Optimisation of cat neutering anaesthesia protocols for use in the community

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Declaration

I declare that the work in this dissertation was carried out in accordance with the requirements of the Universities regulations and code of practice for Research Degree Programmes and that it has not been submitted for any other academic award. Except where indicated by specific reference in the text, the work is the candidate's own work. Work done in collaboration with, or with the assistance of, others, is indicated as such. Any views in the dissertation are those of the author.

SIGNED: *Albert Holgate* DATE: *27.02.2021*

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Abstract

The aim of this study was to compare the two opioids methadone and buprenorphine in sedative combinations administered to cats undergoing castration in a high-volume neutering setting. Both combinations were used prior to orchidectomy in cats (Routine Cat Castrations) as part of a 'drop-in clinic' with no prior appointments required. The overall outcome was to determine a combination to best enable a safe, quick, effective turnover of neuters with limited financial, infrastructure and staffing resources.

A total of 166 cats were recruited as part of this clinical trial. This included 15 cases as part of a pilot study. The aim was to gain two equal numbers for each group over a set period of time. Quantitative planning of the total study was not known as this was incorporated as part of a working teaching unit in conjunction with Nottingham university. The drop-in clinic took place every Friday which allowed an open appointment system from different demographics such as vet triage, owned patients, multi-cat household, stray and ferals as part of an TNR programme.

Cats received one of two possible combinations, medetomidine 600mcg/m² with buprenorphine 180mcg/m² (MB) or medetomidine 500mcg/m² with methadone 5mg/m² (MM) administered intramuscularly (IM).

Sedation was scored using a modified simple descriptive score (SDS) 10 minutes after administering the initial injection. Anaesthesia was induced using isoflurane administered in 100% oxygen via a tight-fitting face mask connected to an Ayres T piece with Jackson Rees modification. Parameters were recorded at 5-minute intervals intraoperatively. At the end of surgery isoflurane was discontinued and one minute later atipamezole was administered IM. The recovery stage was monitored and timing to sternal recumbency followed by portal exploration were recorded. Data collection was recorded on anaesthetic record sheets and transposed to an Excel spreadsheet at a later date.

The medetomidine and methadone combination had significantly higher sedation scores using the SDS modified system. This result included an element of mask induction assessment when compared to the use of the medetomidine and buprenorphine combination, which consistently scored low on the SDS system. Methadone provided superior sedation to buprenorphine prior to anaesthesia maintenance using mask induction as part of the protocol. The recovery data showed both sternal and portal times were significantly shorter with medetomidine and methadone compared to medetomidine and buprenorphine.

Both combinations proved suitable for cat castration anaesthesia. Using the methadone combination can increase the turnover of patients contributing to improved welfare and optimising resources.

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Table of Abbreviations

ASA	American Society of Anaesthesiologists
BSA	body surface area
BUP	buprenorphine
ET	endotracheal tube
HR	heart rate
ISFM	International Society of Feline Medicine
IM	intramuscular
ISO	isoflurane
IV	intravenous
KG	kilogram
MAC	minimum alveolar concentration
MAP	mean arterial pressure
MB	medetomidine and buprenorphine
MG	milligrams
MM	medetomidine and methadone
MET	methadone
NRS	numerical rating scale
OTM	oral transmucosal
OVH	ovariohysterectomy
PPM	parts per million
RR	respiration rate
SC	subcutaneous
SDS	simple descriptive score

SPO_2	arterial haemoglobin saturation with oxygen
TNR	trap, neuter and release
UK	United Kingdom
WEL	work exposure limit

1.0 Introduction

Overpopulation of felines in the United Kingdom (UK) poses a major problem for most welfare organisations. The factors are complex and intertwined, and specific for the owned and unowned population. Relinquishment places enormous demands on shelters in terms of economics and this in turn reduces the ability of rehoming of animals (Stavisky et al. 2012). Understanding the nature of these populations would enable resources to be targeted in the right direction thereby improving animal welfare. The issue of unplanned pregnancies through uncontrolled reproduction in the stray and unowned cats population is also exacerbated by issues such as lifestyles of ownership, pre-expectations of owning a cat and lack of owner education as a strong factor. Statistically it has been shown that there are 7.5 million cats in the UK (Pet Population report 2019, Pet Food Manufacturers Association). There are also an estimated 23% of UK households having at least one cat, with some evidence indicating that up to 39% of the population may own more than one feline, illustrating the potential for overpopulation (Hill et al. 2019). Yet, quantifying the ownership of cats is complex, with Stravinsky et al., (2012) suggesting that it is less common for more than two cats to be owned (Stavisky et al. 2012).

A figure of ownership which is deemed as a ‘problematic’ situation for welfare organisations by way of interventions, is defined as the number of animals exceeding the owner’s capacity for care. Some North

American states have even set thresholds for cat ownership which clearly defines excess or a given concern of hoarding (Hayes 2010).

Hoarding is a huge problem for shelters due to the intermittent yet significant influx of animals in any given period. This creates problems with staffing and space management. Dealing with hoarding is complex in itself as a pathological accumulation of animals are not necessarily focused on cats as a species but could also be an accumulation of inanimate objects which serves to provide a level of comfort due to the underlying cause of trauma. Further research is needed to characterise the reasoning with underlying causes. Hoarding behaviour is typically associated with mental illness which requires managed support usually through a network of specialised counsellors with expertise in areas such as obsessive-compulsive disorders.

Owners' lack of knowledge is also a factor in feline reproduction. This oversight contributed to an estimated shelter intake of 130,000 to 150,000 cats during the period of 2009 and 2010 (Welsh et al. 2014, Welsh 2018). More recently statistics from the R.S.P.C.A have seen 29,432 cats brought into their shelters in 2019 alone (R.S.P.C.A, 2021). The constant influx of animals can have a negative impact on welfare within shelters as those cats kept for prolonged periods of time prior to rehoming are at an increased risk of psychological and physical impairments (Patronek 2012, Jacobson et al. 2020).

Welfare organisations in the UK are now employing innovative approaches through education and awareness programmes to highlight the importance of prepubertal neutering. The traditional accepted age of neutering was 5 to 8 months; however, studies have shown that early age neutered cats (6 - 14 weeks) have lower morbidity, and there are no behavioural or physical differences (Roberts and Clements 2015). The employment of new, safe and reliable anaesthesia and surgical techniques means this can be performed effectively. The implications of prepubertal neutering for welfare charities are enormous especially when resources are considered, for example cost factors of anaesthetic drugs. In the private sector, 28% of all veterinarians are undertaking early age neutering so the welfare principles must continue to be reinforced as an advantage to promote this further (Murray and Skillings 2008, Welsh 2018). A recent study surveying a cross section of the UK public has shown that more than 80% support the practice of routine neutering (Wongsaengchan and McKeegan 2019). It is known that the proportion of accidental litters is as much as 80%. This figure was reported in a survey from 715 cat owning households (Welsh et al. 2014). The informed approach to preventing accidental litters through precautions is effective along with veterinary neutering. Such examples are knowledge of puberty timings, segregation of young pubescent queens and prepubertal neutering.

The Cat Group, which is a collective collaboration of welfare organisations have a policy statement, states that there is a strong case for neutering earlier than the traditional age of six months on the grounds of social, health and population reasons (The Cat Group, 2006). In some cases, feral cats are being neutered as early as eight weeks. This in turn assists the RSPCA which is striving to reduce the acceptable age of neutering to 10-12 weeks and is promoting this through education initiatives. The cost benefit of this approach is difficult to ignore and deny. Equally though, it is important to promote control of unowned cats such as feral colonies which can pose a persistent problem.

It has been suggested that euthanasia as a means of population control could be considered. There has been some success with a dramatic decline in population numbers but only on small islands (under 5km²) successfully, and these were inhabited by people. This is a controversial view and not often favoured by welfare organisations (McCarthy, Levine, and Reed 2013).

One study evaluated three methods of feral cat population control (euthanasia, trap-neuter and release and trap-vasectomy-hysterectomy and release) (McCarthy, Levine, and Reed 2013). This study found that annual capture rates of above 97%, for all the methods appeared to be effective in reducing population sizes but lethal control was most effective out of the three. Trap-vasectomy-hysterectomy appeared to be effective at annual capture rates of between 19% and 97%. From the study it showed that trap, neuter and release did not outperform the other methods. In contrast despite the methods, it is known that lethal control

is unacceptable to the general public and welfare organisations are careful not to have this perception of an acceptable means of control.
One of the RSPCA's neutering campaign involves an initiative having a purpose-built vehicle which can perform 'off site' i.e. away from the hospital work and target specific areas of the community (Figure 1). This is ideal for approaching multi-cat households, a product of hoarding, resulting in owner's poor compliance with their welfare requirements. Such circumstances are often associated with mental health illness in the caregivers, inevitably leading to scenarios of poor husbandry conditions with evidence of poor socialisation and neglect potentially requiring euthanasia (Polak et al. 2014, Hill et al. 2019, Jacobson et al 2020).

Furthermore, confinement of cats in a rehoming facility for a significant period can also potentially cause stress in itself. This could pose health risks to staff such as human related aggression. Studies have shown that neutering male kittens from an early age reduced unwanted behaviours such as urine spraying and also aggression. Castrated males have shown to have a longer lifespan with 62% of neutered cats living longer than entire males (Wongsaengchan and McKeegan 2019). Female cats have been shown to have a 91% reduction in mammary carcinomas if spaying occurred prior to the age of 6 months (Joyce and Yates 2011). From a welfare perspective the duration of hospitalisation of feral animals undergoing neutering and treatment should be minimised, and animals always returned to the place of capture (Sparkes et al. 2013). This supports the development of suitable anaesthetic regimes in mobile facilities in order to reduce time, hospitalisation and cost associated with neutering and improve animal welfare.

To date numerous anaesthetic combinations with different analgesic effects and recovery profiles have been evaluated in cats. A multitude of studies have been undertaken evaluating alpha 2 agonist and opioids combinations followed by volatile agents with and without ketamine. Additionally, protocols incorporating propofol and alfaxalone have been studied. A recent refinement of a benzodiazepine added to the Triple combination of ketamine, alpha 2 agonist and opioid has been employed successfully for early neutering. These combinations are detailed below. (Shah et al. 2019, Polson et al. 2012, Moser et al. 2020, Mahdmina et al. 2020).

Figure 1: - RSPCA vehicle specifically designed for the multicat interventions.

2.0 Literature review

2.1 Surgical Procedures

Neutering of cats is by far one of the most common surgical procedures undertaken in veterinary practice. Population concerns is one of the cited reasons for this from the profession along with welfare concerns such as those shared by the RSPCA. Reproductive diseases involving the prostate, testes, the uterus, ovaries and mammary glands can be reduced. Unwanted behaviours such as vocalising and roaming leading to feral and large colonies in stray populations are also factors to be considered.

2.1 a. Ovariohysterectomy in the cat

The ovariohysterectomy (OVH) surgery can be performed via a midline approach or flank approach. From a veterinary student's perspective, the midline approach is preferred to the flank as this allows for better visualisation of the uterus and also to assist dealing with any potential pregnancies if necessary. In some cases, if access proves difficult, the incision can be extended. The definition of OVH is complete removal of the uterus and ovaries. It is cited that 96% of UK surgeons do in fact use the flank approach (Grint et al. 2006). The procedure involves locating the ovaries by following the uterine horns once the abdominal cavity is entered. Ligaments from the ovaries to the abdominal wall are ruptured.

The ovarian blood vessels are clamped and ligated which allows exteriorisation of the ovaries and uterus, which is then clamped and ligated above the cervix. The is followed by closure of the layers of the abdominal wall using appropriate suture material.

2.1 b. Orchidectomy in the cat.

The orchidectomy procedure is relatively quick surgery involving an incision of each scrotal sac through which each testicle is completely removed. Ductus deferens are used to tie off spermatic vessels in an open castration technique, this method usually involves no sutures. There are other techniques employed such as spermatic bundles ligated with suture material usually absorbable and the latter technique is the use of haemostats in a technique where the spermatic bundle is tied upon itself (Porters et al. 2014). Approximately 1% of all kittens presented especially in early castrations are known to be cryptorchid which emphasises the importance of pre-anaesthesia checks and testes palpation prior to undertaking the procedure (Yates et al. 2003).

2.2 Anaesthetic Drugs

2.2 a Multimodal anaesthesia

The following literature review explores the different components of balanced anaesthesia. From a welfare perspective for charities, it is also necessary to identify practicalities and consider cost as this may be different to the private veterinary sector.

A multimodal approach describes using more than one drug, each having a measured mechanism of action (Corletto 2007). Balanced analgesia using a combination of drugs which affects nociception in different ways in the body is well recognised (Brown, Pavone, and Naranjo 2018). The theory behind the multimodal approach is to combine different mechanisms of action and also reduce the volume of each component, which is also a crucial factor in terms of cost especially from a shelter medicine perspective. This will reduce the incidence of side effects from higher doses of the individual drugs.

In charity practice anaesthesia, the intramuscular (IM) route is often utilised and preferred. The reason for this is both ease of administration and there is a time factor to consider for aseptic venepuncture techniques. Additionally, from an early neuter perspective, venous access may not always be possible because of the size of the kittens. Given that the aim is quick turnover of neuters in a short period of time especially in multi-cat household intervention programmes a quick, simple and easy to administer anaesthetic is paramount.

The multimodal approach can also include a method of producing doses of equal volumes (Mahdmina et al. 2020) facilitating the procedure and reducing the likelihood of error.

Mask induction of anaesthesia can be used as part of the multimodal protocol especially in a charity setting as this ensures a more rapid progression of induction of anaesthesia reducing overall time of anaesthesia.

The following is an overview of each component used individually in a multimodal approach.

2.2.b, Medetomidine

Anaesthetic protocols including alpha-2 adrenoreceptor agonists (a-2 agonist) have frequently been used in neutering programs in shelter medicine. This has been documented since 1994 (Granholm et al. 2007, Ansah, Raekallio, and Vainio 1998, Harrison et al. 2011).

Medetomidine is widely given as part of a Quad protocol which bases the calculation on body surface area (BSA) initially at 1000 ug/m^2 rather than bodyweight. In essence, cats will tend to be given higher volumes of medetomidine based on lower body mass because of the calculation of BSA (Joyce and Yates 2011).

The Quad was developed using medetomidine, buprenorphine, midazolam and ketamine and it is usually prepared in four equal doses using the Kitten Quad calculator (Clancy 2016).

The licensed dose of medetomidine for cats according to the manufacturer's guidelines is 50–100 ug/kg with a volume of 0.25–0.5ml/5kg for moderate sedation and 100–150 μg/kg with a volume of 0.5–0.75 ml/5kg for deep sedation (Dechra products).

Medetomidine is a racemic mixture of two optical enantiomers, dexmedetomidine and medetomidine. Studies have found the L-isomer component of the medetomidine is inactive and has no biological activity although drug interaction has a role. Racemic medetomidine is lipophilic which offers a rapid onset of absorption after administration via the intramuscular route with peak plasma concentrations evident on average after 30 minutes (Lamont 2009). Medetomidine does negatively impact the regulation of body temperature which could be an issue with younger patients and considerations must be made to ensure assistive support is given (MacDonald, Scheinin, and Scheinin 1988). Medetomidine may also cause hyperglycaemia during anaesthesia by a reduction of insulin secretion (Sinclair 2003, Guedes et al. 2013). The impact of this in a short anaesthetic is unknown. The benefits of medetomidine are reliable sedation, muscle relaxation, analgesia and also importantly it reduces the requirements for inhalation agents such as isoflurane (anaesthetic sparing) (Sinclair 2003). The reported duration of action will depend on other components such as the opioid. Studies have shown that the duration of antinociception of medetomidine with buprenorphine is 6–8 hours; when combined with methadone this is shorter at 4–6 hours and lastly the use of butorphanol combined with medetomidine provided 2 hours antinociception (Slingsby, Bortolami, and Murrell 2015).

There have been some studies which have suggested that dexmedetomidine offers marginally superior analgesia compared to those using medetomidine (Bruniges, Taylor, and Yates 2016). Recent studies comparing dexmedetomidine and medetomidine have included antinociceptive effect assessment whereas previously behavioural assessment models were used. Further work in this area is required.

One key advantage of alpha-2 agonists is the ability to antagonise the drugs with an alpha-2 antagonist such as atipamezole. The recovery from medetomidine is commonly associated with ataxia which atipamezole minimises through shortening the duration of recovery or even to the point of eliminating the effects of medetomidine sedation (El-Kammar and Gad 2014). The alpha-2 antagonist can also be used if adverse reactions occur or if poor anaesthesia and / or recovery is evident. Antagonism often utilises a dose of atipamezole equivalent to half the initial medetomidine dose. However, this can cause adverse reactions which are often reported as vomiting and diarrhoea (DeClementi 2007). The effects of atipamezole on sedation versus antinociception are limited and further study in this area is warranted (Vähä-Vahe 1990).

2.2.c Ketamine

Ketamine use is commonplace in veterinary anaesthesia. Ketamine is a dissociative anaesthetic and has antinociceptive properties. A dissociative (cataleptic) state is characterised by increased muscle tone, and unconsciousness. Some physical signs such as excessive eye movements (nystagmus), limb movements and open eyes are also evident which can be counteracted with a combination of additional drugs. Ketamine has a wide safety margin and is a component of many multimodal protocols.

Ketamine is rarely used as a sole agent due to the poor anaesthesia and muscle rigidity hence the use of other drugs as part of a combination to offset these undesirable effects (Glen 1973). Respiration and cardiovascular systems are only depressed when ketamine is used in high doses (Giroux et al. 2015). However, in one study using medetomidine administered with ketamine, 80% were reported to have developed a decreased rate of respiration and apnoea due to vasoconstriction (Verstegen, Fargetton, and Ectors 1989). Ketamine can be administered either IM or intravenously (IV) although it is most commonly given via the IM route for ease of administration.

Ketamine is particularly useful in feral cat management because these animals cannot be handled easily. Feral cats are often an unknown weight, age and health status. This requires anaesthesia with a wide safety margin, providing a quick recovery, so that the cats can be returned to their natural environment optimising their welfare (Harrison et al. 2011).

Ketamine can also be used to improve the plane of anaesthesia in lengthy procedures, such as ovariohysterectomy in pregnant feline patients or those requiring additional diagnostic or surgical procedures (Harrison et al. 2011).

Early studies using ketamine as part of a protocol, such as medetomidine (80µg/kg) with ketamine 10mg/kg, showed no reflex responses when the ovarian ligament / pedicle was ligated during surgery (Verstegen et al. 1989). In a similar study using the same combination but lower doses of ketamine at 5 and 7.5mg/kg respectively, there were no differences to heart rates during the same type of surgery (Verstegen et al. 1991). This shows the potential of varying doses of ketamine but with the same outcomes. Further research exploring thresholds of ketamine and its effects on heart rates in relation to pain reflex are warranted.

The administration of drugs via the IM route is occasionally likely to result in incomplete intramuscular delivery, most likely when inexperienced surgeons or veterinary students inject the drugs. In one study it was shown that 11% of cats required supplemental anaesthesia with isoflurane (Harrison et al. 2011). The duration of procedures such as castrations versus ovariohysterectomy could see a variation in the use of supplementary anaesthesia but this is dependent on the success of the initial delivery of IM application.

2.2.d Atipamezole.

Atipamezole is a potent highly selective alpha-2 antagonist with a rapid onset of action. Atipamezole is used to reverse, or more correctly, antagonise the effects of medetomidine and is often referred to as the reversal agent (Baldwin et al. 2008).

The recommended dosage for atipamezole is 0.04 ml/kg (200 µg/kg body weight) using a 5mg/ml formulation (Bruniges, Taylor, and Yates 2016). It is known that the effects of antagonism are reflected in the dose of medetomidine and the time of administration and dose of atipamezole (El-Kammar and Gad 2014).

The action of atipamezole antagonises the peripheral and central effects of alpha 2 agonists. There have been numerous studies which have researched the effects of atipamezole dose in relation to the length of time of recovery (Bruniges, Taylor, and Yates 2016, Warne et al 2016). In this study, atipamezole was administered after 40 minutes as part of a multimodal approach using the Quad. The result showed this significantly reduced the recovery time by as much as 1 hour compared to those not using atipamezole (Bruniges, Taylor, and Yates 2016). The recommendation therefore is the administration of atipamezole after 40 minutes, so the ketamine component has ceased, and this promotes a smooth recovery. There were faster recoveries in patients that were under 6 months old compared to adults. This same study stated that the use of the dexmedetomidine as part of the Quad had a reduced recovery time by 10 minutes with atipamezole compared to 19 minutes without the use of atipamezole (Bruniges, Taylor, and Yates 2016). There were no differences in recovery time between groups given dexmedetomidine and medetomidine, where both groups were antagonised with atipamezole.

Atipamezole should be considered in early neutering protocols. The respiratory depression can become significant when medetomidine is combined with other injectable agents. The cardiovascular effects such as bradycardia and reduced cardiac output can have more significant consequences in a paediatric or young patient compared to an adult (Joyce and Yates, 2011, Grandy and Dunlop, 1991).

2.3 Opioids

2.3.a Methadone

The use of methadone as an analgesic for feline neutering in the UK is on the increase. A recent survey showed that this was the result of greater awareness, increased licensed availability and the improved knowledge of addressing pain management (Hunt et al. 2015).

The dose range is 0.3-0.6mg/kg for feline patients in the UK and the European countries (Bortolami and Love 2015). Methadone is a pure μ synthetic opioid receptor agonist. The methadone used in the UK is licensed as a racemic mixture formed of two isomers. The analgesic effect is obtained when the L-isomer binds to the μ receptor. Prevention of central sensitisation and hyperalgesia is due to the D-isomer which is defined as non-competitive N-methyl D-aspartate (NMDA) antagonist (Shah et al. 2018). Methadone also inhibits serotonin and noradrenaline in the descending pain pathways (Codd et al. 1995).

Full μ opioids agonist such as methadone are easily titrated to effect which offers the ability to adjust dosage in specific scenarios especially in challenging cases.

Methadone could be used as part of a multimodal regime and combined with other drugs such as alpha-2 agonists or it could be administered with a sole analgesic. It is used as an effective approach in management of acute pain and has a wide therapeutic margin and the effects can be antagonised if needed.

There were concerns over excitatory effects historically although at clinical doses this is minimal. Mydriasis does persist for longer than analgesia which could potentially affect vision in the short term (Bortolami and Love 2015).

Methadone has been documented to reduce the minimum alveolar concentration (MAC) of sevoflurane in feline patients as much as 25% so this highlights the care needed when using opioids. It is important to note that MAC reduction is not a substitute for analgesia as pain is associated with supraspinal pathways rather than at the spinal cord level which only measures the potency of the inhalation anaesthetic. The use of a potent opioid such as methadone offers the advantage of less inhalation anaesthetic use in cats hence reduction in costs.

The combination of methadone (0.5mg/kg) and medetomidine (0.02mg/kg) as a premedicant for ovariohysterectomy and castration showed satisfactory analgesia for 6 hours post administration (Slingsby, Bortolami, and Murrell 2015, Bortolami and Love 2015). In one experimental model methadone offered superior analgesia when compared to buprenorphine (Steagall et al. 2006).

The use of IV methadone (administered slowly) in both dogs and cats has been reported to have no adverse cardiovascular effects and respiratory efforts have been documented as minimal. Bradycardia and reduced respiratory rates are reported when methadone is given to anaesthetised patients (Murrell 2011).

2.3.b Buprenorphine

Buprenorphine was developed in the 1970s and has been a crucial aspect of management of pain in cats (Steagall, Monteiro-Steagall, and Taylor 2014). Buprenorphine can be used as the opioid component of the Quad protocol. This is a popular combination offering a good balanced approach. Buprenorphine is typically preferred over butorphanol due to the longevity and potency of postoperative analgesia (6–12 hours compared with 1–2 hours) (Joyce and Yates 2011). Buprenorphine has a delayed onset but is also long acting with moderate analgesia and few adverse effects (Lizasoain, Leza, and Lorenzo 1991).

Buprenorphine is a potent highly lipophilic semi synthetic partial μ agonist opioid, a derivative of thebaine. It has been documented that buprenorphine could be considered as kappa (κ) antagonist or μ receptor antagonist at high doses (Pergolizzi et al. 2010). In some species studies, it is classified as a full μ agonist (Steagall, Monteiro-Steagall, and Taylor 2014). Buprenorphine has market authorisation in cats in the USA and most European countries.

There are wide variations in the analgesic effects, and this is associated with different routes of administration, doses and obviously the variation of different cats presented. Buprenorphine doses of 0.02mg/kg and 0.04mg/kg has been reported to offer a greater degree of mechanical antinociception than that seen with 0.01mg/kg (Steagall, Monteiro-Steagall, and Taylor 2014).

Buprenorphine is very versatile and can be administered IV, IM, subcutaneously (SC), transdermally and via the oral transmucosal route (OTM) (Bortolami and Love 2015). Studies have shown that buprenorphine is an effective analgesic in cats undergoing a variety of procedures, and this has been widely documented especially with ovariohysterectomy and even with complex orthopaedic work (Mollenhoff, Nolte, and Kramer 2005). In one study, the analgesic properties and recovery effects of two doses 0.12mg/kg and 0.24mg/kg of subcutaneous buprenorphine were compared in cats undergoing ovariohysterectomy. This research showed that 0.12mg/kg provided adequate analgesia as part of a multimodal approach. The higher dose buprenorphine in this study was well tolerated and this dose may allow an increase in the interval between doses which is currently advised at 6–8 hours frequency without loss of analgesia with reduced adverse effects (Leedham et al. 2019).

Early studies evaluating antinociception did in fact demonstrate a bell-shaped dose dependent curve where higher doses led to decreased effect or no analgesia produced and in some studies a ceiling effect. This finding has led to further studies into this phenomenon (Slingsby, Taylor, and Murrell 2011).

The thermal effects of buprenorphine are also crucial, as research has suggested that the use of buprenorphine produced a mild to moderate elevation of body temperature (Posner et al. 2010). This effect could reduce the need for additional warming of the patient in the postoperative period. Hypothermia is often a factor to consider with early neutering hence that could pose a valuable contribution to any multimodal regime in addition to the analgesic effects (Joyce and Yates 2011, Posner et al. 2010).

2.4 Anaesthesia combinations

The Quad protocol was originally devised in early 2000 in response to inadequate licensed IM protocols at the time. The difficulties seen initially were primarily due to reliable depths or planes of anaesthesia, particularly in patients with lower body mass i.e., less than 1.5kg. The calculation of the Quad protocol was modified to consider a greater body surface area (BSA) to mass ratio (Joyce and Yates 2011). The formula used is BSA = K x (body weight), this is where K is a shape constant. This is documented in a study evaluating a formula to improve dosing for chemotherapeutic agents in ferrets by Jones et al, (2015). It does state that the value of K differs amongst species which clearly shows that a

Quad protocol such as this would be unsuitable for a ferret for example. One of the problems of estimating BSA is that this increases the risk of under dosing hence the inefficiency of sedation and potentially adverse effects (Jones et al. 2015).

Previous studies using Quad combinations have shown sufficient analgesia for the younger feline patients, lower mortality rates and rapid recoveries (Polson, Taylor, and Yates 2012).

The Quad protocol includes medetomidine which is calculated at BSA (this would be a higher dose if a patient had a lower BSA) and midazolam to provide sedation and muscle relaxation and an indirect way of reducing the medetomidine dose. Buprenorphine is included as the opioid analgesic plus it causes a slight increase in body temperature which is of benefit postoperatively. The last component of the Quad is ketamine, a dissociative anaesthetic and analgesic, the side effects which is offset by the midazolam and alpha 2 agonist. The Quad protocol offers a simple approach to calculations based on accurate weight and results in four equal doses of the individual components.

The Triple combination was formulated in the 1990s and consisted of medetomidine, butorphanol and ketamine. The principle aim of the Triple at that time was to offer reliability, a smooth recovery and incorporate muscle relaxation to offset the effects of ketamine (Ko et al. 2011). In some cases, butorphanol rather than buprenorphine has been used as part of the ‘Triple combination’ although this would have a shorter duration of analgesia of 2 hours. Atipamezole may be given to the patient to reduce the recovery time without adversely affecting the analgesic properties which the Triple offers (Ko et al. 2011).

In dogs the combination of medetomidine with butorphanol produces a profound sedation apparent after 20 minutes of administration based on a dose of 25 μg/kg medetomidine and 0.1mg/kg butorphanol. Dogs are given ketamine (5mg/kg) separately to medetomidine and butorphanol and this will facilitate minor procedures (Yates 2018). In cats, the Triple is given as a single dose of 0.4mg/kg butorphanol, 80μg/kg medetomidine and 5mg/kg of ketamine. The effect is cats become sedated in as little as 2–3 minutes post IM injection.

2.5. Inhalation Anaesthesia

2.5 a, Isoflurane.

Isoflurane was introduced to the UK in 1983. Trials have shown isoflurane to be superior to halothane and enflurane in human studies (Nunn 1985). Isoflurane superseded halothane in small animal practice in the late 1990s.

Maintenance of anaesthesia with volatile inhalation agents is still favoured today and widely used in the veterinary industry. The reasons for the ongoing popularity include qualities of being predictable and accurately titratable with the modern vaporisers (Pottie, Dart, and Perkins 2008). Isoflurane is non-flammable, highly stable and has low blood solubility. Post procedure, it is known that this has very little biodegradation. Smooth induction followed by rapid recoveries were noticeable in early clinical trials (Ball and Westhorpe 2007). Low blood solubility is an important factor ensuring rapid induction of general anaesthesia. Isoflurane has a blood gas partition coefficient of 1:46 which when compared to halothane which has a blood-gas partition coefficient of 2.54. Decreasing blood solubility leads to rapid induction of anaesthesia which is crucial for a satisfactory postoperative recovery. Premedication and choice of drugs such as the intravenous anaesthetics may also impact on both the use of inhalation agents and the quality of recovery.

One study suggested that the use of sevoflurane with a more pleasant odour improves the patient tolerance compared to isoflurane with a more pungent odour. This could be a factor with tolerance of mask inductions (Wallin et al. 1975). Cats tend to be fractious in nature, and sevoflurane is ideal due to its rapid inhalation induction and induces less 'breath holding' compared to isoflurane. Sevoflurane is also ideal in circumstances where a rapid change in the plane of anaesthesia is required. Sevoflurane has shown to have no recovery issues in patients that have liver or kidney disease (Tzannes et al. 2000). One of the key factors of the slow uptake in the use of sevoflurane is cost, this could be offset when hidden factors such as monitoring time postoperatively are considered. (Tzannes et al. 2000). Mask induction without IV access being secured may reduce personnel time.

Respiratory depression occurs commonly in both sevoflurane and isoflurane anaesthesia. Cardiac output is slightly reduced at light planes of anaesthesia and muscle relaxation is excellent. It was stated that diastolic function is conserved during isoflurane and sevoflurane anaesthesia when compared to halothane (Pottie, Dart, and Perkins 2008).

In a review undertaken by Shaughnessy and Hofmeister (2014) in which findings were collated from 17 studies of isoflurane and sevoflurane, 3 of these studies showed that the MAC value for isoflurane ranged from 1.2% to 2.22% and that of sevoflurane between 2.5% to 3.95% (Shaughnessy and Hofmeister 2014). The same review showed that MAC values could potentially be affected by age of patients which could be a crucial factor in early neutering of cats (Shaughnessy and Hofmeister 2014).

A study reviewing the speed of mask induction using sevoflurane and isoflurane for comparison have shown that sevoflurane was quicker to successful intubation compared to isoflurane despite both having ideal conditions for intubation (Lerche et al. 2002).

Surgical anaesthesia is usually achieved at 1.5 times MAC which shows that a higher vaporiser setting is likely to be required for sevoflurane in comparison to that of isoflurane to ensure adequate depth of anaesthesia. MAC is also reduced however by premedication and therefore vaporiser settings will be dependent on many factors (Raue et al. 2019).

2.5 b, Endotracheal intubation

Endotracheal intubation is a common procedure in veterinary anaesthesia, yet it is not without risks and may contribute to perioperative mortality in feline patients (Hofmeister et al. 2007). A study in 2007 found 63% of deaths postoperatively occurred in cats that were intubated compared to 48% that were not intubated. This suggests that tracheal trauma maybe a contributing factor rather than airway obstruction *per se* (Brodbelt et al. 2007). The study was based on a range of cases from 117 veterinary centres across the UK and covered all American Society of Anesthesiologists (ASA) status levels from I - V. The study did go on to state that increasing ASA physical states by one category was associated with a threefold increase in odds of deaths hence the importance of a defined category for patients. The overall risk of anaesthetic and sedation related deaths was 0.24%. Furthermore, the study suggests that endotracheal intubation should be used with caution especially for minor procedures; it may be more appropriate to provide oxygen without an endotracheal tube. Notwithstanding this finding, it was acknowledged that endotracheal tubes have a role in complex procedures where maintaining an airway is paramount (Brodbelt et al. 2007). A significant concern in the feline patient is their airway anatomy, having a much smaller and delicate trachea compared to that of the dog. Cases of tracheal injuries lead to claims against the veterinary surgeon (Adshead 2011). The Veterinary Defence Society (a mutual insurance company insuring veterinary surgeons and registered veterinary nurses) typically deal with 1-3 tracheal injury claims following endotracheal intubation each year (Hird, 2019).

The function of the endotracheal tube is to deliver carrier gases and volatile agents to and from the breathing system to the patient. Capnography, which should be an essential part of routine anaesthetic monitoring, can help confirm correct placement of an endotracheal tube (Bilbrough 2006). However, the use of capnography in veterinary practice may be as low as 10% which could contribute to poor patient safety (Brodbelt et al. 2007).

The use of cuffed endotracheal tubes rather than uncuffed tubes remains controversial and various papers have documented the resulting injuries (Mitchell et al. 2000, Hofmeister et al. 2007). There are some advantages to cuffed tubes which includes delivery of inhaled anaesthetic gases with an airtight seal. The prevention of environmental contamination (Weber et al. 2009) is a crucial factor in health and safety. Other factors include prevention of aspiration of fluid commonly associated with dental procedures, accurate measurements and readout of capnography and reduction in expenditure on medical gases and inhaled anaesthetic agents.

One disadvantage is cuff over-inflation especially when over 3mls of air has been used to inflate the cuff (Wilson et al. 2016). This can cause a longitudinal tear between the trachealis muscle and tracheal rings (Adshead 2011). A study undertaken on cadavers demonstrated tracheal rupture in 70% of cases when >6mls of air was used to inflate the cuff. This over-inflation represents a significant risk for airway trauma (Hardie et al. 1999). Tissue necrosis as a result of large pressure over a small surface area of tracheal mucosa which would otherwise benefit from an evenly distributed pressure or more accurately measured pressure on a given surface area.

Other studies using cuffed endotracheal tubes reported barotrauma from excessive inflow and not allowing excess gas to vent. This causes the patient's lungs to be distended and exposed to excessive pressures (Rezende 2018). Uncuffed tubes are more commonly used in feline patients primarily due to prevention of traumatic injuries through tracheal tears and damage. The main advantages of using such tubes are ease of placement, ease of visualisation of arytenoid cartilages of the larynx when placing tubes, and less likelihood of accidental removal during anaesthesia or movement of patients (Hofmeister et al. 2007). Uncuffed tubes come with their own faults, these being environmental contamination with volatile agents because the seal around the tube is imperfect, leakage of material and liquid, especially during dental procedures which could cause aspiration pneumonia if not monitored.

Simple methods could help to minimise iatrogenic tracheal trauma. For example, gaining sufficient experience in endotracheal placement and minimising movement of the patient both prior to and post placement. Technological advances are continuing to be made, in human practice and veterinary practice; handheld pressure gauges are used to ensure suitable measured inflation (Adshead 2011). These are products which are specifically designed to offer a digital readout of pressure when inflating cuffed tubes. Built-in manometers which should be used, fill the cuff to a pressure between 20-30cm H_2O as recommended by manufacturer guidelines. Recent studies have shown that the lower end of the range: 20cm H_2O, is considered to be safe for cats (Grubb 2019). Using this method offers a simple but effective means of accurately measuring pressure therefore removing potential risks to the patient.

2.5 c, Use of Masks.

Masks used for the induction of inhalation anaesthesia have been used in veterinary practice since the origins of its development (Mutoh et al. 2001). In its design, it is non-invasive and a simple means of delivering gases and equally important for a method of ventilation should it become required. It is also an alternative to intravenous anaesthesia which may be a safer approach especially in compromised patients or in small patients such as prepubertal cats undergoing neutering where venous access can be difficult.

The volatile agent is usually delivered in oxygen (with or without nitrous oxide) through tight fitting masks which have evolved over time in terms of design (Lerche, Muir, and Grubb 2002). Most anaesthetic masks are transparent which have the added advantage of allowing visualisation of fogging, vomiting and any facial abnormalities that require detection. They are designed with a flexible silicone diaphragm which allows minimal air leakage during ventilation. Some designs have moulded integral connectors which allow attachment to breathing systems and also attachment to patients if this added security is required. They vary in size which is significant progress in development especially in terms of the internal volume of the mask which should be as small as possible in order to reduce dead space. In one study in paediatric patients the mask internal volume could be as much as 30% of their tidal volume which is a clear indication that suitable sizes for patients are necessary (Moyle, Davey, and Ward 1999). Additionally, suitable scavenged masks offer a clear advantage compared to the use of chamber induction in terms of environmental pollution (Steffey et al. 2015).

Of the licenced volatile agents, sevoflurane’s profile offers the most favourable mask induction especially in human paediatric patients (Mutoh et al. 2001).

The comparison of the volatile agents with nitrous oxide for anaesthetic induction have shown that there is no difference in the induction time between isoflurane and sevoflurane (Hikasa et al. 1996, Tzannes et al. 2000). It is known that without suitable premedication, mask induction alone offers a slower onset of induction and could potentially be associated with side effects such as excitement, excessive body movements, breath holding and struggling especially during the initial stages of the induction period (Mutoh et al. 2001). A study comparing mask induction of anaesthesia with isoflurane or sevoflurane in premedicated cats showed that sevoflurane offered a shorter time to intubation and induction of anaesthesia compared to isoflurane although it went on to state that mask induction quality was very similar between the two volatile agents (Lerche, Muir, and Grubb 2002). Face mask induction also aids quick placement of the endotracheal tube after the initial period of mask induction thereby allowing rapid control of ventilation and the ability to maintain a suitable plane of anaesthesia (Tzannes et al. 2000).

2.6 Sedation scoring assessment systems

The definition of sedation is a reduced response to an external stimulus. Examples of this could be verbal and physical stimuli (Simon and Steagall 2020). Profound sedation can be used instead of a general anaesthetic for minor procedures and diagnostics (Simon and Steagall 2020).

There are numerous sedation scoring systems which have both been developed and modified over the years (Reader et al. 2019, Ribas et al. 2015). In some cases, studies have influenced and modified this midway depending on the observational behaviours seen. Good, careful use of sedation drugs has shown to decrease morbidity and mortality in patients which is invaluable (Waldmann 2010). It is documented that validation and reliability is key. Validation is important to ensure that each component has a margin of sensitivity in terms of scales which must have the ability to be reproduced for each case in order to ensure the reliability of the data obtained as evidence. The decision-based approach for the choice of sedation scoring should be based on familiarity, and ease of use which would allow the scale to be used in a consistent manner but also reproducibility to allow standardisation in the study.

There are several types of scales commonly used: these being the simple descriptive scale (SDS), numeric rating scale (NRS) and visual analogue scale (VAS). Such scales have primarily been designed for the observational behaviour which relates to pain. Studies have modified these scales using the objective design of this to incorporate the validity and use in sedation scoring.

The (SDS) is best defined as using simple expressions usually in the form of descending pattern which defines the score such as palpebral reflex in a descriptive form, i.e., 0 - brisk, 1 - slow, and 2 - absent. An example of this composite simple descriptive sedation score form is seen in a study by Gurney et al (2009). This is modified from Kuusela et al (2000) (Gurney et al. 2009, Kuusela et al. 2000). The design covers 7 key points which covers spontaneous posture with 0 for standing, 1, sternally recumbent and 2 for laterally recumbent as an example with an overall score of 0 - 15 with 0 = no sedation and 15 = well sedated. Other similar forms are noted in studies by Wagner et al which is derived from a sedation scale obtained from Grint et al (Grint, Burford, and Dugdale 2009, Wagner et al. 2017). Ribas et al (2014) uses a version which covers posture score, behaviour and muscle relaxation as part of the sedation scoring process (Ribas et al. 2015). This scoring method was later adapted in a study evaluating two different IM protocols on sedation, recovery and ease of venepuncture in cats undergoing blood donation. The study included elements such as reaction to injection (0 = none, 1 = mild, 2 = moderate, 3 = severe) (Reader, Barton, and Abelson 2019).

The NRS uses an ascending numerical scale which is usually a scale of 0–10. This leaves an open interpretation of what is observed or collected which could pose problems for validity unless the same personnel are used throughout the study. Having said this, it is noted that NRS can differentiate between minor variations of changes (Tranquilli, Grimm, and Lamont 2004).

The VAS scale consists of a simple line usually 100mm long on which a cross is placed by the observer. The VAS is designed to offer a measured approach of severity (in mm) but errors can occur because the accuracy is open to interpretation as to where one places the level of severity on the line (Holton et al. 1998).

There are other scales which are used but not necessarily for sedation scoring. An example of this is variable rating scale (VRS). These usually take into account specific parameters such as heart rate and blood pressure, which is ideal for measurements of pain. This may cause a data dilemma in terms of incorporating this as there could be wide variations of information to assimilate.

2.7 Recovery assessment systems

The quality of the recovery is important especially in high throughput neutering programmes where time and resources may be limited to accommodate prolonged and poor-quality recoveries from anaesthesia. Pressure mats were first identified as useful to evaluate patients with orthopaedic conditions but could also be re-purposed to evaluate quality and nature of recovery from anaesthesia. One study showed pressure mats could accurately measure gait parameters in healthy cats during walking and jumping (Stadig and Bergh 2015). These may offer additional useful observations to studies that are particularly focused on speed and quality of recovery. Currently their cost precludes their use in most clinical research.

Another method of measuring recovery is by using a cat portal. Burton's Cat Cube is designed to allow movement between two kennels adjoined by a portal (Figure 2). The door is vented and made from toughened glass to promote patient observations. The portal measures 24 inches wide x 30 inches high x 26.4 inches deep. It was originally designed to offer a compartment approach to merge two side by side kennels together to offer a larger surface area especially for those that may require a longer stay (Burtons Medical Ltd). These were originally designed to International Society of Feline Medicine (ISFM) guidelines.

Figure 2: - Cat Portal - ISFM standard - Burtons Medical Ltd.

3.0 Aims and hypotheses

The aim of this research was to evaluate and compare two anaesthetic combinations designed to be used in welfare organisations for neutering programmes. Medetomidine and buprenorphine (MB) were compared to medetomidine and methadone (MM) for their suitability for orchidectomy anaesthesia in cats. The aim was to use a standardised protocol incorporating mask induction prior to maintaining anaesthesia. It was hypothesised that both combinations would provide a rapid recovery period to allow a high-volume turnaround in a charity setting. Additionally, it was hypothesised that MM would provide superior sedation and a shorter but better-quality recovery.

4.0 Methodology

4.1 Design

The prospective study was undertaken during a weekly routine castration clinic at R.S.P.C.A Greater Manchester Animal Hospital between 17/04/19 and 14/02/20. Cats presented to the 'open clinic' originated from five sources: veterinary triage, usually via the inspectorate, TNR / feral cats for population control, multi-cat household intervention, branch and lastly, owned cats. The study was designed to simulate a high volume setting in a mobile clinic which explores the feasibility of employing an approved protocol for routine use. The study aimed to compare two anaesthesia combinations: -

- Medetomidine 500mcg/m² and methadone 5mg/m²
- Medetomidine 600mcg/m² and buprenorphine 180mcg/m²

The protocols used were standardised between groups. The final selection of drugs for the study was determined after iterative work within the hospital during the months prior to study, the study design is outlined in Figure 3.

Careful considerations were made on informed consent due to the differentiation of the sources listed, for example, vet triage animals usually brought in by the inspectorate. In this case, informed consent is already within the remit of the RSPCA ownership. This differs from owned animals where consent is gained via signed consent obtained on admittance. This is further analysed later in the conclusion. Despite varying sources, the protocol for the study remained the same for impartial outcomes avoiding biased and consistency, this is further enhanced by the use of the pilot study initially to explore the feasibility of the main study.

The study was conducted in an environment where there was a blinded view taken to ensure data recording was not influenced through knowledge of type of combination used. The initial sedation assessment through to the end assessment observations were conducted with the view that no knowledge of the combination was known and that the remit was on the supervising surgeon to ensure analgesia was prioritised and a secondary back up measure in the form of rescue anaesthesia was prepared in accordance to the responsibility of the veterinary surgeon under the Veterinary Surgeons Act 1966.

The study was approved by the ethical review board, Nottingham University (2630 181108).

Figure 3: - Flow chart outlining the decision-making processes involved in selecting the final protocol. The key principles such as ease of administration which are necessary to ensure suitable use of protocol.

4.2 Population

A pilot study was undertaken using 15 cases presented to the clinic between 6/3/19 and 3/4/19 to evaluate the differences and design of the study.

In total 166 feline cases were used for this study. Initial cases were used to refine both sedation scoring and recovery scoring methods to ensure accuracy and reliability. These were excluded from final data analysis to ensure accuracy and unform data collection.

Further refinement was also carried out to include portal exploration times which offer an insight into quality and timing of recovery which was crucial to the study.

All cats recruited were deemed healthy and classified as ASA I. A full clinical evaluation was undertaken prior to surgery and post recovery with the aid of Nottingham University final year veterinary students undertaking shelter medicine extramural rotations and in agreement with current RSPCA policy.

4.3 Enrolment and inclusion

One hundred and sixty-six healthy cats were recruited in total for the study including the initial trial and early development. Animals were fasted for a minimum of 8 hours prior to anaesthesia; all were provided with water up until the point of intramuscular injection of the combinations. All animals were weighed. Consent from owned patients formulating part of the study data collection were obtained via incorporated consent declaration on anaesthetic / procedure consent forms on admittance. All data was collected including demographic information which were later analysed.

4.4 Administration of drugs

Premedication consisted of one of the two following combinations at the dose rate listed;

Combination 1 - Medetomidine 600mcg/m² and buprenorphine 180mcg/m² MB

Combination 2 - Medetomidine 500mcg/m² and methadone 5mg/m² MM

The products used were medetomidine (Sedator 10mg/ml; Dechra Veterinary products), methadone 10mg/ml, (Comfortan, Dechra Veterinary Products) and buprenorphine, Buprenodale 0.3mg/ml, Dechra Veterinary Products).

The drugs were drawn up by veterinary students of Nottingham Veterinary School and checked and supervised by an approved teaching supervisor (Veterinary Surgeon). Both drug combinations were administered by students into the *quadriceps femoris*. Ten minutes elapsed from the time of administration to starting measurement and data collection.

4.5 Assessment

The data collection from sedation scoring, anaesthesia, visual observations and recovery were undertaken by the same assessor, who was an experienced registered veterinary nurse.

All procedures were timed and assessment timepoints standardised between groups.

Simple descriptive scale for sedation

Sedation was scored using a modified SDS extending to include how well the mask was tolerated by the patient. The scale consisted of 7 key components with a total score of 18 possible.

Table 1: - Simple descriptive scale for sedation adapted from Gurney et al (2000).

Criteria Score		Score
Spontaneous Posture	Standing	0
	Sternally recumbent	1

	Laterally recumbent	2
Palpebral reflex	Blink Absent	0 1
Eye Position	Forward Rotated ventrally	0 1
Response to sound (hand clap)	Body Movement Head Movement Ear Twitch No Reaction	0 1 2 3
Resistance to lateral recumbency	Full (Stands) Moderate restraint required Mild Restraint required No Resistance	0 1 2 3
Overall Appearance	No Sedation apparent Mild Sedation Moderate Sedation Well sedated	0 1 2 3
Mask Induction	Scratching Head pulling Slight movement No resistance	0 1 2 3
Total possible sedation score		18

4.6 Anaesthesia Protocol

Ten minutes after sedation scoring, animals were transported from the preparatory area to the main theatre. Anaesthesia was induced via a tight-fitting face mask connected to the Mapleson F system using 2% isoflurane (Isoflo, Pfizer) in 100% oxygen for a period of two minutes. During induction of anaesthesia a cuffed endotracheal tube (Portex) was measured and cut to appropriate length for the patient. At the end of the two minutes of induction, the face mask was removed, the breathing system temporarily plugged to prevent environmental contamination, and the cat's larynx was sprayed with lidocaine (Intubeaze, Dechra). Mask induction continued for a further minute and the endotracheal tube was then placed. Anaesthesia was maintained using 1% isoflurane in 2 litres of oxygen. The cuff of the endotracheal tube was inflated using a cuff inflator and manometer (AG Cuffill™) to 30 cm H_2O pressure to prevent tracheal rupture or injury and facilitated an improved monitoring approach using capnography.

Meloxicam (Metacam, Boehringer Ingelheim) was administered prior to surgery via the subcutaneous route after the induction of anaesthesia at a dose rate of 0.3mg/kg.

The steps of the protocol for the study are illustrated in Figure 4.

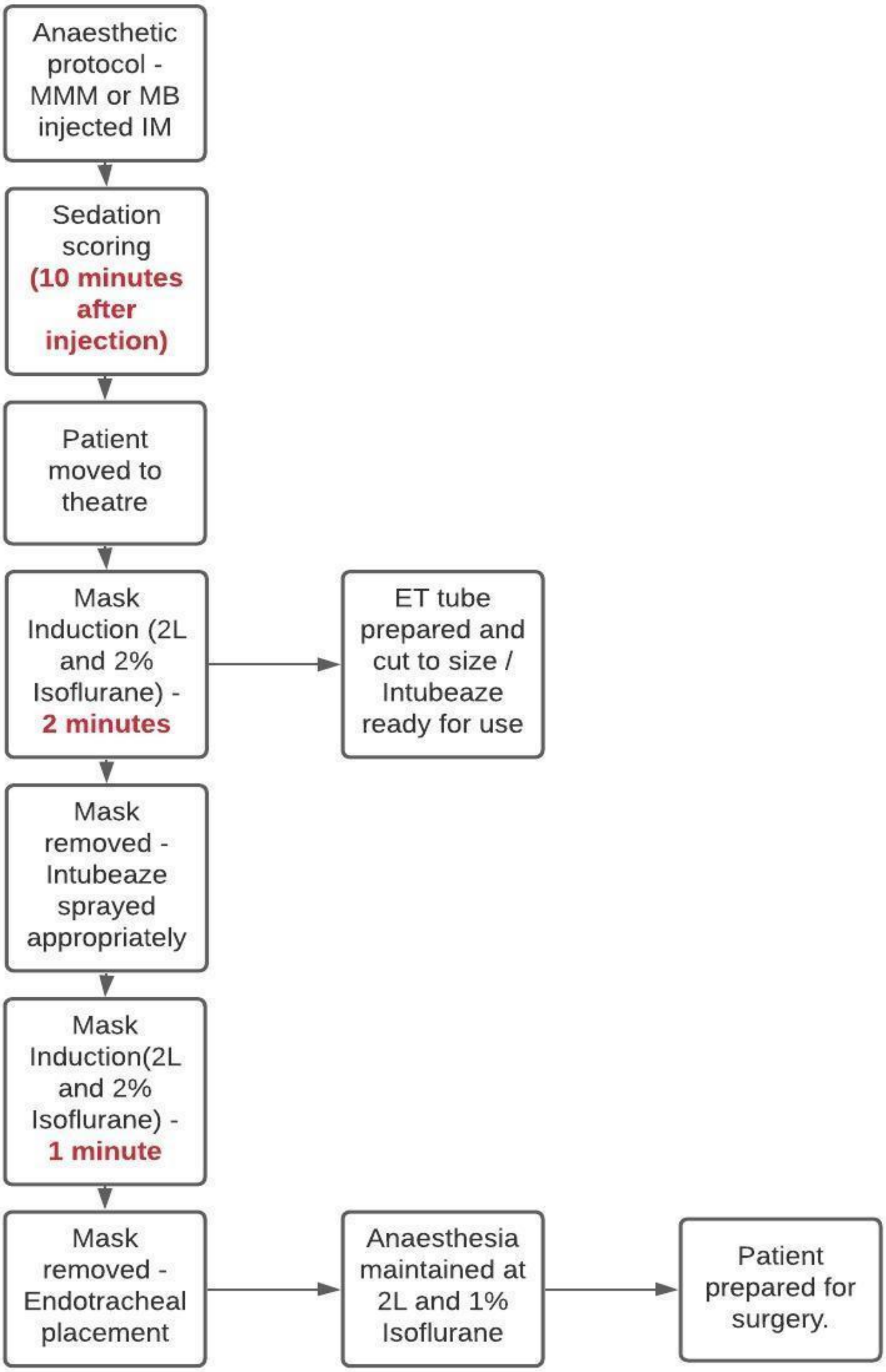


Figure 4: - Anaesthetic protocol for both combinations

4.7 Physiological parameters

Anaesthesia was continuously monitored by a designated person and parameters were recorded at 5-minute intervals. Throughout this study, heart and respiration rate was auscultated. Capnography was used in all patients to ensure accuracy of endotracheal placement and monitoring CO_2 during anaesthesia throughout. Capnography was undertaken using a portable model (Capnoeasy™ Burtons Medical Ltd) which measured end-tidal carbon dioxide and respiration rate. A pulse oximeter (Burton's medical unit) was also used and measured heart rate (HR), and arterial haemoglobin saturation with oxygen (SpO_2%).

4.8 Anaesthesia maintenance

Anaesthesia was maintained with 1% isoflurane in oxygen. Vital signs prior to administration of drugs were conducted for baseline recording. Anaesthetic monitoring occurred throughout the procedures. Muscle tone was monitored along with jaw-tone and palpebral reflexes until the placement of a cuffed endotracheal tube. The Cuffill™ (manometer) was used to fill endotracheal cuffs to the desired inflation to prevent any tracheal trauma. All surgeries were undertaken by veterinary students and anaesthesia was monitored by a second veterinary student. The procedure was under constant supervision by qualified approved veterinary surgeons throughout. Isoflurane was discontinued at the end of surgery. The duration of the surgery was recorded.

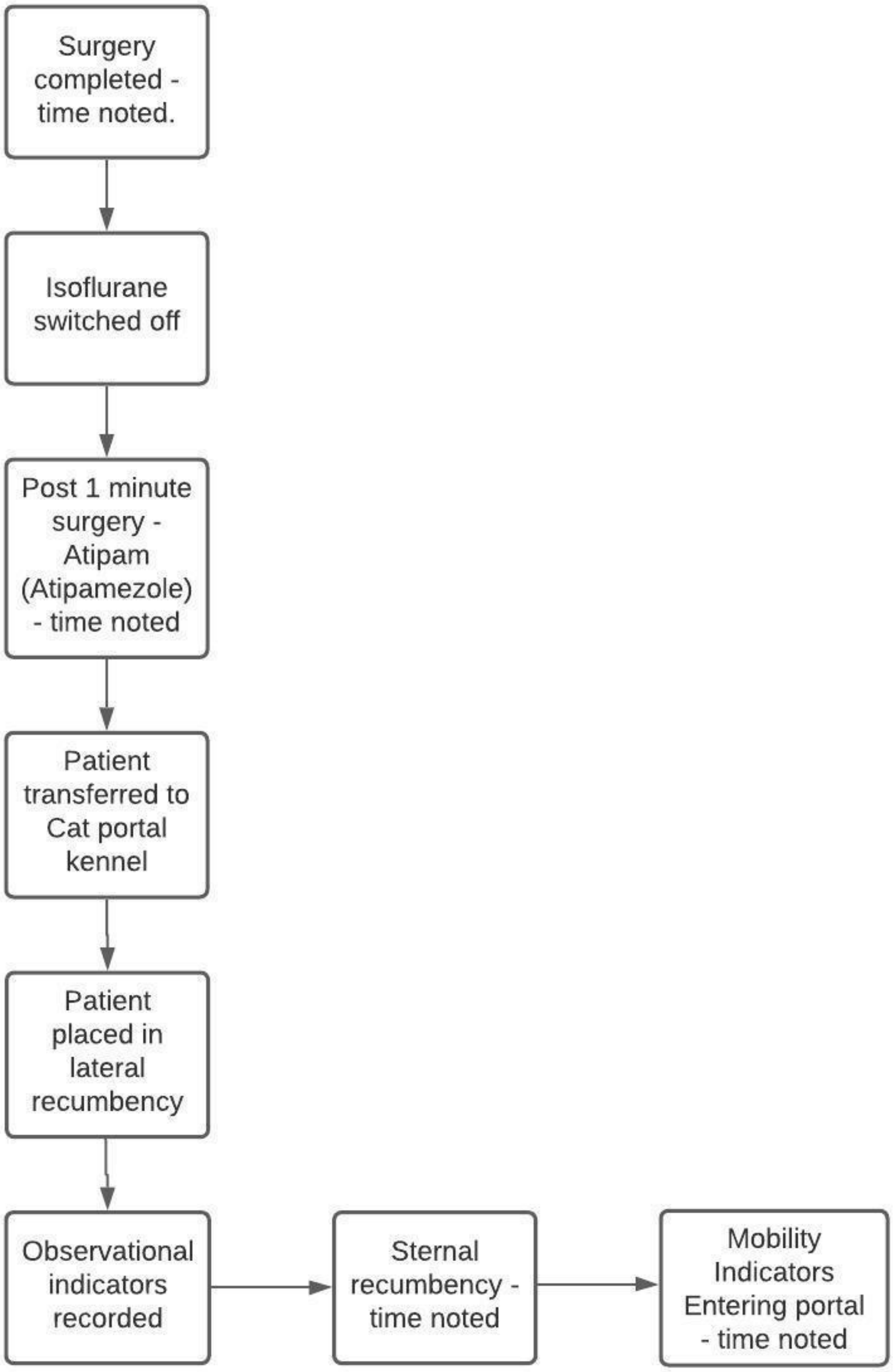


Figure 5: - Recovery protocol.

4.9 Atipamezole and recovery management

Atipamezole was administered IM one-minute post completion of surgery at a dose equivalent to half the volume of medetomidine. Isoflurane was discontinued, but oxygen was administered for a further minute. The endotracheal tube cuff was deflated, and the cat's trachea was extubated prior to the cat being placed in lateral recumbency in the right side of a Cat Portal system. Recovery was timed. Time taken to sternal recumbency and to completely enter the left-hand side of the portal accommodation via the portal were recorded (Figure 5). There was a litter tray and a small, standardised portion of Hills a-d food in the left-hand side of the portal.

4.10 Adverse events

Adverse events were also recorded as free text on the anaesthetic monitoring chart.

5.0 Results

5.0a, Demographic data

Complete data sets for 92 cats were collected. There were 56 cats in the medetomidine and buprenorphine (MB) group and 33 cats in the medetomidine and methadone (MM) group. Those initially excluded based on having no portal times were included in the final analysis. Portal times were later added after initial trial to improve accuracy of numerical data results for the recovery stage.

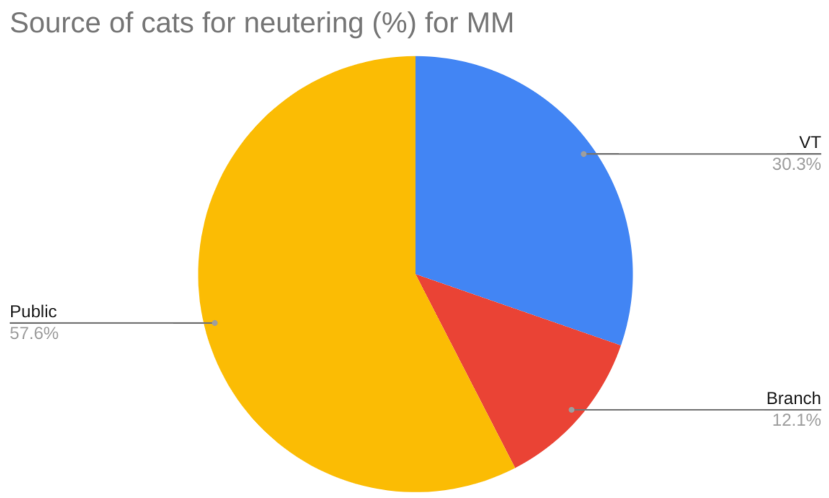
The demographics of cats used in the study showed that more cats were public owned in the MM group (58%) compared to the MB group (36%). There were more neuters of cats from branch practices in the MB group (30%) compared to the MM group (12%). There were marginally more seen from Vet Triage (VT) sources in MB group (33%) in comparison to that of MM (30%).

The demographics are presented in Table 2.

Table 2: - Weight of patients and surgery times

Group	MB (N=56)	MM (N=33)	P value
Surgery duration (Mins)	13 ± 7.9	15 ± 5.5	0.12
Weight (kg)	2.6 ± 1.2	2.7 ± 1.1	0.38
Age (Weeks)	36 (8–356)	32 (8–364)	0.26

Demographics of animals undergoing castration and duration of surgery. Data are presented as mean ± standard deviation or median (range). Significance tested using Student's t test which the confidence interal (CI 95%) could be reported. Mann-Whitney test also factored.



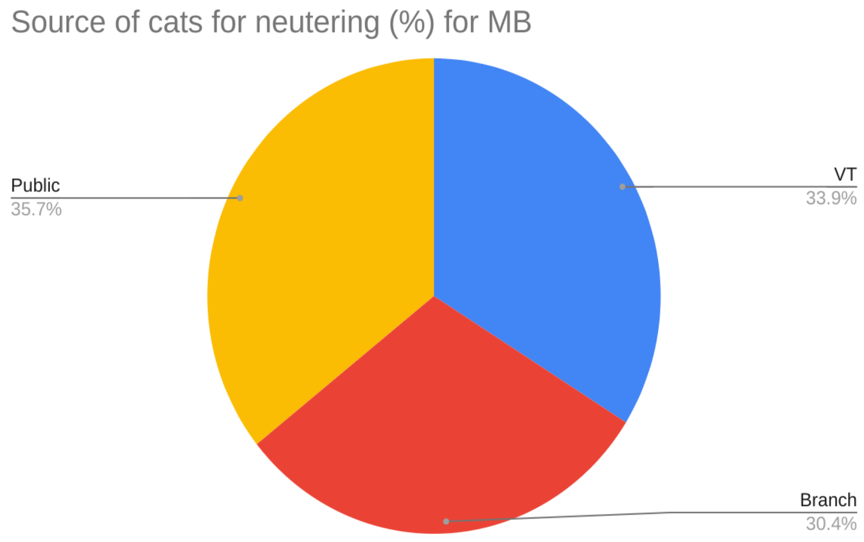


Figure 6: - Pie chart showing the demographic sources of cats for the study.

5.0b, Sedation

The mean sedation score which included the tolerance to mask induction for the two groups is shown in table 3. The mean scores in the MM group were significantly higher compared to cats in the MB group ($p < 0.02$, Student T test).

Table 3: - The sedation quality between two combinations using a modified SDS (Simple Descriptive Score)

	MB (n=56)	MM (n=33)	t-test p value
Sedation score mean	12 ± 2.8	13 ± 2.9	0.024

Data are presented as mean ± standard deviation. Significance tested using Student's t test. MB Medetomidine and Buprenorphine, MM Medetomidine, Methadone.

5.0c, Anaesthesia

Intraoperative variables for heart rate and respiration were collected at 5-minute time points up to a maximum time point of 30 minutes. Physiological variables remained within clinically acceptable limits. HR (Figure 7) showed an increase over 10 minutes time point which coincided with mid-surgery. This data also suggests an increase in HR levels towards the postoperative stage. MM also showed a decrease in both RR but HR showed a return to initial HR measurements throughout the procedure showing sufficient depth of anaesthesia and stabilisation for the postoperative stage.

Table 4: - HR data collated for the duration of the surgical procedure for both combinations.

	0 min	5 min	10 min	15 min	20 min	25 min	30 min
MM (n=33)	113 ± 24	114 ± 24	116 ± 22	126 ± 20	128 ± 34	104	
MB (n=56)	127 ± 28	126 ± 27	125 ± 24	134 ± 21	14 ± 29	138 ± 38	148 ± 35

Heart rate data recorded over a minute period and obtained in 5-minute intervals throughout the duration of the surgery for the two combinations (MM and MB). Data are presented as mean ± standard deviation.

Data were obtained during the average monitoring period, which showed that MB was marginally longer in time than MM hence, no data obtained at the 30 minute interval.

Table 5 - RR data collated for the duration of the surgical procedure for both combinations.

	0 min	5 min	10 min	15 min	20 min	25 min	30 min
MM (n=33)	30 ± 16	26 ± 7	26 ± 8	22 ± 5	21 ± 9	18	
MB (n=56)	37 ± 12	33 ± 9	32 ± 7	34 ± 7	35 ±10	34 ± 10	33 ± 10

Respiratory rate data recorded over a minute period and obtained in 5-minute intervals throughout the duration of the surgery for the two combinations (MM and MB). Data are presented as mean ± standard deviation.

Data were obtained during the average monitoring period, which showed that MB was marginally longer in time than MM hence, no data obtained at the 30 minute interval.

5.0d, - Recovery

The times to gain sternal recumbency and to fully enter the adjacent side of the cat portal were recorded from the time of the atipamezole injection. Both times were significantly quicker to sternal ($p < 0.002$; Student's t test) and entering portal ($p < 0.002$; Student's t test) for the MM group compared to MB group.

Table 6: - The mean times for recovery (minutes)

	MB (n=56)	MM (n=33)	t-test p value
Time to sternal (minutes)	7.3 ± 3.6	4.9 ± 3.6	0.002
Time to enter the portal. (minutes)	9.8 ± 5.9	6.4 ± 4.0	0.002

Data are presented as mean ± standard deviation.

MB Medetomidine and Buprenorphine, MM Medetomidine, Methadone

5.0e, - Adverse effects

The adverse effects were low although isoflurane vaporiser settings had to be increased for MB in 10 cases (18%). Mask resistance was noted for 4 cases (7%) in the MB group. There were no significant differences between groups for vomiting during the initial sedation stage (Table 7).

Table 7: - Adverse effects observed

Adverse reaction	MB (n=56)	MM (n=33)
Vomiting post initial drug administration	2	2
% isoflurane maintenance increase	10	2
Mask resistance	4	0

Data are numbers of cats exhibiting adverse events. MB Medetomidine and Buprenorphine, MM Medetomidine, Methadone.

6.0 Discussion

This is a unique study which explored a novel anaesthetic approach for a high throughout charity establishment with a strong focus on neutering with very little resource.

It was hypothesised that the combination of medetomidine and methadone would be superior for induction, and recovery resulting in a quick turnaround for high volume neutering.

It is furthermore acknowledged the huge progress made previously with the Quad combination and licensed Triple. The purpose was to devise an anaesthetic protocol suitable for mass neutering programmes building on the previous work (Yates and Leedham 2019, Joyce and Yates 2011). A careful approach with the novel aim of having welfare at the forefront was taken. With anaesthetic requirements in mind, the principle was to facilitate a high throughput of cats, neutered *in situ* using a purpose-built mobile theatre. Significant benefits are to those in the community where travel is an issue and to undertake outreach work in multi-cat environments where up to 20 neuters is possible. One study showed that in 10 households identified as a public complaint associated with hoarding behaviour reported to the RSPCA intervention team, there were

176 cats, a median of 16 cats per household which showed the huge scale of the problem (Hill et al. 2019).

A short acting anaesthetic with a fast recovery to allow both quick returns to owners and a rapid cost-effective turnover of neuters was required. This builds on studies that have shown that stress associated from unfamiliar surroundings can be considered to negatively impact on welfare, hence the reason to explore short acting protocols for quick recoveries (Wongsaengchan and McKeegan 2019). Furthermore, the IM route for initial induction of anaesthesia rather than intravenous route was also important and necessary. The primary outcome was a reliable dosing schedule to ensure personnel ease of use for accurate, quick calculations and safe anaesthesia.

It is difficult to differentiate between the MM and MB combinations in terms of analgesia, primarily due to the severity of the pain challenge of each procedure and the combination of analgesic drugs used. The surgical skills and competency of the students vary resulting in different lengths of procedure as a result of the learning process, however this is a realistic environment which utilises resources in a high-volume veterinary practice. The protocol used in this study had a crucial element of assessing the sedation quality. This factor is rarely captured in mortality and morbidity studies (Simon and Steagall 2020) so establishing the metric is an advancement. This is an important factor when validating a combination. The difficulties with such research is that when individual pharmaceutical components are combined it is rather difficult to parse out the factors individually. This supports the notion of sedation scoring, to establish initial differences too at the start of the procedure, rather than only focussing on outcome measures at the end of the procedure. However further studies would still be useful to compare the differences between different combinations as a whole from staff and owner perspectives (Matthews et al. 2017).

The recovery times is an essential purpose of the study to allow a sufficient turnaround in quantity of patients in an given environment. This study concludes that both combinations offer a viable option in regards to reducing recovery times compared to the availability of anaesthesia combinations currently available (Bruniges, et al 2016). However it must be noted, there are literatures and studies which explores different durations of recovery of patients with potential to look at other opioids available such as butorphanol (Moser et al, 2020). There are different opioids at different strengths which have potential to improve on recovery outcomes in terms of timings and quality compared to others widely available through further research (Ko et al 2011, Bruniges et al, 2016 and Mahdmina et al 2020).

Intramuscular combinations are crucial in high volume charity practice as this offers ease of approach for administration. Other advantages are quick preparation of equal dosing protocols, reliability in small patients, non-incremental dosing which reduces implications of errors. Utilising veterinary nurses for administration of non-incremental dosing which they would normally be prevented from carrying out would be of benefit to a reduced staffing environment. Cost factors of drugs when using larger doses in larger patients comparable to that of linear dosing are also crucial to ensure sustainability in use.

In retrospect; there are some disadvantages of the IM approach, these being no IV access for intubation difficulties, post mask placement difficulties and other potential emergencies during surgery. Previous research carried out on small cats showed that IV combinations using alfaxalone are effective, but ease of access and placement is challenging, and dependent upon staff expertise (O'Hagan et al. 2012, Zaki, Ticehurst, and Miyaki 2009).

The limitations of the mask inductions were apparent with two key factors, firstly the MB combination had a lower sedation score as originally hypothesised, and upon mask induction there was some resistance which then posed difficulties for intubation. Secondly the other factor was the use of feral cats. Feral cats in a shelter veterinary environment are prevalent as part of the approach to population control, hence the need to ensure that combinations can accommodate this. The IM approach is useful and far safer for staff and these patients, although these cats were less sedate for mask placement. There are considerations as to whether ketamine as an additional component would prove useful. This would be a natural progression to extend a study to include a contingency factor.

The use of ketamine in one study was found to offer cardiovascular stability during undertaking echocardiographic examinations (Lazzarini et al. 2020). Further research evaluating for example a dose of 1mg/kg of ketamine and the effects on cardiovascular involvement would be beneficial as no studies incorporating it are known in cats (Slingsby and Waterman-Pearson 2000). The benefits of this could prove useful especially in fractious cats or feral cats for neutering purposes. The progression could offer an alternative to the risks posed with mask inductions but in retrospect the current study using the IM route for ease of access, rapid and reliable sedation and profound analgesic effects is highly attractive for high throughput neutering. A study to explore the timings of ketamine administration in a high-volume setting is warranted.

The physiological effects of the alpha 2 agonist such as medetomidine which is used in both combinations in the study is a factor to consider. It is documented that optimum sedation can only be achieved in calm and quiet surroundings with little environmental stimuli. Evidence has shown that pre-existing fear, pain, excitement, stress and even aggression such as in the case of feral cats may delay the onset of sedation (Sinclair 2003). In a high-volume setting noises such as personnel walking past kennels or cleaning in kennel areas which may disturb recoveries is difficult to control for. However, this represents a normal hospital setting so the results from the sedation and recovery scores despite these concerns accurately reflects clinical practice. The degree of environmental noise is recorded in some studies (White and Yates 2017). The addition of the opioid ensures more profound sedation (Slingsby et al. 2015).

The use of medetomidine was used in both combinations, further studies could be undertaken using dexmedetomidine. Studies have shown this to have a shorter duration of onset of around 5 minutes (Simon and Steagall 2020, Reader et al, 2019) which could prove useful for a quicker onset of sedation or if there is an improvement on the sedation scoring used in this study. The same study has shown this combination to have superior analgesic effects and antinociceptive effects were improved when this combination was used (Simon and Steagall 2020). Further research in this area could see potential improvements in sedation using the same protocol of mask inductions.

The duration of surgery with these combinations also has room for further research. The focal point of this study was cat castrations which had an average surgery time of 30 minutes in duration. The question posed is the suitability of the combination for cat spays which inevitably increases surgery time. Earlier studies have shown suitability of the extended period of analgesic effects and this could potentially apply to other species such as ferrets or even other procedures itself.

Thermoregulation is a crucial factor because of the effects of alpha 2 agonists and the importance of maintaining temperature during and after procedures. Research into recovery timings in relation to environmental temperatures such as comparisons to heated and non-heated accommodation for recovery stages would be beneficial. The risk of hypothermia is a factor to consider especially with patients with high body surface area to mass ratio where delays of recovery could be detrimental (Clancy 2016).

Sedation scoring at 10 minutes post injection of the combination was calculated for its effectiveness in this study. This could be expanded to include intervals as early as potentially 5 minutes, 10 minutes and also 15 minutes prior to mask induction. This could give a reliable insight to see if there were any changes in the quality of sedation. Further research could see the optimum time using different time points for quality and onset of sedation prior to surgery.

The implications of using inhalation anaesthetics were considered in the study design due to environmental concerns usually associated with chamber or mask inductions. The study had a strong emphasis on safety but equally factoring in the effectiveness of the combination. Chronic exposures of personnel to anaesthetic gas can cause oxidative stress, DNA damage and carcinogenesis which is a significant concern especially those working as anaesthesiologists (Fay 2018). Equipment to minimise the effects of this such as scavenging systems and waste control systems such as ventilation systems / air conditioning can reduce these but not eliminate the waste gas in total. The thresholds for monitoring waste gas do vary from country to country which governs permissible limits, an example is 50ppm (parts per million) (383mg/m^3) in England comparable to 5ppm (38mg/m^3) in Denmark (Deng et al. 2018). The use of Salus monitoring devices were used in this study to compare differences between normal working environments compared to the use of mask inductions in this study. Salus monitoring devices are designed as badges worn in the clinical environment which measures exposures within a given specified time on an 8 hour time weighted average. This ensures that the limits are within the work exposure limits (WEL). These are usually advised to be performed 6 monthly or annually (by the HSE and the RCVS Practice Standards Scheme). The results were that there were no increased levels using either mask inductions combinations in a duration of 6 hours. There were three personnel involved during the duration of the monitoring process with results of 2.2 ppm, 2.7 ppm and 2.4 ppm which were all well below the levels of maximum limits of 50 ppm and even below the lower levels of limits set by Denmark for comparison. The mask induction process in the combination formed a small step in the process (two-minute process of mask induction followed by a further one minute in between lidocaine administration over the larynx). A circuit cap was used to seal the end of the breathing system during each step to prevent unnecessary leakage. The mask induction was a key element prior to endotracheal intubation to smooth transition to the maintenance phase. It is known that excessive concentrations to achieve sedation and involuntary excitement have an increased risk of mortality (Simon and Steagall 2020). Further studies could be undertaken on anaesthetic masks design and also whether there could be better designed breathing circuits.

The use of cuffed endotracheal tubes in this study with a measured approach to the inflation of the cuff using a manometer cuffill™ syringe. The cuffill™ is widely used in human medicine given the controversial evidence of the use of cuffed endotracheal tubes in relation to tracheal trauma. It is reasonable to suggest that there is no reason why a careful approach could be taken to achieve a seal around the ET tube to ensure suitable maintenance following the initial mask induction. The tube was inflated to 30cm H_2O pressure in accordance with manufacturer guidelines and publications (Grubb, 2019, White et al. 2017). This was furthermore backed up with the use of capnography to aid suitable placement but equally avoiding both under inflation causing leakage of volatile gas and also over inflation which is a well-documented concern in veterinary use in cats. Although this study, and others shows that it is reasonable to use cuffed endotracheal tubes in cats, further research into lengths of tubes and the design of ET tubes are warranted. All too often an estimate of the tube in order to cut to size poses issues with the replacement of connectors allowing a smooth connection to the circuit.

The data obtained during the monitoring process for HR and RR levels, It is noted, that average thresholds through all intraoperative variables are markedly different with HR and RR levels recorded at all time points lower with MM than that of MB. Results are consistent with opioid together with alpha-2 agonists working synergistically due to posts-receptors mechanisms being shared. Methadone compared to buprenorphine clearly showed that sedative and analgesic effects are more profound in methadone than seen in buprenorphine. This is also seen in a similar study by (Mahdmina et al. 2020).

The process of recovery is scrutinised in this study of a high-volume neutering setting. There are risk factors that need to be considered since the recovery period is associated with more problems than the sedation and maintenance phases. It is stated in one study that the prevalence of mortality is 52-60% during the 3 hours postoperatively (Brodbelt et al, 2007). This is one factor that was accounted for to reduce these risks by having a quick recovery process lasting minutes rather than hours. This helps nursing staff in a reduced staffed resource shelter environment to observe a recovery period before discharging which otherwise could stretch personnel time beyond the capacity to deal with a high volume intake (Brodbelt et al. 2007, Matthews et al. 2017).

The recovery period duration is important, but the quality of the recovery still needs to be described too. Future studies could for example include ataxia, mobility, spatial awareness, ocular differences and other factors such as interest in food and time to eating. There are a huge range of parameters which could be explored with further research. Pressure mats would offer a reliable gait analysis of cats however most research has been done involving either dogs or those with orthopaedic conditions (Stadig and Bergh 2015). Very little research has been done using healthy cats which could prove useful in a study such as this (Lascelles et al. 2007). Weight distribution, step cycles, jump analysis could all be developed using the pressure mat system originally designed to assist with diagnosis of orthopaedic conditions for qualities of recoveries. The limitations with the use of pressure mats are the complex technology needed which in turns has cost implications but nevertheless could prove useful with data obtained. This study used parameters including sternal times and portal entry times as key time points, it was felt that these were clear observational outcomes. Standing times are controversial as found by previous studies; for example a cat may stand on its front two paws but could appear as sitting down, so this may offer a flawed timed result (Bruniges et al. 2016). Entering the portal gives a clear indication that the patient would almost certainly would have to stand on all limbs to be able to walk and enter the portal giving a reliable insight to the quality of both mobility but also the recovery process.

The data obtained for the age of each patient were obtained on records prior to admission, it is noted that these are estimated by non-veterinary personnel especially from sources such as the inspectorate, branches and those from large multi-cat households. These account for 64.3% of MB cases and 42.4% of MM cases, respectively.

The demographic data which were obtained showed that VT work is a key component seen in charity practice. This is usually derived from inspectorate generated sources including those from multi-cat households, strays and ferals, and those participating in TNR work. It is important to note that VT sources are likely to have estimated ages on presentation.

Vomiting is an effect of both opioids and alpha-2 agonists and is documented in some papers. It was an occurrence in this study primarily in cats from unknown sources. In these cats it is difficult to ascertain if and when the cat has eaten prior to surgery. This can be minimised as much as possible through recommended fasting before the surgery. There have been some studies undertaken to trial potent antiemetic medication such as maropitant which has been shown to reduce the incident of emesis in dogs and shown to be effective in cats if administered orally prior to sedation (Martin-Flores et al. 2017).

The use of eating as an indicator of recovery was considered in the early stages of the pilot but it was argued that it was open to interpretation of findings and that it varied between cats. There are documented uses in trials using eating times as a factor of the recovery process especially when ketamine is used which evidently prolongs the recovery process. Anaesthetic agents and adjunctive drugs are known to stimulate appetite. This is worth considering if using such drugs as part of the protocol (Armstrong et al. 2018). The same study stated that the length of surgery time could potentially affect the time to eating if measured post-operatively. This is a factor that could prove useful if further studies are performed using feline ovariohysterectomy which tend to be a longer surgery time than orchidectomy. Overall, the standardisation of the study did entail a small proportional of Hills a-d (¼ of tin) which was placed in at the time of recovery for post-op welfare.

Emesis is often reported with alpha 2 agonists due to stimulation of the chemoreceptors. In retrospect the cause of emesis in two cases in both combinations could also be a result of inadequate fasting times prior to admittance from owners or unknown due to mass neutering in multi-cat households.

7.0 Further work

The ability to reduce anxiety and calm animals prior to anaesthesia is desirable. The use of gabapentin could prove useful in future studies. Gabapentin is an antiepileptic which is available in tablet or liquid form which could be given by the pet's owner. Documented evidence suggests that 100-150mg oral gabapentin could prove useful in reducing stress and may improve compliance with mask inductions if administered 90 minutes before transportation in a carrier (Van Haaften et al. 2017).

There is further research required on dose rates and routes of administration of other drugs such as low dose ketamine which has been documented in dogs but not cats, this could be useful to reinforce protocols suitable for early neutering (Slingsby and Waterman-Pearson 2000).

The use of xenon as a novel gas instead of isoflurane has shown to have potential in some studies although notable rare and expensive but has shown to have no toxicity or teratogenic effects. The benefits would be rapid induction and quick recoveries through low blood solubility and minimal metabolism in the body (Lane et al. 1980). There are also cost implications and environmental concerns for production of this so careful consideration if these were brought into use (Neice and Zornow 2016).

One study using methadone in combination with medetomidine as a premedication prior to ovariohysterectomy and castration in the cat by Slingsby et al (2015), acknowledged reliable sedation, however it went on to state that butorphanol could prove a useful component combined with medetomidine to provide a better level of sedation compared to buprenorphine. The study acknowledged there was no data to support this claim. Given the duration of butorphanol is 2 hours in comparison to that of longer durations of methadone and buprenorphine it could be a useful contender for short procedures such as castrations. However, it might be limited to castrations rather than ovariohysterectomy which have a longer duration of surgery and more intense nociception (Slingsby et al. 2015).

It is hoped that the findings from this study will improve anaesthetic protocols particularly in relation to the recoveries. The study will aid the primary objective of improving neutering of cats in a variety of scenarios such as public generated, feral cat population management and multi-cat household management. Use of face masks are well documented, but not widely accepted and research in design for those suitable for brachycephalic cats is needed, aiming for a good seal and reduced dead space to provide better induction but also reduced environmental contamination (Friembichler et al. 2011).

8.0 Conclusion

Our studies have shown that the use of MM offered a superior multimodal approach using mask induction when compared to MB. As the hypothesis suggests, MM offered a higher sedation score compared to the buprenorphine combination although both appear to have quick recovery time overall when compared to other combinations such as the Triple and Quad combination. The modified scoring system which includes the mask induction assessment proves that this protocol enables a smooth process in which maintenance can take place through placement of an ET tube using a standardised process. It is concluded that MM is valid as a combination suitable for orchidectomy in cats and may be suitable for other diagnostic and surgical procedures.

The speed of recovery crucial for a high turnaround in a high volume setting also showed that MM cats were quicker in their sternal and portal times compared to MB.

It is important to note that atipamezole as a reversal agent had an important role in this study. There is research to be undertaken on effects of atipamezole in terms of dose rate and timings of administration which could prove useful to the hypothesis and strengthen the combination through a wide standardisation as a suitable combination for early neutering.

The adverse effects of MB were markedly different to MM when considering the use of initial mask induction. In the MB group 10 cases needed the vaporiser increased which is 18% of total cases compared to 2 cases with MM (6%). This was crucial data to collect to back up evidence of not only a more reliable method of induction but also considering a safe protocol for personnel involved.

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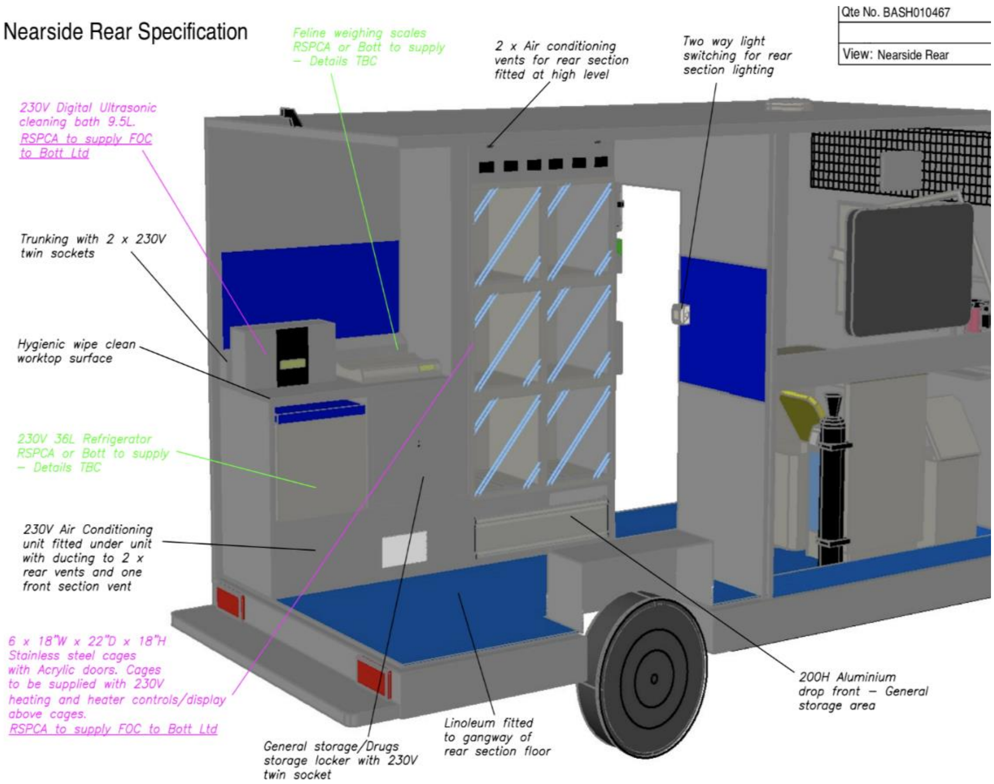
10.0 Appendix

Appendix 10.0 - Architect specification for mobile theatre

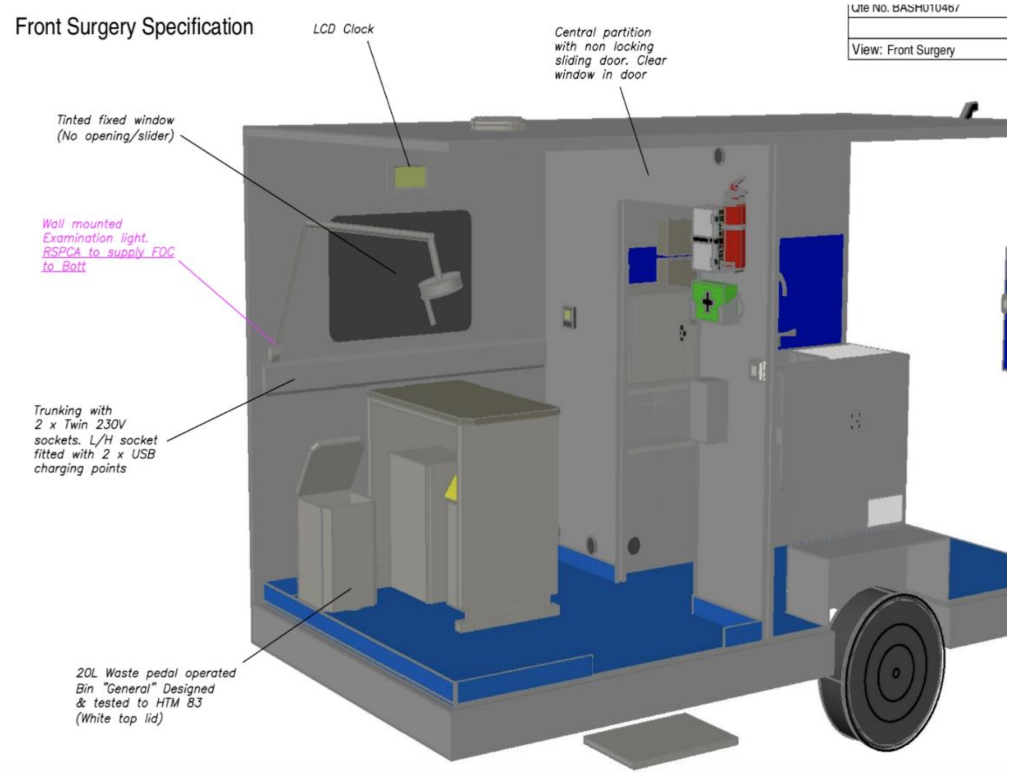
The specifications and design were done in conjunction with Botts Ltd. Designed as requested by Albert Holgate and Ben Faulkner. This vehicle was designed as a multipurpose operating theatre which can attend community outreach programmes, multi-cat households and branches which don’t have facilities to provide for veterinary support. The vehicle is designed to have its own power source and ability to be hooked up to external power. The vehicle has its own water supply and wastewater tank and heating supply. (See appendix diagrams which show the layout and equipment installed)

10.0a, Nearside Rear Specification – this highlights the typical layout with a focal point of 6 heated kennels.



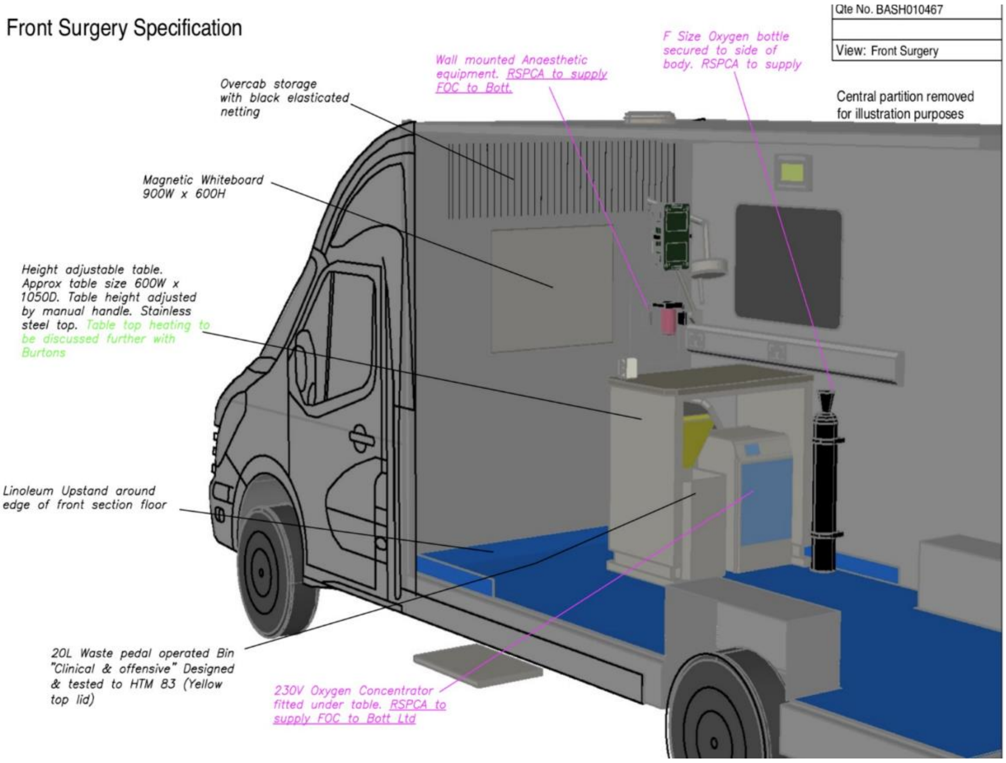
Design plans by Bott Ltd (2018)

10.0b, Front Surgery Specification – This shows the layout of the operating area with enough room for 2 personnel (Veterinary surgeon and nursing support)



Design plans by Bott Ltd (2018)

10.0c, Front Surgery Specification – This shows a viewpoint of anaesthetic machine, operating table but with a focal point of a extension of design of whiteboard intended for student teaching support for those assisting veterinary surgeons during outreach work.



Design plans by Bott Ltd (2018)

Coronavirus statement

This work was done throughout the 2019 pandemic with every attempt made to minimise the impact on the research and compiling this document. This was made possible by the generosity of Nottingham University and the support of Professor Kate White FRCVS and Mr David Yates MRCVS.