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THE ANAESTHETIC MANAGEMENT OF PATIENTS UNDERGOING CAESAREAN SECTION SURGERY AND ITS IMPACT ON POST-OPERATIVE ANALGESIA

Sean Chetty

A Thesis submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, in fulfilment of the requirements for the degree of Doctor of Philosophy

Signed on the 14th October 2016 in Johannesburg

DECLARATION

I Sean Chetty, declare that this thesis is my own, unaided work. It is being submitted for the Degree of Doctor of Philosophy at the University of the Witwatersrand, Johannesburg. It has not been previously submitted for any degree or examination at any other University

This thesis is submitted in the divided block format, which is approved by the Faculty of Health Sciences.

_____
Sean Chetty

14th day of October 2016 in Johannesburg

DEDICATION

To my wife Trusha, for her constant support and encouragement during this journey to complete my PhD

To my children, Keyuri and Tanika, for inspiring me each day to strive to be a better person

To my parents, and my sister, for always supporting my academic goals and applauding my achievements

To my paternal grandmother, for establishing a level of self-confidence in me that has driven my ambitions and goals throughout my life

To my patients, for humbling me and reminding me every day why I chose to become a doctor

PRESENTATIONS ARISING FROM THIS STUDY

Poster Presentations

1. ***European Society of Anaesthesia Congress 2015***
   The recommended Anaesthetic Technique for Caesarean Section surgery in South Africa
   S Chetty, P Kamerman, F Paruk

2. ***European Pain Congress 2015***
   Post-operative Analgesia Practices after Caesarean Section surgery in South Africa: Results of a national survey
   S Chetty, P Kamerman, F Paruk

3. ***World Congress of Anaesthesiologists 2016***
   Low Dose Intrathecal Morphine Reduces Post-Operative Opioid Requirements after Caesarean Section
   S Chetty, P Kamerman, F Paruk

Oral Presentations

1. ***SASA National Congress 2015***
   Obstetric Anaesthetic Practices in South Africa: Results of a national survey
   S Chetty, F Paruk, P Kamerman

Invited Speaker Presentations

1. ***Indoanaesthesia Congress 2016***
   Post-op Caesarean Section pain – How bad can it be?
   S Chetty

2. ***European Society of Anaesthesia Congress 2016***
   Pain after C-section: what does really work and how do you get benefit from participating in PAIN OUT?
   S Chetty

3. ***IASP World Pain Congress 2016***
   Improving management of post-operative pain – Can it be done in low and middle-resource countries?
   S Chetty

ABSTRACT

Poorly controlled pain following caesarean section surgery can have a debilitating effect on the physical and emotional well being of a woman during the post-operative period. Good intra-operative anaesthetic management during caesarean section surgery is requisite to improve post-operative analgesia, and thereby contribute to the well being of the patient.

In South Africa (SA) there are currently no national obstetric anaesthesia practice guidelines. Anaesthetic service providers therefore rely on knowledge acquired during their anaesthetic training and recommendations from international guidelines (which may not be applicable in SA). In order to establish a reference standard of anaesthetic care for obstetric patients in SA, a semi-structured interview was conducted with the heads of department and/or their representatives from the eight anaesthesiology academic departments in SA in 2012. The experts provided recommendations on the intra-operative anaesthetic management of patients for elective and emergency caesarean sections, as well as the post-operative monitoring and analgesic management of these patients. The recommendations were based on the experts' understanding of the uniquely local healthcare environment in SA.

Following the establishment of the SA reference standard, a national survey of anaesthetic service providers was conducted in 2014 to establish what the practises are in South Africa for caesarean section anaesthetics. Nine-hundred-and-thirty-three survey responses were analysed, which equated to a 58% response rate. The majority of anaesthesia providers (97.8%) perform single shot spinal anaesthesia for caesarean sections. Thirty percent of respondents chose to use Quincke spinal needles, despite the increased risk of this needle causing post-dural puncture headaches (PDPH). The preferred local anaesthetic drug was 0.5% bupivacaine with dextrose, and fentanyl was the most commonly used additive agent, as opposed to common international practice, which advocates morphine. The survey also revealed that 58% of doctors work in hospitals that do not have a post-operative monitoring

protocol for patients following caesarean section surgery. This contrasts to recommendations suggested by the national experts regarding patient monitoring requirements.

A clinical trial was then conducted to compare the analgesic efficacy of two different doses of intrathecal morphine (50µg and 100µg) with 25µg fentanyl. Patients in both morphine treatment groups had significantly lower post-operative opioid requirements than patients in the fentanyl group. The pain numerical rating scale (NRS) scores were however not statistically different and there was also no difference in the side effects profile or emotional parameters measured, between the groups.

This study highlights the differences in the recommended practise of obstetric anaesthesia in SA compared to other countries and demonstrates how obstetric anaesthesia is practised in SA. The final component of this study has demonstrated how international best practices can be easily implemented in SA to improve the anaesthetic care of the obstetric patient.

ACKNOWLEDGEMENTS

I would like to acknowledge the following individuals and organisations for their contributions and assistance:

- The University of the Witwatersrand, Faculty of Health Sciences, Faculty Research Grants awarded to me in 2012 and 2015
- The Jan Pretorius Research Fund from the South African Society of Anaesthesiologists
- The South African Medical Research Council (Development grant awarded in 2015)
- The members of staff of the Anaesthesiology department at the University of the Witwatersrand, who reviewed the questionnaires used in this study
- The national experts, who participated in this study
- The SASA secretariat for assisting me with the distribution of the electronic version of the national survey to the society's membership database
- The 2014 SASA congress organising committee for allowing me access to the congress delegates to distribute the national survey
- The anaesthetic service providers, who participated in this study
- The patients who agreed to participate in the clinical trial
- The anaesthesiology registrars and medical officers who administered the spinal anaesthetics to the clinical trial patients, by strictly following the protocol instructions
- Adcock Ingram Critical Care for donating multiport IV extension sets to facilitate the PCA IV access on a separate IV line in the clinical trial
- The following anaesthesiology staff assisted with data collection during their acute pain rotation:
    - Dr P Phukubye
    - Dr K Rathinasamy
    - Dr S Mkize
    - Dr F Desai
    - Dr M Sanders
    - Dr A Rachelson
    - Dr B Rikhotso
    - Dr Leopold-George
    - Dr R Lockhat
- My supervisors, Professors Peter Kamerman and Fathima Paruk, for their valuable guidance and support

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LIST OF ABBREVIATIONS AND SYMBOLS

α2	alpha-2
ANZCA	Australia and New Zealand College of Anaesthetists
APS	American Pain Society
ASA	American Society of Anesthesiologists
CSE	Combined-Spinal-Epidural
CSF	Cerebrospinal fluid
DVT	Deep vein thrombosis
ECG	Electrocardiogram
G	Standard Wire Gauge number
g	gram
HIV	Human Immunodeficiency Virus
HREC	Human Research Ethics Committee – Medical
GDP	Gross domestic product
IASP	International Association for the Study of Pain
ICU	Intensive Care Unit
IM	Intramuscular
IQR	Interquartile Range
IV	Intravenous
L1	Lumbar nerve 1
LOCF	last observation carried forward
mg	milligrams
mm	millimeter
MPQ	The McGill Pain Questionnaire
NaHCO3	Sodium Bicarbonate
NICE	National Institute of Clinical Excellence
NMDA	N-methyl D-aspartate
NNH	Number needed to harm
NRS	Numerical rating scale
NSAIDs	Non-steroidal anti-inflammatory drugs
PCA	Patient controlled analgesia

PCEA	Patient controlled epidural analgesia
PDPH	Post-dural puncture headaches
PI	Principal investigator
PONV	Post-operative nausea and vomiting
PRN	pro re nata
RMMCH	Rahima Moosa Mother and Child Hospital
SBP	Systolic blood pressure
SDS	Simple descriptive scale
SpO2	Peripheral capillary oxygen saturation
SRDS	Self Rating Depression Scale
STAI	State Trait and Anxiety Inventory
SWT	South-west Thames
T10	Thoracic nerve 10
TAP	Transversus abdominus plane
UK	United Kingdom of Great Britain and Northern Ireland
USA	United States of America
USD	US Dollar
VAS	Visual Analogue Scale
VDS	Verbal Descriptor Scale
VRNS	Verbal Numerical rating scale
µg	micrograms

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CHAPTER ONE: INTRODUCTION

Caesarean section rates vary globally. In South Africa this rate exceeds the World Health Organisation (WHO) recommended rate of 10 – 15%, ranging between 16.1% and 20.3% in the public sector district hospitals and metropolitan hospitals, respectively (Moodley, 2010). In the private sector, the caesarean section rate is reported to be as high as 70% (CMS, 2015). The high rate of caesarean sections in South Africa may be due to a more defensive practice of obstetrics by South African doctors and the high rate of maternal requests, but there are no definitive data on the cause. This trend towards high caesarean section rates is not unique to South Africa. The caesarean section rate in the United States of America (USA) in 2013 was 32.7% (Martin *et al.*, 2015). European figures range from 14.8% in Iceland to 52.2% in Cyprus, with a median European rate of 25.2% (Macfarlane *et al.*, 2015). The authors of this European study highlighted that there is evidence that the rising prevalence of caesarean sections across Europe may be due to non-medical reasons, such as maternal request, health system organization and reimbursement policies. However further research is required to make a definitive determination of the rising rate of caesarean sections in Europe (Macfarlane *et al.*, 2015).

The increasing number of caesarean sections being performed means that there is an increasing number of women who require anaesthesia for the procedure and, analgesia for post-surgical pain following the birth of their children. Inadequately treated post-operative pain is associated with its own complications (Stephens *et al.*, 2003), which lead to increased morbidity following delivery. Consequently, the anaesthetic management of the obstetric patient in South Africa, and internationally, has become an increasingly important component in the care of these women.

In South Africa there are no accepted guidelines or protocols for the anaesthetic management of the caesarean section patient. Furthermore,

there are no data available regarding who should take responsibility for the management of the post-operative pain in these patients (eg. obstetrician or anaesthesiologist), or how the pain is being managed. Indeed, even if pain management protocols are used and are correctly implemented, yet they do not result in higher patient satisfaction, then the analgesic regimen has failed.

Good anaesthetic management of the caesarean section patient has the potential to improve patients' birth experiences (Karlstrom, 2007) and decrease the risk of post-operative morbidity (Stephens *et al*., 2003). The period of childbirth can make a woman extremely vulnerable. Women delivering their babies by caesarean section are particularly vulnerable and may feel disempowered during this process. As healthcare providers we have an ethical responsibility to provide high quality pain management to these vulnerable patients. Failure to do this may be considered as a violation of the ethical principles of medicine.

The lack of information surrounding anaesthetic practice and post-operative pain management for South African caesarean section procedures served as the impetus for this study. The ultimate goal of the research described in this thesis is to lay the foundational information required to improve pain management for women having caesarean sections in South Africa. That is, we need basic information on current analgesic practices used for caesarean sections in South Africa, which can inform the establishment of safe, effective, and cost effective pain management protocols, which can be implemented within the resource constraints of the local public healthcare system.

1.1 Study Aims

a) To describe the post-operative pain management practices of doctors managing caesarean section patients in South Africa.

b) To evaluate the safety and efficacy of different intrathecal opioids in women who have undergone caesarean section surgery.

1.2 Specific Objectives

1.2.1 Aim (a)

- To determine what is considered the reference standard in South Africa (as determined by the anaesthesiology academic heads of department) with regards to caesarean section relating to:
    - ❖ Preferred method of anaesthesia
    - ❖ Use of adjuvant drugs for neuraxial anaesthesia
    - ❖ Post-operative monitoring practices
    - ❖ Post-operative pain management

- To determine what the preferences are amongst specialist anaesthesiologists working in the public and private sector with regards to anaesthesia for caesarean section relating to:
    - ❖ Preferred method of anaesthesia
    - ❖ Use of adjuvant drugs for neuraxial anaesthesia
    - ❖ Post-operative monitoring practices
    - ❖ Post-operative pain management

- To determine what the preferences are amongst non-specialist medical practitioners (registrars, medical officers and general practitioners) with regards to anaesthesia for caesarean section relating to:
    - ❖ Preferred method of anaesthesia
    - ❖ Use of adjuvant drugs for neuraxial anaesthesia
    - ❖ Post-operative monitoring practices
    - ❖ Post-operative pain management

1.2.2 Aim (b)

- To evaluate the analgesic effect of three different intrathecal opioid mixtures (100µg morphine, 50µg morphine and 25µg fentanyl) in women who had undergone caesarean section surgery, relating specifically to:
    i. Post-operative analgesic requirements at two time points (12 hours and 24 hours) post surgery
    ii. Pain scores at two time points (12 hours and 24 hours) post surgery
    iii. Sedation scores at two time points (12 hours and 24 hours) post surgery
    iv. Post-operative nausea scores at two time points (12 hours and 24 hours) post surgery
    v. Post-operative pruritus scores at two time points (12 hours and 24 hours) post surgery

- To determine the impact that the patients' post-operative pain has on their activities in the first 24 hours after surgery

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CHAPTER TWO: LITERATURE REVIEW

In this chapter a review of the literature is presented and includes a discussion of the anaesthetic techniques of the caesarean section procedure, evaluation of pain after surgery and the management of pain after caesarean section surgery.

2.1 History of the caesarean section

The first documented successful caesarean section was performed in the Netherlands in 1792 on a woman who had a very small pelvis. In Africa, army surgeon, Dr. James Barry, performed the first documented caesarean section in Cape Town, South Africa, in 1826. (Van Dongen, 2009)

Prior to the advent of anaesthesia, caesarean section surgery was considered to be brutal and the associated mortality was extremely high. In 1846, William T.G. Morton initiated the revolution of modern surgery with the demonstration of the anaesthetic effects of diethyl ether. The discovery of anaesthesia permitted surgeons to take more time during surgery and to refine their methods and therefore improve their techniques. This ultimately resulted in an improvement in surgical outcomes. These purported benefits subsequently also influenced the surgical care of the pregnant patient, culminating in improved survival of women following the abdominal delivery of the foetus. The development of silver wire sutures by J. Marion Simms, to suture the uterine incision, lead to a reduction in women dying from unnecessary blood loss post caesarean sections. These changes together with an improvement in the understanding of sepsis, as well as the introduction of antibiotics, resulted in the caesarean section procedure developing into the relatively safe procedure that it is today. (Sewell, 1998)

The advent of anaesthesia has thus played a vital role in the outcome improvement of surgical procedures. This positive influence has also

extended to the improvement of caesarean section surgery, permitting more women access to this form of delivery. Anaesthesia currently has a very well defined role to play in improving the analgesic outcomes of women following their caesarean sections.

2.2 The caesarean section surgical procedure

A caesarean section constitutes a modern obstetric surgical procedure that is classically defined as "the delivery of a foetus through a surgical incision in the anterior abdominal wall" (Landon, 2007).

The indications for a caesarean section are numerous and may be divided into maternal, foetal or maternal-foetal indications, as depicted in Table 2.1.

TABLE 2.1: Indications for caesarean section

Maternal	Specific cardiac disease (Marfan's syndrome, unstable coronary artery disease)
	Specific respiratory disease (Guillian-Barré syndrome)
	Conditions associated with increased intracranial pressure
	Mechanical obstruction of the lower uterine segment (tumors, fibroids)
	Mechanical vulvar obstruction (condylomata)
Foetal	Non-reassuring foetal status
	Breech or transverse lie
	Maternal herpes
	Congenital anomalies
Maternal-foetal	Cephalopelvic disproportion
	Placental abruption
	Placenta previa
	Elective caesarean delivery

Adapted from (Landon, 2007)

Irrespective of the indication for the procedure, the surgery always involves an incision through the maternal abdominal wall and anterior uterine wall in order to extract the baby. Thereafter the surgeon needs to ensure that haemostasis is effected before surgical closure of the abdominal wound in multiple layers.

The surgical procedure stimulates multiple nociceptors in the skin, muscle and visceral organs. Nociceptors are free nerve endings in the skin, muscle and the viscera that respond to different potentially tissue-damaging stimuli in multiple ways. The tissue trauma leads to the release of a number of nociceptive mediators, such as bradykinin, hydrogen ions and substance P. These substances lead to the development of a pro-inflammatory milieu that sensitizes the nociceptor membranes, increasing their excitability. All these nociceptor stimuli (mechanical, thermal and chemical) are then transduced into electrical signals by membrane depolarization. If these electrical signals are of sufficient magnitude, or distribution across nociceptors, then this electrical potential is transformed into an action potential. (Vadivelu *et al*., 2009, Gold and Gebhart, 2010)

Figure 2.1 illustrates how the different mechanisms (thermal, mechanical or chemical) lead to the release of mediators that act on the nociceptors. The illustration demonstrates how these mediators will ultimately converge on transducers, such as TRPV1, leading to the transduction of the initial stimulation into an electrical signal. The figure also demonstrates how the transduction of noxious stimuli involves several cell types and may require multiple specific proteins, which are uniquely positioned within the nociceptor membrane, for the process of conversion of nociceptor stimulation into electrical signals that will travel to the central nervous system. The electrical signal is then interpreted in the brain as pain. (Gold and Gebhart, 2010)

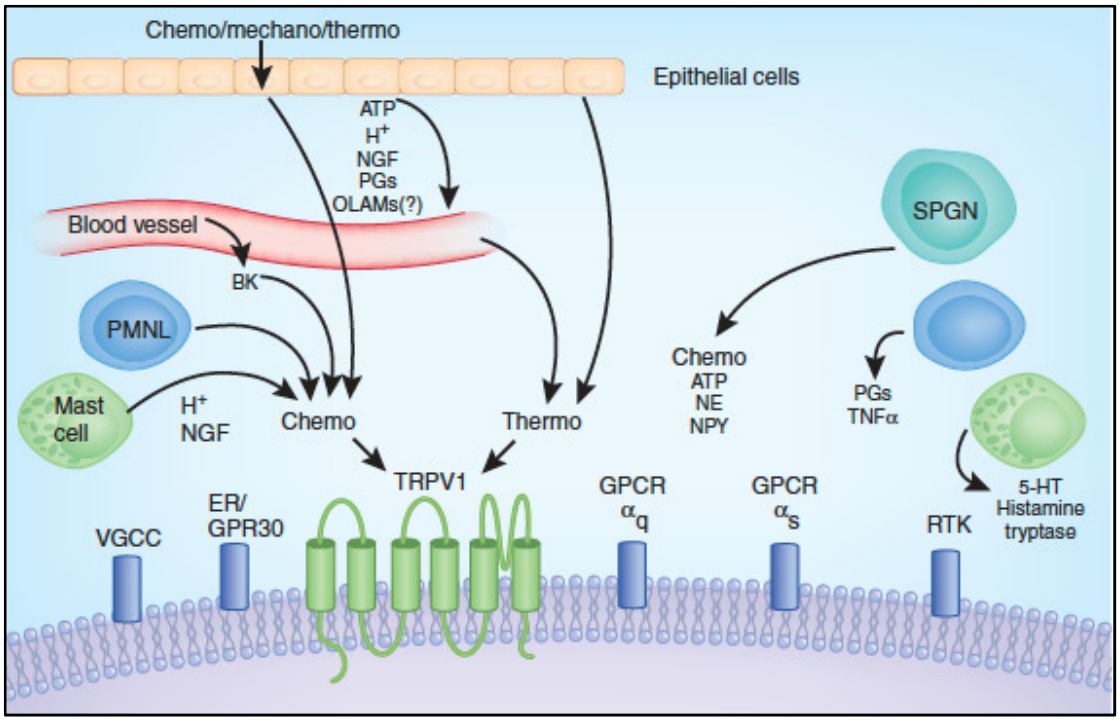


FIGURE 2.1: Transduction of stimuli into electrical signals (Gold and Gebhart, 2010)

The pain that patients experience has at least two components, somatic and visceral. Somatic pain is initiated from the nociceptors in the abdominal wound. These have both deep and cutaneous locations. The signal from these nociceptors is transmitted to the spinal cord through the anterior divisions of the spinal segment nerves from thoracic nerve 10 (T10) to lumbar nerve 1(L1). These nerves run laterally in the abdominal wall between layers of the internal oblique and transversus abdominis muscles. The visceral component of the pain is transmitted from the nociceptors in the uterus through the afferent nerve fibres that pass through the inferior hypogastric plexus. These nerves then enter the spinal cord through the T10 to L1 spinal nerves (McDonnell *et al*, 2009).

The signals travel through the peripheral nerve fibres to the dorsal horn of the spinal cord and then ascend to the brain via the ascending spinal tracts, where they are finally perceived in the sensory cortex as pain. These nerve fibres in the spinal cord have receptors that are responsive to opioid stimulation. Stimulation of these receptors results in the inhibition of the

transmission of nociceptive stimuli to the brain. This endogenous pain modulation system forms an important component of the innate pain control mechanisms. These receptors also provide a useful point of intervention for the management of pain after caesarean section surgery. (Helms and Barone, 2008)

2.3 Anaesthesia for caesarean section surgery

The anaesthesia indicated for caesarean section surgery can be in the form of general anaesthesia or neuraxial anaesthesia. Taking into account the unique anatomical and physiological changes that accompany pregnancy such as a reduced functional residual capacity and profound haemodymanic alterations, the pregnant patient at term (37 completed weeks gestation) poses a greater anaesthetic risk than a non-pregnant female (Birnbach and Browne, 2005). Consequently, neuraxial anaesthesia, which has lower risks associated with its use compared to general anaesthesia, predominates as the preferred anaesthetic method for caesarean section surgery (Tagaloa *et al*., 2009). Amongst the neuraxial anaesthesia techniques, spinal anaesthesia is reported to be more cost effective, less technically challenging and has been reported to achieve adequate surgical anaesthesia in a shorter timeframe as compared with epidural anaesthesia (Riley *et al*., 1995). Both spinal and epidural neuraxial anaesthesia techniques however, allow the mother to be conscious for the birth of her baby, and facilitate bonding to occur sooner with the neonate (within the theatre) as opposed to general anaesthesia (Stevens *et al*., 2014). In addition, there have been reports of a higher prevalence of chronic pain in patients who have had a caesarean section under general anaesthesia as compared to regional anaesthesia (Nikolajsen *et al*., 2004).

Based on the analysis of data from a large registry, Butwick *et al* (2016) demonstrated that there appears to be racial and ethnic disparities between the mode of anaesthesia for caesarean section surgery amongst women in the USA. After analyzing the records of the cohort comprising of 50974 women who had caesarean sections, the authors reported that the rates of general anaesthesia for caesarean section surgery for African American

women, in this study, was 11.3%, compared with rates of 5.2% for Caucasians and 5.8% for Hispanics. Even after correcting for obstetric and non-obstetric covariates, the odds of African American women having general anaesthesia for their caesarean section remained high (OR=1.7, 95%CI = 1.5 – 1.8) compared to other race groups in the USA. (Butwick *et al*., 2016)

Neuraxial anaesthesia involves the administration of a local anaesthetic solution into either the spinal or epidural space through a percutaneous puncture along the vertebral column. The onset of anaesthesia is approximately five minutes with spinal anaesthesia and 15 – 30 minutes with epidural anaesthesia (Kleinman, 2002). The duration, extent and intensity of the neural blockade largely depend on the type, volume and concentration of the local anaesthetic used (Kleinman, 2002), and any additive agents co-administered with the local anaesthetic. Indeed, the addition of non-anaesthetic agents to enhance the intensity and duration of the anaesthesia and analgesia is now commonly practiced (Gadsden, 2005). Additive agents commonly cited in the literature include neostigmine, clonidine, and opioids (Dahlgren *et al*., 1997, Krukowski *et al*., 1997, Benhamou *et al*., 1998). Of these agents, opioids are by far the most commonly used additive (Tagaloa *et al*., 2009). It has been suggested that intrathecal administration of opioid agents allows direct stimulation of the mu opioid receptors in the substantia gelatinosa of the dorsal horn of the spinal cord by suppressing excitatory neuropeptide release from C-fibres (Cousins, 1984). This allows for a more intense neuraxial block with a lower risk of transfer to the foetus (due to the low dose of opioid used).

Irrespective of the mode of anaesthesia provided to a woman for her surgery, the goal remains the same in that the patient should not experience any undue negative physiological response to the surgical incision, including undue pain.

2.4 Consequences of inadequately treated caesarean section pain

The childbirth experience is multidimensional and therefore complex to interrogate and explain (Waldenström *et al*., 1996); there are multiple factors that can influence the patient's emotional experience, and all of these can influence how she will perceive her birthing experience. Waldenström *et al* (1996) identified pain as one of six factors that contributed to explaining the overall birthing experiences of women. Post-operative pain can result in a number of unwanted physical and psychological sequelae for the patient (Breivik, 1998). These sequelae can have a negative impact on the mother as well as the mother-baby relationship if they are not detected or managed appropriately. Karlstrom (2007) reported that women in their study, who experienced more pain than expected after their caesarean section, were more likely to have a negative birth experience. Sixty two percent of women in their study reported that their ability to take care of their babies was adversely affected by their post-operative pain to a large or very large extent in the first 24 hours after delivery.

The physiological response to surgery is an important component of the healing process. The purpose of this response is to promote the development of a catabolic state, which is required for the healing process to occur. However, uncontrolled pain can exacerbate this normal response and this can lead to increased morbidity. Inadequately treated acute post-operative pain can adversely affect a number of different organ systems, but in the post-caesarean section patient, the most significant organ system affected is the central nervous system.

Prolonged activation of peripheral nociceptors can cause central sensitization and may lead to the development of chronic pain syndromes (Woolf, 1983). Therefore, inadequately treated acute post-operative pain increases the risk of development of chronic pain. Cogan *et al* (2002) reported that 19% of patients in the Quebec Post-operative Pain Management study experienced pain beyond three months following surgery.

In 2004, Nikolajsen *et al* (2004) found that 18.6% of post-caesarean section patients experienced persistent scar pain for more than three months after their surgery. The authors sent a postal survey to 244 patients who had caesarean section surgery over a one-year period at their hospital in Denmark, asking questions about chronic pain. Two hundred and twenty patients responded. Of the 41 patients who reported chronic pain following their surgery, 27 still had pain at the time of the survey; and 13 (5.9%) patients reported this to be constant. In addition to the physical burden to the individual patient and her family, chronic pain also incurs an economic cost to the community at large. Gaskin and Richards (2011) estimated that the total cost of pain to the American economy ranged between 560 and 635 billion United States dollars (USD) in 2010. This estimation was based on both the direct cost of care and the indirect costs related to the loss of productivity in the economy. The authors demonstrated that the annual cost of treating pain was greater than the costs related to heart disease, cancer and diabetes in 2010 (Gaskin and Richard, 2011).

Unrelieved post-operative pain can also have a negative psychological effect on the patient. Patients whose pain is inadequately controlled may experience sleep deprivation, anxiety, helplessness and fatigue (Stephens *et al*., 2003). All these physiological disturbances can prevent rapid recovery and rehabilitation of the patient in the post-operative recovery period (Pavlin, 2002).

In patients who have had caesarean section surgery, inadequately treated pain in the post-operative period can also adversely affect the bonding between mother and baby. Poor post-operative pain control has been shown to have a significant negative impact on breastfeeding and infant care (Karlstrom, 2007). The interference with this important nurturing process can lead to impaired bonding between mother and baby during this vital period.

Other organ systems that may be adversely affected by inadequate post-operative pain management include the respiratory system (Stephens *et al*., 2003, Breivik, 1998), the cardiovascular system (Stephens *et al*., 2003),

endocrine and metabolic systems (Stephens *et al*., 2003, Breivik, 1998), haematologic system (Stephens *et al*., 2003), gastrointestinal system (Breivik, 1998, Stephens *et al*., 2003), genitourinary system (Stephens *et al*., 2003) and the immune system (Page, 2000).

The multitude of problems that can develop in post-operative patients whose pain is poorly controlled demonstrates that this important aspect of patient care must be prioritized when planning maternal health care services.

2.5 Patients perception of post-caesarean section surgery pain

Surgery and the associated anaesthesia have the potential to become a frightening experience for many patients. Shafer *et al* (1996) demonstrated that many patients fear anaesthesia more than surgical complications (Shafer *et al*., 1996). Furthermore obstetric patients tend to experience additional anxieties about their surgery, which are related to fears about the baby's exposure to the anaesthetic agents and other drug exposures. In addition to these concerns, expectant mothers are often concerned about their ability to take care of their babies in the post-operative period. Pain, both during and after the caesarean section procedure, has been documented as the most important factor that obstetric patients are concerned about in relation to the entire surgical procedure for a caesarean section. Side effects, such as nausea and vomiting, pruritus and shivering, rank lower on the list of concerns that these patients have (Carvalho *et al*., 2005a).

Pain in the post-operative period is influenced by many different factors, including pre-existing psychological stressors (Keogh *et al*., 2006), intra-operative experiences (Keogh *et al*., 2006) and even the methods used to evaluate the patient's pain (Chooi *et al*., 2013). Pre-operative psychosocial factors have been hypothesized to influence the post-operative experience. Since most women deliver their babies vaginally, the majority of the research done in this field has investigated patients who experience this mode of delivery (Keogh *et al*., 2006). Keogh *et al* (2006) examined the influence of pre-operative psychosocial factors on the post-operative experiences of

women who delivered their babies by caesarean section. The authors evaluated women and their birth partners during the pre-, intra- and post-operative period following caesarean section surgery. Using regression analyses, they concluded that factors that predict the mother's post-operative pain are the patient's pre-operative negative expectations, her level of fear and her level of pain during the surgery and also her partner's level of fear during the surgery. In fact, the birth partner's level of fear during the surgery was the most significant predictor of the patient's post-operative pain in their study.

Based on the results of the Keogh *et al* (2006) study, experiencing pain during surgery has the potential to influence the pain perception that the patient will experience in the post-operative period. As such, a dense regional anaesthetic block will then probably not only provide good intra-operative analgesia but may also positively impact post-operative pain experiences. Keogh and colleagues (2006) also suggested that the anaesthesiologist may play a pivotal role in alleviating the patients' fears during surgery and this may also have a positive impact on the woman's post-operative pain experience as well. These results are supported by findings of a similar study (Jamison *et al*., 1993) investigating the psychosocial influences of women, undergoing abdominal hysterectomy surgery, on their post-operative intravenous analgesic use. Pre-operative emotional distress in this group of patients was significantly associated with the dose of analgesia used in the post-operative period (Jamison *et al*., 1993). Both these studies were however small single centre prospective studies.

In addition to pre-operative anxiety, prenatal depression may also influence post-operative pain experiences. Many studies have shown that depression and pain are comorbid but the interaction between these two conditions is not fully understood. Lou and Kong (2012) investigated the influence that pre-operative depression has on post-operative pain. The authors performed the Self Rating Depression Scale (SRDS) on 764 pregnant women before their surgery and then also evaluated their pain at 24, 48 and 72 hours post-operatively. They found that 29.7% of the women evaluated had positive

depressive symptoms prior to surgery. The authors demonstrated a statistically significant association ($p<0.05$) between pre-natal depression and pain scores in the post-operative period for all three periods evaluated. This study showed that pre-natal depression had a profound negative effect on the pain perception of women in the post-operative period. Considering that close to 30% of the study population had positive symptoms, this implies that this may have a significant impact on pain management in the post-operative period for this population group. It is therefore important that women should be screened and managed for depressive symptoms prenatally. This can have a positive impact on pain perception after surgery (Lou and Kong, 2012). Despite the statistically significant results reported by Lou and Kong, not all research in this field of study has yielded a positive correlation between the presence of psychological factors and post-operative pain. Hansson *et al* (1989) also investigated the influence of pre-operative psychological factors on pain in a different patient population, but could not link levels of pre-operative stress and tension with the post-operative pain experienced in patients undergoing third molar dental surgery (Hansson *et al*., 1989).

In addition to psychosocial factors, there is also evidence to suggest that psychophysical assessment of somatosensory function by quantitative sensory testing can have a predictive value in identifying women who will experience higher levels of pain after their caesarean section. Granot *et al* (2003) conducted pre-operative physical thermal quantitative sensory testing on fifty-eight pregnant women who were scheduled for elective caesarean section surgery. The post-operative pain of these patients was then evaluated on the first day after their surgery. The authors found that the pre-operative quantitative sensory thermal testing at $48^{o}C$ provided the most statistically relevant correlation ($r-0.527$, $p<0.003$) with the post-operative pain experienced by these patients, suggesting that this could be used as a predictive model for post-operative pain in this patient population. Pan and colleagues (2006) attempted to increase the predictive value of pre-operative testing further by combining physical and psychological testing. They evaluated thirty-four patients between one and ten days prior to their scheduled elective caesarean section surgery. Multiple five-second heat

stimuli were applied to the patients and their levels of perceived pain intensity and unpleasantness to the stimuli were recorded. In addition, all patients also completed the State Trait and Anxiety Inventory (STAI), which is a tool used to assess anxiety levels. The authors were able to identify risk factors for rest pain, movement pain and analgesic drug use in the post-operative period. The results of this study suggests that the severity of pain and opioid use in the post-operative period can be determined by a combination of factors that can be tested pre-operatively. The multiple regression analyses from the study suggest the ability to obtain a high probability of the occurrence of severe pain post-caesarean section surgery using these physical and psychological pre-operative tests.

The patient's perception of the post-operative pain may also be influenced by the method used to evaluate their pain. Chooi *et al* (2013) used the verbal numerical rating scale (VRNS) to assess standard pain scores and compared this with comfort scores post caesarean section. Three-hundred patients were randomized into two groups. Patients was asked to either rate their pain after surgery or alternatively to rate their comfort level after surgery. The group of patients who were asked to rate their pain (as opposed to their comfort) had significantly higher scores at rest ($p=0.001$) and with movement ($p<0.001$). The implication was that using words like "pain" when evaluating patients in the post-operative period may actually have a negative connotation for the patient and they may perceive the sensations they have after surgery to be unpleasant. This was in contrast to using neutral words that may not create a negative perception in the patient. In this study, more than half of the women in the group who were questioned directly about pain, reported that they had pain (74%) but also stated they were comfortable (79%), when this was asked directly. This implies that it may actually be more helpful to ask a patient as a direct question if they are comfortable, or if they are bothered by the pain or if they want treatment – in order to assess the patient after surgery, rather than just asking about their pain score. These findings may be explained by the fact that negative suggestions have been shown to influence changes in the anterior cingulate cortex. This area of the brain links the limbic

system to the sensory cortex. Changes in this area of the brain can therefore influence the clinical experience of the patient (Rainville P. *et al*., 1997).

The patient's perception of their post-operative pain is influenced by a multitude of different factors. Many of these are related to the patient's pre-operative physical and mental state however the method of assessment used to evaluate their pain may also have an important influence on how the patient experiences their pain.

2.6 Pain Assessment Tools

Pain is a subjective experience (Merskey *et al*., 1979), which makes the assessment of pain for clinical or research purposes very challenging. Its measurement requires patient compliance and the physical and mental ability to provide a response. This response involves converting the subjective experience of the patient into an objective measurement that can be analyzed and interpreted (Revill *et al*., 1976).

There are a number of different validated tools that have been developed for this purpose. Each of them has advantages and disadvantages depending on the purpose for which they are being used. The most popular pain measurement tools are unidimensional instruments. These pain assessment tools only assess one dimension of the patient's pain such as the intensity of the pain, or the frequency of pain attacks or quality of the pain. To only evaluate one dimension of the patient's pain experience may not adequately uncover the true nature of the pain. Unidimensional pain evaluation instruments are however easier to administer and easier for the patients to understand. The reproducibility and validity of the results obtained with these tests in research studies is a factor that has resulted in these instruments being very popular (Flaherty, 1996).

There are multidimensional pain evaluation instruments available, however these tools are much more complicated and tend to be more difficult for patients to complete. These tools assess the different facets of the patient's

life that may be affected by the pain and addresses important issues like quality of life.

2.6.1. Numerical Rating Scale

The Numerical Rating Scale (NRS) is an eleven-point rating instrument. The scale is made up of numbers from zero to ten, orientated either vertically or horizontally. Zero implies no pain and ten implies maximum pain for the individual patient. This is a unidimensional pain evaluation tool.

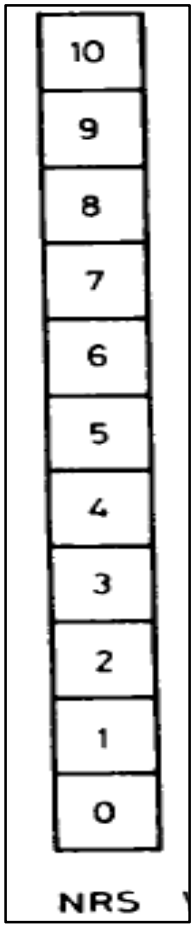


FIGURE 2.2: Format of the Numerical Rating Scale (Downie *et al*., 1978)

The NRS was described by Downie *et al* in 1978 and has been shown to exhibit good correlation with the less complicated 'simple descriptive scale' (SDS) (correlation factor 0.680). It also offers an advantage over the SDS with respect to measurement error (Downie *et al*., 1978). The original NRS was developed as an eleven point scale (0 to 10) however multiple versions

have been developed since in an effort to improve the sensitivity of the scale and the rates of correct response (Flaherty, 1996).

When evaluating a patient using the NRS, the patient is asked to rate their pain (most often the intensity of the pain) on the scale. The instrument allows for the conversion of a subjective experience into an objective value, which can be analysed and interpreted.

The NRS is a popular pain evaluation instrument for both clinical practice and pain research because it offers the clinician and patient a number of practical advantages. The scale is simple to administer and score, and is easy for patients to understand irrespective of the primary language of the patient. In addition to pain intensity, the scale can also be used to evaluate the effect of analgesic therapy (Flaherty, 1996). The main disadvantage associated with the NRS is that it has been found to be less reliable in very young and very old patients (Flaherty, 1996). There are, however, other pain evaluation tools that can be ultilised in these subsets of patients.

2.6.2 The Visual Analogue Scale

The Visual Analogue Scale (VAS) constitutes a simple straight line (either horizontal or vertical) with anchors at each end representing the extreme boundaries of the entity being measured. This is a unidimensional pain evaluation tool. The patient is asked to rate his/her experience of the measured entity by placing a mark on the line at the point on the line that represents their preference.

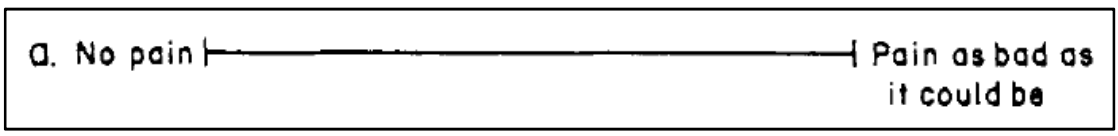


FIGURE 2.3: The Visual Analogue Scale (Wewers and Lowe, 1990)

The VAS has been used as a tool of measure in science for a very long time. The pain VAS originated from the scales used in the field of psychology to measure patient well-being (Pagare *et al*., 2015). Bond and Pilowsky (1966) modified the VAS for the assessment of pain in cancer patients using the anchors of "I have no pain at all" on the left and "My pain is as bad as it could possibly be" on the right sides of the horizontal line. This was followed by Woodford and Merskey (1972), who published one of the earliest uses of the VAS in pain research in the Journal of Psychosomatic Research. These authors correlated the VAS method of pain assessment with a descriptive method used to assess pain in forty-three patients referred to a psychiatrist for pain management.

Many different variations of the VAS exist. Investigators are free to decide if the line should be vertical or horizontal, and the investigator can also determine the length of the line used in a study. However, the 100 millimeter (mm) horizontal line is the most common variation used (Wewers and Lowe, 1990). The use of the horizontal line has been shown to produce a more accurate and uniform distribution of scores than is obtained when the VAS is orientated in vertical format (Scott and Huskisson, 1976). In addition, lines shorter than 100mm are less accurate at determining variations in pain experience than the 10, 15 or 20 centimeter lines (Revill *et al*., 1976).

The score of the VAS scale is calculated by measuring the distance in millimeters from the left sided anchor point to the patient's mark on the line. The VAS scale is therefore able to produce a sensitive measurement of the patient's perception of their pain and avoids categorization of the result, which is generally associated with visual descriptors. The simplicity of the VAS pain scoring system has made this a very popular tool for both clinical practice and research. It can be used in patients with poor eyesight and also in patients where vocabulary level is a concern. Disadvantages of the VAS include the fact that the tool can only be used when the patient is physically present and is able to make a mark on the line. It is therefore not suitable for telephonic follow-up with patients. Some patients also have difficulty in converting their subjective experience of pain into a meaningful mark on a straight line. This

can result in patients recording inaccurate responses on the scale. Researchers have attempted to overcome some of the disadvantages of the VAS by modifying the tool to accommodate for its disadvantages. The Graphic Rating Scale (GRS) is a modification of the VAS where verbal descriptors are placed on the straight line, giving the patient a reference point for their answer (Scott and Huskisson, 1976).

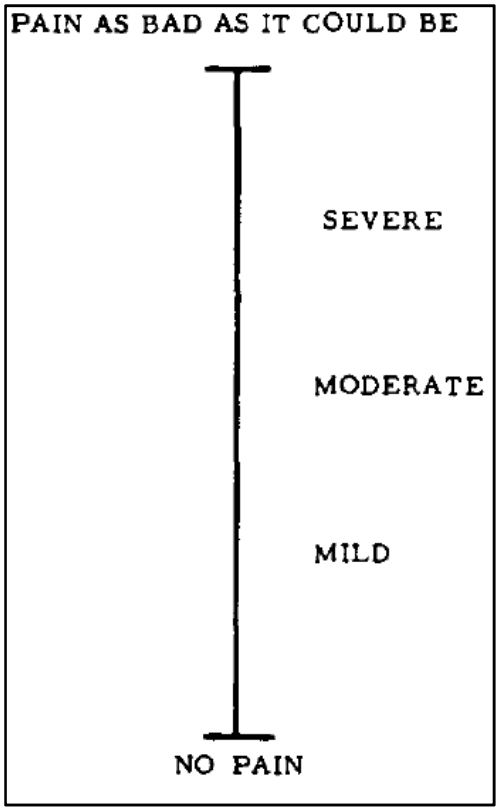


FIGURE 2.4: The Graphical Rating Scale (Scott and Huskisson, 1976)

The NRS, as described in detail in 2.6.1, is also a modified form of the VAS. It includes numbers at set points on the line, which assists the patients in orientating themselves to the scale.

2.6.3 Verbal Descriptor Scale

The Verbal Descriptor Scale (VDS) was first developed and validated by Professor Kenneth Keele in 1948. The chart was developed for evaluating patients' responses to analgesics. Professor Keele commented in his publication: "Pain charts are of value in defining the action of analgesics"

(Keele, 1948). While the VDS and other pain scales have matured into more robust assessment tools, these words were profound at a time when pain assessment was not being appropriately carried out by the medical profession.

The VDS consists of numerically ranked words describing the intensity of the patients' pain at the time of the assessment. This is a unidimensional pain evaluation tool.

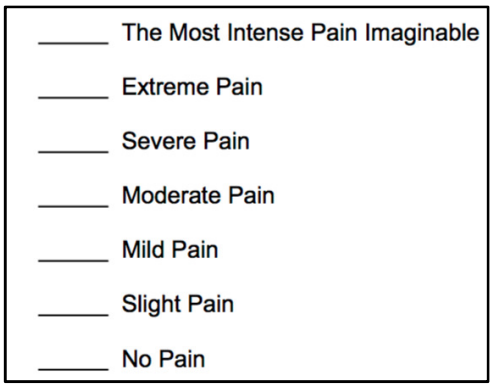


FIGURE 2.4: The Verbal Descriptor Scale (Iowa, 2016)

The patient has a more direct descriptor of the pain that they can identify with. However, a disadvantage of the VDS is that the scale artificially organizes the descriptors into categories by forcing the patient to choose one of the provided descriptors, and this may not actually reflect the true sensation of the patient.

2.6.4 McGill Pain Questionnaire

The McGill Pain Questionnaire (MPQ) is a multidimensional pain assessment instrument. The questionnaire assesses multiple factors that are influenced by or may influence the patient's pain. These include factors such as the pattern of the pain over a period of time, the sensory and affective components of the pain and also the location of the pain. These factors are evaluated in addition to the intensity of the pain. The MPQ was developed by Ronald Melzack, who is considered to be one of the founding fathers of the discipline of pain medicine. In the original publication of the MPQ the author

commented that: " The questionnaire was designed to provide quantitative measures of clinical pain that can be treated statistically" (Melzack, 1975).

The most important advantage of the MPQ is that the instrument addresses the multidimensionality of pain taking into account the psychological and behavioral components of the pain. Despite being a very useful tool, the MPQ is not popular in general clinical practice, especially for acute pain, because it is a complex document and requires a long period of time to complete correctly. In 1987 a short version of the MPQ was published (Melzack, 1987). This abbreviated form of the tool increased the clinical applicability of the MPQ while maintaining most of the advantages of the multidimensional assessment tool.

The screening tools discussed above are only four of many examples of pain assessment tools available for both clinical and research practice. Irrespective of the type of pain assessment tool that is used to evaluate a patient's pain, all these tools require that the relevant patient population is able to understand how to use these tools so that they can convert their subjective experience into an objective quantifiable value on the pain scale. South Africa has a literacy rate of 94.3% (Barrientos and Soria, 2016). Despite this high rate of literacy, there is still a portion of the population who are not able to easily understand pain assessment tools and we need to be cogniscient of the fact that pain assessment tools may not be clinically useful in this population.

Mudgalkar and colleagues (2012) investigated the impact of literacy on the ability to use two different pain assessment tools in a rural community in India. These authors concluded that illiterate patients could easily and reliably use both pain assessment tools that they evaluated (Visual Analogue scale and Numeric Analogue Scale). No studies investigating the validity of pain assessment tools in illiterate South Africans could be identified. However, extrapolating the results of the Indian study (Mudgalkar *et al*, 2012) to South Africa, it is reasonable to conclude that illiterate South Africans can also reliably use simple pain assessment tools.

Another criticism of pain assessment tools is that they only assess the patient's pain once it has already started. Considering the potential severe consequences of poorly treated post-operative pain in the obstetric patient, as discussed previously, it is imperative that we attempt to identify patients who may be at risk for developing severe pain following caesarean section surgery.

Pan and colleagues (2013) have developed a predictive model to identify patients at high risk of developing severe pain following caesarean section surgery. The tool consists of a simple three-item questionnaire assessing the patient's expectation of their pain and their analgesic requirements following surgery, as well as their level of anxiety towards the surgery. The responses to each of the three questions correlated with the pain experienced by the patient at 24 hours after surgery ($r=0.24 - 0.33$, $p<0.001$). The authors concluded that this predicative model could be used to identify high-risk women, who could then have their post-operative analgesia tailored to their specific requirements following surgery.

Identification of high-risk patients, as well as frequent and regular assessment of the patient's pain in the post-operative period will certainly assist the medical staff to manage the patients' pain more effectively.

2.7 Treatment of post-caesarean section surgery pain

Adequate analgesia for the post-operative caesarean section patient is extremely important in order to reduce the risk of side effects associated with poor post-operative pain control (as discussed in 2.4). These new mothers need to have good analgesia so that they can mobilise and take care of their babies. The ideal analgesic regimen should have maximum analgesic effect with minimal side effects and negligible infant exposure through the breast milk (Kwok *et al*., 2014). This is not easy to achieve, especially in developing countries, where many therapeutic options may not be accessible or affordable.

The approach to post-caesarean section pain management has evolved over time, as different drugs and administration techniques have developed. There are many factors that influence the regimen that is used by the anaesthesiologist, to manage a patient's post-operative pain. These factors include patient preferences and expectations, the expected level of difficulty and the duration of the surgery, as well as the preference and level of experience of the anaesthesiologist (McDonnell et al, 2009). The current practice in managing the post-operative pain in these patients is to utilize balanced, multimodal analgesic techniques (Kwok *et al*., 2014). This type of therapy involves the use of different analgesic agents such as opioids, non-steroidal anti-inflammatory drugs (NSAIDs), paracetamol and adjuvant agents; as well as administering these agents using different, synergistic methods. Each of these will be discussed below:

2.7.1 Regional anaesthetic techniques

Regional anaesthetic techniques allow the anaesthesiologist to focus the patient's anaesthetic or analgesic therapy to the specific areas being treated. This decreases the systemic effects and side effects of any agents that are used. Three regional anaesthetic techniques that can be used in the management of post-caesarean section pain are discussed below:

2.7.1.1 Neuraxial Techniques

Neuraxial anaesthetic techniques refer to spinal and epidural anaesthetic techniques. The post-operative analgesic benefits of these techniques are dependent on the adjuvant agents that are used in the neuraxial blocks or on the duration of the infusion of local anaesthetic agents. The administration of intrathecal opioids has proven to be extremely effective in managing the post-operative pain of women following caesarean section surgery (Palmer *et al*., 1999, Salmah and Choy, 2009, Hunt *et al*., 1989, Dahlgren *et al*., 1997, Terajima *et al*., 2003). Intrathecal fentanyl and sufentanil have been demonstrated to be superior to placebo in prolonging the period of effective

analgesia following caesarean section surgery (Dahlgren *et al*., 1997). Dahlgren *et al* (1997) randomized eighty women to receive different doses of intrathecal opioids or placebo, and compared the effects on their post-operative pain VAS scores, and their opioid analgesic requirements in the first 24 hours after surgery. The duration of complete analgesia increased from ninety minutes in the placebo group to up to four hours in the opioid treated groups. This significant increase in the duration of complete analgesia, in the opioid treated patients in this study, was noted by the authors to be similar to other earlier studies using these lipophilic opioid drugs. Despite the improved analgesic effects of these intrathecal opioids, these drugs are also associated with a higher incidence of side effects such as pruritus (Dahlgren *et al*., 1997). This higher side effects association may result in lower patient satisfaction levels after surgery despite improved pain control.

While both these lipophilic opioids (fentanyl and sufentanil) certainly increase the duration of analgesia compared to placebo, the duration of their effect is much shorter when compared to the analgesic effect of intrathecal morphine (Dahl *et al*., 1999). This is because morphine is less lipophilic than fentanyl and sufentanil (Fukuda, 2005), and takes longer to penetrate the nerves, resulting in a longer onset of action and a prolonged duration of action. Palmer *et al* (1999) compared the analgesic effects of eight different doses of intrathecal morphine and placebo, in one-hundred-and-eight women having spinal anaesthesia for elective caesarean section surgery. The post-operative opioid analgesic requirements were significantly higher in the placebo group compared to five of the eight morphine groups. The patient controlled analgesia (PCA) morphine use was 45.7mg lower in the 75µg morphine group compared to the placebo group (95% CI = 4.8mg – 86.6mg). There was however no significant difference in the PCA morphine use between the different intrathecal morphine dose groups.

Palmer *et al* (1999) also found an association in the severity of pruritus experienced by the patients following surgery, with the dose of intrathecal morphine used. The authors noted that the 24-hour pruritus score increased by 0.6 for each 100µg increase in the dose of intrathecal morphine.

Surprisingly, there was no difference in the incidence of nausea and vomiting between the treatment groups and the placebo group in this study (Palmer *et al*., 1999). These results were replicated by a similar study conducted in Turkey. Girgin *et al* (2008) compared the effect of different doses of intrathecal morphine combined with low dose (7.5mg) bupivacaine in women undergoing caesarean section surgery. The authors found no statistical difference in the post-operative opioid requirements between the four doses of intrathecal morphine evaluated. However, there was a significant difference in opioid requirements between the opioid groups and the control group (Mann-Whitney U test, $P<0.001$). In addition, these authors also noted that there was no difference, between all the groups, for the occurrence of nausea and vomiting. Similar to the Palmer *et al* (1999) study, there was a significant increase in pruritus as the dose of intrathecal morphine increased (linear regression, $P=0.0001$). None of the patients in the Girgin *et al* (2008) study developed clinical evidence of severe respiratory depression at any point in this study. Both Palmer *et al* (1999) and Girgin *et al* (2008) agree that the dose response curve for the use of intrathecal morphine for post-operative analgesia, for caesarean section patients, follows a sigmoidal pattern. The minimal effective dose of intrathecal morphine is proposed to be 25µg. There appears to be no significant analgesic advantage to using more than 100µg of intrathecal morphine in these patients, however there is a significant worsening of pruritus as the dose of morphine increases.

Carvalho and Tenorio (2013) conducted a similar comparative study in a developing country setting (Brazil), similar to South Africa. The authors randomized 123 pregnant women scheduled for caesarean section surgery to receive either 50µg or 100µg of intrathecal morphine with the spinal anaesthetic. There was no significant difference in the analgesic effect between the two groups of patients. Pruritus occurred in both groups of patients but this side effect was statistically higher in the 100µg morphine group. There were no cases of sedation or respiratory depression in the entire study population. Nausea occurred in both groups of patients but there was no statistical difference in the occurrence of this side effect ($p=0.512$). The results of this study imply that the lower dose of intrathecal morphine may

provide the same quality of analgesia as the 100µg group but with a lower risk of pruritus.

Most authors agree that the optimal dose of intrathecal morphine is 100µg. However this dosage does not guarantee that 100% of patients will be adequately treated. Swart *et al* (1997) compared 100µg intrathecal morphine with placebo and found that 4/30(13%) patients in the morphine group used more that 40mg of intravenous PCA morphine in the 24 hour period after their surgery. This result implies that not all women will have adequate post-operative pain relief from 100µg intrathecal morphine. The use of rectal diclofenac, as an adjunctive therapy, can increase the effect of intrathecal morphine (Dennis *et al*., 1995), and this may be used, as a treatment option, in patients where intrathecal morphine is not optimally addressing the analgesic needs of the patient.

The most common side effects associated with the use of intrathecal morphine are pruritus [Number needed to harm (NNH) = 2.6 (95% CI=2.1-3.3)], nausea [NNH=6.3 (95% CI=4.2-12.5)] and vomiting [NNH=10.1 (95% CI=5.7-41.0)]. Based on an intrathecal dose of 100µg morphine, it is estimated that 43% of patients will experience pruritus, 12% will experience vomiting and 10% will have nausea as a result of this treatment (Dahl *et al*., 1999). Another important side effect that has been noted with intrathecal morphine is delayed onset of respiratory depression. This is a serious, but fortunately, a rare side effect. The proposed mechanism of this side effect is related to the fact that morphine is highly ionized and does not penetrate the lipid-rich neural tissue easily (Fukuda, 2005). This results in the drug having a long duration of action in the cerebrospinal fluid (CSF). Due to the flow of CSF in the spinal canal, the drug can spread in a cephalad direction and reach the respiratory centre. In pooled data from a meta-analysis that included 485 patients, only one patient developed respiratory depression. The combined NNH for intrathecal opioids (all opioids and different doses) was therefore 476 (95% CI=164 - ∞) and was not statistically different from the control populations (Dahl *et al*., 1999). Kato *et al* (2008) published a retrospective review of 1915 women who received 150µg intrathecal

morphine in their spinal anaesthetics for their caesarean section surgeries. The incidence of bradypnoea occurring in their cohort was 0.26% while the incidence of severe bradypnoea requiring naloxone therapy was only 1/1915 (0.052%). In doses of up to 250µg of intrathecal morphine, Abboud *et al* (1988) could not demonstrate any depression of the ventilatory response to CO_2 that could be attributed to the administration of intrathecal morphine. This finding was in stark contrast to the significant ventilatory depression to rising CO_2 levels observed in response to the administration of subcutaneous morphine (Abboud *et al*., 1988). Based on the results of these studies, it is reasonable to conclude that delayed respiratory depression due to intrathecal morphine (especially low dose intrathecal morphine) is an uncommon side effect. In addition, the higher respiratory rate associated with increased progesterone levels during pregnancy, may offer a wider margin of safety for this side effect, when compared with other patient populations (McDonnell *et al*, 2009).

Reactivation of oral herpes simplex has also been associated with the use of intrathecal morphine. Davies *et al* (2005) found that 38% of patients in their intrathecal morphine group experienced a reactivation of oral herpes simplex within 30 days of their spinal anaesthetic for their caesarean section surgery. This is compared with only 16.6% of patients in the control group. The use of morphine, irrespective of the route of administration (intrathecal or intravenous), appears to be associated with a reactivation of the virus. In South Africa, where there is a high prevalence of the Human Immunodeficiency virus (HIV) infection (Lehohla, 2015), the reactivation of oral herpes simplex may pose a greater problem than in the population investigated in the Davies *et al* study. I am, however, unaware of published or anecdotal evidence to support or detract from this hypothesis.

Urinary retention is another side effect associated with the use of intrathecal opioids. However this is unlikely to pose a problem in women after caesarean section surgery in South Africa, as the use of a urinary catheter after caesarean section surgery is a common global practice (Abdel-Aleem *et al*, 2014).

Intrathecal diamorphine has also been used an alternative to intrathecal morphine. Diamorphine is a more lipophilic derivative of morphine and thus has a faster onset of action than intrathecal morphine (Hindle, 2008). Despite having a short half-life in the CSF, its metabolism into active compounds ensures that its duration of action is comparable to that of morphine. This drug has the advantage of providing both intra-operative and prolonged post-operative analgesia (McDonnell *et al*, 2009). Diamorphine is not registered for use in South Africa and therefore this drug cannot currently be considered for therapeutic use in caesarean section surgery patients in South Africa.

Epidural analgesic techniques can also be used to provide post-operative analgesia for women after caesarean section surgery. The options include administering a continuous infusion of drugs via an epidural catheter, intermittent bolus administration of drugs via an epidural catheter, or a once off bolus of a long acting drug into the epidural space. However, in my experience, using an epidural infusion for analgesia after surgery is not an attractive option for post-operative caesarean section surgery patients, as this form of analgesia will generally require admission to a high-care unit, and will also limit the mobilization of the patient as well as her ability to care for the baby. This will therefore defeat the purpose of good analgesia to increase mobilization and bonding after surgery.

Epidural opioids administration provides the anaesthesiologist with an opportunity to use an epidural without limiting the mobility of the patient that can occur with an epidural local anaesthetic infusion. The choice of technique used will depend on the type of drug that is being used. Morphine has low lipid solubility and therefore can be administered as a single bolus into the epidural space to provide a relatively long duration of therapy. More lipid soluble opioids, like fentanyl and pethidine, have a shorter duration of action and therefore will need to be administered more regularly. These drugs are more suited to patient controlled epidural analgesia techniques or continuous infusions. Palmer *et al* (2000) conducted a dose-response study in sixty patients undergoing elective caesarean section surgery to determine the

effect of different epidural morphine doses in this patient population. The authors concluded that the post-operative analgesic requirements of these patients decreased with increasing doses of epidural morphine. However the ceiling analgesic effect appeared to occur at an epidural morphine dose of 3.75mg. Above this dose there was no significant improvement in analgesia and there was an unacceptable increase in side effects.

When compared with the intrathecal administration of morphine (100µg and 200µg), 3mg of epidural morphine provided the same quality of analgesia to women having elective caesarean section surgery. However the authors of this study noted that the patients in the 100µg intrathecal morphine group required more rescue analgesia in the post-operative period (Sarvela *et al*., 2002). In comparison, Lim *et al* (2005) found that there was no significant difference in the quality of analgesia between patients who received 100µg intrathecal morphine or epidural morphine at the time of their caesarean section. Both methods of analgesia provided adequate analgesia for 12 – 24 hours after surgery, but due to standard hospital procedures the number of patients in the intrathecal morphine study population was much higher than the epidural morphine population (850 vs. 52) in this study and therefore the results need to be interpreted with caution.

Extended release epidural morphine (DepoDur^{TM}) is a novel formulation of morphine developed specifically for epidural use. The drug is a liposome-based morphine delivery system that provides a long duration of analgesia (up to 48 hours) following a single dose. Carvalho *et al* (2005b) demonstrated that the 5mg and 10mg doses of extended release epidural morphine provided comparative analgesia to standard 5mg epidural morphine but the duration of analgesia extended up to 48hours following a single intraoperative dose. (Carvalho *et al*., 2005b) Atkinson Ralls *et al* (2011) however found that patients who received 20 - 35 ml of epidural lignocaine one hour before the administration of the extended release epidural morphine had an increased maximal plasma morphine concentration. This was associated with an increased incidence of side effects. The authors therefore advised extreme caution in the use of the drug in caesarean section patients where the surgery

is performed under epidural top up. (Atkinson Ralls *et al*., 2011) The extended release morphine formulation is currently not registered for use in South Africa and therefore this form of treatment is not accessible for post-operative caesarean section pain relief in South Africa.

Epidural fentanyl is commonly used in combination with low dose local anaesthetics for labour analgesia. There is however a paucity of data regarding the use of epidural fentanyl for post-operative caesarean section analgesia. Cohen *et al* (2002) demonstrated that the mechanism of action of epidural fentanyl following caesarean section surgery is at a spinal level. In this study, the authors compared the effect of epidural fentanyl and intravenous fentanyl; both of which were administered by PCA devices. The groups using intravenous fentanyl required higher total doses of the opioid analgesic ($p<0.0001$), reported greater pain levels ($p<0.001$) and also experienced more side effects, than the epidural groups. (Cohen *et al*., 2002) Indeed, when compared to PCA intravenous morphine, epidural fentanyl, administered by a patient controlled epidural analgesia (PCEA) pump, has been shown to provide improved analgesia with lower rates of nausea and sedation (Cooper *et al*., 1999). This study showed that for caesarean section surgery patients, PCEA fentanyl is probably a better option to use than intravenous morphine. The addition of low dose bupivacaine to a fentanyl epidural infusion has also been shown to improve patient analgesia and reduce the total fentanyl consumption while reducing side effects (Cohen *et al*., 1998). This method of continuous infusion analgesia is however prohibitive in its widespread application because of the increased nursing requirements needed for patients with indwelling epidural catheters, in addition to the risks associated with prolonged indwelling catheter use (Wheatley *et al*., 2001).

Epidural sufentanil has very similar clinical effects to epidural fentanyl (Connelly *et al*., 2000). There is very little published data available on the use of this drug for patients after caesarean section surgery.

Pethidine is an opioid of intermediate lipophilicity, which can be administered epidurally, intravenously or intramuscularly. PCEA pethidine has been used for post-caesarean section analgesia. When compared to intrathecal morphine, epidural pethidine is associated with lower side effects such as pruritus ($p<0.001$), nausea ($p<0.001$) and drowsiness ($p<0.05$) (Paech *et al*., 2000). Paech *et al* (1994) compared epidural pethidine to intravenous pethidine in a double-blind, crossover trial, and demonstrated that epidural pethidine resulted in lower pain scores at rest and with cough ($p=0.0001$), higher patient satisfaction ratings ($p=0.0001$) and lower sedation scores ($p=0.0001$). The authors of this study highly recommended this form of analgesia for the post-caesarean section patient, with the proviso that the neonatal effects of pethidine transfer in breast milk had to be investigated further. Ngan Kee *et al* (1997) also found that patients were more satisfied with PCEA pethidine compared to PCIA pethidine.

In addition to opioids, there are also other drugs that can potentially be administered neuraxially as part of a post-operative analgesic regimen. Neostigmine is an anticholinesterase agent, which results in increased levels of intrathecal acetylcholine (ACh) when administered neuraxially. These increased ACh levels lead to analgesia in both animals and humans, without associated motor or sensory blockade and also without the side effects of respiratory depression and sedation. (Krukowski *et al*., 1997)

Chung *et al* (1998) demonstrated that 25μg of intrathecal neostigmine significantly increased the time to the first analgesic PCA request ($p<0.001$) and resulted in a lower 24 hour analgesic consumption ($p<0.001$) when compared to the placebo group. However, the administration of intrathecal neostigmine led to an increase in the incidence of nausea and vomiting (73.7%) compared to the placebo group (20%, $p<0.005$) and the morphine group (40%, $p<0.01$). This high side effect risk currently limits the clinical effectiveness of using intrathecal neostigmine for post-operative analgesia. In contrast to the effects of intrathecal neostigmine, Kaya *et al* (2004) found that epidural neostigmine administration in pregnant women having caesarean

section surgeries, is not associated with an increased risk of post-operative nausea and vomiting. In addition, these authors also noted that epidural neostigmine results in modest analgesia in this population. The epidural administration of neostigmine was however shown to increase the incidence of post-operative sweating and sedation.

Clonidine is an alpha-2 (α2) receptor agonist and its neuraxial use has been well studied in the peri-operative period. The mechanism of action of neuraxial clonidine is proposed to be due to the fact that α2 adrenergic receptors are found in the dorsal horn of the spinal cord, and it appears likely that α2 agonists act by both pre- and postsynaptic mechanisms to produce antinociception (Chan *et al*., 2010). In experimental studies, the lumbar injection of clonidine led to pain relief in the lower extremities, but not in the upper extremities of healthy volunteers, and the CSF levels of clonidine also corresponded to the degree of antinociception experienced (Eisenach *et al*., 1996). Paech *et al* (2004) conducted a randomized double-blind trial in 240 women having caesarean sections, with the aim of investigating the analgesic efficacy of different formulations of intrathecal drug combinations, which included clonidine at different doses. The authors concluded that a combination of intrathecal morphine (100μg) and clonidine significantly improved post-operative pain relief. However this combination also increased intra-operative sedation. The authors recommended that clonidine in doses of between 30 – 60μg, in combination with intrathecal opioids was the most effective therapeutic combination to use. The use of intrathecal clonidine without intrathecal morphine did not provide any analgesic advantage for these patients.

The combination of intrathecal clonidine (75μg) with fentanyl (12.5μg) and hyperbaric bupivacaine was also demonstrated by Benhamou *et al* (1998) to significantly increase the duration of post-operative analgesia after caesarean section to 215 (± 79) minutes ($p<0.05$) when compared with other groups in the study. This combination of intrathecal drugs was however also associated with increased sedation, but the authors commented that the level of sedation never exceeded grade 2 (moderate). Capogna *et al* (1995) demonstrated that

the administration of clonidine into the epidural space, in combination with 2mg morphine, also significantly increased the duration of analgesia up to 13.25 hours with the 75µg dose and 21.55 hours with the 150µg dose, when compared with the placebo dose, which only provided adequate analgesia for 6.27 hours ($p<0.0001$). The epidural clonidine also reduced the mean total dose of post-operative morphine required from 9.40 mg in the placebo group to 5.0mg in the 75µg group down to 3.60mg in the 150µg group ($p<0.0001$). The authors found no significant difference in side effects between the three groups.

Dexmedetomidine, like clonidine, is also an α2 receptor agonist. This drug is however a more highly selective alpha-2 adrenergic receptor agonist with an α2 to α1 receptor ratio of 1620:1 (Virtanen *et al*., 1988). This is approximately eight times more specific than clonidine for the α2 receptors, and has been reported to have significant analgesic and opioid sparing effects post-operatively when administered via the intravenous route (Unlugenc *et al*., 2005). Based on experimental studies using clonidine, the analgesic properties of dexmedetomidine are suggested to involve both peripheral and central mechanisms. There is however, currently no published work on the neuraxial use of dexmedetomidine in humans for post-operative analgesia. The paucity of data in human trials is most likely due to the suggestion from a 2008 animal study, that dexmedetomidine may have a neurotoxic effect on the myelin sheath when administered via the epidural route (Konakci *et al*., 2008). This was however a single centre animal study in rabbits, and more animal studies need to be conducted before a verdict can be rendered on this issue.

2.7.1.2 Peripheral Nerve Blocks

Blocking peripheral nerves using local anaesthetic agents are popular methods of providing intra- and post-operative analgesia for a variety of different surgical procedures. A major part of the pain experienced after abdominal surgery is related to nociceptive input from the anterior abdominal wall (McDonnell *et al*, 2009). Peripheral nerve blocks have been investigated

for their efficacy in ameliorating the input from these nociceptors and reducing the pain experienced by the patients in the post-operative period.

Ilioinguinal and iliohypogastric nerve blocks have shown that they can be used to decrease the post-operative opioid requirements of patients after caesarean section surgery. Bell *et al* (2002) found that post-operative PCA morphine consumption significantly decreased from 67±28mg in the placebo group to 48±27mg in the experimental group. The investigators in this study used a blind landmark-based technique to perform the blocks. Due to the double-blinded nature of the trial, block success was not assessed following the procedure and the investigators assumed a 95% success rate in the block procedures (based on a previous study in their institution). Despite the decreased opioid requirements in the patients who received the peripheral nerve blocks, there was however no statistical difference in the opioid related side effects (pruritus, p=0.25 and nausea, p=0.79) between the two groups. The results of the study by Bell *et al* (2002) are in conflict with results published earlier by Huffnagle *et al* (1996). In this study the investigators performed bilateral ilioinguinal and iliohypogastric nerve blocks also using a blind landmark-based technique. The results of the study were negative, finding no additional benefit to using these blocks for post-operative pain relief in caesarean section patients (Huffnagle *et al*., 1996). Interestingly, the investigators in this study did evaluate for block success and had a high incidence of block failure in the group where the blocks were performed before surgery. This is also in contrast to the Bell *et al* study, which assumed a 95% block success rate. The success of peripheral nerve blocks is an extremely important requirement in order to make a definitive evaluation of the role of these blocks for post-operative analgesia. The use of ultrasound technology to perform these blocks has been shown to result in positive analgesic effects after surgery (Gucev *et al*., 2008). This publication is however only a case series of three patients, and further randomized studies evaluating this ultrasound technique are needed before a firm recommendation can be made on the usefulness of these blocks for post-caesarean section analgesia.

The transversus abdominus plane (TAP) block involves injecting local anaesthetics into the tranversus abdominus plane in the abdominal wall, blocking the sensory nerves as they pass through this tissue plane, before they pass into the musculature to innervate the anterior abdominal wall. In patients undergoing non-obstetric abdominal surgery, the TAP block has demonstrated a clear reduction in post-operative opioid requirements in the first 24 hours after surgery. In addition, the patients in the TAP block group in this study also reported lower pain scores at three different evaluation points after surgery. (McDonnell *et al*., 2007) However, the use of the TAP block for post-operative analgesia after caesarean section surgery has been mired in controversy with conflicting results being published. The first post-caesarean section surgery TAP block study was published in 2008 by McDonnell *et al*. The authors of this study randomized fifty women undergoing elective caesarean section surgery to receive bilateral TAP blocks with either 0.75% ropivacaine or placebo. The patients in the TAP block group had a 30% reduction in visual analogue pain scores and also had a 70% reduction in their mean post-operative morphine dose requirements in the first 48 hours after surgery (McDonnell *et al*., 2008). In 2009, Belavy *et al* evaluated the effect of the ultrasound guided TAP block technique on post-operative pain in caesarean section surgery patients. The investigators also found that the patients in the TAP block group had lower pain scores and had a 40% reduction in post-operative morphine requirements. While the treatment effect was not as dramatic as the original McDonnell *et al* study, this study also showed benefit in using the TAP block as part of the analgesic regimen in this group of patients (Belavy *et al*., 2009). McMorrow *et al* (2011) compared the efficacy of 100µg intrathecal morphine with bilateral TAP blocks for the effect on post-operative analgesia in a randomized double-blind placebo controlled trial. The investigators concluded that the "single shot" TAP block was not superior to spinal morphine for post-operative caesarean section analgesia and also that the use of bilateral "single shot" TAP blocks in patients who receive 100µg intrathecal morphine during their spinal anaesthetic, offers no additional analgesic benefit for the patients.

Bollag *et al* (2012) have proposed the concept of pain relief from repeated local anaesthetic injections through bilateral TAP catheters, in a case series published in 2012. The authors of this paper have proposed that repeated local anaesthetic dosing through bilateral TAP catheters might be a viable therapeutic alternative in patients in whom the administration of intrathecal long acting opioids is not possible. Further randomized trials are needed to evaluate if this is a reasonable treatment option for post-caesarean analgesia.

2.7.1.3 Wound infiltration

Wound infiltration can be performed using a "single shot" approach at the end of surgery or by continuous infusion of drugs via wound infusion catheters. The efficiency of this treatment option is dependent on the type of administration method used and also on the drugs that are used. Results from trials evaluating wound infusion catheter systems have been mixed and this is most probably due to the different implantation techniques applied (subcutaneous, subfascial or sub-rectus), drug dosing regimens employed (continuous or bolus) and types of drugs used (Kwok *et al*., 2014, Tan, 2012)

In a prospective, randomized, double-blind placebo controlled trial comparing epidural analgesia and subfascial wound catheters using an intermittent local anaesthetic (0.25% levobupivacaine) bolus technique, Ranta *et al* (2006) found that both techniques had similar outcomes in terms of pain scores (3 or less) after the initial four hour period. O'Neill *et al* (2012) conducted a similar study comparing a continuous infusion of 0.2% ropivacaine, via a subfascial wound catheter, with epidural morphine boluses, and found that the pain scores at rest were lower in the wound catheter group for up to 48 hours after surgery, and that these patients experienced lower side effects as well. Fredman *et al* (2000) compared the effect of a subcutaneous catheter connected to a patient controlled elastomeric pump containing either 0.2% ropivacaine or placebo (saline), and found decreased movement-associated pain and decreased post-operative opioid requirements in the ropivacaine group. Chandon *et al* (2014) found no difference in the analgesic effect between ultrasound guided bilateral TAP blocks and continuous wound

infusion with levobupivacaine. This study was however stopped prematurely due to an adverse reaction in one of the patients in the TAP block group. This patient experienced generalized seizures shortly after the administration of the TAP block, which was attributed to the partial systemic absorption of the local anaesthetic. The results of this trial therefore need to be interpreted with caution.

While most trials utilize local anaesthetics in the wound infiltration catheters, Lavand'homme *et al* (2007) assessed the post-operative analgesic effects of continuous wound infiltration with diclofenac in elective caesarean section patients and found that the infusion of 300mg diclofenac over 48 hours decreased the 48 hour post-operative morphine requirements compared with a 0.2% ropivacaine infusion and with intravenous diclofenac. The results of this study not only opened up a previously unknown area of use for diclofenac, but it also raises the possibility that NSAIDs may have peripheral analgesic effects directly at the site of injury.

The multiple regional anaesthetic techniques that anaesthetic service providers can use to manage post-operative pain in caesarean section patients can lead to confusion and under-use of these valuable techniques. Neuraxial regional anaesthetic techniques have been shown to be extremely effective in managing post-operative pain in this patient population. The proviso is that these techniques should be used to administer opioids into the neuraxial spaces (intrathecal or epidural). Opioids (morphine in particular) have a longer duration of effect than using local anaesthetic drugs alone. This longer analgesic effect can also be prolonged with the addition of other neuraxial adjuvant drugs such as neostigmine or clonidine, but this also raises the side effects experienced by patients. Other regional anaesthetic options such as peripheral nerve blocks and wound infiltration techniques have therapeutic benefits when compared with placebo, however these techniques do not seem to have any therapeutic superiority when compared to neuraxial opioids.

2.7.2 Systemic Analgesia

The systemic administration of analgesics following surgery is a commonly used modality of care. The advantage of this method of drug administration is that it is more cost effective, easier for nursing staff to administer and has a long history of successful use in post-partum women. However, the pain relief attained by this method of administration is generally considered less effective than that achieved following the neuraxial administration of medication. (Gadsden, 2005)

2.7.2.1 Intravenous (IV) and intramuscular analgesia (IM)

Patient controlled intravenously administered opioids are a popular method of administering medication to patients after caesarean section surgery, especially when neuraxial techniques are not possible or after a general anaesthetic.

Based on my clinical experience, the IM administration of opioids is very popular in South Africa because of the lower cost and reduced level of monitoring required when compared to IV or neuraxial administration of these analgesics. In a blinded, randomized comparison between epidural opioids, PCA opioids and IM opioids following caesarean section surgery, Harrison *et al* (1988) demonstrated that neuraxial drug administration provided superior analgesia to the other two techniques; however this was overshadowed by the higher side effect profile in this group. When comparing PCA administration to IM administration, the patients had comparable pain relief and post-operative opioid use. Despite the relatively higher pain scores in the PCA group (compared to the epidural group), the patient satisfaction levels with this method of analgesia was comparable with that of the neuraxial group. The authors postulated that this might be due to the more stable level of analgesia, lower side effects and knowledge that analgesia was more accessible to the patients in the PCA group. This higher level of patient satisfaction for PCA opioids compared with IM opioids following caesarean section was also reported in another similarly designed study (Eisenach *et al*.,

1988). The authors in this study found that the number of instances where patients reported being uncomfortable was highest in the IM group and lowest in the epidural group. The lower satisfaction levels seen with IM opioids is most likely due to the fact that plasma concentrations of opioids are unpredictable following IM injections, the injections are painful to receive and the patients are probably reluctant to request the injections from the nurses.

In most publications reviewed, morphine is the most common opioid used in IV PCA regimens for the management of post-caesarean section pain. It is generally also the standard against which most other analgesic interventions are evaluated. Fentanyl is a synthetic, more potent opioid that is a popular drug administered intraoperatively, but has not been shown to provide superior analgesia for post-operative caesarean section surgery patients when administered via PCA pump (Howell *et al*., 1995). Woodhouse *et al* (1996) published similar results of non-inferiority with regards to analgesic efficacy, when fentanyl PCA was compared to morphine and pethidine PCA's. Based on the results of both these studies and the higher cost of fentanyl compared to morphine, this drug does not appear to be a suitable alternative to morphine for post-operative analgesia.

From my own clinical experience, I have noted that pethidine is a popular opioid in South Africa for post-operative pain management in both general surgical patients and for obstetric post-surgical patients. The drug can be administered intramuscularly and with a long time period between administrations so that it does not impact too greatly on nursing workload. In studies comparing the use of this drug to other opioids for post-operative analgesia after caesarean section surgery, PCA pethidine has been found to provide the same quality of analgesia to PCA fentanyl (Ngan Kee *et al*., 1997) and to both PCA morphine and PCA fentanyl (Woodhouse *et al*., 1996). However there have been serious concerns raised about the secretion of pethidine's active metabolite, nor-pethidine, into breast milk (Shnider and Moya, 1964) and its effect on the neurological function of the neonate (Wittels *et al*., 1997). Based on the risk to the neonate, pethidine should be avoided in post-caesarean section patients who are breastfeeding their babies.

Tramadol is a weak opioid and is readily available in South Africa, even in the public health sector. In a randomized, double-blinded study conducted in a South African academic hospital, Wilder-Smith *et al* (2003) showed that a single combined dose of intramuscular tramadol (100mg) and diclofenac (75mg) provided superior analgesia to either drug alone and to placebo. Unfortunately this study did not include neuraxial opioids or PCA morphine in the comparator groups.

NSAIDs are commonly used analgesic agents globally and they are known to be effective against the visceral pain associated with uterine incision and involution after caesarean section surgery (Tan, 2012). Cardoso *et al* (1998) combined intrathecal morphine (at three different doses) with 75mg IM diclofenac and found that the addition of IM diclofenac enhanced the analgesic effect of the intrathecal morphine, to such an extent that the authors recommended that there was no advantage to using intrathecal doses of morphine larger than 25µg if this is used in combination with systemic diclofenac. This combination proved to be as effective as higher intrathecal morphine doses with and without NSAIDS.

Methadone has also been proposed as an analgesic option in patients having caesarean section surgery under general anaesthesia. In a retrospective case-control study, Russell *et al* (2013) demonstrated that a single bolus dose of intravenous methadone intraoperatively, improved the quality of analgesia and significantly reduced the post-operative opioid requirements for up to 48 hours after surgery. This novel analgesic option needs to be investigated further especially for use in patients undergoing neuraxial anaesthesia. There is limited data available on the transfer of methadone across the human placenta. Laboratory investigations conducted by Nekhayeva and colleagues (2005) indicated that the transfer of methadone across the placenta favours movement of the drug in the direction towards the maternal circulation, and is probably affected by enzymatic transport mechanisms in the placenta. There are however no clinical reports available on the effects of methadone on the foetus. In South Africa, methadone is registered as a schedule 6 drug and is

not readily available for use in the public health sector (Division of Clinical Pharmacology, 2012).

Ketamine is a N-methyl D-aspartate (NMDA) receptor antagonist. It is an old IV anaesthetic agent that produces a state of dissociative anaesthesia when used at higher doses. The drug however leads to a number of unwanted side effects (such as hypertension and hallucinations) that limits its widespread clinical use (Aroni *et al*., 2009). At sub-anaesthetic doses, this drug has been shown to have analgesic effects and therefore it has the potential to contribute to the post-operative analgesia of women after caesarean section surgery. Menkiti *et al* (2012) investigated the effect of an intra-operative bolus dose of ketamine on the post-operative analgesia of women having a caesarean section in a developing country, where access to intrathecal opioids is limited. The authors demonstrated lower pain scores in the ketamine group ($p=0.022$) and also reduced post-operative analgesic requirements ($p<0.001$) when compared to the control group. This drug should therefore be considered for post-operative analgesia for caesarean section surgery, especially in developing countries.

Paracetamol is well known analgesic drug that is believed to act at both central and peripheral levels of the nociceptive pathways (Tan, 2012). It has a significant opioid sparing effect when used in combination with PCA morphine (Remy *et al*., 2005) and therefore offers an attractive option to be used as part of a post-caesarean section pain management regimen. However results of studies investigating the effect of paracetamol in obstetric patients have been conflicting. Siddik *et al* (2001) compared the analgesic effect of intravenous paracetamol and rectal diclofenac and found that while diclofenac had a significant opioid sparing effect for post-caesarean section surgery patients, paracetamol offered no such benefit. Inal *et al* (2006) however, compared the analgesic effects of a single dose of IV paracetamol with a single dose of IV pethidine at the end of surgery and demonstrated lower VAS scores and a longer time to first supplementary analgesic request in the paracetamol group. Abu Omar *et al* (2011) also showed positive results demonstrating that the addition of regular intravenous paracetamol to the

treatment of patients who received intrathecal morphine during their spinal anaesthetic decreased the need for rescue analgesia in the 24hours after their caesarean section. There appears to be a trend that IV paracetamol can offer a viable alternative to reduce supplementary opioid requirements for post-caesarean section patients.

While there are many effective IV and IM alternatives for pain management after caesarean section surgery, alternative routes of administration of drugs have also been evaluated and proven to be effective in many cases.

2.7.2.2 Oral analgesia

Administering medication via the oral route is simple, cost-effective and generally more convenient for nursing staff and patients (Tan, 2012). Almost all classes of drugs that are available in IV and IM formulations are available as oral medications. In South Africa, caesarean section surgery patients generally have their IV lines removed 24 hours after surgery in order to facilitate mobilization and promote interaction with the newborn baby. At this point of treatment, oral analgesia (usually a combination of opioids, paracetamol and NSAIDs) becomes a necessity. There are however studies which have also evaluated the efficacy of oral analgesia in the early post-operative period following caesarean section.

Jakobi *et al* (2000) assessed patient satisfaction levels towards two oral analgesic regimens for pain management following caesarean section surgery under epidural analgesia. Group 1 (109 patients) were given one-gram (g) of oral dipyrone at regular intervals, on request, also and allowed access to 30mg immediate release oral morphine for rescue analgesia. Group 2 (90 patients) were given immediate release oral morphine (30mg) at regular intervals, on request, and then given access to 1g oral dipyrone if they requested additional analgesia. The patient satisfaction scores were high in both groups (90±9.6 in group 1 and 83.7±8.9 in group 2). The patients in group 1 had an average effective analgesic time of 6.5±0.6 hours compared to 5.05±0.5 hours in group 2. The authors concluded that oral analgesics

provided satisfactory and cost effective analgesia for this group of patients. These authors did not however do a direct comparison with neuraxial, IV or IM analgesic options in this study. In South Africa, dipyrone is not registered for use. However, there are a number of oral NSAIDs available for post-operative use and paracetamol is also easily accessible. Valentine *et al* (2015), demonstrated that regular doses of paracetamol after surgery decreased the opioid use, without compromising the quality of analgesia after caesarean section surgery.

When comparing an oral opioid regimen with PCA morphine in 93 women having caesarean section surgery, Davis *et al* (2006) demonstrated that patients using regular doses of oral oxycodone-acetaminophen experienced less pain at six and twenty-four hours after surgery than those using PCA morphine. The patients using the oral regimen also had less side effects than the IV group. Based on the results of this study the authors recommended that consideration should be given to expanding the use of oral analgesia for pain relief following caesarean section surgery. McDonnell *et al* (2010) did a direct comparison between regular oral oxycodone and intrathecal morphine, comparing the quality of post-operative pain relief afforded by each analgesic regimen. One hundred and twenty women scheduled for elective caesarean section surgery were randomized into two groups. The authors concluded that while the oral oxycodone regimen provide comparable pain relief to the intrathecal morphine regimen, with a lower incidence of pruritus, the patient satisfaction score was significantly lower in the oral oxycodone group ($p=0.010$).

A recent Cochrane Collaboration review on "*Oral analgesia for relieving post-caesarean pain*" assessed data from eight trials with 962 patients to determine the effectiveness, safety and cost-effectiveness of oral analgesia for post-caesarean pain relief. The authors found that due to the limited data available, "no conclusions can be made regarding the safest and the most effective form of oral analgesia for post-caesarean pain" (Mkontwana and Novikova, 2015). Further studies are needed in this field.

Gabapentin is an oral alpha-2 delta ligand calcium channel blocking agent. The analgesic effect of the drug is due to its inhibition of the release of excitatory neurotransmitters in the dorsal horn of the spinal cord. A preoperative dose of 600mg gabapentin was demonstrated by Moore *et al* (2011) to reduce the 24 hour VAS pain scores from 41mm in the placebo group to 21mm in the gabapentin group (p=0.001). These authors have proposed that 600mg gabapentin, when used as part of a multimodal analgesic regimen, will improve post-operative caesarean pain and improve patient satisfaction. In 2012, Short *et al* compared two different preoperative doses of gabapentin (300mg and 600mg) with placebo to investigate their analgesic effects following caesarean section surgery. The authors did not find any difference in the analgesic effects of either of the gabapentin doses compared to placebo (p=0.61). They did however conclude that the study was underpowered and a larger study is required to confirm these results. In light of these conflicting results, it is not possible to determine if gabapentin can offer any analgesic benefit for patients after caesarean section surgery.

2.7.2.3 Rectal analgesia

Medication can be absorbed from the rectum with the same mechanism of absorption as medication is absorbed from the upper gastrointestinal tract. This route of administration is advantageous especially when the patient does not have IV access, and severe nausea and vomiting precludes oral drug administration. The negative factors associated with rectal administration of drugs are that absorption may be interrupted by defecation and patients may also not be fond of the technique. (de Boer *et al*., 1982)

Based on my clinical experience, it appears that the rectal route of administering post-operative analgesia is very popular in South Africa. Paracetamol suppositories are commonly used for post-operative pain relief in paediatric patients and NSAIDs suppositories are routinely inserted into the rectum at the end of surgery during caesarean sections. The use of NSAIDs after caesarean section surgery is however controversial. There are valid concerns about the risk of increased bleeding after surgery, together with the

concerns about bronchospasm, gastrointestinal bleeding and renal dysfunction due to NSAIDs use (Dahl and Raeder, 2000). Dahl *et al* (2002) conducted a randomized, double-blind placebo controlled trial to evaluate the opioid sparing effect of diclofenac suppositories in patients following caesarean section surgery. Eighty-two women were randomized to receive 100mg diclofenac suppositories or placebo suppositories every twelve hours after surgery. The NSAIDs group used significantly less morphine during the 32 hour evaluation period (14 ± 1.5mg) as compared to the placebo group (21.5 ± 1.6mg, $p<0.05$). The VAS pain scores were however not significantly different between the groups. In addition, there was no difference in bleeding or any other NSAIDs associated side effects between the two groups during the evaluation period.

2.7.2.4 Transdermal analgesia

At present only fentanyl and buprenorphine transdermal patches are registered for use in South Africa. Both these patches are indicated for moderate to severe chronic pain.

There is no published literature on the use of transdermal opioid analgesics for pain relief following caesarean section surgery. Lehmann *et al* (1997) studied the safety and effectiveness of transdermal fentanyl patch administration on the post-operative pain relief following abdominal surgery. The authors found that similar post-operative analgesia was achieved with less IV analgesics in the fentanyl group compared to the placebo group. In addition, there was no difference in the respiratory rate or heamoglobin oxygen saturation between the two groups.

Transdermal analgesia may provide a novel way of providing analgesia to women following caesarean section surgery, however more research is needed in this area before any recommendations can be made.

Irrespective of the method of anaesthesia used or the choice of post-operative analgesia techniques or medication, every caesarean section patient should

be monitored in the post-operative period. The Obstetric Anaesthesia Guidelines (Wee *et al*., 2005) in the United Kingdom state that the post-operative care of the caesarean section patient should meet the same standard of care as that required for any post-operative patient. The American Practice Guidelines (Horlocker *et al*., 2009) state that patients who receive neuraxial opioids should be monitored for up to 24 hours following intrathecal administration of hydrophilic opioids and for at least 2 hours following the administration of a single dose of a lipophilic opioid. The current South African Society of Anaesthesiologists Practice Guidelines (Bettings *et al*., 2013) make no specific recommendations on the post-operative management of caesarean section patients or of patients who have received neuraxial opioids.

2.8 Guidelines for the management of post-caesarean section pain

In 2003, John R Hampton, the Emeritus Professor of Cardiology at the University of Notingham, wrote "*A fool – loosely defined as someone who does not know much about a particular area of medicine – will do well to follow guidelines when treating patients, but a wise man (again, loosely defined as someone who does know about the disease in question) might do better not to follow them slavishly*" (Hampton, 2003). These words succinctly explain the usefulness of practice guidelines for clinicians.

Practice guidelines should be considered as being basic recommendations for the safe and efficient management of patients with particular clinical conditions. Guidelines are generally based on a synthesis of current scientific evidence, expert opinion, open forum commentary and clinical feasibility data (Apfelbaum *et al*., 2016). These documents should be used to supplement, strengthen and validate institutional policies rather than be used as a blanket set of rules that may not be feasible in every clinical environment. It is the obligation of every health care practitioner to ensure that their patients are provided with the best care possible within the constraints of the environment in which they are working. Practice guidelines can be used to advocate for an improvement in these environments. This is especially true in developing

countries where practitioners are often faced with a shortage of drugs, consumables and equipment that may be considered essential in the developed world.

Practice guidelines for obstetric anaesthesia are generally very comprehensive and include recommendations on a wide variety of obstetric anaesthesiology topics ranging from management during labour, pre-operative management, operative delivery and post-operative care. For the purposes of this literature review, I will limit the review to aspects of anaesthesiology practice guidelines that relate only to the pain management of the obstetric patient.

The American Society of Anesthesiologists (ASA) Task Force on Obstetric Anesthesia published Practice Guidelines for Obstetric Anesthesia in 2016 (Apfelbaum *et al*., 2016). These comprehensive guidelines addressed the pre-, intra- and post-operative anaesthetic management of the obstetric patient in detail, basing recommendations on scientific evidence and expert opinion. These guidelines state that the choice of a particular anaesthetic technique for a caesarean section must be individualized and based on the circumstances of each patient. However, the document does indicate that neuraxial techniques are preferred over general anaesthesia in most cases. Moreover, the ASA guidelines advise that for patients who have a neuraxial anaesthetic for their caesarean section surgery, neuraxial opioids should be used preferentially over intermittent injections of parenteral opioids to manage post-operative pain. The guidelines are clear that there is evidence for better analgesia with epidural opioids as opposed to intermittent IV or IM opioids (Apfelbaum *et al*., 2016). While the ASA guideline is very comprehensive and well researched, it falls short in that it does not make any recommendations on the type of opioids that should be used in the neuraxial anaesthetic techniques. The authors fail to discuss the implications of using hydrophilic opioids vs. lipophilic opioids in the neuraxial techniques. The use of different types of opioids will result in different durations of effective analgesia and side effects. In addition, there was no discussion about the benefit of multimodal analgesic techniques in this patient group.

In 2009, the ASA Task force on Neuraxial Opioids did however publish practice guidelines for the prevention, detection, and management of respiratory depression associated with neuraxial opioid administration (Horlocker *et al*., 2009). Following detailed analyses of the literature, these guidelines recommend that the "lowest efficacious dose of neuraxial opioids should be administered to minimize the risk of respiratory depression". Caution is also advised in using neuraxial opioids together with parenteral opioids, sedatives, hypnotics or magnesium as this practice increases the risk of respiratory depression. The techniques that are currently available for the detection of respiratory depression (pulse oximetry, end-tidal carbon dioxide monitoring, respiratory rate count, depth of respiration assessment and sedation level) are discussed in the guidelines, however there is insufficient evidence available to be able to make a firm recommendation on the preferred techniques that should be used. (Horlocker *et al*., 2009)

The 2009 guideline (Horlocker *et al*., 2009) does discuss the consequences of using lipophilic versus hydrophilic opioids with regards to the duration of risk. In addition, the different administration techniques are discussed and the duration of risk of the single injection techniques vs. the continuous infusion techniques is explained. The recommendation from the guidelines committee is that all patients receiving neuraxial opioids should be monitored for adequacy of ventilation, oxygenation and level of consciousness. The duration of this monitoring ranges from two hours for lipophilic opioids (eg. Fentanyl) up to twenty-four hours for hydrophilic opioids (eg. Morphine).

The National Institute of Clinical Excellence (NICE) in the United Kingdom of Great Britain and Northern Ireland (UK) updated its 2004 guidelines on Caesarean section in November 2011(Griffiths *et al*., 2011). This is a very comprehensive document addressing many aspects of a caesarean section including surgical and anaesthetic management. The guidelines recommend that women should be offered intrathecal or epidural diamorphine for intra- and post-operative analgesia as this reduces the need for supplemental analgesia after caesarean section surgery. In the absence of the neuraxial

option, PCA opioids are recommended. In addition, NSAIDs should be used as an adjunctive analgesic agent because of their opioid sparing effects. The guideline also indicates that wound infiltration or ilioinguinal nerve blocks have also been found to be effective alternatives to systemic analgesics following caesarean section surgery.

The Australian and New Zealand College of Anaesthetists (ANZCA) and Faculty of Pain Medicine (FPM) updated their Acute Pain Management Guidelines in 2015 (Schug *et al*., 2015). These guidelines include a section on the management of pain after caesarean section surgery. Analysis of the literature evaluating oral analgesia after caesarean sections did not allow the guidelines committee to make any conclusions regarding their use. The document states that they were only able to identify small trials and these had contradictory results. The studies on parenteral analgesics were also deemed to be inadequate. Trials assessing synthetic IV opioids were not remarkable. The guidelines do mention that there are trials that show some benefit in using IV dexamethasone, ketamine or dexmedetomidine, however none of these studies were overwhelmingly encouraging (Schug *et al*., 2015).

Neuraxial analgesia (intrathecal and epidural) was also discussed in the ANZCA guideline, in addition to peripheral regional anaesthetic blocks. The ANZCA and FPM guideline (Schug *et al*., 2015), unlike the NICE guidelines (Griffiths *et al*., 2011), do not however advise the reader to use any particular drug regimen or analgesic technique. Users of the ANZCA guideline are expected to interpret the data provided and to make their own decisions about the analgesia that should be used.

The Procedure Specific Post-operative Pain Management (PROSPECT) Working group is dedicated to providing recommendations on pain management interventions that are related to specific surgical procedures (Neugebauer *et al*., 2007). These recommendations are available online so that they are freely accessible and easily available for use. The PROSPECT recommendations for caesarean section surgery are very specific and are categorized into pre-operative, intra-operative (pre-delivery), intra-operative

(post-delivery), surgical techniques and post-operative recommendations. Recommended analgesic options include the use of intrathecal morphine intraoperatively, together with IV paracetamol and IV NSAIDS after the delivery of the baby. In addition, regional anaesthetic techniques are also recommended as adjunctive analgesic techniques for these patients (PROSPECT Working Group, 2015).

The South African Acute Pain Management Guidelines were originally published in 2009 as an official publication of the South African Society of Anaesthesiologists. The guideline has been updated in 2016 (Lundgren *et al*., 2016) to reflect changes in practice and drugs that have become available in South Africa during the seven-year period since the guidelines were first published. The South African guideline (Lundgren *et al*., 2016) recommends a neuraxial anaesthetic technique for all women having caesarean sections unless there is a contraindication to this technique. The rationale behind this bold recommendation is that this anaesthetic technique will provide analgesia for the surgery and for a period of time after surgery as well. The guideline provides details on the use of intrathecal bupivacaine with or without the addition of fentanyl (12.5 – 20μg). The guideline specifically does not recommend intrathecal morphine for these patients, despite overwhelming evidence in the international literature regarding the superior efficacy of this mode of analgesia for patients having caesarean sections. For those patients, where general anaesthesia is necessary, the guideline provides recommendations on the use of drugs to blunt the intubation response and also on the use of opioids during the procedure. There is no recommendation pertaining to the requirements for monitoring of patients for the side effects of analgesics in the post-operative period; however this may be beyond the mandate of the guidelines committee.

Despite the widespread availability of practice guidelines for the management of pain after caesarean section surgery, it is the implementation of these guidelines that will ultimately influence the experience of women after their caesarean sections. Unfortunately, evidence exists (from other specialities)

that there are often multiple barriers to the implementation of clinical practice guidelines at the grass roots level of care. Organisational limitations are often cited as important factors to the poor uptake (Ebben *et al*., 2013). Cabana *et al* (1999) also discussed the barriers to implementing guidelines by medical practitioners. They identified a number of factors such as knowledge, attitude and behavior, which act as barriers. Based on their assessment of implementation barriers, Cabana and colleagues (1999) proposed a rational approach towards improving the implementation of clinical guidelines. These suggestions included addressing doctors' lack of knowledge and lack of awareness of guidelines, as well as teaching the medical practitioners to deal with external barriers that will influence guideline implementation.

2.9 Anaesthetic practices for the management of pain after caesarean section surgery

Anaesthetic practices tend to differ across different regions of the world depending on local practices, drug availability, equipment standards and staff availability. Surveys of obstetric anaesthetic and analgesic practices have been conducted in a number of regions around the world to document practices in different regions.

Tagaloa *et al* (2009) conducted an online survey investigating obstetric anaesthesia practices amongst the members of the Society of Obstetric Anesthesia and Perinatology (SOAP), in the USA. The majority of respondents in this survey (85%) indicated that single shot spinal anaesthesia was their preferred regional anaesthetic technique for elective caesarean sections. The popularity of this technique was anticipated considering that spinal anaesthesia has been shown to be more cost effective, easier to perform and faster in onset compared to epidural anaesthesia (Riley *et al*., 1995). In a study performed in the UK, Jenkins and Khan (2003) published data on caesarean section anaesthesia for the South-west Thames (SWT) region of England from 1992 to 2002 using a regional database. During this period the caesarean section rate in the SWT region rose from 13.9% in 1992 to 24.2% in 2002. The rate of general anaesthesia for caesarean section

surgery decreased in the SWT region of the UK from 43.1% in 1992 to only 9.8% in 2002. There was a subsequent increase in the use of regional anaesthesia during this period from 69.4% to 94.9% for elective caesarean sections, and 49.3% to 86.7% for emergency caesarean sections. The authors commented that the rise in regional anaesthesic techniques for obstetric patients might have contributed to the decline in the maternal mortality rate during this period. This study did not discuss the types of drugs used in the regional anaesthetics nor the monitoring of patients after their surgeries. A survey of obstetric anaesthesia practices in Belgium (Van Houwe *et al*., 2006), published in 2006, reported that 80% of respondents used a spinal anaesthetic technique for caesarean sections; either alone (34%) or as part of a combine spinal-epidural technique (46%). General anaesthesia was not a common modality used for obstetric patients. These results differed from other European countries where practice surveys have been done. Reports from a German study (Stamer *et al*., 2005) exploring obstetric anaesthetic practice for the period 2000 to 2002 (3 years), revealed that a spinal anaesthesia technique was only used in 50% of scheduled caesarean sections. For urgent and emergency cases the spinal anaesthesia rate decreased to 34.6% and 4.8% respectively during the evaluation period. This spinal anaesthetic rate is much lower than has been reported in the surveys from the USA, the UK and Belgium. Chan and Ng (2000) conducted a survey in 1996 to determine the obstetric anaesthesia and analgesia practices in Malaysia during this period. Malaysia is a middle income Asian country with maternal mortality rate of 40 per 100000 live births in 2015. Data submitted from 35 hospitals were analysed in this survey. These hospitals comprised of 17 government hospitals and 18 private hospitals. The authors reported that the regional anaesthesia rate for caesarean sections in their sample was 41.9%. Spinal anaesthesia was the most popular form of regional anaesthesia used for these procedures (84.6%). Epidurals were performed in only 12.2% of cases.

Practices related to post-operative pain control for patients also vary widely across the world. Most respondents in the Tagaloa *et al* (2009) survey used intrathecal opioids in their spinal anaesthetic to improve the post-operative

pain relief for their patients. The median dose of morphine reported in this survey was 200µg. This is higher than doses that have been shown to provide effective analgesia in the obstetric population (Abboud *et al*., 1988). Systemic analgesic therapy was not popular with only 12% of respondents using IV PCA therapy but NSAIDs were used by 81% of the respondents as part of their analgesic regimen. In 2003, Faboya and Uncles (2006) conducted a study in the SWT region of England investigating the practice of post-operative analgesia after elective caesarean section surgery. Only 33% of the hospitals surveyed had a written protocol for post-operative analgesia. Sixty-seven percent of respondents routinely used intrathecal diamorphine (200-500µg) for post-operative analgesia for caesarean section surgery patients. The remaining 33% used fentanyl in a dose range of 10-25µg. Morphine PCA was used in 33% of the hospitals when fentanyl was used intrathecally. All hospitals used diclofenac after surgery, with 90% of the respondents initiating this therapy at the end of surgery by using a rectal suppository for patients. This survey confirmed that hospitals in the SWT region of the UK practiced multimodal analgesic techniques during the period reviewed (Faboya and Uncles, 2006). In Belgium, Van Houwe *et al* (2006) reported that intrathecal opioids were not used in the spinal anaesthetics for caesarean sections. There appeared to be an even distribution of hospitals using epidural analgesia vs. IV/IM analgesia for post-operative pain management. The majority of epidural analgesia (81%) was provided using patient controlled epidural analgesia (PCEA). When IV/IM regimens were used, the respondents preferred a multimodal analgesic technique, which included NSAIDs (Van Houwe *et al*., 2006). Data from the 2005 German survey (Stamer *et al*., 2005) indicated that one third of the hospitals (143/397) who responded to the survey reported combining opioids with local anaesthetics for the spinal anaesthesia. Sufentanil was the most commonly used agent (77%) followed by fentanyl (15%) and morphine (13%). CSE was performed by a minority of the respondents (10.6%), where sufentanil was also the most popular opioid additive used. In Israel, only 12% of obstetric anaesthesia units surveyed reported routinely using intrathecal morphine for post-operative pain control for patients after a caesarean section. Most units

(68%) removed the epidural catheter after surgery and did not use it for post-operative analgesia. Only two units (9%) reported using TAP blocks occasionally for post-operative analgesia but the majority did not utilize this form of analgesia. NSAIDs were only used in 47% of the units surveyed (Orbach-Zinger et al., 2014).

The practices related to post-operative monitoring are also different in the various countries. Sixty-three percent of the respondents in the SOAP study reported that they monitor patients who received neuraxial opioids for up to 24-hours, and 93% of the respondents indicated that their hospital had a protocol for monitoring of these patients (Tagaloa *et al*., 2009). No details regarding the post-operative monitoring practices of patients after caesarean section were reported by Faboya and Uncles (2006) in their study of practices in the SWT region of England. Similarly, no details regarding post-operative monitoring practices were reported by Stamer *et al* (2005) or Chan and Ng (2000) in their respective surveys. In Israel, there were 72% of hospitals where anaesthesiologists did not monitor patients' post-operative pain control. However, in the few units where intrathecal morphine is used for caesarean section patients, patients are monitored for respiratory depression every two hours for 24 hours after surgery (Orbach-Zinger *et al*., 2014).

There is a paucity of data from Africa regarding anaesthetic practices for obstetric patients. No studies on obstetric anaesthesia practices in Central Africa have been found in the medical literature. A letter published in the International Journal of Obstetric Anesthesia in 2006, discussing the evolution of obstetric anaesthesia in West Africa made reference to obstetric anaesthesia practices in Nigeria. The author reported that the mainstay of obstetric anaesthesia in West Africa was general anaesthesia, despite regional anaesthesia being available, safer and cheaper in this region. Ketamine anaesthesia was very common, and this resulted in a high number of maternal deaths due to aspiration and cerebrovascular accidents (Okafor, 2006)

In 1978, Buley *et al* (1978) published the results of a survey they conducted in the Republic of South Africa and South West Africa (now called Namibia) on the obstetric anaesthesia practices in these countries. The authors reported that the majority of obstetric anaesthetics (90%) were performed by non-specialist practitioners. General anaesthesia was the preferred method of anaesthesia in an overwhelming majority of the hospitals surveyed (125/131, 95%). Only 7 hospital in Natal and KwaZulu (now called KwaZulu Natal) and 1 in the Transvaal (this former province is now divided into Gauteng, Limpopo and Mpumulanga provinces), used regional anaesthetic techniques for caesarean section surgery. This data from South Africa is very outdated and the anaesthetic practice reported in this study, while acceptable during the 1970's, is considered inappropriate care in 2016. There are unfortunately no other reports in the medical literature regarding obstetric anaesthetic practices in South Africa since this 1978 publication.

A worrying factor in the delivery of obstetric anaesthesia in South Africa is the level of training of the service providers. Lamacraft *et al* (2008) conducted a study investigating the experience and training of doctors performing obstetric anaesthesia in the Free State province in South Africa and found most obstetric anaesthetics in this province were administered by junior doctors, who had very little prior anaesthetic training. And, in a 2012 editorial in the Continuing Medical Education journal, Diedericks commented that the majority of anaesthetics in South Africa are provided by non-specialists, and in most cases this is for caesarean sections (Diedericks, 2012). If this is the case, it brings us back to first part of the statement made by John R Hampton, "*A fool – loosely defined as someone who does not know much about a particular area of medicine – will do well to follow guidelines when treating patients…"*, highlighting the need for clear, succinct guidelines on anaesthesia for caesarean sections in South Africa.

There is a significant paucity of information in the medical literature pertaining to the current obstetric anaesthesia practices in South Africa. Without this knowledge it is impossible for the country to develop an effective plan to improve the anaesthetic care of women having caesarean section surgery in

South Africa. Hence, I undertook a series of studies to describe the post-operative pain management practices of doctors managing caesarean section patients in South Africa and to evaluate the safety and efficacy of different intrathecal opioids on post-operative pain experiences in women who have undergone caesarean section surgery. The results of these studies will be presented in the forthcoming chapters.

2.10 Summary

In this chapter the literature review was presented. In the following chapter the study titled "*Developing a reference standard for anaesthesia for caesarean sections in South Africa*" will be presented.

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CHAPTER THREE: Expert opinion on anaesthesia for caesarean sections in South Africa

3.1 **Introduction**

South Africa has a high caesarean section rate (Moodley, 2010, CMS, 2015), and the anaesthetics for these procedures can be performed by many different categories of doctors ranging from junior medical officers to experienced specialists (Bettings *et al*., 2013). These procedures are performed in many different types of hospitals ranging from rural district hospitals to tertiary academic hospitals. Moreover, there are currently no national guidelines for the anaesthetic management of caesarean sections in South Africa.

A number of international caesarean section anaesthesia guidelines exist (Apfelbaum *et al*., 2016, Griffiths *et al*., 2011), however resource limitations mean that these guidelines may not be locally applicable. Compared to the public healthcare sector, the private health sector in South Africa is relatively well-provisioned in terms of doctor: patient ratio, equipment, and access to medicines. The high financial and resource availability in private healthcare means that international guidelines may be followed, but this sector services only a minority of the South African population. The bulk of the population is serviced by the public healthcare sector, which faces severe financial and other resource restrictions. For example, in 2013/4 the private sector spent 146 million rands on 8 million people (17% of the population), while during the same period the total public health expenditure on health was 141 million rands, to service the health needs of the remaining 83% of the population (Blecher *et al*., 2011). The resource constraints faced by the public sector means that they are less able to match the resources international guidelines call for to implement an effective caesarean section anaesthesia and post-operative analgesia service. Thus, a bespoke service, which takes into account local resource constraints, needs to be established.

Before locally appropriate guidelines can be developed it is essential to ascertain the current status quo in South Africa so that we have a reference point from which the country can gauge improvements in its obstetric anaesthetic services when aspiring towards a benchmark.

3.2 **Aim**

To describe the current reference standards for obstetric anaesthesia practices in South Africa

3.3 **Objectives**

To describe the reference standard in South Africa (as determined by the anaesthesiology academic heads of department at the eight medical schools) for anaesthesia for caesarean section surgery relating specifically to:

a. Preferred method of anaesthesia
b. Use of adjuvant drugs for neuraxial anaesthesia
c. Post-operative monitoring practices
d. Post-operative pain management

3.4 **Ethical considerations**

This was a prospective study involving an interview with the academic heads of the eight university anaesthesiology departments in South Africa. All anaesthesiology specialist training in South Africa takes place in these eight university departments.

Participants voluntarily participated in the study and provided written informed consent.

The protocol was reviewed and approved by the Human Research Ethics Committee – Medical (HREC) of the University of the Witwatersrand - Approval number M111124 (APPENDIX A).

3.5 **Research Methodology**

A semi-structured interview was conducted with the academic heads of departments of anaesthesiology at the eight South African medical schools in 2012. A semi-structured interview method was chosen in order to ensure that all pre-determined areas of discussion points are covered, while also allowing the interviewees to freely discuss points which they deemed to be appropriate for the topic of caesarean section anaesthesia.

The interview questionnaire was formulated to determine what the interviewees considered to be the reference standard for caesarean section anaesthesia in South Africa, with specific reference to:

i. Method of anaesthesia
ii. Use of adjuvant drugs for neuraxial anaesthesia
iii. Post-operative monitoring practices
iv. Post-operative pain management practice

The questions used in the interview were based on the questionnaire developed by Tagaloa *et al* (2009) and used in a 2011 survey conducted in the USA (APPENDIX B). The questionnaire was modified to take the local South African healthcare environment into account, and also to include questions related to the post-operative practices applicable to caesarean section patients. These changes related to the following points:

- Questions related to demographics and the experts' experience were omitted
- Some questions were rephrased to take into account that the questionnaire was directed at an expert for their opinion rather than what their personal practice was
- Drugs used for spinal anaesthesia were adjusted to include only drugs available in South Africa and also allowed for volume used to be indicated (Questions 4, 5 and 6)

- Drugs used for epidural anaesthesia were adjusted to include only drugs available in South Africa (Question 11)
- The experts were given more alternatives regarding their choice of management of a labouring patient requiring a caesarean section (Question 13)
- The experts were asked if they thought that maternity units should have a monitoring protocol, as opposed to whether their hospital had a protocol (Question 18)
- The options for NSAIDs were adjusted to include more drugs available in South Africa (Question 27)
- Route of administration of NSAIDs was included (Question 29)
- Use of IV paracetamol was included (Question 30)
- Oral analgesic options were adjusted to include drugs available in South Africa (Question 31)
- The experts were asked for comments or questions they thought may be relevant to obstetric anaesthesia in South Africa (Question 33)

To ensure face validity of the questionnaire, the modified questionnaire was reviewed by 12 senior members of staff of the Department of Anaesthesiology at the University of the Witwatersrand. Feedback was used to refine the survey questionnaire further. Following the validation process, changes were made to the punctuation of certain questions. The modifications made to the original questionnaire are indicated in APPENDIX C.

The interviews were recorded using an electronic voice recorder (Philips Digital Voice Tracer LFH0862).

The interview questions, participant information sheet and consent forms are referenced in the appendix.

APPENDIX D: Semi-structured Interview Questionnaire
APPENDIX E: Participant Information Sheet
APPENDIX F: Participant Consent Form
APPENDIX G: Participant Consent for Electronic recording

3.5.1 **Data Analysis**

Recordings were transcribed within one week of the interview being completed and the data analysed using qualitative data analysis methods including content analysis (Mayring, 2000). The responses to each of the questions were categorized into themes based on the options given to the interviewees. The categories were then quantified and interpreted in conjunction with any supporting statements made by the interviewees while answering the questions.

Data Description:

Continuous parametric data are described using mean and standard deviation. Continuous non-parametric data is described using median and interquartile ranges. Categorical data is presented using frequencies and percentages.

In order to maintain confidentiality of the respondents, responses are not linked to specific institutions in the reporting of the data.

3.6 **Results and Discussion**

All eight medical faculties in South Africa in 2012 participated in this study. During the interviews, the departments were represented by the head of department, or the head of department and the departmental obstetric anaesthesia expert or only the departmental obstetric anaesthesia expert (at the behest of the head of department) (Table 3.1).

TABLE 3.1: Participating universities and interviewees

Head of Department only	Head of Department and Departmental Obstetric Anaesthesia Expert	Departmental Obstetric Anaesthesia Expert
University of Limpopo (MEDUNSA Campus) University of the Witwatersrand	University of Cape Town University of KwaZulu Natal University of Pretoria University of the Free State	University of Stellenbosch Walter Sisulu University

At the four universities that were represented by both the head of department and the obstetric anaesthesia expert, the representatives came to a consensus and provided an 'institutional response' to the questions. Thus the denominator used to calculate proportions was eight (the number of institutions), and not the total number of participants.

3.6.1 **Preferred method of anaesthesia**

3.6.1.1 **The use of spinal anaesthesia for caesarean sections**

There was unanimous agreement at all the institutions, that the preferred anaesthetic technique for the majority of patients having an elective caesarean section should be a single shot spinal anaesthetic. Epidural anaesthesia, combined spinal-epidural anaesthetic technique and general anaesthesia were not recommended as the preferred technique by any of the institutions.

The agreement amongst all the institutions (n=8) was that the single shot spinal anaesthetic offers the quickest, most reliable and safest anaesthetic option for patients having an elective caesarean section. These claims are consistent with findings that spinal anaesthetic techniques are easier and more cost effective to perform than other neuraxial anaesthetic techniques (Riley *et al*., 1995). In addition, these recommendations are also in alignment with international guideline recommendations from the USA (Apfelbaum *et al*.,

2016) and the United Kingdom of Great Britain and Northern Ireland (UK) (Griffiths *et al*., 2011), which advocate regional anaesthetic techniques for caesarean section surgery.

Type of needle for spinal anaesthesia

The needle design and size can influence the effects and side-effects experienced by patients from the spinal anaesthetic procedure (O'Connor *et al*., 2007), and thus selection of needle is an important consideration when delivering spinal anaesthesia. There was agreement from all the institutions that a pencil point needle should preferentially be used when performing a spinal anaesthetic for a caesarean section. The pencil point needle seperates the fibres of the dura rather than cutting through them (Calthorpe, 2004). This atraumatic entrance into the subarachnoid space reduces the risk of a dural flap developing, thereby decreasing the risk of a post-dural puncture headache (PDPH) occuring.

The suggested pencil point needle types included: (*multiple options were possible)*

- Whittacre© (5/8)
- Sprott© (3/8)
- Pencan© (1/8)

These recommendations are in line with those of the ASA, which state that "pencil-point spinal needles should be used instead of cutting-bevel spinal needles" (Apfelbaum *et al*., 2016).

All institutions agreed that the Quincke© needle should never be used to perform a spinal anaesthetic for obstetric patients. The Quincke© needle is a cutting spinal anaesthetic needle that is associated with a greater risk of developing PDPH (O'Connor *et al*., 2007). Respondents at all institutions however, conceded that the reality was that this cutting needle is sometimes all that is available in the public sector hospitals, and therefore doctors often

may not have any choice but to use this needle. The frequency of this problem was not quantified.

Gauge of needle for spinal anaesthesia

The gauge of the spinal anaesthestic needle refers to the external diameter of the needle and is based on the Standard Wire Gauge system (Poll, 1999). The higher the gauge number, the smaller is the outer diameter of the needle. Using a wide diameter needle to perform a spinal anaesthetic is associated with an increased risk of the patient developing a PDPH (O'Connor *et al.*, 2007).

All institutions recommended that smaller gauge needles should be used to perform spinal anaesthetics for patients having caesarean section surgery. Half (4/8) of the institutions recommended that a 26G needle be used. About one third (3/8) of the institutions recommended that the 25G needle was preferable, citing easier needle control as the reason for using the slightly larger diameter needle. Only one institution recommended that the 27G needle was appropriate. (Figure 3.1)

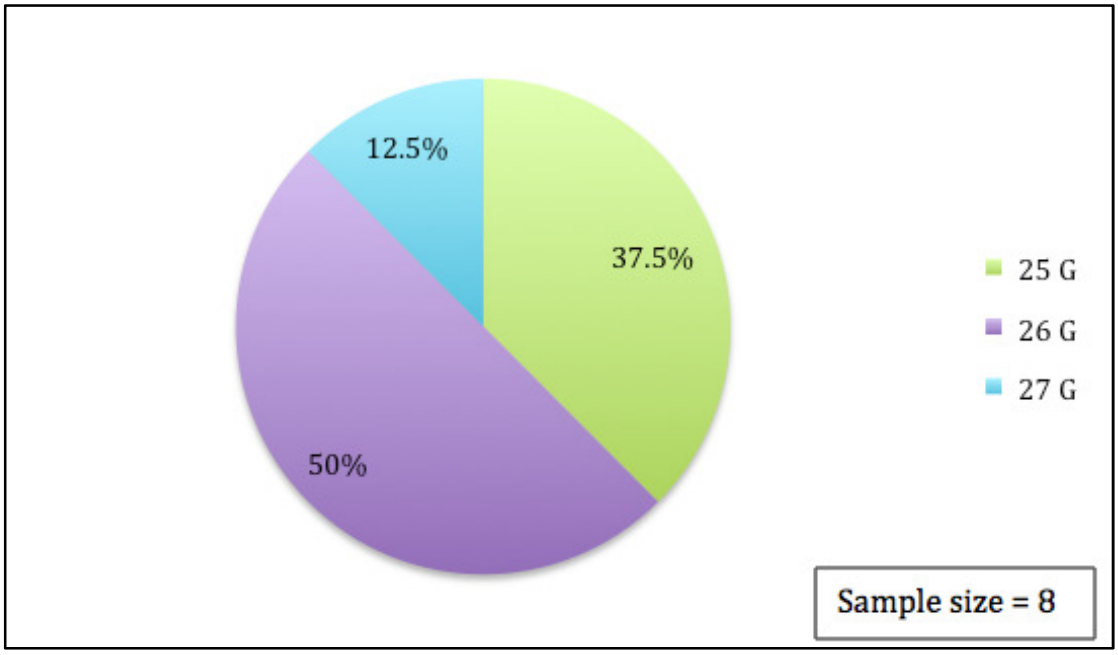


FIGURE 3.1: Choice of gauge of spinal anaesthetic needle

The 27G needle is the smallest gauge needle that is currently available for clinical use in South Africa. Most institutions (7/8) were of the opinion that this size of needle should be reserved for use by experienced practitioners because the needle is very small and is more difficult to manoeuvre when performing a spinal anaesthetic. The risk associated with its use therefore outweighs the benefit of a lower PDPH risk.

The 22G needle is a relatively large bore needle that has a higher association with PDPH (O'Connor *et al*., 2007). There was unanimous agreement that this needle should not be routinely used to perform a spinal anaesthetic in pregnant patients. However, three institutions highlighted that the caveat is that, in certain cases (eg. morbidly obese patients) this needle may be more appropriate to use as it easier to manoeuvre and can decrease the tissue trauma. This is an important point as 42% of South African women are reported to be overweight (Ng *et al*., 2014).

Local anaesthetic choice for spinal anaesthesia

Current international guidelines (Apfelbaum *et al*., 2016, Griffiths *et al*., 2011) do not recommend any specific local anaesthetic for use in obstetric spinal anaesthetics, but there was unanimous agreement across the institutions that the local anaesthetic of choice for obstetric spinal anaesthetics is 0.5% bupivacaine with dextrose. None of the institutions recommended using any of the other available local anaesthetics (bupivacaine 0.5%, lignocaine 2%, ropivacaine 0.75% or levobupivacaine 0.5%). Bupivacaine 0.5% with dextrose is a hyperbaric local anaesthetic solution that spreads towards the thoracic kyphosis when the patient is in the supine position (Kleinman, 2002). This cephalad spread results in an attenuation of the nerve impulses from approximately the T4 level of the spinal cord.

Bupivacaine with dextrose is available as a pre-mixed solution for intrathecal use in South Africa. One expert commented that in their center, the availability of the pre-mixed solution is often erratic, and they advocate that

anaesthetic service providers mix their own hyperbaric solution of bupivacaine by adding dextrose to plain 0.5% bupivacaine. This practice is potentially dangerous if strict attention to detail is not maintained with regards to dilutions and aseptic techniques.

Dose of local anaesthetic for spinal anaesthesia

The dose of local anaesthetic administered for a spinal anaesthetic has an impact on the quality of the anaesthesia and the incidence of hypotension (Kleinman, 2002). The experts interviewed in this study had varied responses regarding the appropriate dose of intrathecal local anaesthetic that should be used. Four of the institutions recommended a range of doses while the other four were very specific in what dose they felt was the most appropriate. These results are illustrated in figure 3.2.

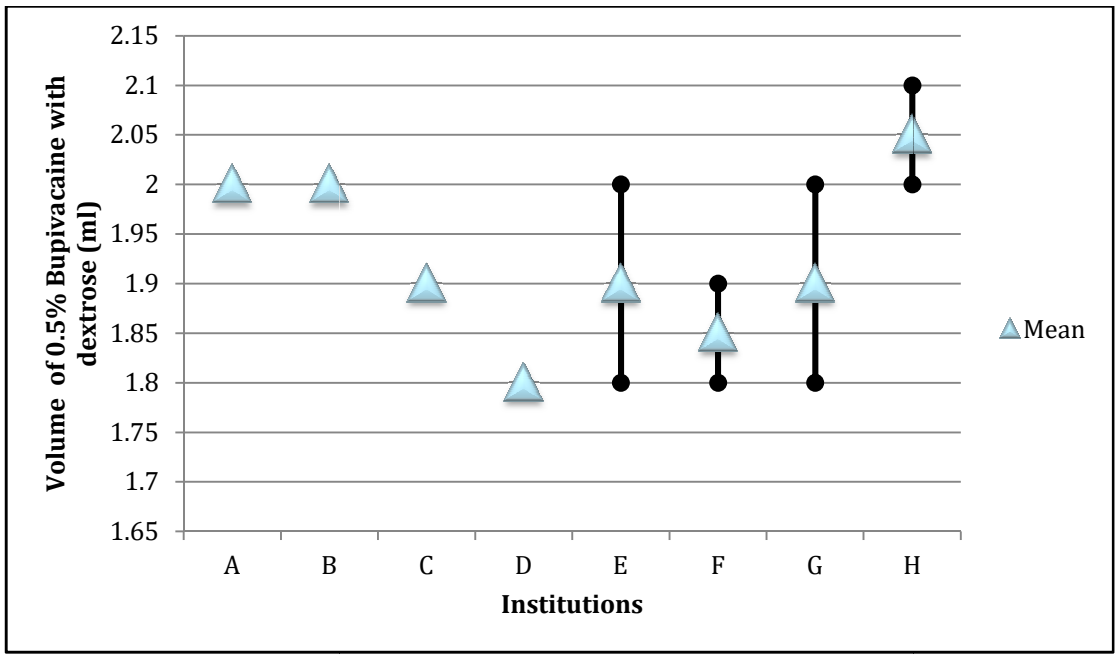


FIGURE 3.2: Recommended doses of 0.5% bupivacaine with dextrose for single shot spinal anaesthetic

The range of recommended doses of 0.5% bupivacaine with dextrose, ranged between 1.8ml and 2.1ml (9mg – 10.5mg). The median recommended dose of 0.5% bupivacaine with dextrose was 1.9ml (9.5mg). Yet, using doses of

≤10mg bupivacaine (2ml of a 0.5% solution) for obstetric spinal anaesthesia has been demonstrated to be associated with a higher incidence of visceral pain during the surgical procedure (Kiran and Singal, 2002).

One expert was highly critical about using doses lower than 2ml of 0.5% bupivacaine with dextrose, correctly indicating that this increases the risk of a failed spinal anaesthetic. Therefore the minimum dose recommended by this expert was 2ml. Nevertheless, the lowest dose recommended across the institutions was above the 8mg bupivacaine dose Arzola and Wieczorek (2011) identified as being associated with severely compromised anaesthetic efficacy.

The use of adjuvant drugs for elective spinal anaesthesia

All the experts recommended the use of an opioid additive with the intrathecal local anaesthetic to improve the efficacy of the spinal block. One expert stated:

"It is wrong not to use an opioid"

Neuraxial opioid administration allows for a more direct stimulation of the opioid receptors in the spinal cord, which improves the intensity of the anaesthetic and, depending on the opioid used, will also prolong the analgesic efficacy of the block (Cousins, 1984). This theory also applies to lipophilic opioids such as fentanyl.

This institutional recommendation is in line with the 2016 American Pain Society (APS) Guidelines (Chou *et al*., 2016), which recommend intrathecal opioids as one of the therapeutic analgesic options for caesarean section patients. Fentanyl was universally recommended as the opioid that should be used as an additive agent for the spinal anaesthetic in order to improve the efficacy of the block and to provide better intraoperative analgesia. This recommendation is certainly justified, as intrathecal fentanyl has been

demonstrated to increase the effectiveness and duration of analgesia when compared to control groups (Hunt *et al*., 1989).

The recommended fentanyl dosage ranged between 10 – 25µg (median = 20µg). Experts from three institutions gave a specific dose that should be used while the remaining five institutions provided a range of doses that anaesthetic service providers should work between. (Figure 3.3)

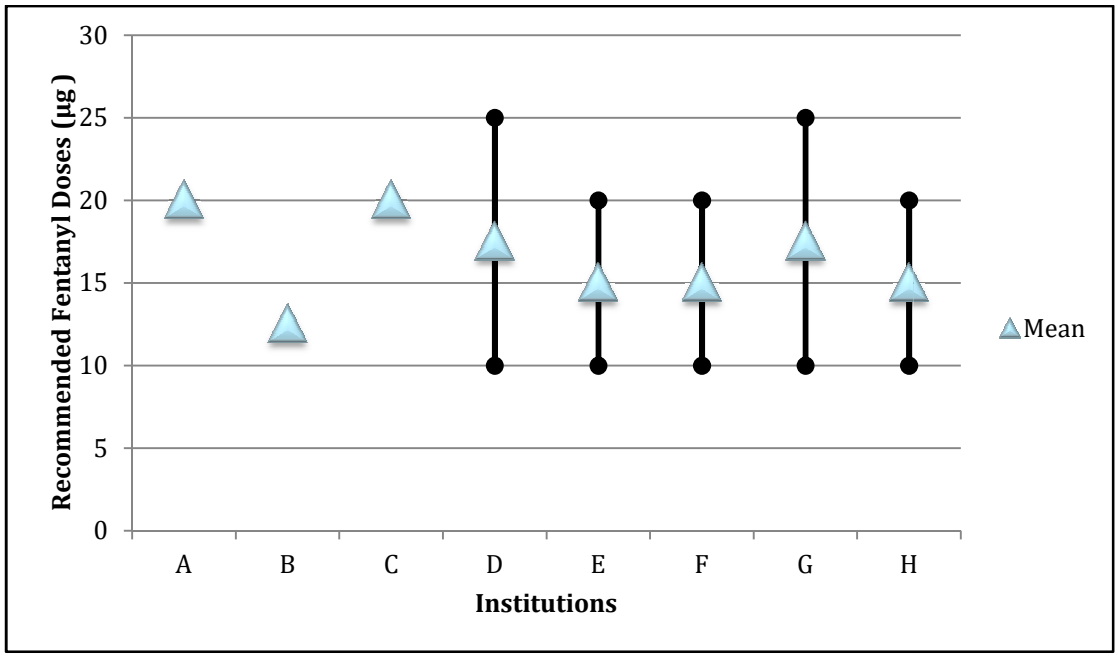


FIGURE 3.3: Recommended doses of fentanyl for single shot spinal anaesthetic

These recommended dosages of fentanyl may be higher than is actually required. Intrathecal fentanyl doses as low as 6.25µg, have been shown to provide effective intra-operative analgesia for caesarean section surgery, with doses above this level not increasing the effectiveness of the intraoperative analgesia (Hunt *et al*., 1989).

There was unanimous agreement that intrathecal morphine should not be used because of concerns regarding the potential delayed respiratory depressant effects of morphine following neuraxial administration. The concern was that there is inadequate nursing monitoring standards in the

post-operative obstetric wards in South Africa to be able to detect this complication timeously. One of the experts commented:

"It would worry me if we're using morphine in our caesar patients because of the lack of effective nursing and monitoring in the wards"

The area of the hospital where the patients recover is dependent on the level of nursing care available in each hospital.

These opinions are contrary to the recommendations of the Australia New Zealand College of Anaesthetists (ANZCA) 2015 Acute Pain Guidelines (Schug *et al*., 2015), which emphasizes the positive analgesic effects of intrathecal morphine for patients having caesarean section surgery. The Procedure-specific post-operative pain management (PROSPECT) working group also specifically recommends that intrathecal morphine (below 200µg) should be used for patients having a spinal anaesthetic for caesarean section (PROSPECT Working Group, 2015).

One expert from a different university did however concede that the risk of delayed respiratory depression was very low, especially if the doses of morphine recommended in the international literature for obstetric patients, are used. In addition, pregnant women are less likely to develop delayed respiratory depression due to their high progesterone levels, which causes them to develop an increased respiratory rate (McDonnell *et al*, 2009). However, it appears that current teaching in South Africa is governed by fear of this low risk of delayed respiratory depression and the inability to detect it timeously.

3.6.1.2 **The use of epidural anaesthesia for caesarean section**

Experts from all the institutions agreed that an epidural anaesthetic technique should not be used as the sole anaesthetic for elective caesarean sections. The reasons cited for this recommendation included:

- Longer time required to administer compared to spinal anaesthetic

- Cannot be used post-operatively in the general ward
- Does not provide as good surgical anaesthesia compared to spinal anaesthesia

However, there was unanimous agreement across the institutions that the technique can be used as part of a combined spinal-epidural (CSE) technique. The epidural should then be used for post-operative analgesia in a high-care setting.

For an urgent caesarean section, where the patient already has an indwelling epidural catheter, experts from seven institutions (87.5%) agreed that the anaesthetic should be a "top-up" of the labour epidural. At one of the institutions the recommendation was that the anaesthetic service provider should perform a general anaesthetic if they did not insert the epidural. If they inserted the epidural catheter then it would be appropriate to "top-up" for the surgical procedure.

There was a variation in the choice of local anaesthetic that the experts recommend for the epidural "top-up". Six (75%) of the institutions recommended 2% lignocaine, so that surgical anaesthesia could be achieved quickly for the surgery. One institution suggested levobupivacaine, citing the relative cardiac safety of the agent and one institution recommended using bupivacaine. No reason was provided for this choice.

Of note, is that three of the six institutions, which recommended 2% lignocaine as the preferred local anaesthetic for "top-up", indicated that 0.5% bupivacaine could be used if time was not a constraining factor. The reason cited was that it has a longer duration of action and will probably not require additional dosing intraoperatively. One expert commented:

"I think bupivacaine is probably better but lignocaine might be quicker. Could be either, but I think lignocaine might be quicker and there again it depends on the indication and on your time available"

The use of adjuvant drugs for emergency epidural "top-up"

Experts from all the institutions agreed that an epidural top-up is an appropriate strategy to use to attain surgical anaesthesia for a laboring patient with an *in-situ* labour epidural that requires a caesarean section. At one institution however, a *proviso* that the provider who inserted the epidural must be the same person administering the anaesthetic for the surgery, was stipulated. The expert at this institution reiterated that if there is a different anaesthetic provider for the surgery, then the anaesthetic should be a general anaesthetic.

Four institutions advocated for no additive agents being used in the epidural top-up, and that the anaesthetic service provider should be limited to using local anaesthetic only. At the remaining four institutions the experts felt that using additives is appropriate and that multiple additive agents could be used. The additives recommended are listed in table 3.2

TABLE 3.2: Table of recommended epidural "top-up" additives

Additives recommended that may be used in the epidural top-up solution	Number of institutions advocating use
No agents added	4
Fentanyl	3
Sodium Bicarbonate 8.4%	3
Morphine	3
Adrenaline	2
Sufentanil	0
Other	0

Despite fentanyl being a lipophilic opioid, the analgesic effect of epidural fentanyl has been shown to occur primarily by a spinal mechanism and not from systemic absorption of the drug (Cohen *et al*., 2002). This is despite of the easier systemic absorption of lipophilic drugs.

The analgesic effect of epidural morphine for post-caesarean section patients is well established and has been shown to increase with increasing doses of morphine up to 3.75mg (Palmer *et al*., 2000). Three institutions indicated that they recommend the use of epidural morphine for post-operative analgesia only if the patient was being transferred to a high-care environment after surgery. The addition of opioids to the epidural local anaesthetic solution is in line with the recommendations of the APS (Chou *et al*., 2016), which recommends that epidural anaesthetics (with or without opioid) can be used for caesarean sections.

Two institutions' experts recommended the addition of adrenaline to the epidural "top-up" solution. The associated vasoconstriction and decreased systemic absorption of the local anaesthetic drugs was cited as the motivation for the addition of adrenaline. One expert made the comment that:

"Adrenaline gives you a slightly better margin of safety because of the vasoconstriction and decreased absorption."

Indeed, laboratory studies have demonstrated that the vasoconstrictive effect of adrenaline has a dual influence on the local anaesthetic when used in an anaesthetic block. Vasoconstriction decreases the systemic absorption of the local anaesthetic resulting in lower peak plasma concentrations and thereby reducing the risks of systemic toxicity, and in addition, the resultant higher drug concentration around the nerves (as a result of the reduced absorption) prolongs the duration of the drug. However, this prolongation of effect does not apply to the long acting local anaesthetic agents such as bupivacaine or ropivacaine. (Neill, 2007, Hurley *et al*., 1991)

Sodium bicarbonate is an alkaline solution. Experts at three institutions recommended that the 8.4% sodium bicarbonate solution be used as an additive agent for the epidural top-up. This drug is added to local anaesthetic solutions to increase the pH of the solution resulting in an increased ratio of unionized to ionized local anaesthetic molecules. It is the unionized local anaesthetic molecules that are able to penetrate the lipophilic cell membrane

of the nerves. This higher concentration of unionized molecules results in a more rapid onset of action of the local anaesthetic solution. (Neill, 2007)

The Faculty of Pain Medicine in the Royal College of Anaesthetists in the UK issued recommendations in 2010 titled “Best practice in the management of epidural analgesia in the hospital setting” (Rowbotham *et al*., 2010). The document is not specifically for obstetric epidurals but makes general recommendations about epidural analgesia. These guidelines do not make any recommendations on which drugs are most appropriate to use in epidural analgesia but they do make the following stipulations:

- “ There should be a limited number of solutions approved and available for epidural infusions in every hospital”
- “They should be prepared under strict sterile conditions in specifically designed units. Many are available commercially. Any variation from this should occur in exceptional circumstances only and with the agreement of the responsible consultant after a risk/benefit analysis”
- “Epidural infusions should be labeled : ‘For epidural use only’ “
- “Epidural infusions should be stored in separate cupboards or refrigerators from those holding intravenous and other types of infusions in order to reduce the risk of wrong route of administration”
- “The lowest possible effective concentration of local anaesthetic should be used in order to preserve motor function as much as possible. This improves patient satisfaction and aids detection of neurological complications. If higher concentrations are required, the infusion rate should be reduced periodically to allow assessment of motor block”
- “The use of drugs beyond license should be consistent with local hospital guidelines and informed by recommendations of the British Pain Society”

The use of additive agents for epidural anaesthetic solutions is not prescribed by any international guidelines. The use of these agents is generally left at the discretion of the doctor administering the epidural anaesthetic. These additive agents may provide specific advantages for the patient and therefore the use of these agents should be dependent on the clinical scenario.

3.6.2 **Post-operative Monitoring Practices**

Monitoring of patients in the post-operative period is an important aspect of post-operative care. The National Institute of Clinical Excellence (NICE) guidelines (Griffiths *et al*., 2011) state:

"After recovery from anaesthesia, observations (respiratory rate, heart rate, blood pressure, pain and sedation) should be continued every half hour for two hours and hourly thereafter provided that the observations are stable or satisfactory. If these observations are not stable, more frequent observations and medical review are recommended"

Efficient monitoring can alert healthcare providers to any complications related to the surgery or anaesthesia that may have an adverse effect on the patient's surgical outcome. Post-operative monitoring begins in the recovery room and should continue (albeit less intensively) in the post-operative wards (Bettings *et al*., 2013). The APS guidelines (Chou *et al*., 2016) recommend that every patient that receives systemic opioids for post-operative analgesia should be monitored for sedation, respiratory status and other adverse events in the initial hours after surgery, but the guidelines do not stipulate the exact duration of monitoring required.

The administration of neuraxial opioids intraoperatively can result in side effects that can extend into the post-operative period (Mikuni *et al*., 2009). This is especially applicable to hydrophilic opioids such as morphine, which have a long duration of effect following neuraxial administration (Salmah and Choy, 2009). The short-term side effects include symptoms such as pruritus, nausea and vomiting. However, the most feared side effect of neuraxial opioids is respiratory depression (Kato *et al*., 2008).

Experts from all eight institutions agreed that maternity units must have a monitoring protocol for patients who receive neuraxial opioids as part of their anaesthetic. The recommended duration of monitoring depended on the neuraxial opioid used. For short acting opioids such as fentanyl and

sufentanil, the mean duration of monitoring recommended was 4 hours (0 – 12 hours).

The majority of the institutions (7/8) recommended a specific duration of monitoring. Only one institution suggested a range (6 - 12 hours) of time that patients should be monitored. At two institutions the experts did not believe that monitoring for respiratory depression was necessary beyond the recovery room, as they felt that the duration of effect of fentanyl and sufentanil did not warrant concern regarding respiratory depression beyond the surgical period. The American Society of Anesthesiologists (ASA) guidelines (Horlocker *et al*., 2009) recommend that monitoring for respiratory depression following a single neuraxial dose of lipophilic opioids should be done for a minimum of two hours after administration.

For patients who receive neuraxial hydrophilic opioids, 7/8 (87.5%) institutions recommended that these patients must be monitored for 24 hours after the administration of the drug. Only 1/8 (12.5%) of the institutions recommended that monitoring should be performed for eight hours. The ASA guidelines (Horlocker *et al*., 2009) recommend that monitoring of these patients must be performed for a minimum of 24 hours after the administration of the medication. The monitoring should be done once per hour for the first 12 hours and then once every two hours for the second 12 hours. (Horlocker *et al*., 2009)

Monitoring of patients must be guided by the clinical condition of the patients. Patients who are at increased risk for developing respiratory depression (obese patients, history of sleep apnoea, elderly, concomitant administration of opioids via different routes, and those patients in an unstable medical condition) must be monitored for an extended period of time (Horlocker *et al*., 2009).

The ASA Task force on Neuraxial Opioids practice guidelines (Horlocker *et al*., 2009) recommends that patients who receive neuraxial opioids should be monitored, as a minimum, for adequacy of ventilation, oxygenation and also

for level of consciousness. The recommendations from the interviewed experts varied in the number of modalities that should be assessed. Four institutions recommended that respiratory rate, sedation scores and pulse oximetry should be monitored. Respiratory rate monitoring and sedation monitoring was recommended by two of the institutions. Only one institution recommended that respiratory rate monitoring be used as the sole monitoring tool.

Capnography allows the continuous measurement of expired carbon dioxide and can serve as a measure of the adequacy of ventilation in a patient (Kodali, 2013). Only five institutions expressed that capnography was a useful monitor of respiratory depression following neuraxial opioid administration, and should be a preferred monitor. However the opinion was expressed at all eight institutions that the cost of the device was too prohibitive for capnography to be implemented as a routine measure in the South African public healthcare sector environment. I have highlighted three responses from the expert panel regarding the use of capnography in patients who received intrathecal opioids:

"…it's a sophisticated monitor and certainly costly. If you're looking at it for effective analgesia in state hospitals, its not an option really."

"…well, it would be great if we could have that. Its not like pulse oximetry and the respiratory rate can do everything for you…. yes but I don't think its possible"

"Excellent, if you can get it"

At two institutions, opinions were expressed that patients given intrathecal morphine could be nursed in a normal post-operative ward provided that the ward was adequately staffed, and that the nursing staff regularly monitored patients for respiratory depression using acceptable monitoring protocols.

The comments made by both the institutional experts were:

"…. if the nurses are trained, yes, I'll be happy."

"Not high-care necessarily, but a ward with equipment and nursing vigilance"

3.6.3 **Post-operative pain management**

The experience of pain after a caesarean section is influenced by a number of different factors including the psychological and emotional preparedness of the patient for the birth of her child. The level of pain that a woman experiences following caesarean section surgery has an impact on her ability to take care of and bond with her baby (Karlstrom, 2007). It is therefore important that health care providers implement and evaluate analgesia in these patients.

The path to successful post-operative pain management begins in the pre-operative period. Patients should be educated about the surgical procedure and also about what to expect with regards to post-operative pain after surgery. The APS guidelines recommend that patients should be provided with information about their post-operative pain management options before the surgery so that they are informed and aware of their options in advance (Chou *et al*., 2016). For patients having caesarean section surgery, these options should include regional and systemic analgesic options.

Seven institutional experts felt that epidural analgesia should not be routinely used for post-operative pain management in South Africa. They reasoned that this would require that these patients be admitted to a high-care unit in order to ensure correct management of the epidural anaesthetic after surgery. The same experts also felt that the benefit of the epidural can be closely matched using other analgesic techniques, such as intrathecal morphine. They did however concede that intrathecal morphine use would also require intensive monitoring. Quotes, from the expert panel, related to the use of epidural post-operative analgesia include:

"… I don't think its sustainable care and also there are potential complications with the epidural catheter…."

"… because we've got other modalities of post-op analgesia…."

"I'd rather give intrathecal morphine and take the epidural out … and it also goes with monitoring. I can't send a woman to the post-natal ward with an epidural catheter in… "

Other reasons cited as to why routine use of epidural analgesia was inappropriate in the public healthcare sector in South Africa included: Inadequate monitoring in postnatal wards (n=6), no additional gain for the patient (n=6), no standard epidural protocols available (n=5), nursing staff shortages (n=5), lack of nursing staff education in epidural care (n=5), no epidural pumps in postnatal wards (n=4) and anaesthesiology staff shortages (n=4).

If we compare the response from the interviewees to international practices, Palmer *et al* (2000) reported that the use of epidural morphine for post-caesarean analgesia may not be optimal and that supplementation with systemic analgesics may be required in order to optimise pain management. Cooper *et al* (1999) compared the analgesic efficacy of epidural fentanyl and intravenous patient controlled analgesia (PCA) morphine and found that while the PCA morphine utilization was significantly lower ($p=0.0007$) for patients in the epidural fentanyl arm of the study, the patient satisfaction levels were similar in both groups. Based on the findings of these studies, the recommendations from the experts appears to be justified, especially considering the relative shortage of high care beds in South Africa. The APS guidelines are neutral in their recommendations regarding epidural opioids, indicating that a local anaesthetic epidural can be used with or without opioids (Chou *et al*., 2016)

Patient controlled opioid administration allows patients to administer their medication as and when they require it, and is associated with increased patient satisfaction with their pain management (Harrison *et al*., 1988). This increased satisfaction is postulated to be due to the more stable plasma analgesic levels (when compared with intermittent administration techniques) and the greater sense of empowerment for patients (Harrison *et al*., 1988). Despite the documented higher satisfaction levels that PCA offers, experts at six of the eight institutions (75%) did not recommend PCA for routine post-operative analgesia in caesarean section patients. They felt that the limitation on patient mobility (n=5), the risks associated with intravenous (IV) opioids (n=4), and the requirement that the IV line be in place for prolonged periods (n=3), were factors that collectively made PCA an unsuitable analgesic technique for routine use following caesarean section surgery. There was however two institutions that argued that PCA would provide an ideal form of analgesia, but they felt that its routine use was currently impractical and expensive for both the private and public health care sectors in South Africa. These same institutional experts indicated that this modality should be reserved for challenging cases where pain is likely to be high (e.g. difficult surgery). The comment from one of these experts was:

"Patients who have had a difficult caesar. So, for example a previous caesar X2 who's now come for another caesar, or a patient who has had a caesar for twins or perhaps a patients who needed a classical incision for whatever reason or even where a caesar has progressed to hysterectomy… "

The UK guideline (Griffiths *et al*., 2011) however, recommends that all patients should be offered PCA opioids after their caesarean section.

Despite 75% of institutions not being in favour of PCA, there was unanimous agreement (8/8) that when a PCA is used, the most appropriate drug to use is morphine. No direct reasons were offered for this preference however it is likely that this is due to the longer duration of action of morphine compared to other opioids.

Non-steroidal anti-inflammatory drugs (NSAIDs) are anti-hyperalgesic agents that provide good post-operative pain relief due to their anti-inflammatory effects (Lavand'homme *et al*., 2007). These drugs also have well documented benefits for pain associated with uterine incision and uterine involution after caesarean section surgery (Tan, 2012). All the institutional experts (8/8, 100%) recommended that NSAIDs should be routinely used after caesarean section surgery, except in patients where contraindications to the drugs exist. These contraindications included: bleeding diatheses (n=8), severe pre-eclampsia (n=8), and renal dysfunction (n=8).

At one institution, concerns were raised about using NSAIDs in HIV positive patients because, anecdotally, they have observed nephropathy developing in HIV positive patients following NSAIDs use.

"… I think it's contra-indicated in a few settings ... We are cautious in HIV positive patients because we have seen a few cases of nephropathy developing in these patients…. the number one thing here is the renal dysfunction."

This concern regarding NSAIDs used was raised at the first expert interview, therefore the point was specifically raised at subsequent interviews. Other institutional experts (7/8) however, did not share this concern, when the issue was raised directly with them.

No opinions were expressed with regards to which NSAIDs were preferable (TABLE 3.3), and the decision on which NSAIDs to use was based on personal experiences with particular drugs their centres.

TABLE 3.3: NSAIDs preferences following caesarean section

NSAIDs	Number of institutions
Ibuprofen	4
Diclofenac	4
Ketorolac	1
Parecoxib	1*

** Stipulated that the drug should only be used as the initial dose of NSAIDs in the operating theatre and thereafter the NSAIDs should be changed to another drug in the same class, but administered via a non-parenteral route.*

Similarly, there was no consensus across the institutions regarding the route of administration of the NSAIDs. Half of the institutions advised an oral route of administration while the other half recommended rectal suppositories. At one institution, the expert stated that there is no scientific justification for rectal administration of NSAIDs, and is inappropriate for caesarean sections. The ANZCA 2015 Acute Pain guideline (Schug *et al*., 2015) provides good evidence for the use of NSAIDs in the post-operative period however the guideline stated that there was conflicting evidence regarding the benefits of using NSAIDs in the post-caesarean section patient. The UK (Griffiths *et al*., 2011) and APS (Chou *et al*., 2016) guidelines, as well as the PROSPECT recommendations (PROSPECT Working Group, 2015), however state clearly that NSAIDs should be offered as an adjunctive analgesic after caesarean section surgery, provided that there are no contraindications to the use of NSAIDs.

Intravenous paracetamol is a good analgesic agent that has a significant opioid sparing effect when used in combination with opioids (Remy *et al*., 2005). The drug therefore offers an attractive option to be used as part of a post-caesarean section pain management regimen. The majority of institutions (6/8, 75%) agreed that IV paracetamol should be routinely used following caesarean section surgery. These experts agreed that the opioid sparing effect of IV paracetamol is superior to other drugs and will therefore be beneficial to these patients. There was however concern expressed by this group, that the costs of the drug are prohibitive for widespread application

in South Africa. At two institutions, it was felt that that the routine use of IV paracetamol could not be justified within the resource-constrained environment in South Africa. The PROSPECT guidelines are the only international recommendations that make specific mention of IV paracetamol use for caesarean section surgery. No other international guidelines have specifically recommended IV paracetamol for use after surgery but paracetamol has been recommended by guidelines from two different countries (Chou *et al*., 2016, Schug *et al*., 2015).

In addition to the medications discussed above, the experts at the eight institutions also recommended other oral agents that should be used to manage post-caesarean pain, especially after the first 24-hour post-operative period. (TABLE 3.4)

TABLE 3.4: Oral analgesic agents to be used for caesarean section analgesia

Oral Analgesic	Number of institutions
Paracetamol	5
Codeine	5
Tramadol	3

Seven institutions recommended that analgesics must be administered as regular scheduled doses in order to have maximum effectiveness. Only one institution recommended *pro re nata* (PRN) administration. The use of oral agents is in line with other international guideline recommendations (Chou *et al*., 2016).

The experts also made recommendations on what they felt was needed in South Africa to improve post-caesarean section analgesia. The highlighted areas include the following:

- Development of guidelines for post-caesarean analgesia

"…establishment of the special interest group that would be responsible for the establishment of guidelines for post-caesarean analgesia… "

- Standardise care in the country

"I think we need to standardise management. When I say management I mean the peri-operative management and how we manage complicated obstetrics"

- Develop a post-operative monitoring chart

"We need to have…. similar to Ireland or the UK (I am not sure which), where they have a specific chart for post-op caesar observations…"

- Improved anaesthesia training for obstetric cases

"…my biggest concern is that we are sending out very junior doctors to go and do difficult anaesthetics when they're not ready for it. We need to improve the standards of training, especially for obstetric anaesthesia."

3.7 Summary of results

Table 3.5 summarises the key results of this study and compares the opinions expressed at the eight institutions with currently available international guidelines.

TABLE 3.5: Summary of the recommendations of the South African institutional experts compared with current international guidelines

SOUTH AFRICAN EXPERT RECOMMENDATIONS	INTERNATIONAL GUIDELINES
Method of anaesthesia	
Single shot spinal anaesthetic	ASA – Neuraxial anaesthetic technique (does not specify intrathecal or epidural)[(a)] UK – Regional anaesthetic technique (does not specify intrathecal or epidural)[(b)]
Type of spinal anaesthetic needle	
Pencil point needle ** Quincke needles should not be used*	ASA – Pencil point needle[(a)] ** Recommendation is to use pencil point needle instead of cutting-bevel needle*
Local anaesthetic for spinal block	
0.5% bupivacaine with dextrose	No recommendations
Use of adjuvant drugs for neuraxial anaesthesia	
Opioids – Fentanyl (10 – 25µg)	ASA – Neuraxial opioids are recommended. No specific drug is recommended[(a)]

** Morphine should not be used*	UK – Neuraxial diamorphine[(b)] APS – Intrathecal and epidural opioids. No specific drug is recommended[(c)] ANZCA – Intrathecal morphine[(d)] PROSPECT – Intrathecal morphine [(f)] ** There are no explicit recommendations against morphine*
Post-operative monitoring practices	
Monitoring for respiratory depression in patients given neuraxial opioids. The duration of monitoring depends on the drug used: • Lipophilic opioids - 0 – 12 hours • Morphine - 24 hours after the administration of the drug	ASA - Monitoring for respiratory depression should be done in patients who receive neuraxial opioids. The duration of monitoring depends on the drug used: • Lipophilic opioids – minimum of two hours after administration[(e)] • Morphine - The monitoring should be done once per hour for the first 12hours and then once every two hours for the second 12 hours[(e)] APS – Sedation and respiratory status in the initial hours after surgery for patients who receive systemic opioids[(c)]

Post-operative pain management practice	
Epidural analgesia – should not be routinely used for post-operative analgesia	APS – Epidural analgesia (with or without opioids) can be offered[(c)]
PCA opioids – should be reserved for challenging cases	UK – PCA opioids should be offered to patients[(b)]
NSAIDS – should be routinely used for post-operative pain management	UK – NSAIDS should be routinely used[(b)] APS - NSAIDS should be routinely used[(c)] ANZCA – Conflicting evidence regarding benefits of NSAIDs use[(d)] PROSPECT – Oral NSAIDs should be used [(f)]
Paracetamol – should be routinely used for post-operative pain management. The intravenous formulation is preferred but the cost is a concern	APS - Paracetamol should be routinely used[(c)] ANZCA – Paracetamol should be routinely used [(d)] PROSPECT – Oral paracetamol should be used [(f)]

[(a)] (Apfelbaum *et al*., 2016)[(b)] (Griffiths *et al*., 2011) [(c)] (Chou *et al*., 2016) [(d)] (Schug *et al*., 2015) [(e)] (Horlocker *et al*., 2009) [(f)] (PROSPECT Working Group, 2015)

3.8 **Conclusions**

This study was conducted as a series of semi-structured interviews with senior representatives of the eight academic anaesthesiology training departments in South Africa in 2012. These experts in anaesthesia were asked a series of questions related to the anaesthetic management of caesarean sections in the South African environment. The aim of these interviews was to determine a reference standard for performing an anaesthetic for caesarean section in South Africa taking into account the limited healthcare resources available in a developing country such as South Africa. Given that all training of anaesthesiology registrars in South Africa takes place in these eight centres, it is reasonable that the views expressed at the institutions informs training standards for obstetric anaesthesia in South Africa. Not all the heads of departments were experts in obstetric anaesthesia, but the opinions they provided were considered to be representative of the obstetric anaesthesia teaching in their departments. The experts provided input into four areas of anaesthetic management related to caesarean section anaesthesia. These were: i) method of anaesthesia, ii) use of adjuvant drugs for neuraxial anaesthesia, iii) post-operative monitoring practices and iv) post-operative pain management practice.

Spinal anaesthesia was the recommended anaesthetic technique for elective caesarean sections. The experts recommended that 0.5% bupivacaine with dextrose (at doses between 9 and 10.5mg) should be used for these spinal anaesthetics. Fentanyl was the preferred opioid adjuvant for spinal anaesthesia. Morphine was not recommended because of concerns regarding the risk of delayed respiratory depression.

For emergency patients with an indwelling epidural catheter, 2% lignocaine was recommended to “top-up” the epidural in order to attain surgical anaesthesia. Adjuvant drugs can be added to the top-up solution, including fentanyl, sodium bicarbonate and adrenalin. The experts indicated that the addition of morphine to the epidural solution should be reserved for patients who are going to be nursed in a post-operative high care unit.

All patients who had received neuraxial opioids intraoperatively need to be monitored for respiratory depression in the post-operative period. The opinions on the duration of monitoring varied, depending on the type of opioid used. For lipophilic opioids such as fentanyl, recommended monitoring times range between 0 – 12 hours. For patients in whom intrathecal morphine was used, the recommended duration of monitoring ranged between 8 – 24 hours. Most experts recommended that respiratory rate, pulse oximetry and level of consciousness should be monitored as part of the monitoring process.

A number of different post-operative analgesic techniques were discussed with the experts in order to try and develop a common protocol that can be applied in South Africa. Epidural analgesia, PCA pumps and intrathecal morphine were not recommended for the routine analgesic regimen for caesarean section patients in South Africa. There was agreement that NSAIDs must be included in the pain management protocol. The majority of the experts recommended using IV paracetamol, but concerns were raised about the cost sustainability of this. Other oral analgesics such as paracetamol, tramadol and codeine have also been recommended.

Some of the therapeutic options recommended by the South African experts are contrary to international guidelines and established effective global analgesic options. These expert recommendations will be compared to the actual practice of obstetric anaesthesia in South Africa in chapter four.

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CHAPTER FOUR: National survey of anaesthesia practices for caesarean sections in South Africa

4.1 Introduction

Improving maternal health is the fifth millennium development goal of the Millennium Declaration, which was endorsed by 189 countries at the United Nations in September 2000 (United Nations Foundation, 2016). Obstetric anaesthesia services are an important component of a maternal healthcare package of services that are required for us to achieve this goal in South Africa (SA) and around the world. South Africa has a reported caesarean section rate of 16 – 20% (Moodley, 2010). This rate implies that up to one fifth of all pregnant women in South Africa will require an anaesthetic for the delivery of their babies. Good anaesthetic management has the potential to improve patients' birth experiences and decrease the risk of post-operative morbidity (Tan, 2012).

In order to understand the training and educational needs of the anaesthetic profession with regards to obstetric anaesthesia practices, it is important to be aware of the current anaesthetic practices in the country. This information will allow South Africa to benchmark its obstetric anaesthesia services against international standards and will also provide valuable information of training and educational needs of the country's anaesthesiology professionals.

In 1978 Buley *et al* (1978) published data on obstetric anaesthesia practises in South Africa and South West Africa (Namibia), but since then no comprehensive assessments of these practises have been undertaken in the region. Since that 1978 study there have been many changes and improvements in the practise of obstetric anaesthesia and analgesia.

In chapter three, the results of interviews with South Africa academic anaesthesiology leaders, to determine the current training standard for

obstetric anaesthesia practice in South Africa, was presented. In this chapter, we explore what practitioners are doing in the field. We conducted a national survey amongst doctors who work as anaesthesia service providers in the Republic of South Africa. A detailed description of the survey methodology and results will be discussed in this chapter.

4.2 Aim

The aim of this study was to describe the post-operative pain management practises of doctors managing caesarean section patients in South Africa.

4.3 Objectives

The specific objective of this study was to determine what the preferences are amongst:

I. Specialist anaesthesiologists working in the public and private sector with regards to anaesthesia for caesarean section relating to:
    a. Preferred method of anaesthesia
    b. Use of adjuvant drugs for neuraxial anaesthesia
    c. Post-operative monitoring practices
    d. Post-operative pain management

II. Non-specialist medical practitioners (registrars, medical officers and general practitioners) who predominantly administer anaesthetics in the public and private sector with regards to anaesthesia for caesarean section relating to:
    a. Preferred method of anaesthesia
    b. Use of adjuvant drugs for neuraxial anaesthesia
    c. Post-operative monitoring practices
    d. Post-operative pain management

4.4 Demarcation of the study field

The survey was conducted in the Republic of South Africa.

4.5 Ethical considerations

- This study was conducted in accordance with the ethical principles of the Declaration of Helsinki (World Medical Association, 2013) and Good Clinical Practice (Department of Health, 2006).
- The protocol was reviewed and approved by the Human Research Ethics Committee – Medical (HREC) of the University of the Witwatersrand - Approval number M140123 (APPENDIX H).

4.6 Research Methodology

4.6.1 **Sample Size Calculation**

There are 1700 names on the membership database of the South African Society of Anaesthesiologists (SASA). The Health Professions Council of South Africa also has a register of specialist anaesthesiologists registered with the Council, however neither this list nor SASAs database represents all anaesthetic providers in South Africa because some registered specialists may no longer be practising in South Africa. In addition, there are a large number of non-specialist anaesthesiologists working as anaesthetic providers in South Africa. Assuming a total population of anaesthetic providers (specialist and non-specialist) of 2500 practising in South Africa, a 5% margin of error and a 95% confidence level, a minimum sample of 333 respondents was deemed a statistically representative sample of the population.

4.6.2 **Sample Method**

A consecutive convenience sampling method was used. The convenience sampling method was chosen due to limited accessibility to the study population. All eligible doctors (specialists and non-specialists) were approached either at anaesthesiology-community events, or electronically, using the database of the South African Society of Anaesthesiologists, and invited to participate in the survey. Participants were asked not to complete

the survey more than once. All participants voluntarily completed the questionnaire. It is acknowledged that a convenience sample may not fully represent the study population (Hultsch *et al*., 2002)

4.6.3 **Methodology**

A modified version of the questionnaire used by Tagaloa *et al* (2009), in the United States, to address a similar aim was used in this study. The questionnaire developed by Tagaloa *et al* (2009) can be seen in APPENDIX B. The questionnaire was modified to take into account the local South African environment. The changes made related to the following points:

- Demographic details specific to South Africa (Questions 1, 2 and 3)
- Practitioners exposure to anaesthesia and to obstetric anaesthesia (Questions 4 and 5)
- Allowances were made for the respondents to not have a preference for or not know the type of spinal needle or the needle gauge used for spinal anaesthesia (Questions 9 and 11)
- Drugs used for spinal anaesthesia were adjusted to include only drugs available in South Africa and also allowed for volume to be indicated (Questions 13, 14 and 15)
- Drugs used for epidural anaesthesia were adjusted to include only drugs available in South Africa (Questions 20)
- More details were asked on the use of epidural morphine (Question 21 and 26)
- Practitioners were given more alternatives regarding their choice of management of a labouring patient requiring a caesarean section (Question 22)
- Monitoring of patients following neuraxial opioid administration (Question 30)
- Responsibility of care regarding analgesia following caesarean section (Questions 31 and 32)

- More options were added regarding the use of the epidural catheter for post-operative analgesia (Question 33)
- The options for NSAIDs were adjusted to include more drugs available in South Africa (Question 39)
- Route of administration of NSAIDs was included (Question 41)
- Use of IV paracetamol was included (Question 42)
- Oral analgesic options were adjusted to include drugs available in South Africa (Questions 43)
- Patient satisfaction regarding post-operative analgesia (Question 44)

The questions that were added to or modified from the Tagaloa *et al* (2009) questionnaire are listed in APPENDIX I.

To ensure face validity of the questionnaire, the modified questionnaire was reviewed by 12 senior members of staff of the Department of Anaesthesiology at the University of the Witwatersrand. Feedback was used to refine the survey questionnaire further. Following the validation process, changes were made to the punctuation of certain questions, and, in addition, two questions (Question 10 and Question 12) were added to the questionnaire in order to assess the impact shortages of consumables had on practices.

The final questionnaire (APPENDIX J) was distributed to all eligible doctors in South Africa. Distribution of the survey was done at selected anaesthetic-community events, between March and December 2014, throughout the Republic of South Africa. The survey was distributed in person, by the principal investigator (PI), so that any queries about the study, raised by the invited doctors, could be addressed. In addition, an electronic version of the survey (using the Survey Monkey® platform) was distributed to the database of the South African Society of Anaesthesiologists. The electronic survey was sent out in October 2014 and followed by two reminder e-mails (two weeks and four weeks after the original invitation to participate was sent out). The survey was closed on the 31st December 2014. The survey was completed anonymously. In order to improve the response rate to the survey, participants were offered the opportunity to be entered into a lucky draw

competition to stand a chance to win a tablet computer. The names of those participants who chose to enter the competition were separated from the survey answers before the data were analysed.

4.6.4 **Data Analysis**

We analysed the prospectively collected data from survey respondents. Data from manually completed questionnaires were entered into a spreadsheet using Microsoft® EXCEL® for MAC (Version 14.6.2). Data from the electronically completed survey were imported from the Survey Monkey® server into a Microsoft® EXCEL® spreadsheet. Continuous parametric data were described using mean and standard deviation. Continuous non-parametric data were described using median and interquartile ranges. Categorical data were described using frequencies and percentages. Baseline characteristics of the study sample were summarized using simple proportions. Data were analysed using StatPlus, AnalystSoft Inc. - statistical analysis program for Mac OS® (Version v6) and the statistical analysis program R (Version 3.2.3) (R Core Team, 2015).

Comparisons were made between specialists and non-specialists in areas that may be impacted on by clinical insight and level of training (Questions: 8, 9, 13, 14, 15, 22, 30 and 31). Comparisons were also made between practitioners in the public and private sectors, in areas where resources may have an impact on the ability to provide clinical services (Questions: 4, 5, 6, 7, 9, 10, 13, 27, 28 and 29).

4.7 Results and Discussion

Nine hundred and seventy-three survey questionnaires were completed. Forty of these responses were excluded from analysis (Figure 4.1): 38 were incomplete questionnaires and two questionnaires were completed by doctors who were not practising in South Africa.

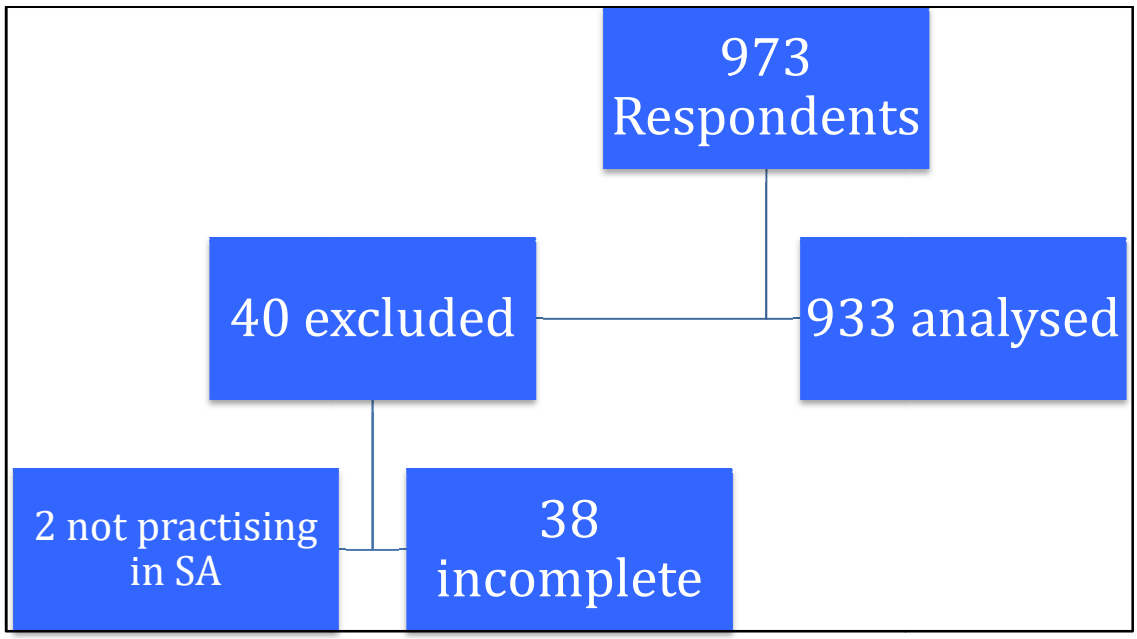


FIGURE 4.1: Summary of survey responses

There were approximately 1700 doctors on the database of the SASA. From my interactions with a large number of doctors while carrying out this survey, I determined that there are many doctors involved in the provision of anaesthesia who do not practice any obstetric anaesthesia. These doctors did not answer the survey, which may have contributed to the survey response rate being less than 60%. The average response rate for surveys conducted by the Obstetric Anaesthetists Association between 1998 and 2012 was 65% (Robson *et al*., 2015). The response rate of 57% in this survey is comparable. Tagaloa *et al* (2009) reported a 36% response rate to their electronic survey distributed amongst 1081 members of the Society for Obstetric Anesthesia and Perinatology.

4.7.1 **Demographics of the Respondents**

4.7.1.1 **Geographical distribution**

There were responses from practitioners across all nine provinces in South Africa. The largest proportion of respondents was from Gauteng province (53%), followed by the Western Cape (19%) and KwaZulu-Natal (17%). Responses from the other 6 provinces in the country were relatively small. The geographical distribution of the survey responses is listed in Table 4.1.

Table 4.1: Geographical distribution of survey responses

Province	Number of Responses	Percentage of total responses	Percentage of the national population *	Percentage of national gross domestic product $
Gauteng	493	52.8	23.7	34.5
Western Cape	179	19.2	11.3	14.2
KwaZulu Natal	155	16.6	19.8	15.7
Free State	35	3.7	5.3	5.3
Eastern Cape	26	2.8	12.7	7.5
North West	23	2.5	6.8	6.5
Mpumulanga	12	1.3	7.8	7.0
Limpopo	7	0.8	10.4	7.1
Northern Cape	3	0.3	2.2	2.2
Total	933	100	100	100

* (Lehohla, 2011) $ (Bouwer, 2011)

This geographical distribution of the respondents is not surprising considering that Gauteng, KwaZulu-Natal and the Western Cape are the most populated provinces in South Africa (Lehohla, 2011) and are home to six of South Africa's eight academic anaesthesiology departments. Gauteng province has three medical schools and is considered the economic hub of the country, contributing 35% to the national economy in 2011 (Bouwer, 2011). The distribution of anaesthetic service providers across the provinces in South

Africa does not however match the general population distribution across the country. The membership distribution of the SASA across the provinces of SA is as follows: Gauteng – 47.5%, Western Cape – 23.6%, KwaZulu Natal – 15.4%, Free State- 5.7%, Eastern Cape – 4.5%, North West – 1.1%, Mpumulanga – 1.2%, Limpopo – 0.6%, and the Northern Cape - 0.5% (SASA, 2016). The geographical distribution of the survey responses is similar to the geopgraphical distribution of anaesthetic service providers across South Africa.

4.7.1.2 **Anaesthesiology qualifications**

Five-hundred-and-forty (57.9%) specialist anaesthesiologists and 393 (42.1%) non-specialists answered the survey. Of the non-specialists, 303 had a diploma in anaesthetics, while 90 only had a basic undergraduate medical degree. (Figure 4.2)

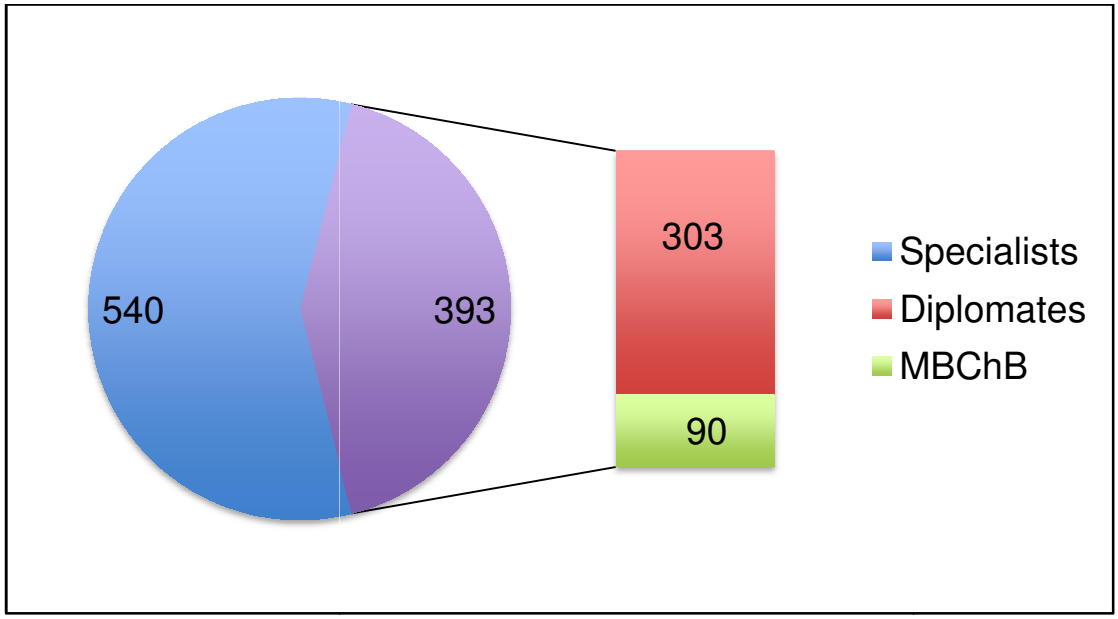


FIGURE 4.2: Qualifications of survey respondents

Many doctors who do not have any experience in anaesthesiology will join anaesthesiology departments in the public sector hospitals to be trained. The minimum requirement for these jobs is an undergraduate medical degree. During their training, these doctors are able to write the exam for the Diploma

in Anaesthetics. Diplomates have completed at least 6 months of anaesthesia training in an accredited centre, and have passed the diploma exam from the College of Anaesthetists of South Africa. In comparison, specialist anaesthesiologists have completed four years of registrar training in an academic institution and passed the fellowship exam of the College of Anaesthetists of South Africa.

The Practice Guidelines of the South African Society of Anaesthesiologists (SASA) (Bettings *et al*., 2013) states that no doctor should administer an anaesthetic unsupervised without having passed the exam for the Diploma in Anaesthetics. These guidelines permit the administration of anaesthesia to patients by non-specialist doctors based on the clinical risk profile of the patient. This risk profile is determined by the American Society of Anaesthesiology (ASA) physical status classification system (Appendix K). Diplomates are only permitted to provide an unsupervised anaesthetic for ASA1 and ASA2 patients. They may administer an anaesthetic for an ASA3 patient under the supervision of a specialist. The diplomate should not treat ASA 4 and ASA 5 patients for elective procedures. There is no limitation on the provision of anaesthetic care to the obstetric patient provided that the ASA physical status of the patient is ASA 3 or less.

4.7.1.3 **Main area of work**

South Africa has a dual health care system. The private sector caters mainly to the middle and upper classes. Patients who access the private health sector services are generally employed and are members of private medical aid schemes (CMS, 2015). There is a small percentage of the patients who are privately funded. The private healthcare system functions on a fee-for-service model, with healthcare providers invoicing the patients or funders for the cost of the service that is rendered. The private health system has a health budget equivalent to about 4.3% of gross domestic product (GDP) and covers about 16% of the population (HST, 2015, Benatar, 2013).

The public health system is funded by the government and is responsible for the health care of about 84% of the population, delivered on a budget equivalent to about 4% of the GDP (Benatar, 2013, Blecher *et al*., 2011). The public health system caters mainly for the lower income classes and the indigent. Each provincial department of health manages the public health services within the provinces. The public health services are divided into district, regional, tertiary, central and specialist services. Anaesthesiology services are available at all tiers of care in the hospital environment (except in dedicated psychiatric hospitals). Caesarean sections can be performed at all hospitals where obstetric services are offered.

All specialist training is done within the public health care system. However, most specialists move into the private sector after qualifying (about 77% of specialist members of SASA are in full time private practice). This may be due to the higher remuneration structure for doctors in the private sector and the perception of better working conditions and easier access to better drugs and equipment.

There was an equitable distribution of respondents to this survey between the public and private heath care systems. Four-hundred-and-sixty-five (49.8%) respondents were from the private sector, and 468 (50.2%) from the public sector. The majority of all respondents from the private sector had specialist qualifications (83%), but there was a variation between each of the provinces. The highest number of private sector non-specialists was in Gauteng (56/232, 24%). There were no private sector non-specialist respondents from the Free State, Mpumalanga or the Northern Cape provinces. (Figure 4.3)

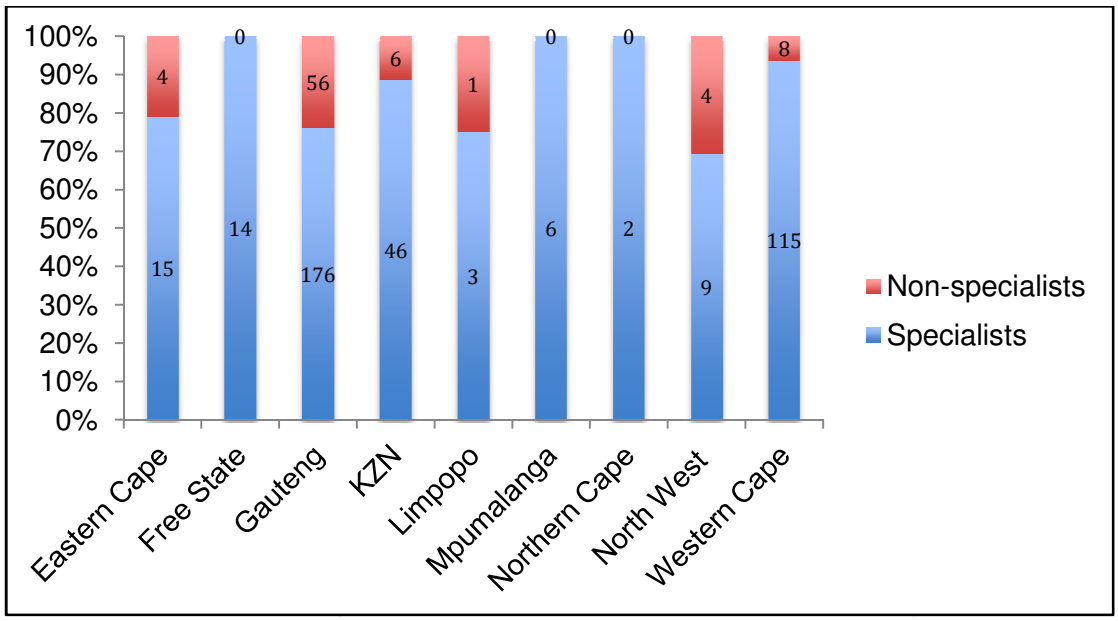


FIGURE 4.3: Provincial distribution of specialists and non-specialists in the private sector cohort

Nationally there were 79 private sector non-specialists who participated in this survey. Of these, 19 (24%) only had a basic undergraduate medical degree. Based on the recommendations of the SASA Practice Guidelines (Bettings *et al.*, 2013), these individuals should not be providing unsupervised anaesthesia to patients, yet they are working unsupervised in the private sector.

Of the 468 public sector doctors who responded to the survey, 148/468(32%) were specialists, 191/468(41%) were registrars, 58/468 (12%) were medical officers with more than 5 years of experience in anaesthesia, and 71/468(15%) were junior medical officers. (Figure 4.4)

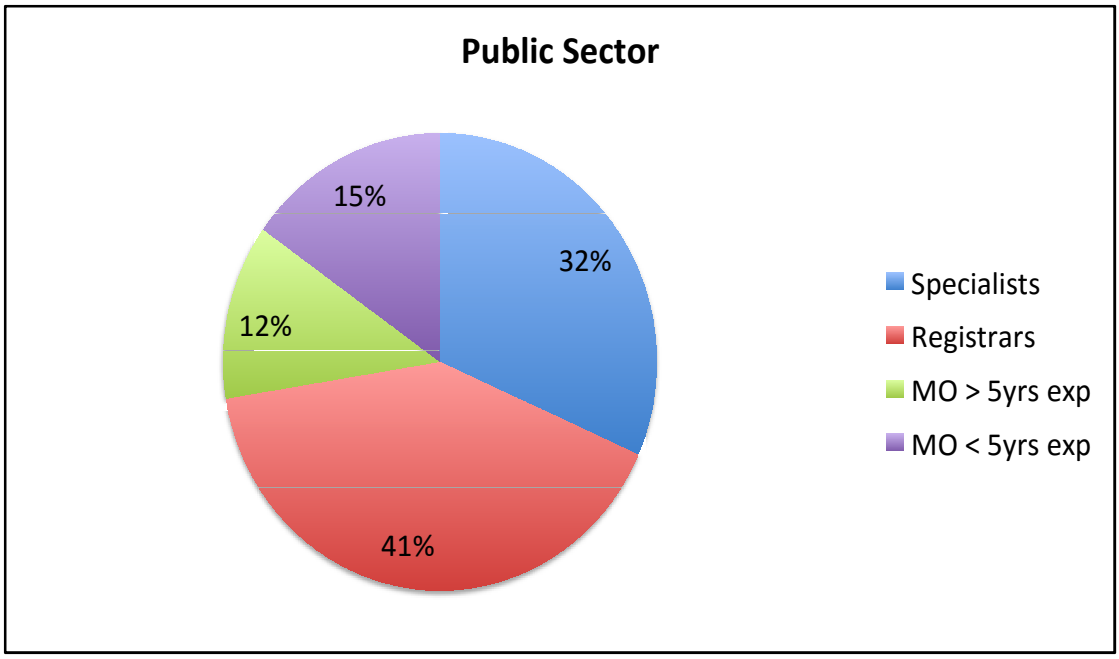


FIGURE 4.4: Distribution of specialists and non-specialists in the public sector cohort

The majority of all respondents from the public sector were non-specialist doctors except from Limpopo and the Northern Cape provinces. However this discrepancy is most likely due to the low number of respondents from these provinces. (Figure 4.5)

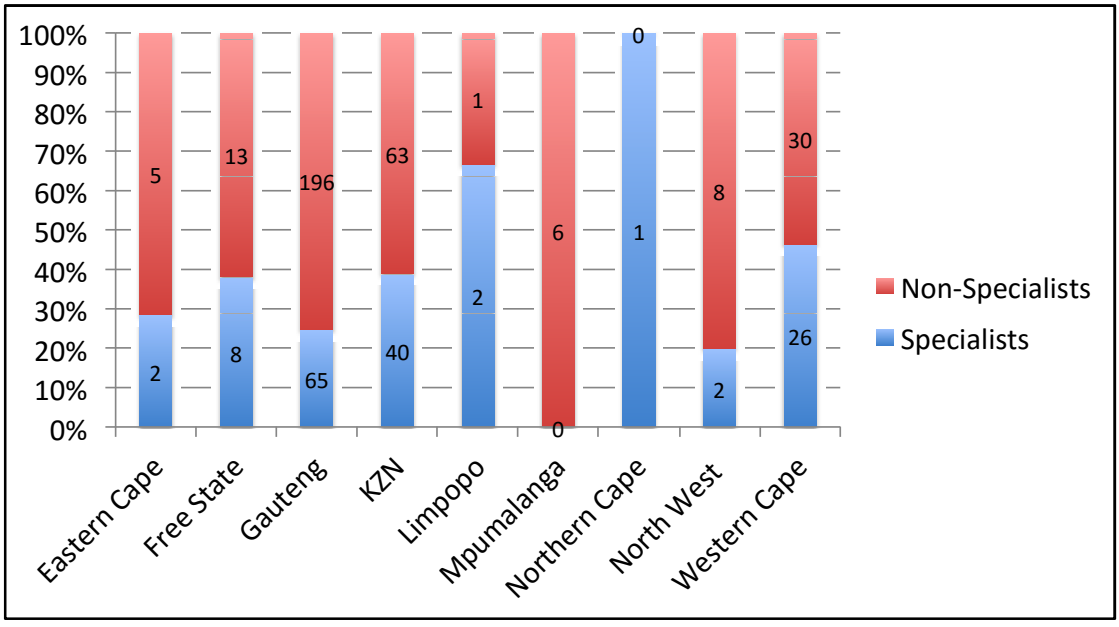


FIGURE 4.5: Provincial distribution of specialists and non-specialists in the public sector cohort

Table 4.2 provides a breakdown of the respondents from each province, based on their qualification and their primary area of employment.

TABLE 4.2: Summary of the respondents based on province, sector of employment and qualifications

	Private Sector		Public Sector	
	Specialists	Non-specialists	Specialists	Non-specialists
Eastern Cape	15	4	2	5
Free State	14	0	8	13
Gauteng	176	56	65	196
KZN	46	6	40	63
Limpopo	3	1	2	1
Mpumalanga	6	0	0	6
Northern Cape	2	0	1	0
North West	9	4	2	8
Western Cape	115	8	26	30
TOTALS	386	79	146	322

4.7.1.4 **Work Load**

The workload of anaesthetic providers varied depending on the level of seniority of the doctor, and the sector in which they were primarily employed.

The number of anaesthetics that respondents to this survey were involved with on average each month is summarized in Figure 4.6. The median number of cases performed by private sector doctors was 100 while the median number of cases performed by public sector doctors per month was 80. The Wilcoxon-Mann-Whitney-U statistical analysis of this data indicates that there is a statistical difference between the medians of the two groups ($p<0.001$) indicating that practitioners in private practice perform statistically more anaesthetics per month than their public sector colleagues.

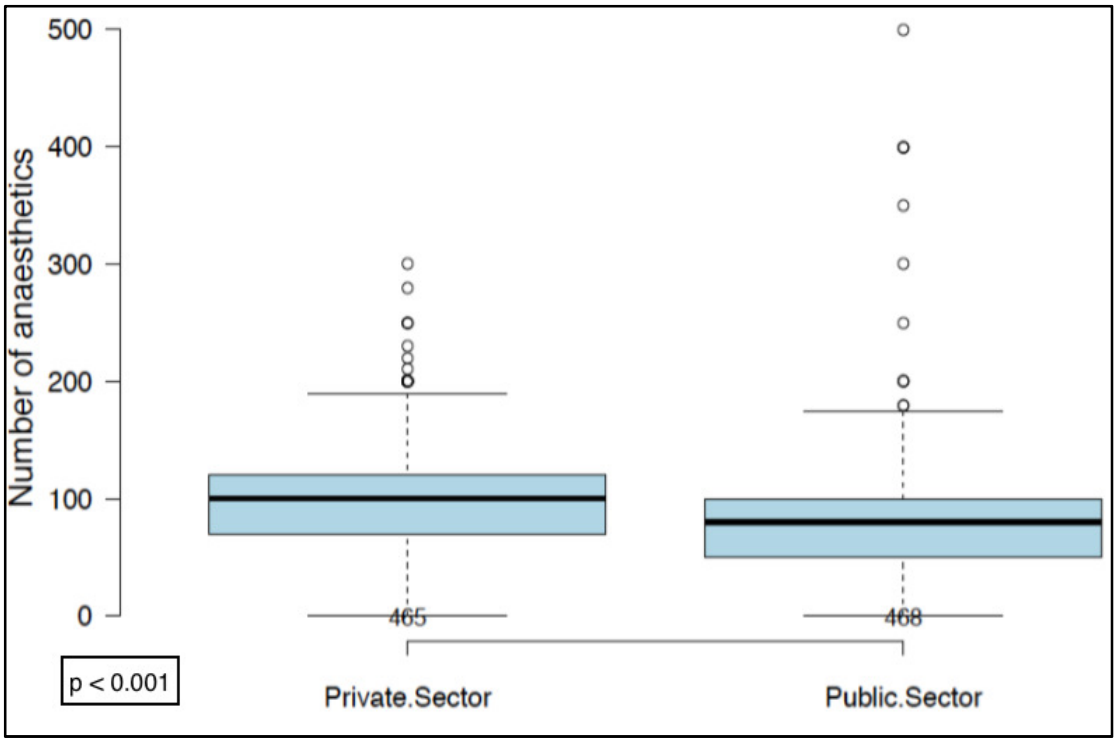


FIGURE 4.6: Summary of the average number of anaesthetics performed per month

These results have been plotted as a histogram below showing the spread of the responses (Figures 4.7)

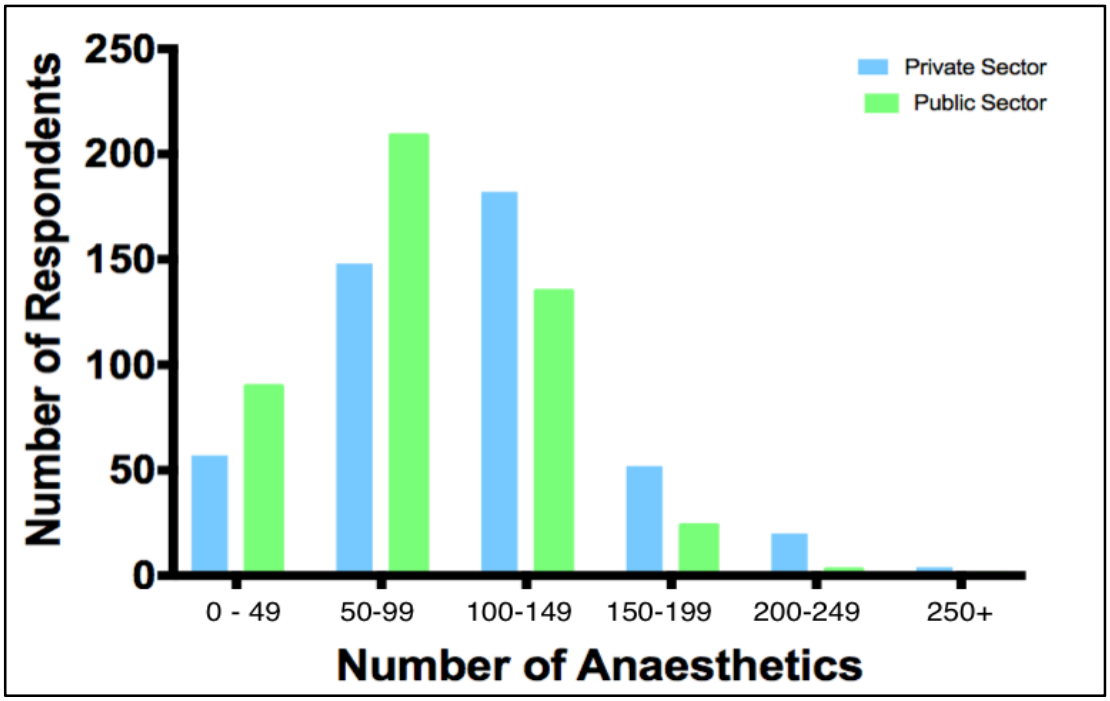


FIGURE 4.7: Histogram of the total number of anaesthetics performed by private sector and public sector doctors in one month

The caesarean section rate in SA is high (Moodley, 2010), however obstetric anaesthesia only forms a portion of the caseload that any one doctor will be exposed to. In this survey, the doctors were asked to state approximately how many caesarean section anaesthetics they administered each month. The median number of caesarean section anaesthetics performed by private sector doctors was 10. In the public sector, the median number of caesarean section anaesthetics was 15 (Figure 4.8). Wilcoxon-Mann-Whitney-U statistical analysis of this data indicates that there is a statistical difference between the medians of the two groups ($p<0.001$), such that the public sector practitioners are doing more caesarean section anaesthetics than the doctors in the private sector.

The very high number of caesarean section anaesthetics that is being performed by some practitioners in the public sector is anomalous when compared to the responses of the majority of the respondents. However, individual practices differ and there are some public sector hospitals where there is a high rate of caesarean sections, which may lead to anaesthetic service providers performing a very high number of caesarean section anaesthetics.

Despite doctors in the private sector performing more anaesthetics, on average, per month than their public sector counterparts, they are doing significantly fewer caesarean section anaesthetics than doctors in the public sector.

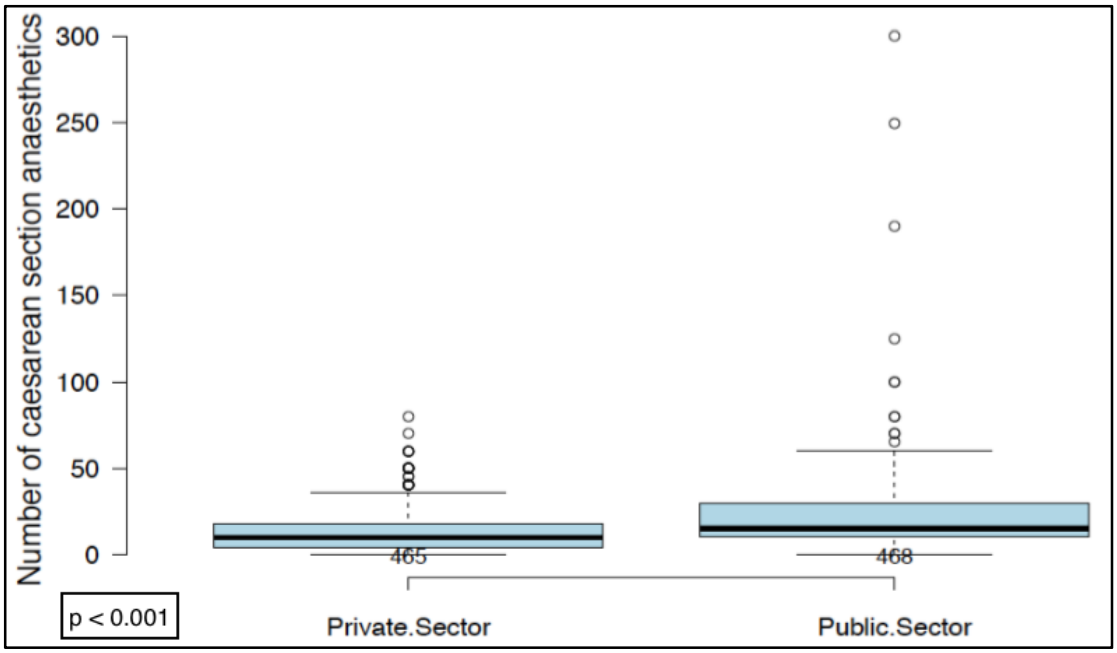


FIGURE 4.8: Average number of caesarean section anaesthetics administered per month

These results have been plotted as a histogram below showing the spread of the responses (Figures 4.9)

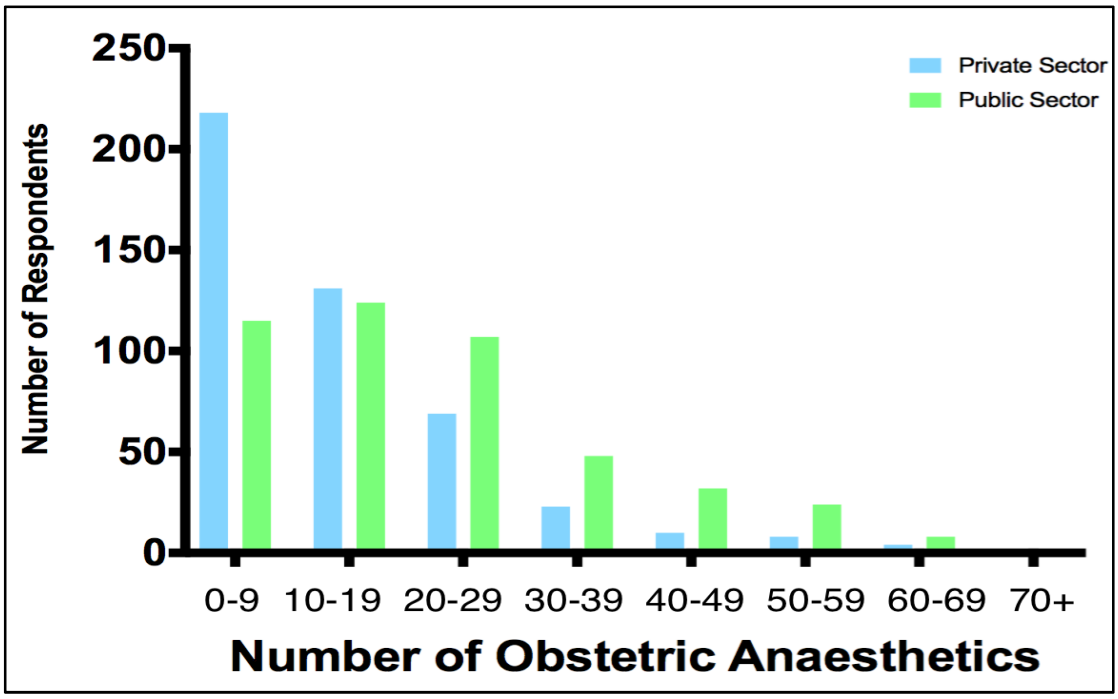


FIGURE 4.9: Histogram of the total number of caesarean section anaesthetics performed by private sector and public sector doctors in one month

The majority of respondents in both the public and private sector are involved in obstetric anaesthetics during office-hours and after-hours. There is a small percentage of people who either only perform anaesthetics for caesarean sections during the day, or on call. A few respondents indicated that they only perform anaesthetics for caesarean sections for dire emergencies or in a supervisory capacity (in the public sector). These results are summarized in Table 4.3 below:

TABLE 4.3: Degree of involvement with obstetric anaesthesia by both health care sector doctors

	Daytime Only	On Call Only	Daytime and On Call	Other	p-value
Public Sector	49	56	350	13	$p < 0.01$
Private Sector	51	104	279	31	

Chi square analysis of these results shows that there is a statistically significant difference in the work exposure of doctors in the private and public sectors with regards to performing anaesthetics for caesarean sections ($p<0.01$), such that doctors in the public sector have a statistically greater exposure to caesarean section anaesthetics than their private sector colleagues. The greater involvement of doctors with both daytime and on-call duties is similar to international data (Tagaloa *et al*., 2009).

Obstetric anaesthesia caseload is dependent on the frequency with which a doctor works in the obstetric anaesthesia environment. In this survey, 406/933(44%) of the respondents were involved with obstetric anaesthesia <1 day per week. 388/933(42%) perform obstetric anaesthetics 1-2 days/week, while only 139/933(14%) do obstetric cases >2 days/week. There was a higher percentage of doctors in the public sector who work in obstetric anaesthesia for 1-2 days per week. (Figure 4.10)

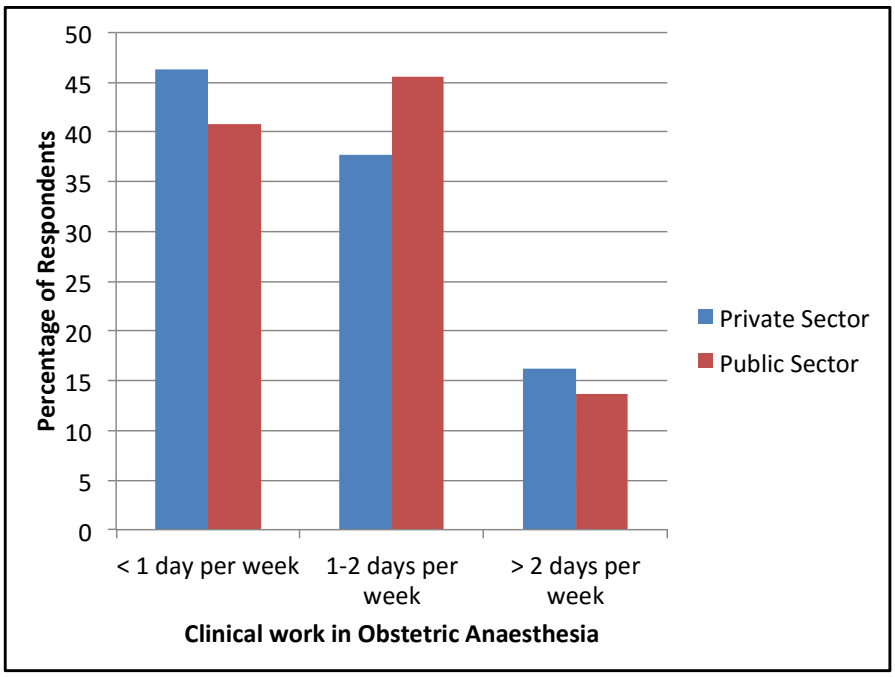


FIGURE 4.10: Clinical involvement in obstetric anaesthesia

There was a higher percentage of respondents in the 2009 survey of SOAP members in the United States of America (USA) who worked in obstetric anaesthesia >2 days per week (43%) compared to the respondents in this survey (14%) for the same clinical exposure period (Tagaloa *et al*., 2009). However, the SOAP membership is predominantly made up of anaesthesiologists who have an interest in obstetric anaesthesia, which may explain the greater exposure to obstetric anaesthesia each week. This South African survey was conducted amongst all doctors involved with all anaesthetic services in South Africa. From these data, the general anaesthetic service provider in South Africa, spends a small proportion of time providing obstetric anaesthesia.

4.7.2 **Intraoperative anaesthetic management**

4.7.2.1 **Preferred anaesthetic technique**

Anaesthesia for caesarean section can be performed using a general anaesthetic or regional anaesthetic technique. The choice of technique is dependent on the individual patient's clinical condition and preference, the skill of the anaesthetic service provider and the accessibility to the drugs and consumables needed to provide each type of anaesthetic. The risks associated with general anaesthesia in the pregnant patient has steered provider preferences toward regional neuraxial anesthetic techniques for this patient group (Tan, 2012). Consistent with this view, we found that the majority of respondents (97.8%) preferred to use a single shot spinal anaesthetic technique for caesarean section anaesthesia. Only a small number of respondents chose other anaesthetic techniques as their techniques of choice (Figure 4.11).

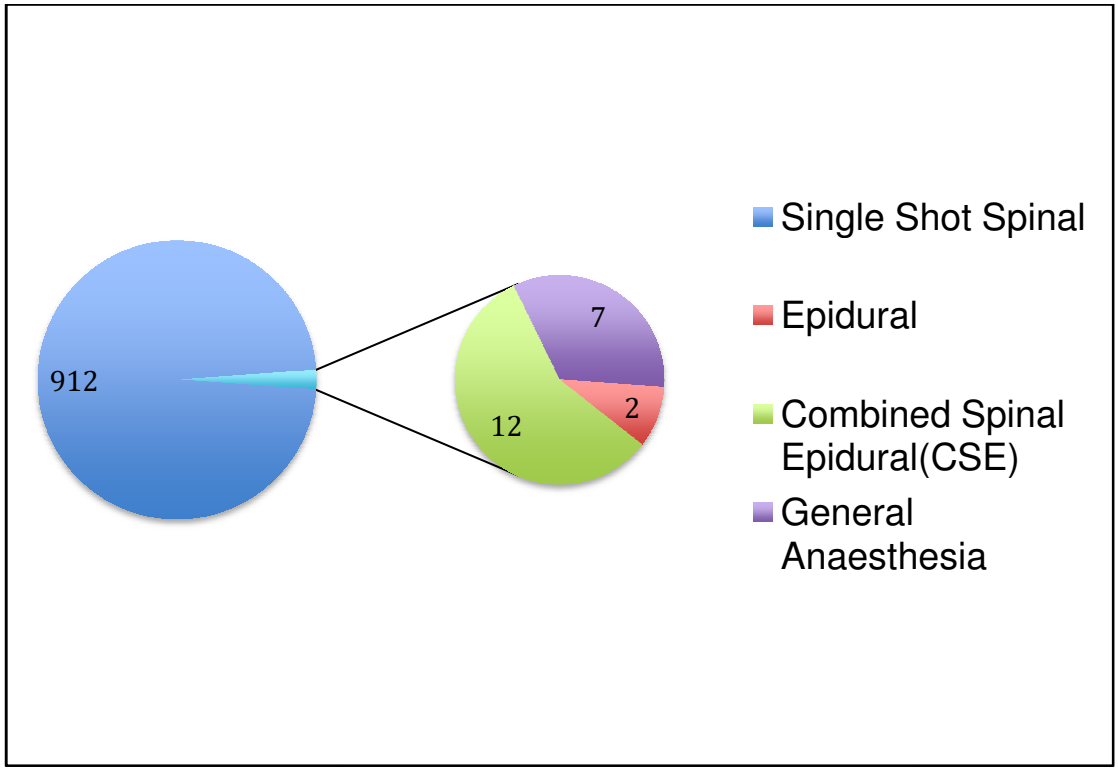


FIGURE 4.11: Preferred techniques for caesarean anaesthesia

An analysis of the responses of specialists and non-specialists in the cohort reveals that there is no statistical difference in the preference for spinal anaesthetics between the two groups (Table 4.4).

TABLE 4.4: Doctors' choices for caesarean section anaesthetic technique

	Single Shot Spinal	Other Techniques	p-value
SPECIALISTS	524	16	p = 0.08
NON-SPECIALISTS	388	5	

The high use of a single shot spinal anaesthetic technique is similar to the use of this technique reported in Germany (91.4%) (Stamer *et al*., 2005). Tagaloa *et al* (2009) reported a preference for single shot spinal anaesthetics in 85% of respondents from a study in the USA. The use of the combined-spinal-epidural (CSE) and epidural techniques were reported as 11% and 4% respectively in the American survey (Tagaloa *et al*., 2009). This is similar to our results. Data from a Malaysian survey of anaesthetic practise indicates that regional anaesthesia is performed in only 41.9% of caesarean section cases. Of these, the majority is performed as spinal anaesthetics (84.6%) (Chan and Ng, 2000).

General anaesthesia did not feature at all in the anaesthetic preferences in the Tagaloa *et al* (2009) study. In our study, 7/933 (0.8%) of the respondents (6/465 private sector doctors and 1/468 public sector doctors) preferred to perform a general anaesthetic for caesarean sections. This was a decrease from the 90% prevalence of general anaesthesia being performed for caesarean sections in a previous South African survey (Buley *et al*., 1978). Despite the developments in anaesthesiology that make obstetric spinal anaesthesia safer, more cost effective and technically easier, general anaesthesia continues to be practiced around the world, especially in developing countries. In West Africa, general anaesthesia is the predominant anaesthetic technique used for caesarean sections (Okafor, 2006). This

practise is however not isolated to developing countries. Van Houwe *et al* (2006) reported that one hospital, in their 2004 survey in Belgium, performed general anaesthesia in 34% of caesarean sections. General anaesthesia was however only used in 5% of cases when all hospitals were included in the results in this survey (Van Houwe *et al*., 2006). The increased risk associated with general anaesthesia in the obstetric patient behooves us to ensure that we move away from this form of anaesthesia in this patient population, unless there is an appropriate contraindication to performing a regional anaesthetic technique. However, some experts argue that it is important that practitioners remain clinically adept at performing general anaesthetics in the obstetric patient population so that this skill can be used when the need arises during an unexpected emergency situation (Dyer, 2011).

4.7.2.2 **Preference of Spinal Needles**

The design and gauge of a spinal anaesthetic needle has an effect on the risks of complications associated with spinal anaesthesia. Larger gauge needles and needles with a cutting tip (such as the Quincke© needle) increase the risk of cerebrospinal fluid (CSF) leakage from the spinal canal, and resultant development of post-dural puncture headache (PDPH). (O'Connor *et al*., 2007)

The Wittacre© spinal anaesthetic needle was the most popular needle for administering a spinal anaesthetic (299/933, 32%) in our survey. The next most popular choice was the Quincke© needle (282/933, 30%). Figure 4.12 is a graphical representation of the preferred choices of spinal needles for doing a spinal anaesthetic for the obstetric patient

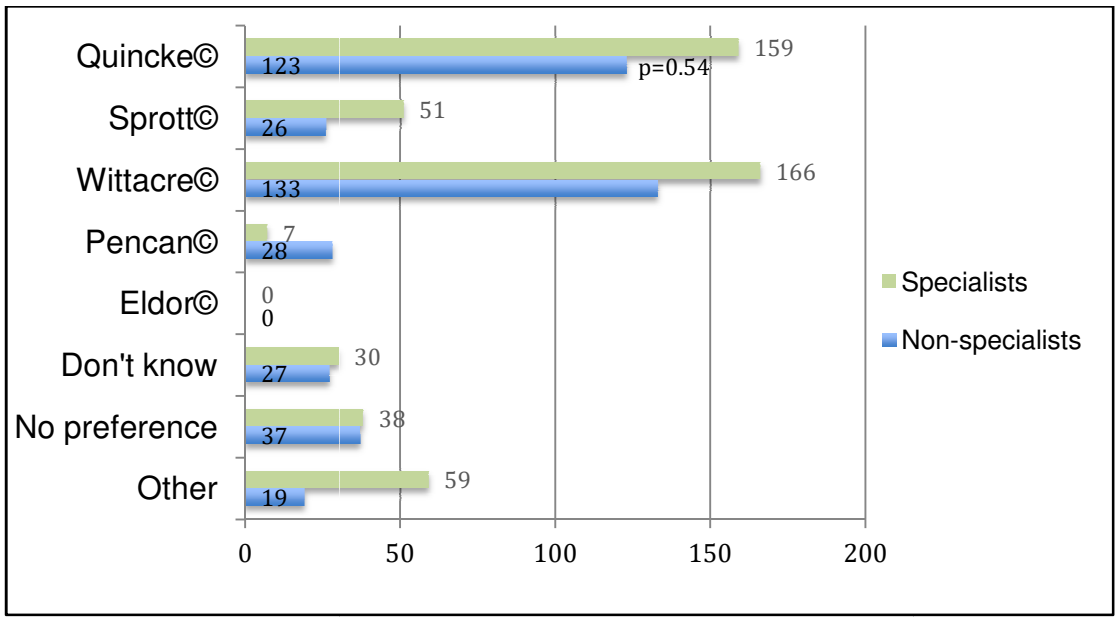


FIGURE 4.12: Preferred spinal needle choices for performing a spinal anaesthetic for caesarean section anaesthesia

The Sprott©, Wittacre©, Eldor© and Pencan© needles are pencil point needles. Current research promotes the use of pencil point needles for obstetric spinal anaesthetics in order to reduce the risk of PDPH (O'Connor *et al.*, 2007).

None of the respondents in the survey chose the Eldor© needle as their first choice. The Eldor© needle is a pencil point needle with a two holes near the tip of the needle to allow a faster and better distribution of local anaesthetic into the CSF (Cothon.Net, 2014). It is concerning that 30% of the respondents preferred to use a Quincke© needle. The Quincke© needle is a cutting spinal anaesthetic needle. Cutting needles are associated with a greater risk of causing PDPH (O'Connor *et al.*, 2007). There were 159 specialists and 123 non-specialists who indicated that the Quincke© needle was their preferred spinal anaesthetic needle. Chi-squared analysis of the data identified no statistical difference in the choice of the Quincke© needle between specialists and non-specialists (p=0.54).

57/933 (6%) of respondents did not know what needle they preferred to use for a spinal anaesthetic, and 75/933 (8%) had no needle preference for the procedure. The cumulative group of 132/933 (14%) individuals consisted of

64 non-specialists and 68 specialists (Figure 4.13). Chi-squared analysis revealed that there was no statistical difference in these results between these two categories of doctors (p=0.11).

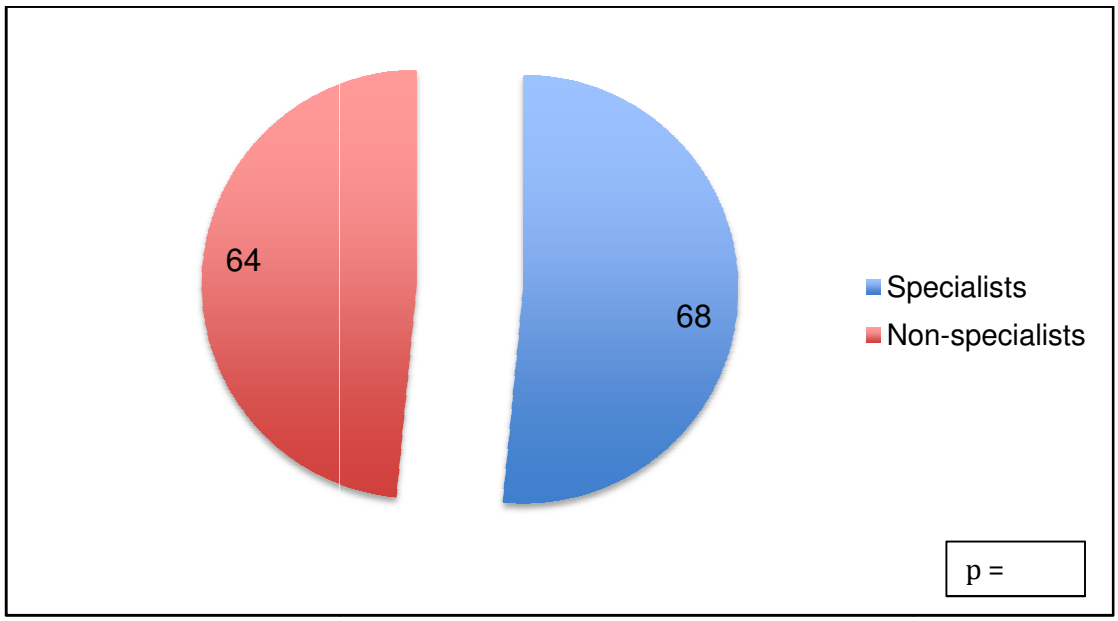


FIGURE 4.13: Doctors who have no spinal needle preference

When the responses with regards to the spinal needle preference are categorized according to the employment sector of the respondents, we find that 70/468(15%) of public sector doctors have no needle preference or don't know what needle they prefer as opposed to 62/465 (13%) of private sector doctors. (Figure 4.14)

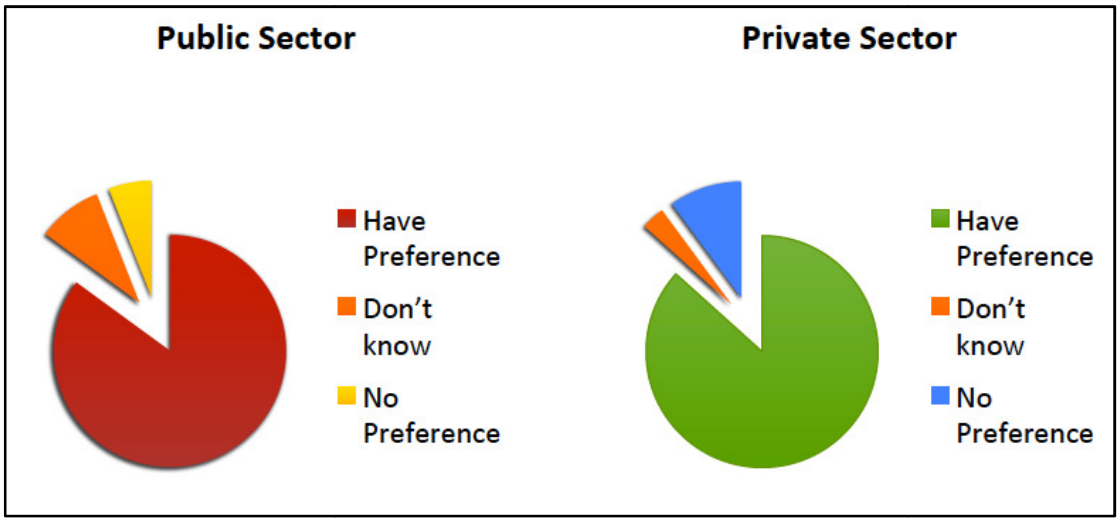


FIGURE 4.14: Spinal needle preferences of private and public sector doctors

Seventy-eight of the 398 public sector doctors (19.5%) who had a needle preference for administering a spinal anaesthetic reported that their preferred needle was not available, compared to 26 of the 403 private sector doctors (6%) with a needle preference. The difference between the two sectors was statistically significant ($p<0.01$). This difference hints at greater restrictions on the selection of needles available in the public sector compared to the private sector, but unfortunately we did not probe the reason for a preferred needle being available. The implication of these data is that there is reduced freedom of choice to doctors in the public sector vs. the private sector with regards to the spinal anaesthetic needle that the doctor would prefer to use. This is not surprising considering that the private sector has greater levels of funding and access to consumables than the public sector (Benatar, 2013).

The gauge of the spinal needle used is also an important factor to consider when administering a spinal anaesthetic. Large gauge needles (22G) are known to increase the risk of PDPH. Current literature recommends that smaller gauged needles should be used to perform a spinal anaesthetic as this reduces the risk of complications (O'Connor *et al*., 2007). In our study, 460/933(49%) of the respondents preferred to use a 26G spinal needle to perform a spinal anaesthetic for a caesarean section. There were 294/933 (31.5%) of the respondents who preferred the 25G needles. Only 28/933(3%) of doctors preferred to use the 22G needle, which is known to increase the risks of PDPH (O'Connor *et al*., 2007). (Figure 4.15)

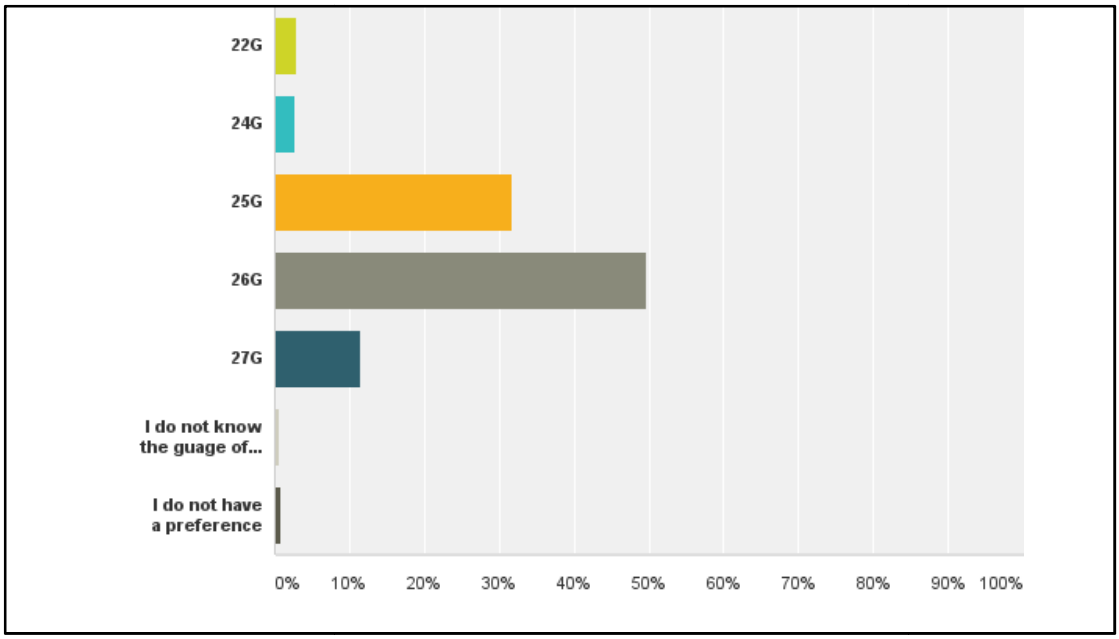


FIGURE 4.15: Gauge preference of spinal anaesthetic needles

4.7.2.3 **Drugs used for spinal anaesthesia**

There are a number of different local anaesthetic agents that can be used for spinal anaesthesia. The physiochemical properties of the drug, including the baricity and concentration, influence the quality of the anaesthetic block (Kleinman, 2002).

There were 886/933 (95%) respondents who preferred to use 0.5% bupivacaine with dextrose as the local anaesthetic for obstetric spinal anaesthesia. This is a hyperbaric local anaesthetic solution that spreads in a cephalad direction towards the normal thoracic kyphosis when the patient lies supine (Kleinman, 2002). This upward spread of the local anaesthetic results in a higher block level. Tagaloa et el (2009) reported that 90% of respondents in their survey in the USA preferred using hyperbaric bupivacaine, however the concentration preferred in their study was 0.75%. In South Africa, 0.75% bupivacaine is not available for clinical use.

There was a similar distribution in the use of hyperbaric bupivacaine between the specialist and non-specialist doctors (Figure 4.16), as well as between the public and private healthcare sectors (Figure 4.17).

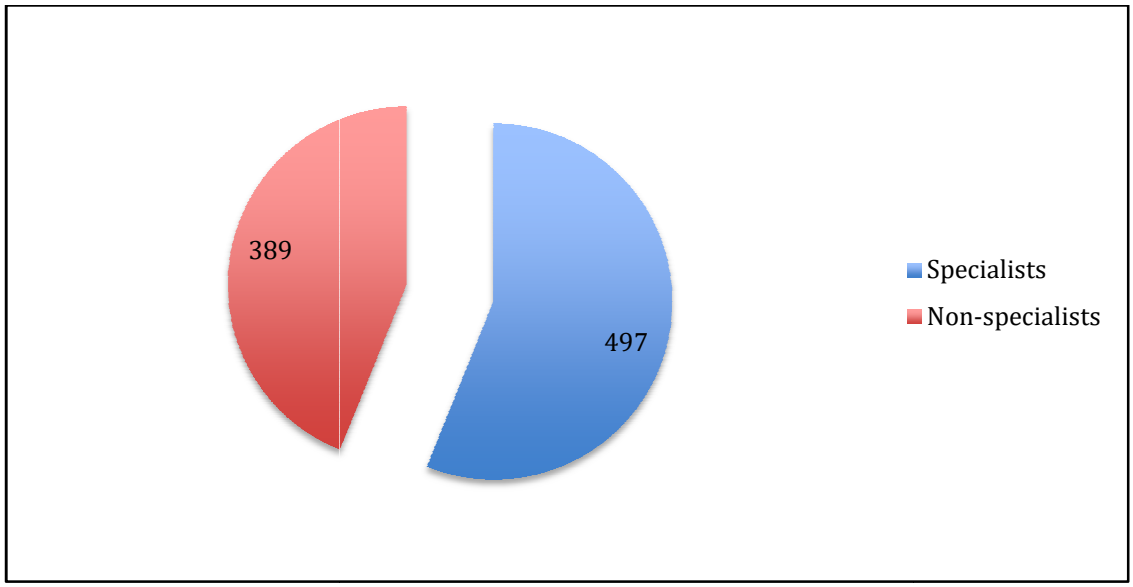


FIGURE 4.16: Distribution between specialists and non-specialists amongst doctors who prefer to use 0.5% bupivacaine with dextrose for spinal anaesthetics

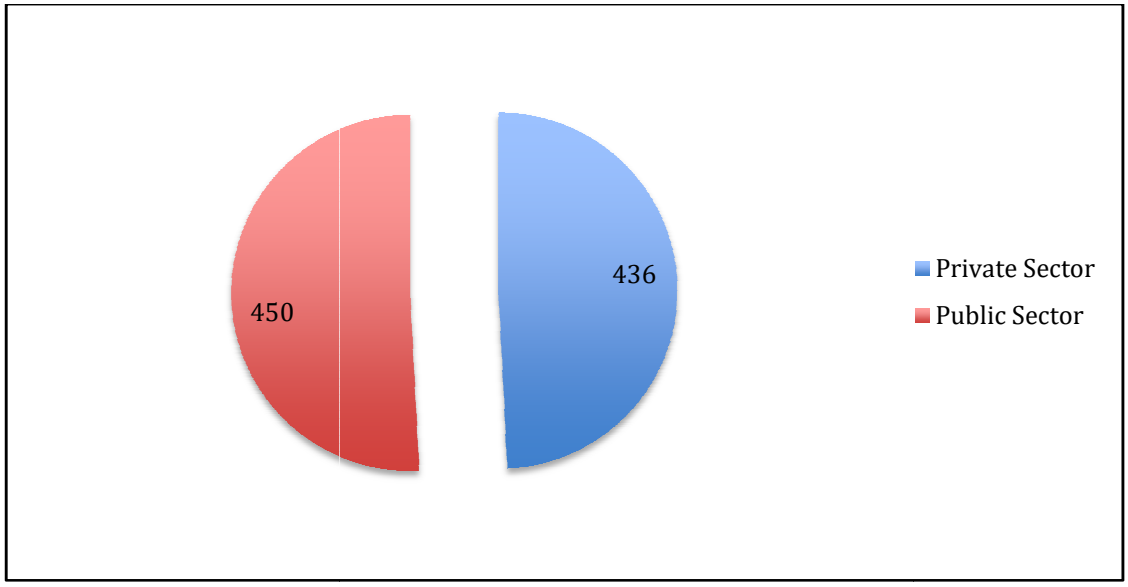


FIGURE 4.17: Distribution between private and public sector doctors who prefer to use 0.5% bupivacaine with dextrose for spinal anaesthetics

Bupivacaine is an amide local anaesthetic. The 0.5% concentration solution contains 5mg/ml of local anaesthetic. Its duration of action, following spinal administration, is up to 150 minutes (Strichartz and Charles, 2005). Plain

0.5% bupivacaine was the most popular drug used by the 5% of doctors who do not use hyperbaric bupivacaine (Figure 4.18). The difference between plain bupivacaine and bupivacaine with dextrose is the baricity of the solutions. This has an effect on the spread of the local anaesthetic and the level of the spinal block achieved in a supine patient (Kleinman, 2002).

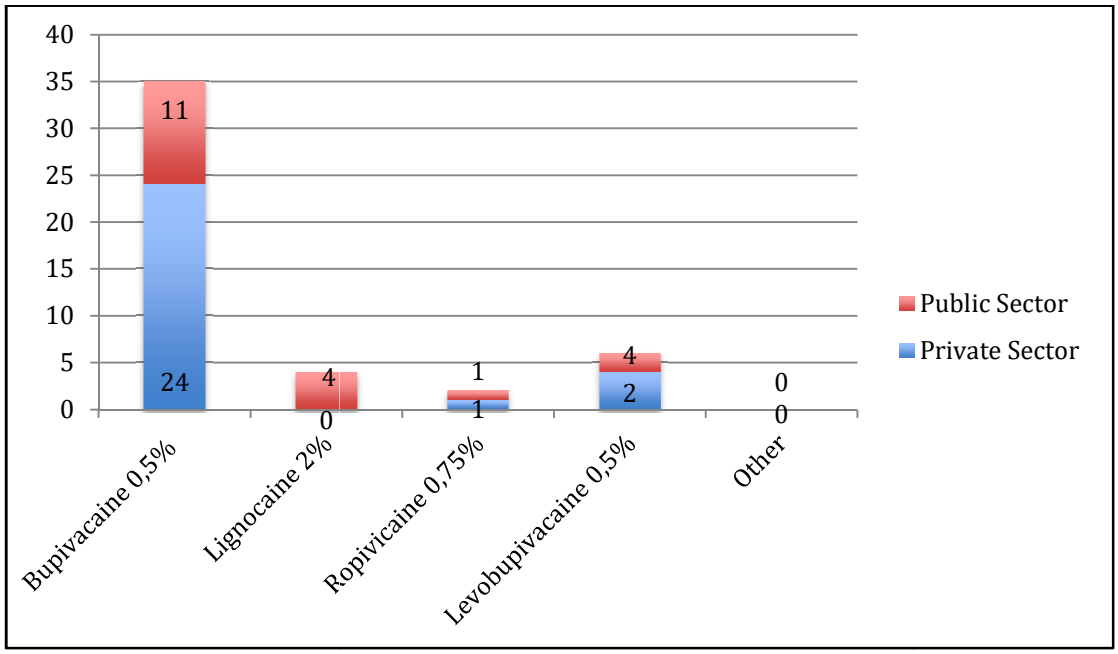


Figure 4.18: Preferences of private and public sector doctors who prefer not to use 0.5% bupivacaine with dextrose for spinal anaesthetics

The median volume of local anaesthetic used by the 886/933 doctors who prefer to use 0.5% bupivacaine with dextrose was 2.00ml (10 mg). Van Houwe *et al* (2006) reported that the average dose of hyperbaric bupivacaine used in their study, conducted in Belgium, was 9mg (1.8ml of the 0.5% solution); lower than the median dose reported here.

There was a statistically significant difference between the local anaesthetic volume used by specialists and non-specialists (Wilcoxon-Mann-Whitney-U test, $p<0.001$) with the non-specialists group using a lower median volume of local anaesthetics than specialists group (Table 4.5).

TABLE 4.5: Volume of 0.5% bupivacaine used in spinal anaesthetics

	SPECIALISTS	NON-SPECIALISTS
NUMBER	509	377
MAX (ml)	4	5
MIN (ml)	1.44	1.25
MEDIAN (ml)	2.00	1.80

In spinal anaesthesia, the volume of local anaesthetic administered is a significant factor affecting the extent of the spread of the anaesthetic and therefore the level of the block (King and Wooten, 1995). Pregnant patients have a higher intra-abdominal pressure and this exerts an effect on the spinal canal, effectively reducing the volume of the spinal canal (Hirabayashi *et al*., 1996). These patients therefore require a lower volume of intrathecal local anaesthetic to achieve the same block level as a non-pregnant patient. A higher block level increases the risks associated with spinal anaesthesia such as hypotension, nausea and cardiac arrest. However, using a higher volume of local anaesthetic decreases the risk of a failed spinal anaesthetic (Axelsson *et al*., 1982). One possible explanation for the higher volume used by the specialists is that these doctors are better trained to deal with the side effects of a high spinal block, and they may be more inclined to ensure their spinal anaesthetic is successful (so as to avoid general anesthesia for these patients) rather than fearful of the effects of a higher block.

The addition of additive agents to an intrathecal local anaesthetic mix is used to potentiate the effect of the local anaesthetic in the spinal canal, or to offer additional benefits via stimulation of central receptors in the spinal cord (McDonnell *et al*, 2009). There are a number of drugs that can be used for this purpose. These include agents such as opioids, neostigmine and clonidine.

In our survey, the doctors were asked what agents they routinely add to their intrathecal local anaesthetic mix for caesarean sections. They could choose

multiple drugs from the list provided. Table 4.6 summarizes the responses to this question.

TABLE 4.6: Preferences of specialists and non-specialist doctors for intrathecal additives

	Specialists	Non-specialists	Total	p-value
Fentanyl	342	312	654	p<0.001
Morphine	24	8	32	p=0.067
Sufentanil	88	33	121	p<0.01
No Drugs Routinely Added	96	44	140	p<0.01
Other	3	2	5	

Fentanyl is the most commonly used additive agent for spinal anaesthesia for caesarean sections, accounting for 80% of additives used (Table 4.6). Although the use of fentanyl was high in both specialists (61%) and non-specialists (78%), fentanyl use was marginally (but significantly) greater amongst non-specialists (Fisher's Exact, p<0.001). Tagaloa *et al* (2009) described that 54% of respondents in their study used a combination of fentanyl and morphine.

The average dose of intrathecal fentanyl used by specialists was 15.12 µg and by non-specialists is 13.77 µg (Students t-test, p=0.04) (Table 4.7).

TABLE 4.7: Doses of intrathecal fentanyl used by specialists and non-specialists

	SPECIALISTS (n = 340)*	NON-SPECIALISTS (n = 308)*
MAXIMUM (µg)	100	100
MINIMUM (µg)	5	2
MEAN (µg)	15.12	13.77
SD	7.75	8.66

*2 specialists and 4 non-specialists did not stipulate the dose of fentanyl used and were excluded from this calculation

The minimum dose of fentanyl used by the non-specialist group was 2 μg and 5 μg by the specialist group. These are extremely low doses of fentanyl and will probably have no analgesic effect on the patient. The minimal effective dose of intrathecal fentanyl has been documented to be 6.25 μg (Hunt *et al*., 1989).

Sufentanil is a synthetic lipophilic opioid analgesic that is very similar to fentanyl (Fukuda, 2005). In this survey, sufentanil was reported to be used by 121 doctors as an intrathecal additive drug. There was a statistically higher ratio of sufentanil users and non-users between the specialist and non-specialist groups of doctors (Fishers exact test, $p<0.01$) (Table 4.6).

Morphine was used by a very small number of the respondents in this survey. Only 24 specialists and 8 non-specialists added morphine to their intrathecal spinal anaesthetic mix. A statistical comparison of this data, using the Fishers Exact test, indicated that there was no statistical difference in the ratio of intrathecal morphine users and non-users between specialists and non-specialists ($p=0.067$) (Table 4.6). Tagaloa *et al* (2009) reported that 79% of respondents in their survey used morphine as an additive agent for spinal anaesthesia. The high use of morphine in their study is most likely related to the well-documented superior analgesic effect of intrathecal morphine for post-operative caesarean section patients (Palmer *et al*., 1999, Girgin *et al*., 2008, Carvalho and Tenório, 2013). In contrast, a similar survey conducted in Israel (Orbach-Zinger *et al*., 2014), reported that 72% of obstetric anaesthesia units never used intrathecal morphine for caesarean sections, while only 12% of units reported routine use of intrathecal morphine. The main reason cited for not using intrathecal morphine in these units was the lack of nursing staff to monitor patients for respiratory depression. In South Africa, the low use of intrathecal morphine for caesarean sections is most probably due to the teaching in the academic institutions that this drug is not safe to use in the South African setting, as discussed in chapter three. However, concerns about nursing care may also have been a consideration of the practitioners influencing their choice of intrathecal opioid.

One hundred and forty people did not add any additive drug routinely to their spinal anaesthetic mix for caesarean sections. There were a statistically greater number of specialists who do not use intrathecal additives compared to non-specialists (Fishers Exact Test, $p<0.01$) (Table 4.6).

4.7.2.4 **Management of anaesthesia for non-elective caesarean sections**

In a labouring woman with an *in situ* epidural catheter, who requires an urgent caesarean section, 662/933 (71%) respondents chose to "top-up" the epidural in order to proceed with surgery. Only 48/933 (5%) people would proceed with an emergency general anaesthetic for these patients. 209/933 (22%) respondents indicated that they would remove the epidural catheter and perform a spinal anaesthetic. Table 4.8 summaries the responses of the survey respondents regarding the choice of anaesthetic in a laboring woman requiring a caesarean section.

TABLE 4.8: Choice of anaesthetic in a labouring woman requiring a caesarean section

	TOTAL	SPECIALISTS	NON-SPECIALISTS	p-value
Top-Up Epidural	662	416	246	p<0.01
Spinal Anaesthetic	209	102	107	p<0.01
General Anaesthetic	48	17	31	p<0.01
Other	14	5	9	p=0.106

A Fishers Exact test of the differences between specialists and non-specialists for each of the four anaesthetic options reveals that there is a statistical difference in the ratios of users and non-users for top-up epidurals (specialists > non-specialists, $p<0.01$), spinal anaesthetics (non-specialists> specialists, $p<0.01$) and general anaesthesia (non-specialists > specialists, $p<0.01$).

Of the 662 people who chose “topping up” the epidural as their choice of anaesthetic for this type of patient, 314(47%) would use 0.5% bupivacaine, 221(33%) would choose 2% lignocaine, 111(17%) would use 0.75% ropivacaine and 3(0.45%) would choose 0.5% levobupivacaine (Figure 4.19).

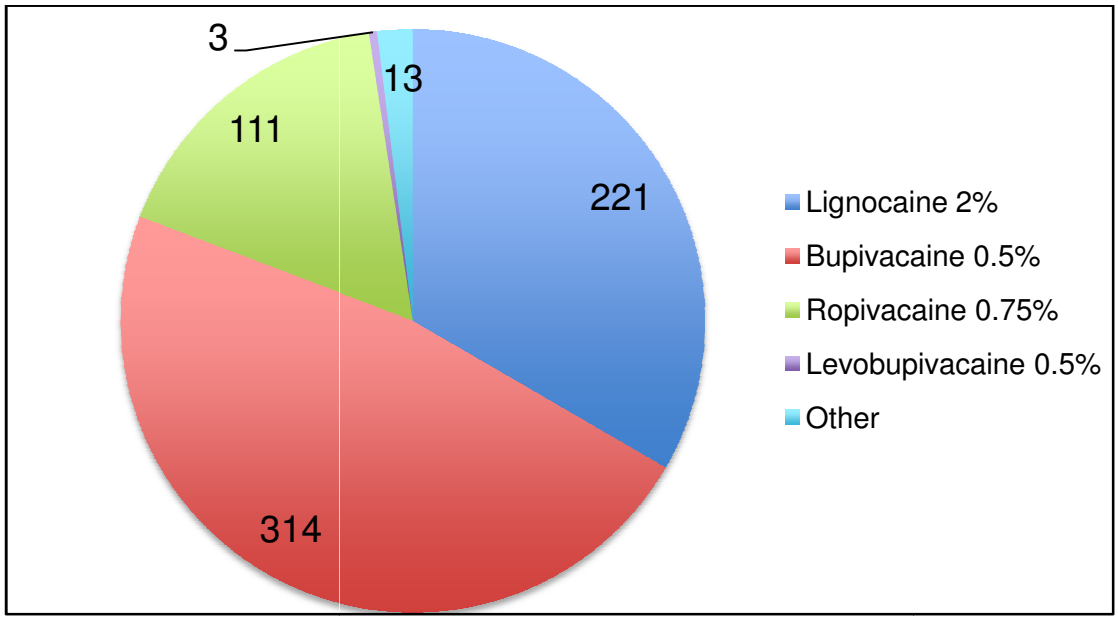


FIGURE 4.19: Choice of local anaesthetic for epidural “top-up”

Similar results were reported by Regan and O’Sullivan (2008), who found that 41.5% of respondents in a practice survey done, in the United Kingdom of Great Britain and Northern Ireland (UK), preferred to use 0.5% bupivacaine to “top up” a preexisting labour epidural for caesarean section anaesthesia. Tagaloa *et al* (2009) however, found that 74% of the respondents in their survey preferred to “top-up” the preexisting labour epidural with 2% lignocaine. This is markedly higher than the 33% preference for 2% lignocaine in our study. A minority of the respondents in their study (5%) preferred the longer acting local anaesthetic agents such as bupivacaine or ropivacaine (Tagaloa *et al*., 2009).

Of the 662 people who use an epidural “top-up” for a labouring patient, 284/662 (43%) do not add any other drugs to the epidural local anaesthetic. For those people that do add drugs to the epidural local anaesthetic, fentanyl

was the most common drug used (281/662, 42%). Fentanyl was also the most commonly used additive agent in the USA survey (Tagaloa *et al.*, 2009). Adrenalin and sodium bicarbonate (NaHCO3) are the next two most common agents used in our survey respondents. Only 4/662 (0.6%) people used morphine routinely as an additive agent into the epidural mix. (Figure 4.20)

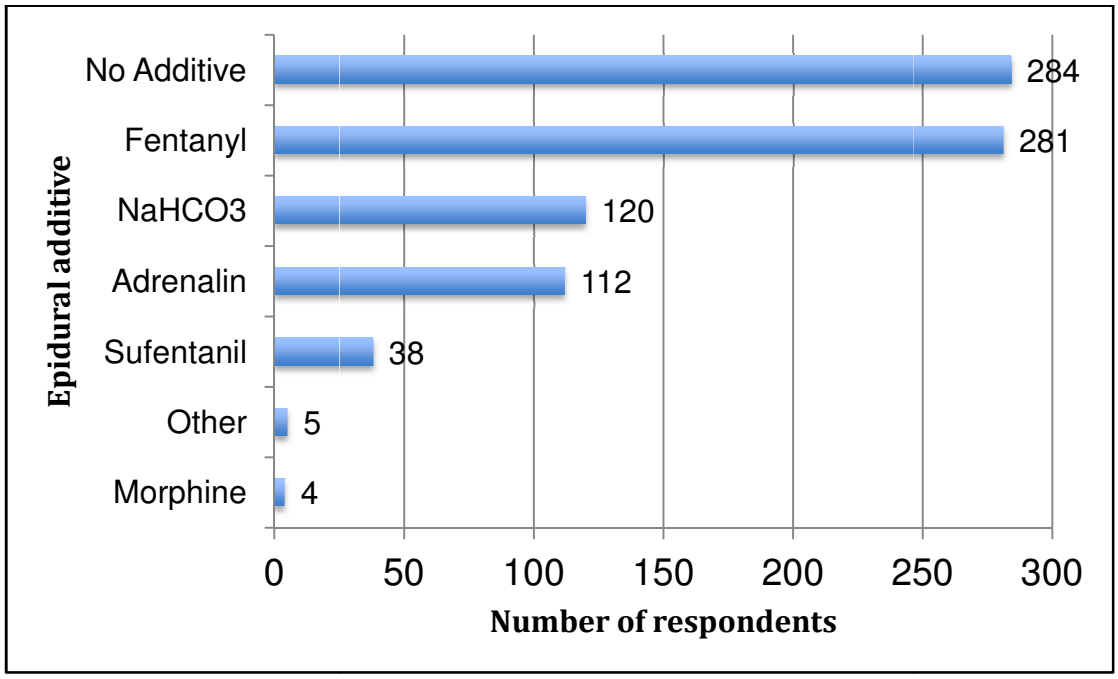


FIGURE 4.20: Use of additive agents for epidural "top-up"

4.7.3 **Post-operative monitoring practices**

All patients who have an anaesthetic need to be monitored for a requisite period of time after their anaesthetic (Bettings *et al.*, 2013). For patients who are given intrathecal opioids, the duration of observation may be increased in order to detect any delayed effects of the intrathecal opioids. This duration of observation will depend on the intrathecal opioid that is used.

In this survey, there were 389/933 (42%) individuals who practiced in hospitals that have a protocol for monitoring patients who had received neuraxial opioids. These were divided into 216/389 (56%) from the private sector and 173/389 (44%) from the public sector. Of the remaining 544 people who did not work in hospitals with a monitoring protocol, 249/544

(46%) people worked in the private sector and 295/544 (54%) worked in the public sector. A similar survey question in the USA revealed that 93% of respondents worked in an institution that had a protocol for monitoring patients (Tagaloa *et al.*, 2009). Figure 4.21 summarises the responses of doctors regarding their hospitals' post-operative monitoring protocols.

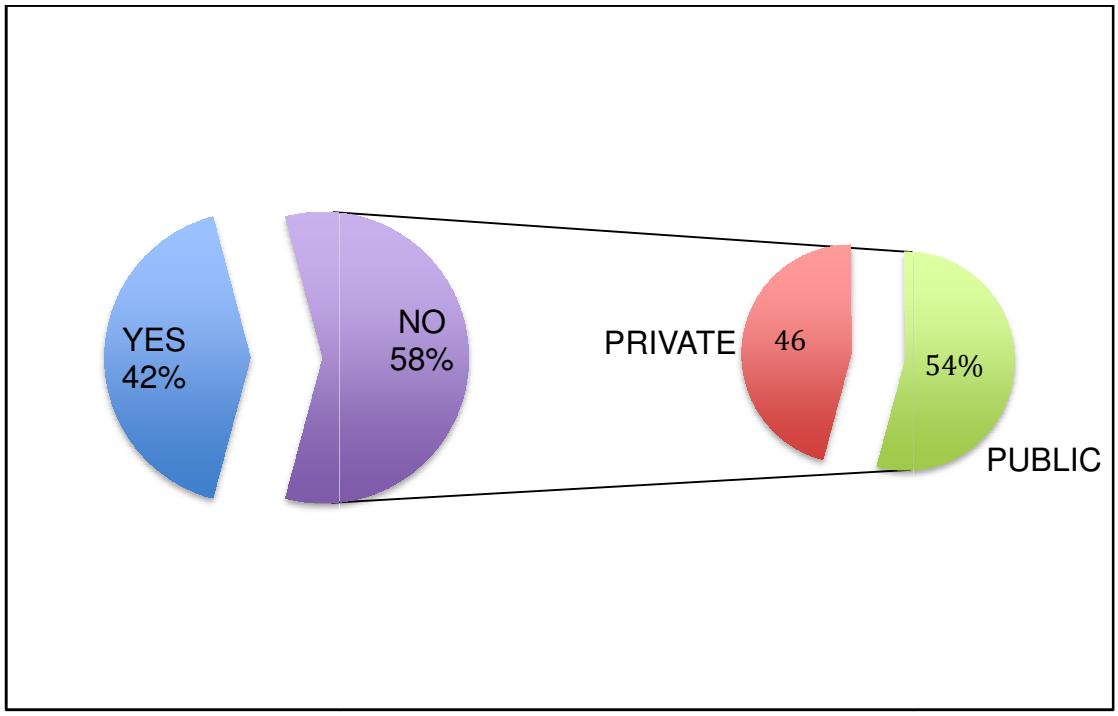


FIGURE 4.21: Availability of post-operative monitoring protocols in hospitals

Using the Fishers Exact statistical test we compared the use of a monitoring protocol for patients receiving intrathecal opioids between public sector and private sector hospitals and found that there is a significant difference in the ratio of the use-of to no-use-of protocols between the two sectors ($p<0.001$), such that protocols are more often used in the private sector compared to the public sector.

The 389 doctors who follow a post-operative monitoring protocol were asked how many hours patients are monitored for signs of respiratory depression after neuraxial opioid administration. Their responses are graphically illustrated in Figure 4.22.

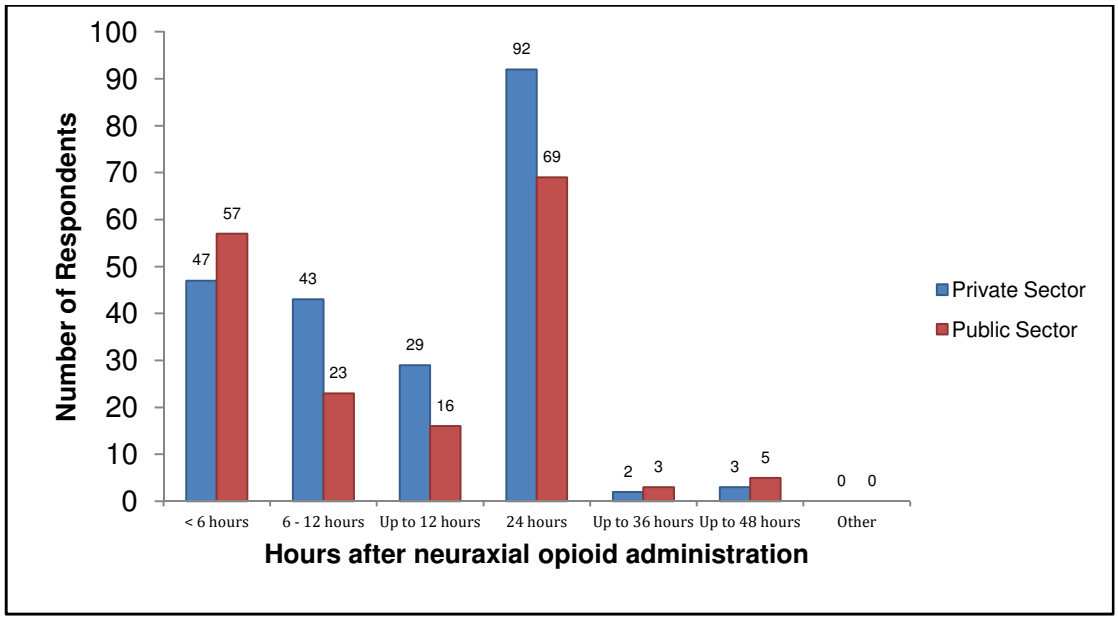


FIGURE 4.22: Duration of monitoring of patients following neuraxial opioid administration

The ASA task force on neuraxial opioids recommended that monitoring should be continued for up to two hours in patients who are treated with intrathecal fentanyl and for up to 24 hours in patients who have received intrathecal morphine (Horlocker *et al*., 2009). In our study, we did not determine if the type of neuraxial opioid used influenced the monitoring practice. However, as 95% of doctors who use intrathecal additives, are using lipophilic opioids it is likely that these monitoring practices are associated with the use of lipophilic opioids in the majority of responses.

Respondents were asked to indicate all the monitoring modalities used to monitor these patients. Each respondent could choose multiple options. The results are listed in Table 4.9.

TABLE 4.9: Choice of monitoring modalities used to assess patients for respiratory depression

Monitoring Modality	Total number of responses	Private Sector	Public Sector	p value
Respiratory rate	320	181	139	p = 0.424
Sedation score	167	102	65	p = 0.064
Pulse oximetry	263	136	127	p < 0.05
Other	5	3	2	p = 1

The most commonly used modality for monitoring patients for respiratory depression is respiratory rate monitoring. Pulse oximetry is used statistically more in the public sector than in the private sector (Fishers Exact test, $p<0.05$). There was no statistical difference in the use of the other monitoring modalities between the public and private sectors. Measurements indicated in the "Other" category include blood pressure monitoring (n=1), electrocardiogram (ECG) (n=1) and return of mobility (n=1). There is currently insufficient evidence in the literature to support any recommendation of which monitoring modalities should be used (Horlocker *et al*., 2009).

The 544 respondents, who indicated that their hospitals do not have a post-operative monitoring protocol in place, were asked if they think it is necessary to monitor patients for respiratory depression after neuraxial opioid administration. The majority (504/543*, 92.8%) responded that this is necessary. (Table 4.10)

* One person did not answer this question

TABLE 4.10: Responses of specialists and non-specialists regarding the need for post-operative monitoring following intrathecal opioid administration

	SPECIALISTS	NON-SPECIALISTS	p-value
YES	274	230	p = 0.409
NO	24	15	

These responses were analysed according to level of qualification to determine if there was a difference in the opinions of the more highly trained specialists compared to the non-specialists. There was no statistical difference in the responses between specialists and non-specialists to this question (p=0.409).

4.7.4 **Post-operative pain control**

When asked who should be responsible for the management of the patient's post-operative analgesia, the majority of respondents (587/933, 62.9%) felt that the anaesthesiologist should be the only health care professional responsible for this aspect of care. Only 39/933(4.1%) doctors felt that the post-operative pain should be managed using a team approach involving the obstetrician, anaesthesiologist and the nurse. 186/933(19.9%) of the respondents were of the opinion that the obstetrician should be the only person responsible for the patient's post-operative pain control. The responses to this question are tabulated in Table 4.11.

TABLE 4.11: Choices of respondents regarding who should be responsible for the management of patients' post-operative pain control

Professional who should be responsible	Number of responses
Anaesthesiologist + Obstetrician + Nurse	39 (4.2%)
Anaesthesiologist + Obstetrician	76 (8.2%)
Anaesthesiologist + Nurse	6 (0.6%)
Obstetrician + Nurse	1 (0.1%)
Anaesthesiologist	587 (63%)
Obstetrician	186 (20%)
Nurse	34 (3.6%)
No one	3 (0.3%)

As a generally accepted principle of pain management, a team approach to address a patient's pain is always better than one individual being solely responsible (Ballantyne, 2012). The team approach allows for different aspects of the patient's pain to be taken into consideration and also facilitates discussion between the members of the team, which can prevent important aspects of management being overlooked. It is unfortunate that there were three respondents in this survey (one specialist and two non-specialists – both of whom do not have a diploma in anaesthesia) who felt that no one should be responsible for the patient's post-operative pain management.

While a team approach to the management of the patients' post-operative pain control is ideal, the elucidated actual state of practice in South Africa was that the anaesthesiologist is the professional responsible for the patient's analgesia in 62% of cases.

The responses are illustrated in Figure 4.23.

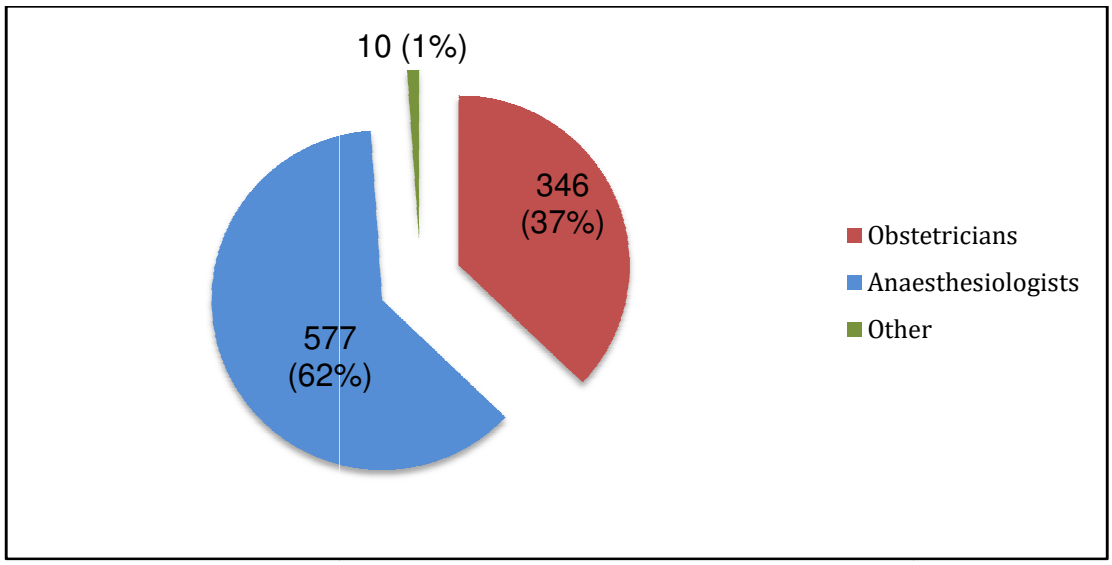


FIGURE 4.23: Professionals who are responsible for patients' pain control

The majority of the survey respondents (853/933, 91%) did not routinely use an epidural catheter for post-operative pain management for the caesarean section patient. 80/933 (9%) indicated that they use a labour epidural catheter for post-op analgesia. This is similar to the published practise in Israel, where only 8% of obstetric anaesthesia units use the labour epidural catheter post-operatively for patient-controlled epidural analgesia (Orbach-Zinger *et al.*, 2014). None of the respondents in our study indicated that they would insert an epidural catheter for post-operative analgesia if the patient did not have one pre-operatively. (Figure 4.24)

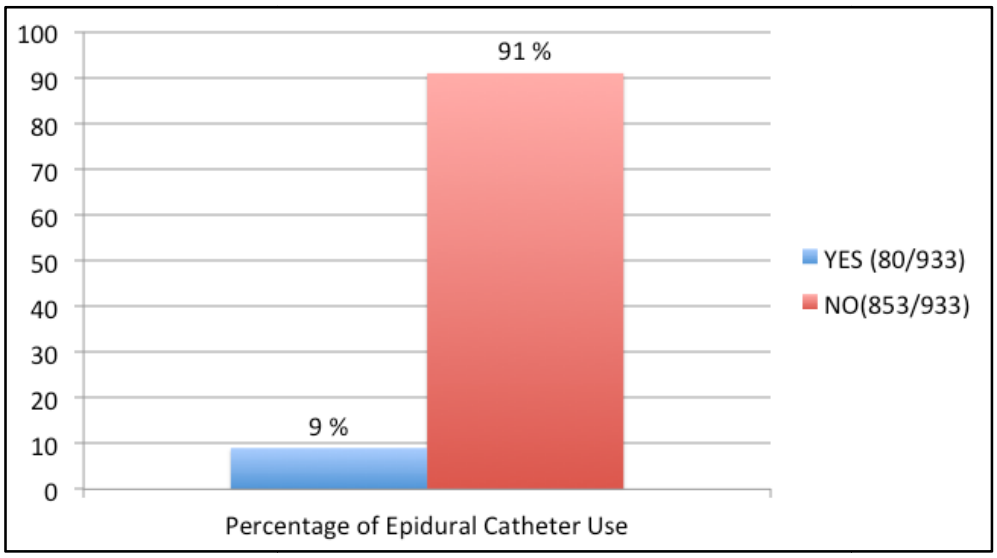


FIGURE 4.24: Use of epidural catheter for post-operative pain control

Only 164/933 (17%) of people in this survey would routinely use a patient controlled analgesic pump (PCA) to manage post-operative pain for the caesarean section patient. When this pain control technique is utilized, the most popular medication used in the PCA is morphine (110/164). Other drugs used are: pethidine (mepiridine) (49/164, 40 specialists and 9 non-specialists) and fentanyl (3/164, 3 specialists). Tagaloa *et al* (2009) reported that 12% of respondents in their survey would routinely use a PCA pump for post-operative analgesia. In Israel, where the routine use of intrathecal morphine is low (similar to our findings in South Africa), the routine use of PCA pumps for post-operative analgesia is 4% (Orbach-Zinger *et al*., 2014), which is much lower than the findings in our study. The low preference of PCA pumps for post-operative analgesia in South Africa may be related to the relative limitation of movement that this form of analgesia may cause for the patient. This is related to the fact the patient will have an intravenous line connected to a stand that may hinder movement. Figure 4.25 illustrates the choice of respondents for PCA use, as well as the preference of drugs used in the PCA's.

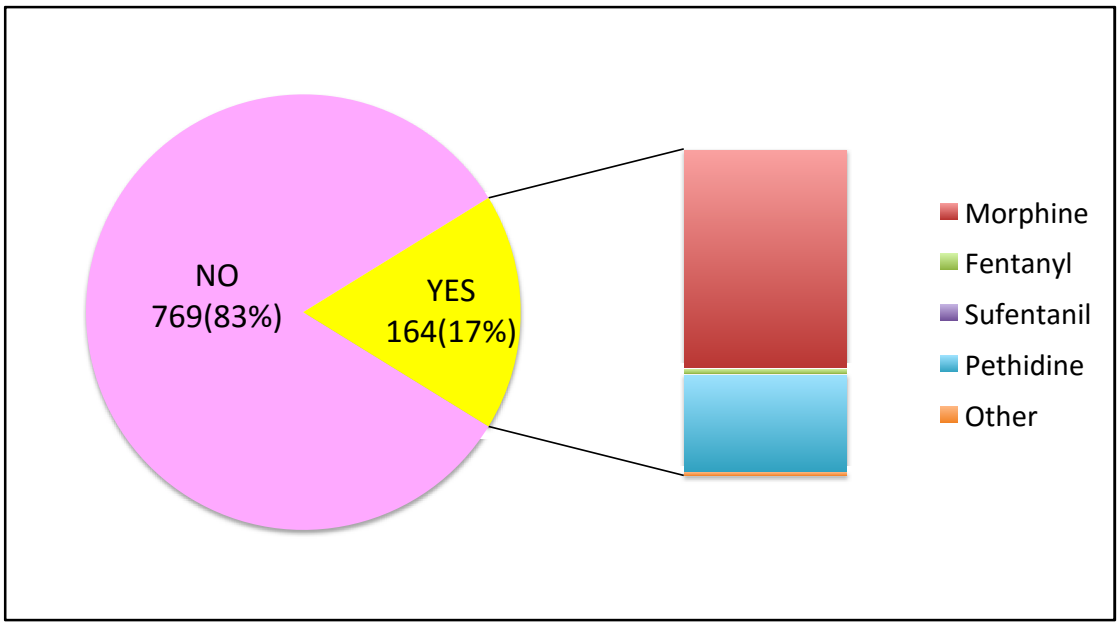


FIGURE 4.25: Preference of use of PCA pumps and drugs used in these pumps

Seventy five percent of the respondents in this survey routinely prescribed NSAIDs for post-operative analgesia after caesarean section (Figure 4.26). These results are similar to results published by Tagaloa *et al* (2009) from the USA, where 81% of respondents in their survey reported using NSAIDs for post-operative analgesia. Orbach-Zinger *et al* (2014) reported that only 54.5% of obstetric anaesthesia units in Israel use NSAIDs post-operatively as part of an analgesic regimen. The most commonly used NSAID in our study was diclofenac (445/933). Indomethacin (146/933) and parecoxib (75/933) were also popular choices of NSAID's. The rectal administration route was preferred by 49.1% of the respondents. Rectal administration of NSAIDs has a proven opioid sparing effect following caesarean section surgery (Dahl *et al*., 2002)

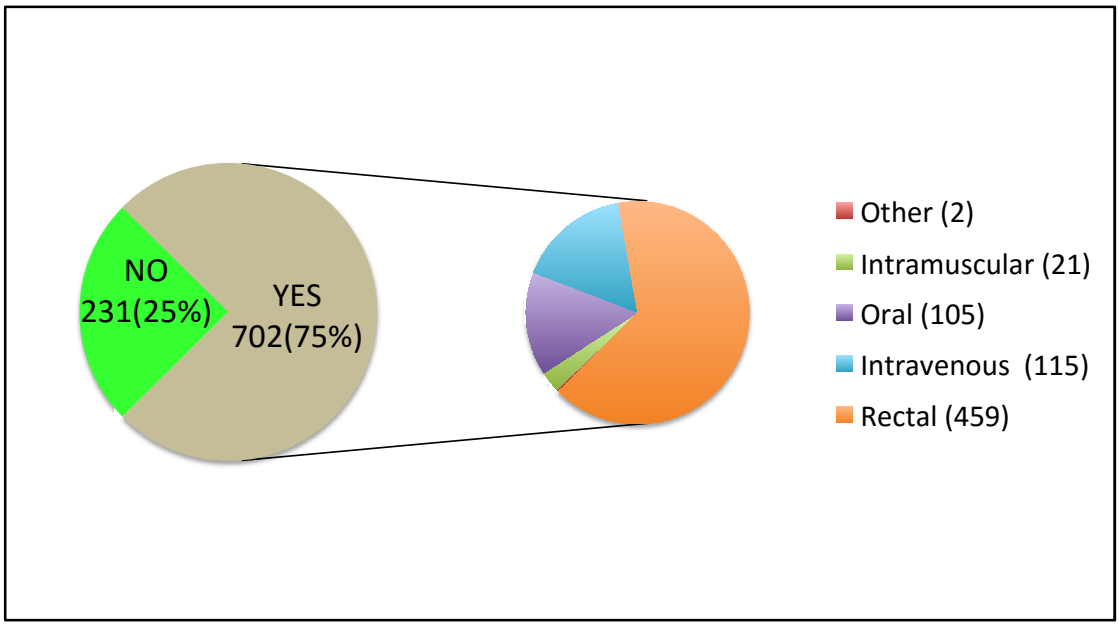


FIGURE 4.26: NSAIDs use after caesarean section surgery and preferred route of administration

Intravenous (IV) paracetamol is categorized as a schedule 3 drug in SA (Division of Clinical Pharmacology, 2012) and is available for use in hospitals. The drug is known to have an opioid sparing effect (Remy *et al*., 2005) and has also been shown to have superior analgesic effects compared to intravenous pethidine in the post-operative period (Inal *et al*., 2006). In this

study, 64% of respondents reported routinely prescribing intravenous paracetamol after caesarean section surgery. (Figure 4.27)

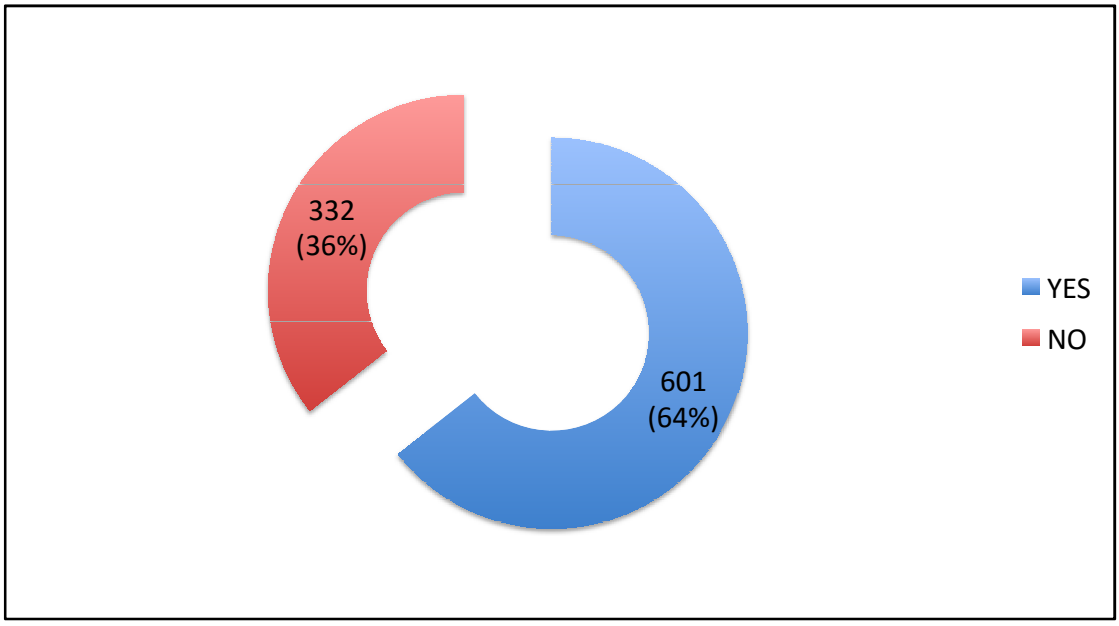


FIGURE 4.27: IV paracetamol use after caesarean section surgery

Paracetamol was the most popular oral analgesic used for post-operative pain management. It was prescribed by 501(54%) respondents in this survey as part of their patients' analgesic regime. This is similar to the results reported by Tagaloa *et al* (2009). Forty-five percent of respondents in their survey used oral paracetamol for post-operative pain relief (Tagaloa *et al*., 2009). Tramadol, despite not being registered in SA for use in breastfeeding mothers, is a very popular drug (prescribed by 369 respondents (40%) in our survey).

4.7.5 **Patient satisfaction**

Based on their current obstetric anaesthesia practise, 76% of the respondents to this survey are of the opinion that their patients are satisfied with their post-operative analgesia. This is the perception of the anaesthetic service provider and not the actual level of satisfaction of their patients. These results are illustrated in Figure 4.28.

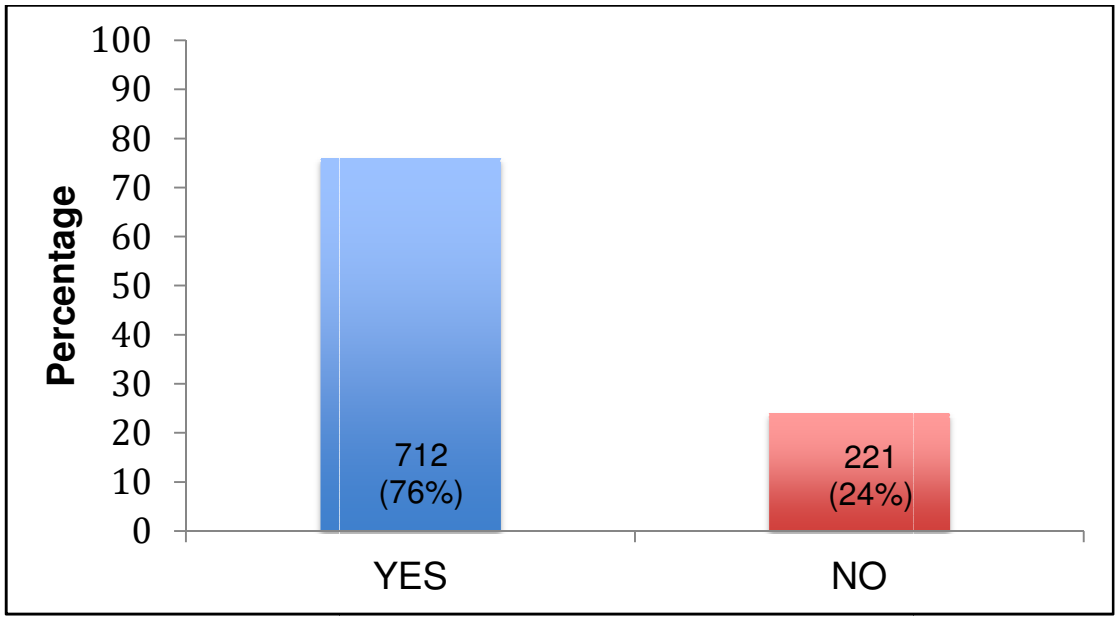


FIGURE 4.28: Practitioners' perceptions of their patients' satisfaction of their post-operative analgesia

4.8 Study Limitations

There was a risk of selection bias in the study population. The respondents to this survey were doctors attending anaesthesiology-community events or who may have had a special interest in obstetric anaesthesia, and therefore responded to the electronic survey. The risk was that there was a positive bias in that people who participated in this study may have been more motivated and may have attended additional training, and as such the results obtained in this survey may present a more positive result than the reality. These findings may therefore not be indicative of the overall practice of obstetric anaesthesia in SA.

4.9 Conclusions

We conducted a national survey to determine the current obstetric anaesthesia practices in SA. The survey was based on a similar survey conducted in the USA by Tagaloa *et al* (2009) but was adapted to take the unique South African health care environment into consideration.

Data from 933 respondents to this survey were analysed. The response rate was 57%. All provinces were represented however the majority of the respondents were from Gauteng, the Western Cape and KwaZulu-Natal. There was similar representation from both the private and public sectors.

The median number of obstetric anaesthetics performed each month by private sector respondents was 10 while public sector doctors performed a median of 15 obstetric anaesthetics per month. There was a statistical difference between the exposure of doctors in the private and public sectors to obstetric anaesthesia. The majority of the survey respondents were involved in obstetric anaesthesia services during daytime hours and after hours.

97.8% of all respondents in this survey preferred to use a single shot spinal anaesthetic technique for patients having an elective caesarean section. This popular choice of anaesthetic technique is similar to results from other international studies (Tagaloa *et al*., 2009, Stamer *et al*., 2005). The most commonly used spinal anaesthetic needle was the Whittacre needle, which is a pencil point needle. However, up to 30% of the survey respondents preferred to use a cutting spinal anaesthetic needle. These needles increase the risk of developing PDPH (O'Connor *et al*., 2007). There was a greater risk of not being able to use one's preferred spinal needle for doctors working in the public sector compared to those doctors working in the private sector.

The most commonly used local anaesthetic for obstetric spinal anaesthetics was 0.5% bupivacaine with dextrose. The median volume of 0.5% bupivacaine with dextrose, used by the respondents, was 2.00ml (10mg). There was however a statistically significant difference in the volume of local anaesthetic used between specialists and non-specialists. The majority of the survey respondents added an additive agent to the local anaesthetic mix for the spinal anaesthetic block, and the most commonly used additive agent was fentanyl. Morphine was used by a very small number of individuals.

In the labouring patient requiring an emergency caesarean section, the majority of respondents preferred to “top-up” a pre-existing labour epidural for the surgery. The preferred local anaesthetic for this epidural “top-up” was 0.5% bupivacaine.

With regards to post-operative monitoring practices, the majority of respondents (58%) did not work in hospitals that have protocols for monitoring patients who have received neuraxial opioids. Despite working in this environment, 92.8% of these doctors felt that it was necessary to monitor these patients for respiratory depression.

For the majority of the respondents (62%) the anaesthesiologist was the person who is responsible for the patient’s post-operative pain management. PCA pumps and epidural analgesia were not popular techniques utilized for post-operative analgesia. NSAIDs and intravenous paracetamol were commonly used drugs for post-operative pain control. Oral tramadol was also a popular drug.

Based on current practices, 76% of the respondents felt that their patients are satisfied with their post-operative analgesia after their caesarean section.

Table 4.12 compares the results of our study with the results reported by Tagaloa *et al* (2009).

TABLE 4.12: Comparison of the national survey results with the results of the USA study reported by Tagaloa *et al* (2009)

TAGALOA *et al* STUDY	SOUTH AFRICAN NATIONAL SURVEY
Survey Response Rate	
36 %	57%
Clinical Time Doing Obstetric Anaesthesia	
< 1 day per week = 18% 1 – 2 days per week = 39% > 2 days per week = 43%	< 1 day per week = 44% 1 – 2 days per week = 42% > 2 days per week = 14%
Level of Involvement in Obstetric Anaesthesia	
Daytime cover = 9% On Call only = 4% Daytime and on call = 87%	Daytime cover = 11% On Call only = 17% Daytime and on call = 67% Other = 5%
Preferred method of anaesthesia	
Single shot spinal anaesthetic = 85% Epidural = 4% General Anaesthetic = 0% CSE = 11%	Single shot spinal anaesthetic = 97.8% Epidural = 0.2% General Anaesthetic = 0.8% CSE = 1.2%
Type of spinal anaesthetic needle	
Pencil point needle = 94% Quincke© needle = 5%	Pencil point needle = 70% Quincke© needle = 30%
Gauge of Spinal Anaesthetic Needle	
24G = 13% 25G = 63% 27G = 16% Other needle sizes = 8%	22G = 3% 24G = 2.6% 25G = 31.5% 26G = 49% 27G = 11.4%

Local anaesthetic for spinal block	
*Hyperbaric 0.75% bupivacaine = 90% Plain 0.5% bupivacaine = 8% * 0.75% hyperbaric bupivacaine is not available in South Africa	*Hyperbaric 0.5% bupivacaine = 95% Plain 0.5% bupivacaine = 4% * 0.75% hyperbaric bupivacaine is not available in South Africa
Median Dose of Hyperbaric Bupivacaine	
12mg	10mg
Use of adjuvant drugs for neuraxial anaesthesia	
Adjuvant drugs used: • *Fentanyl = 77% • *Sufentanil = 2% • *Morphine = 79% * Reported as percentage of respondents who indicated that they use these drugs	Adjuvant drugs used: • *Fentanyl = 80% • *Sufentanil = 15% • *Morphine = 4% * Reported as percentage of respondents who indicated that they use these drugs
Choice of local anaesthetic for labour epidural "top up" for surgery	
2% lignocaine = 74% * Chloroprocaine = 21% Others = 5% * Chloroprocaine not available in South Africa	0.5% bupivacaine = 47% 2% lignocaine = 33% 0.75% ropivacaine = 17% 0.5% levobupivacaine = 0.45%
Post-operative monitoring practices	
Respondents who work in a hospital with a monitoring protocol = 93% The duration of monitoring varies. • < 6hrs = 3% • 6 – 12hrs = 3% • Up to 12hrs = 12% • 24hrs = 63% • Up to 36hrs = 0% • Up to 48hrs = 0%	Respondents who work in a hospital with a monitoring protocol = 42% The duration of monitoring varies. • < 6hrs = 27% • 6 – 12hrs = 17% • Up to 12hrs = 12% • 24hrs = 42% • Up to 36hrs = 1% • Up to 48hrs = 1%

Post-operative pain management practices	
79% of respondents will not routinely use an epidural for post-operative pain management	91% of respondents will not routinely use an epidural for post-operative pain management
12% of respondents will routinely use a PCA pump for post-operative analgesia	17% of respondents will routinely use a PCA pump for post-operative analgesia
NSAIDs are used by 81% of practitioners	NSAIDs are used by 75% of practitioners
IV paracetamol not specifically reported. 45 % of respondents use oral paracetamol	64% of respondents prescribe IV paracetamol for their patients in the post-operative period. 54% of respondents use oral paracetamol

The large cohort of this study has provided an accurate demonstration of the current state of obstetric anaesthesia in South Africa. The results of this study have provided us with new information on the practice of obstetric anaesthesia in South Africa. The survey has highlighted some important and interesting differences in anaesthetic practices for caesarean sections between the public sector and private sector. In addition, we have also highlighted issues relating to differences in the practices between specialists and non-specialists providing obstetric anaesthetic services in South Africa. This study has brought to the fore major concerns relating to the practice of anaesthesia by practitioners with no anaesthetic qualifications, which is in direct contravention to the practice guidelines of the SASA (Bettings *et al.*, 2013), and also the inappropriate use of Quincke needles by a large number of practitioners. This study has also highlighted the stark differences in the obstetric anaesthetic practices in South Africa compared to other published global practices (Table 4.13).

Based on the results of the study presented in chapter three, there are a number of areas where the practises of South African anaesthetic service providers do not conform to the suggested reference standards for anaesthetic management for caesarean sections. These include the widespread use of cutting Quincke© spinal anaesthetic needles to perform spinal anaesthesia for pregnant women, and the high percentage of practitioners that work in hospitals that do not have post-operative monitoring protocols for patients who have received neuraxial opioids. Areas where current practice complies with the expert recommendations include the widespread use of regional anaesthesia for caesarean sections and the preference for using 0.5% bupivacaine with dextrose as the local anaesthetic for spinal anaesthesia in these patients. Practitioners also prefer to use fentanyl as an intrathecal additive to all other opioids including morphine (which is not recommended by South African experts). NSAIDs and paracetamol are commonly prescribed drugs for post-operative analgesia, which complies with recommendations from the expert panel.

Table 4.13 compares the results of our study with recommendations made by the national experts (Chapter three) and with published international guidelines.

TABLE 4.13: Comparison of the national survey results with the recommendations of the South African institutional experts and current international guidelines

SOUTH AFRICAN EXPERT RECOMMENDATIONS	INTERNATIONAL GUIDELINES	RESULTS OF THE SOUTH AFRICAN NATIONAL SURVEY
Method of anaesthesia		
Single shot spinal anaesthetic	ASA – Neuraxial anaesthetic technique (does not specify intrathecal or epidural techniques)[(a)] UK – Regional anaesthetic technique (does not specify intrathecal or epidural techniques)[(b)]	Method of anaesthesia reported: • Single shot spinal anaesthetic = 97.8% • Epidural = 0.2% • General Anaesthetic = 0.8% • CSE = 1.2%
Type of spinal anaesthetic needle		
Pencil point needle ** Quincke© needles should not be used*	ASA – Pencil point needle[(a)] **Recommendation is to use pencil point needle instead of cutting-bevel needle*	Pencil point needle = 70% Quincke© needle = 30%

Gauge of Spinal Anaesthetic Needle		
25G, 26G and 27G	No recommendations	22G = 3% 24G = 2.6% 25G = 31.5% 26G = 49% 27G = 11.4%
Local anaesthetic for spinal block		
0.5% bupivacaine with dextrose	No recommendations	0.5% bupivacaine with dextrose = 95%
Use of adjuvant drugs for neuraxial anaesthesia		
Opioids – Fentanyl (10 – 25µg) ** Morphine should not be used*	ASA – Neuraxial opioids are recommended. No specific drug is recommended[(a)] UK – Neuraxial diamorphine[(b)] APS – Intrathecal and epidural opioids. No specific drug is recommended[(c)]	Adjuvant drugs used: • *Fentanyl = 80% • *Sufentanil = 15% • *Morphine = 4% * Reported as percentage of respondents who indicated that they use these drugs

	ANZCA – Intrathecal morphine[(d)] PROSPECT – Intrathecal morphine [(f)] ** There are no explicit recommendations against morphine*	
Post-operative monitoring practices		
Monitoring for respiratory depression in patients given neuraxial opioids. The duration of monitoring depends on the drug used: • Lipophilic opioids - 0 – 12 hours • Morphine - 24 hours after the administration of the drug	ASA - Monitoring for respiratory depression should be done in patients who receive neuraxial opioids. The duration of monitoring depends on the drug used: • Lipophilic opioids – minimum of two hours after administration[(e)] • Morphine - The monitoring should be done once per hour for the first 12hours and then once every two hours for the second 12 hours[(e)]	Only 42% of respondents work in hospitals with a protocol for monitoring patients who have received neuraxial opioids. The duration of monitoring varies. • < 6hrs = 27% • 6 – 12hrs = 17% • Up to 12hrs = 12% • 24hrs = 42% • Up to 36hrs = 1% • Up to 48hrs = 1% We did not however determine if the duration of monitoring varied with the type of neuraxial opioid used.

	APS – Sedation and respiratory status in the initial hours after surgery for patients who receive systemic opioids[(c)]	Respiratory rate monitoring is the most commonly used monitoring modality. Pulse oximetry and sedation scores are also used.
Post-operative pain management practice		
Epidural analgesia – should not be routinely used for post-operative analgesia	APS – Epidural analgesia (with or without opioids) can be offered[(c)]	91% of respondents will not routinely use an epidural for post-operative pain management
PCA opioids – should be reserved for challenging cases	UK – PCA opioids should be offered to patients[(b)]	17% of respondents will routinely use a PCA pump for post-operative analgesia
NSAIDS – should be routinely used for post-operative pain management	UK – NSAIDS should be routinely used[(b)] APS - NSAIDS should be routinely used[(c)]	NSAIDs are used by 75% of practitioners 49.1% of practitioners prefer to administer NSAIDs as a rectal suppository

	ANZCA – Conflicting evidence regarding benefits of NSAIDs use[(d)] PROSPECT – Oral NSAIDs should be used [(f)]	
Paracetamol – should be routinely used for post-operative pain management. The intravenous formulation is preferred	APS - Paracetamol should be routinely used[(c)] ANZCA – Paracetamol should be routinely used [(d)] PROSPECT – Oral paracetamol should be used [(f)]	64% of respondents prescribe IV paracetamol for their patients in the post-operative period. Oral paracetamol is used by 54% of respondents

[(a)](Apfelbaum *et al.*, 2016) [(b)](Griffiths *et al.*, 2011) [(c)](Chou *et al.*, 2016) [(d)](Schug *et al.*, 2015) [(e)](Horlocker *et al.*, 2009) [(f)] (PROSPECT Working Group, 2015)

The results of this study can be used to modify and improve anaesthetic training programmes so as to improve the obstetric care of women in South Africa.

4.10 Summary

In this chapter the results of the national survey of anaesthetic practices in South Africa was presented. In the next chapter we will present the results of a clinical trial investigating the differences in the analgesic effects of three different intrathecal opioid regimens for the management of post-operative caesarean section pain.

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CHAPTER FIVE: The influence of two different intrathecal morphine doses compared to intrathecal fentanyl on the post-operative pain experiences of women undergoing neuraxial anaesthesia for caesarean section

5.1 Introduction

Adequate and appropriate pain management post-caesarean section constitutes an essential component of post-operative care of the new parturient. Mothers in pain have greater difficulty taking care of their newborns, including the ability to breastfeed, therefore appropriate pain management can facilitate the bonding process between mother and baby in the early post-operative period (Karlstrom, 2007). Indeed, from the patient perspective, in a survey amongst pregnant patients at Stanford University, USA, patients ranked pain associated with caesarean section surgery as one of their greatest concerns related to their pregnancies (Carvalho *et al*., 2005).

Intrathecal opioids, and morphine in particular, have been shown to provide good post-operative analgesia for women after caesarean section surgery (Carvalho and Tenório, 2013). Morphine is poorly lipophilic in comparison to the more lipophilic opioids, fentanyl and sufentanil (Fukuda, 2005). As a result of its relative hydrophilicity (compared to fentanyl and sufentanil), intrathecal morphine does not penetrate the nervous tissue quickly and this results in the drug having a relatively long onset of action and a prolonged duration of effect. Internationally, intrathecal morphine is considered the gold standard for providing post-caesarean section analgesia, and is the therapy against which other therapies are measured (Palmer *et al*., 1999, Dahl *et al*., 1999, Tan, 2012, Sarvela *et al*., 2002).

Based on our investigations (chapters 3 and 4), the vast majority of anaesthetic service providers in South Africa do not use intrathecal morphine for post-caesarean section analgesia. This may be due to individual

practitioners' preferences and not drug availability, as morphine is listed as an essential medicine on the South African formulary (Zeeman, 2012) and is readily available for use in hospitals and for outpatient use in both the public and private healthcare sectors.

5.2 Aim

The aim of this study was to evaluate the analgesic effect of two intrathecal opioids (morphine and fentanyl) in women who have undergone caesarean section surgery in a South African public sector hospital.

5.3 Objectives

The specific objectives of the study were:

i. To evaluate the analgesic effect of three different intrathecal opioid mixtures (100µg morphine, 50µg morphine and 25µg fentanyl) in women who had undergone caesarean section surgery, relating specifically to:
    a. Post-operative analgesic requirements at two time points (12 hours and 24 hours) after surgery. *This was the primary outcome. All subsequent objectives listed here address secondary outcomes.*
    b. Pain scores at two time points (12 hours and 24 hours) after surgery.
    c. Sedation scores at two time points (12 hours and 24 hours) after surgery.
    d. Post-operative nausea scores at two time points (12 hours and 24 hours) after surgery.
    e. Post-operative pruritus scores at two time points (12 hours and 24 hours) after surgery.

ii. To determine the impact that the patients' post-operative pain had on their activities (movements in and out of bed, deep breathing or coughing, and sleeping), their emotional states and their perception of relief in the first 24 hours after surgery.

5.4 Demarcation of the study field

The study was performed at a single center, the Rahima Moosa Mother and Child Hospital (RMMCH), Johannesburg, South Africa. RMMCH is a tertiary, public sector hospital, serving the western areas of Johannesburg. There are approximately 12000 deliveries per year at the hospital, with a caesarean section rate of approximately 30% (data extracted from hospital records). RMMCH is a teaching hospital affiliated to the Faculty of Health Sciences at the University of the Witwatersrand.

5.5 Ethical considerations

- This study was conducted in accordance with the ethical principles of the Declaration of Helsinki (World Medical Association, 2013) and Good Clinical Practice (Department of Health, 2006).
- The protocol was reviewed and approved by the Human Research Ethics Committee – Medical (HREC) of the University of the Witwatersrand (Approval number M141181- APPENDIX L).
- The following ethical considerations were taken into account when planning this study
    - Beneficence – The investigated treatment options in this trial would potentially improve the post-operative pain management of the patients recruited into the clinical trial.
    - Non-maleficence – All planned interventions in the clinical trial were aimed at improving the patient's post-operative experience. The increased patient follow up afforded to the trial participants ensured that no harm came to the patients.

- Autonomy – All women at the hospital received equal and fair treatment. Patients who were invited to participate in the trial were reassured that they would get the same treatment as all other patients irrespective of whether they participated in the trial or not.
- Justice – This trial was aimed at investigating a cost-effective and accessible pharmaceutical option for post-operative analgesia for women after caesarean section surgery. Evidence generated from this study could be utilized to make analgesia more accessible to patients having caesarean sections in SA

- The study has been registered on the www.clinicaltrials.gov website. Registration number: NCT02577809.

5.6 Research Methodology

5.6.1 **Study design**

The study was a single-centre, double-blind, parallel-group, randomised trial of two doses of intrathecal morphine versus a single dose of fentanyl. Two doses of intrathecal morphine were compared with the current hospital standard of care (25µg fentanyl) in order to determine what was the lowest effective dose of intrathecal morphine in our patient population.

5.6.2 **Study Population**

The study population included all patients having caesarean section surgery under single shot spinal neuraxial anaesthesia at RMMCH, and who provided informed consent to take part in the study.

Sample Size Calculation

- The sample size was calculated taking into account the primary objective of the study (post-operative analgesic requirements after surgery), in order to ensure that the study was adequately powered.

  The calculation was based on an F-test with repeated measures (two time periods) and interaction (three groups), and assumed 0.5

correlation between repeated measures, a small effect size of 0.2, and 90% power to detect a difference

The calculated sample size was 28 patients per group or 84 patients in total.

- We aimed to recruit 100 patients into the study in order to allow for loss of patients from the study.

5.6.3 **Sample Method**

A consecutive convenience sampling method was used. The convenience sampling method was chosen because of the time constraints and scope of the research. The most readily accessible patients presenting for surgery were included. It is acknowledged that a convenience sample cannot fully represent the study population (Hultsch *et al*., 2002).

5.6.4 **Criteria for the study**

5.6.4.1 INCLUSION CRITERIA:

All patients > 18years having caesarean section surgery under single shot spinal neuraxial anaesthesia at RMMCH.

5.6.4.2 EXCLUSION CRITERIA

- Pre-operative:
    - *a)* Patient refusal or inability to give informed consent
    - *b)* Severe pre-eclampsia
    - *c)* Eclampsia
    - *d)* Patient unable to understand how to use the Patient Controlled Analgesia (PCA) pump, after appropriate counseling and training
- Intra-operative:
    - *a)* Obstetric Complications:
        - *i)* Post-partum Haemorrhage
        - *ii)* Ruptured Uterus
        - *iii)* Still Birth
    - *b)* Conversion to general anaesthesia intra-operatively
    - *c)* Administration of supplementary intravenous opioid analgesics

- Post-operative:
    a) Patients who had babies that required additional care, for a prolonged period, after birth (eg. Neonatal intensive care unit (ICU) admission for ≥ 12 hours or congenital abnormalities).
    b) Patients who require ICU or high-care admission post-operatively for any intra-operative complications

5.6.5 **Methodology**

- The trial was conducted from July – September 2015. The trial ended after 100 patients were recruited.
- Patients were approached pre-operatively and the study was explained to them. They were then invited to participate in the study.
- A graphical representation of the patient flow is illustrated in Figure 5.1

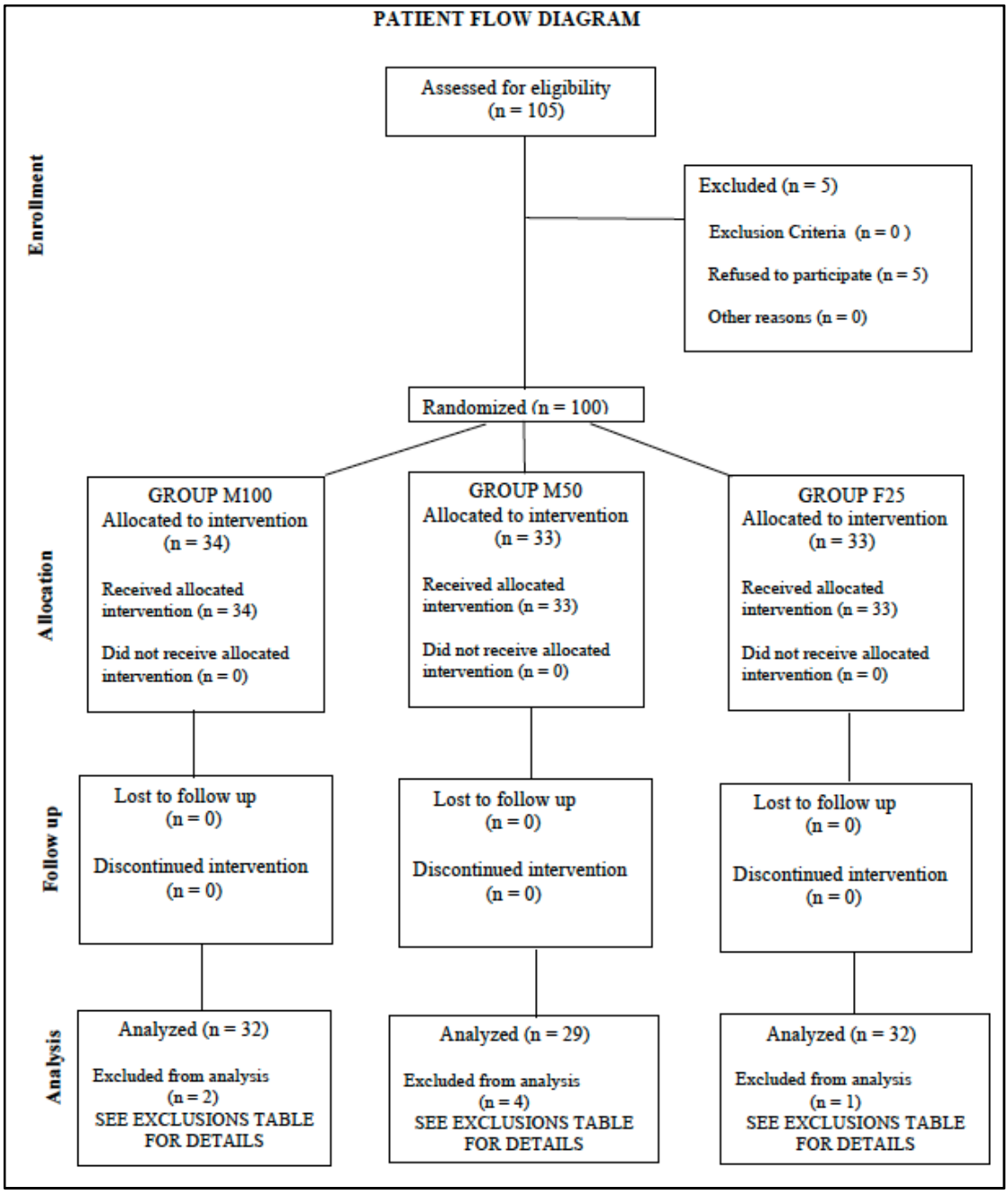


FIGURE 5.1: Patient flow diagram

The CONSORT checklist for this study is in APPENDIX M.

- After obtaining written informed consent from the patients (APPENDIX N), the following data were recorded on the patient data sheet (APPENDIX O)
    - Baseline weight
    - Baseline blood pressure
    - Age
    - Parity
    - Previous pregnancy losses
    - Relevant medical history and relevant pre-operative investigation results
    - ASA status
    - Indication for caesarean section
- Each patient was taught how to use a PCA pump.
- The standard of care, in the hospital, for intraoperative aspiration prophylaxis for obstetric patients is 10ml sodium citrate given orally and 10mg metoclopramide administered intramuscularly. Both these drugs were administered by the nursing staff in the ward prior to the patient being transferred to theatre.
- Patients were randomized, by the principal investigator (PI), when they arrived in the waiting area in the theatre complex, after the doctor performing their anaesthetic evaluated them.
- Patients were randomised using a computer generated block randomisation list generated from www.sealedenvelope.com (Sealed Envelope Ltd, 2015)
- Patients were randomized into one of three groups. The group that they were allocated into determined the intrathecal medication that they received as part of their anaesthetic:
    - **Group M100** - 1.8ml 0.5% hyperbaric bupivacaine with 100µg morphine (mixed in 0.4ml normal saline to a volume of 2.3ml)
    - **Group M50** – 1.8ml 0.5% hyperbaric bupivacaine with 50µg morphine (mixed in 0.4ml normal saline to a volume of 2.3ml)
    - **Group F25** - 1.8ml 0.5% hyperbaric bupivacaine with 25µg fentanyl (2.3ml volume)

- Once the patient was randomised, the PI (S Chetty) handed over the sealed randomisation envelope to the anaesthetist delivering the anaesthetic service so that the appropriate medication could be used in the spinal anaesthetic. The sealed envelope contained an instruction sheet to the anaesthetist informing them of the patient's group allocation and giving them instructions on how to mix the intrathecal local anaesthetic mixture (APPENDICES P, Q and R). The PI remained blinded to the group that the patient was allocated to and hence the medication that was used in the spinal anaesthetic. This design (i.e., the anaesthetic service provider knowing the drug) was used for safety reasons in the event of complications occurring during or after the procedure.
- In the operating theatre, standard American Society of Anesthesiologists (ASA) monitoring was used (blood pressure, electrocardiogram (ECG) and pulse oximetry)
- Each patient was pre-loaded with a 500ml bolus of colloid solution (hydroxyethyl starch) prior to the procedure. Thereafter an infusion of Modified Ringer's Lactate was infused at a rate of 60ml/hr. This protocol was used to decrease the risk of post-spinal hypotension and is the current standard of care at the hospital.
- Spinal anaesthesia was performed, by the attending anaesthetist, with the patient in the sitting position, using an aseptic technique, inserting a spinal needle into the lumbar spine.
- Once there was back-flow of cerebrospinal fluid (CSF), the patient was given 2.3ml of the local anaesthetic solution with opioid (as per the allocated group indicated in the randomisation instructions). Thereafter, all instruments were removed from the patient's back and a dressing was applied to the skin.
- After the performance of the spinal anaesthesia procedure, the patient was placed in a supine position with 15º left uterine displacement using a Crawford wedge.
- The level of sensory loss to temperature was determined by the attending anaesthetist using a cold metal instrument in theatre eg. forceps. Surgery only commenced after a satisfactory sensory blockade was achieved.

- Oxygen at 8 l/min flow was administered via a 40% venturi face mask.
- Blood pressure was monitored at one minute intervals until the baby was delivered then continued every three minutes thereafter until the end of surgery.
- In this study, hypotension was defined as a 20% reduction from baseline systolic blood pressure (SBP) or a SBP of 100mm Hg or less. Should this have occurred in theatre after the spinal anaesthetic, the patient was treated with a rapid infusion of 100ml of Ringers Lactate solution and intravenous boluses of 50µg of phenylephrine (unless the patient had a bradycardia (heart rate <40 beats per minute) – in which case 5mg boluses of intravenous ephedrine was used) .
- At the end of the surgery, a 100mg indomethacin suppository was inserted into the patient's rectum by the surgeon, as per standard hospital practice.
- After surgery, the patient was transferred to the recovery room for monitoring.
- The investigator issued the post-operative analgesia prescription for the patient before the patient left the recovery room. The post-operative prescription used for all patients was:
    - Morphine PCA pump
    - Indomethacin suppository 100mg per rectum 12 hourly
    - Prochlorperazine Maleate 12,5mg intramuscular (IM) 8hourly
    - Antibiotic (as per the surgeon's request)
- In the recovery room the patient was shown again how to use the intravenous PCA pump. The PCA pump contained morphine. The PCA pump had the following settings:
    - dilution of 1mg/ml of morphine
    - 1ml bolus
    - 5 minute lock-out period
    - 10mg/hr maximal dose
    - no background infusion
- The baby remained in the incubator in the recovery room (as per the standard hospital procedures)

- After 30 minutes of monitoring in the recovery room, if the patient met the standard hospital discharge criteria for the recovery area, the patient was discharged to the obstetric ward for observations.
- Standard ward monitoring of vital signs was performed by the ward staff
- Study observations
    - Data was collected using the study data collection form (APPENDIX O) at 12 hours ± 1 hour and 24 hours ± 1 hour after surgery
    - Data was collected on the following parameters:
        - ✓ Time from end of surgery to the first demand of analgesia from the PCA pump and the total amount of morphine used after 12hours and 24 hours after surgery.
        - ✓ Pain scores at time of assessment using an 11 point numerical rating scale (0 – 10)
            - ❖ With cough
            - ❖ At rest
        - ✓ Side-effects of morphine at two time points (12 hours and 24 hours) after surgery as follows:

a) Level of sedation, using the following scoring system:
0 = Awake
1 = Mild drowsiness
2 = Moderate drowsiness, easily awaken
3 = Difficult to arouse

Sedation was considered clinically relevant if the patient was not easily awakened.

b) Respiratory rate – Respiratory depression was defined as respiratory rate of less than eight breaths per minute.

Any respiratory rate of less than 8 was reported to the attending doctors for intervention with nalaxone

c) Nausea and vomiting, using the following scale:
   0 = No nausea
   1 = Presence of nausea without vomiting
   2 = Mild to moderate vomiting (not requiring treatment)
   3 = Severe vomiting (treatment required)

*Severe vomiting (more than two episodes) was treated with intravenous metoclopramide 10mg**

d) Pruritus, using the following scale:
   0 = No pruritus
   1 = Mild to moderate pruritus (not requiring treatment)
   2 = Severe pruritus (treatment required)

*Severe pruritus (more than two episodes) was treated with 25mg Phenergan**

** Patients who received treatment for nausea, vomiting and pruritus were excluded from the statistical analysis of the particular side effect parameter for which they received treatment (nausea & vomiting or pruritus) for the subsequent assessments. This was done so as to negate the false-negative side effect profile that the administration of the treatment would create.*

- Data were also collected using the Pain OUT registry format (PAIN OUT, 2016). The patient questionnaire (APPENDIX S) was completed at two time points (12 hours and 24 hours) after surgery. The process form (APPENDIX T) was completed after the second patient evaluation.

- After 24 hours, the PCA pump was removed and the patient was continued on standard oral analgesic treatment (as per the hospital protocol).

All data were collected by the principal investigator and/or the research assistants (who were anaesthesiology registrars doing their acute pain rotation).

5.6.6 **Data Analysis**

We analysed the prospectively collected data from patients who completed all trial requirements (per protocol cohort). Clinical data from manually completed data collection sheets (APPENDICES O, S and T) were entered into a spreadsheet using Microsoft® EXCEL® for MAC (Version 14.6.2).

Data was analysed using StatPlus, AnalystSoft Inc. - statistical analysis program for Mac OS®. (Version v6) and the statistical analysis program R (Version 3.2.3) (R Core Team, 2015)

Continuous parametric data was described using mean and standard deviation. Continuous non-parametric data was described using median and interquartile ranges. Categorical data was described using frequencies and percentages.

Baseline characteristics of the study sample were summarized using simple proportions and means or medians with ranges. Kruskal Wallis statistical analysis was performed on patient baseline data relating to age, weight, systolic and diastolic blood pressures and duration of surgery. Chi-squared statistical tests were performed on the patient baseline data of parity, previous pregnancy losses (data of all primiparous patients were removed from this statistical calculation), number of emergency procedures and number of patients who experienced a drop in blood pressure following administration of spinal anaesthesia. The post-operative analgesic requirements were described as median doses and interquartile ranges for each group, and compared using a Kruskal Wallis test. Further comparisons between pairs of treatment groups were performed using the Wilcoxon sum-ranked test.

5.7 Results and Discussion

The results and discussion of the primary objective (analgesic requirements post-operatively) are presented in this chapter (chapter five). The results and discussion of all secondary objectives are presented in chapter six.

One hundred patients were recruited into the trial. Seven of these patients were excluded from the data analysis due to protocol violations (two in Group M100, four in Group M50 and one in Group F25). The details of these patients are listed in table 5.1.

Six of the seven patients excluded from the data analysis were because their babies were admitted to the high-care unit. As per the study protocol, any patient whose baby was not with them at the time of the 12-hour assessment was excluded from the data analysis. The rationale behind this exclusion was that these patients may have been very anxious about the condition of their infants and these high levels of anxiety may have had impact on their pain perception. One patient was excluded from data analysis because she chose to withdraw from the trial before the first 12-hour assessment. All patients (including excluded patients) were monitored until the end of the study period at 24-hours after surgery

TABLE 5.1: Characteristics of the excluded patients

Treatment Group	Age (years)	ASA Status	Parity	Previous Pregnancy Loss	Weight (kg)	Indication for Caesarean Section	Emergency or Elective	Reason for Exclusion
F25	27	1	1	0	105	Previous Caesar	Elective	Baby in ICU for > 12hours
M100	45	2	4	0	74	CPD	Emergency	Baby in ICU for > 12hours
M50	24	1	1	0	67	Breech Presentation	Emergency	Baby in ICU for > 12hours
M50	23	2	1	0	53	Pre-eclampsia	Emergency	Baby in ICU for > 12hours
M50	32	1	4	0	85	Previous Caesar	Elective	Baby in ICU for > 12hours
M100	40	2	3	2	154	Multiple previous miscarriages	Elective	Baby in ICU for > 12hours
M50	26	1	1	0	92	Failed VBAC	Emergency	Patient chose to withdraw from study after surgery

The data from 93 patients were included in the analysis. Following unblinding of the patient allocations, there were 32 patients in Group M100, 29 patients in Group M50 and 32 patients in Group F25, after the excluded patients were removed from their respective groups. Based on the study sample size calculation, these group numbers met the requirements of the study power calculation.

The characteristics of the patients in each treatment group are summarized in Table 5.2.

TABLE 5.2: Characteristics of the study patients

	TREATMENT GROUP			
	Group M100	**Group M50**	**Group F25**	**p-value**
Intervention	Morphine 100µg	Morphine 50µg	Fentanyl 25µg	
Number of Patients	32	29	32	
Age (years) [mean(range)]	31 [21-40]	30[23-39]	30[21-41]	p = 0.88
Primaparity[n(%)]	2(2)	1(1)	5(5)	p = 0.20
Previous Pregnancy Loss [n(%)]	6(6)	4(4)	6(6)	p = 0.74
Weight [mean(range)] *kg*	80.32[49-101]	80.61[50-106]	84.79[55-164]	p = 0.89
SBP [mean(range)] *mm Hg*	124.71[100-163]	121.44[95-160]	121.66[99-167]	p = 0.60
Diastolic Blood Pressure [mean(range)] *mm Hg*	76.15[57-97]	77.69[56-101]	70.52[50-104]	p = 0.09
Emergency Procedure [n(%)]	9(10)	10(11)	11(12)	p = 0.83
Drop in blood pressure [n(%)]	22(24)	17(18)	24(26)	p = 0.39
Surgery duration (minutes) [median[range]]	55[22-106]	65[27-108]	55[28-115]	p = 0.43
Indication for caesarean section				
Previous caesarean section	26	20	23	
Foetal distress	1	2	5	
Breech presentation	0	3	0	
Cephalo-pelvic-disproportion	2	1	1	
Delayed 2nd stage of labour	0	0	1	
Twin pregnancy	0	1	0	
Pre-eclampsia	0	0	0	
Failed augmentation of labour	1	1	0	
Macrosomia	1	0	1	
Multiple previous miscarriages	0	0	0	
Prolonged rupture of membranes	0	0	1	
Failed attempt at vaginal birth after caesarean section	1	0	0	
Post-dates	0	1	0	

The three groups of patients were homogenous in terms of patients' characteristics. There were no statistically significant differences between the groups in terms of age, weight, number of primiparous patients, previous pregnancy losses, ASA status, blood pressure measurements, number of emergency procedures, the number of patients who experienced hypotension and the durations of the surgeries.

5.7.1 **Post-operative analgesic requirements**

The morphine used in the first 12 hours, second 12 hours and in total for the 24 hours after surgery was compared for each of the treatment groups. These results are summarized in table 5.3.

TABLE 5.3: Summary of the post-operative analgesic requirements of the three treatment groups

	Group M100 (n = 32)	**Group M50 (n = 29)**	**Group F25 (n = 32)**	**p-value**
Morphine used in first 12 hours (mg) [MEDIAN(IQR)]	8.0 (9.25)	8.0 (13.0)	16.0 (14.5)	$p < 0.001$
Morphine used in the second 12 hours (mg) [MEDIAN(IQR)]	3.5 (6.0)	5.0 (4.0)	10.0 (9.25)	$p = 0.01$
Total morphine used in 24 hours (mg) [MEDIAN(IQR)]	12.5 (14.25)	15.0 (16.0)	26.5 (19.3)	$p < 0.001$

There was a statistically significant difference in the dosage of morphine used between the three groups for all three of the periods analysed. This is illustrated in figures 5.2, 5.3 and 5.4

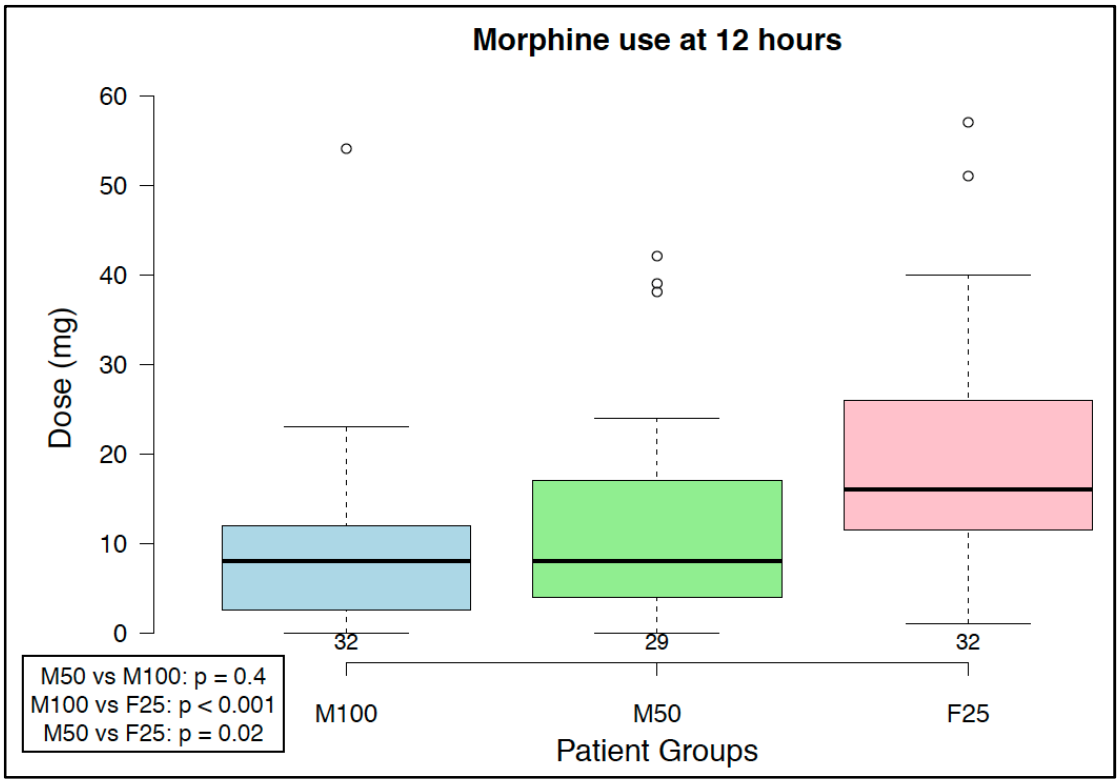


FIGURE 5.2: Box and Whisker plot of morphine doses used at 12-hour assessment

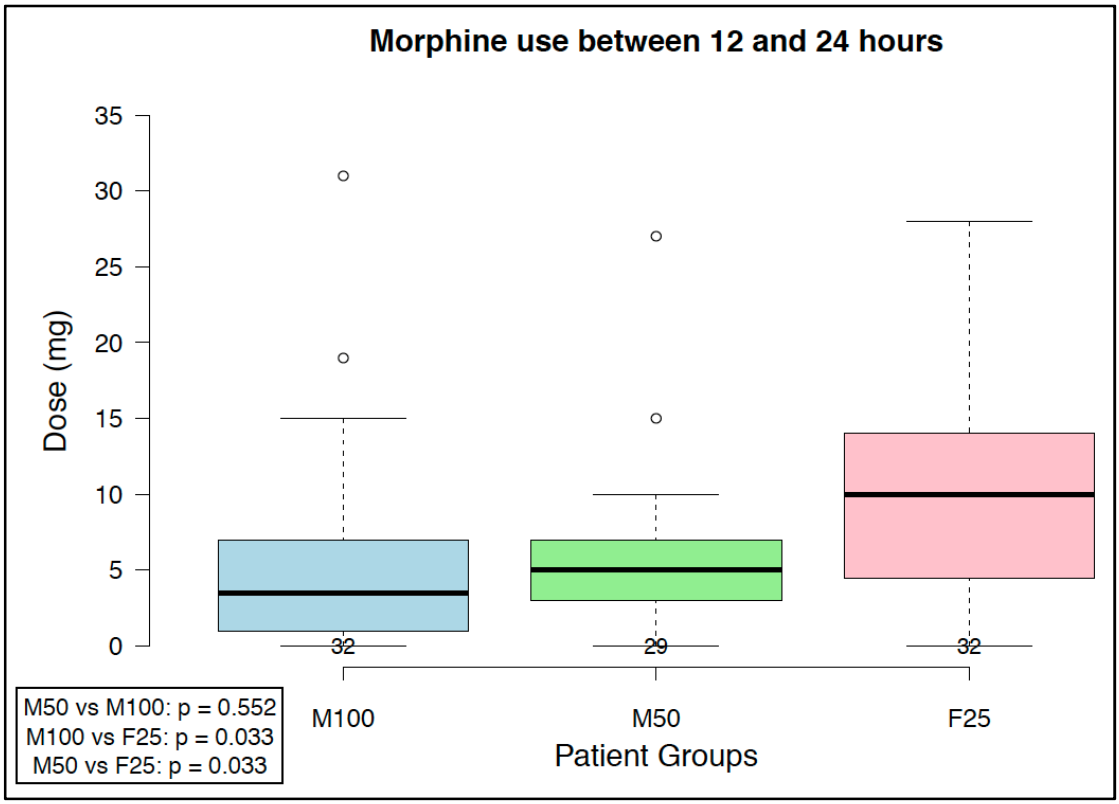


FIGURE 5.3: Box and Whisker plot of morphine doses used between 12 and 24 hours

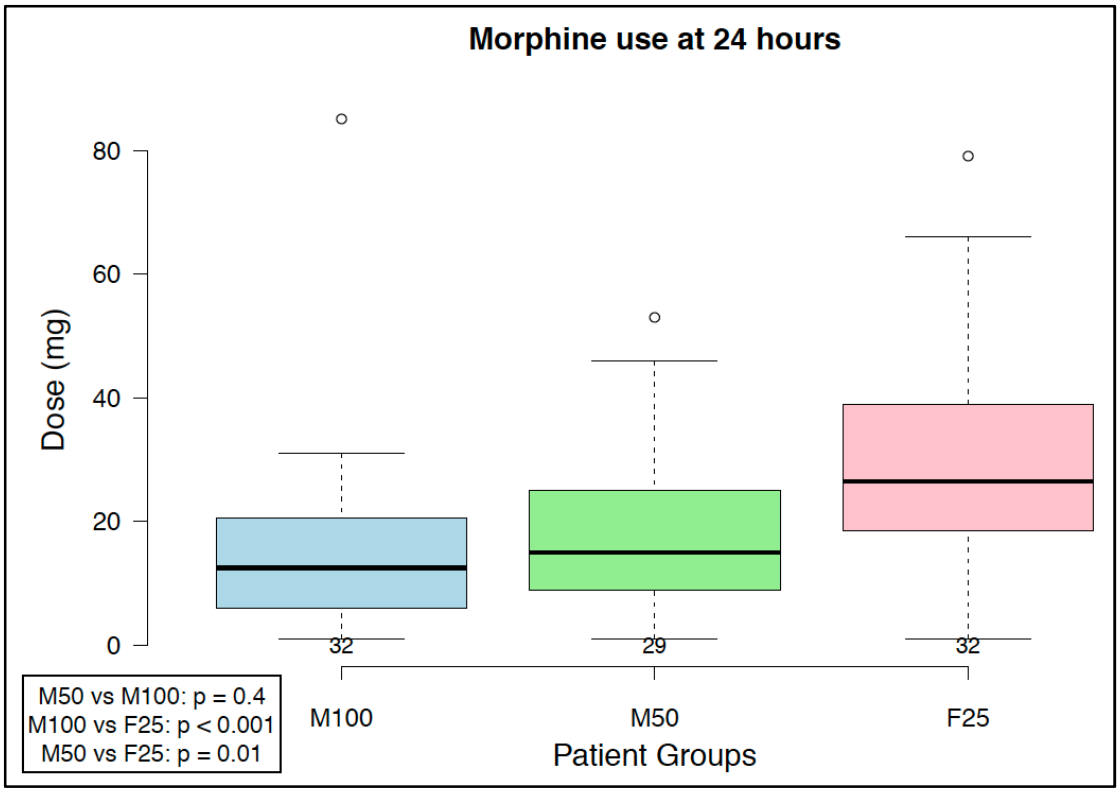


FIGURE 5.4: Box and Whisker plot of morphine doses used over the full 24-hour period

Using the Wilcoxon sum-rank test we compared each of the three groups with each other and also found that there was a statistically significant difference in the doses of morphine used between groups M100 and F25 and also between groups M50 and F25 for all of the time periods analysed (Figures 5.2, 5.3 and 5.4). Both the intrathecal morphine patient groups (Groups M100 and M50) used significantly less PCA morphine in all three time periods analysed, compared to the intrathecal fentanyl patient group (Group F25). When comparing the 50µg intrathecal morphine group (Group M50) with the 100µg intrathecal morphine group (Group M100), there was no difference in the morphine used between these groups for all the time periods analysed.

Based on the study exclusion criteria, 7 patients were excluded from the data analysis. In order to examine the results in the intention to treat cohort, we additionally analysed the data for all randomized patients. We used last observation carried forward (LOCF) to interpolate missing values in participants with missing 24-hour data. For the single patient who withdrew

before the 12-hour measurement, we used the median morphine dose at each time point from the group she was randomized to (Group M50).

TABLE 5.4: Summary of the post-operative analgesic requirements of the intention to treat cohort

	Group M100 (n = 34)	Group M50 (n = 33)	Group F25 (n = 33)	p-value
Morphine used in first 12hours (mg) [MEDIAN(IQR)]	9.0 (9.0)	8.0 (11.0)	16.0 (16.0)	$p < 0.001$
Morphine used in the second 12hours (mg) [MEDIAN(IQR)]	4.5 (6.0)	6.0 (5.0)	10.0 (9.0)	$p < 0.001$
Total morphine used in 24hours (mg) [MEDIAN(IQR)]	13.5 (14.5)	15.0 (12.0)	27.0 (20.0)	$p < 0.001$

The Kruskal Wallis statistical calculation performed on this data set indicated that there was a statistical difference between the three treatment groups for all three of the periods analysed (first 12 hours, second 12 hours and the full 24 hour period after surgery). This was in keeping with the statistical results of the original data analysis. This implied that the data from the excluded patients did not affect the statistical outcomes with regards to the analysis of the post-operative opioid requirements.

Emergency surgery can be considered to be a confounding factor that may have an influence on a patient's post-operative pain experience. In this study there were 9 patients in group M100, 10 patients in group M50 and 11 patients in group F25 who had emergency surgery. The emergency surgery population sample size was however too small to perform a meaningful analysis and this was therefore not done. The sample is underpowered to determine if this is a significant confounder.

The efficacy of intrathecal opioids for post-operative analgesia is well established in the obstetric anaesthesia setting. Palmer *et al* (1999) evaluated eight different doses of intrathecal morphine, ranging from 25μg to 500μg, and found that intrathecal morphine doses above 75μg were significantly more efficacious than placebo in providing post-operative analgesia following caesarean section surgery. When isolating the results of the two doses of intrathecal morphine that were investigated in our study, the Palmer *et al* (1999) study revealed that mean PCA morphine use in the 50μg and 100μg groups were 30± 26mg and 26± 23mg respectively. These doses are higher than the cumulative PCA morphine used in our study (18.2 ± 13.6mg and 15.4 ± 15.5mg) over the same time period. Girgin *et al* (2008) showed very similar PCA morphine requirements (28 ± 18mg) as Palmer *et al* (1999), in the group of patients who were given 100μg intrathecal morphine. These authors also reported that the PCA requirements of the 400μg morphine group were 20 ± 14mg, which is more similar to the PCA morphine requirement of the 100μg group in our study.

The discrepancy in PCA morphine doses between these two previous studies and our study may be explained, in part, by the fact that all patients in our study were given rectal NSAIDs as part of their analgesic regimen. Cardoso *et al* (1998) compared different doses of intrathecal morphine, with and without the use of intramuscular (IM) diclofenac, and showed that the addition of NSAIDs to the analgesic regimen had a significant opioid sparing effect. The author recommended that doses as low as 25μg intrathecal morphine, in combination with NSAIDs, can provide very effective analgesia after caesarean section surgery, with a reduced side-effect profile.

Palmer *et al* (1999) demonstrated that the post-operative PCA morphine requirements decreased as the dose of intrathecal morphine increased in their study. However these authors did not perform a direct comparison between 50μg and 100μg doses of intrathecal morphine. The results of our study however do not concur with this trend. There is no statistical difference between the PCA morphine doses used by patients in Group M100 and Group M50 despite the Group M100 patients receiving double the dose of

intrathecal morphine compared to patients in Group M50. The similarity in the efficacy of the two doses of intrathecal morphine assessed is suggestive that, in this group of patients, 50µg intrathecal morphine, in combination with rectal NSAIDs, can provide as good analgesia as 100µg intrathecal morphine.

This assumption of clinical equivalence between the two intrathecal morphine doses investigated in our study, was corroborated by Carvalho and Tenório (2013). These authors also compared the efficacy of the 50µg and 100µg doses of intrathecal morphine, and concluded "intrathecal 50µg provided the same quality of analgesia as 100µg, with a lower incidence of side effects". These authors did not use PCA morphine requirements as the basis of their conclusions and instead used patient pain Visual Analogue Scale (VAS) scores and overall patient satisfaction scores to make their determinations. Despite similar pain VAS scores in both groups, 70% of patients in the 50µg group reported pain to be their main reason for discomfort after surgery, compared with only 32% in the 100µg group.

The patients in Group F25 in our study had significantly higher post-operative PCA morphine requirements compared to those of each of the morphine groups. These results are similar to results published by Salmah and Choy (2009). These authors compared the analgesic efficacy of 100µg intrathecal morphine with that of 25µg intrathecal fentanyl, in women having caesarean section surgery under spinal anaesthesia. Patients in their morphine group had a mean post-operative PCA morphine consumption of 9.2 ± 1.2mg compared to 30.8 ± 2.3mg in the fentanyl group ($p<0.05$). These results were not surprising considering that the expected duration of action of intrathecal fentanyl ranges from one to four hours (Lundgren *et al*., 2016). Fentanyl is more lipophilic than morphine (Fukuda, 2005) and is able to penetrate into the nerves in the spine more quickly giving it a quick onset of action, and making it suitable for intra-operative analgesia. However, its short duration of action means that it is not able to provide adequate post-operative analgesia for most of the first 24-hours after surgery, and therefore patients will have higher analgesic requirements during this period.

The results and discussion of the secondary objectives of this study are presented in chapter six.

5.8 Conclusions

We investigated the effects of three different regimens of intrathecal opioids (Group M100 - 100µg morphine, Group M50 - 50µg morphine, and Group F25 - 25µg fentanyl) as part of the spinal anaesthetic for women having caesarean section surgery at RMMCH. A comparison of the analgesic effects, side effects and the impact on patients' post-operative experiences of all three regimens, were evaluated and compared in this randomized double-blinded study.

One hundred patients were recruited into the study. The data from 93 patients were analysed and reported on. There was no statistical difference in the basic characteristics of the patient populations between the three treatment groups.

Patients in the two morphine groups (Group M100 and Group M50) used less PCA morphine than patients in Group F25 during the 24-hour evaluation period following surgery (Kruskal Wallis, $p<0.001$). This difference in PCA morphine use was established in the first 12-hour evaluation period (Kruskal Wallis, $p<0.001$) and continued into the 2nd 12-hour evaluation period (Kruskal Wallis, $p=0.01$). There was however, no statistical difference in the PCA morphine use between Group M100 and Group M50, implying that the analgesic efficacy of these two treatment regimens is the same. It is important to note that the analgesic regimen that was used in this study included rectal indomethacin suppositories for 24 hours after surgery. The synergistic effects of NSAIDs with intrathecal morphine have been previously demonstrated in patients having caesarean section surgery (Cardoso *et al.*, 1998). The post-operative opioid requirements of the entire intention to treat cohort (n = 100) was also analysed, and corresponded with the results calculated for the 93 patients who fulfilled the study inclusion criteria. This

implied that the data of the seven excluded patients did not materially affect the study outcome.

The results of this objective of the study confirmed that intrathecal morphine, included as a component of the neuraxial anaesthetic solution for women having caesarean section surgery under single shot spinal anaesthesia at RMMCH, decreased the post-operative opioid requirements of these patients in the first 24 hours after surgery.

5.9 Summary

In this chapter the results of the primary objective of the clinical trial investigating the influence of different intrathecal opioid regimens on the post-operative pain experiences of women having caesarean sections at RMMCH has been presented. In the next chapter, the results of the secondary objectives of this study will be presented and discussed. The study limitations and acknowledgements related to this study will also be presented.

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CHAPTER SIX: The influence of two different intrathecal morphine doses compared to intrathecal fentanyl on patients' post-operative pain experiences and its impact on the activities and emotions of women undergoing neuraxial anaesthesia for caesarean section

6.1 Introduction

Poorly treated pain can have an adverse psychological effect on a patient (Stephens *et al*., 2003). The use of intrathecal morphine during anaesthesia for caesarean sections can provide good analgesia for the patient for a significant period after discharge from the recovery room (Palmer *et al*., 1999). Despite international evidence of the analgesic effects of intrathecal morphine for post-operative caesarean section analgesia, this method of analgesia is not popular in South Africa, as described in chapters 3 and 4.

The background to the study, the study design, and description of the cohort were provided in chapter 5, and are therefore not recalculated here. For clarity, I have repeated the description of the secondary objectives of the study.

6.2 Secondary objectives

The specific secondary objectives of the study were:

iii. To evaluate the analgesic effect of three different intrathecal opioid mixtures (100µg morphine, 50µg morphine and 25µg fentanyl) in women who had undergone caesarean section surgery, relating specifically to:
    a. Pain scores at two time points (12 hours and 24 hours) after surgery.

b. Sedation scores at two time points (12 hours and 24 hours) after surgery.
c. Post-operative nausea scores at two time points (12 hours and 24 hours) after surgery.
d. Post-operative pruritus scores at two time points (12 hours and 24 hours) after surgery.

iv. To determine the impact that the patients' post-operative pain had on their activities (movements in and out of bed, deep breathing or coughing, and sleeping), their emotional states and their perception of relief in the first 24 hours after surgery.

6.3 Research Methodology

The research methodology for this study was presented in chapter five.

6.3.1 **Data Analysis**

We analysed the prospectively collected data from patients who completed all trial requirements (per protocol cohort). Clinical data from manually completed data collection sheets (APPENDICES O, S and T) were entered into a spreadsheet using Microsoft® EXCEL® for MAC (Version 14.6.2).

Data were analysed using StatPlus, AnalystSoft Inc. - statistical analysis program for Mac OS®. (Version v6) and the statistical analysis program R (Version 3.2.3) (R Core Team, 2015)

Continuous parametric data was described using mean and standard deviation. Continuous non-parametric data was described using median and interquartile ranges. Categorical data was described using frequencies and percentages.

The post-operative pain scores at rest and with cough for both evaluation periods (12 hours and 24 hours) were described with minimum, maximum,

median values with interquartile ranges and compared using the Kruskal Wallis test. The side effect profiles of each treatment group for respiratory depression, sedation, nausea and pruritus were described using the frequencies of each of the allocated scores and compared using a Kruskal Wallis statistical test. The effect of pain on patient activities in bed (moving in bed, breathing deeply or coughing and sleeping), and out of bed were described using frequencies of the score categories and compared using a Chi-squared statistical analysis. The effects of pain on the patients' levels of anxiety were presented as a summary of the Numerical Rating Scale (NRS) scores of each group using minimum, maximum, median and interquartile ranges. These were compared between the three treatment groups using a Kruskal Wallis statistical test. The data were also categorized into four groups based on the impact of the pain on the patients' levels of anxiety. These data were described using the frequencies of the categories and compared using the Chi-squared test. The effects of pain on the patients' feelings of helplessness were presented as a summary of the NRS scores of each group. These were compared between the three treatment groups using a Kruskal Wallis statistical test. Pairwise comparisons between the three treatment groups were also performed using the Wilcoxon rank sum test. The patients' perception of their pain relief was described as a summary of the scores of each group and a comparison between the groups was made using the Kruskal Wallis statistical test. These data were also categorized into four groups based on the degree of pain relief that the patients felt, and reported as frequencies of the categories. The patients need for additional pain treatment was reported as the frequencies of two categories (yes and no), and the three treatment groups were compared using a Chi-squared test. Patients' scores of their level of satisfaction with their pain treatment was presented as a summary of the NRS scores of each group using minimum, maximum, median values and interquartile ranges. Comparisons between the three treatment groups were performed using a Kruskal Wallis statistical test. The data were also categorized into four groups based on the levels of satisfaction with treatment. These data were described using the frequencies of the categories and compared using the Chi-squared test.

6.4 Results and Discussion

The results and discussion of the primary objective of this study were presented in chapter five. In this chapter, the results and discussion related to the secondary objectives will be presented. The patient characteristics of the study population and the list of excluded patients have been presented in chapter five.

6.4.1 **Post-operative pain scores**

Patients' pain scores at rest and with cough were evaluated, using the NRS, at 12 hours and 24 hours after surgery. These results are summarized in table 6.1.

TABLE 6.1: NRS pain scores of patients at 12 and 24 hours after surgery

Pain Assessment	Group M100 (n=32)	Group M50 (n=29)	Group F25 (n=32)	p-value
Pain at rest at 12-hour assessment	Median = 1 Min = 0 Max = 6 IQR = 2.25	Median = 1 Min = 0 Max = 6 IQR = 2	Median = 1 Min = 0 Max = 9 IQR = 3.25	p = 0.1
Pain with cough at 12-hour assessment	Median = 2 Min = 0 Max = 9 IQR = 5	Median = 2 Min = 0 Max = 7 IQR = 3	Median = 3.5 Min = 0 Max = 10 IQR = 7	p = 0.08
Pain at rest at 24-hour assessment	Median = 2 Min = 0 Max = 8 IQR = 2.5	Median = 1 Min = 0 Max = 7 IQR = 3	Median = 2.5 Min = 0 Max = 10 IQR = 4	p = 0.3
Pain with cough at 24-hour assessment	Median = 3 Min = 0 Max = 8 IQR = 4.25	Median = 3 Min = 0 Max = 8 IQR = 4	Median = 5 Min = 1 Max = 10 IQR = 5	p = 0.08

In our study, pain was evaluated at rest and with cough at 12 and 24 hours after surgery. Pain measurement with cough was used to determine the level of pain that the patient experienced on movement as opposed to lying still in bed. Evaluation of pain with movement was a more accurate reflection of the real world situation that these women are exposed to, where they have to take care of their newborn babies.

Our results showed that there was no statistically significant difference in the pain scores at rest or with cough between the three groups at either of the two evaluation periods. The minimum pain score in all the groups at all evaluation times was zero. Maximum pain score reached 10/10 only in Group F25 for three out of the four evaluation points. This was in contrast to the statistically different pain VAS scores noted by Cardoso *et al* (1998). The authors of this study found that the pain scores of patients decreased as the dose of intrathecal morphine increased from 25µg to 50µg to 100µg. In addition, with each different dose of intrathecal morphine, the pain VAS scores were also reduced in the groups of patients who received regular doses of intramuscular diclofenac. However, pain scores in our study are in line with the results reported by Carvalho and Tenório (2013), who also evaluated the same doses of intrathecal morphine at two time periods after surgery (12 and 24 hours). Similar to our results, these authors did not find any statistically significant difference in patient pain scores between the two groups, at rest or with cough, at either time period evaluated. The patients in their study did not have access to PCA morphine in the post-operative period. Patients were given tramadol hydrochloride as rescue analgesia when required. Girgin *et al* (2008) also reported no difference in pain VAS scores at four hours and 24 hours after surgery between all the intrathecal opioid groups they evaluated (100µg, 200µg, 300µg and 400µg), and also in comparison with the control group (no intrathecal opioid used). Despite the similar pain VAS scores in these groups, there was a significant decrease in PCA morphine used with the increasing doses of intrathecal morphine evaluated, which is similar to what we have observed in our study.

One explanation of why there is no statistical difference in the pain NRS scores between each of the three groups in our study is that patients were repeatedly counseled on how to use the PCA pump to manage their pain, and could therefore freely administer analgesics to themselves (within the confines of the safety parameters set on the PCA pumps). The patients were therefore able to effectively manage their pain with intravenous opioids, and subsequently the pain NRS score reflected good analgesia and cannot be considered to be a true reflection of the effectiveness of their intrathecal opioid.

6.4.2 **Side effects profile**

Patients were monitored and evaluated for the common side effects associated with intrathecal opioids i.e. respiratory depression, sedation, nausea and vomiting, and pruritus.

6.4.2.1 **Respiratory Depression**

Respiratory depression is an important side effect of opioid use and is of particular concern with regards to the use of intrathecal opioids, as discussed in chapters 3 and 4. Current literature states that the risk of respiratory depression after the use of intrathecal morphine is low. Dahl *et al* (1999) calculated that the number needed to harm (NNH) for respiratory depression with all types of opioids and using multiple doses, is 476 and is not significantly different from control groups.

We assessed the respiratory rate of patients in our study at two time points after surgery (12 hours and 24 hours). The Box and Whisker plot illustrating the respiratory rates for each of the three patient groups at the 12-hour and 24-hour assessments is shown in Figures 6.1 and 6.2.

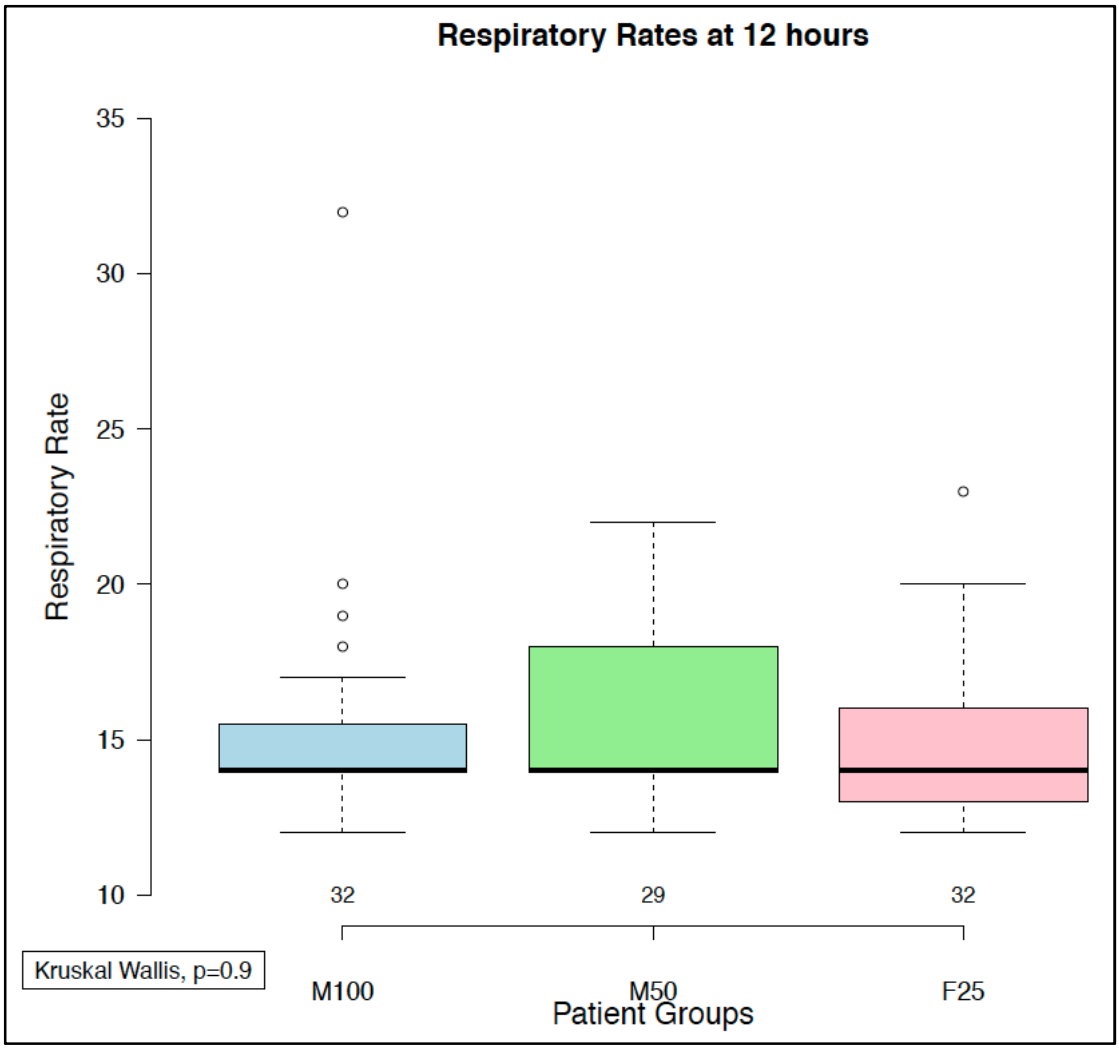


FIGURE 6.1: Box and Whisker plot of respiratory rates at 12-hour assessment

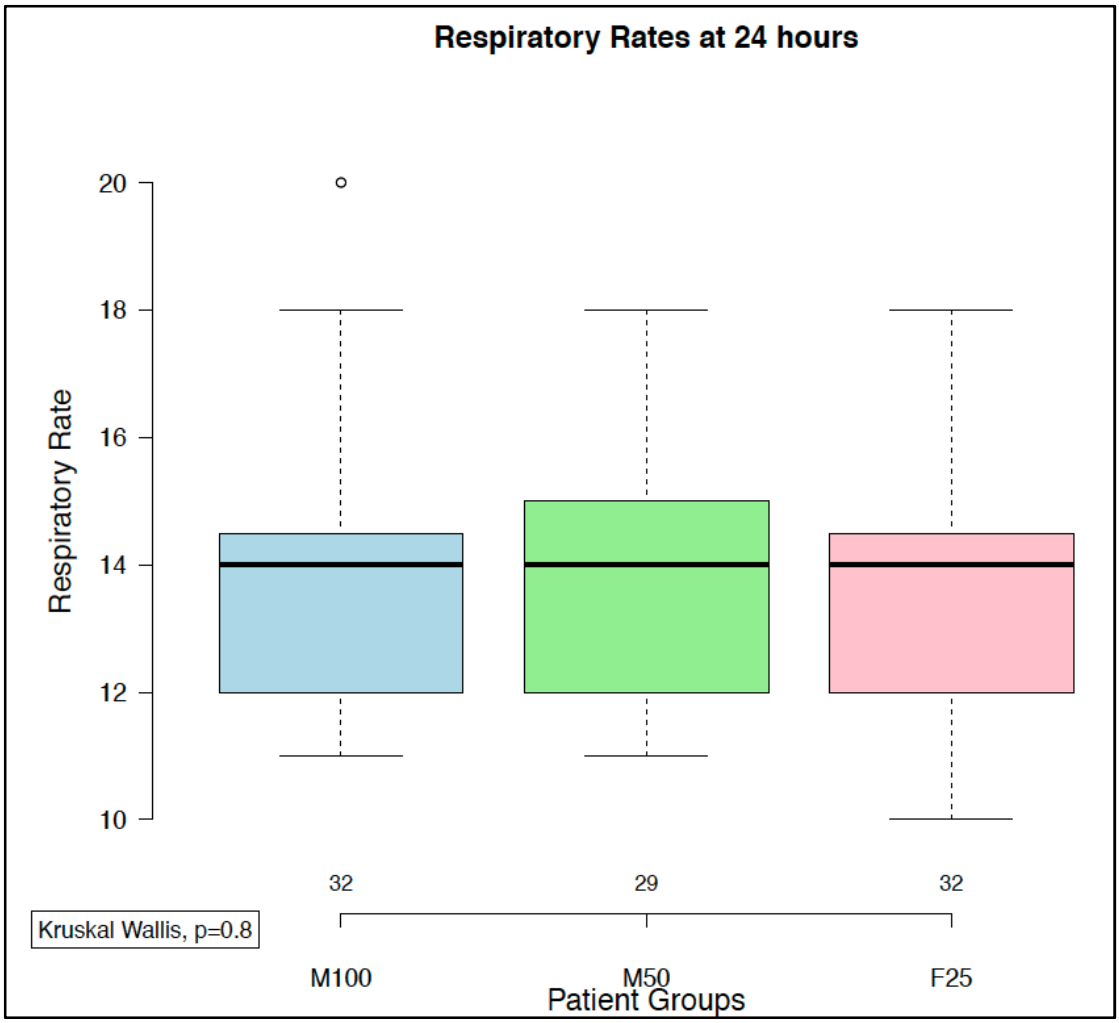


FIGURE 6.2: Box and Whisker plot of respiratory rates at 24-hour assessment

There were no cases of bradypnoea in our study. The median respiratory rate was 14 for all three treatment groups at both the 12-hour and 24-hour assessments. The lowest respiratory rate documented was ten, and was documented at the 24-hour assessment in Group F25. Since intrathecal fentanyl only has a duration of action of one to four hours (Lundgren *et al.*, 2016), it is unlikely that this respiratory rate of ten was related to the intrathecal opioid. Statistical comparisons of the three treatment groups confirmed that there was no significant statistical difference in the respiratory rates between the three groups at the 12-hour assessment (Kruskal Wallis, p=0.9) or the 24-hour assessment (Kruskal Wallis, p=0.8).

The consequences of respiratory depression can be catastrophic, especially if a serious case is not detected and treated appropriately, however the risk of this side effect appears to be very low, especially when using low doses of intrathecal morphine, as was done in our study. Kato *et al* (2008) conducted a retrospective review of 1915 obstetric patients who had received 150µg intrathecal morphine during their spinal anaesthetics, over a seven-year period, and reported that only 5/1915 patients experienced respiratory depression that could be attributed to the intrathecal opioids. Of these patients, only one patient had severe respiratory depression that required naloxone therapy. Abouleish *et al* (1991) studied the effects of 200µg intrathecal morphine in 856 women having caesarean section surgeries. These authors defined respiratory depression as an arterial oxygen saturation(SpO2) < 85% or a respiratory rate < 10 breaths per minute. Only 8/856 (0.93%) of patients were documented to experience respiratory depression. All of these patients were noted to be markedly obese. The morphine doses used in our study were 33% (Group M100) and 66% (Group M50) lower than the doses studied in the Kato *et al* (2008) review and also at least 50% lower than the dose evaluated in the Abouleish *et al* (1991) study. Based on the results of their clinical investigations, Palmer *et al* (1999) concluded that the side effects of intrathecal morphine are directly proportional to the dose of morphine used, however their study was not designed to detect respiratory depression. The very low doses of intrathecal morphine that we have studied are therefore less likely to cause to respiratory depression, than the risks quoted by both Kato *et al* (2009) and Abouleish *et al* (1991).

The dose of intrathecal morphine that is used in an obstetric spinal anaesthetic is an important factor to consider when evaluating the risk of respiratory depression. Carvalho and Tenório (2013) reported no cases of respiratory depression in their series of 123 patients using doses of intrathecal morphine similar to what we used in our study (50µg and 100µg). The authors noted that the absence of respiratory depression in their cohort did not mean that the risk is negligible but rather that the sample size of their study may have been too low to detect it considering that this is a rare side

effect. Mikuni *et al* (2009) also investigated the effects of 50µg and 100µg intrathecal morphine and reported no cases of respiratory depression in their study of 76 patients. Cardoso *et al* (1998) and Salmah and Choy (2009) reported that no patients experienced respiratory depression in their studies of 120 and 60 patients respectively. While we also had no cases of respiratory depression in any of our treatment groups, our study was not powered to detect respiratory depression differences. The results that we obtained in our study, with regards to the incidence of respiratory depression, does however appear to be corroborated by similar findings of comparatively sized studies investigating similar doses of intrathecal opioids.

6.4.2.2 **Sedation**

Patients' levels of sedation were evaluated at the two post-operative evaluation periods using the three-point scale described in the methodology section of chapter five (section 5.6.5)

The levels of sedation were low in all patients. The majority of patients had a sedation score of zero or one in all the treatments groups at both time points. No patients were evaluated to have a sedation level of three in any of the treatment groups. We determined that there was no statistical difference in the sedation scores of patients between any of the treatment groups at 12 hours (Kruskal Wallis, p=0.8) and 24 hours (Kruskal Wallis, p=0.2). These results are illustrated in Figures 6.3 and 6.4.

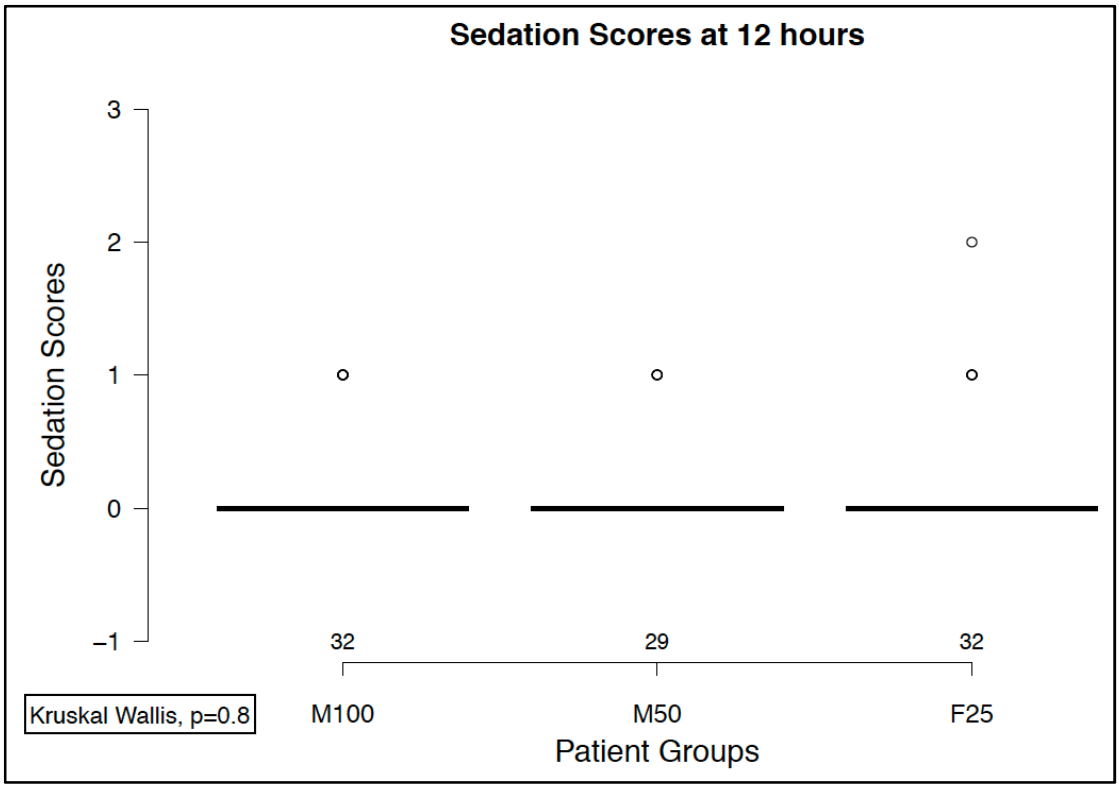


FIGURE 6.3: Box and Whisker plot of sedation scores at 12-hour assessment

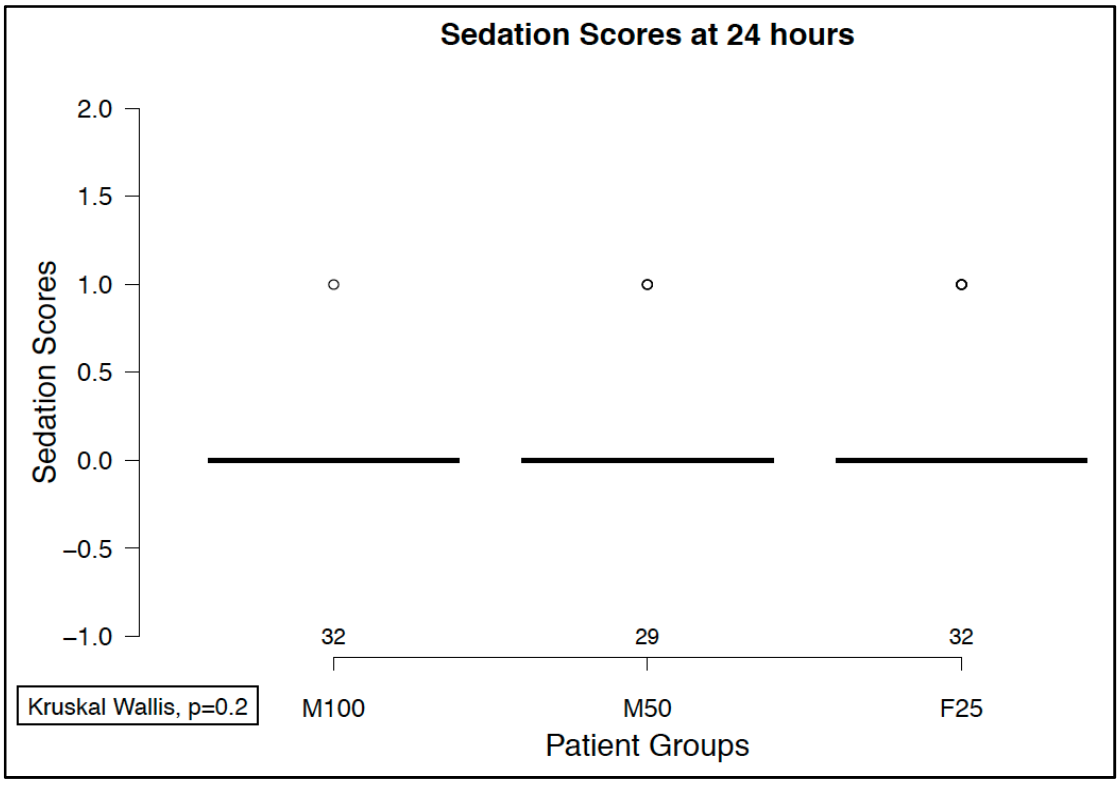


FIGURE 6.4: Box and Whisker plot of sedation scores at 24-hour assessment

Using the same intrathecal morphine doses that we have used, Carvalho and Tenório (2013) reported that there were no cases of sedation in their cohort of 123 patients being evaluated for differences in efficacy and side effects of the two different doses of intrathecal morphine. In a double-blinded placebo controlled evaluation of oral treatments to manage the side-effects of intrathecal morphine, Abboud *et al* (1990) reported a 23% incidence of somnolence in patients receiving 250µg intrathecal morphine as part of their anaesthetic for their caesarean section. Side effects associated with intrathecal morphine tend to increase as the dose of morphine increases (Palmer *et al*., 1999). The lower doses of morphine used in our study, and in the study by Carvalho and Tenório (2013), were mostly likely to be the reason that somnolence was not a problem for any of the patients in these studies.

The goal of improved analgesic levels in women after caesarean section surgery is to support mother-baby interactions in the early post-operative period. High levels of sedation would be counter-productive to this goal. The absence of high levels of sedation in our study was therefore an important finding, as this could facilitate bonding between the mother and baby in the post-operative period.

6.4.2.3 **Nausea**

We evaluated patients for nausea at 12 and 24 hours after surgery. The majority of patients had no nausea at the 12-hour assessment (68/92) and 24-hour assessment (78/82). There were however six patients (5/32 (15%) in Group M100 and 1/31 (3%) in Group F25) who had severe vomiting and required treatment at the 12-hour assessment. Their data were excluded from the 24-hour analysis. One patient in Group F25 had severe vomiting which required treatment prior to the 12-hour assessment, and therefore this patient's 12-hour assessment was excluded from analysis. At the 24-hour assessment only 2/30 (6.7%) patients in Group F25 reported severe vomiting requiring treatment. The nausea and vomiting scores are illustrated in Figures 6.5 and 6.6.

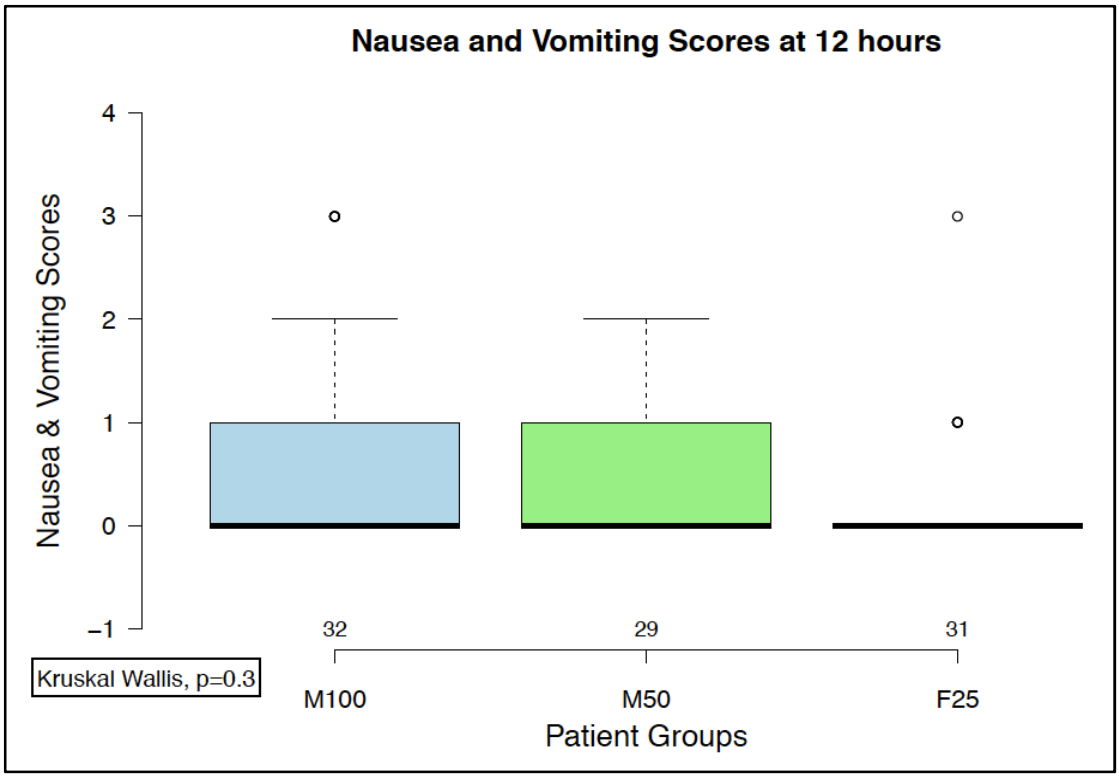


FIGURE 6.5: Box and Whisker plot of nausea scores at 12-hour assessment

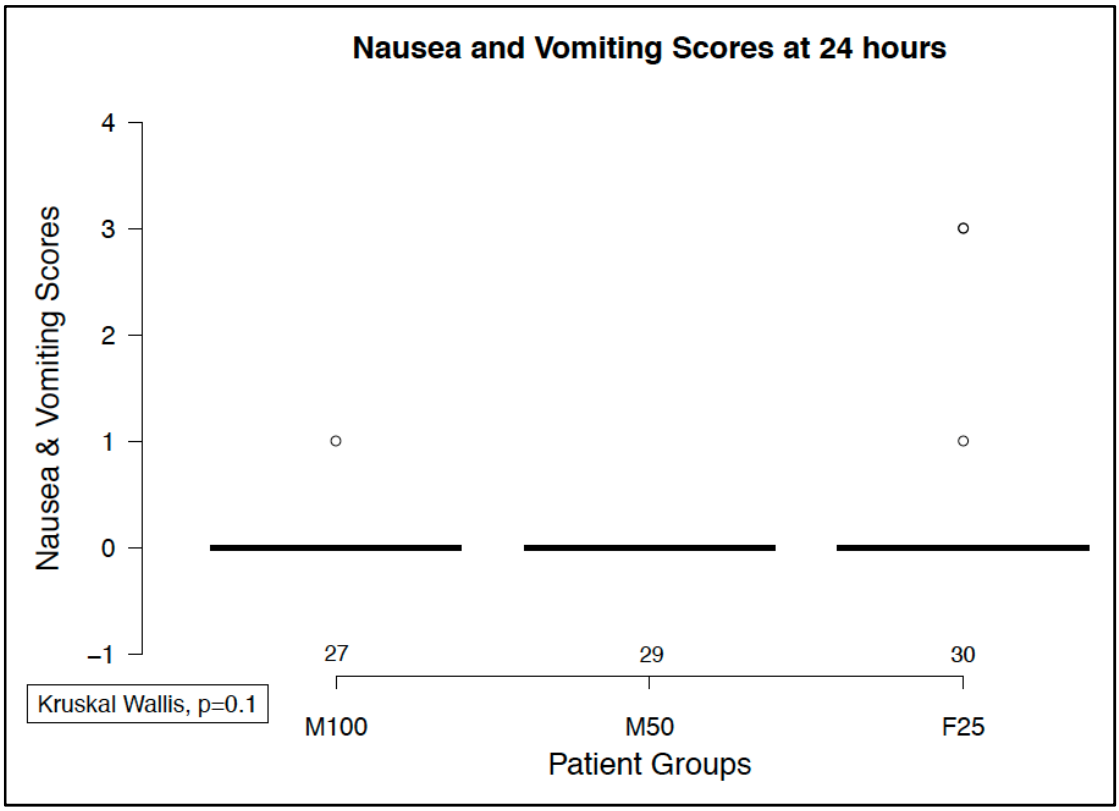


FIGURE 6.6: Box and Whisker plot of nausea scores at the 24-hour assessment

The occurrence of post-operative nausea and vomiting (PONV) following neuraxial morphine administration is reported to occur in up to 80% of patients (Dominguez and Habib, 2013). In our study only 15% of patients had severe nausea and there was no statistical difference between the three groups of patients for the occurrence of nausea and vomiting at 12 hours (Kruskal Wallis, p=0.3) and 24 hours (Kruskal Wallis, p=0.1).

Mikuni *et al* (2009) compared similar doses of intrathecal morphine as we have investigated, and reported PONV in 8% (2/25) of patients in the 50µg morphine group and 20% (5/25) in the 100µg morphine group, but did not find a statistical difference in the occurrence of PONV between any of the patient groups (0µg, 50µg and 100µg intrathecal morphine). Sarvela *et al* (2002) also found that PONV occurred in 16% of patients in the 100µg intrathecal morphine group and this increased to 28% in the 200µg intrathecal morphine group, but again there was no statistical difference in the occurrence of PONV between these groups. The results of these studies and of our study concur with the opinions expressed by Palmer *et al* (1999), that there does not appear to be a relationship between the dose of intrathecal morphine used and the occurrence of PONV. Salmah and Choy (2009) found a high incidence of PONV in both the fentanyl and the morphine groups (48.1% vs. 63.6%) in the first six hours after surgery in their study. There was also a statistically higher number of patients, in the 100µg intrathecal morphine group, that required intravenous treatment for PONV compared to the 25µg fentanyl group (54.5% vs. 14.8%) ($p<0.04$). These results are higher than those found in our study where only 15%(5/32) and 6.3%(2/32) of patients required treatment for PONV in the 100µg morphine and 25µg fentanyl groups respectively. No patients required treatment for PONV in the 50µg morphine group. Based on the results of Salmah and Choy (2009) and of our study, it appears that 50µg intrathecal morphine is the most suitable dose to use, with regards to having the lowest risk of PONV. However, our study was not powered to detect any differences in PONV between the three treatment groups and the recommendations regarding the appropriate dose of intrathecal morphine must be read with this in mind.

6.4.2.4 **Pruritus**

Itchiness after surgery is an issue of great concern for patients who are having a caesarean section (Carvalho *et al*., 2005). Pruritus can have a negative influence of a patient's level of satisfaction with the post-operative care after a caesarean section. We scored patients' pruritus based on their experiences at two time points after surgery (12-hours and 24-hours). The results of these evaluations are illustrated in Figures 6.7 and 6.8.

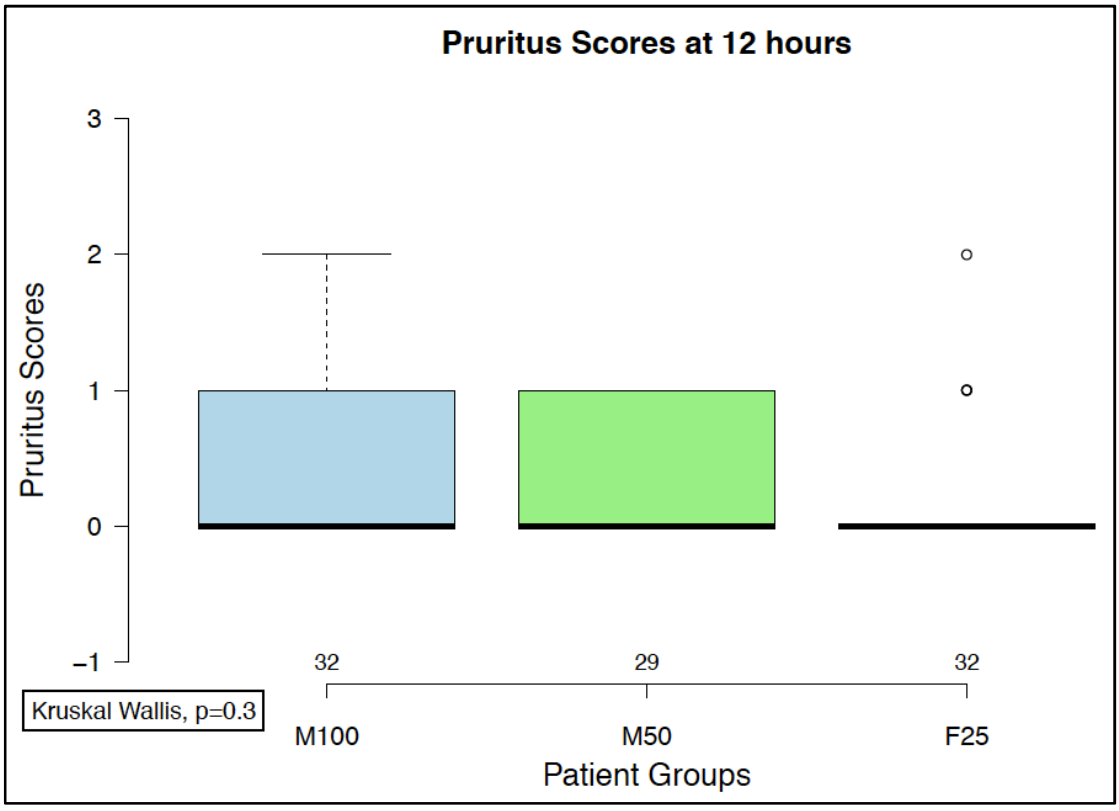


FIGURE 6.7: Box and Whisker plot of pruritus scores at the 12-hour assessment

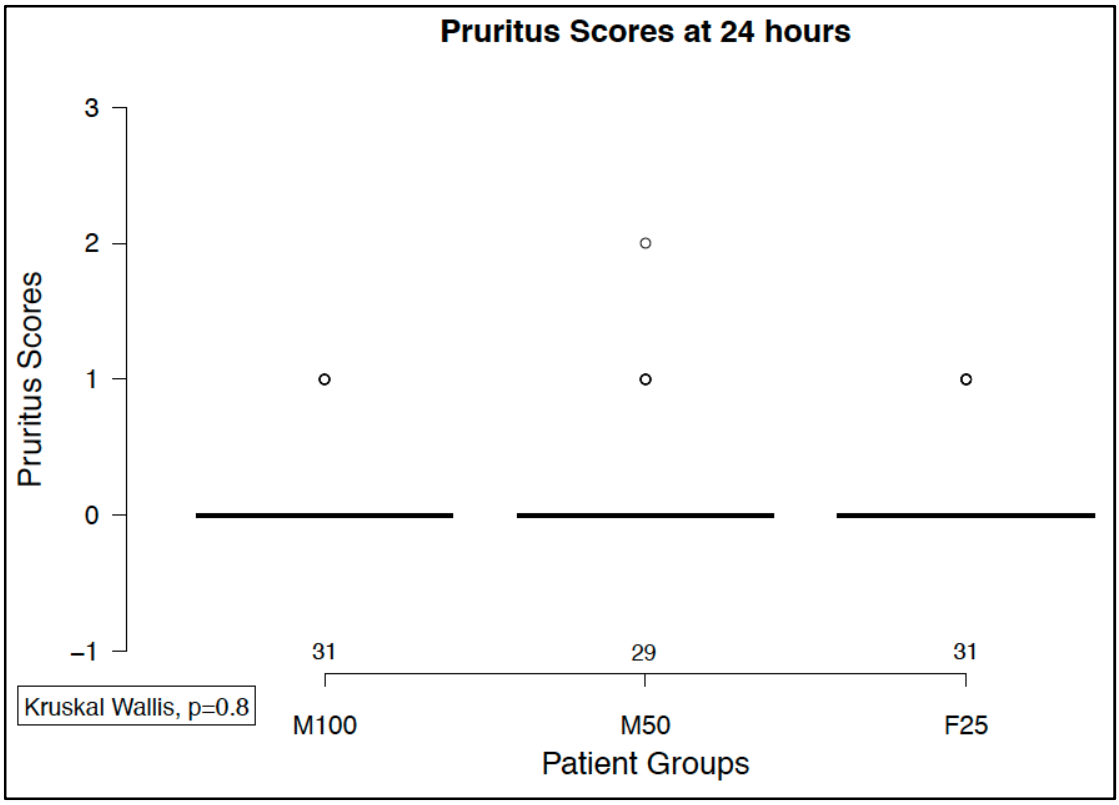


FIGURE 6.8: Box and Whisker plot of pruritus scores at the 24-hour assessment

Most patients in the study had no pruritus or only mild to moderate pruritus that did not require treatment. Only 1/32 (3.125%) patient from Group M100, and 1/32 (3.125%) patient from Group F25 had severe pruritus, which required treatment, in the first 12 hours after surgery. These patients' data were excluded from the pruritus data analysis at the second assessment because they received treatment for pruritus at the 12-hour assessment. At the 24-hour assessment 1/29 (3.4%) patient in the M50 group had severe pruritus, however the patient refused treatment, and was included in the data analysis. There was no statistical difference between the three groups for pruritus at either the 12-hour assessment (Kruskal Wallis, p=0.3) or the 24-hour assessment (Kruskal Wallis, p=0.8).

Dahl *et al* (1999) conducted a systematic review of randomized controlled trials addressing the analgesic efficacy and adverse effects of intrathecal opioids used for anaesthesia for caesarean section surgery. The authors calculated that the NNH for pruritus with intrathecal morphine was 2.6

(95%CI, 2.1 – 3.3) and with fentanyl was 2.2 (95%CI, 1.8 – 2.7). McDonnell *et al* (2009) estimated that 43% of patients would experience pruritus when given a 100µg dose of intrathecal morphine. The results of our study do not agree with this calculation. Only 3% of patients in Group M100 in our study experienced pruritus that required treatment. If we include the patients who experienced mild pruritus (not requiring treatment), the incidence of pruritus for patients in Group M100 is still only 9/32 (28%) at the 12-hour evaluation and 5/31 (16%) at the 24-hour assessment. Mikuni *et al* (2009) found no difference in the frequency of pruritus between patients in the 50µg and 100µg intrathecal morphine groups, but did find a statistically significant difference in the frequency of pruritus between the 100µg morphine group and the control group. The frequency of pruritus was 10/25(40%) in the 50µg group and 16/25(64%) in the 100µg morphine group in their study. This was higher than the occurrence of pruritus in the same groups in our study. Carvalho and Tenório (2013) reported that in both their 50µg and 100µg intrathecal morphine groups there was a higher incidence of pruritus experienced at the first post-operative evaluation (12 hours) compared to the second evaluation (24 hours) (67% and 83% vs. 17% and 30% respectively). In their 100µg group, patients ranked pruritus as the 2nd most important factor that caused them discomfort over the 24 hours after surgery. Pain was ranked as the most important factor. Cardoso *et al* (1998) used a combination of intrathecal morphine and IV NSAIDs to treat post-caesarean section pain and also found a statistically greater incidence of pruritus in the 100µg morphine groups irrespective of whether NSAIDs were used. Palmer *et al* (1999) found that the risk of developing pruritus and the need for treatment increases in direct proportion to the dose of intrathecal morphine. In our study there was no statistical difference in the occurrence of pruritus between the two morphine groups despite the increased dosage used in Group M100. Salmah and Choy (2009) compared 100µg intrathecal morphine to 25µg intrathecal fentanyl and similar to our study, found no difference in the incidence of pruritus between the morphine and fentanyl groups. However, the incidence of pruritus in each group was 54.1% vs. 51.8% respectively. This is much higher than the incidence observed in our study.

The low incidence of pruritus in all groups in our study is not in keeping with comparative studies investigating the efficacy of similar doses of intrathecal opioids. This discrepancy may be explained by our patient population having a higher tolerance of pruritus, or a fear to report the side effects. Investigating the reasons behind this statistical anomaly is warranted for future studies but is beyond the scope of this study.

6.4.3 **Effect of pain on patient activities**

Pain and medication side effects are important considerations when evaluating the success of post-operative analgesia, however it is also important to assess the effect that pain has on the patients activities in the post-operative period.

Good pain management after surgery will enable the recovering patient to be more physically active and mentally alert (Breivik, 1995). It is important for a new mother to be mobile in order to allow her to take care of, and bond with, her newborn baby. Pain can have a negative impact on her ability to do this by limiting the mother's ability to move around and also because of the negative emotional impact that it can have on her psyche (Stephens *et al.*, 2003).

We evaluated the effect that the patients' pain had on their post-operative experiences in the first 24-hours after surgery addressing issues related to their activities, the impact on their emotional state and also their level of satisfaction with their analgesia after surgery. These results are discussed below.

6.4.3.1 **Activities in bed**

Patients were asked to rate, on a scale from 0 to 10, how much their pain interfered with or prevented them from:

a) Doing activities in bed

The responses were categorized into groups based on the score they allocated to the level of interference. The results of the impact of the pain on their activities in bed are illustrated in Figure 6.9.

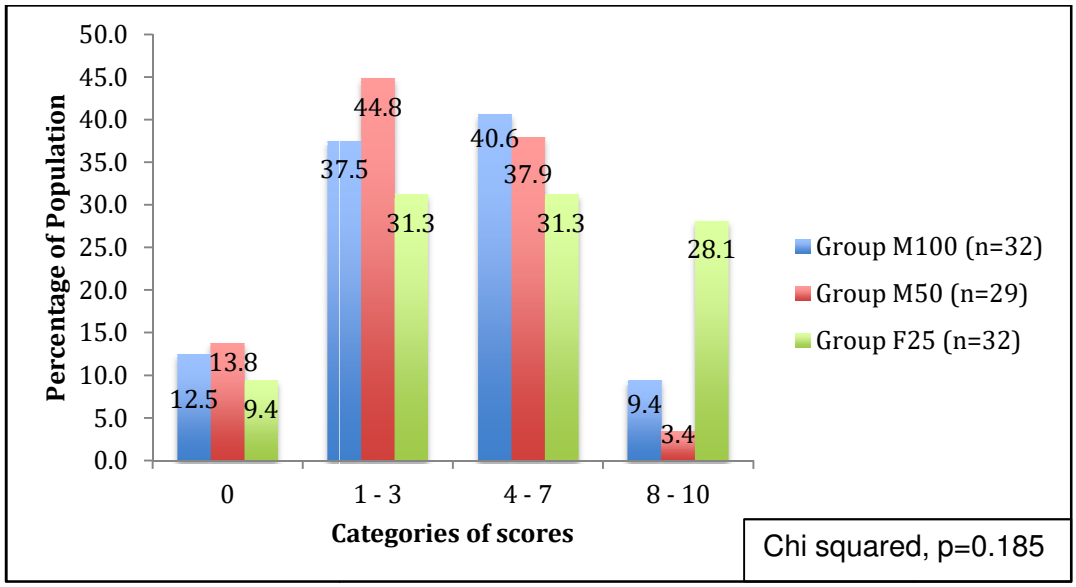


FIGURE 6.9: Influence of pain on patients' activities in bed

In our study, 9/32 (28%) of patients in Group F25 reported that their pain severely impaired (scores = 8 – 10) their activities while they were in bed. This was compared with 3/32 (9%) in Group M100 and 1/29 (3%) in Group M50. Analysis of these results indicated that there was no statistical difference between the different groups responses regarding the impact of the pain on their activities (Chi-squared, p=0.185).

b) Breathing deeply or coughing

Patients scored the level of interference that their pain had on their ability to breath deeply or cough. This data was sorted into four categories according to level of impact and is graphically depicted in Figure 6.10.

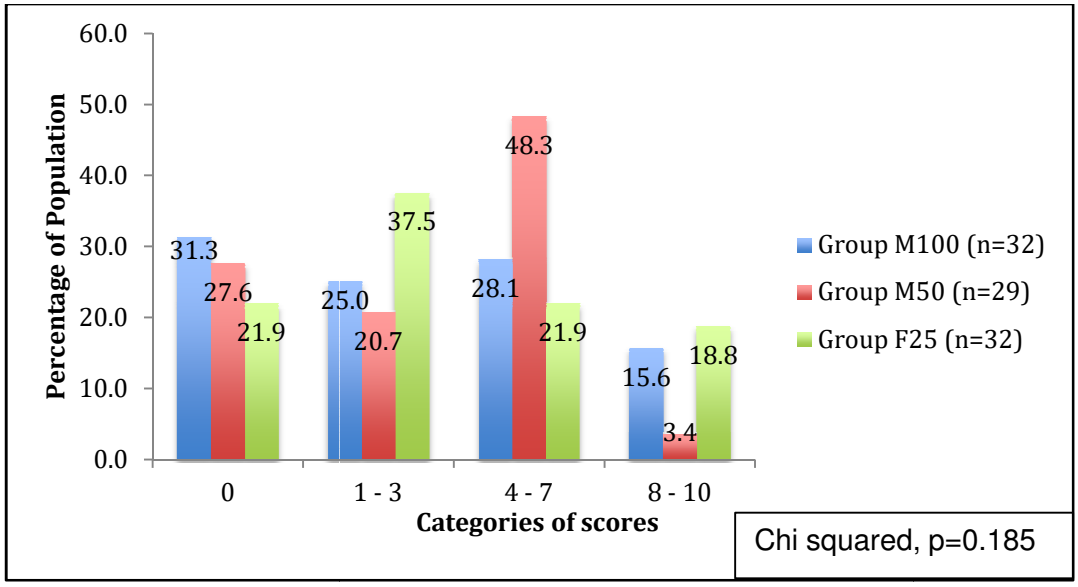


FIGURE 6.10: Influence of pain on patients' ability of breath deeply or cough

30/93 (32%) of patients across all three treatment groups (Group M100 - 9, Group M50 - 14, Group F25 - 7) reported that their pain only moderately (scores = 4 - 7) affected their ability to breathe deeply or cough in the 24 hours after surgery. Surprisingly, more patients in Group M100 (5/32) indicated that their breathing was severely affected (scores = 8 – 10) by pain than in Group M50 (1/29), despite the fact that the patients in Group M50 received a lower dosage of intrathecal morphine. Reduction of breathing movements can result in lower tidal volumes, and decreased minute ventilation during the post-operative period and this can lead to collapse of the alveoli and a reduction in oxygen transport across the pulmonary membranes (Stephens *et al*., 2003). Pulmonary complications following surgery can have dire long-term consequences for the patients. Statistical analysis showed that there was no significant difference between the treatment groups with

regards to the effect of pain on the patients' abilities to breathe deeply or cough (Chi-squared, p=0.185).

c) Sleeping

Most patients only regarded their pain as mildly affecting their ability to sleep (scores = 1 – 3), and there was no statistical difference between the three treatment groups in this study (Chi-squared, p=0.851). A summary of the responses to this question is illustrated in Figure 6.11.

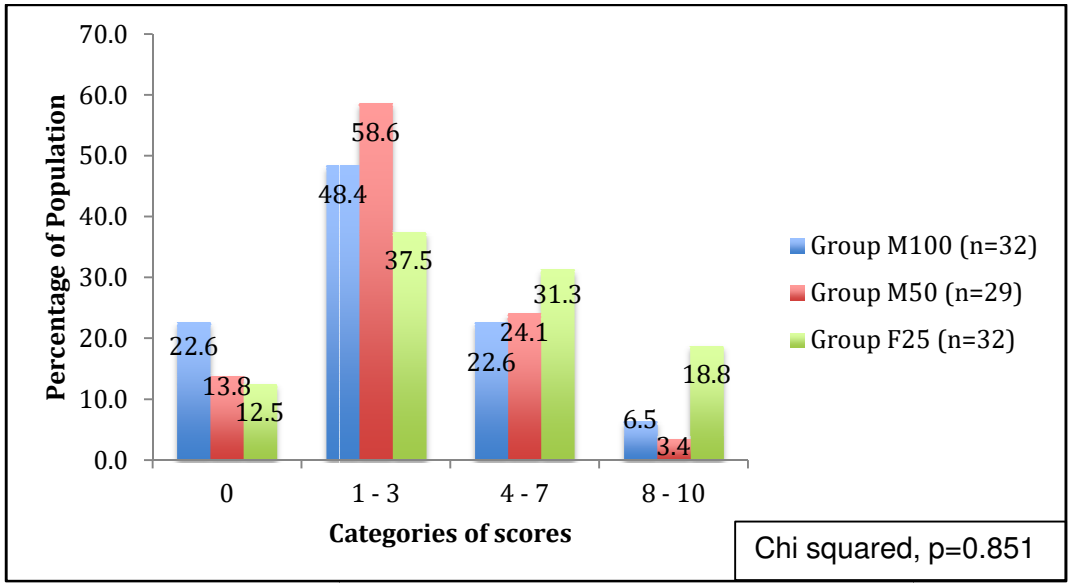


FIGURE 6.11: Influence of pain on patients' ability to sleep

6.4.3.2 **Activities out of bed**

Patients were asked, if they had been out of bed, how much did their pain interfere with or prevent them from doing activities out bed.

One patient in Group M100 and one patient in Group F25 had not been out of bed at the time of the 24-hour assessment and therefore did not respond to this question. The results of this question are illustrated in Figure 6.12.

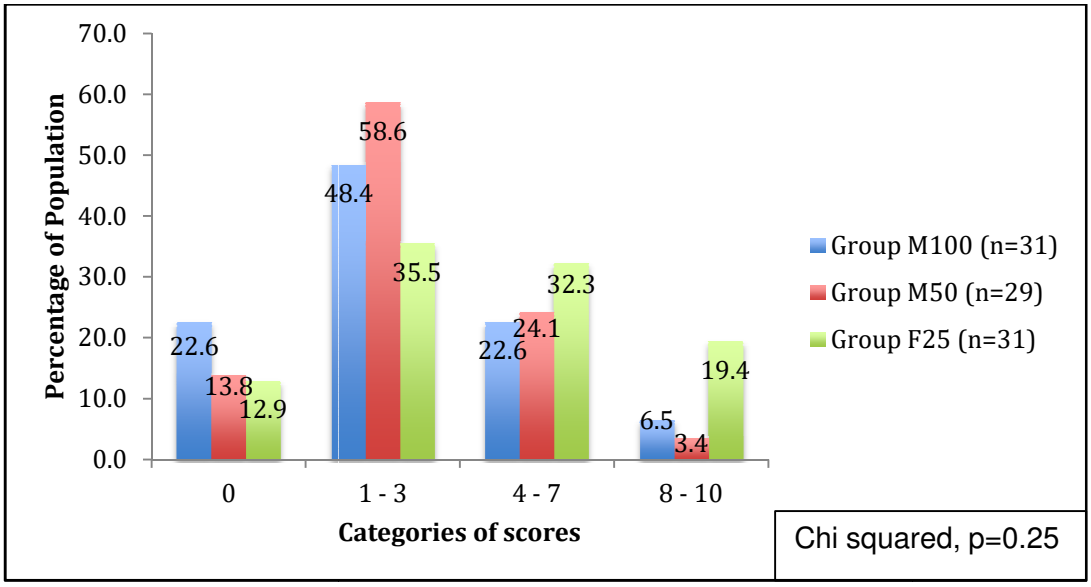


FIGURE 6.12: Influence of pain on patients' activities out of bed

Of the 91/93 patients who had mobilized out of their bed by the time the 24-hour assessment was done, there were 6/31 (19%) patients from Group F25 who indicated that the pain severely limited (scores = 8 – 10) their activities while out of bed. Fewer patients in groups M100 (2/31, 6.5%) and M50 (1/29, 3.4%) found the pain to be severely limiting to their out of bed activities. There was however no statistical difference between the three groups with regards to the interference caused to out-of-bed activities (Chi-squared, p=0.25). The post-operative pro-inflammatory state increases the risk of developing a DVT (Stephens *et al*., 2003) therefore early mobilization is an important preventative measure to avoid this complication. Practically, the limitation of out-of-bed activities will impact the mother's ability to bath and change her baby in the first day after birth. Karlstrom *et al* (2010) reported that half of the patients in their study described their post-operative pain as having a large negative impact on their ability to take care of their babies. Feeding and caring for the newborn infant is an important part of bonding process between the mother and baby, and therefore should be assisted by good pain control as much as possible. The trend towards fewer patients in the intrathecal morphine groups having their activities severely affected by their pain, implies that patients in these treatment groups may have been more likely to take care of their babies with less strain.

6.4.4 **Effect of pain on emotional state**

The International Association for the Study of Pain defines pain as "an unpleasant sensory or emotional experience associated with actual or potential tissue damage or described in terms of such damage" (Merskey *et al*., 1979). Pain can therefore have an important influence on a patient's state of mind. This is especially true in the post-partum patient, who is experiencing changes in their hormone levels (Smith *et al*., 1990), which places them at increased risk of emotional lability.

We asked patients to rate the impact that their pain had on their emotional state with particular reference to their levels of anxiety and of feelings of helplessness.

Patients were asked how much the pain caused them to feel:

a) Anxious

These results are summarized in table 6.2.

TABLE 6.2: Summary of NRS scores on the impact of pain on patients' state of anxiety

Assessment	Group M100 (n=32)	Group M50 (n=29)	Group F25 (n=32)	p-value
Level of Anxiousness	Median = 0 Min = 0 Max = 9 IQR = 4	Median = 3 Min = 0 Max = 10 IQR = 5	Median = 2 Min = 0 Max = 8 IQR = 5	p = 0.25

The median score in all three groups was low. There was no statistical significance between the three treatment groups (Kruskal Wallis, p=0.25).

In order to make this data more meaningful, we categorized the data in to four groups based on the significance of the impact on their state of anxiety: no impact (score = 0), mild impact (scores = 1 - 3), moderate impact (scores = 4 - 7), extreme impact (scores = 8 - 10). These results are illustrated in Figure 6.13.

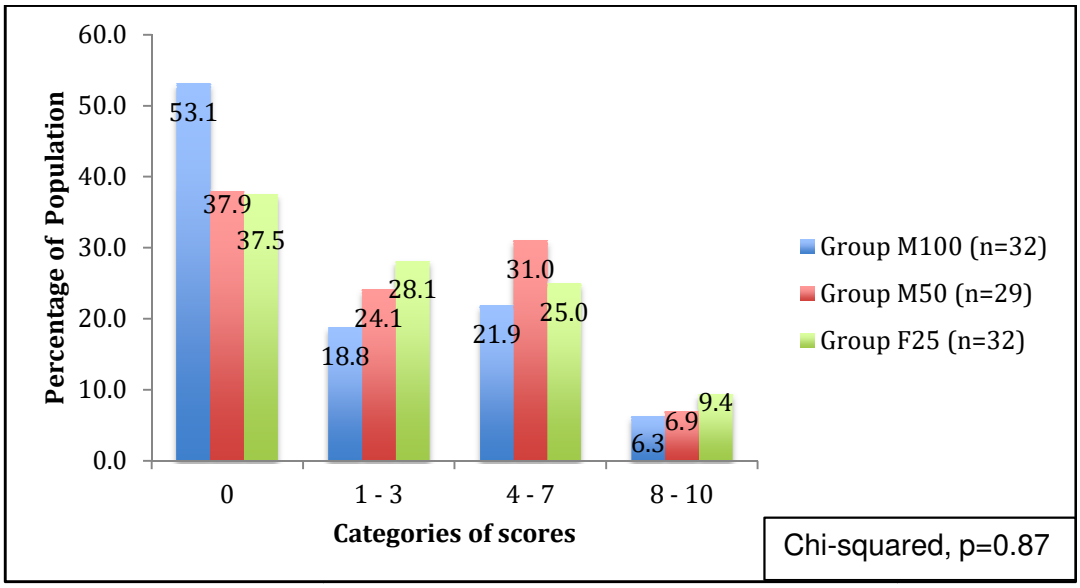


FIGURE 6.13: Summary of the categories of impact of pain on anxiety

Pain and discomfort can have a profound impact on a patient's perception of their quality of life and their sense of health (Skevington, 1998). In addition, inadequate pain management or increased side effects from analgesics can reduce a patient's quality of life, especially if this poor analgesia occurs over an extended period (Breivik, 1995). The majority of patients in all three treatment groups in our study, did not think that their pain had any impact on their level of anxiety (Group M100-17/32, Group M50-11/29, Group F25-12/32) by indicating a score of zero. There is no significant difference, either, in the categories of impact between the three treatment groups (Chi-squared, p = 0.87). However, this does not necessarily imply that patients were not experiencing anxiety. It merely means that the patients did not think that their pain was impacting their anxiety. As all patients in the study were new mothers, it is not unreasonable to assume that they all were experiencing some level of anxiety associated with being a new parent. This study was however not designed to evaluate levels of anxiety in the treatment groups.

b) Helplessness

The scores of each of the three treatment groups for this question are summarized in Figure 6.14.

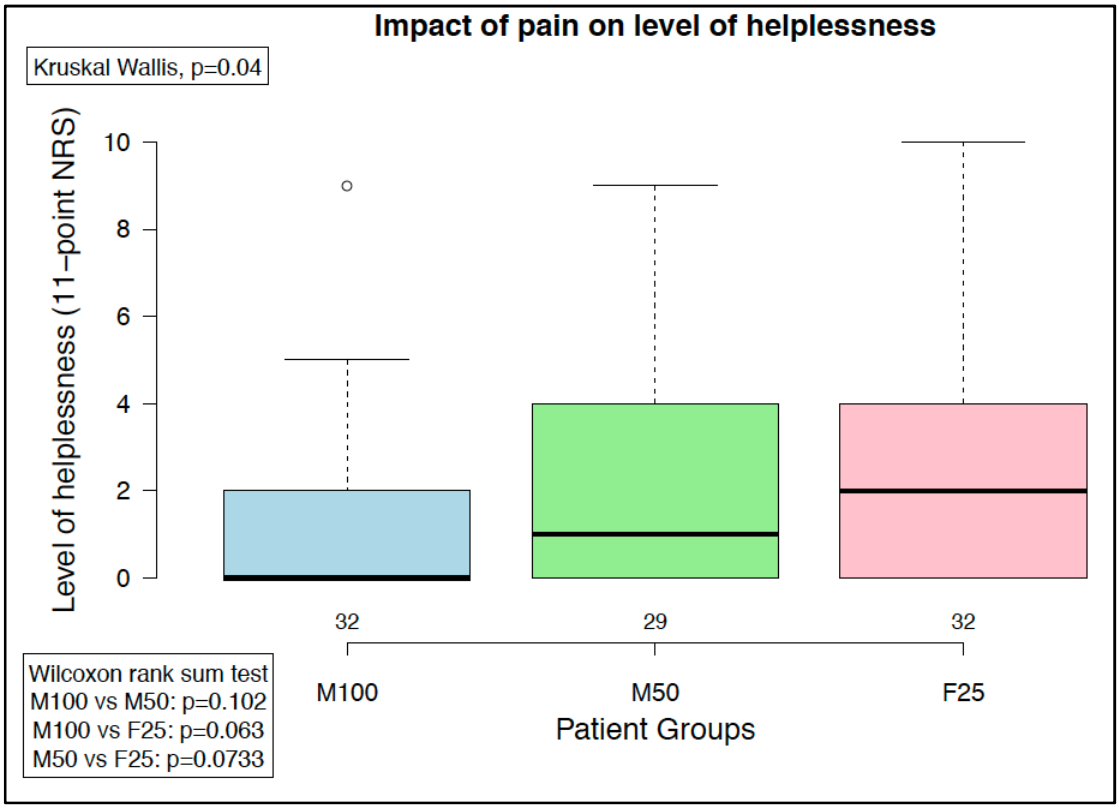


FIGURE 6.14: Summary of NRS scores on the impact of pain on patients' level of helplessness

Initial analysis of the scores rating the impact of pain on patients' feelings of helplessness, using the Kruskal-Wallis analysis, showed that there was a statistical difference between the three treatment groups with regards to the effect that their pain had on their state of helplessness (Kruskal Wallis, p=0.04). We then conducted pairwise comparisons using the Wilcoxon rank sum test on the data, to determine exactly where this difference occurs. The more detailed analysis of the groups showed that there was no statistical difference between the groups. This anomaly in the statistical significance was due to the sample not being powered to determine a difference in this parameter.

Our results seemed to indicate that there was a trend that pain has an increased impact on patients' perceptions of helplessness in the treatment Group F25. This was also the group that used a statistically higher amount of PCA morphine in the first 24-hours after surgery. This may imply that poor pain control contributes to greater feelings of helplessness, however this relationship will have to be investigated further in a study powered to assess this relationship.

6.4.5 **Patient satisfaction**

The level of patient satisfaction after surgery is a complex issue to probe. There are many confounding factors that will influence whether a patient is satisfied with their post-operative experience. Pain forms one part of this complex issue.

Patients were asked how much pain relief (in percentage) they have received since their surgery. The results of this question are summarized in Figure 6.15.

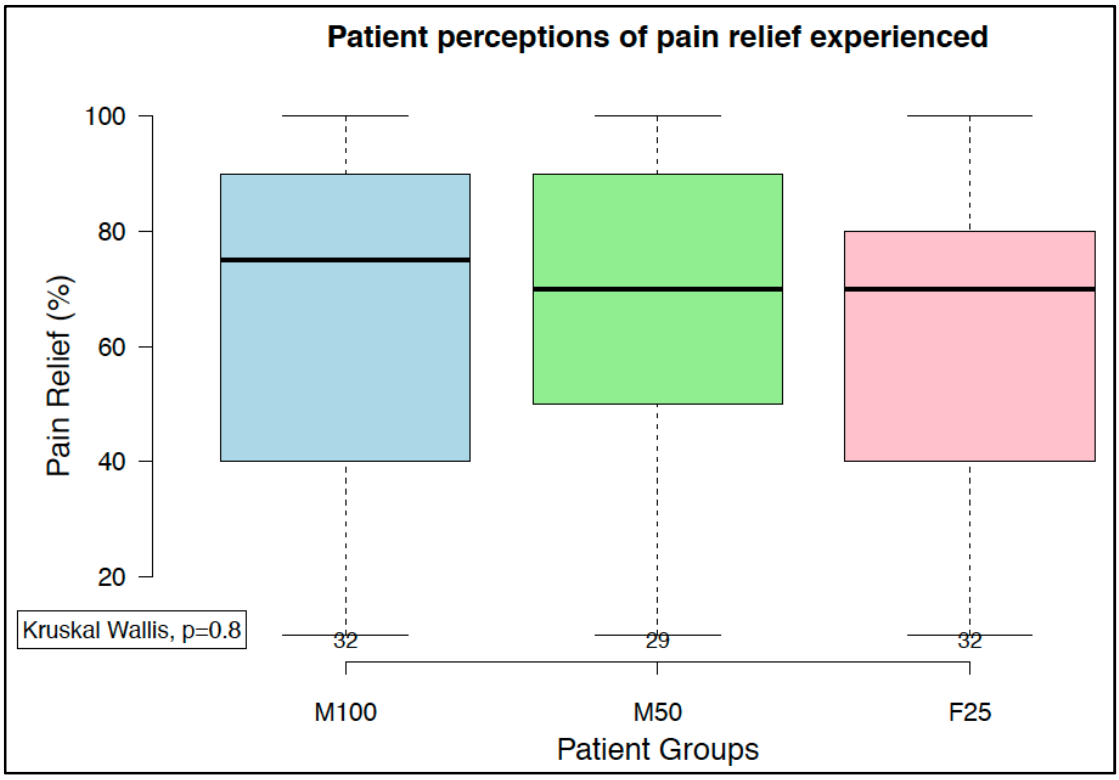


FIGURE 6.15: Summary of scores of percentage of pain relief perceived by the patient

The pain relief experienced by patients in all three treatment groups was very similar. The maximum relief recorded in all groups was 100% and all groups had a similar median (Group M100=75, Group M50=70, Group F25=70). No patient in this study, irrespective of their allocated treatment group expressed that they had no pain relief. Statistical analysis showed that there was no statistical difference between the three treatment groups (Kruskal Wallis, p=0.8).

Categorizing the same data into groups, based on impact, also reveals that the majority of patients in all groups in our study experienced a high level of pain relief after surgery. These results are illustrated in figure 6.16.

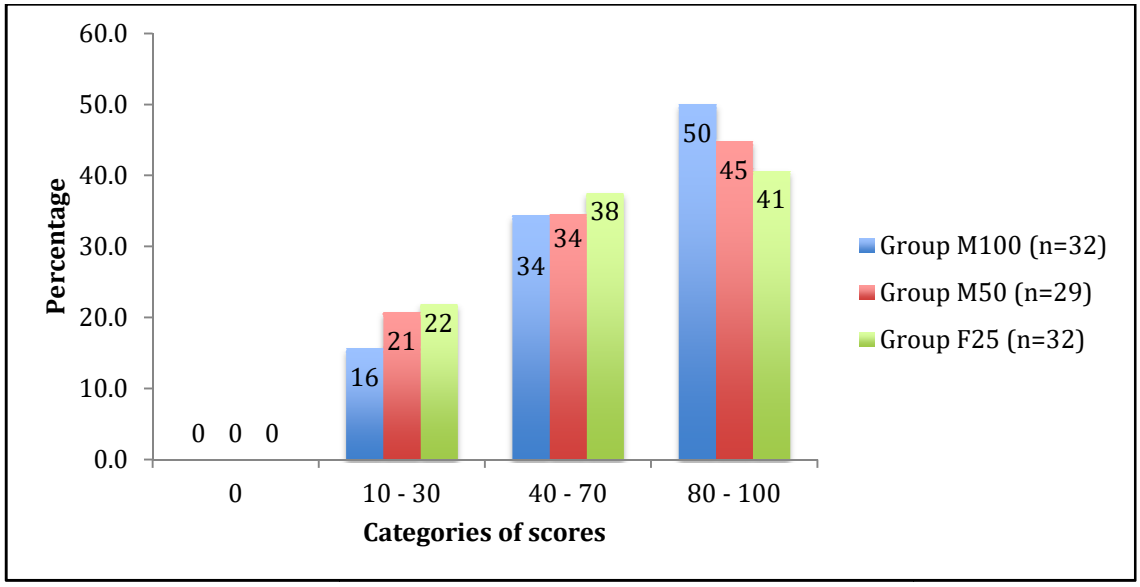


FIGURE 6.16: Categories of scores of the patients' perceptions of pain relief

One explanation for this is that all patients, irrespective of the treatment group to which they were allocated, had access to PCA morphine, and could therefore freely and effectively manage their pain after surgery. This is a confounding factor in studies such as this one. All subjects have access to PCA morphine (which is used to primarily evaluate the effect of the intervention being investigated) and this access will influence the patients' pain NRS scores and also their perception of the success of their pain control treatment.

Patients were asked if they would have liked more pain treatment than they received. These results are summarised in Table 6.3.

TABLE 6.3: Perceptions of need for more pain treatment

Assessment	Group M100 (n=32)	Group M50 (n=29)	Group F25 (n=32)	p-value
Need for more pain treatment	YES = 13(45%) NO = 19(65%)	YES = 6(21%) NO = 23(79%)	YES = 15(47%) NO = 17(53%)	p = 0.8

The majority of women in all the treatment groups did not want more pain treatment than they received. This finding extended across all the treatment groups and there was no statistical difference between the three treatment groups (Chi-squared, p=0.8). Karlstrom *et al* (2010) had similar findings in their study, where despite 44% of the women reporting a VAS score ≥ 4, most of the patients felt that they received the all pain relief that they needed. One possible reason for these findings is that many women seem to have a perception that there should be pain as part of the birthing process and therefore are accepting of any pain that they may have after their caesarean section surgery.

Patients were asked to rate their level of satisfaction with their pain relief since their surgery, on a scale of 0 to 10. The results of this question are tabulated in Table 6.4.

TABLE 6.4: Scores of satisfaction with pain relief provided

Assessment	Group M100 (n=32)	Group M50 (n=29)	Group F25 (n=32)	p-value
Level of satisfaction	Median = 9 Min = 1 Max = 10 IQR = 2.25	Median = 8 Min = 0 Max = 10 IQR = 3	Median = 8 Min = 0 Max = 10 IQR = 4	p = 0.5

Statistical analysis shows that there is no statistical difference between the three treatment groups with regards to the patients' satisfaction of their pain management following surgery (Kruskal Wallis, p=0.5).

Categorizing the data into groups based on the levels of satisfaction shows that most patients are extremely satisfied (scores = 8 – 10) with their analgesia across all the treatment groups. These results are illustrated in figure 6.17.

As stated above, there are many factors that contribute towards satisfaction levels following surgery. This must be considered when we interpret these results.

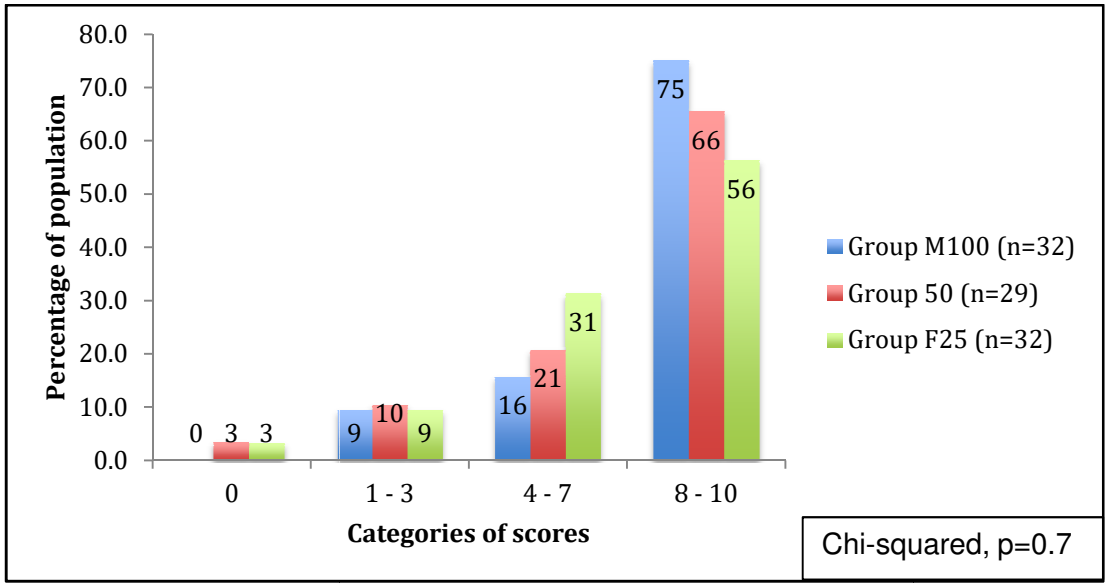


FIGURE 6.17: Categories of scores of the patients' level of satisfaction of their pain relief

In the group of patients who rated their satisfaction as 8/10 or above, the highest percentage of satisfied patients are from Group M100 (75%), however there is no statistical significance to this finding (Chi-squared, p=0.7).

6.5 Study limitations

- A consecutive convenience sampling method was used to recruit patients into the study. This is not an ideal method to recruit patients into a clinical trial as the method may result in a false representation of the patient population. The convenience sampling method was chosen because of the time constraints and scope of the research. I would recommend that any future investigation into this topic should ensure that consecutive patients are recruited for the clinical trial.
- The patient treatment group allocations were not completely concealed, as the treating anaesthetic service provider was aware of the patients' group allocation. This was necessary in order to allow the treating doctor to

administer the correct medication in the spinal anaesthetic and also to be aware of the medication that the patient was given in the event that an emergency occurred during surgery. The PI however remained blinded to the treatment groups until the study was completed and the patient groupings were unblinded.

- The exclusion of women whose babies were not with them by the 12-hour assessment may have masked potential side effects of the study medication in these babies. However, all these babies were (for other clinical indications) admitted to the paediatric intensive care unit and therefore any medication side effects would have been detected and treated. Furthermore, it is extremely unlikely that any of the study medication could have been transferred to the baby due to the fact that the medication was administered intrathecally to the mother and the baby was delivered shortly after this administration, leaving very little time for systemic absorption in the mother and transfer to the baby via the placenta.
- The study was only powered to detect a significant difference for the primary objective. Some of the secondary objectives revealed results that pointed towards trends in the data but no statistically significant results were found.
- Many of the secondary objectives investigated e.g. activities out of bed, levels of anxiety and feeling helplessness are not validated measures

6.6 Conclusions

The analgesic effects of three different intrathecal opioid regimens were evaluated in 100 patients undergoing caesarean section surgery at RMMCH. The treatment groups were Group M100 - 100µg morphine, Group M50 - 50µg morphine and Group F25 - 25µg fentanyl. Seven patients were excluded from the data analysis. The data from 93 patients were analysed.

We presented and discussed the results related to the impact of the three treatment regimens on post-operative analgesic requirements in chapter five.

In chapter six, we have presented and discussed the results of this study pertaining to the side effects of intrathecal opioids and also on the effect of the investigated intrathecal opioid regimens on the patients' post-operative activities, their emotional states and the perception of their pain relief in the first 24 hours after surgery.

Despite the statistically significant difference in PCA morphine use between the different treatment groups in our study, we found that there was no difference in the side effect profile between the three treatment groups. No serious side effects occurred in this study. The side effects profile with regards to sedation, nausea, pruritus and respiratory depression were similar across all the treatment groups. We also found that the pain NRS scores between the groups at rest and with cough were similar. This discrepancy between the PCA morphine use and the patients' pain scores is most likely due to the patients having access to PCA morphine and therefore they were able to effectively manage their pain and keep their pain scores low.
The effect of the pain on the patients' activities and emotions were similar between the three treatment groups. There was also no statistical difference in the levels of patient satisfaction between the treatment groups in this study.

Based on the results of this study presented in chapters five and six, patients treated with 50µg and 100µg intrathecal morphine require less post-operative analgesia than patients who are treated with 25µg fentanyl in the first 24 hours after caesarean section surgery. There is no difference in the physical or emotional side effects of the three treatment regimens. It is therefore feasible and advisable that the use of 50µg intrathecal morphine should be advocated in patients having caesarean sections in South Africa.

6.7 Summary

In this chapter the results of the secondary objectives of the clinical trial investigating the influence of different intrathecal opioid regimens on the post-operative pain experiences of women having caesarean sections at RMMCH has been presented. In the next chapter, the conclusion of this PhD research project will be presented.

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CHAPTER SEVEN: Conclusion

The caesarean section rate in South Africa is high and is above the World Health Organisation (WHO) recommended rate of 10 – 15% (Moodley, 2010). This phenomenon is not unique to South Africa. There appears to be a global trend towards increasing surgical deliveries (Macfarlane et al., 2015). The rise in surgical deliveries is likely to be due to the more defensive practice of obstetrics, due to an upsurge in malpractice litigation against obstetricians, as well as from an increase in maternal requests. As a result of this high percentage of caesarean section deliveries, the anaesthetic management of the obstetric patient in South Africa has become increasingly important. This refers to both the intra-operative and post-operative management of these patients. Good anaesthetic management has the potential to improve patients' birth experiences and decrease the risk of post-operative morbidity.

There are a number of international guidelines (Apfelbaum et al., 2016, Griffiths et al., 2011, Horlocker et al., 2009, Schug et al., 2015) available with recommendations about the anaesthetic management of patients who are having caesarean section surgery. However all these guidelines have been established in developed countries that have relatively sophisticated health care systems and lower resource constraints as compared to South Africa and other developing countries.

My PhD research study has developed a reference standard for caesarean section anaesthesia in South Africa by canvassing the expert opinion of anaesthesiology academic leaders in the country on this topic. This South African reference standard has been discussed in relation to current international standards from more affluent countries and compared to the practice of South African anaesthetic service providers, which has been determined from a national survey of anaesthetic practice that I conducted over a 10-month period in South Africa in 2014. The national survey also attempted to establish the opinions of practitioners about their impressions of

their patients' levels of satisfaction with their post-operative pain management following caesarean section surgery.

The final component of my PhD research study was a double blind clinical trial comparing the analgesic effects of the current standard of caesarean section anaesthetic care in South Africa with analgesic modalities proposed in the international literature, taking cognisance of the resource limitations within the South African health care environment. This clinical trial was the first randomized double-blinded clinical trial to evaluate the effect of different intrathecal opioids on post-operative pain experiences in women who have undergone caesarean section surgery in South Africa. The unique South African health care environment, and our patient populations that are different from the populations in developed countries, makes this a distinctive clinical investigation.

7.1 **Summary of the results**

To develop a reference standard for the anaesthetic management of patients having caesarean section surgery in South Africa, the heads of department of the eight academic anaesthesiology departments in South Africa were invited to participate in a process to develop such a standard. All South African trained specialist anaesthesiologists train in one of these departments and therefore the standard set by the academic departments ultimately determines the reference standard of anaesthetic care for patients having caesarean sections in South Africa. All universities participated in this process of reference standard setting. Departments were represented either by the head of department and/or the obstetric anaesthesia expert from the department.

The national survey of obstetric anaesthesia practices in South Africa was the only survey of this kind ever conducted in South Africa. Anaesthesiology service providers were invited to participate in this survey to provide details on their practice of obstetric anaesthesia. The responses of 933 anaesthetic service providers were analysed. Practitioners from all nine provinces in South Africa participated in the study, with the majority of the respondents

being from the three most populated provinces in the country – Gauteng, Western Cape and KwaZulu-Natal. There was equivalent representation from the public and private health care sectors. Analysis of the responses showed that there was a statistical difference between the obstetric anaesthesia work exposure of doctors in the private and public sectors in South Africa.

In the clinical trial one hundred patients were randomized into three different treatment groups, each of which received different intrathecal drugs / dosages (Group M100 - 100µg morphine, Group M50 - 50µg morphine and Group F25 - 25µg fentanyl). Patients were evaluated on their post-operative analgesic requirements, pain scores, side effects profile and level of satisfaction with treatment.

During the expert interviews, the South African experts unanimously proposed single shot spinal anaesthesia as the preferred anaesthetic technique for patients having elective caesarean sections. They also recommended 0.5% bupivacaine with dextrose, at a dose of 1.8 – 2.1 ml (9 – 10.5mg), as the preferred local anaesthetic for obstetric spinal anaesthesia. The national practice survey revealed that the majority of the respondents (97.8%) performed single shot spinal anaesthesia as their primary anaesthetic for elective caesarean sections. The preferred choice of local anaesthetic for the neuraxial block, for 95% of the survey respondents was 0.5% bupivacaine with dextrose. The median volume of this local anaesthetic used by specialists was 2.00ml and 1.80ml by non-specialists. This difference in volume of local anaesthetic used in the spinal anaesthetic (0.20ml) was statistically significant ($p<0.001$) and may be reflective of the difference in the understanding by these two categories of doctors of the importance of ensuring a successful spinal block in the parturient.

The lipophilic opioid, fentanyl, at a dose of 10 – 25mcg, was recommended as the reference standard adjuvant drug to be added to the spinal anaesthetic mixture. The use of intrathecal morphine was not recommended due to concerns about side effects of this drug. The majority of respondents (654/933) in the survey reported that they used fentanyl as an adjuvant agent

in their spinal anaesthetic solution. Of these, 342 were specialists and 312 were non-specialists. Statistical analysis showed that there was a statistical difference in the use of fentanyl between specialists and non-specialists. The mean dose of fentanyl used by each group was also statistically different. Specialists used a mean fentanyl dose of 15.12µg while the non-specialists used a mean dose of 13.77µg. Both these dosages fell within the dosage range recommended by the experts for use in South Africa. A much lower number of anaesthetic service providers used sufentanil as an adjuvant agent in their spinal anaesthetics. There was also a statistical difference in the use of this agent between specialists and non-specialists. Only 32/933 people responded that they used intrathecal morphine for their obstetric spinal anaesthetics. This was in line with recommendations from South African experts and this was most likely due to the current teaching practices in the anaesthesiology academic departments. The recommendation that morphine not be used in post-caesarean section patients was in line with the South African Acute Pain Management guidelines (Lundgren et al., 2016) but was contrary to multiple international studies which demonstrated that intrathecal morphine offered good, safe and effective analgesia for post-caesarean section pain (Cardoso et al., 1998, Palmer et al., 1999, Salmah and Choy, 2009, Abboud et al., 1988, Girgin et al., 2008, Swart et al., 1997).

With regards to the needle that should be used to perform the spinal anesthetic, all the experts interviewed agreed that the pencil point needles (Wittacre, Sprott, Pencan or Eldor) were the recommended spinal anaesthetic needles**.** There was also consensus that the cutting Quincke spinal needle should not be used to perform a spinal anaesthetic for obstetric patients. The Qunicke needle is associated with a greater risk of developing post-dural puncture headaches (PDPH) (O'Connor et al., 2007). The majority of respondents to the survey reported that they preferred to use a pencil point needle to perform the spinal anaesthetic. However there were still 30% of the doctors who indicated that they choose to use the cutting Quincke spinal needle. This practice was contrary to the proposed reference standards of practice for South Africa, and may be considered to constitute negligent

practice, considering the increased risks associated with using this type of needle.

For emergency cases, where the patient has an indwelling labour epidural catheter, a “top up” of the epidural was recommended to create an adequate level of surgical anaesthesia for the procedure. The recommended local anaesthetic for the epidural top-up was 2% lignocaine. No consensus was reached by the experts, on the appropriate adjuvant agent that should be added to the local anaesthetic solution for the epidural top-up. The experts recommended that fentanyl, morphine, sodium bicarbonate and adrenalin could be considered. The current South African practice was that 71% of anaesthetic service providers choose to “top-up” the epidural anaesthetic for the caesarean section in a labouring patient with an in situ epidural catheter. This was in accordance with the reference standard proposed. There were 22% of the survey respondents who removed the epidural catheter and performed a spinal anaesthetic, while only 5% would perform a general anaesthetic for these patients. There was a statistical difference between the practises of specialists and non-specialists for each of these three anaesthetic techniques. 0.5% bupivacaine was the local anaesthetic of choice for the epidural “top-up” in 47% of respondents while 33% of respondents preferred to use 2% lignocaine. It appeared that a large proportion of practitioners in South Africa do not use the local anaesthetic recommended by the proposed reference standard. Fentanyl was the most common drug additive used for epidural “top-up’s” however a similar number of respondents preferred not to use any additive agent in the “top-up” solution. This division in common practises regarding epidural adjuvants is most probably a reflection of the non-committed standpoint of the experts regarding this issue.

Epidural anaesthesia was not recommended, by the experts, as a primary anaesthetic technique for caesarean sections unless it was part of a combined-spinal-epidural (CSE) technique, and the patient was then managed in a high-care environment post-operatively, where the epidural could be utilized for post-operative analgesia.

The reference standard with regards to post-operative monitoring practices was that all patients who received neuraxial opioids as part of their anaesthetic should be monitored for respiratory depression in the post-operative period. The recommended duration of monitoring was dependent on the type of opioid used. For lipophilic opioids, monitoring for up to 12 hours was recommended. When hydrophilic opioids were administered neuraxially, the recommended duration of monitoring was 24 hours. No consensus was reached on the ideal mechanism of monitoring, however at least one type of monitor should be used. The recommended monitors were sedation score measurements, pulse oximetry and respiratory rate monitoring. Capnography was accepted as a good monitor however the cost of the equipment was prohibitive and it was therefore not recommended for use in South Africa. Only 41.7% of the survey respondents worked in hospitals that had a protocol for monitoring patients who received neuraxial opioids. Respiratory rate monitoring was the most popular monitoring technique used to monitor these patients. Of those doctors who worked in hospitals without a monitoring protocol, the majority of them were in the public sector. 92.8 % of the 544 doctors who worked in hospitals without monitoring protocols agreed that monitoring these patients was important.

There were 4.1% of the survey respondents who felt that a multidisciplinary team, made up of the anaesthesiologist, obstetrician and nurse, should manage the patient's post-operative pain. The majority of respondents (587/933, 62.9%) felt that the anaesthesiologist should be the only health care professional responsible for the patient's post-operative analgesia. There were three respondents who felt that no one should take responsibility for the patients' post-operative pain.

Routine use of epidural analgesia and patient controlled analgesia (PCA) pumps was not recommended within the reference standards of care. Non-steroidal anti-inflammatory drugs (NSAIDs), IV paracetamol and other oral analgesics were recommended for routine post-operative analgesia for caesarean section patients. Survey results indicated that epidural analgesia and PCA pumps were not popular choices for post-operative pain

management. None of the anaesthetic service providers surveyed would insert an epidural catheter exclusively for post-operative analgesia and only 9% of the respondents would use a labour epidural catheter for post-operative analgesia. There were only 17% of respondents who routinely used a PCA pump for post-operative pain management. Morphine was the most popular analgesic agent used in the PCA pumps. The reported practices regarding post-operative epidural analgesia and PCA pump use were in accordance with the recommended reference standards for obstetric anaesthesia care in South Africa. NSAIDs suppositories and IV paracetamol were very popular forms of analgesia prescribed for post-caesarean analgesia. Oral paracetamol and tramadol were the most commonly prescribed oral analgesics used for post-operative pain in women who had caesarean sections.

Based on their practice, 76% of the survey respondents were of the opinion that their patients were satisfied with their post-operative analgesia. When patients enrolled in the clinical trial were asked to rate their level of satisfaction with their treatment, 75% of patients in Group M100 rated their level of satisfaction between 8 and 10 (out of a maximum of 10). This is compared to 65.5% of the patients in Group M50 and only 56.3% of the patients in Group F25. These differences may be indicative of a trend towards greater satisfaction in the intrathecal morphine groups however these results were not statistically significant. Considering that the majority of the national survey respondents preferred to use fentanyl as the adjuvant drug in their obstetric spinal anaesthetics, it is very likely, based on the above results, these doctors are overestimating their patients' levels of satisfaction with their post-operative analgesia.

Analysis of the data from the clinical trial revealed that there was a statistically significant difference in the post-operative opioid requirements between the morphine groups (M100 and M50) and the fentanyl group (F25). Patients in the fentanyl group required more opioid analgesics in the first 12 hours, second 12 hours and cumulatively for the full 24-hour period after surgery. There was no difference in the post-operative opioid requirements between

groups M100 and M50, which implied that the two different doses of intrathecal morphine provided equivalent levels of analgesia in this study. There was however no difference in the pain scores between the three treatment groups. This unexpected result was most likely due to the fact that patients had unrestricted access to PCA analgesia and therefore could adequately manage their pain (and ensure their pain scores were lowered) with higher doses of intravenous opioids, when the pain was greater.

There was no statistical difference in the side effects experienced by patients in all three groups with reference to levels of sedation, respiratory depression, pruritus or nausea and vomiting. Of importance in this study was that there were no cases of respiratory depression (immediate or delayed) in the entire study cohort. The impact of the pain on the patients' activities (in and out of bed) and emotional states were also similar in all the treatment groups.

7.2 **Discussion of the results**

The first study (chapter three) established a reference standard of care for obstetric anaesthesia in South Africa. These standards allow us to compare the expected standard of care for South Africa to other international regions and may possibly also be extrapolated to other developing countries in Africa and globally. In addition South African practitioners would also able to benchmark their individual obstetric anaesthesia practices with the reference standards for the country.

The standards of care with regards to the anaesthetic technique used for the obstetric spinal anaesthesia is very similar to those proposed by current guidelines from the United States of America (USA) (Apfelbaum et al., 2016) and the United Kingdom of Great Britain and Northern Ireland (UK) (Griffiths et al., 2011). Neuraxial anaesthetic techniques are proposed to be safer and more effective forms of anaesthesia for pregnant patients than general anaesthesia and are also associated with lower neonatal morbidity. The decision on what anaesthetic technique to use for each patient however

needs to be individualized and depends on a number of different factors including the patient's clinical condition and patients' anaesthetic preferences.

A small gauge pencil point needle was strongly recommended as the needle of choice for performing obstetric spinal anaesthetics. This recommendation was in line with recommendations from the American Society of Anesthesiologists (ASA) (Apfelbaum et al., 2016).

The choice of the local anaesthetic agent to be used in the spinal anaesthetic was not stipulated in any current international guidelines. However, the South African experts recommended that 0.5% bupivacaine with dextrose be used as the reference standard of care in South Africa. This hyperbaric drug facilitates the cephalad spread of the local anaesthetic towards the thoracic kyphosis when the patient is in a supine position (Kleinman, 2002). This ensures that the spinal block is established at a high enough level so that the patient does not feel any pain during the caesarean section surgery. This recommendation will mostly address the 5.04% of South African practitioners who are using different local anaesthetics for their obstetric spinal anaesthetics.

The median volume of 0.5% bupivacaine recommended for obstetric spinal anaesthesia was 1.9ml (9.5mg). There were no international guidelines that made dosage recommendations for the local anaesthetic drug however the South African recommendations were substantiated by results of the review by Arzola and Wieczorek (2011), which found that using low doses of bupivacaine (≤8mg) in the spinal anaesthetic compromises the anaesthetic efficacy of the neuraxial block. Kiran and Singal (2002) also demonstrated a greater incidence of visceral pain in patients where ≤10mg bupivacaine was used in the spinal anaesthetic.

The use of intrathecal opioids for post-operative pain management was advocated by both the ASA and National Institute of Clinical Excellence (NICE) guidelines (Apfelbaum et al., 2016, Griffiths et al., 2011). The South African recommendations (chapter three) on the use of intrathecal opioid

adjuvant drugs were however controversial when discussed in relation to international publications on the analgesic efficacy of intrathecal opioids for post-operative analgesia following caesarean section surgery. The South African reference standard was to use fentanyl at doses between 10 – 25 mcg. Intrathecal fentanyl has better post-operative analgesic effects than using no intrathecal opioids (Hunt et al., 1989). However, when compared to intrathecal morphine, fentanyl's shorter duration of action offers very limited post-operative analgesic benefits (Salmah and Choy, 2009). The motivation of the expert panel for the use of fentanyl, instead of morphine, as an intrathecal adjuvant was fear of the risks of the side effects of intrathecal morphine, with specific reference to delayed respiratory depression. The risk of developing this side-effect has however been demonstrated to be very low (0.26%) (Kato et al., 2008) and can be further reduced by selectively excluding patients who are at increased risk of developing post-operative respiratory complications (such as patients with obstructive sleep apnoea), and avoiding concomitant use of systemic opioids. The intra-operative use of intrathecal fentanyl necessitates using additional analgesics for post-operative pain relief after surgery. This practice can also increase the risk of respiratory depression. Abboud et al (1988) demonstrated marked ventilatory depression in patients after administration of subcutaneous morphine for analgesia in elective caesarean section patients. Therefore the use of intrathecal fentanyl in obstetric anaesthesia in South Africa will only serve to reduce the success of analgesic treatment without reducing the risk of respiratory depression, unless systemic opioids are completely eliminated from the treatment options for these patients.

Despite current evidence of the lower analgesic effects of intrathecal fentanyl compared with morphine, the majority of respondents (654/933) to the national survey (chapter four) preferred fentanyl as an opioid additive for obstetric spinal anaesthesia. Only 32/933 respondents used morphine as the intrathecal adjuvant. This was in stark contrast to practices in the USA, where 79% of anaesthetic doctors used intrathecal morphine for caesarean section anaesthesia (Tagaloa et al., 2009).

The clinical trial evaluating the analgesic effects of intrathecal morphine and fentanyl in caesarean section patients (chapters five and six) clearly demonstrated reduced post-operative analgesic requirements in patients who received intrathecal morphine compared to patients who received intrathecal fentanyl. Furthermore, there were no incidences of respiratory depression in the entire study population, however this study was not powered to detect differences in the incidence of respiratory depression between the three treatment groups. The results of this study were similar to other international studies evaluating the analgesic effects of intrathecal opioids (Cardoso et al., 1998, Salmah and Choy, 2009, Palmer et al., 1999, Girgin et al., 2008). Intrathecal morphine provides good post-operative pain relief to patients after caesarean section surgery. Furthermore, the results of this study confirmed that a low intrathecal morphine dose of 50µg has the same quality of analgesia as the 100µg intrathecal morphine dose. Carvalho and Tenorio (2013) demonstrated similar results and in addition also concluded that this lower morphine dose is associated with a lower side effect profile.

The combination of NSAIDs with intrathecal morphine improves the analgesic effects of the treatment and has opioid sparing effects (Cardoso et al., 1998). An NSAID suppository is a popular analgesic choice used by practitioners in South Africa. In addition, IV paracetamol, despite concerns about the high cost of the drug by the South African experts, was used by 64% of South African anaesthetic service providers. IV paracetamol also has good opioid sparing effects (Remy et al., 2005). The combination of NSAIDs, paracetamol and intrathecal opioids satisfy the components of a multimodal analgesic regime and will ultimately lead to better patient analgesia with a lower side effect profile (Kehlet and Dahl, 1993).

Many of the concerns from the South African anaesthesia experts around the use of long acting intrathecal opioids, related to the perceived poor post-operative monitoring practices in the obstetric wards in South Africa. The American Practice Guidelines (Horlocker et al., 2009) state that patients who receive neuraxial opioids should be monitored for up to 24 hours following intrathecal administration of hydrophilic opioids. These sentiments were

echoed in the reference standards for South Africa. However 58.3% of anaesthetic service providers in South Africa stated that the hospitals that they work in do not have protocols for monitoring patients who have received neuraxial opioids. The reference standard for monitoring only required that at least one monitoring modality was used to monitor these patients. Respiratory rate monitoring and sedation score monitoring are low cost, simple and effective monitoring strategies that can easily be implemented in all obstetric units in South Africa. The perceptions of poor post-operative monitoring practices can be overcome with simple interventions such as staff training programmes for the post-operative ward nurses. The clinical trial that we conducted demonstrated that intrathecal morphine could be safely used in low doses in a public sector hospital where patients can be clinically monitored for respiratory depression.

7.3 **Limitations of the Study**

a. The development of the reference standard for obstetric anaesthesia practice was done by conducting eight individual interviews with representatives of the eight academic anaesthesiology departments in South Africa. This process excluded any experts in obstetric anaesthesia from the private sectors and may also have excluded obstetric anaesthesia experts who work in the academic departments but were not included in the process by the head of the department. Ideally the reference standard development process should be a two-phase process. The first phase is the identification phase, as conducted in this study. The second phase should be a validation phase where a larger group of experts review and validate the items from the first phase. This could not be done in my study because there are very few recognized obstetric anaesthesia experts in South Africa. The heads of departments, as the developers of training standards for specialists were then accepted as appropriate surrogates for this process.
b. The national survey only had 973 respondents, of which 933 were included in the data analysis. There are approximately 1700 doctors on the South African Society of Anaesthesiologists (SASA) database. This

implies the survey response rate is 57%. However, in South Africa anaesthesia may be administered by specialist anaesthesiologists and also by general practitioners. Not all these doctors may be affiliated to the SASA and therefore it is not possible to know how many doctors are actually providing anaesthetic services in South Africa. The survey response rate may be lower than 58%.

c. In the clinical trial, all clinicians involved in the study, and the patients, were blinded to the intervention drug used. However, the doctor administering the anaesthetic was not blinded to the intervention, as he/she was required to mix up the opioid and local anaesthetic solution before administering it for the spinal anaesthetic. This was done to ensure that the doctor had all the necessary information for the anaesthetic they were performing. Also, due to study budget limitations, it was not possible to have a pharmacist available who could prepare the intrathecal drugs after randomization.
d. Patient data collected in the clinical trial did not include height, and therefore the patients' BMI's could not be calculated. In addition, history of previous caesarean section surgery was not documented.
e. The clinical trial was not powered to detect differences in the side effects profile of each treatment group.
f. The clinical trial did not evaluate patients pain beyond 24 hours after surgery

7.4 **Recommendations and future research agenda**

a. The reference standards for obstetric anaesthesia practices in South Africa need to be developed into a set of national guidelines for the management of obstetric anaesthesia in South Africa. The results of this study will be used as a basis on which future South African guidelines will be developed. We plan to develop these guidelines in conjunction with a wider panel of obstetric anaesthesia experts from both the public and private sectors.

b. A study evaluating the acceptance by nursing personnel of new monitoring protocols for patients who receive neuraxial opioids should be conducted in South Africa.
c. Request the SASA to issue a statement warning anaesthetic service providers of the increased risk posed to patients by the use of Quincke spinal needles for spinal anaesthesia for caesarean sections.
d. Based on the results of the clinical trial, the post-operative pain treatment protocols for caesarean section surgery must be updated in South Africa to include low dose intrathecal morphine in combination with NSAID suppositories and IV paracetamol.

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CHAPTER EIGHT: Appendices

APPENDIX A: Human Research Ethics Committee Approval M111124

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG
Division of the Deputy Registrar (Research)

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
R14/49 Dr Sean Chetty

CLEARANCE CERTIFICATE	M111124
PROJECT	The Anaesthetic Management of Patients Undergoing Caesarean Section Surgery and Its Impact onn Post-Operative Analgesia
INVESTIGATORS	Dr Sean Chetty.
DEPARTMENT	Department of Anaesthesiology
DATE CONSIDERED	25/11/2011
M1111240DECISION OF THE COMMITTEE*	Approved Part 1 (Aim 1)

Unless otherwise specified this ethical clearance is valid for 5 years and may be renewed upon application.

DATE 19/01/2012 **CHAIRPERSON** .....
(Professor PE Cleaton-Jones)

*Guidelines for written 'informed consent' attached where applicable
cc: Supervisor : Prof Fathima Paruk

DECLARATION OF INVESTIGATOR(S)
To be completed in duplicate and **ONE COPY** returned to the Secretary at Room 10004, 10th Floor, Senate House, University.
I/We fully understand the conditions under which I am/we are authorized to carry out the abovementioned research and I/we guarantee to ensure compliance with these conditions. Should any departure to be contemplated from the research procedure as approved I/we undertake to resubmit the protocol to the Committee. **I agree to a completion of a yearly progress report.**

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES...

APPENDIX B: Survey questionnaire developed by Tagaloa et al (2009)

Survey of Obstetric Anaesthesia Practice for Caesarean Delivery

1) What is your study number (Please refer to the Title line of the original email)?

42895805 | | 1

2) Please select from the following the best description of the institution where you provide obstetric anaesthesia services.

12895814

- ○ Private Hospital
- ○ University/Teaching Hospital
- ○ District General Hospital
- ○ Other (Please Specify):

2

3) Approximately how many deliveries are there in your unit per annum?

12895819

- ○ <500
- ○ 500 - 1499
- ○ 1500 - 2999
- ○ 3000 - 5000
- ○ >5000
- ○ Other (Please Specify):

3

4) What is the rate of Caesarean delivery (expressed in percentages) in your unit per annum?

42895822 | | 4

5) What best describes the DAYTIME level of consultant obstetric anaesthetic coverage at your

institution?

12895890

- Dedicated in-house 24 hour obstetric anaesthesia coverage
- In-house anaesthetic coverage shared with operating rooms
- Off-site obstetric anaesthesia coverage
- Other (Please Specify):

5

6) What best describes the NIGHTTIME level of consultant/attending obstetric anaesthetic coverage at your institution?

12895896

- Dedicated in-house 24 hour obstetric anaesthetic coverage
- In-house anaesthetic coverage shared with operating rooms
- Off-site obstetric anaesthesia coverage
- Other (Please Specify):

6

7) What is YOUR level of involvement in obstetric anaesthesia?

12901349

- Daytime cover
- On-call only
- Daytime and on-call
- Other (Please Specify):

7

8) On average, how often do you work in obstetric anaesthesia?

12901354

- <1 day a week
- 1 - 2 days a week
- > 2 days a week

8

9) What is your preferred technique for healthy patients requiring elective Caesarean delivery?

12901372

- Single shot spinal
- Epidural
- Combined spinal-epidural
- General anaesthetic

9

10) If a SPINAL is your preferred technique, which type of spinal needle do you routinely use?

12901385

- Quincke
- Sprotte
- Whitacre
- Pencan
- Eldor
- Other (Please Specify):

10

11) What needle gauge do you routinely use?

12901402

- 22G
- 24G
- 25G
- 26G
- 27G
- Other (Please Specify):

11

12) For a healthy non-obese patient, what is your preferred choice of **intrathecal** local anaesthetic?

12901420

- Heavy Bupivacaine 0.75%
- Heavy Bupivacaine 0.5%
- Plain Bupivacaine 0.5%
- Plain Lignocaine 2%
- Plain Ropivacaine 0.75%
- Plain Levobupivacaine 0.5%
- Other (Please Specify):

12

13) For a healthy non-obese patient, what is your **standard** dose of intrathecal local anaesthetic (in mg)?

42901425 13

14) For a healthy non-obese patient, what other agents do you **routinely** add to your intrathecal mixture? (mark all that apply)

22901448

- None
- Fentanyl
- Morphine
- Diamorphine

Other (Please Specify):

14

15) If **morphine** is one of the agents you routinely add to your intrathecal mixture, please state your preferred dose (in mcg).

42901457 15

16) For **EPIDURAL** placement, what is your preferred technique for loss of resistance?

12901476

- Air
- Saline

- ○ Both
- ○ Other (Please Specify):

16

17) Do you routinely use EPIDURAL anaesthesia for **elective** Caesarean delivery?

12901484

- ○ Yes
- ○ No

17

18) (If **NO**, please skip the next **five** questions, and go straight to Q23)
If **yes**, what is your preferred choice of epidural local anaesthetic?

12901537

- ○ Lignocaine 2%
- ○ Bupivacaine 0.5%
- ○ Ropivacaine 0.75%
- ○ Levobupivacaine 0.5%
- ○ Other (Please Specify):

18

19) Please state the volume of local anaesthetic that you routinely use (in ml)

42901544 | | 19

20) For **elective** Caesarean delivery, what other agents do you routinely add to your epidural local anaesthetic? (mark all that apply)

22901571

- ☐ None
- ☐ Fentanyl
- ☐ Sufentanil
- ☐ Morphine
- ☐ Diamorphine

☐ Sodium Bicarbonate 8.4%

☐ Adrenaline

Other (Please Specify):

20

21) For **elective** Caesarean delivery, do you routinely give morphine via the epidural catheter for postoperative pain relief?

12901624

○ Yes

○ No

21

22) If **yes**, please state the dose (in mg)

42901628 22

23) In a laboring patient with an epidural in situ requiring **urgent** Caesarean delivery, what is your preferred choice of epidural local anaesthetic?

12901552

○ Lignocaine 2%

○ Bupivacaine 0.5%

○ Ropivacaine 0.75%

○ Levobupivacaine 0.5%

○ Chlorprocaine 3%

○ Other (Please Specify):

23

24) Please state the volume of local anaesthetic that you routinely use (in ml).

42901558 24

25) For **urgent** Caesarean delivery, what other agents do you routinely add to your epidural local anaesthetic?

12901592

○ None

- Fentanyl
- Sufentanil
- Morphine
- Diamorphine
- Sodium Bicarbonate 8.4%
- Adrenaline
- Other (Please Specify):

25

26) For **urgent** Caesarean delivery, do you routinely give **morphine** via the epidural catheter for postoperative pain relief?

12901612

- Yes
- No

26

27) If **yes**, please state the dose (in mg).

42901656 27

28) Does your institution have a protocol for monitoring patients after neuraxial opioids?

12901659

- Yes
- No

28

29) If **yes**, how long are patients monitored for signs of respiratory depression after neuraxial opioid administration?

12901661

- <6 hrs
- 6 - 12hrs
- 12hrs
- 24hrs

- ○ 36hrs
- ○ 48hrs
- ○ Other (Please Specify):

29

30) How are healthy patients who received neuraxial opioids for Caesarean delivery routinely monitored to detect respiratory depression? (mark all that apply)

22901663

- ☐ Respiratory rate
- ☐ Sedation score
- ☐ Pulse oximetry

Other (Please Specify):

30

31) Do you routinely use the epidural catheter for postoperative analgesia?

12901666

- ○ Yes
- ○ No

31

32) If **yes**, what method and agents do you routinely use?

22901710

- ☐ Patient Controlled Epidural Analgesia (PCEA)bolus administration only
- ☐ PCEA with continuous infusion
- ☐ Intermittent epidural boluses, local anaesthetic only
- ☐ Intermittent epidural boluses, opioid only
- ☐ Continuous infusion, local anaesthetic only
- ☐ Continuous infusion, local anaesthetic plus opioid

Other (Please Specify):

32

33) If **no**, please indicate why you do not use the catheter for postoperative analgesia (mark all that apply).

22901675

- [ ] Not standard protocol
- [ ] No epidural pumps on postnatal wards
- [ ] Inadequate monitoring on postnatal wards
- [ ] Lack of nursing staff education in epidural care
- [ ] Anesthesia staff shortage
- [ ] Nursing staff shortage

Other (Please Specify):

33

34) Do you routinely prescribe an intravenous PCA following Caesarean delivery?

12901724

- ○ Yes
- ○ No

34

35) If **yes**, what intravenous analgesic agent do you routinely use?

12901727

- ○ Morphine
- ○ Fentanyl
- ○ Pethidine
- ○ Other (Please Specify):

35

36) Do you **routinely** prescribe NSAIDS for postoperative analgesia?

12901729

- ○ Yes
- ○ No

36

37) If **yes**, what NSAIDS do you routinely prescribe?

12901732

- Ibuprofen
- Ketorolac
- Diclofenac
- Other (Please Specify):

37

38) What dosing regimen do you use for your **NSAID** prescription?

22901735

- PRN
- Regular scheduled doses 'around the clock'

Other (Please Specify):

38

39) What other **oral analgesics** do you routinely prescribe following Caesarean delivery (mark all that apply)?

22901737

- Acetaminophen
- Codeine
- Hydrocodone
- Oxycodone
- Tramadol

Other (Please Specify):

39

40) What dosing regimen do you use for these other oral agents?

22901738

- PRN
- Regular scheduled doses 'around the clock'

Other (Please Specify):

40

41) Thank you for your participation! Study numbers will be entered into the draw and the lucky winners will be contacted once the study has been completed.

0	82901754	41
41		

Finish Survey

APPENDIX C: Questions modified for Semi-structured Interview questionnaire

The following questions were either added to or modified from the original questionnaire used by Tagaloa *et al* (2009)

2. For a spinal anaesthetic, what would you consider the most appropriate needle to use?

Quincke

 Sprotte

Whitacre

Pencan

Eldor

Other (Please Specify):

_____

3. What needle gauge do you recommend?

22G

24G

25G

26G

27G

Other (Please Specify): _____

4. For a healthy, non-obese patient for a caesarean section, what would you recommend as the preffered choice of intrathecal local anaesthetic?

 Bupivacaine 0.5% with Dextrose

 Bupivacaine 0.5%

 Lignocaine 2%

 Ropivacaine 0.75%

 Levobupivacaine 0.5%

 Other (Please Specify):

_____

5. **For a healthy, non-obese patient, what should be the standard dose of the <u>above mentioned</u> intrathecal local anaesthetic?**

_____ mg **OR** _____ ml

6. **For a healthy, non-obese patient, what other agents do you think should be routinely added to the intrathecal local anaesthetic mixture?** *(mark all that apply)*

No drugs routinely added

Fentanyl Dose used = _____ µg

Morphine Dose used = _____ µg

Sufentanil Dose used = _____ µg

Other (Please Specify):

7. **For EPIDURAL placement, what do you consider to be the best technique for loss of resistance?**

Air

□ Saline

□ Both

□ Other (Please Specify):

_____

11. **For ELECTIVE caesarean delivery, what other agents should one routinely add to the epidural local anaesthetic?** *(mark all that apply)*

No other agents added

□ Fentanyl

□ Sufentanil

□ Morphine

□ Sodium Bicarbonate 8.4%

□ Adrenaline

Other (Please Specify):

_____

12. **For elective caesarean delivery, should you give morphine via the epidural catheter for post-operative pain relief?**

Yes

Please state the dose : _____ mg

□ No

13. In a labouring patient with an epidural in situ requiring an URGENT caesarean section, what should be the preferred method of anaesthesia?

□ (a) Top up the in-situ epidural

□ (b) Remove epidural and administer spinal anaesthesia

□ (c) General Anaesthesia

□ (d) Other (Please Specify):

_____

17. For an URGENT Caesarean section, would you routinely give morphine via the epidural catheter for post-operative pain relief?

Yes

Please state the dose : _____ mg

□ No

21. Should you routinely use an epidural catheter for postoperative analgesia after a caesarean section?

Yes

No

27. If YES, what NSAIDs do you recommend?

□ Ibuprofen

□ Ketorolac

□ Diclofenac

□ Lornoxicam

□ Parecoxib

□ Other (Please Specify):

_____

29. What is your preferred route of administration of NSAID's after a caesarean section?

- □ Oral
- □ Intravenous
- □ Rectal
- □ Intramuscular

Other (Please Specify): _____

30. Should we routinely prescribe intravenous Paracetamol for post-operative analgesia?

- □ Yes
- □ No

31. What other oral analgesics do you routinely prescribe after a caesarean delivery ? *(mark all that apply)*

- □ Paracetamol
- □ Codeine
- □ Oxycodone
- □ Tramadol
- □ Other (Please Specify): _____

33. Do you have any other comments or questions which you think would be relevant to this discussion on the anaesthetic management of Obstetric Anaesthesia in South Africa?

APPENDIX D: Semi-structured Interview Questionnaire

1. What do you consider to be the preferred technique for healthy patients requiring elective Caesarean delivery?

    a. Single shot spinal
    b. Epidural
    c. Combined spinal-epidural
    d. General anaesthetic

COMMENTS:

_____

_____

_____

2. For a SPINAL anaesthetic, what would you consider the most appropriate needle to use?
    a. Sprotte
    b. Whitacre
    c. Pencan
    d. Eldor
    e. Other (Please Specify): _____

3. What needle gauge do you recommend?
    a. 22G
    b. 24G
    c. 25G
    d. 26G
    e. 27G
    f. Other (Please Specify): _____

COMMENTS:

_____

_____

_____

4. For a healthy non-obese patient, what would you recommend as the preferred choice of intrathecal local anaesthetic?
    a. Bupivacaine 0.5% with Dextrose

    b. Plain Bupivacaine 0.5%

    c. Plain Lignocaine 2%

    d. Plain Ropivacaine 0.75%

    e. Plain Levobupivacaine 0.5%

    f. Other (Please Specify): _____

5. For a healthy non-obese patient, what should be the standard dose of intrathecal local anaesthetic (in mg)? _____

COMMENTS:

_____

_____

_____

6. For a healthy non-obese patient, what other agents do you think should be routinely added to the intrathecal mixture? (mark all that apply)
    a. No drugs routinely added
    b. Fentanyl
       DOSE USED = ___ mcg
    c. Morphine
       DOSE USED = ___ mcg
    d. Sufentanil
       DOSE USED = ___ mcg
    e. Other (Please Specify):

COMMENTS:

_____

_____

_____

7. For EPIDURAL placement, what do you consider to be the best technique for loss of resistance?

    a. Air

    b. Saline

    c. Both

    d. Other (Please Specify):

COMMENTS:

_____

_____

_____

8. Should EPIDURAL anaesthesia be used routinely for elective Caesarean delivery?

    a. Yes

    b. No

COMMENTS:

_____

_____

_____

9. What would you recommend as the preferred choice of epidural local anaesthetic for this group of patients?
    a. Lignocaine 2%

    b. Bupivacaine 0.5%

    c. Ropivacaine 0.75%

    d. Levobupivacaine 0.5%

e. Other (Please Specify):

10. Please state the volume of local anaesthetic that should routinely be used (in ml) for these patients? _____

11. For elective Caesarean delivery, what other agents should one routinely add to the epidural local anaesthetic? (mark all that apply)

    a. No other agents added

    b. Fentanyl

    c. Sufentanil

    d. Morphine

    e. Sodium Bicarbonate 8.4%

    f. Adrenaline

    g. Other (Please Specify):

12. For elective Caesarean delivery, should you give morphine via the epidural catheter for postoperative pain relief?

    a. Yes
       If yes, please state the dose (in mg) _____

    b. No

COMMENTS:

_____

_____

13. In a labouring patient with an epidural in situ requiring urgent Caesarean delivery, what should be the preferred method of anaesthesia?

    a. Top up the in-situ epidural

    b. Remove epidural and administer spinal anaesthetic

c. General Anaesthesia

d. Other (Please Specify): _____

14. What would you recommend as the preferred choice of epidural local anaesthetic in these patients?

    a. Lignocaine 2%

    b. Bupivacaine 0.5%

    c. Ropivacaine 0.75%

    d. Levobupivacaine 0.5%

    e. Other (Please Specify): _____

15. Please state the volume of local anaesthetic that should be routinely used (in ml) in these patients? _____

16. For urgent Caesarean delivery, what other agents do you routinely add to your epidural local anaesthetic?

    a. No agents added

    b. Fentanyl

    c. Sufentanil

    d. Morphine

    e. Sodium Bicarbonate 8.4%

    f. Adrenaline

    g. Other (Please Specify): _____

17. For urgent Caesarean delivery, would you routinely give morphine via the epidural catheter for postoperative pain relief?
    a. Yes
       If yes, please state the dose (in mg) _____
    b. No

COMMENTS:

_____

_____

_____

18. Should all maternity units have a protocol for monitoring patients who receive neuraxial opioids?

    a. Yes

    b. No

19. For how long should patients be monitored for signs of respiratory depression after neuraxial opioid administration?
    a. <6 hrs

    b. 6 - 12hrs

    c. 12hrs

    d. 24hrs

    e. 36hrs

    f. 48hrs

    g. Other (Please Specify): _____

20. How do you think healthy patients, who received neuraxial opioids for Caesarean delivery, should be routinely monitored to detect respiratory depression? (mark all that apply)
    a. Respiratory rate
    b. Sedation score
    c. Pulse oximetry
    d. Other (Please Specify):

COMMENTS:

_____

_____

_____

21. Should you routinely use the epidural catheter for postoperative analgesia after Caesarean Section surgery?
    a. Yes

    b. No

22. If yes, what method and agents do you recommend?

    a. Patient Controlled Epidural Analgesia (PCEA)bolus administration only

    b. PCEA with continuous infusion

    c. Intermittent epidural boluses, local anaesthetic only

    d. Intermittent epidural boluses, opioid only

    e. Continuous infusion, local anaesthetic only

    f. Continuous infusion, local anaesthetic plus opioid

g. Other (Please Specify):

23. If no, please indicate why you would not use the catheter for postoperative analgesia (mark all that apply)

a. Not standard protocol

b. No epidural pumps in postnatal wards

c. Inadequate monitoring in postnatal wards

d. Lack of nursing staff education in epidural care

e. Anaesthesia staff shortage

f. Nursing staff shortage

g. Other (Please Specify):

COMMENTS:

_____

_____

_____

24. Should you routinely prescribe an intravenous PCA following Caesarean delivery?
    a. Yes
    b. No

25. If yes, what intravenous analgesic agent would you recommend?

a. Morphine
b. Fentanyl
c. Pethidine
d. Other (Please Specify): _____

COMMENTS:

_____

26. Should NSAID's be routinely prescribed for postoperative analgesia?
    a. Yes
    b. No

27. If yes, what NSAIDS do you recommend?
    a. Ibuprofen
    b. Ketorolac
    c. Diclofenac
    d. Lornoxicam
    e. Parecoxib
    f. Other (Please Specify):_____

28. What dosing regimen would you recommend for NSAID prescription?
    a. PRN
    b. Regular scheduled doses 'around the clock'
    c. Other (Please Specify): _____

29. What is your preferred route of administration of NSAID's
    a. Oral
    b. Intravenous
    c. Rectal
    d. Intramuscular

COMMENTS:

_____

_____

30. Should we routinely prescribe intravenous Paracetamol for postoperative analgesia and why?
    a. YES
    b. NO

COMMENTS:

_____

_____

_____

31. What other oral analgesics do you routinely prescribe following Caesarean delivery (mark all that apply)?
    a. Paracetamol
    b. Codeine
    c. Dextropropoxyfene
    d. Tramadol
    e. Other (Please Specify): _____

32. What dosing regimen do you use for these other oral agents?
    a. PRN
    b. Regular scheduled doses 'around the clock'
    c. Other (Please Specify):

COMMENTS:

_____

_____

_____

33. Do you have any other comments or questions which you think would be relevant to this discussion on the anaesthetic management of Obstetric Anaesthesia in South Africa?

_____

_____

_____

Thank you for your participation!

APPENDIX E: PARTICIPANT INFORMATION SHEET

This Participant Information Sheet is for the Academic Heads (or their designated alternate) of the Anaesthesiology Departments at the eight medical schools in South Africa, who have been requested to take part in a structured interview regarding their opinions on the Anaesthetic management of Obstetric patients in South Africa. The title of this research project is "A determination of what should be considered the Current GOLD standard practices for the management of Obstetric Anaesthesia and post-operative monitoring in South Africa"

Name of Principal Investigator: Dr Sean Chetty
Name of Organization: University of the Witwatersrand
Name of Proposal: The anaesthetic management of patients undergoing caesarean section surgery and its impact on post-operative analgesia

Introduction

Good Day, I am Sean Chetty, a specialist Anaesthesiologist working in the public sector in Johannesburg. I am currently registered for my PhD at the University of the Witwatersrand. My research centers around anaesthesia for caesarean section surgery in South Africa.

The purpose of this document is to give you information and invite you to be part of this research. You are not obliged to participate in the research study; however your participation will contribute to a better understanding of obstetric anaesthesia services in South Africa.

Purpose of the research

Currently, pain management for women who have babies by caesarean section is difficult. We must be able to give these women medicines which are good enough to treat their pain but will also not cause problems for them or the baby. If the pain is not properly controlled then it may be more difficult for the mother to take care of the baby.

In addition, there are no guidelines for the post-operative management of obstetric patients who have had neuraxial anaesthesia. I would like to determine, what should be considered the acceptable standard of practice for obstetric anaesthesia and post-operative monitoring, by interviewing the Heads of Anaesthesiology from the 8 medical Schools in South Africa.

Type of Research Intervention

This research will involve you being interviewed for approximately 1 hour. The format is a structured interview, with room for discussion of matters that you feel need to be discussed in detail.

Participant selection

I am inviting all Anaesthesiology Academic Heads of Departments in South Africa (or their designated alternatives) to participate in this research.

Voluntary Participation

Your participation in this research is entirely voluntary. It is your choice whether to participate or not. You may change your mind later and stop participating even if you agreed earlier.)

Procedures and Protocol
Description of the Process

If you agree to be part of this research study, I will make an appointment to meet with you at your convenience. I will send you the structured interview questions, in advance, so that you are able to prepare for the interview.

The interview will be recorded to allow an accurate description of your thoughts. These recordings will be destroyed after 5 years.

Duration
This interview will take approximately 1 hour.

Benefits

There will be no direct individual benefit to you for participation in this interview. However, the collective comments made by all the heads of department, will lead to an understanding of how obstetric anaesthesia should be conducted in South Africa. This will hopefully be a forerunner to the development of Guidelines for the country.

Confidentiality

The information that we collect from this research project will be kept confidential. Information about you that will be collected during the research will be put away and no-one but the researchers will be able to see it.

Sharing the Results

After this research is finished, the information will be analysed and the results will be published so that other interested people will learn from this research. Information about you will not be published.

Right to Refuse or Withdraw

You do not have to take part in this research if you do not wish to do so. You may also stop participating in the research at any time you choose. It is your choice and all of your rights will still be respected

Who to Contact
If you have any questions you may ask them now or later, even after the study has started. If you wish to ask questions later, you may contact any of the following: Dr Sean Chetty 083 707 44444 or e-mail: sean.chetty@wits.ac.za

This proposal has been reviewed and approved by the University of the Witwatersrand Post-graduate Committee. It has also been reviewed by the Human Research Ethics Committee of the University of the Witwatersrand. Any queries may be directed to the Chair of the HREC, Professor PCJ at 011 7171234.

APPENDIX F: PARTICIPANT CONSENT FORM FOR RESEARCH STUDY

Study Number:
Name of Interviewee: _____

Title of Project: A determination of what should be considered the Current GOLD standard practices for the management of Obstetric Anaesthesia and post-operative monitoring in South Africa

Name of Researcher: Dr Sean Chetty

	Please tick to confirm
I confirm that I have read and understood the participant information sheet for the above study.	☐
I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	☐
I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my legal rights being affected.	☐

I agree to take part in the above research study

_____	_____	_____
Name of Patient	Date	Signature

_____	_____	_____
Researcher	Date	Signature

APPENDIX G: PARTICIPANT CONSENT FORM FOR ELECTRONIC RECORDING OF INTERVIEW

Study Number: _____

Name of Interviewee: _____

Title of Project: A determination of what should be considered the Current GOLD standard practices for the management of Obstetric Anaesthesia and post-operative monitoring in South Africa

Name of Researcher: Dr Sean Chetty

I confirm that I have read and understood the participant information sheet for the above study.

I agree that the structured interview with Sean Chetty can be electronically recorded in order to allow an accurate description of my responses. I understand that these recordings will be destroyed after 5 years.

I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my legal rights being affected.

I agree to take part in the above research study

_____	_____	_____
Name of Interviewee	Date	Signature

_____	_____	_____
Researcher	Date	Signature

APPENDIX H: Human Research Ethics Approval M140123

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M140123

NAME: (Principal Investigator) Dr Sean Chetty

DEPARTMENT: Department of Anaesthesiology
Rahima Moosa Mother and Child Hospital

PROJECT TITLE: The Anaesthetic Management of Patients Undergoing Caesarean Section surgery and

DATE CONSIDERED: 31/01/2014

DECISION: Approved unconditionally

CONDITIONS:

SUPERVISOR: Prof Fathima Paruk

APPROVED BY: Professor PE Cleaton-Jones, Chairperson, HREC (Medical)

DATE OF APPROVAL: 31/01/2014

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Secretary in Room 10004, 10th floor, Senate House, University.

I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. **I agree to submit a yearly progress report**.

Principal Investigator Signature M140123Date

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

Appendix I: Questions modified for Questionnaire

The following questions were either added to or modified from the original questionnaire used by Tagaloa et al (2009):

34. Which province do you work in?

Gauteng
 Western Cape
 Eastern Cape
 KwaZulu Natal
 Mpumalanga
 North West
 Limpopo
 Northern Cape
 Free State

35. Description of your practice *(Choose one of the following options)***:**

Private practice

 Private practice with public sector sessions
 Private practice with no public sector involvement

Public sector

 Medical officer with less than 5 years experience in anaesthesia
 Medical officer with more than 5 years experience in anaesthesia
 Registrar
 Specialist with RWOPS
 Specialist without RWOPS

36. Highest South African Anaesthetic Qualification:

 MBChB / MBBCh
 DA (SA)
 FCA (SA) / FFA (SA) / MMed (Anaes)
 International Fellowship in Obstetric Anaesthesia

37. **Approximately how many anaesthetics do you administer per month?**
(Please indicate an average number and NOT a range)

Number: _____

38. **Approximately how many CAESAREAN SECTION anaesthetics do you administer per month?** *(Please indicate an average number and NOT a range)*

Number: _____

9. When administering a SPINAL anaesthetic, which type of spinal needle do you <u>prefer</u> to use?

Quincke

 Sprotte

Whitacre

Pencan

Eldor

I do not know the type of needle

I do not have a preference

Other (Please Specify): _____

10. When administering a SPINAL anaesthetic, which type of spinal needle do you routinely <u>have</u> to use?

Quincke

 Sprotte

Whitacre

Pencan

Eldor

Other (Please Specify): _____

I do not know the type of needle

I do not have a preference

11. When administering a SPINAL anaesthetic, what needle gauge do you <u>prefer</u> to use?

22G

24G

25G

26G

27G

Other (Please Specify): _____

I do not know the guage of needle

I do not have a preference

12. When administering a SPINAL anaesthetic, what needle gauge do you routinely <u>have</u> to use?

22G

24G

25G

26G

27G

Other (Please Specify): _____

I do not know the guage of needle

I do not have a preference

13. When administering a spinal anaesthetic for a healthy, non-obese patient for a caesarean section, what is your preferred choice of intrathecal local anaesthetic?

□ Bupivacaine 0.5% with Dextrose

□ Bupivacaine 0.5%

□ Lignocaine 2%

□ Ropivacaine 0.75%

□ Levobupivacaine 0.5%

□ Other (Please Specify): _____

14. For a healthy, non-obese patient, what is your standard dose of the <u>above mentioned</u> intrathecal local anaesthetic?

_____ mg **OR** _____ ml

15. For a healthy, non-obese patient, what other agents do you routinely add to your intrathecal local anaesthetic mixture?

(mark all that apply)

No drugs routinely added

Fentanyl Dose used = _____ µg

Morphine Dose used = _____ µg

Sufentanil Dose used = _____ µg

Other (Please Specify):

Name of additive : _____ Dose used = _____

Name of additive : _____ Dose used = _____

20. For ELECTIVE caesarean delivery, what other agents do you routinely add to your epidural local anaesthetic? *(mark all that apply)*

□ No other agents added

□ Fentanyl

□ Sufentanil

□ Morphine

□ Sodium Bicarbonate 8.4%

□ Adrenaline

□ Other (Please Specify): _____

21. For elective caesarean delivery, do you routinely give morphine via the epidural catheter for post-operative pain relief?

Yes

(i) Please state the dose : _____ mg

(ii) When do you administer this medication?

□ BEFORE the baby is delivered

□ AFTER the baby is delivered

□ No

22. In a labouring patient with an epidural in situ requiring an URGENT caesarean section, what is your preferred method of anaesthesia?

□ (a) Top up the in-situ epidural

□ (b) Remove epidural and administer spinal anaesthesia

□ (c) General Anaesthesia

□ (d) Other (Please Specify): _____

26. For an URGENT Caesarean section, do you routinely give morphine via the epidural catheter for post-operative pain relief?

Yes

(i) Please state the dose : _____ mg

(ii) When do you administer this medication?

□ BEFORE the baby is delivered

□ AFTER the baby is delivered

□ No

30. If you answered <u>NO to QUESTION 27</u> , do you think it is necessary to monitor patients who have been administered neuraxial opioids for respiratory depression?

□ YES

□ NO

31. Following surgery for a caesarean section, who do you believe should be responsible for the management of the patients post-operative analgesia?

□ Obstetrician
□ Anaesthesiologist
□ Nurse
□ Other (Please specify): _____

32. In your practice, following surgery for a caesarean section the patient's post-operative analgesia is prescribed by:

□ Obstetrician
□ Anaesthesiologist
□ Other (Please specify): _____

33. Do you routinely use an epidural catheter for postoperative analgesia after a caesarean section?

Yes – Only if the patient has an epidural catheter pre-operatively

Yes – I will insert an epidural catheter if the patient does not have one

No

39. If you answered <u>NO to QUESTION 38</u> , please skip the next three questions (Q 39 - 41) , and go straight to QUESTION 42

If you answered <u>YES to QUESTION 38</u> , what NSAIDs do you routinely prescribe?

- □ Ibuprofen
- □ Ketorolac
- □ Diclofenac
- □ Lornoxicam
- □ Parecoxib
- □ Other (Please Specify): _____

41. What is your preferred route of administration of NSAID's after a caesarean section?

- □ Oral
- □ Intravenous
- □ Rectal
- □ Intramuscular

Other (Please Specify): _____

42. Do you routinely prescribe intravenous Paracetamol for post-operative analgesia?

- □ Yes
- □ No

43. What other oral analgesics do you routinely prescribe after a caesarean delivery ? *(mark all that apply)*

- □ Paracetamol
- □ Codeine
- □ Oxycodone
- □ Tramadol
- □ Other (Please Specify): _____

44. In your current practice of obstetric anaesthesia, do you think that your patients are satisfied with their post-operative analgesia?

- □ Yes
- □ No

APPENDIX J: Survey of Obstetric Anaesthesia Practice for Caesarean Section

Dear Colleague

My name is Sean Chetty and I am currently conducting a survey on the current obstetric anaesthesia practices in South Africa. This survey is being conducted as part of a PhD research project at the University of the Witwatersrand and has been approved by the Human Research Ethics Committee Medical (Approval no: M 140123).

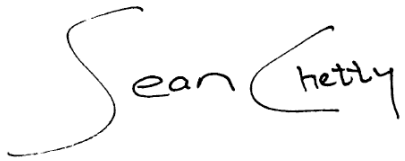
I would like to invite you, as a provider of anaesthetic services in South Africa, to participate in this research survey. The results of this survey will provide valuable information to determine current obstetric anaesthesia practice in South Africa. The survey will take approximately 3 - 5 minutes to complete.

Your answers are confidential and data will be recorded anonymously. However, should you wish to receive the results of the survey, please indicate your e-mail address at the end of the survey and the results will be forwarded to you.

All participants who complete the survey will be offered an opportunity to be entered into a lucky draw for a tablet computer. Should you wish to be entered into the lucky draw for a tablet computer, you can enter your contact details at the end of the survey. All entries will be detached from the survey responses to ensure anonymity of participants.

Thank you in advance for your participation.

Kind Regards



SURVEY

PLEASE USE "X" IN THE CHECKBOX TO MARK YOUR ANSWERS TO THE QUESTIONS BELOW:

1. **Which province do you work in?**

Gauteng
□ Western Cape
□ Eastern Cape
□ KwaZulu Natal
□ Mpumalanga
□ North West
□ Limpopo
□ Northern Cape
□ Free State

2. **Description of your practice** *(Choose one of the following options)***:**

Private practice

□ Private practice with public sector sessions

□ Private practice with no public sector involvement

Public sector

□ Medical officer with less than 5 years experience in anaesthesia

□ Medical officer with more than 5 years experience in anaesthesia

□ Registrar

□ Specialist with RWOPS

□ Specialist without RWOPS

3. **Highest South African Anaesthetic Qualification:**

□ MBChB / MBBCh

□ DA (SA)

□ FCA (SA) / FFA (SA) / MMed (Anaes)

□ International Fellowship in Obstetric Anaesthesia

4. **Approximately how many anaesthetics do you administer per month?**

(Please indicate an average number and NOT a range)

Number: _____

5. **Approximately how many CAESAREAN SECTION anaesthetics do you administer per month?** *(Please indicate an average number and NOT a range)*

   Number: _____

6. **What is YOUR extent of involvement in obstetric anaesthesia?**

   - ☐ Daytime cover
   - ☐ On-call only
   - ☐ Daytime and on-call
   - ☐ Other (Please specify): _____

7. **On average, how often do you work in obstetric anaesthesia?**

   - ☐ <1 day a week
   - ☐ 1 - 2 days a week
   - ☐ > 2 days a week

8. **What is your preferred anaesthetic technique for healthy patients requiring an elective caesarean section?**

   - ☐ Single shot spinal anaesthesia
   - ☐ Epidural anaesthesia
   - ☐ Combined spinal-epidural
   - ☐ General anaesthesia

9. **When administering a SPINAL anaesthetic, which type of spinal needle do you <u>prefer</u> to use?**

   - Quincke
   - ☐ Sprotte
   - Whitacre
   - Pencan
   - Eldor
   - I do not know the type of needle
   - I do not have a preference
   - Other (Please Specify): _____

10. When administering a SPINAL anaesthetic, which type of spinal needle do you routinely <u>have</u> to use?

Quincke

 Sprotte

Whitacre

Pencan

Eldor

Other (Please Specify): _____

I do not know the type of needle

I do not have a preference

11. When administering a SPINAL anaesthetic, what needle gauge do you <u>prefer</u> to use?

22G

24G

25G

26G

27G

Other (Please Specify): _____

I do not know the guage of needle

I do not have a preference

12. When administering a SPINAL anaesthetic, what needle gauge do you routinely <u>have</u> to use?

22G

24G

25G

26G

27G

Other (Please Specify): _____

I do not know the guage of needle

I do not have a preference

13. When administering a spinal anaesthetic for a healthy, non-obese patient for a caesarean section, what is your preferred choice of intrathecal local anaesthetic?

□ Bupivacaine 0.5% with Dextrose

□ Bupivacaine 0.5%

□ Lignocaine 2%

□ Ropivacaine 0.75%

□ Levobupivacaine 0.5%

□ Other (Please Specify): _____

14. For a healthy, non-obese patient, what is your standard dose of the <u>above mentioned</u> intrathecal local anaesthetic?

_____ mg **OR** _____ ml

15. For a healthy, non-obese patient, what other agents do you routinely add to your intrathecal local anaesthetic mixture? *(mark all that apply)*

No drugs routinely added

Fentanyl Dose used = _____ µg

Morphine Dose used = _____ µg

Sufentanil Dose used = _____ µg

Other (Please Specify):

Name of additive : _____ Dose used = _____

Name of additive : _____ Dose used = _____

16. In general, for an EPIDURAL placement, what is your preferred technique for loss of resistance?

Air

Saline

Both

□ Other (Please Specify): _____

17. Do you routinely use EPIDURAL anaesthesia for ELECTIVE Caesarean sections?

□ Yes

□ No

18. If you answered <u>NO to QUESTION 17</u>, please skip the next four questions (Q 18 – 21), and go straight to QUESTION 22

If you answered <u>YES to QUESTION 17</u>, what is your preferred choice of epidural local anaesthetic?

□ Lignocaine 2%

□ Bupivacaine 0.5%

□ Ropivacaine 0.75%

□ Levobupivacaine 0.5%

□ Other (Please Specify): _____

19. **Please state the volume of local anaesthetic that you routinely use (on average) in an standard sized pregnant patient:** _____ml

20. **For ELECTIVE caesarean delivery, what other agents do you routinely add to your epidural local anaesthetic?**
(mark all that apply)

No other agents added

□ Fentanyl

□ Sufentanil

□ Morphine

□ Sodium Bicarbonate 8.4%

□ Adrenaline

Other (Please Specify): _____

21. For elective caesarean delivery, do you routinely give morphine via the epidural catheter for post-operative pain relief?

Yes

(i) Please state the dose : _____ mg

(ii) When do you administer this medication?

- □ BEFORE the baby is delivered
- □ AFTER the baby is delivered

□ No

22. In a labouring patient with an epidural in situ requiring an URGENT caesarean section, what is your preferred method of anaesthesia?

□ (a) Top up the in-situ epidural

□ (b) Remove epidural and administer spinal anaesthesia

□ (c) General Anaesthesia

□ (d) Other (Please Specify): _____

23. If you answered <u>(b) (c) or (d) in QUESTION 22</u> , please skip the next 4 questions (Q 23 – 26) and go straight to question 27

If you answered <u>(a) in QUESTION 22</u> , What is your preferred choice of local anaesthetic for the epidural Top-up?

□ Lignocaine 2%

□ Bupivacaine 0.5%

Ropivacaine 0.75%

Levobupivacaine 0.5%

Other (Please Specify): _____

24. **Please state the average volume of local anaesthetic that you would routinely use in an average sized pregnant patient:** _____ml

25. For an URGENT caesarean section, what other agents do you routinely add to your epidural local anaesthetic?

□ No agents added

□ Fentanyl

□ Sufentanil

□ Morphine

□ Sodium Bicarbonate 8.4%

□ Adrenaline

Other (Please Specify): _____

26. For an URGENT Caesarean section, do you routinely give morphine via the epidural catheter for post-operative pain relief?

Yes

(i) Please state the dose : _____ mg

(ii) When do you administer this medication?

□ BEFORE the baby is delivered

□ AFTER the baby is delivered

□ No

27. Do you or the hospital/s where you practice obstetric anaesthesia, have a protocol for monitoring patients who receive neuraxial opioids?

Yes

No

28. If you answered <u>YES to QUESTION 27</u> , how long are patients monitored for signs of respiratory depression after neuraxial opioid administration?

□ <6 hrs

□ 6 – 12 hrs

□ Up to 12 hrs

□ 24 hrs

□ Up to 36 hrs

□ Up to 48 hrs

□ Other (Please Specify): _____

29. **If you answered <u>YES to QUESTION 27</u> , how are healthy patients who receive neuraxial opioids for caesarean delivery routinely monitored to detect respiratory depression?**

(mark all that apply)

□ Respiratory rate

Sedation score

Pulse oximetry

Other (Please Specify): _____

30. If you answered <u>NO to QUESTION 27</u> , do you think it is necessary to monitor patients who have been administered neuraxial opioids for respiratory depression?

□ YES

□ NO

31. Following surgery for a caesarean section, who do you believe should be responsible for the management of the patients post-operative analgesia?

□ Obstetrician

□ Anaesthesiologist

□ Nurse

□ Other (Please specify): _____

32. In your practice, following surgery for a caesarean section the patient's post-operative analgesia is prescribed by:

□ Obstetrician

□ Anaesthesiologist

□ Other (Please specify): _____

33. Do you routinely use an epidural catheter for postoperative analgesia after a caesarean section?

Yes – Only if the patient has an epidural catheter pre-operatively

Yes – I will insert an epidural catheter if the patient does not have one

No

34. If you answered <u>YES to QUESTION 33</u> , which of the following is your preferred method of medication administration?

□ Patient Controlled Epidural Analgesia with bolus administration only

□ Patient Controlled Epidural Analgesia with continuous infusion

□ Intermittent epidural boluses, local anaesthetic only

□ Intermittent epidural boluses, opioid only

□ Continuous infusion, local anaesthetic only

□ Continuous infusion, local anaesthetic plus opioid

Other (Please Specify): _____

35. **If you answered <u>NO to QUESTION 33</u>, please indicate why you do not use an epidural catheter for post-operative analgesia** *(mark all that apply*)

□ No standard protocol

□ No epidural pumps in postnatal wards

□ Inadequate monitoring in postnatal wards

□ Lack of nursing staff education in epidural care

□ Anaesthesia staff shortage

□ Nursing staff shortage

□ Other (Please Specify): _____

36. Do you routinely prescribe an intravenous Patient Controlled Analgesic (PCA) pump following a caesarean section?

□ Yes

□ No

37. If you answered <u>YES to QUESTION 36</u> , what intravenous analgesic agent do you routinely use in the PCA pump?

Morphine

□ Fentanyl

□ Sufentanil

□ Pethidine

Other (Please Specify): _____

38. Do you routinely prescribe non-steroidal anti-inflammatory drugs (NSAIDs) for postoperative analgesia after a caesarean section?

□ Yes

□ No

39. If you answered <u>NO to QUESTION 38</u> , please skip the next three questions (Q 39 - 41) , and go straight to QUESTION 42

If you answered <u>YES to QUESTION 38</u> , what NSAIDs do you routinely prescribe?

□ Ibuprofen

□ Ketorolac

□ Diclofenac

□ Lornoxicam

□ Parecoxib

□ Other (Please Specify): _____

40. What dosing regimen do you use for your NSAID prescription?

□ As required (PRN)

Regular scheduled doses 'around the clock'

Other (Please Specify): _____

41. What is your preferred route of administration of NSAID's after a caesarean section?

□ Oral

□ Intravenous

□ Rectal

□ Intramuscular

Other (Please Specify): _____

42. Do you routinely prescribe intravenous Paracetamol for post-operative analgesia?

□ Yes

□ No

43. **What other oral analgesics do you routinely prescribe after a caesarean delivery ?**

(mark all that apply)

□ Paracetamol

□ Codeine

□ Oxycodone

□ Tramadol

□ Other (Please Specify): _____

44. What dosing regimen do you use for these other oral agents?

□ PRN

□ Regular scheduled doses 'around the clock'

□ Other (Please Specify): _____

45. In your current practice of obstetric anaesthesia, do you think that your patients are satisfied with their post-operative analgesia ?

□ Yes

□ No

Thank you for your participation!

THIS SECTION WILL BE DETACHED FROM YOUR ANSWERS ABOVE

Should you wish to be sent the results of this survey, please write your e-mail address here:

e-mail address: _____

THIS SECTION WILL BE DETACHED FROM YOUR ANSWERS ABOVE

Should you wish to be entered into a lucky draw for a tablet computer please enter your contact details here:

Name : _____

e-mail address: _____

Contact Telephone Number: _____

APPENDIX K: The ASA Classification

ASA Physical Status Classification System

ASA PHYSICAL STATUS CLASSIFICATION SYSTEM

Last approved by the ASA House of Delegates on October 15, 2014

Current definitions (NO CHANGE) and Examples (NEW)

ASA PS Classification	Definition	Examples, including, but not limited to:
ASA I	A normal healthy patient	Healthy, non-smoking, no or minimal alcohol use
ASA II	A patient with mild systemic disease	Mild diseases only without substantive functional limitations. Examples include (but not limited to): current smoker, social alcohol drinker, pregnancy, obesity (30 < BMI < 40), well-controlled DM/HTN, mild lung disease
ASA III	A patient with severe systemic disease	Substantive functional limitations; One or more moderate to severe diseases. Examples include (but not limited to): poorly controlled DM or HTN, COPD, morbid obesity (BMI ≥40), active hepatitis, alcohol dependence or abuse, implanted pacemaker, moderate reduction of ejection fraction, ESRD undergoing regularly scheduled dialysis, premature infant PCA < 60 weeks, history (>3 months) of MI, CVA, TIA, or CAD/stents.
ASA IV	A patient with severe systemic disease that is a constant threat to life	Examples include (but not limited to): recent (< 3 months) MI, CVA, TIA, or CAD/stents, ongoing cardiac ischemia or severe valve dysfunction, severe reduction of ejection fraction, sepsis, DIC, ARD or ESRD not undergoing regularly scheduled dialysis
ASA V	A moribund patient who is not expected to survive without the operation	Examples include (but not limited to): ruptured abdominal/thoracic aneurysm, massive trauma, intracranial bleed with mass effect, ischemic bowel in the face of significant cardiac pathology or multiple organ/system dysfunction
ASA VI	A declared brain-dead patient whose organs are being removed for donor purposes	

*The addition of "E" denotes Emergency surgery: (An emergency is defined as existing when delay in treatment of the patient would lead to a significant increase in the threat to life or body part)

Reference

https://www.asahq.org/resources/clinical-information/asa-physical-status-classification-system#

APPENDIX L: Human Research Ethics Approval: M141181

R14/49 Dr Sean Chetty

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M141181

NAME: (Principal Investigator)	Dr Sean Chetty
DEPARTMENT:	Anaesthesiology Rahima Moosa Mother and Child Hospital
PROJECT TITLE:	An Investigation of the Influence of Different Intrathecal Opiods on the Post-Operative Pain Experiences of Woman at Rahima Moosa Mother and Child Hospital
DATE CONSIDERED:	28/11/2014
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Prof Fathima Paruk
APPROVED BY:	Professor P Cleaton-Jones, Chairperson, HREC (Medical)
DATE OF APPROVAL:	25/02/2015

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Secretary in Room 10004, 10th floor, Senate House, University.
I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. **I agree to submit a yearly progress report**.

Principal Investigator Signature _____ Date _____

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	V
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	169
	2b	Specific objectives or hypotheses	170
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	171
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	N/A
Participants	4a	Eligibility criteria for participants	173
	4b	Settings and locations where the data were collected	172
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	175
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	170
	6b	Any changes to trial outcomes after the trial commenced, with reasons	
Sample size	7a	How sample size was determined	172
	7b	When applicable, explanation of any interim analyses and stopping guidelines	N/A
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	175
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	176
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	176
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	175/176
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those	176

		assessing outcomes) and how	
	11b	If relevant, description of the similarity of interventions	N/A
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	179
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	179
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	183
	13b	For each group, losses and exclusions after randomisation, together with reasons	181
Recruitment	14a	Dates defining the periods of recruitment and follow-up	173
	14b	Why the trial ended or was stopped	173
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	183
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	183
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	184
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	N/A
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	197
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	223
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	224
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	224
Other information			
Registration	23	Registration number and name of trial registry	171
Protocol	24	Where the full trial protocol can be accessed, if available	171
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	vii

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.

INFORMED CONSENT FOR PATIENT PARTICIPATION

Dear Madam

My name is Sean Chetty and I am a doctor working in the Anaesthesiology department at the Rahima Moosa Mother and Child Hospital. I am conducting a study that is investigating how different types of anaesthetics, used for patients who are having caesarean sections, make patients feel after surgery.

The aim of the study is to determine if we can improve the management of pain after caesarean section surgery. If you decide to take part in the study you will be randomly assigned to one of three groups to receive either Fentanyl 25mcg or Morphine 50mcg or Morphine 100mcg with the local anaesthetic for your spinal anaesthetic for your surgery. All three of these drugs are opioid agents and all are registered for use in a spinal anaesthetic in South Africa.

After your surgery, you will be given a medication pump with pain medication in it, which you can use to manage any pain or discomfort you may have after the surgery. I will teach you how to use this pump, before and after your surgery.

You will be asked to complete two questionnaires in the first 24 hours after your surgery. Each of these questionnaires should take you approximately 5 minutes to complete. In addition, I would like permission to record some information from your hospital records. The information you provide will be made anonymous once you hand in this questionnaire. This means that your name or other form of identification will be deleted from the questionnaire after you hand it in and will not be included in any records we will hold.

Your answers in these questionnaires will not be shared with your medical or nursing team. Your participation is voluntary and your medical team will treat you in the same way whether or not you choose to participate in this study. Should you wish to withdraw from the study, you may do so without any problem.

I would be grateful if you would consider participating in this study.

CONSENT

I have had the purpose of the INTRATHECAL OPIOID study explained to me and have been given the opportunity to ask questions about my participation.

I agree to participate in the study

_____	_____	_____
Name	Signature	Date

(To be retained by investigator)

PATIENT INFORMATION SHEET

Dear Madam

My name is Sean Chetty and I am a doctor working in the Anaesthesiology department at the Rahima Moosa Mother and Child Hospital. I am conducting a study that is investigating how different types of anaesthetics, used for patients who are having caesarean sections, make patients feel after surgery.

The aim of the study is to determine if we can improve the management of pain after caesarean section surgery. If you decide to take part in the study you will be randomly assigned to one of three groups to receive either Fentanyl 25mcg or Morphine 50mcg or Morphine 100mcg with the local anaesthetic for your spinal anaesthetic for your surgery. All three of these drugs are opioid agents and all are registered for use in a spinal anaesthetic in South Africa.

After your surgery, you will be given a medication pump with pain medication in it, which you can use to manage any pain or discomfort you may have after the surgery. I will teach you how to use this pump, before and after your surgery.

You will be asked to complete two questionnaires in the first 24 hours after your surgery. Each of these questionnaires should take you approximately 5 minutes to complete. In addition, I would like permission to record some information from your hospital records. The information you provide will be made anonymous once you hand in this questionnaire. This means that your name or other form of identification will be deleted from the questionnaire after you hand it in and will not be included in any records we will hold.

Your answers in these questionnaires will not be shared with your medical or nursing team. Your participation is voluntary and your medical team will treat you in the same way whether or not you choose to participate in this study. Should you wish to withdraw from the study, you may do so without any problem.

If you have any questions or queries about this study at a later time, I can be contacted on 081 055 4761

(To be detached and given to patient)

INTRATHECAL OPIOID STUDY

Pre-Operative Data:

INFORMED CONSENT SIGNED	YES	NO

Study number	
Patient name	
Hospital number	

ASA	1	
	2	
	3	
	4	
	5	
	E	

Age	
Weight	
Blood Pressure	
Parity	
No. of previous pregnancy losses	

Indication for Caesarean Section	

Relevant Medical History	

Relevant Investigations	

FIRST PCA PUMP TEACHING DONE	YES	NO

In theatre Data:

HAS THE PATIENT RECEIVED HER PRE-OPERATIVE MEDICATION ?	YES	NO

BLOCK RANDOMISATION NUMBER	

DID THE PATIENT'S BLOOD PRESSURE DECREASE MORE THAN 20% FROM BASELINE OR TO LESS THAN 100mmHg DURING SURGERY ?	YES	NO

IF YES ABOVE, DID SHE RECEIVE ANY TREATEMENT AS PER HOSPITAL PROTOCOL	YES	NO

Surgery START Time	
Surgery END Time	

Recovery Room Data:

SECOND PCA PUMP TEACHING DONE	YES	NO

HAS THE PATIENT POST-OPERATIVE PRESCRIPTION BEEN WRITTEN AND THE PCA PUMP SET UP?	YES	NO

APPENDIX O: Data Collection Form

Ward Data:

FIRST TIME POINT COLLECTION (12hours after surgery)

TIME OF DATA COLLECTION	

HAS THE PAIN-OUT QUESTIONNAIRE BEEN COMPLETED?	YES	NO

PATIENT Pain Score at **Rest**

0	1	2	3	4	5	6	7	8	9	10

PATIENT Pain Score with **Cough**

0	1	2	3	4	5	6	7	8	9	10

TIME OF FIRST ANALGESIC REQUEST ON PUMP	

MORPHINE USED (in milligrams)	

SEDATION SCORE AT EVALUATION TIME	0	1	2	3

RESPIRATORY RATE	_____ breaths per minute

*** If <8 bpm – report to medical team for Nalaxone treatment**

N & V SCORE AT EVALUATION TIME	0	1	2	3

If score of 3 above, has the patient received treatment ?

YES	NO

PRURITIS SCORE AT EVALUATION TIME	0	1	2

If score of 2 above, has the patient received treatment ?

YES	NO

Ward Data:

SECOND TIME POINT COLLECTION (24 hours after surgery)

TIME OF DATA COLLECTION	

HAS THE PAIN-OUT QUESTIONNAIRE BEEN COMPLETED?	YES	NO

PATIENT Pain Score at **Rest**

0	1	2	3	4	5	6	7	8	9	10

PATIENT Pain Score with **Cough**

0	1	2	3	4	5	6	7	8	9	10

TOTAL MORPHINE USED (in milligrams)	

SEDATION SCORE AT EVALUATION TIME	0	1	2	3

RESPIRATORY RATE	_____ breaths per minute

*** If <8 bpm – report to medical team for Nalaxone treatment**

N & V SCORE AT EVALUATION TIME	0	1	2	3

If score of 3 above, has the patient received treatment ?

YES	NO

PRURITIS SCORE AT EVALUATION TIME	0	1	2

If score of 2 above, has the patient received treatment ?

YES	NO

HAS THE PCA PUMP BEEN REMOVED	YES	NO
HAS THE PATIENTS PRESCRIPTION BEEN UPDATED?	YES	NO

INSTRUCTIONS TO ANAESTHETISTS FOR INTRATHECAL OPIOID ADMINISTRATION CLINICAL TRIAL

Dear Anaesthetist

This patient has been recruited to be part of the current research study investigating the effect of different intrathecal opioid doses on patients' post-operative pain relief

As the doctor administering her anaesthetic, you are requested to please follow the instructions below regarding the administration of the anaesthetic in order to ensure that the study protocol is adhered to.

If you have any queries please speak to Dr Sean Chetty, who is the principal investigator for this clinical trial.

Please can you do the following:

1. Familiarise yourself with the study protocol including ALL exclusion criteria.
2. Once you have completed your pre-operative assessment, please consult the study investigator to let him know if there is any reason the patient cannot be included in the trial.
3. Patients will only be randomized when they arrive in the waiting area in the theatre complex, and after you have evaluated them.
4. Patients will be randomized into three groups according to the medication to be used in the spinal anaesthetic.
5. This patient has been randomised into **Group A** and must receive the following intrathecal anaesthetic mixture:

1.8ml 0.5% hyperbaric bupivacaine with 0.1mg preservative-free morphine (mixed in 0.4ml normal saline to a volume of 2.3ml)

She will receive a total of 2.3ml of the solution for her spinal anaesthetic

This is a double blinded clinical trial therefore DO NOT discuss the intrathecal medication with the investigator. The investigator MUST remain blinded to the intervention.

6. In theatre, standard, ASA monitoring must be used (Blood Pressure, ECG and Pulse Oximetry)
7. Each patient must be pre-loaded with a 500ml bolus of colloid solution (HES) prior to the procedure. Thereafter an infusion of Modified Ringers Lactate should be infused at a rate of 60ml / hr. This protocol is used to decrease the risk of post-spinal hypotension.
8. Spinal anaesthesia should be performed with the patient in the sitting position using an aseptic technique using a spinal needle in the lumbar spine.

9. HOW TO MIX THE SPINAL ANAESTHETIC MIX
    - *Using a 1 ml syringe (insulin syringe) draw up 0.1 ml of the morphine from the MORPHINE 10mg/ml AMPULE. This is 1mg of morphine.*
    - *Dilute this 0.1ml (1mg) up to 1ml in the insulin syringe to make a concentration of 0.1mg / 0.1ml*
    - *Mix 0.1ml (0.1mg) of this solution with 0.4ml of normal saline in a 2ml syringe. You should now have 0.5ml in this syringe. This is 0.1mg morphine in a 0.5ml volume*
    - *In a 5ml syringe, draw up 1.8ml of the spinal bupivicaine with dextrose*
    - *Add the 0.5ml of the 0.1mg morphine solution (from the 2ml syringe) to the bupivicaine. You should now have a volume of 2.3ml (1.8ml Bupivicaine + 0.5ml morphine) in the 5ml syringe.*

- Once there is back-flow of cerebrospinal fluid, the patient must be given 2.3ml local anaesthetic solution with opioid, as prepared following the above instructions. Thereafter, all instruments must be removed from the patient's back and a dressing is applied to the skin.
- After spinal anaesthesia, the patient must be placed in a supine position with 15º left uterine displacement using a crawford wedge.
- The level of sensory loss to temperature must be determined. Surgery can only commence after a satisfactory blockade up to level of T4 is achieved.
- Oxygen at 8 L/min flow must be administered via a 40 % venturi face mask.
- Blood pressure must be monitored at 1-minute intervals until the baby is delivered then continued every 3 minutes thereafter until the end of surgery.
- Hypotension is defined as a 20% reduction from baseline systolic blood pressure or a systolic blood pressure of 100mmHG. If this occurs, the patient must be treated with a rapid infusion of 100ml of Ringers Lactate solution and intravenous phenylephrine 50 microgram boluses (unless the patient has a bradycardia (HR<40bpm) – in which case 5mg intravenous boluses of Ephedrine must be used) .
- At the end of the surgery, please ensure that the surgeon inserts the Indomethacin suppository into the rectum. This is enclosed in this envelope.
- After surgery, the patient must be transferred to the recovery room for monitoring.
- The post-operative analgesia prescription will be issued by the investigator for the patient before she leaves the recovery room. This will be:
    - Morphine PCA Pump
    - Indomethacin Suppository 12hrly
    - Stemetil 12,5mg imi 8hrly

20. After 30 minutes of monitoring in the recovery room, if the patient is stable, and meets the discharge criteria for the recovery area, the patient will be discharged to the obstetric ward for observations.
21. Please complete the "in-theatre" data on the data collection sheet and hand over to the investigator in the recovery room

INSTRUCTIONS TO ANAESTHETISTS FOR INTRATHECAL OPIOID ADMINISTRATION CLINICAL TRIAL

Dear Anaesthetist

This patient has been recruited to be part of the current research study investigating the effect of different intrathecal opioid doses on patients' post-operative pain relief

As the doctor administering her anaesthetic, you are requested to please follow the instructions below regarding the administration of the anaesthetic in order to ensure that the study protocol is adhered to.

If you have any queries please speak to Dr Sean Chetty, who is the principal investigator for this clinical trial.

Please can you do the following:

1. Familiarise yourself with the study protocol including ALL exclusion criteria.
2. Once you have completed your pre-operative assessment, please consult the study investigator to let him know if there is any reason the patient cannot be included in the trial.
3. Patients will only be randomized when they arrive in the waiting area in the theatre complex, and after you have evaluated them.
4. Patients will be randomized into three groups according to the medication to be used in the spinal anaesthetic.
5. This patient has been randomised into **Group B** and must receive the following intrathecal anaesthetic mixture:

1.8ml 0.5% hyperbaric bupivacaine with 0.05mg preservative-free morphine (mixed in 0.45ml normal saline to a volume of 2.3ml)

She will receive a total of 2.3ml of the solution for her spinal anaesthetic

This is a double blinded clinical trial therefore DO NOT discuss the intrathecal medication with the investigator. The investigator MUST remain blinded to the intervention.

6. In theatre, standard, ASA monitoring must be used (Blood Pressure, ECG and Pulse Oximetry)
7. Each patient must be pre-loaded with a 500ml bolus of colloid solution (HES) prior to the procedure. Thereafter an infusion of Modified Ringers Lactate should be infused at a rate of 60ml / hr. This protocol is used to decrease the risk of post-spinal hypotension.
8. Spinal anaesthesia should be performed with the patient in the sitting position using an aseptic technique using a spinal needle in the lumbar spine.

9. HOW TO MIX THE SPINAL ANAESTHETIC MIX
   - *Using a 1 ml syringe (insulin syringe) draw up 0.1 ml of the morphine from the MORPHINE 10mg/ml AMPULE. This is 1mg of morphine.*
   - *Dilute this 0.1ml (1mg) up to 1ml in the insulin syringe to make a concentration of 0.1mg / 0.1ml*
   - *Discard 0.5ml of this solution*
   - *Mix the remaining 0.5ml of solution in the insulin syringe with 0.5ml normal saline. You now have a mixture of 0.05mg/0.1ml morphine*
   - *Mix 0.1ml (0.05mg) of this solution with 0.4ml of normal saline in a 2ml syringe. You should now have 0.5ml in this syringe. This is 0.05mg morphine in a 0.5ml volume*
   - *In a 5ml syringe, draw up 1.8ml of the spinal bupivicaine with dextrose*
   - *Add the 0.5ml of the 0.05mg morphine solution (from the 2ml syringe) to the bupivicaine. You should now have a volume of 2.3ml (1.8ml Bupivicaine + 0.5ml morphine) in the 5ml syringe.*

- Once there is back-flow of cerebrospinal fluid, the patient must be given 2.3ml local anaesthetic solution with opioid, as prepared following the above instructions. Thereafter, all instruments must be removed from the patient's back and a dressing is applied to the skin.
- After spinal anaesthesia, the patient must be placed in a supine position with 15° left uterine displacement using a crawford wedge.
- The level of sensory loss to temperature must be determined. Surgery can only commence after a satisfactory blockade up to level of T4 is achieved.
- Oxygen at 8 L/min flow must be administered via a 40 % venturi face mask.
- Blood pressure must be monitored at 1-minute intervals until the baby is delivered then continued every 3 minutes thereafter until the end of surgery.
- Hypotension is defined as a 20% reduction from baseline systolic blood pressure or a systolic blood pressure of 100mmHG. If this occurs, the patient must be treated with a rapid infusion of 100ml of Ringers Lactate solution and intravenous phenylephrine 50 microgram boluses (unless the patient has a bradycardia (HR<40bpm) – in which case 5mg intravenous boluses of Ephedrine must be used) .
- At the end of the surgery, please ensure that the surgeon inserts the Indomethacin suppository into the rectum. This is enclosed in this envelope.
- After surgery, the patient must be transferred to the recovery room for monitoring.
- The post-operative analgesia prescription will be issued by the investigator for the patient before she leaves the recovery room. This will be:
  - Morphine PCA Pump
  - Indomethacin Suppository 12hrly
  - Stemetil 12.5mg iml 8hrly

20. After 30 minutes of monitoring in the recovery room, if the patient is stable, and meets the discharge criteria for the recovery area, the patient will be discharged to the obstetric ward for observations.
21. Please complete the "in-theatre" data on the data collection sheet and hand over to the investigator in the recovery room

APPENDIX Q: Instruction to anaesthetists for administering 50µg intrathecal morphine

INSTRUCTIONS TO ANAESTHETISTS FOR INTRATHECAL OPIOID ADMINISTRATION CLINICAL TRIAL

Dear Anaesthetist

This patient has been recruited to be part of the current research study investigating the effect of different intrathecal opioid doses on patients' post-operative pain relief

As the doctor administering her anaesthetic, you are requested to please follow the instructions below regarding the administration of the anaesthetic in order to ensure that the study protocol is adhered to.

If you have any queries please speak to Dr Sean Chetty, who is the principal investigator for this clinical trial.

Please can you do the following:

1. Familiarise yourself with the study protocol including ALL exclusion criteria.
2. Once you have completed your pre-operative assessment, please consult the study investigator to let him know if there is any reason the patient cannot be included in the trial.
3. Patients will only be randomized when they arrive in the waiting area in the theatre complex, and after you have evaluated them.
4. Patients will be randomized into three groups according to the medication to be used in the spinal anaesthetic.
5. This patient has been randomised into **Group C** and must receive the following intrathecal anaesthetic mixture:

1.8ml 0.5% hyperbaric bupivacaine with 25µg fentanyl (2.3ml volume)

She will receive a total of 2.3ml of the solution for her spinal anaesthetic

This is a double blinded clinical trial therefore DO NOT discuss the intrathecal medication with the investigator. The investigator MUST remain blinded to the intervention.

6. In theatre, standard, ASA monitoring must be used (Blood Pressure, ECG and Pulse Oximetry)
7. Each patient must be pre-loaded with a 500ml bolus of colloid solution (HES) prior to the procedure. Thereafter an infusion of Modified Ringers Lactate should be infused at a rate of 60ml / hr. This protocol is used to decrease the risk of post-spinal hypotension.
8. Spinal anaesthesia should be performed with the patient in the sitting position using an aseptic technique using a spinal needle in the lumbar spine.

9. HOW TO MIX THE SPINAL ANAESTHETIC MIX
    - *Using a 2ml syringe, draw up 0.5ml Fentanyl from the FENTANYL 100mcg/2ml AMPULE*
    - *This is 25mcg of Fentanyl*
    - *In a 5ml syringe, draw up 1.8ml of the spinal bupivicaine with dextrose*
    - *Add the 0.5ml of Fentanyl (from the 2ml syringe) to the bupivicaine. You should now have a volume of 2.3ml (1.8ml Bupivicaine + 0.5ml fentanyl) in the 5ml syringe.*

- Once there is back-flow of cerebrospinal fluid, the patient must be given 2.3ml local anaesthetic solution with opioid, as prepared following the above instructions. Thereafter, all instruments must be removed from the patient's back and a dressing is applied to the skin.
- After spinal anaesthesia, the patient must be placed in a supine position with 15º left uterine displacement using a crawford wedge.
- The level of sensory loss to temperature must be determined. Surgery can only commence after a satisfactory blockade up to level of T4 is achieved.
- Oxygen at 8 L/min flow must be administered via a 40 % venturi face mask.
- Blood pressure must be monitored at 1-minute intervals until the baby is delivered then continued every 3 minutes thereafter until the end of surgery.
- Hypotension is defined as a 20% reduction from baseline systolic blood pressure or a systolic blood pressure of 100mmHG. If this occurs, the patient must be treated with a rapid infusion of 100ml of Ringers Lactate solution and intravenous phenylephrine 50 microgram boluses (unless the patient has a bradycardia (HR<40bpm) – in which case 5mg intravenous boluses of Ephedrine must be used) .
- At the end of the surgery, please ensure that the surgeon inserts the Indomethacin suppository into the rectum. This is enclosed in this envelope.
- After surgery, the patient must be transferred to the recovery room for monitoring.
- The post-operative analgesia prescription will be issued by the investigator for the patient before she leaves the recovery room. This will be:
    - Morphine PCA Pump
    - Indomethacin Suppository 12hrly
    - Stematil 12,5mg imi 8hrly

20. After 30 minutes of monitoring in the recovery room, if the patient is stable, and meets the discharge criteria for the recovery area, the patient will be discharged to the obstetric ward for observations.
21. Please complete the "in-theatre" data on the data collection sheet and hand over to the investigator in the recovery room





PATIENT OUTCOMES QUESTIONNAIRE

Dear Madam

My name is Sean Chetty and I am the head of the department of Anaesthesiology at the Rahima Moosa Mother and Child Hospital. My colleagues and I are collaborating on an international survey investigating how patients feel after surgery. The aim of the survey is to improve the management of pain after surgery in this department.

We would be grateful if you would consider participating in our survey. If you decide to join the study you will complete a questionnaire that should take approximately 5 minutes to complete. In addition, we would like permission to record some information from your hospital records. The information you provide will be made anonymous once you hand in this questionnaire. This means that your name or other form of identification will be deleted from the questionnaire after you hand it in and will not be included in any records we will hold.

Your answers in this questionnaire will not be shared with your medical or nursing team,

Your participation is voluntary and your medical team will treat you in the same way whether or not you choose to participate in our survey. Should you wish to withdraw from the study, you may do so without any problem.

CONSENT

I have had the purpose of the PAIN OUT study explained to me and have been given the opportunity to ask questions about my participation.

I agree to participate in the study

_____ _____

Signature Date

Version2.4 110225





PATIENT OUTCOMES QUESTIONNAIRE

Dear Madam

My name is Sean Chetty and I am the head of the department of Anaesthesiology at the Rahima Moosa Mother and Child Hospital. My colleagues and I are collaborating on an international survey investigating how patients feel after surgery. The aim of the survey is to improve the management of pain after surgery in this department.

We would be grateful if you would consider participating in our survey. If you decide to join the study you will complete a questionnaire that should take approximately 5 minutes to complete. In addition, we would like permission to record some information from your hospital records. The information you provide will be made anonymous once you hand in this questionnaire. This means that your name or other form of identification will be deleted from the questionnaire after you hand it in and will not be included in any records we will hold.

Your answers in this questionnaire will not be shared with your medical or nursing team,

Your participation is voluntary and your medical team will treat you in the same way whether or not you choose to participate in our survey. Should you wish to withdraw from the study, you may do so without any problem.

Version2.4 110225

PATIENT CODE:

PATIENT OUTCOMES QUESTIONNAIRE

The following questions are about pain you experienced since your surgery.

P1. On this scale, please indicate the **worst pain** you had since your surgery:

0	1	2	3	4	5	6	7	8	9	10
no pain										**worst pain possible**

P2. On this scale, please indicate the **least pain** you had since your surgery:

0	1	2	3	4	5	6	7	8	9	10
no pain										**worst pain possible**

P3. How often were you in **severe pain** since your surgery?
Please circle your best estimate of the percentage of time you experienced **severe pain**:

0%	10%	20%	30%	40%	50%	60%	70%	80%	90%	100%
never in severe pain										**always in severe pain**

P4. Circle the one number below that best describes how much, since your surgery, **pain interfered with or prevented you from ..**

a. doing **activities in bed** such as turning, sitting up, changing position:

0	1	2	3	4	5	6	7	8	9	10
did not interfere										**completely interfered**

b. **breathing deeply** or **coughing**:

0	1	2	3	4	5	6	7	8	9	10
did not interfere										**completely interfered**

c. **sleeping**:

0	1	2	3	4	5	6	7	8	9	10
did not interfere										**completely interfered**

d. Have you been **out of bed** since your surgery?

☐ Yes ☐ No

If yes, how much did pain interfere or prevent you from doing activities out of bed such as walking, sitting in a chair, standing at the sink:

0	1	2	3	4	5	6	7	8	9	10
did not interfere										**completely interfered**

Version 2.6 1 10 2015

PATIENT CODE:

PATIENT OUTCOMES QUESTIONNAIRE

P5. Pain can affect our mood and emotions.
On this scale, please circle the one number that best shows how much, since your surgery, **pain caused you to feel ..**

a. **anxious**

0	1	2	3	4	5	6	7	8	9	10
not at all										**extremely**

b. **helpless**

0	1	2	3	4	5	6	7	8	9	10
not at all										**extremely**

P6. Have you had any of the following **side effects** since your surgery?
Please circle **"0" if** no; if yes, circle the one number that best shows the severity of each:

a. **Nausea**

0	1	2	3	4	5	6	7	8	9	10
none										**severe**

b. **Drowsiness**

0	1	2	3	4	5	6	7	8	9	10
none										**severe**

c. **Itching**

0	1	2	3	4	5	6	7	8	9	10
none										**severe**

d. **Dizziness**

0	1	2	3	4	5	6	7	8	9	10
none										**severe**

P7. Since your surgery, how much **pain relief** have you received?
Please circle the one percentage that best shows how much relief you have received from all of your **pain treatments** combined (medicine and non-medicine treatments):

0%	10%	20%	30%	40%	50%	60%	70%	80%	90%	100%
no relief										**complete relief**

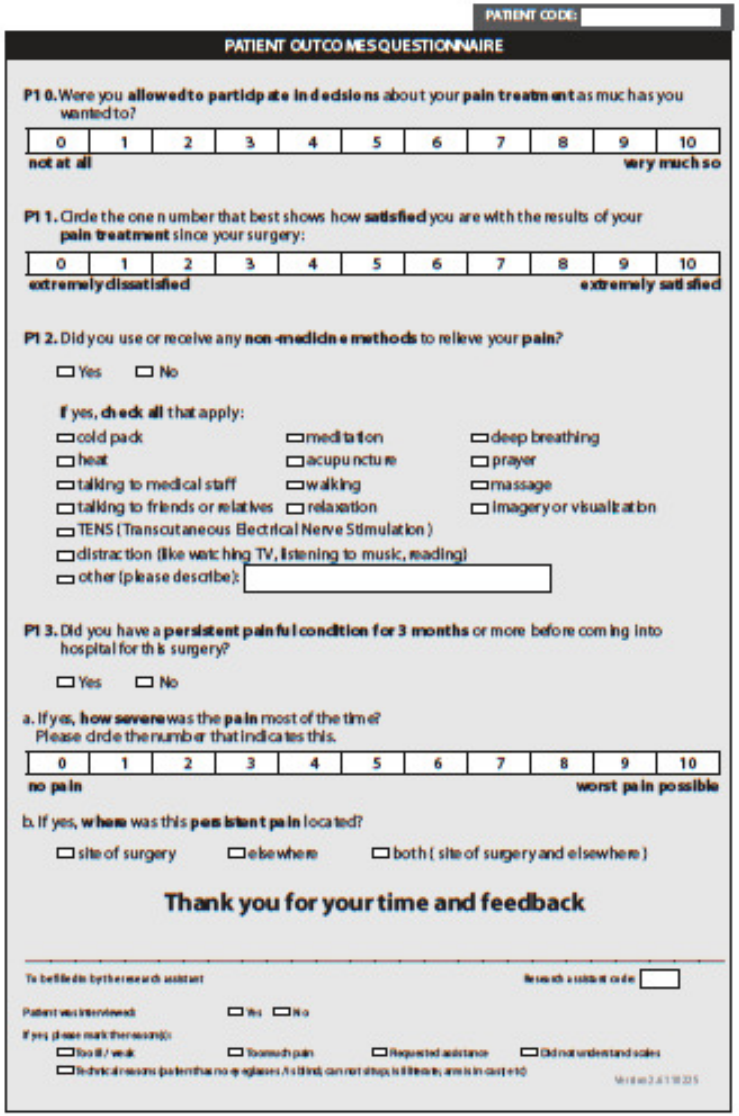
P8. Would you have liked **MORE pain treatment** than you received?

☐ Yes ☐ No

P9. Did you receive any **information** about your **pain treatment** options?

☐ Yes ☐ No

Version 2.6 1 10 2015



PATIENT CODE:

PATIENT OUTCOMES QUESTIONNAIRE

P1 0. Were you **allowed to participate in decisions** about your **pain treatment** as much as you wanted to?

0	1	2	3	4	5	6	7	8	9	10

not at all — **very much so**

P1 1. Circle the one number that best shows how **satisfied** you are with the results of your **pain treatment** since your surgery:

0	1	2	3	4	5	6	7	8	9	10

extremely dissatisfied — **extremely satisfied**

P1 2. Did you use or receive any **non-medicine methods** to relieve your **pain**?

☐ Yes ☐ No

If yes, check all that apply:

- ☐ cold pack
- ☐ heat
- ☐ talking to medical staff
- ☐ talking to friends or relatives
- ☐ meditation
- ☐ acupuncture
- ☐ walking
- ☐ relaxation
- ☐ deep breathing
- ☐ prayer
- ☐ massage
- ☐ imagery or visualization
- ☐ TENS (Transcutaneous Electrical Nerve Stimulation)
- ☐ distraction (like watching TV, listening to music, reading)
- ☐ other (please describe):

P1 3. Did you have a **persistent painful condition for 3 months** or more before coming into hospital for this surgery?

☐ Yes ☐ No

a. If yes, **how severe** was the **pain** most of the time?
Please circle the number that indicates this.

0	1	2	3	4	5	6	7	8	9	10

no pain — **worst pain possible**

b. If yes, **where** was this **persistent pain** located?

☐ site of surgery ☐ elsewhere ☐ both (site of surgery and elsewhere)

Thank you for your time and feedback

To be filled in by the research assistant — Research assistant code:

Patient was interviewed: ☐ Yes ☐ No

If yes, please mark the reason(s):

☐ Too ill / weak ☐ Too much pain ☐ Requested assistance ☐ Did not understand scales

☐ Technical reasons (patient has no eyeglasses / is blind, can not stay still / is illiterate, arm is in cast etc)

Version 2.4.1 18.2.05

A DATE OF DATA COLLECTION: 2 0 1 Y M M D D

B TIME OF DATA COLLECTION: H H M M

C WARD WHERE DATA IS COLLECTED:

D RESEARCH ASSISTANT CODE:

PATIENT CODE:

ROOM NUMBER:

SCREENING - INCLUSION CRITERIA

	yes	no
S1 Time of data collection is POD1 AND patient is 6 hrs (minimum) in the ward Endosurgery: Date 2 0 1 Y M M D D Time H H M M PODTT Back in ward: Date 2 0 1 Y M M D D Time H H M M #####1	☐	☐
S2 Patient is consenting age or over	☐	☐
S3 Patient has given his assent (or consent) to participate	☐	☐

If yes to 1 and 2 and 3
- Give the Outcomes questionnaire to the patient
- Complete the Process questionnaire

If no to 1 or 2 or 3:
- Do not fill in the rest of the Process questionnaire
- Do not give the Outcomes questionnaire to the patient
- Input the screening data (up to the point you have reached) into the web mask

Special case if yes to 1 and 2 and 3* and you have permission from the Ethics Committee in your hospital:
- Complete the Process questionnaire

If no to S3, mark the reason(s):

- ☐ a. Patient is not on the ward
- ☐ b. Patient does not wish to participate*
  - ☐ b1. too ill
  - ☐ b2. too much pain
  - ☐ b3. other
- ☐ c. Patient is asleep
- ☐ d. Patient has visitors
- ☐ e. It is not possible to communicate with the patient (e.g., patient is deaf, does not read/write in any of the languages in which the Outcomes questionnaire is available)
- ☐ f. Patient is cognitively impaired (e.g., Down's syndrome, dementia, Alzheimer's disease, Cerebral Palsy)
- ☐ g. Other, specify:

* Remember: You may interview patients who need help, eg., arrive ill or is too much pain or illiterate

DEMOGRAPHIC INFORMATION

D1 Gender	☐ Male ☐ Female	D2 Year of birth	1 9 Y Y
D3 Weight	kg	D4 Height	cm
D5 Nationality (check one only)		D6 Country of birth (check one only)	

D7 Language of Outcome questionnaire (select one)

☐ Arabic ☐ Bahasa Malaysia ☐ Danish ☐ Dutch ☐ English ☐ Finnish ☐ French
☐ German ☐ Hebrew ☐ Italian ☐ Korean ☐ Mandarin ☐ Romanian ☐ Russian
☐ Serbo-Croatian ☐ Spanish ☐ Swedish

BLANK FIELDS

Blank field 1:

Blank field 2:

Blank field 3:

Blank field 4:

Version2.6 110217

Page 1

Mark medications *given* to patient; record *cumulative* doses.

PATIENT CODE:

MEDICAL HISTORY

H1 Comorbidities

☐ yes ☐ no ☐ not possible to obtain the information

If yes, which (check all that apply):

Cancer	☐ **Cancer**
Renal	☐ **Renal** insufficiency or disease **without dialysis** ☐ **Renal** disease **requiring dialysis**
Psychiatric	☐ **Affective disorders** (depression, anxiety, phobia, PTSD, bipolar disorder) ☐ **Schizophrenia** ☐ **Alcohol** use disorder ☐ Current **smoker** ☐ **Substance abuse** of drugs (legal and illegal)
Cardiovascular	☐ **Hypertension** ☐ **Coronary artery** disease or **myocardial infarction** or **cerebral vascular accident**
Hematology	☐ **Sickle cell disease**
GI disease	☐ **Liver Cirrhosis** ☐ History or current upper or lower **GI ulcer** (peptic or duodenal ulcer disease) ☐ **Irritable bowel disease** (Crohn's disease, ulcerative colitis)
Pulmonary disease	☐ **Asthma** ☐ **Sleep apnea** ☐ Chronic Obstructive Pulmonary Disease (**COPD**)
Neurologic	☐ **Fibromyalgia**
Steroid use	☐ Regular administration of **oral or parenteral corticosteroid** medications
Multiple trauma	☐ At least 1 **fracture**(s) / **laceration**(s) / **tissue damage** in addition to the current reason for surgery
Other surgery	☐ Patient has already undergone **another surgery** during current hospitalization
	☐ **Other**, specify:

H2 Existing condition (check medical record)

☐ Pregnancy, Week: ☐☐ ☐ not relevant ☐ not possible to obtain the information

☐ Lactation ☐ not relevant ☐ not possible to obtain the information

H3 Did the patient receive any opioid(s) before the current admission?

☐ yes ☐ no ☐ not possible to obtain the information

If yes, which (multiple answers possible):

	Immediate release (PO & other)	Controlled release (PO & other)
Buprenorphine	☐ mg\day	☐ µg\hr (transdermal)
Codeine	☐ mg\day	☐ mg\day
Fentanyl	☐ µg\hr (transdermal / transmucosal)	☐ µg\hr (transdermal)
Hydrocodone	☐ mg\day	☐ mg\day
Hydromorphone	☐ mg\day	☐ mg\day
Morphine	☐ mg\day	☐ mg\day
Oxycodone	☐ mg\day	☐ mg\day
Oxycodone (with Naloxone)	☐ mg\day	☐ mg\day
Pethidine (Meperidine)	☐ mg\day	☐ mg\day
Tapentadol	☐ mg\day	☐ mg\day
Tilidin (often Naloxone)	☐ mg\day	☐ mg\day
Tramadol	☐ mg\day	☐ mg\day
Other, specify:	☐	☐
Other, specify:	☐	☐

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Page 3

Mark medications *given* to patient; record *cumulative* doses. PATIENT CODE:

PRE - MEDICATION

M1 Sedatives (pre-medication)

☐ yes ☐ no ☐ not possible to obtain the information

If yes, which (multiple answers possible)

	p.o.	i.v.
Diazepam	☐ mg	☐ mg
Dikaliumchlorazepat	☐ mg	☐ mg
Haloperidol	☐ mg	☐ mg
Lorazepam	☐ mg	☐ mg
Midazolam	☐ mg	☐ mg
Promethazine	☐ mg	☐ mg
Other, specify:	☐ mg	☐ mg

M2 Non-opioids (pre-medication)

☐ yes ☐ no ☐ not possible to obtain the information

If yes, which (multiple answers possible)

	p.o.	i.v.	i.m.	supp.
Celecoxib	☐ mg	☐ mg	☐ mg	☐ mg
Diclofenac	☐ mg	☐ mg	☐ mg	☐ mg
Etoricoxib	☐ mg	☐ mg	☐ mg	☐ mg
Gabapentin	☐ mg	☐ mg	☐ mg	☐ mg
Ibuprofen	☐ mg	☐ mg	☐ mg	☐ mg
Ketoprofen	☐ mg	☐ mg	☐ mg	☐ mg
Ketorolac	☐ mg	☐ mg	☐ mg	☐ mg
Metamizol	☐ mg	☐ mg	☐ mg	☐ mg
Naproxen	☐ mg	☐ mg	☐ mg	☐ mg
Nefopam	☐ mg	☐ mg	☐ mg	☐ mg
Paracetamol (Acetaminophen)	☐ mg	☐ mg	☐ mg	☐ mg
Parecoxib	☐ mg	☐ mg	☐ mg	☐ mg
Pregabalin	☐ mg	☐ mg	☐ mg	☐ mg
Other, specify:	☐	☐	☐	☐
Other, specify:	☐	☐	☐	☐

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Page 4

Mark medications *given* to patient; record *cumulative* doses. PATIENT CODE:

PRE - MEDICATION

M3 Opioids & Clonidine (pre-medication)

☐ yes ☐ no ☐ not possible to obtain the information

If yes, which (multiple answers possible):

	Immediate release (PO & other)	Controlled release (PO & other)	i.v.	i.m.	supp.	s.c.
Buprenorphine	☐ mg	☐ µg/hr	☐ µg	☐ µg	☐ µg	☐ µg
Codeine	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg
Fentanyl	☐ µg (transmucosal)	☐ µg/hr (transdermal)	☐ µg	☐ µg	☐ µg	☐ µg
Hydrocodone	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg
Hydromorphone	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg
Morphine	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg
Nalbuphine	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg
Oxycodone	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg
Oxycodone (with Naloxone)	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg
Pethidine (Meperidine)	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg
Piritramide	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg
Tapentadol	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg
Tilidin (with Naloxone)	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg
Tramadol	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg
Other, specify:	☐	☐	☐	☐	☐	☐
Other, specify:	☐	☐	☐	☐	☐	☐
Clonidine	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg

SURGICAL PROCEDURE(S)

P1 Surgical procedure(s)

use ICD-9 codes link: http://icd9cm.chrisendres.com/index.php?action=proclist

	ICD-9 Procedure Code		Text (only if your code is not necessary/unknown)
1		1	
2		2	
3		3	
4		4	

P2 Duration of surgery

Start surgery: Date: 2 0 1 Y M M D D Time: H H M M

End surgery: Date: 2 0 1 Y M M D D Time: H H M M

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Page 3 **Mark medications *given* to patient; record *cumulative* doses.** PATIENT CODE:

INTRA-OPERATIVE

M4 General anaesthesia (intra-op)

☐ yes ☐ no ☐ not possible to obtain the information

If yes, which (multiple answers possible):

☐ Inhalational	☐ IV

M5 Regional anaesthesia (RA) (intra-op)

☐ yes ☐ no ☐ not possible to obtain the information

If yes, which (multiple answers possible):

☐ Epidural	☐ Spinal	☐ Brachial plexus	☐ Femoral
☐ Sciatic	☐ Paravertebral	☐ Other:	☐ Other:

M6 Non-opioids (intra-op)

☐ yes ☐ no ☐ not possible to obtain the information

If yes, which (multiple answers possible):

	i.v.	i.m.	supp.
Diclofenac	☐ mg	☐ mg	☐ mg
Ibuprofen	☐ mg	☐ mg	☐ mg
Ketamine	☐ mg	☐ mg	☐ mg
Ketoprofen	☐ mg	☐ mg	☐ mg
Ketorolac	☐ mg	☐ mg	☐ mg
Metamizol	☐ mg	☐ mg	☐ mg
Naproxen	☐ mg	☐ mg	☐ mg
Nefopam	☐ mg	☐ mg	☐ mg
Paracetamol	☐ mg	☐ mg	☐ mg
Parecoxib	☐ mg	☐ mg	☐ mg
Other, specify:	☐	☐	☐
Other, specify:	☐	☐	☐
	i.v.	i.m.	supp.

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Page 4 **Mark medications *given* to patient; record *cumulative* doses.** PATIENT CODE:

INTRA-OP

M7 Wound infiltration (intra-op)

☐ yes ☐ no ☐ not possible to obtain the information

If yes, which (multiple answers possible; analgesia is not recorded):

☐ Single shot by surgeon ☐ Indwelling catheter ☐ Other, specify: ☐ Other, specify:

M8 Opioids & local anaesthetics & Clonidine (intra-op)

☐ yes ☐ no ☐ not possible to obtain the information

If yes, which (multiple answers possible):

	RA (see M5)	i.v.	i.m.	s.c.
Alfentanil	☐ µg	☐ µg	☐ µg	☐ µg
Buprenorphine	☐ µg	☐ µg	☐ µg	☐ µg
Codeine	☐ mg	☐ mg	☐ mg	☐ mg
Fentanyl	☐ µg	☐ µg	☐ µg	☐ µg
Hydrocodone	☐ mg	☐ mg	☐ mg	☐ mg
Hydromorphone	☐ mg	☐ mg	☐ mg	☐ mg
Morphine	☐ mg	☐ mg	☐ mg	☐ mg
Nalbuphin	☐ mg	☐ mg	☐ mg	☐ mg
Oxycodone	☐ mg	☐ mg	☐ mg	☐ mg
Pethidine (Meperidine)	☐ mg	☐ mg	☐ mg	☐ mg
Piritramid	☐ mg	☐ mg	☐ mg	☐ mg
Remifentanil	☐ µg	☐ µg	☐ µg	☐ µg
Sufentanil	☐ µg	☐ µg	☐ µg	☐ µg
Tramadol	☐ mg	☐ mg	☐ mg	☐ mg
Bupivacaine	☐	☐	☐	☐
Levobupivacaine	☐	☐	☐	☐
Lidocaine	☐	☐	☐	☐
Prilocaine	☐	☐	☐	☐
Ropivacaine	☐	☐	☐	☐
Other, specify:	☐	☐	☐	☐
Other, specify:	☐	☐	☐	☐
Clonidine	☐ µg	☐ mg	☐ mg	☐ mg
	RA	i.v.	i.m.	s.c.

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Mark medications *given* to patient; record *cumulative* doses. PATIENT CODE:

RECOVERY ROOM

M9 Non-opioids (recovery room)

☐ yes ☐ no ☐ not possible to obtain the information

If yes, which (multiple answers possible):

	p.o.	i.v.	i.m.	supp.
Celecoxib	☐ mg	☐ mg	☐ mg	☐ mg
Diclofenac	☐ mg	☐ mg	☐ mg	☐ mg
Etoricoxib	☐ mg	☐ mg	☐ mg	☐ mg
Gabapentin	☐ mg	☐ mg	☐ mg	☐ mg
Ibuprofen	☐ mg	☐ mg	☐ mg	☐ mg
Ketamine	☐ mg	☐ mg	☐ mg	☐ mg
Ketoprofen	☐ mg	☐ mg	☐ mg	☐ mg
Ketorolac	☐ mg	☐ mg	☐ mg	☐ mg
Metamizol	☐ mg	☐ mg	☐ mg	☐ mg
Naproxen	☐ mg	☐ mg	☐ mg	☐ mg
Nefopam	☐ mg	☐ mg	☐ mg	☐ mg
Paracetamol	☐ mg	☐ mg	☐ mg	☐ mg
Parecoxib	☐ mg	☐ mg	☐ mg	☐ mg
Pregabalin	☐ mg	☐ mg	☐ mg	☐ mg
Other, specify: ☐	☐	☐	☐	☐
Other, specify: ☐	☐	☐	☐	☐
	p.o.	i.v.	i.m.	supp.

M10 Regional analgesia (recovery room)

☐ yes ☐ no ☐ not possible to obtain the information

If yes, which (multiple answers possible):

☐ Epidural	☐ Spinal	☐ Brachial plexus	☐ Femoral
☐ Sciatic	☐ Paravertebral	☐ Other:	☐ Other:

[illegible]
(2) If the medication was given as PCA, tick appropriate box in the PCA column

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Mark medications *given* to patient; record *cumulative* doses. PATIENT CODE:

RECOVERY ROOM

M11 Opioids & local anaesthetics & Clonidine (recovery room)

☐ yes ☐ no ☐ not possible to obtain the information

If yes, which (multiple answers possible)

	Immediate release (PO & other)	Controlled release (PO & other)	RA (see M10)	i.v.	i.m.	supp.	s.c.	PCA (see M10)
Buprenorphine	☐ mg	☐ µg/hr	☐ µg	☐ µg	☐ µg	☐ µg	☐ µg	☐
Codeine	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐
Fentanyl	☐ µg	☐ µg/hr	☐ µg	☐ µg	☐ µg	☐ µg	☐ µg	☐
Hydrocodone	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐
Hydromorphone	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐
Morphine	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐
Nalbuphin	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐
Oxycodone	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐
Oxycodone (with Naloxone)	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐
Pethidine (Meperidine)	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐
Piritramid	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐
Sufentanil	☐ µg	☐ µg	☐ µg	☐ µg	☐ µg	☐ µg	☐ µg	☐
Tapentadol	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐
Tilidin (with Naloxone)	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐
Tramadol	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐
Bupivacaine	☐	☐	☐	☐	☐	☐	☐	☐
Levobupivacaine	☐	☐	☐	☐	☐	☐	☐	☐
Lidocaine	☐	☐	☐	☐	☐	☐	☐	☐
Prilocaine	☐	☐	☐	☐	☐	☐	☐	☐
Ropivacaine	☐	☐	☐	☐	☐	☐	☐	☐
Other, specify: ☐	☐	☐	☐	☐	☐	☐	☐	☐
Other, specify: ☐	☐	☐	☐	☐	☐	☐	☐	☐
Clonidine	☐ µg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐
Naloxone (only as an antagonist for respiratory depression)	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐
	Immediate release (PO & other)	Controlled release (PO & other)	RA	i.v.	i.m.	supp.	s.c.	PCA

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Mark medications *given* to patient; record *cumulative* doses. PATIENT CODE:

WARD

M12 Non-opioids (ward)

☐ yes ☐ no ☐ not possible to obtain the information

If yes, which (multiple answers possible):

	p.o.	i.v.	i.m.	supp.
Celecoxib	☐ mg	☐ mg	☐ mg	☐ mg
Diclofenac	☐ mg	☐ mg	☐ mg	☐ mg
Etoricoxib	☐ mg	☐ mg	☐ mg	☐ mg
Gabapentin	☐ mg	☐ mg	☐ mg	☐ mg
Ibuprofen	☐ mg	☐ mg	☐ mg	☐ mg
Ketamine	☐ mg	☐ mg	☐ mg	☐ mg
Ketoprofen	☐ mg	☐ mg	☐ mg	☐ mg
Ketorolac	☐ mg	☐ mg	☐ mg	☐ mg
Metamizol	☐ mg	☐ mg	☐ mg	☐ mg
Naproxen	☐ mg	☐ mg	☐ mg	☐ mg
Nefopam	☐ mg	☐ mg	☐ mg	☐ mg
Paracetamol	☐ mg	☐ mg	☐ mg	☐ mg
Parecoxib	☐ mg	☐ mg	☐ mg	☐ mg
Pregabalin	☐ mg	☐ mg	☐ mg	☐ mg
Other, specify:	☐	☐	☐	☐
Other, specify:	☐	☐	☐	☐
	p.o.	i.v.	i.m.	supp.

M13 Regional analgesia (ward)

☐ yes ☐ no ☐ not possible to obtain the information

If yes, which (multiple answers possible):

☐ Epidural	☐ Spinal	☐ Brachial plexus	☐ Femoral
☐ Sciatic	☐ Paravertebral	☐ Other:	☐ Other:

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Mark medications *given* to patient; record *cumulative* doses. PATIENT CODE:

WARD

M14 Opioids & local anaesthetics & Clonidine (ward)

☐ yes ☐ no ☐ not possible to obtain the information

If yes, which (multiple answers possible):

	Immediate release (PO & other)	Controlled release (PO & other)	RA (see M15)	i.v.	i.m.	supp.	s.c.	PCA (see M15)
Buprenorphine	☐ mg	☐ µg/hr	☐ µg	☐ µg	☐ µg	☐ µg	☐ µg	☐
Codeine	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐
Fentanyl	☐ µg	☐ µg/hr	☐ µg	☐ µg	☐ µg	☐ µg	☐ µg	☐
Hydrocodone	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐
Hydromorphone	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐
Morphine	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐
Nalbuphin	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐
Oxycodone	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐
Oxycodone	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐
Pethidine (Meperidine)	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐
Piritramid	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐
Sufentanil	☐ µg	☐ µg	☐ µg	☐ µg	☐ µg	☐ µg	☐ µg	☐
Tapentadol	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐
Tilidin	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐
Tramadol	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐
Bupivacaine	☐	☐	☐	☐	☐	☐	☐	☐
Levobupivacaine	☐	☐	☐	☐	☐	☐	☐	☐
Lidocaine	☐	☐	☐	☐	☐	☐	☐	☐
Prilocaine	☐	☐	☐	☐	☐	☐	☐	☐
Ropivacaine	☐	☐	☐	☐	☐	☐	☐	☐
Other, specify:	☐	☐	☐	☐	☐	☐	☐	☐
Other, specify:	☐	☐	☐	☐	☐	☐	☐	☐
Clonidine	☐ µg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐
Naloxone	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐ mg	☐
	IR	CR	RA	i.v.	i.m.	supp.	s.c.	PCA

M15 Measurement of pain: Was pain documented as defined in the SOPs?

☐ yes ☐ no ☐ not possible to obtain the information

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APPENDIX U: Turnitin Report

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG | FACULTY OF HEALTH SCIENCES

18 May 2016

The Chairperson
Postgraduate Committee
Faculty of Health Sciences
University of the Witwatersrand

Dear Madam

Re: PhD: **The anaesthetic management of patients undergoing caesarean section surgery and its impact on post-operative analgesia**

Dr Sean Chetty, student number: 9500971P has submitted his thesis to Turnitin which revealed a similarity index of 13%. These similarities appear not to be plagiarism but mainly the use of common terminology and phrases.

Yours sincerely

Peter Kamerman (Supervisor)
Associate Professor
School of Physiology

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ORIGINALITY REPORT

13%	10%	8%	2%
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