibility of some of the recommendations, both in general and specifically in the pre-hospital environment (Cheketts, 2016; Denning & Barley, 2015; Lumb & McLure, 2016).

Pre-hospital emergency anaesthesia is an advanced clinical intervention performed for severely ill or injured patients in a highly challenging setting. It is therefore not surprising that when displayed graphically we can see that this a complex multi-faceted issue, with many interacting logistical, practical, and clinical considerations (Figure 5.) Some of the most significant factors implicated in the

delivery of PHEA include drug choice and administration, monitoring standards and practices and equipment availability and utilisation (Figure 6)

Recommendations

Pre-hospital emergency anaesthesia should meet the same standards expected in the operating theatre or emergency department (The Association of Anaesthetists of Great Britain and Ireland (AAGBI), 2008; The Faculty of Intensive Care Medicine (FICM), 2019; Lockey et al., 2017). Anaesthetic standards of care including adequate anaesthesia, analgesia and neuromuscular blockade must be maintained throughout the pre-hospital/transport phase and until definitive treatment (AAGBI, 2008; Lockey et al., 2017; Paal et al., 2010).

Human resources

Most pre-hospital practitioners cannot and should not perform PHEA (Lockey & Porter, 2007). Only appropriately trained practitioners, who deliver PHEA sufficiently regularly and frequently to maintain competence should do so (AAGBI, 2008; Lockey & Porter, 2007; Paal et al., 2010). PHEA should not be performed in professional isolation and an appropriately trained assistant should always be present (AAGBI, 2008; Lockey & Porter, 2007). It is, however, acknowledged that in the pre-hospital setting good quality assistance is not always available (AAGBI, 2008).

Pharmacological considerations

A hypnotic drug is usually required to maintain anaesthesia for transfer following pre-hospital induction of emergency anaesthesia (AAGBI, 2008; Lockey et al., 2017). No drug/ drug combination is recommended as superior (AAGBI, 2008) and with appropriate consideration the most commonly used anaesthetic drugs can be used for the maintenance of PHEA (i.e., ongoing anaesthesia) (Lockey et al., 2017). The choice of hypnotic drug will be dictated by patient physiology and the operator's familiarity with the drug (AAGBI, 2008; Lockey et al., 2017; Luck & Morgan, 2019). Various drugs and combinations thereof may be used, including boluses of ketamine, midazolam, and opiate or infusions of propofol, with or without opiate (Luck & Morgan, 2019). Long-acting drugs with almost inert haemodynamic properties are preferable (Paal et al., 2010) and small, frequent doses may help to minimise the adverse haemodynamic effects associated with sedatives (AAGBI, 2008; Lockey et al., 2017).

No sedative dose nor effect-site concentration will be appropriate for all patients and clinical calibration of the patient's response to anaesthetic, with subsequent dose adjustment is

recommended (Nimmo et al., 2019). Processed electroencephalography (pEEG - a form of depth of anaesthesia monitoring) in the period prior to transfer may assist with the determination of the appropriate target concentration or infusion rate (Nimmo et al., 2019).

Total intravenous anaesthesia (TIVA)

Total intravenous anaesthesia is a method of inducing and maintaining general anaesthesia using drugs given only by the intravenous route, without the use of inhalational agents (Nimmo et al., 2019). TIVA is almost always used for PHEA. TIVA encompasses a range of techniques including bolus dosing, manual infusions and target controlled infusion pumps. Nimmo et al., (2019) acknowledge the relative advantages and disadvantages of these techniques and state that whilst infusions may be preferable, they are bulky, heavy and may increase the complexity of transfer (AAGBI, 2008; Lockey et al., 2017).

Despite earlier attempts to improve and streamline the practice of TIVA, until 2019 there were no universally accepted comprehensive guidelines pertaining to the use of total intravenous anaesthesia. In response to the 5th National Audit Project (NAP5) report which found that a large proportion of adverse events associated with the use of TIVA were caused by inadequate training and education (Pandit et al., 2014), the AAGBI and SIVA together produced a set of standards and guidelines for the best practice of TIVA (Nimmo et al., 2019). The same standards of practice apply regardless of the location in which TIVA is administered. The AAGBI and SIVA consider that all anaesthetists should be trained and competent in the delivery of TIVA (Nimmo et al., 2019).

When general anaesthesia is to be maintained by propofol infusion, use of a target-controlled infusion is recommended (Nimmo et al., 2019). The initial target concentration should be determined considering patient, pharmacological and clinical factors (Nimmo et al., 2019). Only one concentration of propofol and one standard concentration of remifentanil should be stored within a department or team (Nimmo et al., 2019).

To be able to achieve and maintain an appropriate concentration of an intravenous anaesthetic or analgesic drug all anaesthetists must have a firm understanding of the principles underpinning TIVA (Nimmo et al., 2019). Achieving a stable concentration will require varying drug infusion rates in different patients/circumstances (Nimmo et al., 2019). It should be noted that the TCI pump relies upon a pharmacokinetic model, which is only truly applicable to patients similar to the population upon which it was developed (De Baerdemaeker, 2004; Gepts, 2008; Schnider & Minto, 2008). Administering TIVA manually, without a TCI pump, is not without its challenges either and as with TCI pumps, a sound understanding of pharmacokinetics is necessary (Nimmo et al., 2019). Any given

infusion rate may cause rising, declining or stable concentrations depending on prior administration rate and duration (Nimmo et al., 2019). The drug concentration achieved should cause loss of consciousness and prevent movement in response to noxious stimuli, but should not be excessive, as this may cause marked hypotension and delayed recovery from anaesthesia (Nimmo et al., 2019).

Programming should only be input after the drug-filled syringe has been placed in the pump and options should be restricted to those routinely used (Nimmo et al., 2019). Pumps should be stacked consistently to reduce the risk of incorrectly programming a pump to administer a different drug (Nimmo et al., 2019).

After reviewing data from the National Reporting and Learning System, the Safe Anaesthesia Liaison Group (SALG) (2009) identified various issues associated with the use of TIVA and made early recommendations to improve practice. The SALG (2009) constructed and disseminated a diagram illustrating the correct arrangement for an intravenous fluid line incorporating a multi-lumen connector, anti-reflux valves on fluid administration lines, anti-syphon valves, a clamp on the intravenous infusion line and side clamps on drug delivery lines, a Luer-lock connector and "Microbore Siamese tubing". There has been some discussion regarding the use of side clamps on the drug administration lines (Denning & Barley, 2015), but the overarching recommendations remain valid. The SALG's early recommendations (2009) have been largely endorsed by the AAGBI and SIVA (Nimmo et al., 2019). They further recommend that the infusion lines should have as few sites for leakage as possible and drug and fluid lines should join as close to the patient as possible to minimise the space in which anaesthetic agents may accumulate (Nimmo et al., 2019). The use of standard TIVA administration sets is recommended to facilitate this. At the end of the procedure all vascular access devices should be flushed with at least twice the dead space volume of the device.

The intravenous cannula should always remain in sight (Nimmo et al., 2019; SALG, 2009). When the intravenous cannula or central venous catheter cannot be visualised during anaesthesia the anaesthetist should have a higher index of suspicion for problems, should regularly inspect the cannula site and should have a lower threshold for using pEEG. Anaesthetists should be familiar with the use of pEEG monitoring. pEEG monitoring is recommended when a neuromuscular blocking drug is given with TIVA. Observation of the EEG trace and electromyography will augment the utility of the pEEG monitoring (Nimmo et al., 2019).

Monitoring

Minimum monitoring should be maintained regardless of duration, location, or method of anaesthesia (Checketts et al., 2016; Lockey & Porter, 2007; Nimmo et al., 2019; Paal et al., 2010) and

any period without monitoring must be kept to a minimum (Cheketts et al., 2017; Lockey et al., 2017). The AAGBI (2008) stipulate that both clinical assessment and non-invasive monitoring be made and recorded at least every three minutes (AAGBI, 2008; Lockey et al., 2017). Automated electronic records may be beneficial in reducing clinician workload (Checketts et al., 2016; Checketts et al., 2017; Lockey et al., 2017). 'Minimum monitoring' requirements include pulse oximetry, heart rate, non-invasive blood pressure monitoring, electrocardiography, inspired and expired gases, airway pressures, temperature, peripheral neuromuscular transmission and depth of anaesthesia monitoring (Checketts et al., 2016; FICM, 2019; Lockey et al., 2017).

Quantitative capnography is essential in all patients with an endotracheal tube, supraglottic airway device, or those who are deeply sedated (Checketts et al., 2017; Lumb & McLure, 2016, Paal, 2010). In contrast to the hospital setting, anaesthetics gas monitoring is rarely indicated in the pre-hospital environment (Lockey et al., 2017).

Monitoring of neuromuscular blockade is now mandatory and quantitative monitoring should be used whenever feasible (Checketts et al., 2017; Lumb & McLure, 2016). Despite this recommendation electromyography is rarely used in the pre-hospital setting (Lockey et al., 2017). Instead, repeat doses of a long-acting nondepolarising muscle relaxant are administered to ensure ongoing paralysis (Luck & Morgan, 2019).

Depth of anaesthesia (DOA) monitoring is necessary when total intravenous anaesthesia (TIVA) is used with neuromuscular blockade (Checketts et al., 2017, NICE, 2012; Nimmo et al., 2019) and it can be used in any scenario that the anaesthetist deems appropriate (AAAGBI, 2008). The AAGBI, and the Society for Intravenous Anaesthesia (SIVA) recommend the use of a processed EEG (pEEG) monitor (Nimmo et al., 2019), of which the Bispectral Index (BIS) monitor is one example. NICE recommend the Bispectral Index (BIS), E-Entropy and Narcotrend-Compact M monitors (NICE, 2012) as suitable options, but give preference to the BIS monitor. pEEG monitoring should begin before neuromuscular blockade is given and be continued until full recovery is demonstrated by a nerve stimulator (Nimmo et al., 2019). Data should be used in conjunction with clinical observation and experience (Nimmo et al., 2019). If portable pEEG is not available, pEEG monitoring in the period immediately prior to transfer may assist determination of the appropriate target concentration or infusion rate (Nimmo et al., 2019). The utility of depth of anaesthesia monitoring with volatile gaseous anaesthesia is debatable (though rarely relevant in the pre-hospital setting) and is thus not mandated (Checketts et al., 2017).

The AAGBI now recommend monitoring of cuff pressures in all tracheal tubes and supraglottic airway devices (Checketts et al., 2017; Lumb & McLure, 2016).

It is recommended that temperature monitoring forms part of minimal monitoring throughout anaesthesia and recovery in all circumstances (Lumb & McLure, 2016) and certainly when general anaesthesia is maintained >30 minutes (Checketts et al., 2016). Temperature monitoring should be considered in pre-hospital emergency cases (Lockey et al., 2017).

Some have described reservations regarding the role of the anaesthetic monitoring recommendations and argue that they do not reflect best clinical care, that they cannot be applied to all clinical scenarios (including the pre-hospital setting), and that they allow room for departments to vary practice and not adhere to the standards (Lumb & McLure, 2016). However, whilst it may initially be challenging to meet these standards it is argued that the guidelines represent the 'gold standard' that all anaesthetic teams should strive for (Checketts, 2016).

Equipment

The equipment used to monitor the patient should be of an equivalent standard to that used in hospital (Lockey et al., 2017).

It should be appropriate, functional and maintained to a similarly high standard (AAGBI, 2008; Lockey et al., 2017). All anaesthetic and monitoring equipment must be portable, robust and weather-resistant, be effective under varying lighting conditions and have adequate battery power (Lockey et al., 2017). The choice of equipment for very adverse conditions must be carefully considered (AAGBI, 2008; Lockey et al., 2017).

Audible alarms must be set and verified before the induction of anaesthesia (AAGBI, 2008; Checketts et al., 2016) and they must be loud enough to be heard in the noisy pre-hospital environment (AAGBI, 2008; Checketts et al., 2016). Audio-visual devices may offer additional benefits (Lumb & McLure, 2016).

All anaesthetic equipment must be checked before use and it is the responsibility of the anaesthetist to oversee this (Checketts et al., 2016).

Given the extensive array of equipment required, care should be taken to construct an appropriate monitoring setup (Checketts et al., 2016), ensuring that all ventilator displays, and any syringe drivers are visible (FICM, 2019).

Transport

In the pre-hospital setting extraction and transport factors must also be considered. In every case the 'scene time' should be kept to a minimum, but all anticipated practical procedures must be performed prior to transfer (AAGBI, 2008; Lockey et al., 2017). Patients should be stabilised prior to transfer in order to decrease the risk of deterioration during transfer (FICM, 2019). Monitoring may need to be suspended during extraction, but must otherwise continue throughout (Lockey et al., 2017). Transport should be supervised by a clinician experienced in caring for the anaesthetised patient.

3. Synthesis of research strands

Results from this scoping review successfully address the aims of each of the two strands of research and can be used to describe the extent to which pre-hospital emergency anaesthetic practice complies with the current guidance.

Results from Research strand 1 give a good overview of practices surrounding PHEA in the UK (Table 2). The articles from which this data were collected are relatively recent suggesting that the conclusions remain highly relevant today. Several aspects of PHEA practice were described in sufficient detail to enable comparison with the guidelines (Figure 7). In all of the domains assessed national practices surrounding PHEA aligned well with the clinical practice guidelines. For example, PHEA is only routinely performed by senior physicians with a high level of training and experience in the delivery of anaesthesia to critically unwell patients (Burgess et al., 2018; Cowan et al., 2012; McQueen et al., 2015) and basic monitoring practices are also consistent with key recommendations (Burgess et al., 2018; Cowan et al., 2012; McQueen et al., 2015).

However, after reviewing the guidelines in detail (Table 5) it became clear that there are a large number of published recommendations comprehensively guiding the practice of PHEA and many of the variables that relate to these recommendations have not yet been collected nor reported in the literature. Examples of these 'missing' variables include the method of drug administration, intravenous line arrangement and details of routine monitoring practices (Figure 7).

It is therefore not possible to comprehensively assess the extent to which the current practices for the maintenance of anaesthesia in the pre-hospital environment are aligned with the published guidance.

Figure 7. A Venn diagram demonstrating the variables of interest collated from research strand 1 data compared with those from research strand 2

4. Discussion

A scoping review was conducted to investigate the research question "What are the current practices for the maintenance of anaesthesia in the pre-hospital environment and are these practices aligned with the published guidance". This was explored as two separate research strands: Research strand 1 – The maintenance of anaesthesia following pre-hospital induction of emergency anaesthesia in the UK and Research strand 2 – Guidelines for the maintenance of pre-hospital emergency anaesthesia.

In total 17 articles met criteria for inclusion in the scoping review. Three articles met eligibility criteria for Research strand 1 (Burgess et al., 2018; Cowan et al., 2012; McQueen et al., 2015) and fourteen articles met eligibility criteria for Research strand 2 (AGGBI, 2008; Checketts et al., 2016; Checketts 2016; Checketts et al., 2017; Denning & Barley, 2015; FICM, 2019; Lockey & Porter 2007; Lockey et al., 2017; Luck & Morgan, 2019; Lumb & McLure, 2016; NICE, 2012; Nimmo et al., 2019; Paal et al., 2010; SALG, 2009).

Results from this scoping review successfully address the aims of each of the two separate research strands and can be used to describe the extent to which pre-hospital emergency anaesthetic practice complies with the current guidance. All aspects of UK PHEA practice that could be assessed align well with the current guidelines. However, the relatively poor depth and breadth of the evidence base limits the extent to which this assessment can be made without further investigation

Research strand 1

This strand of the scoping review demonstrated that there is a relative paucity of literature which describes the current practices surrounding the maintenance of pre-hospital emergency anaesthesia in the UK. Only three relevant journal articles (Burgess et al., 2018; Cowan et al., 2012; McQueen et al., 2015) were included after systematic searches in both MEDLINE and EMBASE databases. This review is therefore likely to serve as an initial step in investigating and understanding more about anaesthetic practice in this challenging environment.

The most frequently occurring themes within the extracted data were the "conduct of pre-hospital callouts and PHEA" and the "provision of PHEA in the UK" (Figure 3.). These themes correspond closely to the research question; "The Maintenance of Anaesthesia following Pre-hospital Induction of Emergency Anaesthesia in the UK", reflecting an effective search strategy and appropriate inclusion and exclusion criteria. Schematic mapping demonstrated that a large proportion of the themes could be linked (Figure 3), highlighting the overall complexity of the subject and providing

contextual information. When considering potential quality improvement ventures it will be important to consider all aspects of this multi-dimensional topic.

The conclusions that can be drawn from this research strand are limited by the fact that the three articles were published up to nine years ago, so may no longer provide an accurate reflection of the rapidly developing field of pre-hospital emergency medicine and the articles were written with different primary aims and objectives to this research question, which may have affected the way that the data has been collected and interpreted.

Research strand 2

There is a relative abundance of articles available which either describe or discuss clinical practice guidelines relevant to the practice of PHEA (AGGBI, 2008; Checketts et al., 2016; Checketts 2016; Checketts et al., 2017; Denning & Barley, 2015; FICM, 2019; Lockey & Porter 2007; Lockey et al., 2017; Luck & Morgan, 2019; Lumb & McLure, 2016; NICE, 2012; Nimmo et al., 2019; Paal et al., 2010; SALG, 2009).

Two of these papers are of fundamental importance (Lockey et al., 2017; Nimmo et al., 2019). They are the most up-to-date, comprehensive, and well endorsed guidelines available which guide UK practice. Nevertheless, of these two key papers only the AAGBI guidelines from 2017 (Lockey et al., 2017) were written with the specific aim of improving pre-hospital anaesthesia. In contrast the joint guidelines from the Association of Anaesthetists and the Society for Intravenous Anaesthesia were written to serve as a guideline for the safe practice of TIVA, wherever and whenever it is used (Nimmo et al., 2019). It is unclear whether this lack of specificity will have a significant impact on the utility and application of this key guideline in the unique and challenging pre-hospital environment.

One of the inherent difficulties associated with the use of clinical practice guidelines is the relatively common circumstance in which multiple professional bodies or experts publish conflicting guidelines concerning the same clinical problem. Overall, the recommendations included demonstrate a high degree of consistency, but there are some minor points of disagreement, for example the set-up/ arrangement of a dedicated intravenous line and the use of monitoring such as electroencephalography or depth of anaesthesia monitors. The lack of consensus is likely to serve as source of confusion or frustration for practitioners (Woolf et al., 1999) and make any assessment of practice against the guidelines difficult.

Synthesis

Pre-hospital emergency anaesthesia and advanced airway management have been some of the most controversial areas of pre-hospital emergency and critical care medicine (Lockey et al., 2014). Whilst there is some residual controversy regarding the need for and the conduct of pre-hospital anaesthesia, it is now widely accepted that PHEA should be performed in a small but significant number of pre-hospital callouts (Lockey et al, 2014; National Confidential Enquiry into Patient Outcome and Death, 2007; NICE, 2018). Consistent with this recommendation, evidence demonstrates that PHEA is performed on approximately 10% of pre-hospital callouts (Burgess et al., 2018; McQueen et al., 2015).

This study found that 44 advanced pre-hospital care services can provide pre-hospital emergency anaesthesia in the UK (Burgess et al., 2018; Cowan et al., 2012). These services work on a regional basis, but their cumulative temporal and geographical coverage remains unknown.

The conduct of pre-hospital callouts and PHEA is not widely known and schematic mapping demonstrated that many interacting factors including human resources, equipment and drug considerations may all influence practice. The complexity of the topic should be acknowledged when pre-hospital emergency anaesthetic practice is evaluated.

In line with important recommendations (Lockey & Porter, 2007; Lockey et al., 2017) this study found that PHEA is only performed by senior doctors with a minimum level of anaesthetic experience and competence, usually with a background in anaesthetics or emergency medicine (Burgess et al., 2018; Cowan et al., 2012; McQueen et al., 2015). Whilst there are common elements to the training path for these doctors their everyday anaesthetic practice is likely to be dissimilar in terms of both case number and patient case mix. This may impact clinician competence, and confidence with different anaesthetic techniques, thereby influencing PHEA practice. It would be interesting to further explore whether the way in which PHEA is maintained varies in association with the background, experience and/or seniority of the practicing clinician.

PHEA should not be performed if the pre-hospital team does not have an adequate skill mix (Crewdson et al., 2019) and despite a clear reliance upon senior physicians, doctors are not always present on callouts (Cowan et al., 2012). AAGBI guidelines also state that a trained assistant should be available (AAGBI, 2008; Lockey et al., 2017), however, unlike most hospital settings this is not always possible (Cowan et al., 2012). It remains unclear whether PHEA would be performed more frequently if experienced, competent physicians and assistants were present on a greater proportion of pre-hospital callouts. This would have implications for the funding and development of training programmes necessary to equip a greater number of healthcare professionals with the necessary

skills. It is notable that there is now an established subspecialty training programme in Pre-hospital Emergency Medicine (IBTPHEM, 2020) and it is possible that the frequency with which PHEA is provided will increase.

Trauma was found to be by far the most common indication for PHEA and in the UK, this usually arises in the context of road traffic accidents (Burgess et al., 2018; McQueen et al., 2015). Major trauma is defined as serious and often multiple injuries where there is a strong possibility of death or disability. The National Institute for Health and Care Excellence support the provision of PHEA in this patient cohort and recommend that "people with major trauma who cannot maintain their airway and/or ventilation have drug-assisted rapid sequence induction (RSI) of anaesthesia and intubation within 45 minutes of the initial call to the emergency services" (NICE, 2018).

Catastrophic haemorrhage is the leading cause of early preventable death following traumatic injury (Eastridge et al., 2012; Kauvar & Wade, 2005) and this has important implications for the way in which PHEA is maintained. These often hypovolaemic patients are at risk of severe haemodynamic instability and clinicians may therefore favour agents with relative haemodynamic stability, such as ketamine. However, whilst ketamine is not uncommonly used for the maintenance of PHEA, this scoping review found that boluses of midazolam and opioid were together the most common drugs given to achieve ongoing anaesthesia (Cowan et al., 2012; McQueen et al., 2015). Small, frequent doses of sedatives may help to reduce the adverse haemodynamic risks, but unfortunately this review could not explore the drug administration approach due to limitations of the evidence base.

The Association of Anaesthetists of Great Britain and Ireland appropriately support autonomous decision making for clinicians choosing how to pharmacologically maintain ongoing anaesthesia in the pre-hospital environment, as they do for those working in the operating theatre or intensive care setting. They acknowledge that consideration will be given to patient factors and clinician familiarity with the drug (Lockey et al., 2017).

The intravenous route is used to induce and maintain pre-hospital anaesthesia and recently published guidelines are available (Nimmo et al., 2019), which specifically address issues surrounding this anaesthetic technique. The extent to which pre-hospital services follow TIVA guidelines could not be investigated in this scoping review due to limited data. This is an important area for future research, as training in TIVA is inconsistent, many do not feel confident in its use (Nimmo et al., 2019) and the recent NAP5 (the 5th National Audit Project) report found adverse events to be significantly associated with TIVA (Pandit et al., 2014). The AAGBI's and SIVA's TIVA guidelines were

not however written with the aim of specifically improving *pre-hospital* practice and it remains to be seen whether their application in this setting is feasible and beneficial.

Checklists have been shown to improve practice and safety in a wide range of clinical (Thomassen et al., 2014) and other high-risk settings including aviation and the nuclear industry (Rognas et al., 2013). It is therefore not surprising that pre-hospital medical services are encouraged to use checklists for all anaesthetic procedural steps (Lockey et al., 2017). Burgess et al., (2018) found the routine use of checklists by pre-hospital emergency medical services to be variable, but a third of UK pre-hospital services use checklists to ensure the maintenance of anaesthesia (Burgess et al., 2018). There is scope to encourage and further increase the use of pre-hospital checklists.

Many clinical guidelines pertaining to monitoring during pre-hospital anaesthesia have been published, each with a large number of salient points (AAGBI, 2008; Checketts et al., 2016; Lockey & Porter, 2007; Lockey et al., 2017; Nimmo et al., 2019; Paal et al., 2010). The standard of monitoring in the pre-hospital environment is expected to meet the same high standard as that performed in the operating theatre (AAGBI, 2008; Checketts et al., 2016; Lockey et al., 2017; Nimmo et al., 2019). Pre-hospital medical services in the UK meet the basic recommended standards including ECG, SpO2, non-invasive blood pressure (NIBP) monitoring and capnography (Cowan et al., 2012). There are however much more extensive monitoring guidelines, which for example also refer to depth of anaesthesia, electromyography, and temperature monitoring (Checketts et al., 2016; Lockey et al., 2017; Nimmo et al., 2019). Unfortunately, limitations in the current literature did not permit the evaluation of all recommended aspects of monitoring.

Pre-hospital medical services in the UK travel by road and air (Cowan et al., 2012) and it is possible that the method of transport will affect what anaesthetic techniques, monitoring and wider clinical practices can be successfully used. Depth of anaesthesia monitoring for example is now routinely used with TIVA in the operating theatre and recommendations appear to support its use in the pre-hospital setting (Nimmo et al., 2019; NICE, 2012). This method of monitoring, however, is susceptible to mechanical and electrical interference and it would be interesting to assess whether it can be used reliably during pre-hospital retrieval and transfer.

When considering the provision of anaesthesia in the pre-hospital environment attention must be paid to the equipment used, ensuring that it is functional and appropriate for the setting (Lockey et al., 2017). The equipment required is both costly and extensive (Lockey et al., 2017; Nimmo et al., 2019). Little reference is made within the literature to the equipment used for PHEA and it would be interesting to know whether clinicians have access to all of the equipment that they would like and

whether it is fit for purpose. It may be difficult for services to meet high demands for resources given their reliance upon charity donations (The Air Ambulance Service, 2020; The British Association for Immediate Care 2020).

5. Methodological evaluation

The use of scoping review methodology enabled the inclusion of a broad range of articles from both the published and grey literature and allowed the construction of a holistic picture of pre-hospital practice in the context of the current clinical guidelines. Given the relative shortage of literature in this specialist area this approach was appropriate.

Scoping reviews do not normally incorporate a formal quality assessment and the impact of this on study conclusions remain unclear. It may have been useful to assess the quality of included articles, especially given questions regarding the degree of relevance and specificity to pre-hospital practice and documented inconsistencies of some guidelines.

6. Study limitations

Unfortunately, some important characteristics and variables relevant to the practice of PHEA have not been collected or reported in the literature and the depth of evaluation is therefore limited.

7. Conclusions

PHEA is indicated in a small, but significant number of patients. PHEA is an advanced intervention with contextual complexity and the conduct of PHEA is not well known. This scoping review found that a small number of studies have been published which describe clinical practices surrounding the maintenance of PHEA. In contrast many articles are available which guide the maintenance of PHEA. The scoping review helps to build a picture of nationwide practice and suggests that the main aspects of UK PHEA practice comply well with the available guidelines.

8. Implications and further research

Further research is required to build a more detailed picture of how pre-hospital teams currently maintain emergency anaesthesia and to examine the extent to which practice complies with the guidelines for the maintenance of PHEA. This will likely involve the collection and examination of a greater number of variables, including drug availability and choice, method of drug administration, safety practices and equipment/resource availability.

Ultimately this research will highlight any interesting patterns or inconsistencies in practice and identify opportunities to optimise clinical care and patient outcome.

Chapter Three

The Maintenance of Anaesthesia following Pre-hospital Induction of Emergency Anaesthesia in the UK: A Secondary Data Analysis

1. Introduction

The scoping review (Chapter Two) helped to build an initial picture of nationwide practice and suggests that the main aspects of UK PHEA practice comply well with the available guidelines. The conclusions that could be drawn were limited by weaknesses in the published literature.

Further research is required to comprehensively describe how pre-hospital teams currently maintain emergency anaesthesia. Important variables that should be elucidated include drug choice and method of drug administration, safety practices and equipment/resource availability. Practice should be examined with a view to ascertaining the degree of compliance with the current guidelines and to subsequently explore factors affecting the conduct of PHEA and compliance with the guidelines. This research may demonstrate inconsistencies in practice and highlight opportunities to improve clinical care and patient outcome.

This chapter aimed to investigate how emergency anaesthesia is currently maintained following pre-hospital induction by services across the UK and to ascertain to what extent current practice aligns with PHEA guidelines. The study is based upon secondary data analysis methodology whereby qualitative and quantitative analyses were performed upon data that had already been collected by researchers in the field of pre-hospital medicine, in this case from EMRTS Cymru (Emergency Medical Retrieval and Transfer Service, Wales). The guidelines against which practice was compared originate from two key papers (Lockey et al 2017; Nimmo et al 2019). This study also sought to determine whether participation in the survey would potentially influence future practice.

2. Methods

Ethics

Ethical approval was obtained from both Bangor University Healthcare and Medical Sciences Academic Ethics Committee and the Emergency Medical Retrieval and Transfer Service (EMRTS Cymru) Research & Development committee (EMRTSRD024). The study was deemed to not require

NHS REC review according to the MRC HRA decision tool (Health Research Authority, 2021).

This study relied upon secondary data analysis, defined as the analysis of data collected by another person for a different primary purpose (Smith et al., 2011) and was thus led by secondary data methodology as described by Boslaugh (2007), Johnston (2017) and Smith et al. (2011). Secondary data analysis is a well-established methodology that offers several efficiency advantages, most notably in time and resources (Boslaugh, 2007; Johnston, 2017; Smith et al., 2011). It employs the same basic research principles as those used in primary data analysis and can be used in a broadly similar manner (Boslaugh, 2007; Johnston, 2017; Smith et al., 2011). High quality secondary data analysis is underpinned by robust methodological steps that have been described in the aforementioned key articles (Boslaugh, 2007; Johnston, 2017; Smith et al., 2011). These steps can be summarised as: 1) Developing the research question, 2) Identifying the dataset, 3) Evaluating the dataset, 4) Data analysis, and 5) Data presentation/reporting.

Methodology for this study followed a bespoke five-stage approach (Table 1) that was developed from models reported by Boslaugh (2007), Johnston (2017) and Smith et al. (2011) considering the relative advantages of each. The model was revised to optimise suitability for the nature and purpose of this study. Minor amendments included removing a suggested literature review from Step 1 (as a scoping review had been completed immediately prior to beginning secondary data analysis) and not searching for datasets using suggested resources such as The Society of General Internal Medicine's Online Compendium (www.sgim.org/go/datasets), but instead contacting known key stakeholders/professionals working within this small specialist field.

Secondary data analysis approach		
Step 1	Identifying the research topic and defining a research question	Identify a meaningful and relevant research topic. *Conduct a literature review (Chapter 2 – Scoping review).* Define the research question considering the results and implications of the scoping review.
Step 2	Locating appropriate secondary data/ Selecting a dataset.	Consider desired characteristics of the dataset. Locate possible dataset(s) considering their cost and availability. Compare the attributes of the dataset with the research question.
Step 3	Evaluating the dataset	Familiarisation with the dataset. Answer the questions: 1) Who collected the data? 2) For what purpose was the data collected? 3) How was the data collected? 4) When was the data collected? 5) What was done to the data after it was collected? Evaluate the data itself by: 1) Assessing the validity of the measures 2) Evaluating the completeness of the dataset; is any missing data random or

		non-random?
Step 4	Analysing the data	Conduct appropriate quantitative and/or qualitative analyses.
Step 5	Presenting findings	Structure the analysis and presentation of findings in a way that tells a meaningful story.

Table 7. A bespoke five-stage approach to secondary data analysis.

The principles and processes of secondary data analysis can be conceived as a series of five essential stages as described in Table 1 and below (Smith et al., 2011).

Step 1: Identifying the research topic and defining a research question

The research topic had been defined during the initial stages of the study as "The Maintenance of Anaesthesia following Pre-hospital Induction of Emergency Anaesthesia". By conducting a scoping review (Chapter 2) I was able to ascertain what was already known regarding PHEA and what outstanding questions required further investigation. The scoping review found that there was a relative paucity of data generally describing clinical practices for the maintenance of PHEA and important characteristics and variables had not been collected or reported in available literature. There are several documents available which are together intended to guide clinical practice in relation to PHEA, yet it was unclear to what extent current practice reflects these guidelines. This research ultimately aimed to highlight inconsistencies in practice with a view to identifying opportunities to improve clinical care.

I thus defined my research question as: "What are the current practices for the maintenance of anaesthesia in the pre-hospital environment and are these practices aligned with the published guidance?"

Step 2: Selecting a dataset

First of all, I considered the population that I wanted to study, what type of data would be most useful for my research question and what variables I wanted to include in my analysis. I concluded that I wanted to base my analysis on a nationally representative sample, that categorical data would be most useful for this initial investigation and that a broad spectrum of variables, which together could build a multi-dimensional picture of pre-hospital emergency anaesthetic practice would be most useful. I proceeded to search for an appropriate dataset.

By conducting the scoping review, I had identified key stakeholders in the field including pre-hospital emergency services, key professional bodies and active researchers. After discussions with the

Research and Development team from one such pre-hospital service (EMRTS Cymru (The Emergency Medical Retrieval and Transfer Service, Wales)) I was able to locate a dataset that appeared suitable for my research question. The researchers were happy for me to use this dataset in its entirety without any financial implications or other restrictions. An initial assessment of the dataset suggested that it would fit the research question well. As the key to ensuring meaningful secondary data analysis is to ensure "a good fit between the research question and the dataset" (Johnston, 2017), I proceeded to evaluate the dataset to confirm relevance and suitability for my research purpose.

Step 3: Evaluating the dataset

After locating a dataset that seemed viable in meeting the aims of my research question, I familiarised myself with the data and evaluated its suitability for my research question. I aimed to learn as much as I could about the dataset itself to place the data in context and understand if this would influence the quality of the subsequent analysis. I sought to find out who had collected the data, for what purpose and how and when the data was collected. Fortunately, the two clinical researchers (Dr Jon Birks and Dr David Green) who had initially collected the data were happy to provide me with this information, discuss the data collection process in detail and send me a copy of the data collection tool (the online survey; Appendix 1). They had collected and kept evidence of careful, well thought data collection.

The data was collected specifically for the research question "The Maintenance of Anaesthesia following Pre-hospital Induction of Emergency Anaesthesia in the UK" from November 2018 to March 2019. Dr Jon Birks (JB) and Dr David Green (DG) had designed the data collection tool, sent out the online survey (Appendix 1) and collected the responses, but had not analysed the data. No one else had had access to the data. JB & DG consented to the data being used for my research question and ultimately for the purpose of the Masters by Research study. I was sent the complete set of raw data and supporting documentation. A list of all the organisations included in the study is available as Appendix 2. I was fortunate that both JB & DG were happy to discuss the dataset and provide me with any further information necessary to evaluate the dataset.

This dataset offered several advantages. As the data was current and had not been previously used it could be analysed with the aim of bringing novel, up-to-date, meaningful information to the field. The research question for which the data was originally collected was similar to this study's research question, so the variables that had been collected were likely to be highly relevant. JB & DG were experts in the field of pre-hospital anaesthesia, without any competing interests, meaning the data

collection process benefitted from expert knowledge and experience, free of bias.

The data was collected by online survey using a bespoke, structured questionnaire (Appendix 1). Survey content was informed by both relevant literature and expert knowledge (JB & DG). The survey was designed to establish whether PHEA was provided by the organisation and to capture further data relating to the maintenance of pre-hospital anaesthesia following Rapid Sequence Induction (RSI). If the service responded that they did not have provision for pre-hospital anaesthesia, the survey ended at this initial question.

UK pre-hospital care organisations that were likely to routinely provide PHEA were identified from the Air Ambulances UK (previously The Association of Air Ambulances) and the BASICS websites (Association of Air Ambulances, 2018; British Association for Immediate Care, 2018). A list of 55 services was compiled and contact details were sought.

Two BASICS schemes were withdrawn from the survey, as they only had postal addresses available. The remaining 53 organisations were approached using the standardised electronic invitation. Individuals were asked to complete the survey in a manner that reflected the practices of the organisation that they worked for rather than their individual preferences. Survey responses were received and collated over a four-month period from 17/11/18 to 17/03/19. A follow up 'reminder' email was sent to individuals or services that had not replied on 05/01/2019. The survey was formally closed on 17/03/2019. Responses were received from 42 services, equating to a response rate of 79%. Unfortunately, one organisation was no longer practising as a service, thus leaving adequate data from 41 pre-hospital services.

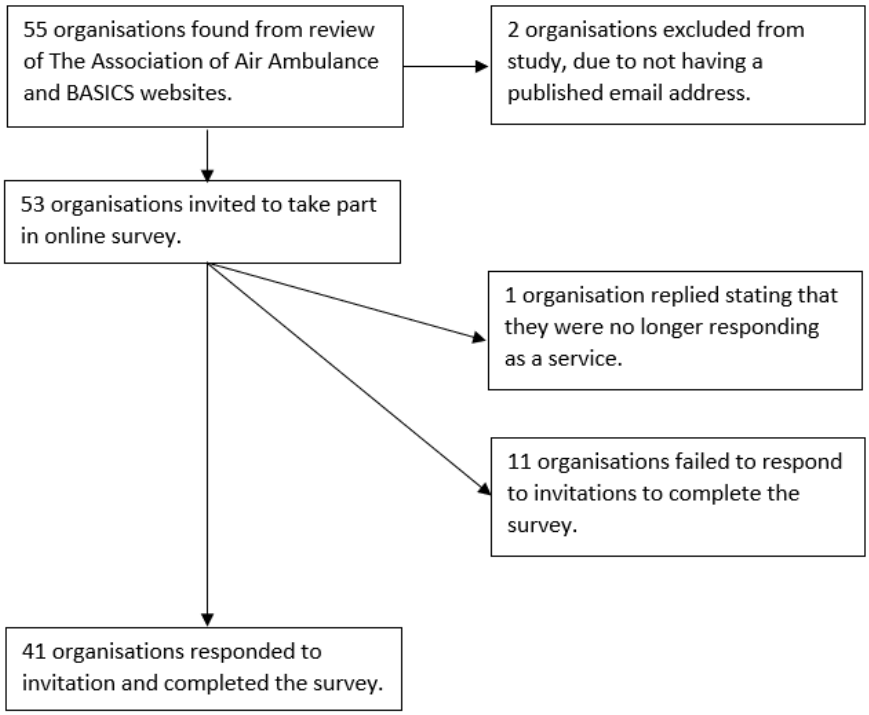


Figure 8 CONSORT diagram illustrating the process for inclusion in the study.

Data was collected regarding the preferred technique(s) for maintaining anaesthesia (bolus, manual infusion or target-controlled infusion) and the range of available and routinely used drugs, as well as the transport method used to convey the anaesthetised patient to medical facilities. Participants were also asked to complete questions regarding the precautions undertaken to ensure that PHEA was maintained in accordance with safety and best practice guidelines. Data concerning the funding status of the services was also collected. Free text comments were invited to assess whether future clinical practice would change after completing the survey and reading the attached SALG document (Safe Anaesthesia Liaison Group, 2009).

The data consisted largely of categorical variables with some free text responses. The variables collected were sufficient to comprehensively describe pre-hospital anaesthetic practice in a good amount of detail and to enable comparison of clinical practice with standards and guidelines. Free text answers allowed the participants to express their opinions without being restricted to a small number of responses and facilitated deeper conceptual and thematic analysis. Whilst no other researchers had collected the same dataset the data was broadly consistent with recent key pieces of literature obtained from other sources (Burgess et al., 2018; Cowan et al., 2012; McQueen et al., 2015).

Finally, I checked what had been done to the data after it had been collected including whether there

had been any cleaning or coding of the data or imputation of missing data items. The survey responses had been compiled and input into Microsoft Excel software, then stored securely. There was only one item of 'missing data' where two letters had been entered instead of a word response for funding status. This had not been altered/amended and the data sent to me was entirely original.

Step 4: Data analysis

The overall goal for the secondary data analyses were the same as for other methods, so once Step 1-3 had been completed data analysis took the same format as for primary data.

Thematic analysis

Firstly, I used thematic analysis techniques, as described by Braun & Clark (2006), to search for patterns across the entire dataset. This was useful as an initial method of analysis due to the inherent theoretical freedom and flexibility of the approach. During this iterative process I became more familiar with the data and was able to pick out and explore apparent patterns. Ultimately, I was able to define key codes and themes (fundamental and recurring key topics or issues) and then label small data segments with code(s) belonging to the main themes of service capability/provision of PHEA, conduct of PHEA, safety and monitoring practices, resources, drugs, clinical governance, audit and quality improvement and funding. The codes can be thought of as 'sub-topics' or elements of the major themes. For example, the major theme of 'Drugs' is composed of the codes: a) drugs carried by the team, b) drugs routinely used and c) method of drug administration.

During this phase I also searched for practical and conceptual links between the major themes and codes.

Inductive analyses employed during this phase suggested that some results may be stratified by drug administration method. Therefore, given the risk of distorting meaningful results by only analysing the data as a whole, a small number of additional subgroup analyses were performed (see "Safety precautions" section below).

Quantitative analyses

Descriptive statistics constituted the fundamental methodological approach used during data analysis. This approach was used to describe the basic features of the data and provide simple summaries, facilitating the presentation of a relatively large amount of novel data in both a manageable and meaningful way. This ultimately allowed the identification of emerging patterns and constructs of interest.

This method was most appropriate for several reasons. Firstly, the primary research question sought to "*describe* how PHEA is maintained" thus necessitating an informative but illustrative approach. Secondly, the collected data was largely categorical in nature meaning that it was more amenable to this descriptive, flexible approach. It may have been possible to code the data and perform inferential statistical analyses, but this would have detracted from the meaningful presentation of results and according to the research question inferential statistics were not required. Descriptive statistics were particularly useful as this represented one of the first studies of its kind in this small, subspecialist field of medicine, and by describing the characteristics of the data and summarising the results in a simple yet meaningful way it will serve as a foundation from which further research can be developed.

Due to the categorical nature of the variables, results have been described using percentages to express proportions and the modal average to describe the central tendency of data. Results have been presented descriptively, graphically and in tabular form.

Results from the scoping review demonstrated that a large number of articles had been published which were either guidelines for PHEA themselves or which discussed the PHEA guidelines as a principal objective. Analysis of these articles indicated that two were fundamentally important in guiding PHEA and they have been widely accepted as such (Lockey et al., 2017; Nimmo et al., 2019). These two guideline reports were both the most up to date articles of their type, they were well resourced and referenced, and they were highly comprehensive, including specific recommendations published by other organisations, for example the National Institute for Health and Care Excellence (NICE) recommendations regarding the role of PHEA in the management of pre-hospital trauma (NICE, 2019) and depth of anaesthesia monitoring (NICE, 2016). The articles written by Lockey et al., (2017) and Nimmo et al., (2019) have been endorsed by an extended list of major professional bodies including the Association of Anaesthetists of Great Britain and Ireland, the Royal College of Emergency Medicine, the Royal College of Anaesthetists (RCOA), the Faculty of Pre-hospital Care the Royal College of Surgeons of Edinburgh, BASICS and BASICS Scotland. Their recommendations constitute the standards against which practice has been compared in this secondary data analysis.

The specific recommendations against which practice has been assessed are:

- Does the service provide PHEA? – PHEA is indicated in a small but significant number of pre-hospital callouts (Lockey et al., 2017).
- How is the patient transported to hospital? – The transport process should be carefully considered before undertaking pre-hospital anaesthesia. It may comprise air or road transfer (Lockey et al., 2017).

- Which primary method is used for delivering ongoing pre-hospital anaesthesia? – No particular anaesthetic technique preferred (Lockey et al., 2017)
- When general anaesthesia is maintained with propofol is a TCI pump used? - TCI is recommended when general anaesthesia is maintained with propofol (Nimmo et al., 2019)
- What drugs are available for maintaining PHEA? – The most commonly used anaesthetic drugs can be used for PHEA with appropriate consideration (Lockey et al., 2017).
- Drug chosen for maintaining PHEA – The most commonly used anaesthetic drugs can be used for PHEA with appropriate consideration (Lockey et al., 2017).
- Is depth of anaesthesia monitoring routinely used for patients undergoing PHEA? – Depth of anaesthesia monitoring is recommended when TIVA is given with neuromuscular blockade (Nimmo et al., 2019).
- When administering fluid or blood products via the same IV cannula as the anaesthetic/sedative agent(s), is there always a one-way valve on the IV line? – One-way valves should be used on all lines where more than one infusion is being given (Nimmo et al., 2019).
- Are one-way valves clearly labelled as such? - One-way valves should be used on all lines where more than one infusion is being given (Nimmo et al., 2019).
- Is the intravenous cannula inspected at regular intervals? - The intravenous cannula used to deliver the sedative/anaesthetic agent should be visually inspected at regular intervals (Nimmo et al., 2019).
- Do the IV infusion lines used for PHEA all include anti-syphon values at the syringe end of the line? – There should be an anti-syphon valve on the drug delivery line (Nimmo et al., 2019).
- Are the IV infusion lines used for PHEA made from ‘kink resistant material’ - IV infusion lines used for PHEA should be made from ‘kink resistant’ material (SALG, 2009).

Qualitative analyses

Free text responses were analysed using thematic analysis and results have been presented descriptively.

3. Results

This survey found that most pre-hospital medical services in the UK are able to provide PHEA. Results demonstrate that UK clinical practices aimed at maintaining PHEA vary and whilst they comply with standards endorsed by the Association of Anaesthetists of Great Britain and Ireland, the Royal College of Emergency Medicine, the Royal College of Anaesthetists, the Faculty of Pre-hospital Care,

BASICS and BASICS Scotland (Lockey et al., 2017), they do not appear to comply well with the current TIVA guidelines (Nimmo et al., 2019).

PHEA is always maintained using TIVA (n=41, 100%) and most services utilise bolus administration (n=24, 75%). National TIVA guidelines are more relevant for anaesthesia maintained by infusion, as opposed to boluses and this may explain why compliance with the guidelines appears to be poor. The TIVA guidelines may not be appropriate for pre-hospital use.

Clinicians stated that drug choice is influenced by patient physiology, drug pharmacodynamics/ pharmacokinetics and resource availability. It is unclear whether clinical practice should change to become more uniform, or whether present variation in practice represents the best management for each unique patient and scenario.

Most of these crucial services rely upon charity funding (n=23, 72%), so before pre-hospital services commit to investing significant resources in augmenting compliance with the guidelines, there should be clear demonstration of clinical utility and benefit of the guidelines in the pre-hospital setting.

Survey responses highlighted clear evidence of a continued desire to "improve pre-hospital medical services", however that may be.

Thematic analysis

The entire dataset was examined using thematic analysis and key themes were identified as service capability/provision of PHEA, conduct of PHEA, safety and monitoring, resources, drugs, clinical governance, audit and quality improvement and funding (Table 2). The labels which defined these themes encompassed multiple smaller codes, which represented topics and constructs of interest, for example the theme "resources" included data coded by both "equipment" and "human resources" (Table 2).

Secondary data codes and themes		
Coding	Codes	Themes
1.1		Service capability/ Provision of PHEA
1.1.1	Pre-hospital care services	
1.1.2	Service capability/provision of PHEA	
1.2		Conduct of PHEA
1.2.1	Standard operating procedures/protocols/ written guidance	
1.2.2	Transport	

1.3		Safety and monitoring practices
1.3.1	Safety	
1.3.2	Monitoring	
1.4		Resources
1.4.1	Equipment	
1.4.2	Human resources	
1.5		Drugs
1.5.1	Drugs carried	
1.5.2	Drugs used	
1.5.3	Method of drug administration	
1.6		Clinical governance, audit and quality improvement
1.6.1	Clinical governance	
1.6.2	Clinical audit	
1.7		Funding

Table 8. Codes and themes defined following thematic analysis of the secondary dataset.

Many links, both practical and conceptual, existed between themes (and subserving codes) and together these links established a network of factors which influence the delivery of PHEA. Data mapping visually demonstrates the complexity of the topic (Figures 2-8). Themes were weighted by relative importance judged according to how many times they appeared within the data. The 'Conduct of PHEA' and issues related to 'Drugs' emerged as key themes (Figures 9-15).

Inductive analyses suggested that certain measures, including safety and monitoring variables were systematically associated with method of drug administration. A small number of additional subgroup analyses were therefore conducted.

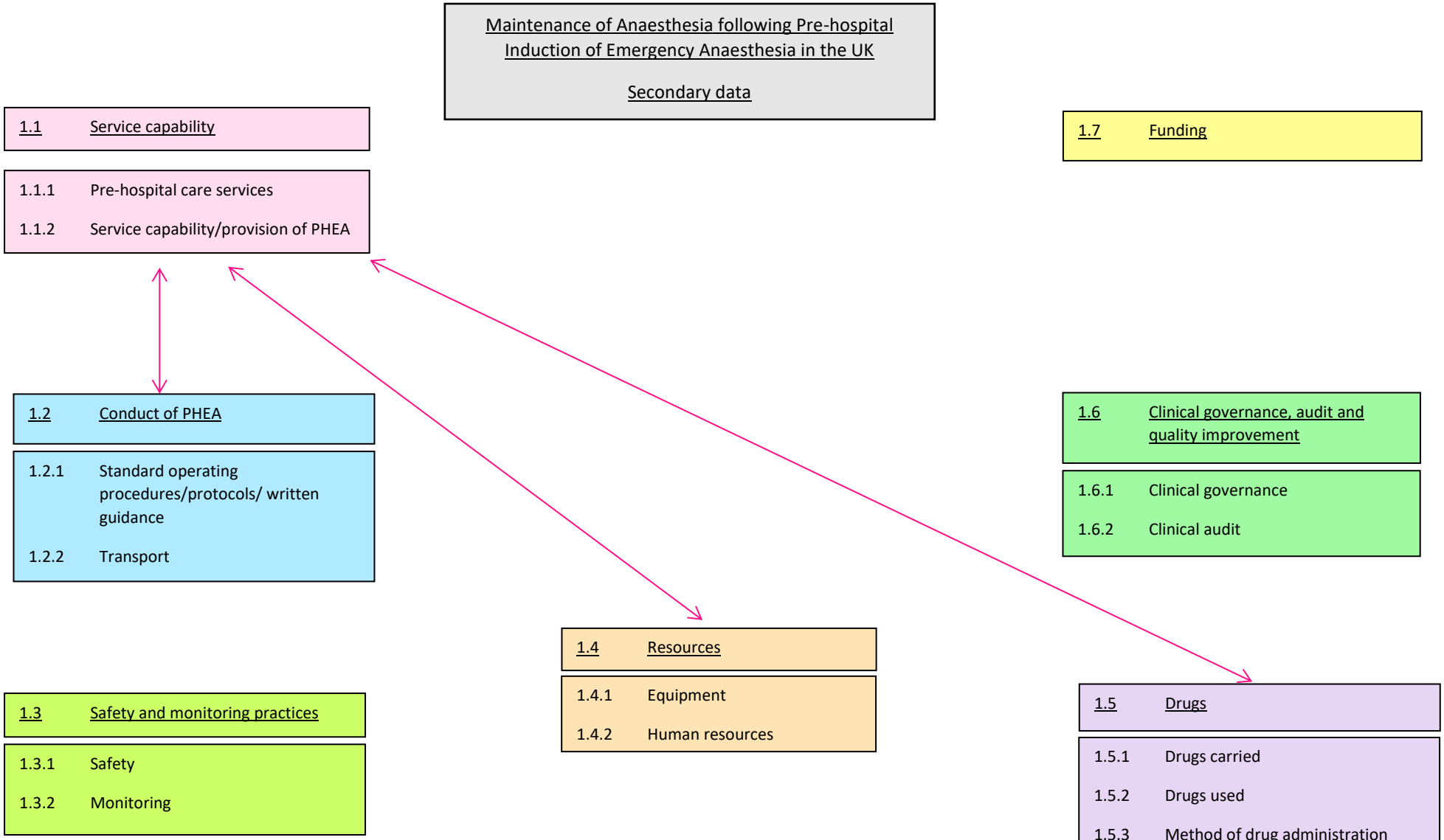


Figure 9. Data mapping demonstrating factors which link, either conceptually or practically, with 'Service capability'.

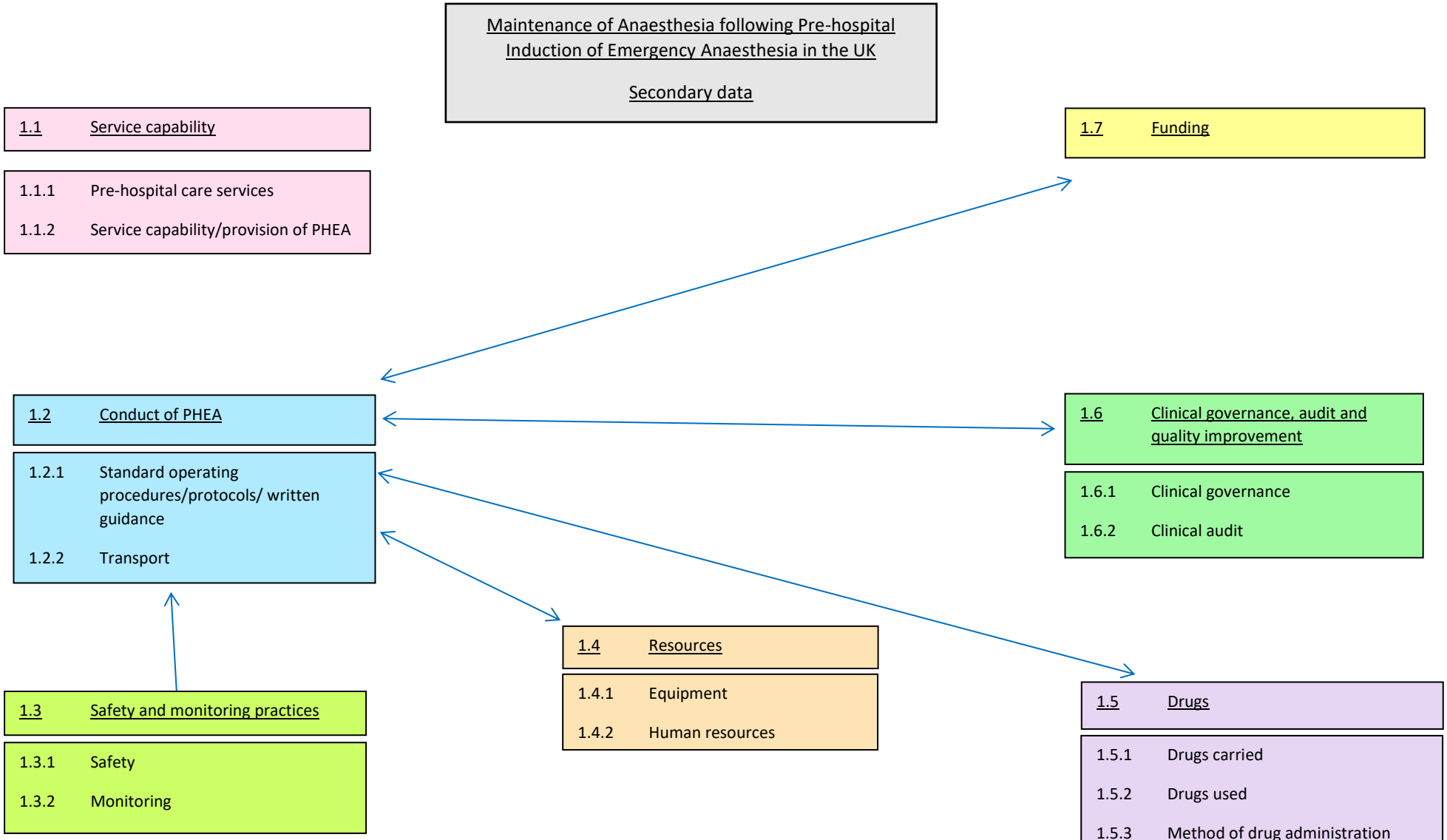


Figure 10. Data mapping demonstrating factors which link, either conceptually or practically, with the 'Conduct of PHEA'.

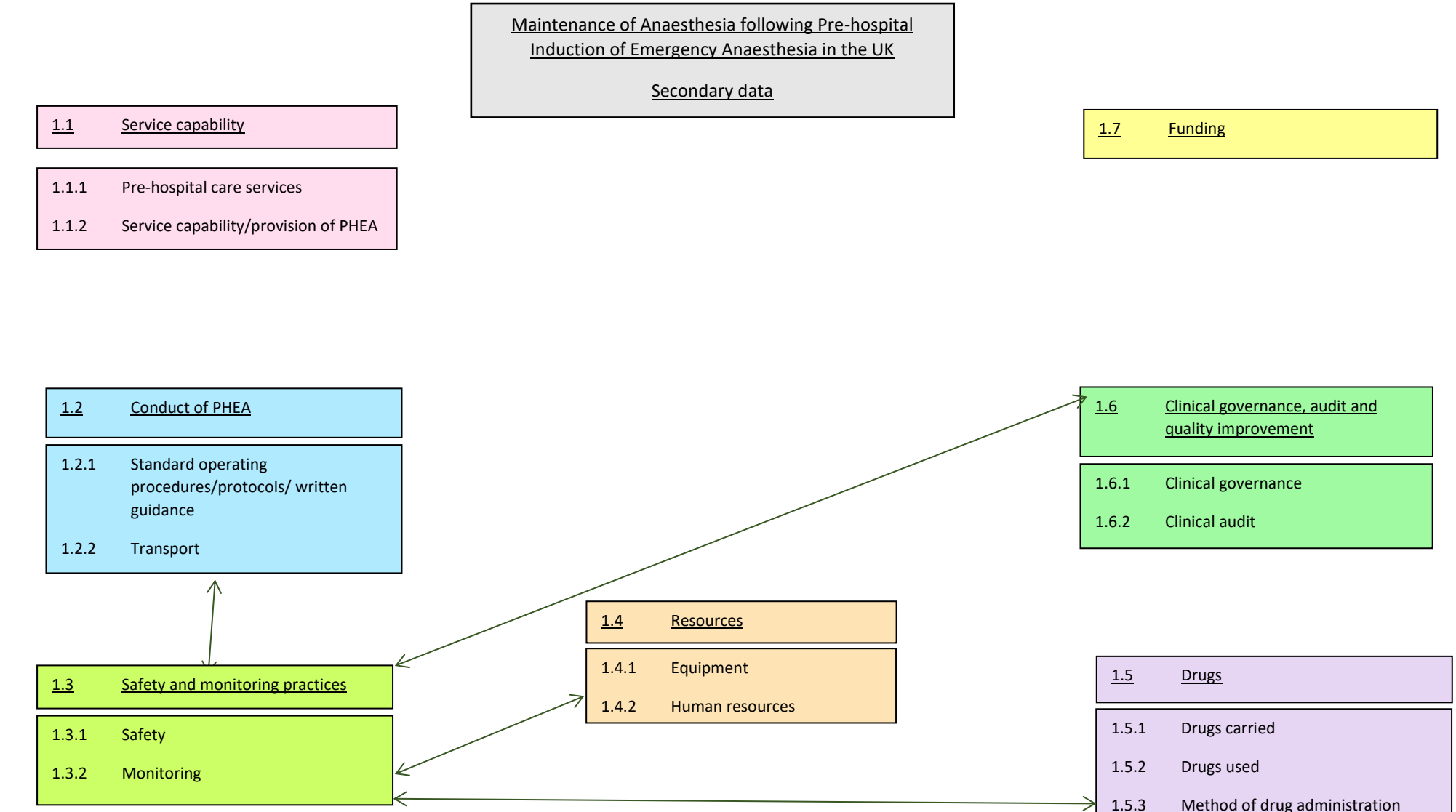


Figure 11. Data mapping demonstrating factors which link, either conceptually or practically, with 'Safety and monitoring practices'.

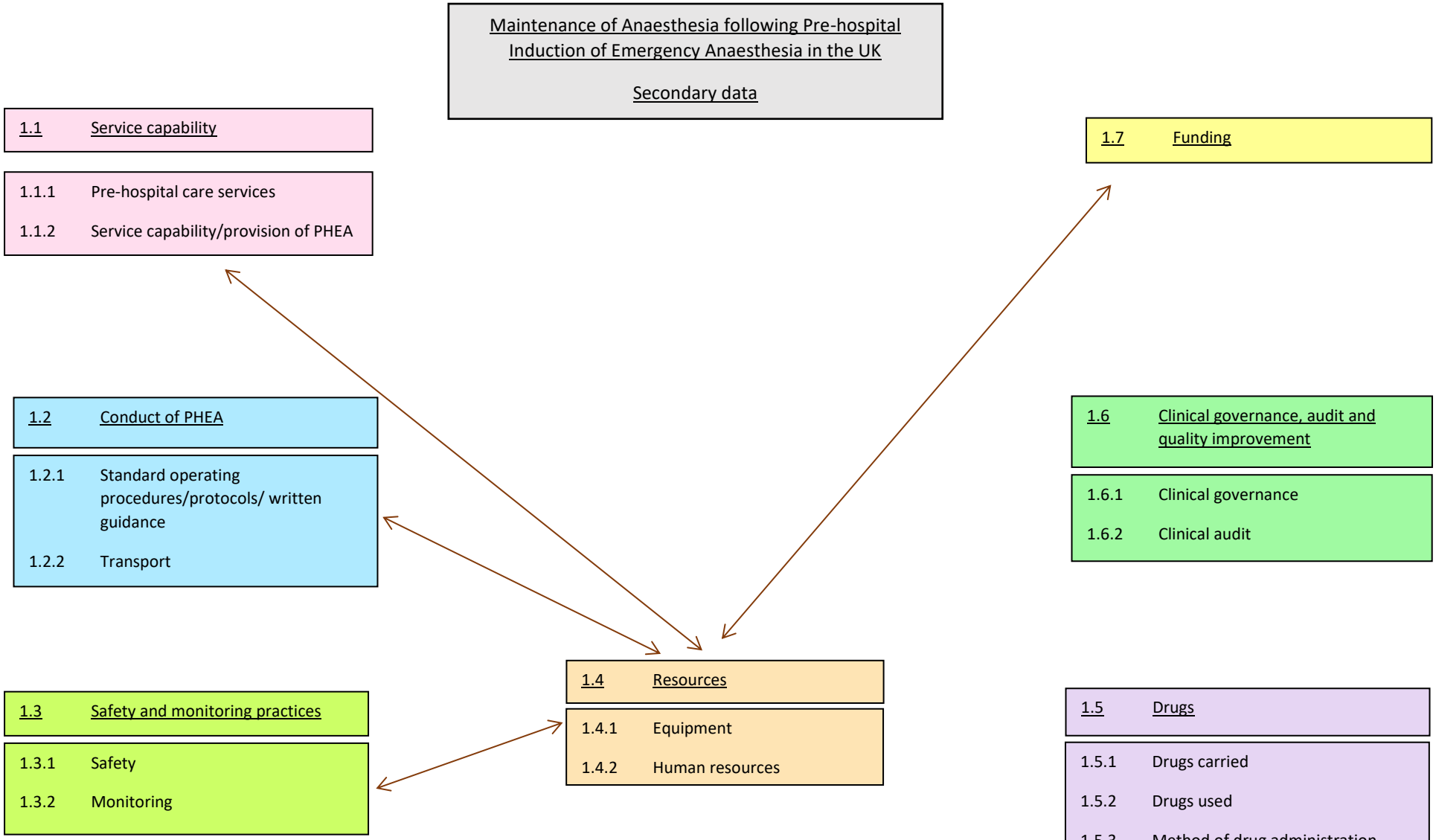


Figure 12. Data mapping demonstrating factors which link, either conceptually or practically, with "Resources".

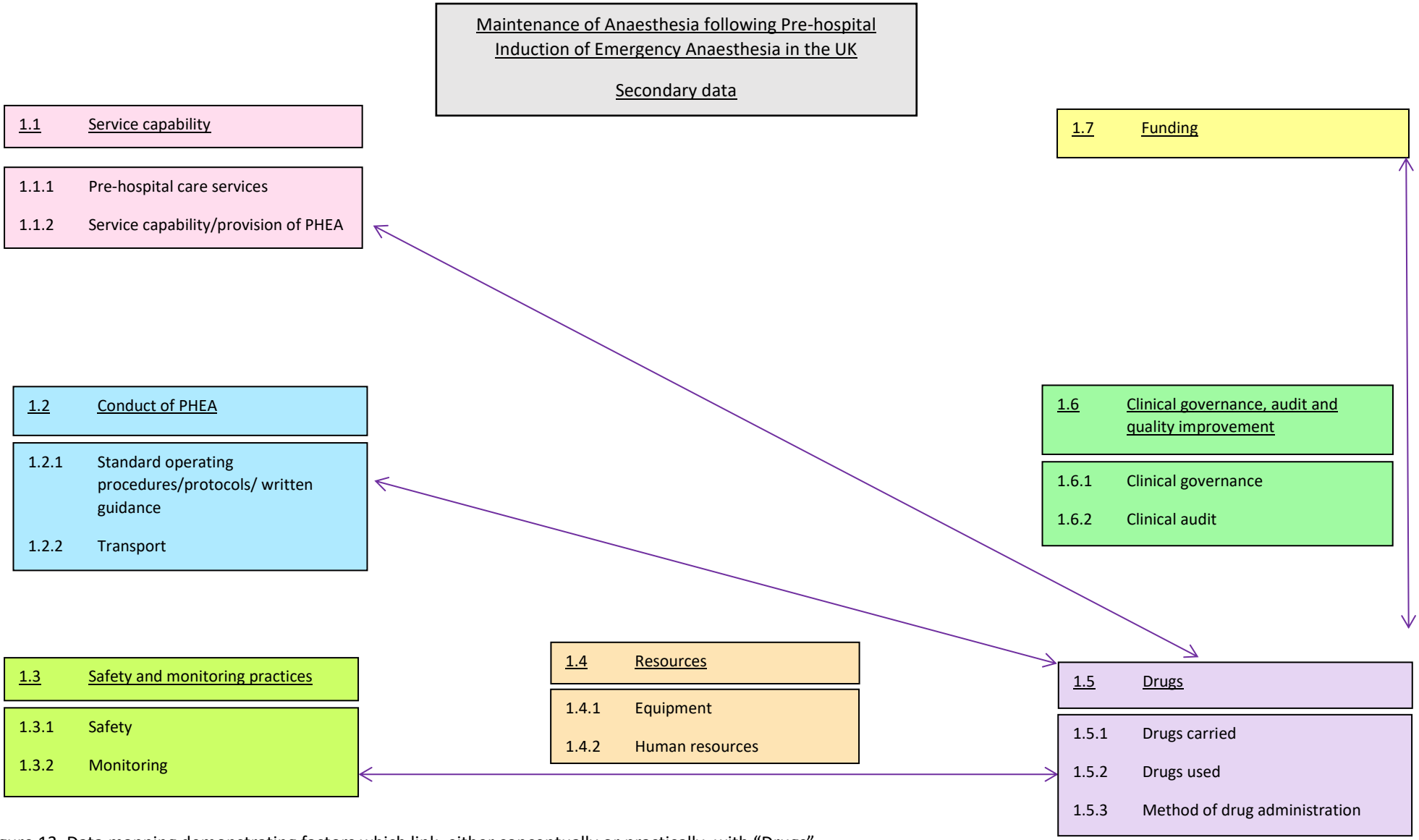


Figure 13. Data mapping demonstrating factors which link, either conceptually or practically, with "Drugs".

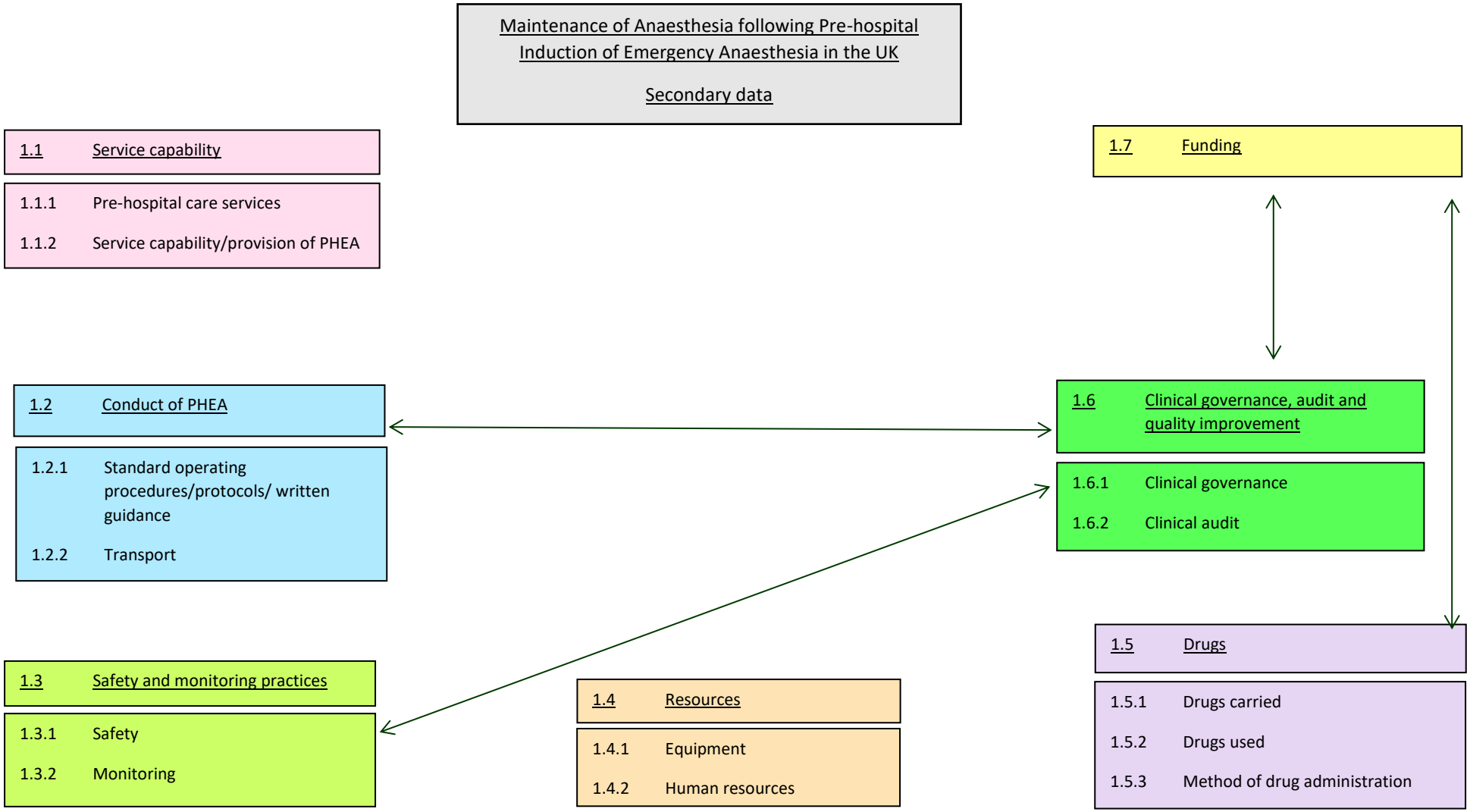


Figure 14. Data mapping demonstrating factors which link, either conceptually or practically, with 'Clinical governance, audit and quality improvement'.

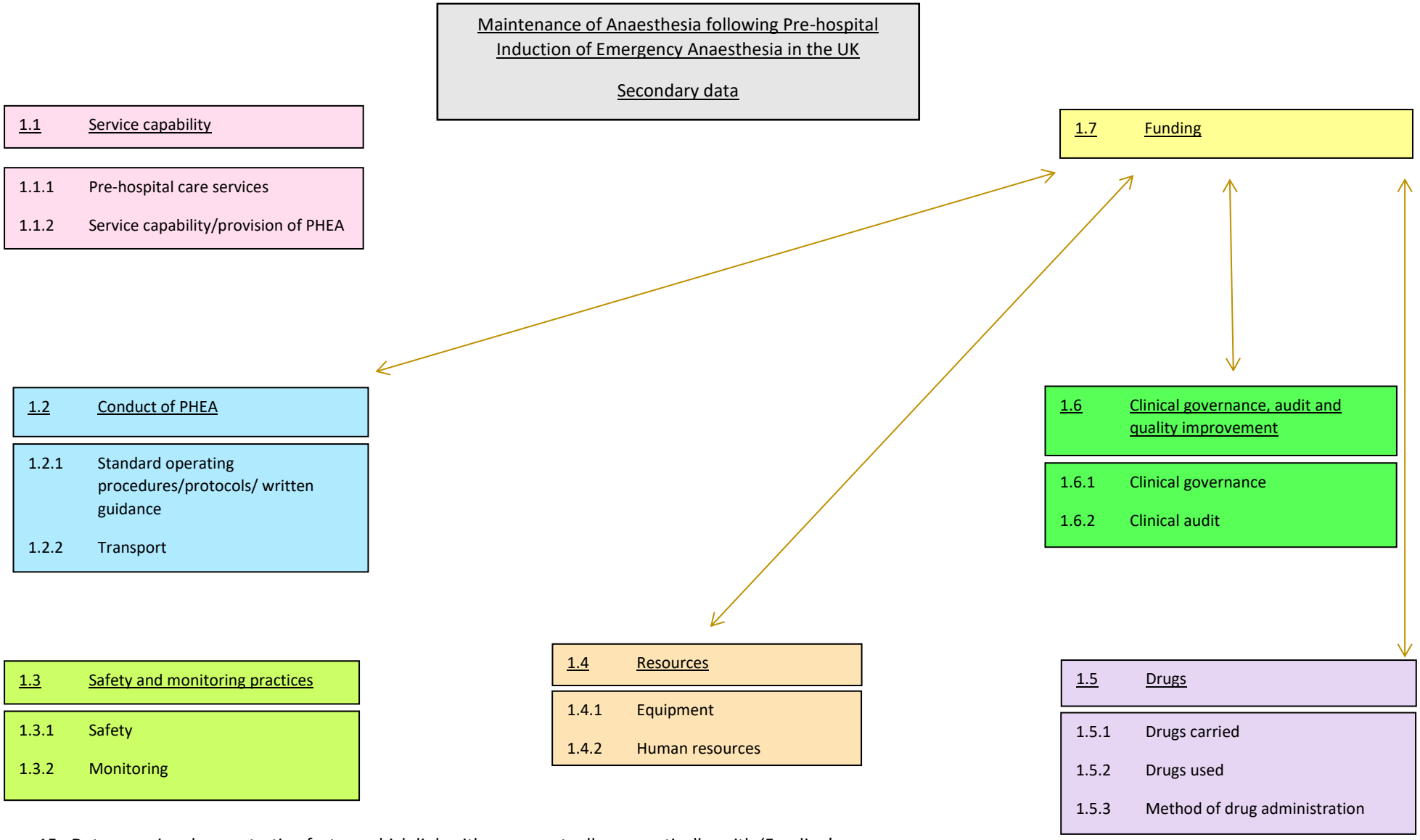


Figure 15. Data mapping demonstrating factors which link, either conceptually or practically, with 'Funding'.

Maintenance of Anaesthesia following Pre-hospital Induction of Emergency Anaesthesia in the UK

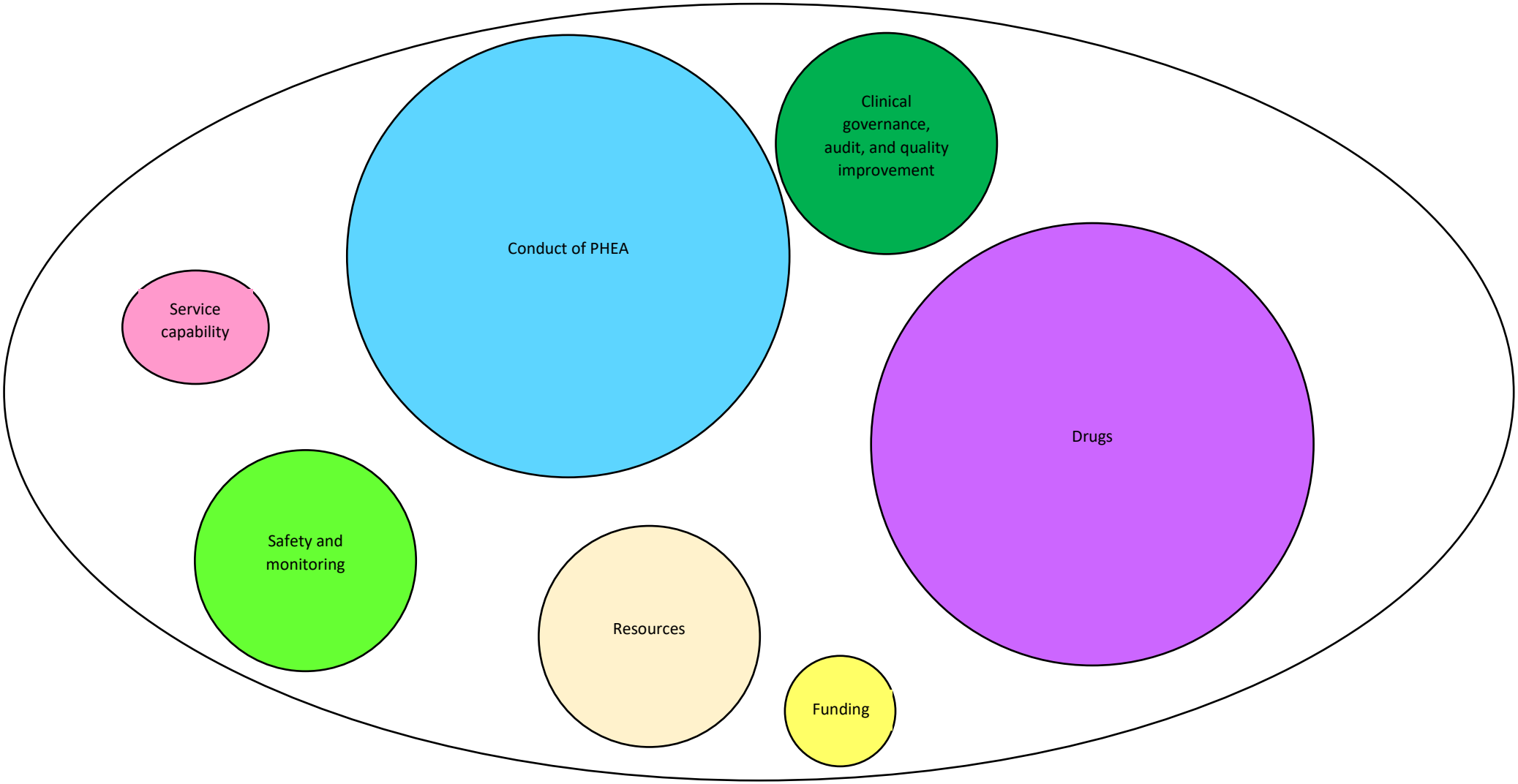


Figure 16. Graphic representation of the themes/factors that influence the maintenance of PHEA. Themes have been weighted by relative importance.

Provision of pre-hospital emergency anaesthesia (PHEA) by UK pre-hospital medical services.

The results demonstrate that most pre-hospital services provide PHEA (n=32, 78%). Of these, 28 (87.5%) provide pre-hospital emergency anaesthesia during both road and air transport and four (12.5%) during road transport only.

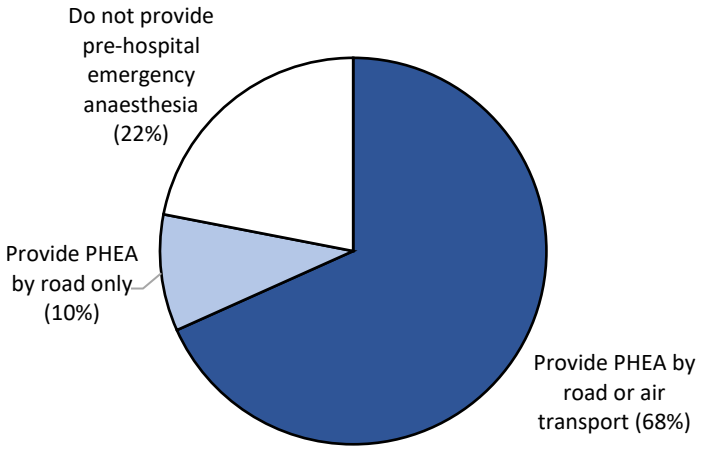


Figure 17 Provision of PHEA by UK pre-hospital medical services.

Anaesthetic drugs

Most UK pre-hospital care teams that provide anaesthesia have access to midazolam, ketamine, morphine, fentanyl and propofol (Table 1).

Drugs carried by organisation	Number	Percentage (%)
Midazolam	32	100
Ketamine	31	97
Morphine	30	94
Fentanyl	25	78
Propofol	19	59
Thiopentone	8	25
Alfentanil	1	3

Table 9. Drugs available for the maintenance of pre-hospital emergency anaesthesia.

Most services using a bolus only technique used a combination of morphine and midazolam for on-going anaesthesia (Table 2). Practice was variable however and several other drugs/ drug combinations were reported as 'standard practice' (Table 2). Free text responses highlighted that choice is "*operator dependent*". Several respondents stated that whilst morphine and midazolam boluses would be their first choice, if the patient were not haemodynamically stable, they would instead use boluses of ketamine.

For services maintaining anaesthesia using continuous infusions, propofol or ketamine are the most frequently used drugs (Table 2). One service stated that they only have one infusion pump, and this limits clinical choice.

Drug combinations most commonly used	Number	Percentage (%)
Bolus only	24	75
Midazolam and morphine	16	50
Ketamine and fentanyl	2	6
Midazolam and fentanyl	1	3
Midazolam and fentanyl +/- ketamine	1	3
Morphine and midazolam or ketamine (dependent on haemodynamic stability)	1	3
Ketamine	1	3
Variable - operator dependent	2	6
Continuous infusion	8	25
Propofol	3	9
Ketamine	3	9
Propofol with fentanyl boluses	2	6

Table 10 Drug combinations most commonly used for the maintenance of pre-hospital emergency anaesthesia.

Primary method used to maintain emergency anaesthesia (i.e., to deliver ongoing sedation)

PHEA was always maintained by TIVA (n=32, 100%), which is defined as the use of any combination of intravenous agents, without inhaled hypnotics to achieve general anaesthesia. This definition encompasses manual dosing, fixed rate infusions, and TCI pumps.

Following on-scene induction of anaesthesia, most services choose to use a bolus only technique to maintain emergency anaesthesia (n=24, 75%), with the remainder using fixed rate, continuous infusion on a millilitres/hour basis (n=8, 25%). Whilst two services (6.25%) have equipment capable of providing TCI none use this technique.

Safety precautions

Routine adherence to the TIVA safety guidelines varied between the pre-hospital medical services; 13 (41%) of the teams reported not routinely meeting any of the guidelines, but a small number of services met a maximum of three of the six guidelines of interest. The reported average compliance with safety precautions for TIVA was 17%, but there was a considerable difference between the continuous infusion group and the bolus only group, with the former meeting 31% of safety precautions and the latter meeting only 10%.

In terms of equipment 10% of services stated that one-way valves are clearly labelled as such, with 23% of services routinely placing these on lines being used for co-administration of fluids/blood products. 25% of services using continuous infusion use IV lines with an anti-syphon valve at the syringe end of the line and 16% of this group report that their infusion lines are made from 'kink-resistant' material. Over a third (38%) regularly inspect the cannula being used to deliver the anaesthetic agent. No teams carry out depth of anaesthesia monitoring.

Safety precautions used	Number	Percentage (%)
The cannula being used to deliver the sedative/anaesthetic agent is visually inspected at regular intervals.	12	38
An anti-reflux valve is always used when administering fluid or blood products by the same IV cannula as the anaesthetic/sedative agents.	7	22
IV infusion lines used for PHEA lines are made from 'kink resistant' material	5	17
IV infusion lines used for PHEA all include anti-siphon values at the syringe end of the line.	4	13
All anti-reflux valves are clearly labelled as such.	3	10
Depth of anaesthesia monitoring is used	0	0

Table 11 Safety precautions applicable when providing intravenous anaesthesia in the pre-hospital setting.

Changes to future practice

As a result of participation in the survey, most respondents (72%) stated that they would suggest a review or change within their service. Most of those that said they would suggest a change were "*not certain all minimum suggested safety criteria [were being] met by their organisation*". 60% of the quality improvement changes conceived involved the introduction of new equipment.

The remainder felt that despite non-concordance with the guidelines a change in practice was either not desired or not feasible. One respondent stated that changes to practice were *"unworkable in the current climate*", suggesting that resource availability is a key limiting factor in clinical choice. Another respondent stated that "*TIVA as use[d] in hospital is not appropriate, [because] there is a massive difference between pre and in hospital* [*practice]"*.

Funding

The majority (72%) of pre-hospital care services rely, at least in part, on charitable donations with only nine teams (28%) being funded solely by the NHS (Figure 17).

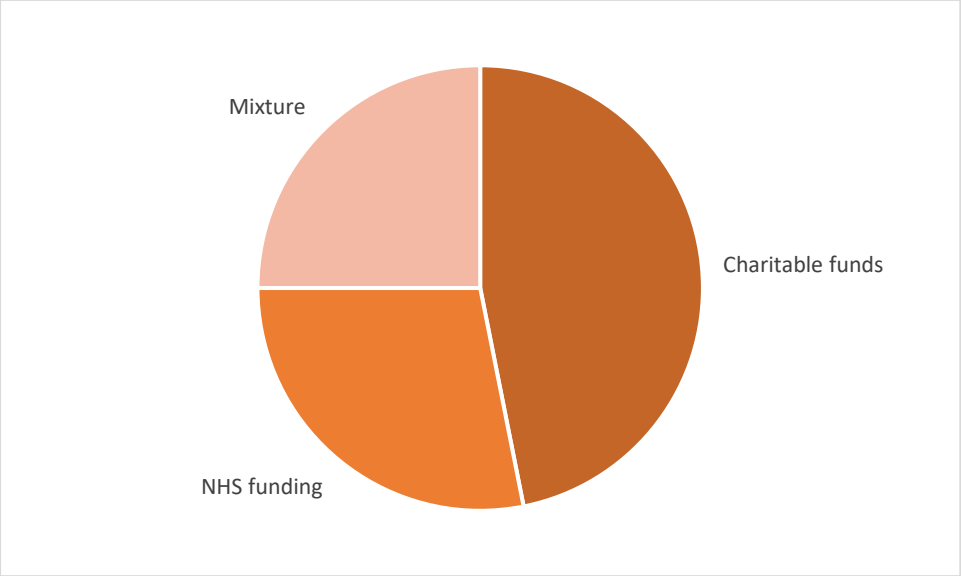


Figure 18. Funding sources of UK medical services providing pre-hospital anaesthesia

4. Discussion

This is the only study to date to specifically investigate the way that anaesthesia is maintained following emergency pre-hospital induction in the UK.

This research was conducted using secondary data analysis and this method brought advantages of time and resource efficiency. The chosen dataset was fit for purpose and benefited from a robust, well described data collection process led by experts in the field of pre-hospital emergency

medicine.

Results show that the maintenance of PHEA is a fundamentally complex topic influenced by a network of interlinked factors including human factors and resources, equipment, drug availability, safety recommendations and funding.

This analysis demonstrated that UK clinical practices aimed at maintaining PHEA vary. Different drug combinations and methods of administration are used by teams throughout the UK. However, taken together with results from the scoping review, findings from this secondary data analysis suggest that many aspects of PHEA practice comply well with the AAGBI endorsed guidelines for safer pre-hospital anaesthesia (Lockey et al., 2017). UK pre-hospital emergency anaesthetic practice does not appear to comply well with the guidelines for TIVA though (Nimmo et al., 2019).

The major TIVA guidelines are not specific to the pre-hospital setting and they assume continuous infusion of anaesthesia, whereas this analysis demonstrated that UK teams predominantly rely upon bolus administration. Some may feel that it is unfair to assess pre-hospital anaesthetic practice against these guidelines, but the widely supported guidelines state that they should be used whenever anaesthesia is maintained by TIVA. Before pre-hospital services commit to investing significant resources in meeting these potentially inappropriate standards, these guidelines should be validated for pre-hospital emergency scenarios or separate pre-hospital specific guidelines should be developed. Either way, there should be a clear demonstration of benefit in this setting.

Synthesis

This study relies upon secondary data analysis, thus data that had initially been collected by other investigators has been used to address the research question: “The Maintenance of Anaesthesia following Pre-hospital Induction of Emergency Anaesthesia”. A major advantage of this technique is that of economy (Boslaugh, 2007). As someone else had already collected the data I did not have to dedicate time nor financial resources to designing, developing, and distributing the data collection tool nor receiving and storing the responses. This was an appropriate use of available resources in the current scientific period where large amounts of data are continually being collected and stored across the world.

The chosen dataset offered several advantages: the variables that had been collected were highly relevant to the research question, there was evidence of a clear, robust data collection process that was free of bias and the initial investigators were experts in the field of anaesthesia, thus the data collection process had benefited from expertise and knowledge that may not otherwise have been

available. The breadth of coverage that had been achieved by the initial researchers was notable. From their position of expertise and experience in the field the investigators had managed to attain national coverage, thereby enhancing the generalisability of the dataset. The initial researchers agreed to supply the comprehensive dataset without restriction (financial or otherwise) and were happy to discuss the data collection process in detail.

A sufficient number and range of variables had been collected to gain a good understanding of current practice and free text responses allowed me to further explore the research question and gain an insight into expert opinion regarding current practice and possible changes to future practice. Nevertheless, as I did not develop the data collection tool and the data was not collected specifically for my research question, several variables that I would have liked to analyse to build a more complete, multi-dimensional picture of PHEA were not collected. For example, I would have liked to gather information about the clinicians who perform PHEA including their background, and experience, as well as previous and current training/professional development. Additionally, I would like to have been able to investigate the indications for PHEA, and if there are any factors which limit the provision of PHEA on a day-to-day basis. Whilst this research question focusses more on the anaesthetic agents delivered after pre-hospital induction of anaesthesia, it would also be useful to have data regarding the pharmacological achievement of neuromuscular blockade. In summary there remains a small number of variables to be collected that may help to complete the picture of UK PHEA practice.

The free text responses received allowed me to further explore clinical practice and decision making and I would have liked to use more open questions to investigate the rationale underpinning clinical decision making generally in the context of pre-hospital emergency anaesthesia and in common or conceivable pre-hospital scenarios. To further investigate the role and effectiveness of the current guidelines I would have included open questions which sought to ascertain the respondents' opinions of the guidelines.

This study was based on an analysis of secondary data obtained through a survey of all practising pre-hospital medical services in the UK. A total of 55 teams were identified and asked to participate. The response rate of 79% was good and allowed a representative analysis of nationwide services. Failing to identify and receive responses from all practising organisations in the UK reflects a potential source of bias, however other researchers in the field have recently reported finding a similar number of practising UK pre-hospital teams (Burgess et al., 2018; Cowan et al., 2012).

Thematic analysis

Key codes and themes identified during secondary data analysis showed considerable overlap with codes and themes identified during the scoping review phase (Chapter 2), suggesting that the dataset was well suited to investigating the research question and building upon initial findings from the scoping review.

Further analysis of these themes demonstrated a complex network of practically and conceptually linked factors, which influence the maintenance of PHEA (Figure 9 - 15). This finding adds strength to results from the scoping review: clinical practice surrounding PHEA is a complex issue and many clinical and non-clinical factors are implicated in the provision and delivery of this specialised service.

5. Results in context

Provision of PHEA

Most pre-hospital medical services in the UK (n=32, 78%) can provide pre-hospital emergency anaesthesia, but nine services are unable to meet the AAGBI (Lockey et al., 2017) and NICE guidelines (NICE, 2019) that recommend the provision of PHEA in a select group of patients. Participation in the survey guaranteed anonymity and confidentiality and few details were collected regarding the composition and characteristics of the pre-hospital emergency care services/organisations themselves. These organisations work on a regional basis, but little is known about the characteristics of the organisations that can provide PHEA compared with those that cannot. The significance and relative impact of the nationally disparate provision of PHEA may be influenced by regional variations in population demographics and/or geographical characteristics.

Even when teams are capable of providing PHEA, it remains unclear whether PHEA can always be provided or whether this varies day-to-day or even shift-to-shift according to staff availability and team composition, operational hours, or environmental conditions. It may have been more meaningful to assess whether PHEA can *always* be provided, or in what proportion of indicated cases it can be delivered. Literature suggests that temporal coverage falls short of other European nations (Adnet & Lapostolle, 2004; Burgess et al., 2018; Cowan et al., 2012; Dick, 2003; Jeremie et al., 2006; Kruger et al., 2010; McQueen et al., 2015). It would be interesting to calculate the total temporal, geographical and population coverage achieved by UK based services with a view to enhancing the uniformity and equity of service provision. It is important to acknowledge that this study, and others based on similar methodology, may fail to identify and/or include all organisations currently working in the UK and this may present a risk of selection bias and incomplete data.

Transport process

This study found that most UK services have the capacity to provide PHEA during road or air transport. National guidelines state that the transport process should be carefully considered before PHEA is planned or conducted (Lockey et al., 2017). Schematic mapping (Figure 3) demonstrated that transport considerations are closely linked with resource factors, as well as clinical/pharmacological and safety/monitoring practices. To build a complete picture of PHEA it would be useful to further explore these potentially bi-directional links and characterise exactly why and how transport factors are considered during the planning and conduct of PHEA.

Anaesthetic drugs

This study has highlighted variation in practice between UK services, with differing drug combinations and methods of drug administration being used. The use of local standard operating procedures (SOPs) is now widespread, with many clinical institutions developing and implementing protocols with the aim of improving patient safety and outcome and reducing human error. One such freely available article is MAGPAS Air Ambulance's pre-hospital emergency anaesthesia SOP (MAGPAS, 2018). It is conceivable and highly likely that other UK pre-hospital services operating independently have their own SOPs which guide their teams' practice. Without shared policy making between the regional teams, it is possible that differences in SOPs may account for the lack of uniformity in practice. It is also possible that practice varies to some extent between clinicians within the same service or indeed for the same clinician presented with different patients with differing pathology and needs. One inherent weakness of this study's methodology lies in the fact that one individual was asked to respond on behalf of the organisation for which they work. This approach is susceptible to reporting bias and may fail to capture differences in practice between clinicians working for the same service.

It is possible that this variation in practice is not a weakness but represents best practice for each clinical scenario in the context of highly interchangeable and often challenging patient and human factors and austere environmental conditions. An in-depth analysis of a large sample of individual cases would be needed to confirm this, but the AAGBI acknowledge the complex rationale underpinning anaesthetic drug choice and do not recommend any particular drug as superior. They argue that that with appropriate consideration the most commonly used anaesthetic drugs can be used for PHEA (Lockey et al., 2017). My results showed that in practice boluses of midazolam and morphine are used most frequently to maintain anaesthesia. Free text responses indicated that the drugs chosen for the maintenance of anaesthesia were based upon clinician familiarity and patient physiology, particularly the relative haemodynamic stability of the patient. Conducting interviews with clinicians serving in the field of PHEM and delivering PHEA would serve to elucidate the

comprehensive list of factors considered in this critical decision and their relative importance.

Primary method used to maintain emergency anaesthesia

The AAGBI do not stipulate whether bolus dosing, fixed rate infusion or TCI should be used to maintain anaesthesia during patient retrieval and transfer (Lockey et al., 2017) and many pre-hospital services, such as MAGPAS Air Ambulance have their own standard operating procedures (SOPs) (MAGPAS, 2018) which guide this step but do not give direction regarding method of administration. However, SIVA and AAGBI guidelines recommend that *if* general anaesthesia is maintained with propofol, TCI should be used (Nimmo et al., 2019)

Clinician responses demonstrated that bolus administration is used by most pre-hospital services in the UK, with 75% of teams maintaining PHEA in this way. Bolus dosing has the advantages that the clinician may inspect the cannula site more frequently, they may get biofeedback of resistance to flow and they may be more likely to manually occlude the line during drug administration, preventing back flow (if a one-way valve is not in situ). This may help mitigate some of the risks associated with unintended interruption of continuously infused hypnotic agents (Cook & Pandit, 2012). However, bolus dosing is more prone to inconsistent drug concentrations at plasma and effect-site, risking awareness or hypotension with under or over-dosing of sedative. The AAGBI suggest that small, frequent doses titrated to physiological variables may help mitigate these risks (Lockey et al., 2017) and it is likely that UK pre-hospital teams do indeed administer ongoing anaesthesia in this way.

Infusion pumps may be preferable (Lockey et al., 2017) as they should help avoid peak and trough concentrations, but survey responses demonstrated that this method is less commonly used for PHEA in the UK. Free text responses indicated that pump availability is one factor which limits the frequency with which they are used. This may be related to the fact many pre-hospital organisations rely on charitable funds to purchase equipment (results from this study) and the need to test the air-worthiness of this equipment would further increase associated costs. The use of infusion pumps is also likely to pose more logistical and practical challenges in the pre-hospital setting. When one considers the relatively short duration and the time pressure under which UK pre-hospital retrievals and transfers are conducted the setting up of fixed rate infusions may seem a poor use of limited, valuable time (Burgess et al., 2018; Lockey & Deakin, 2005; NICE, 2019).

Manual infusion regimes are also prone to errors in the determination and delivery of the required infusion rate of the sedative, as reported by NAP5 (Nimmo & Cook, 2014). TCI pumps have been developed with the aim of overcoming these problems and ensuring the attainment of a user-

defined drug concentration in the plasma or at the effect-site. These models rely upon pharmacokinetic models that have been developed and modelled for a specific drug. The pharmacokinetic models most anaesthetists may be familiar with are the Marsh and Schnider models for propofol TCI (Absalom et al., 2009).

It is recommended that when anaesthesia is maintained with propofol, TCI should be used (Nimmo et al., 2019). Presumably, this recommendation is limited to propofol as this is the only sedative for which there are commonly used pharmacokinetic models available. Whilst guidelines state that TCI should be used when anaesthesia is maintained with propofol, propofol TCI models have never been validated in pre-hospital trauma patients (Absalom et al., 2009) and the pump algorithms are unable to easily account for drugs commonly co-administered during pre-hospital retrieval and transfer (Struys et al., 2016). Furthermore, TCI is a specialist anaesthetic technique and doctors delivering PHEA from backgrounds other than anaesthetics (Harris & Lockey, 2011) may be unfamiliar with its use. These reasons may partially explain why pre-hospital teams in the UK do not use this technique to deliver ongoing anaesthesia. Interestingly, whilst most teams do carry propofol only two teams have equipment capable of delivering propofol by TCI. This suggests that in reality TCI is rarely considered.

Safety precautions

TIVA is always used for PHEA, however evidence suggests that training in TIVA is often inconsistent and many do not feel comfortable using this technique (Nimmo et al., 2019). The 5th National Audit project (NAP5) found that the most common contributory factor in serious complications associated with TIVA was inadequate education and experience (Cook & Pandit, 2012). Specific training in the practical aspects of TIVA is required and non-anaesthetists delivering anaesthesia should have special training in the administration of anaesthesia (Cook & Pandit, 2012).

To help address the relative lack of confidence associated with the use of TIVA, The Society for Intravenous Anaesthesia and the Association of Anaesthetists of Great Britain and Northern Ireland published guidelines for the safe practice of TIVA (Nimmo et al., 2019). They state that the infusion device used should have a Luer-lock connector at each end, an anti-syphon valve on the drug delivery line and an anti-reflux valve on all lines where more than one infusion is being given. The peripheral or central venous cannula being used for the anaesthetic infusion should be visible at all times and if this is not possible it should be regularly inspected (Nimmo et al., 2019).

Results clearly demonstrated that compliance with the TIVA guidelines is poor. The possible reasons for poor compliance are multiple and may include resource or financial restrictions, human factors,

training, or clinical governance arrangements. Some argue that the recommended setup for TIVA is overly complex and that proper implementation of the guidelines could result in an increased risk of user error (Denning & Barley, 2015). Most important though is the fact that the key guidelines (Nimmo et al., 2019) are generic and largely relate to the use of infusions, as is standard practice in hospital. In contrast, this study found that most services do not use infusions but did go on to fill in the questions relating to the TIVA safety recommendations, thus average compliance appeared to be poor. Nevertheless, considering only services utilising continuous infusion, the compliance with SIVA safety guidelines was still only 31%. It will be important to clarify the reasons for the apparent poor compliance with safety guidelines. It may be that pre-hospital practice has not been considered in the development of the current guidelines and they are not appropriate for use in this setting, though this may be a surprising finding considering that the guidelines represent essential safety precautions. Alternatively, there may be yet unexplored reasons for the apparent poor compliance.

Depth of Anaesthesia monitoring is strongly recommended whenever TIVA is used with neuromuscular blockade (NICE, 2016; Nimmo et al., 2019) and especially when the cannula is not in view (Nimmo et al., 2019), as is often the case in PHEA scenarios. The rationale for this recommendation is to mitigate the risk of accidental awareness under anaesthesia (Pandit et al., 2014), which can be associated with considerable physiological and psychological harm for the patient as well as medicolegal difficulties for the clinician. According to the National Audit Project 5 (NAP5) report, published by the RCOA and AAGBI, the incidence of intra-operative awareness is approximately 1 in every 19,000 cases (Pandit et al., 2014). Respective data for pre-hospital patients is not available.

The AAGBI, the Society for Intravenous Anaesthesia (SIVA) and NICE support the use of Bispectral Index (BIS), E-Entropy, or Narcotrend-Compact M monitors (NICE, 2016; Nimmo et al., 2019). These monitors are however never used by UK pre-hospital teams. Key issues for the teams include the lack of clarity regarding the relative risk of accidental awareness in this patient group and the ideal depth of anaesthesia target for pre-hospital trauma patients, many of whom have a reduced level of consciousness prior to the induction of anaesthesia. There is, in general, a lack of compelling evidence supporting their pre-hospital use and well documented difficulties interpreting their output. Ketamine, a general anaesthetic with unique dissociative properties and relative haemodynamic stability is frequently used during pre-hospital callouts (Chapter Three, Results), but is associated with a paradoxical increase in BIS and E-Entropy values (Hajat et al., 2017; Lobo & Schraag, 2011). Many other patient and environmental factors, including hypoxaemia, bradycardia, brain injury and patient position have all been documented to affect depth of anaesthesia values

given by the monitors (Lobo & Schraag, 2011). Further issues include the reliability of the monitors during transport, (especially given the vibration encountered during transport) (Lobo & Schraag, 2011), the time and space consumed by the monitors and the financial implications for organisations largely funded by charitable donations (Duchateau et al., 2014; NICE, 2016; Ontario, 2004; Pandit & Cook, 2003). Before DOA monitors are incorporated into routine pre-hospital care, there should be strong evidence that they are effective, robust, and appropriate for use in pre-hospital conditions.

After participating in the survey most UK pre-hospital care services stated that they would suggest a review or change within their service, as they felt that their organisation was not meeting minimum safety standards. This is a positive reflection on the pre-hospital community's desire to continually enhance the services that they deliver. Most of the quality improvement changes envisioned involved the introduction of new equipment, which would have significant resource and funding implications, especially considering that the vast majority of pre-hospital care services rely on charitable donations. This illustrates the multi-factorial nature of the practice of PHEA and demonstrates the need for targeted funding.

It was interesting that some respondents felt that there was no indication for a change in practice, despite variable adherence to the guidelines. Many cited the lack of pre-hospital specific guidelines and stated that changes made to make practice more consistent with the guidelines were unreasonable, infeasible, and inappropriate. It is undeniable that human factors, weather conditions, patient physiology and stability, as well as resource and equipment availability all differ markedly from in hospital and increase the complexity of pre-hospital practice. The lack of relevance of the current guidelines to pre-hospital emergency practice is a notable weakness. Up-to-date evidence-based guidelines that are specific for PHEA and go further than stating that practice "*should meet hospital standards"* should be developed and disseminated.

6. Conclusion

Overall, these results show that UK PHEA practice conforms well with key national guidelines. The findings illustrate a variation in practice, which is likely to be appropriate and is supported by major professional bodies (Lockey et al., 2017). It is necessary to now continue to collect more data to facilitate a more comprehensive evaluation of pre-hospital practice with reference to a broader spectrum of recommendations.

The results do however suggest poor compliance with some of the published recommendations for TIVA. However, the TIVA guidelines were written primarily for the management of patients receiving

a continuous infusion of anaesthetic drugs in hospital, which differs from pre-hospital practice in many important ways. Whilst most clinicians stated that they would endeavour to improve their service's practices, there was disagreement regarding the utility and feasibility of fully adopting these guidelines.

Before pre-hospital services commit to investing substantial resources in meeting TIVA standards, further research is needed to investigate the optimal way of maintaining and monitoring pre-hospital emergency anaesthesia. Pre-hospital emergency anaesthesia is in many respects more challenging than routine anaesthesia in hospital and simply stating that PHEA "should meet the same standards as in hospital practice" (Lockey et al., 2017) whilst inspirationally sound, is perhaps unrealistic. Professional bodies may need to produce more tailored recommendations for pre-hospital anaesthetic practice given the unique nature of each scenario, however this remains a key area of future research.

Thematic analysis and schematic mapping demonstrated the multi-dimensional nature of UK PHEA practice and illustrated the network of interacting factors at play. Which of these factors are the most crucial and how they drive clinical decision making and clinical practice in this challenging and high-pressure environment remain to be fully elucidated. Once UK PHEA practice has been comprehensively described it will be necessary to further characterise the influence and contribution of these factors. It would be most valuable to conduct interviews with key stakeholders, such as personnel working for UK pre-hospital care services.

Chapter Four

The Maintenance of Anaesthesia following Pre-hospital Induction of Emergency Anaesthesia in the UK: Discussion

1. Introduction

The aim of this study was to investigate and thence describe how PHEA is maintained following pre-hospital induction by services across the UK, and to identify to what extent current practice reflects PHEA guidelines. This is the only survey to date to focus on the way in which PHEA is maintained. Given the importance of the topic, the lack of previously published literature is remarkable.

The research question has been investigated as follows: Chapter One – Introduction, Chapter Two – Scoping Review, Chapter Three – Secondary Data Analysis and Chapter Four – Discussion. Chapter 1 serves as an introduction to the topics of PHEM and PHEA, describes relevant background and contextualises the information. The structure of the thesis is also described in Chapter One and the research question is thence defined. Chapter Two takes the form of a scoping review that was conducted with the aim of determining the breadth and depth of the available literature and providing an overview of the evidence base. This chapter describes current practice and summarises key guidelines, later making an initial evaluation of practice with reference to the clinical guidelines. Chapter Three is based upon the analysis of a robust dataset that has recently been collected by expert clinical researchers from EMRTS Cymru, an example of an advanced pre-hospital care service. This stage of secondary data analysis builds upon findings from the scoping review and allows a deeper exploration of the topic. Results from Chapter Two and Three suggest that the way in which PHEA is maintained in the UK conforms well with major clinical guidelines but highlights a discrepancy between safety practices employed during the administration of TIVA and key TIVA recommendations that theoretically should be applied in all settings. It remains to be elucidated whether this discrepancy represents a weakness in the suitability of these guidelines for pre-hospital care, or whether clinical practice could be optimised.

2. Research approaches

The investigative approaches employed in this study were both appropriate and effective.

Scoping review

The scoping review successfully facilitated an initial analysis of the literature and provided an overview of both the maintenance of PHEA in the UK and the relevant clinical guidelines. The literature search returned three articles relevant to the first strand of the research question, and fourteen articles for the second strand of the research question

Based upon this early literature review it was possible to deduce that practices surrounding the maintenance of PHEA in the UK did appear to comply well with the guidelines, but that more research was necessary to specifically examine practice against a broader spectrum of key recommendations.

Research strand 1 – The maintenance of anaesthesia following pre-hospital induction of emergency anaesthesia in the UK

PHEM is a relatively new clinical field compared to more traditional specialties such as General Practice or General Internal Medicine and as demonstrated in schematic mapping (in Chapter Two - A Scoping Review, and Chapter Three - Secondary Data Analysis), PHEM and PHEA are subspecialist subjects embedded in a network of contextual complexity. These factors do not immediately facilitate the conduct of high-quality research and as a result there is a relative paucity of high value literature.

In this context strengths of the scoping review approach include the breadth of the search strategy and the volume and range of literature returned by the search. Articles screened for inclusion did not need to meet criteria of being a particular type, design nor methodology and could be heterogeneous in both content and format. This was beneficial considering the small body of available evidence - each article that could be included contributed a significant proportion of the cumulative pooled data. Furthermore, the diversity of literature that was reviewed using this approach aided deeper contextual understanding and mapping of the nuanced topic, even when some articles did not ultimately meet criteria for inclusion in the scoping review itself.

Research strand 2 – Guidelines for the maintenance of pre-hospital emergency anaesthesia

“Clinical practice guidelines have been upheld as an essential part of quality medical practice for several decades” (Kredo et al., 2016), and in recent years they have become even more abundant and popular. They are often used as a ‘simple’ way to try and optimise patient care and support best practice across a range of clinical specialties. Anaesthesia is no exception.

For this reason, the scoping review’s initial advantage of breadth and diversity became a weakness. Following the literature search many articles were returned that were of varying relevance and utility to the research question. It was difficult to establish boundaries and the lack of a quality

assessment process made interpretation and data synthesis challenging. Additionally, the higher number of articles that were included increased the workload and resulted in a less efficient process.

Nevertheless, the scoping review was ultimately successful in identifying guidelines that were relevant and important to the practice of PHEA.

Secondary data analysis

Secondary data analysis methodology was used to build upon initial findings from the scoping review, specifically to further examine the way in which pre-hospital teams currently maintain emergency anaesthesia, assessing practice against a greater number and range of variables.

This approach was based upon analysis of a dataset that had been collected by clinical researchers from EMRTS Cymru (Emergency Medical Retrieval and Transfer Service, Wales).

The key benefits of this approach were advantages of efficiency in both time and resources. As with primary data analysis the utility of data analysis can *theoretically* be limited by the quality of the dataset. In this case, the large dataset had recently been collected, it contained important and meaningful variables that were highly relevant to the research question, and it had been developed by expert clinicians active in the field of pre-hospital emergency medicine. Individuals from a large proportion of UK pre-hospital care services participated in the survey. The dataset benefitted from a sound and robust methodology, which the original researchers were happy to comprehensively share.

Thematic analysis demonstrated that key codes and themes relevant to this dataset showed considerable overlap with codes and themes identified during the scoping review phase (Chapter 2), supporting the utility and relevance of this dataset in supplementing initial investigative findings.

Whilst the dataset was extensive and of good quality, some variables of interest had not been collected or included. This meant that whilst it was still possible to answer the research question, it could, in theory, have been addressed more comprehensively.

On the other hand, the collection of a greater number and breadth of variables would have been more time consuming and demanding for both researchers and participants and may have decreased the survey response rate, thereby detrimentally affecting the generalisability and reliability of the results.

Overall, the secondary data analysis approach was highly effective in meeting the research objectives.

3. Impact of COVID-19 on study design and implementation

I had initially planned to conduct an in-depth case study analysis based upon Robert Yin methodology (Yin, 2012) after the completion of the scoping review and secondary data analysis stages. The aim of this stage was to further explore the factors that influence clinical decision making and practice in the pre-hospital setting and to assess the presence and significance of barriers preventing clinicians from practicing both in accordance with the guidelines and/or what they considered to be best practice. I planned to meet these objectives by conducting several semi-structured interviews with individual personnel from EMRTS Cymru (the Emergency Medical Retrieval and Transfer Service, Wales), an advanced pre-hospital service currently practising in the UK.

I planned to specifically examine: 1) Anaesthetic drug preferences and the rationale 2) Attitudes around the use of bolus, infusion, and TCI administration of sedative 3) Attitudes surrounding pre-hospital emergency anaesthesia guidelines in general, 4) Attitudes surrounding TIVA guidelines, 5) Any clinical issues which influence the maintenance of PHEA, 6) Any additional non-clinical factors which affect practice.

It was a disappointment that due to national COVID-19 restrictions I was unable to conduct this final stage of the study. Video conferencing had been considered as a potential way to overcome the problem imposed by social distancing rules, but due to staff redeployment and increased service pressures on anaesthetics and intensive care departments this was unfortunately not feasible.

This stage serves as a natural progression from the scoping review and secondary data analysis, and I hope that an in-depth case study analysis can be undertaken once restrictions allow.

4. Contextualised results

The aim of this study was to build a picture of how emergency anaesthesia is maintained following pre-hospital induction by services across the UK, and to identify to what extent current practice reflects PHEA guidelines. Despite the limitations imposed by national COVID-19 restrictions, by conducting a scoping review and secondary data analysis I was able to successfully answered the research question.

Thematic analysis and schematic mapping performed during the scoping review and secondary data analysis stages illustrated a network of interacting factors which actively influence the way in which PHEA is delivered. It demonstrated the complex, unique, context in which pre-hospital emergency treatment is delivered.

The results demonstrate a variation in practice but support the conclusion that UK PHEA practice conforms well with many national guidelines. The results do however suggest poor compliance with some of the published recommendations for total intravenous anaesthesia.

The apparent discrepancy between clinical practice guidelines and current practice can be *over*-simplified as resulting from either a weakness of the guidelines, or sub-optimal clinical practice. These possibilities are further explored below.

5. Reflections

During the scoping review process fourteen papers were highlighted as important papers containing recommendations which may be used to guide PHEA (AGGBI, 2008; Checketts et al., 2016; Checketts 2016; Checketts et al., 2017; Denning & Barley, 2015; FICM, 2019; Lockey & Porter 2007; Lockey et al., 2017; Luck & Morgan, 2019; Lumb & McLure, 2016; NICE, 2012; Nimmo et al., 2019; Paal et al., 2010; SALG, 2009).

Conducting the scoping review was an iterative process and it ultimately became apparent that there were two key papers whose summative contribution far outweighed the other papers (Lockey et al., 2017 & Nimmo et al., 2019). They were up-date, comprehensive and well endorsed guidelines, supported by the Association of Anaesthetists of Great Britain and Northern Ireland and other eminent professional bodies. One of these papers was written specifically with the aim of clarifying pre-hospital anaesthetic standards of care and updating relevant guidelines endorsed by key organisations (Lockey et al., 2017). The second paper was written to guide the safe practice of total intravenous anaesthesia, making specific recommendations for *how* intravenous anaesthesia is given, wherever that may be. (Nimmo et al., 2019).

The recommendations from both papers were generalised and applied to the field of PHEA, but one may wonder whether guidelines from the paper written by Nimmo et al., (2019) should have been. PHEA can be considered a distinct entity, different in many ways from anaesthesia given as part of elective/emergency general anaesthesia and anaesthesia given as part of critical care. Trauma is by far the most common clinical indication for PHEA in the UK (Burgess et al., 2018; McQueen et al 2015) and it is associated with a dramatically different spectrum and severity of morbidity and mortality compared to in hospital surgical and procedural intervention or critical care treatment. There is often a considerable risk to life and/or limb and time to definitive care is an essential determinant of outcome in PHEM (Abhilash & Sivanandan, 2020). Priority is understandably placed

upon achieving and maintaining physiological stability and expediting transfer to a trauma centre where definitive treatment can be given (Moran et al., 2018).

The administration and provision of ongoing anaesthesia (PHEA) during on scene emergency retrieval and transfer is thus performed in the context of a different set of primary and secondary aims and objectives. Key priorities include the facilitation of comprehensive patient and scene evaluation, the attainment of physiological stability, and the administration of emergency limb or life-saving treatment. Relieving the pain and suffering of patients is also a necessary priority for pre-hospital teams. In contrast hospital anaesthetic guidelines aim to address and minimise some of the more common and/or serious risks associated with general anaesthesia in hospital. Accidental awareness is a relatively rare (one to two patients per 1000 (Shepherd et al., 2013)), but serious complication associated with general anaesthesia. It occurs when a patient gains a degree of consciousness during a general anaesthetic and can recall surgical or procedural events during this period. It can be devastating for patients, and is a 'never event' for clinicians, representing the failure of successful anaesthesia. Serious risks to life, limb or major organ dysfunction are appreciably less common during routine anaesthesia, so in hospital anaesthesia guidelines tend to focus on mitigation of the more relevant risks. This helps us understand why emphasis in the TIVA guidelines is placed upon monitoring practices and devices used to ensure adequate 'depth of anaesthesia'.

In contrast the opposing risk of oversedation is appreciably more problematic in the field of PHEM. The administration of excessive doses of sedatives can exacerbate haemodynamic instability in already hypovolaemic trauma patients. The associated risks of multiorgan dysfunction, secondary brain injury and cardiac arrest confer major causes of morbidity and mortality and must be recognised. The use of TCI pumps may unnecessarily increase the risk of haemodynamic compromise associated with the administration of sedative drugs. TCI pumps rely upon the user inputting key patient characteristics, such as age and body weight, and then selecting a target effect-site concentration. The pump achieves the effect-site concentration by administering an initial bolus and subsequent infusion. The initial bolus of sedative is not user controlled and may cause cardiovascular compromise and risk exacerbating shock and/or causing major secondary injury. Indeed, the AAGBI advise that small, frequent boluses are used to mitigate this well recognised risk (Lockey et al., 2017).

The TIVA guidelines (Nimmo et al., 2019) recommend several pieces of equipment and monitoring devices that are likely to be available and beneficial in hospital, however several factors specific to the pre-hospital setting and the transport vehicle limit what equipment can realistically be used during pre-hospital callouts. As previously mentioned, time is of critical importance to pre-hospital care and any intervention that delays arrival in hospital may detrimentally affect outcome (Brown et

al., 2016; Moran et al., 2018). Equipment that is time intensive to set up or use is therefore unlikely to be advantageous. Denning & Barley (2015) argued that the setup for TIVA infusion pump systems as recommended by SALG (2009) and Nimmo et al., (2019) was overly complex and unlikely to be time efficient. The utility of equipment and monitoring devices used for PHEM is also restricted by space (on board the transport vehicle and at the scene), the weather and environmental factors including lighting, and other transport considerations. Depth of anaesthesia monitors are recommended whenever TIVA is given with neuromuscular blockade (Nimmo et al., 2019), however these monitors have been shown to be susceptible to vibrations from air warming blankets used in hospital (Kertai et al., 2012) and are therefore unlikely to be reliable in the context of vibrations arising from air or road transport.

The economic implications of practice recommendations must also be carefully considered by pre-hospital care organisations. These services rely upon charitable donations and operate within financial constraints. Costly interventions will only be supported if they confer a significant benefit to patient outcome that is well supported in the literature. The cost of a single depth of anaesthesia monitor alone varies from almost £5000 to more than £10,0000 and further costs arise from the acquisition of single-use sensors (NICE, 2012). Before pre-hospital organisations commit to investing considerable funds in the acquisition and application of these monitors, they must first consider the evidence of impact on patient outcomes and the cost-effectiveness of the intervention. The relative benefit of the intervention must then be balanced against any compromise that must be made in the procurement of alternative resources. At present strong evidence of benefit of depth of anaesthesia monitors is lacking and they are therefore unlikely to be a cost-effective investment.

In contrast to the guidelines written by Nimmo et al., (2019) Lockey et al., (2017) produced a set of guidelines that are more general in nature. They assert standards of practice that should be met during pre-hospital anaesthetic practice, suggesting that with few exceptions standards should meet the usual AAGBI guidelines for hospital anaesthesia. Whilst Lockey et al., (2017) make recommendations for monitoring, equipment and clinical practices they do not dictate how PHEA should be pharmacologically maintained. The authors acknowledge that the quality of the evidence base guiding PHEA (and pre-hospital care in general) is still relatively poor and they recommend that due consideration be taken before such decisions are made. This appears to be an appropriate recommendation and allows highly skilled, experienced clinicians the freedom to meet the needs of their patients in the most appropriate manner.

As previously described, pre-hospital emergency medicine is a relatively new subspecialty, for which training was only formally approved in 2012 (Hyde et al., 2014). When the paper authored by Lockey

et al., (2017) was written, pre-hospital emergency medicine was still in its infancy, and it was understandable that leading experts in the field supported the extrapolation of standards of practice and guidelines used in closely related fields of anaesthesia, emergency medicine or critical care. However, decision making in pre-hospital emergency medicine must consider not only clinical care, but also scene management skills and wider environmental factors, rescue competencies, resource issues and extraction and retrieval logistics (Wilson et al., 2015). Time is also critically important in pre-hospital care, as evidenced by the remarkable impact that the early use of simple interventions such as tourniquets and tranexamic acid have (CRASH-2 trial collaborators, 2010; Kragh et al., 2009). As PHEM is increasingly recognised as its own subspecialty, with unique characteristics and incomparable demands there is a growing need for the specialty to establish its own set of guidelines and standards of practice rather than merely stating that "practice should meet the same standards as hospital" (Lockey et al., 2017). At present the evidence base for pre-hospital interventions is relatively weak and the sparsity of publications specifically addressing PHEA is remarkable. This is a key area for future research.

Pre-hospital care services in the UK are regional organisations that operate independently of one another. These services usually develop their own standard operating procedures (SOPs) which influence clinical decision making on a day-to-day basis. Many pre-hospital care services document recommendations for primary anaesthetic agents in their SOPs (Lockey et al., 2015). MAGPAS Air Ambulance, for example recommends ketamine (10 mg/ml), fentanyl (50 micrograms/ml) and rocuronium (10mg/ml) as first choice anaesthetic drugs (MAGPAS, 2018). They discuss special circumstances and make suggestions for modifications in the context of the haemodynamically compromised, elderly or moribund patients. Clinicians working for these organisations may not have ultimate freedom of choice when deciding which anaesthetic agents to use. Their choice will be limited by what drugs are favoured and procured by their service.

Clinical practice guidelines have been used throughout this piece of research as indicators of performance and whilst they should reflect best practice in most circumstances, they were never intended for this purpose (Tetreault et al., 2019). Quality pre-hospital care, as in any setting, relies upon the sound integration of evidence, clinical knowledge and experience and individual clinical and patient circumstances. There is therefore some flexibility in the application of guidelines (Eddy, 1990) and lack of concordance with the guidelines does not necessarily equate to poor practice. Similarly, compliance with the guidelines does not ensure optimal patient outcome. One could argue that comparison of practice against the guidelines does not represent the best nor the fairest method of practice evaluation. In future research it may be better to identify patient outcomes of

genuine importance, whether that be survival or functional outcome, and use these values as indicators of performance.

It is highly plausible that there is no one optimal way of maintaining PHEA that can be described in a single set of guidelines. PHEA is typically performed for critically ill patients with markedly perturbed physiology, where clinical information is scarce and environmental conditions are often challenging. These factors are highly interchangeable and combine to create a unique scenario with specific patient care priorities. PHEA is a complex intervention, which is itself associated with significant risks. It must be appropriately tailored to the individual patient's requirements with a view to maintaining physiological stability, administering lifesaving treatment, and expediting transfer to a definitive care setting, whilst minimising risks of iatrogenic harm. It has been argued that the efficacy of pre-hospital emergency care services is strongly determined by the ability of clinicians to appropriately individualise the care they give (Voelckel et al., 2018). The argument for high level clinical decision making is supported by the fact that only senior clinicians with years of training and experience can perform PHEA.

Some argue that there and now too many clinical practice guidelines and that we rely upon them too heavily (Baker, 2014; Carthey et al., 2011). Regardless, it may ultimately not be possible to develop a set of guidelines for the maintenance of pre-hospital emergency anaesthesia. Instead, a set of standards of practice that pays due attention to the varying circumstances in which PHEA is delivered may be most appropriate. This would highlight the most important universally accepted standards of practice but still allow clinicians the freedom to tailor management to the patient and setting.

6. Recommendations for future research

Initially it would be useful to conduct further research to 'complete the picture' of how PHEA is conducted. This would involve the collection of more data and an evaluation of practice against a greater number and range of variables. For example, these variables may include: a) the indication for PHEA, b) factors restricting the provision of PHEA, c) factors restricting the way in which it can be delivered, c) the clinician providing PHEA (background, training and experience/seniority) and d) other health care professionals present in a supportive position. Ideally this survey would again include all currently practising UK services in order to enhance the generalisability of the results.

As previously discussed, the literature review for this study was based upon scoping review methodology that was associated with key advantages of breadth and heterogeneity of included literature. One potential weakness of this study lies in the fact that pre-hospital practice was

principally evaluated against two guideline papers (Lockey et al., 2017; Nimmo et al., 2019), neither of which had been critically appraised. To increase the strength and reliability of similar studies, in the future if would be advantageous to perform a formal a critical appraisal of the relevant clinical practice guidelines either as part of, or after the initial literature review.

Next it would be important to investigate factors affecting clinical decision making surrounding PHEA. This would be best met by conducting an in-depth case study analysis, similar in many ways to the one which had been planned as Phase III of this study. This case study analysis would benefit from methodology as described by Yin (2012) and would look to consider the *whys* rather than the *hows*. This exploratory analysis is unlikely to provide a single clear-cut answer, but will help deepen our understanding of the human factors at play as well as the clinical, logistical and organisational issues.

As part of the original survey developed and conducted by clinicians from EMRTS (and later analysed in Chapter Three), participants were asked whether they would consider making changes to their practice in light of the guidelines mentioned. A brief follow-up study to establish if any changes had been made and if so, what changes, would be interesting.

There is a need to further build the evidence base upon which pre-hospital care is delivered. Whilst current guidelines have been developed using the best available evidence, increased focus should be placed on identifying and clearly defining gaps in our knowledge and making efforts to address these areas. Where previous pre-hospital recommendations for practice have been extrapolated from 'similar' clinical scenarios during in-hospital anaesthesia or critical care, increased focus must now be placed upon developing the subspecialties own research with a view to establishing pre-hospital specific CPGs.

Whilst it may seem easy to make recommendations for future research in the field of PHEM, the reality is that conducting research of high value in this field is inherently difficult. For example, when considering how you could accurately record (and later evaluate) on-scene management of pre-hospital cases, the time critical nature, combined with unpleasant or problematic environmental conditions and critically ill patients make it challenging to prioritise 'real-time' research. Options include implementing automatic recording systems (video or equipment-based records), which could be supplemented by post-event interviews with clinicians. Video recording may be most accurate but may be practically challenging to set up and may feel invasive to the lead clinician and wider team, adding an unnecessary level of stress to the high-pressure environment. On the other hand, if used alone post-events interviews may be subject to incomplete/inaccurate recollections and may be influenced by stress experienced during the case.

7. Conclusion

This study contributes to the development of the evidence base for PHEM and is the only study to date to specifically investigate the way that anaesthesia is maintained following pre-hospital induction in the UK. Overall, these results show that UK PHEA practice conforms well with key national guidelines (Lockey et al., 2017) but there is a discrepancy between the recommended method of administering TIVA (Nimmo et al., 2019) and how ongoing anaesthesia is administered during pre-hospital extraction and retrieval. Further research is required to build the evidence base surrounding PHEM and PHEA with a view to establishing the subspecialties own comprehensive yet specific standards of practice.

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Appendix 1

Pre-hospital maintenance of sedation/anaesthesia study - data collection form

We are conducting a short, UK wide, survey reviewing how sedation/anaesthesia in maintained following a pre-hospital rapid sequence induction. For clarity, please only consider patients who are given anaesthetic induction agents (for example disregard patients who were intubated during cardiac arrest and then had sedation maintained) as part of a Pre-Hospital Emergency Anaesthetic (PHEA). Medical and trauma patients can be considered and you will find the answers very generic. Please answer all questions and make comments in the free text areas if you wish. Please note that Q1 has been included so we can monitor the responses easily and send reminders as appropriate. We will not use this data to present specific organisations results/responses, rather the results will be presented in a generic fashion.
Thank you for your help. Kind regards Dr Jon Birks (Consultant in Anaesthesia & PHEM) and Dr David Green (Anaesthetic ST6)
*Required

Which organisation are you answering for? (Please choose one option only. If you have been asked to complete this for 2 organisations, please do the survey twice) *
Choose

Scotland's Charity AA
EMRS Scotland
Great North AA
Yorkshire AA
North West AA Charity
Lincs and Notts AA
Wales AA/EMRTS
Midlands AA Charity
TAAS
Magpas
East Anglian AA
London's AA
Thames Valley AA
Kent, Surrey, Sussex AA
Essex and Herts AA
Great Western AA
Wiltshire AA
Hampshire and Isle of Wight AA
Dorset and Somerset AA
Cornwall AA trust
Devon AA
Air Ambulance NI
BASICS Scotland - Highland

BASICS Scotland – Grampian
BASICS Scotland – East and Borders
BASICS Scotland – West Region
BASICS Scotland – Central
BASICS Scotland – Highland; Western Isles, Orkney and Shetland
BASICS Ambulance North East
BASICS North West
Penrith BEEP
SMART – South Manchester Accident Rescue Team
Cheshire and Shropshire BASICS
Yorkshire Ambulance Service BASICS
LIVES
EMICS
West Midlands CARE Team
Mercia Accident and Rescue Service
North Staffordshire BASICS
Norfolk Accident and Rescue Scheme
Suffolk Accident and Rescue Scheme
BASICS Essex Accident Rescue Scheme
BASICS Hertfordshire
North Wales Emergency Doctor Service
MEDSERVE Wales
Montgomery Emergency Doctor Service
BASICS Thames Valley
BASICS London
Millwall FC Medical Team
BASICS Cornwall
BASICS Devon
SAVES – Somerset
Swift Medics – Wiltshire
BASICS – Gloucestershire
SIMCAS

Does your service/organisation perform pre-hospital emergency anaesthesia (PHEA)? *

- ☐ Yes
- ☐ No

Pre-Hospital Emergency Anaesthesia

Following a PHEA, how does your service routinely convey patients to hospital?

- ☐ Road only
- ☐ Air Only
- ☐ Road & air

During the journey to hospital following on-scene PHEA, how does your service routinely give ongoing anaesthesia?

- ☐ Bolus only
- ☐ Continuous infusion (ml/hr)

- ☐ Continuous infusion using target-controlled infusion e.g. plasma/effect site (TCI)

Depth of anaesthesia

Does your service routinely use depth of anaesthesia monitoring systems in patients who have undergone PHEA (e.g. BIS, Entropy)?

- ☐ Yes
- ☐ No

Lines

Considering the infusion lines, Y-connectors, 3-way taps etc that your service utilizes to deliver anaesthetic agent(s), please indicate which of the following features are satisfied by selecting the appropriate boxes. Please select all that apply.

- ☐ When administering fluid/blood products via the same IV cannula as the anaesthetic/sedative agents, is there always one-way valve on the IV line?
- ☐ Our service's PHEA Standard Operating Procedure/Guideline suggest that the IV cannula being used to deliver the sedative/anaesthetic agent is visually inspected at regular intervals.
- ☐ Our service always ensures that all one-way valves purchased are clearly labelled as such.
- ☐ Our services' IV infusion lines used for PHEA all include anti-siphon values at the syringe end of the line.
- ☐ Our IV infusion lines used for PHEA lines are made from 'kink resistant' material.
- ☐ None of the above

Pre-hospital maintenance of sedation/anaesthesia study

Intravenous agents

Which of the following drugs does your service have available for use in ongoing maintenance of anaesthesia/sedation? Please select all that are available.

- ☐ Morphine
- ☐ Midazolam
- ☐ Ketamine
- ☐ Thiopentone
- ☐ Propofol
- ☐ Remifentanil
- ☐ Fentanyl
- ☐ Other:

Which of these drugs/drug combinations is the MOST COMMONLY used for sedation/maintenance of anaesthesia within your service? Please select one option only.

- ☐ Ketamine infusion
- ☐ Ketamine boluses
- ☐ Propofol infusion
- ☐ Propofol boluses
- ☐ Midazolam and morphine boluses
- ☐ Midazolam infusion with morphine boluses
- ☐ Midazolam and morphine infusions
- ☐ Midazolam and ketamine infusion

- ☐ Propofol and morphine infusions
- ☐ Propofol infusion with morphine boluses
- ☐ Propofol and fentanyl infusions
- ☐ Propofol infusion with fentanyl boluses
- ☐ Propofol and remifentanil infusions
- ☐ Thiopentone infusion and morphine boluses
- ☐ Thiopentone infusion and fentanyl boluses
- ☐ Unable to comment
- ☐ Other:

Infusion Pumps

Does your service have pumps that have a target controlled infusion (TCI) capability within their programming (effect or plasma site)?

- ☐ Yes
- ☐ No

Funding

How is your service's equipment that is used for maintenance of anaesthesia (eg the infusion lines and pumps etc) purchased?

- ☐ NHS funding
- ☐ Charitable funds
- ☐ Mixture of above
- ☐ Other:

Untitled section

Having participated in this survey and been sent a copy of the 'Safe anaesthesia Liaison Group 'Guaranteeing Drug Delivery in Total Intravenous Anaesthesia' document as part of the invitation, will you, with help from any relevant colleagues within your organization or service...? Please select one answer only.

- ☐ Not suggest any reviews or changes within your service as you are not convinced there is any need
- ☐ Not suggest any reviews or changes within your service as you are certain all minimum suggested safety criteria are already being met
- ☐ Suggest a review or change within your service as you are not certain all minimum suggested safety criteria have been met
- ☐ Suggest a review or change within your service as although you feel all minimum suggested safety criteria have been met, you consider that some potentially aspirational standards could be introduced
- ☐ Other:

If in the question above you selected 'suggest a review', which would be the area of your focus?

Your answer

Thank you for your help!!

BACK

Appendix 2

List of pre-hospital organisations practising in the UK & included in the study

Scotland's Charity AA

EMRS Scotland

Great North AA

Yorkshire AA

North West AA Charity

Lincs and Notts AA

Wales AA/EMRTS

Midlands AA Charity

TAAS

Magpas

East Anglian AA

London's AA

Thames Valley AA

Kent, Surrey, Sussex AA

Essex and Herts AA

Great Western AA

Wiltshire AA

Hampshire and Isle of Wight AA

Dorset and Somerset AA

Cornwall AA trust

Devon AA

Air Ambulance NI

BASICS Scotland - Highland

BASICS Scotland – Grampian

BASICS Scotland – East and Borders

BASICS Scotland – West Region

BASICS Scotland – Central

BASICS Scotland – Highland; Western Isles, Orkney and Shetland

BASICS Ambulance North East

BASICS North West

Penrith BEEP

SMART – South Manchester Accident Rescue Team

Cheshire and Shropshire BASICS

Yorkshire Ambulance Service BASICS

LIVES

EMICS

West Midlands CARE Team

Mercia Accident and Rescue Service

North Staffordshire BASICS

Norfolk Accident and Rescue Scheme

Suffolk Accident and Rescue Scheme

BASICS Essex Accident Rescue Scheme

BASICS Hertfordshire

North Wales Emergency Doctor Service

MEDSERVE Wales

Montgomery Emergency Doctor Service

BASICS Thames Valley

BASICS London

Millwall FC Medical Team

BASICS Cornwall

BASICS Devon

SAVES – Somerset

Swift Medics – Wiltshire

BASICS – Gloucestershire

SIMCAS