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Clinical outcomes and costs: a comparison between spinal anaesthesia and intra-venous general anaesthesia for emergency caesarean sections at a regional hospital in Swaziland.

By

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Declaration

I, Dr Edgar T Majirija, hereby declare that this dissertation presented to the University of Pretoria for the degree Masters of Science in Clinical Epidemiology, is my own work and has not been presented previously by me for a degree at any other tertiary institution.

E. Majirija *06/06/2013*

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ABSTRACT

Background: Spinal anaesthesia (SA) was introduced for emergency caesarean sections (c/sections) at Hlathikhulu Government Hospital in December 2010. Previously only general anaesthesia (GA) was used.

Objective: To determine the more cost-effective of the two interventions for emergency c/section.

Methods: Complications, clinical outcomes and costs were compared. Patients' charts were collected retrospectively for the period 01 January 2010 to 31 December 2011. Costs were assessed from a health-care provider perspective.

Results: Charts for 100 GA and 95 SA patients were compared. No cases of maternal mortality or ICU admission were recorded. Complications and outcomes were similar for SA versus GA groups: - post partum haemorrhage (7 vs 12, p = 0.28), neonatal mortality (3 vs 3, p = 0.63), neonatal intensive care admission (5 vs 5, p = 0.59), wound sepsis (2 vs 3, p = 0.52), blood transfusion (0 vs 2, p = 0.26), one minute APGAR (7.9 vs 7.5, p = 0.97), five minute APGAR (9.6 vs 9.7, p = 0.28), maternal blood loss (278 ml vs 322 ml, p = 0.073) and length of hospital stay (3.5 days vs 3.4 days, p = 0.68). Compared with GA, mean cost of anaesthetic drugs was lower for SA (Rand 24.01 vs Rand 75.07, p <0.001) and, similarly, mean costs of c/section were also lower for SA (Rand 837.20 vs Rand 902.43, p <0.001).

Conclusion: SA and GA are similar in terms of clinical outcomes but SA is the less expensive alternative.

Key words: emergency caesarean section; spinal anaesthesia, general anaesthesia; complications; costs; clinical outcomes.

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Appendix 7: University of Pretoria Faculty of Health Sciences Research Ethics committee approval.

Appendix 8: Scientific and Ethics Committee of Swaziland approval for study.

List of Abbreviations

95% CI:	95% confidence interval
<:	is less than
>:	is greater than
=:	is equal to
€:	Euro (European Union currency)
£:	British pound
$:	United States dollar
ANC:	Ante-natal care
APGAR:	Appearance Pulse Grimace Activity Respirations
C/section:	Caesarean section
Chi2:	Chi square test
CMS:	Central Medical Stores
CNS:	Central nervous system
CPD:	Cephalo-pelvic disproportion
DALYs:	Disability adjusted life years
GABA:	Gamma-aminobutyric acid receptor
HIV:	Human Immunodeficiency Virus
hrs:	hours
ICER:	Incremental cost effectiveness ratio
ICU:	Intensive care unit
L2, L3, L4, L5:	Level of lumbar vertebrae
ml:	millilitres
NMDA:	N-methyl-D-aspartate receptor
NSAIDs:	Non-steroidal anti-inflammatory drugs
PNC:	Post-natal care
PPH:	Post partum haemorrhage
PRN:	Per rising need
P value:	α value
QALYs:	Quality Adjusted Life Years

R:	South African Rand
RCTs:	Randomised Controlled Trials
SWILK:	Shapiro-Wilk test for assessing normality
vs:	versus
WHO:	World Health Organisation
WHO-CHOICE:	World Health Organisation – Choosing Interventions that are Cost-Effective

CHAPTER 1: BACKGROUND AND LITERATURE REVIEW

1.1 INTRODUCTION

Caesarean section (c/section) was introduced into clinical practice as a life saving procedure for both the mother and the baby. The first modern c/section was performed in the nineteenth century.[1] A c/section is usually performed when a vaginal delivery would put the mother's or baby's life at risk. The procedure has become one of the most important obstetric interventions in the management of labour, its use resulting in reduced maternal and neonatal mortalities.

C/section rates have been reported to be as high as 20% to 40% in high income countries, with low income countries having rates of 1 to 10% of all deliveries carried out. Most Southern African countries have c/section rates below 10% with the exception of South Africa. In 2010, c/section rates were noted to be - South Africa 20.6%, Zimbabwe 4.8%, Zambia 3.0%, Mozambique 1.9% and Swaziland 7.9% compared to high income countries such as China 25.9%, United States of America 30.3%, Germany 27.8%, United Kingdom 22% and Brazil 45.9% in 2008.[2] The majority of c/sections carried out worldwide are emergency cases as opposed to elective cases, this is more evident in developing countries where a few elective cases are performed. According to the World Health Organisation (WHO) in 2008, c/section rates between 5 to 20% were deemed adequate, the reasoning being that low rates were associated with higher maternal and perinatal mortalities and higher rates were associated with unnecessary procedures and were also associated with increased morbidity and cost to governments.[2] The average cost of performing a c/section to the healthcare provider ranges from country to country and also varies according to the methods used.

The decision on whether to perform a c/section and when and how the procedure is to be performed usually lies with the physician and his team. The issue of costs is not usually considered, the main focus being the outcomes for both the mother and the baby. Issues of costs are, however, important to the health service provider. Interventions with better outcomes or equivalent outcomes but greater ease of performing and monitoring are more likely to be favoured by physicians, whereas the healthcare provider will probably favour the less expensive intervention.[2]

Two types of anaesthesia are commonly used for performing c/sections - general anaesthesia and regional anaesthesia. Of the two methods regional anaesthesia is the most recent intervention and is the preferred option for most physicians and anaesthetists. Spinal anaesthesia was used in up to 95% of elective c/sections in the United Kingdom in 2002 and up to 86% overall. In Germany the figures for the same period were 50.5% for elective cases and 34.6% for emergency cases, the remainder being intra-venous general and epidural anaesthesia.[3,4] C/section has been found to be safe under both modalities in developed countries.

In Swaziland and other Sub-Saharan countries, spinal anaesthesia is still relatively new when compared to developed countries. Spinal anaesthesia was introduced on a large scale at Hlathikhulu Hospital in December 2010. There is still considerable debate between anaesthetists and medical officers on the use of the intervention locally. Issues of its comparability with the more traditional general anaesthesia for emergency caesarean section have been raised, considering that with general anaesthesia there are few apparent major complications or mortalities noted in the hospital. Initial impressions are that the two modes of anaesthesia are comparable. However, spinal anaesthesia seems to have the added advantage that it is easier to perform and monitor, giving it an advantage in settings where resources are limited. The economic impact of using spinal anaesthesia as opposed to general anaesthesia also needs to be considered, as a less expensive alternative will free up funds for use elsewhere.

By collecting data using a retrospective analytical study design, this study aims to compare some of the clinical outcomes and costs to the healthcare provider associated with performing c/section under general anaesthesia and spinal anaesthesia.

1.2 CAESAREAN SECTION

1.2.1 Definition

A c/section is defined as a surgical procedure in which one or more incisions is made through the mother's abdomen and the uterus to deliver one or more foetuses.[5,6] The operation has been developed to resolve obstetric complications not amenable to vaginal delivery.[5] C/section rates have been noted to be as high as 40% in some developed countries, with some developing countries having rates as low as 1%.[2] C/section has been used effectively over the years to reduce both maternal and perinatal mortality and the procedure now plays a very significant part in modern day obstetrics.

1.2.2 Techniques for caesarean section

Different techniques for performing c/sections have been developed over the years in an attempt to come up with the easiest procedure to perform with the fastest time to reach the foetus, the least haemorrhage, the least complications and more recently the best cosmetic result. The most common methods of performing caesarean section are the Pfannenstiel, Misgav Ladach, Joel Cohen, Maylard and the midline incision. The first four named are all transverse incisions, with the most commonly used being the Pfannenstiel incision.[7,8] Transverse incisions are associated with less blood loss, shorter operating times, reduced time to oral intake, less risk of fever, shorter duration of postoperative pain, lower analgesic requirements, and shorter time from skin incision to birth of the baby.[5] Two types of incisions to the uterus are also used, the classical (midline) incision and the lower transverse incision in the lower uterine segment. The lower transverse uterus incision is commonly used because of lower blood loss when compared to the classical incision and is used in up to 90% of all cases.[5]

1.2.3 Classification of Caesarean section

C/sections can be classified either as emergency or elective. An emergency c/section is when the procedure is performed when there is an immediate threat to the life of the woman or baby, or when there is maternal or foetal compromise which might not immediately be life-threatening but requiring early intervention as opposed to an elective c/section which is performed at a time that suits both the mother and the maternity team.[9] Rates of emergency c/section tend to be higher than for elective procedures, the extent of the difference differs

according the population being studied. Studies in Nigeria in 2009 showed elective versus emergency rates of 9.6% versus 34.4%, in England rates observed in 2010 were 9.3% versus 14.5%, and in Greece rates in 2010 were 18.2% versus 11% of all deliveries.[10-12]

1.2.4 Indications for caesarean section

Indications for c/section usually determine whether the procedure will be performed as an emergency or as an elective. Common indications for elective c/section include maternal request (commonest indication), breech presentation, hypertensive disorders, previous caesarean or uterine procedure, multiple pregnancies, Human Immunodeficiency Virus (HIV). The most common indications for emergency c/section include foetal distress, cephalo-pelvic disproportion (CPD), breech presentation, placental complications, previous caesarean or uterine procedure, prolonged labour, mal-presentation, hypertensive complications, cord accidents and multiple pregnancies. The most common indications for emergency c/section are foetal distress and cephalo-pelvic disproportion (CPD). Studies in African settings in 2009 showed that up to 30.9% of c/sections were for CPD, 25% for foetal distress, 21.5% for previous c/section and 13.5% for malpresentations.[5,12-14]

1.2.5 Complications

Complications are usually as a result of the condition necessitating the procedure, the anaesthesia used or the procedure itself. Both intra-operative and post-operative complications for c/section are generally rare with the most common complications noted being infection and bleeding. Despite complication rates being relatively low, they are higher for c/section than for normal vaginal delivery. Emergency c/sections also tend to have higher complication rates than elective c/sections. Compared to vaginal deliveries, maternal mortality and especially morbidity is increased with c/sections to approximately twice the rate after vaginal delivery (approximately one third to one half of maternal deaths post c/section being attributable to the surgical procedure or the indication of the procedure).[5] Major sources of morbidity and mortality can be related to sequelae of infection, anaesthetic complications, surgical injury and thromboembolic disease. Intra-operative surgical complications include uterine lacerations, bladder injury, injury to ureters (0.1% of all cases), bowel injuries (less than 0.1% of all cases), uterine atony and bleeding. Post-operative complications include endomyometritis (less than 5% with use of prophylactic antibiotics), wound infection (2.5 to 15% of all cases), urinary tract infection, slow return of bowel motility,

thromboembolic complications and bleeding.[5] Most post-operative complications are managed without any major long term consequences. Complication rates also depend to some extent on the level of competency of the physician so there are some institutional variations. Complication rates play a role in determining which intervention is preferred by health workers, interventions with lower complication rates tend to be favoured.

1.3 ANAESTHESIA FOR CAESAREAN SECTION

1.3.1 Definitions

Anaesthesia is a pharmacologically induced and reversible general or local insensibility to pain with or without loss of consciousness. Types of anaesthesia include general, local and regional anaesthesia. Local anaesthesia inhibits sensory perception within a specific location in the body. Regional anaesthesia renders a larger area of the body insensitive to pain by blocking transmission of nerve impulses between a part of the body and the spinal cord. Regional anaesthesia is normally divided into epidural and spinal anaesthesia. General anaesthesia refers to inhibition of sympathetic, sensory and motor nerve transmission at the level of the brain leading to loss of consciousness and lack of sensation. For c/section both regional and general anaesthesia are used. Regional anaesthesia is now the most commonly used technique.[3-5]

1.3.2 Types of anaesthesia for caesarean section

Two methods of anaesthesia are commonly used for c/section, namely general and regional anaesthesia. Regional anaesthesia is further classified into spinal and epidural anaesthesia or combined techniques. As previously mentioned, spinal anaesthesia is now the most popular method for obstetric anaesthesia with rates in some developed countries as high as 95% of elective procedures and 86% overall.[3,4] Rates of use for emergency c/section are also on the ascendency. Compared with general anaesthesia, regional anaesthesia has been associated with reduced maternal mortality, the need for fewer drugs, faster neonatal-maternal bonding, decreased blood loss and excellent pain control.[15]

1.3.3 General anaesthesia

General anaesthesia brings about reversible loss of consciousness and usually involves assisted ventilation for the patient and reversal of the anaesthesia when the procedure is completed. Drugs are usually administered intravenously to induce anaesthesia and then through inhalational means gases are used to maintain anaesthesia throughout the procedure. General anaesthesia usually requires use of special anaesthetic machines and monitors both to drive gases during the procedure and monitor vital signs of the patient during the procedure. Rapid sequence induction is normally used in obstetric cases because of the risk of aspiration as it is assumed that pregnant women have a full stomach. Induction

of anaesthesia in our setting is performed using sodium thiopentone, propofol or ketamine after pre-oxygenating the patient for about five minutes. Suxamethonium, a short acting paralyzing agent is also given after which intubation can be done using an endotracheal tube. Halothane is then used to maintain anaesthesia until the procedure is completed, oxygen and nitrous oxide are also given concurrently with the halothane. No agents for reversing paralysis are given when suxamethonium is used because of is short half life.[16-18]

1.3.3.1 General anaesthetic agents and their mechanisms

Sodium thiopentone is a short acting barbiturate that depresses the central nervous system (CNS) to produce hypnosis and anaesthesia without analgesia. It is given intravenously and is thought to act by enhancing responses to gamma-aminobutyric acid (GABA), diminishing glutamate responses, and directly depressing excitability by increasing membrane conductance and thereby producing a net decrease in neuronal excitability to provide anaesthetic action. Termination of its action is as a result of redistribution from the brain to other body compartments.[18,19]

Propofol is a newer intravenous anaesthetic agent which is a sedative-hypnotic agent with a short duration of action due to rapid redistribution from CNS to other tissues, high metabolic clearance and high lipophilicity. Loss of consciousness occurs rapidly and smoothly, usually within one arm-brain circulation (about 40 seconds). The action of propofol involves a positive modulation of the inhibitory function of the neurotransmitter GABA through $GABA_A$ receptors.[18,20]

Ketamine is a cyclohexanone derivative used for induction of anaesthesia. Ketamine has analgesic properties and less cardiorespiratory depressant effects than other anaesthetic agents. It also stimulates the cardiovascular system. Ketamine interacts with N-methyl-D-aspartate (NMDA) receptors, opioid receptors, monoaminergic receptors, muscarinic receptors and voltage sensitive calcium ion channels. It produces a state of profound anaesthesia, normal pharyngeal-laryngeal reflexes, normal or slightly enhanced skeletal muscle tone, cardiovascular and respiratory stimulation, thereby making it useful in states where there is hypovolaemia.[18,21]

Suxamethonium also called succinylcholine is a skeletal muscle relaxant which acts in about 30 seconds with a duration of effect of three to five minutes. It is used to facilitate intubation in general anaesthesia and to provide skeletal muscle relaxation during surgery or mechanical ventilation. The drug acts by mimicking the effect of acetylcholine causing a

persistent depolarisation of the neuromuscular junction, the depolarisation resulting in desensitization.[22]

Halothane is an inhalational anaesthetic agent that can be used for induction and maintenance of anaesthesia. It is a non-flammable, halogenated hydrocarbon anaesthetic that provides rapid induction with little or no excitement. Analgesia may not be adequate so it is usually administered with nitrous oxide. It acts on multiple ion channels resulting in depression of nerve conduction, breathing, cardiac contractility. Halothane binds to potassium channels in cholinergic neurons, and also binds to NMDA and calcium channels causing hyperpolarisation. Halothane also reduces blood pressure, decreases the pulse rate and depresses respiration.[23]

Nitrous oxide is an inhalational anaesthetic used as a carrier gas during general anaesthesia and also has some anaesthetic and analgesic properties. It is thought that gas molecules bind to proteins within neuronal membranes and modify ion fluxes and subsequent synaptic transmission thereby causing the anaesthetic effect. The analgesic effect is most likely as a result of interaction with the endogenous opioid system.[24]

1.3.4 Spinal anaesthesia

Spinal anaesthesia involves the introduction of a local anaesthetic into the subarachnoid space through the lumbar vertebrae usually between the levels L2 to L5, resulting in nerve blockage of nerve roots and consequently the analgesic effect. Spinal anaesthesia is now the main anaesthetic technique for c/sections in most developed countries with combined rates for elective and emergency as high as 86% in some developed countries. It is a sterile procedure which requires some positioning and draping of the patient before a spinal needle can be inserted into the vertebral space. Subarachnoid block is the most commonly administered regional anaesthetic for c/section because of its speed of onset and reliability.[3,4]

1.3.4.1 Spinal anaesthetic agents and their mechanisms

Bupivacaine is the most commonly used spinal anaesthetic agent. It is an amide and the duration of action is 4 to 8 hours. Bupivacaine is introduced into the subarachnoid space between L2 to L5 intervertebral space using a spinal needle. Bupivacaine blocks the generation and the conduction of nerve impulses by increasing the threshold for electrical

excitation in the nerve, by slowing the propagation of the nerve impulse, and by reducing the rate of rise of the action potential. It prevents depolarisation by blocking the influx of sodium into cells by binding to the intracellular portion of sodium channels. Analgesic effects come about as a result of binding to prostaglandin E2 receptors thereby inhibiting production of prostaglandins. The order of loss of function on administration of bupivacaine is pain – temperature – touch – proprioception then skeletal muscle tone.[25]

1.3.5 Epidural anaesthesia

Epidural anaesthesia is the second type of regional anaesthesia used for c/section. It involves insertion of an indwelling catheter through the lumbar vertebrae at levels L3 and L4, into the epidural space. An anaesthetic is then injected into the epidural space through the indwelling catheter resulting in nerve blockage. Epidural techniques can be used alone or in combination with other anaesthetic techniques. Epidural anaesthesia is normally performed by an anaesthetist or physician with specialist training. Because of the time it takes to perform the procedure and the expertise required, epidural anaesthesia is not very common in developing countries and is not commonly used for emergency c/sections. Drugs used for epidural anaesthesia are similar to those for spinal anaesthesia.[25,26]

1.3.6 Comparison of clinical outcomes: spinal versus general anaesthesia

The gradual shift from general anaesthesia to spinal anaesthesia has been necessitated by some advantages spinal anaesthesia has over the latter. Studies have shown that use of spinal anaesthesia for c/section is associated with reduced maternal blood loss because of a fall in blood pressure and maternal heart rate and improved venous drainage resulting in a decrease in oozing.[27-30] Estimated mean blood loss of 632 millilitres (ml) for spinal compared to 787 ml for general anaesthesia ($p<0.02$) was noted in a study performed in the West Indies in 2006, transfusion rates were also noted to be higher for general anaesthesia (13.6% versus 2.2%, $p<0.05$).[31] Other advantages of spinal anaesthesia include good muscle relaxation, a patent airway during the procedure and a faster return of normal gut function.[31] Evidence of the effect of anaesthesia on APGAR scores (Appearance, Pulse, Grimace, Activity, Respiration) at 1 minute and 5 minutes has been contradictory with some studies suggesting better outcomes with spinal anaesthesia than general anaesthesia and others showing no difference between the two interventions.[27,28,32] Pain management post operatively has also shown to be better in spinal anaesthesia by some studies, in terms of

both the time taken from completion of procedure to the first dose of analgesia using a per rising need (PRN) schedule or when total consumption during the first 24 hours was compared.[32,33] General anaesthesia does have some documented advantages in that the anaesthetist has reliable airway throughout the procedure, there are no concerns about anxiety for the patient during the procedure and no contraindications for general anaesthesia have been noted.[33,34] Studies have also shown a lower incidence of post-operative wound infection for general anaesthesia when compared to spinal anaesthesia (8.7% versus 20%, $p<0.0001$).[33,34] However, the incidence of maternal and perinatal mortality have been shown to be higher for general anaesthesia mainly as a result of failed intubation and aspiration of gastric contents.[31]

1.3.7 Anaesthetic related complications of caesarean section

Despite the increased use of c/section for delivery of babies, the incidence of anaesthetic complications still remains relatively low. The majority of complications encountered are minor or treatable complications with the incidence of major complications very low. It is however difficult in most cases to classify a complication as purely anaesthetic or surgical. Major complications such as maternal mortality directly as a result of anaesthesia are higher in general anaesthesia as opposed to regional techniques. It has also been noted that complication rates are higher in emergency c/sections as opposed to elective cases. Anaesthetic complications depend on the anaesthetic agents used and the type of anaesthesia.[35]

1.4 COSTS/ECONOMIC EVALUATION

1.4.1 Definitions

An economic evaluation is the comparative analysis of alternative courses of action in terms of both their costs and their consequences.[36] Economic evaluations are now being used more frequently in health care decision making when comparing different interventions and their outcomes in order to get the best outcomes with the least expenditure. The availability of several alternatives of attaining a particular goal has necessitated this approach. This is valuable in government settings in which resources are limited and where use of funds in one area often means the money is unavailable for other initiatives, often referred to as opportunity cost of the intervention. When making clinical decisions issues of costs are not usually considered, but when making healthcare resource allocation decisions, the aim is to minimise opportunity cost and come out with the most economically efficient intervention.[36]

1.4.2 Types of health economic evaluations

There are four main types of economic evaluations, namely cost minimisation, cost effectiveness, cost utility and cost benefit analysis. All types of health care evaluations measure the cost of a health care intervention in monetary terms but they differ in how the clinical benefit is measured.

1.4.2.1 Cost minimisation analysis

Cost minimisation analysis is an analysis in which all the relevant outcome measures of two or more comparators are assumed to be equal, resulting in the assessment being based solely on the comparative cost of the interventions. The assumption usually needs some clinical evidence for the study to be considered a full economic evaluation.[37]

1.4.2.2 Cost effectiveness analysis

A cost effectiveness analysis is an economic evaluation in which comparison is made of the costs and the benefits are reported in clinical outcomes appropriate for the group of patients being studied or in naturally occurring units, for example changes in mortality or complication rates. In instances where one intervention turns out to be cheaper than the other, an

incremental cost effectiveness ratio (ICER) is calculated depicting costs per unit of outcome obtained.[38] In this study we set out to compare clinical outcomes of caesarean section performed under two methods of anaesthesia, namely spinal anaesthesia and intra-venous general anaesthesia, therefore the incremental cost per complication averted can be estimated. Not all cost effectiveness analysis end up with an ICER as clinical outcomes may be found to be the same with both interventions, in such a case the study can be treated like a cost minimisation analysis were the focus is on the costs of the interventions.[37,38]

1.4.2.3 Cost utility analysis

Cost utility analysis compares alternatives similar as in cost effectiveness analysis, but a more generic outcome measure is used directly on patients using health utilities, for example, quality adjusted life years (QALYs) or disability adjusted life years (DALYs). This allows broader comparisons to be made between treatments or different disease groups. Cost per unit of outcome, for example, cost per QALY or DALY can then be derived.[39]

1.4.2.4 Cost benefit analysis

Costs and outcomes are compared using a generic monetary outcome, for example rands or dollars. This approach allows for assessment of whether programme is worthwhile or not. Cost benefit analysis has similar indications as cost utility analysis, the main difference being that subjective decisions regarding the value of health outcomes are made by techniques such as willingness-to-pay rather than by utilities.[40]

1.4.3 Perspective in economic evaluations

Perspective in health economic evaluations is the viewpoint from which the study is conducted. The perspective gives a guide as to which costs and outcomes will be considered relevant and are included in the analysis. Perspective can be from a societal view or from a health care provider perspective. The health care provider's perspective will look at the costs and benefits of providing an intervention and will also include direct medical costs. This may look at how much it will cost government and what benefits will be attained when using the intervention. A societal perspective is broader than a health care provider perspective and it includes all costs irrespective of who incurs them and considers all consequences whether good or bad, regardless of who experiences them.[36]

1.4.4 Costing

Costs in health economic evaluations are usually reported in monetary terms, the costs included being determined by the perspective of the study. Costing requires measurement of the quantities of resources used and the unit price of the resources. Health care provider perspective will normally look at the direct medical costs of an intervention.[36] In the analysis, the cost of c/section looked at cost of consumables, cost of drugs and gases, cost of sterilisation, cost of hospital stay post caesarean section and cost of therapeutic regimes from a healthcare provider perspective. Capital costs and wage costs for theatre staff were excluded in the analysis. Total costs are a product of the quantity of consumables used and the price per unit consumed.

1.4.5 Sensitivity analysis

Sensitivity analysis is a technique by which assumptions underlying estimates are varied in order to test for the robustness of the conclusions by varying the items around which there is uncertainty. The results of the evaluation are recalculated after systematically substituting values for each of the variables of interest. If the conclusions are unaltered after the re-analysis, the results are said to be robust.[41] Techniques available for sensitivity analysis include univariate/one-way sensitivity analysis, multivariate sensitivity analysis, threshold analysis and probabilistic sensitivity analysis. One way sensitivity analysis is the simplest type of analysis whereby input values for a parameter are varied one at a time across a plausible range while the remaining values are kept constant, range of values can be within minimum or maximum range or within 95% confidence intervals.[42] Sensitivity analysis allows the researcher to assess the effect uncertainties may have on their conclusions.

1.4.6 Study design in economic evaluations

Prospective studies, retrospective studies and modelling techniques can all be used for health economic evaluations. Retrospective studies assess costs that have already been incurred and outcomes that have already been realised when the study begins. Both clinical and cost data can be obtained from different sources and the data is readily available making the data collection phase only long enough for the researcher to collect the data. This has the advantage that both time and resources can be saved, the main disadvantage of retrospective studies being that the available data might not be as comprehensive and detailed as desired.[43] When compared to retrospective studies, prospective studies grant the

researcher better control on the type and quality of data collected but are also resource and time intensive and are susceptible to observer bias. Prospective studies are usually based on randomised clinical trials (RCTs) and are considered the standard in economic evaluations.[43] Retrospective studies are not as vigorous as prospective studies but do provide some credible results and may provide the basis for bigger and more robust studies.

1.4.6.1 Observational studies

Observational studies can be useful in collecting data for costs and clinical outcomes for health economic studies. Observational studies are normally less expensive, easier to perform and usually have fewer ethical considerations to deal with than randomised clinical trials which provide higher levels of evidence for clinical and economic studies, thus making them useful in resource limited settings. Observational studies have the advantage of providing data obtained in a more natural setting so results tend to resemble what would be found in the general population. Limitations of observational studies include the potentially large number of confounders because the symmetry of unknown confounders cannot be maintained since allocation to treatment groups is not under the influence of the investigator.[44]

Because imbalance of covariates between the intervention groups is often a problem and assignment of anaesthetic groups is not based on random allocation, special statistical techniques such as multivariate adjustment or propensity scores often need to be used to adjust for such differences at baseline using statistical techniques such as multivariable linear and logistic regression methods depending on the type of outcome in order to give the results some credibility.[44] Propensity scores, defined as the conditional probability of receiving a treatment rather than the alternative treatment given a collection of observed covariates, aim to simultaneously balance many covariates in the two treatment groups thereby reducing bias. Propensity scores are obtained using regression methods and can be used in conjunction with matching, stratification or regression methods to ensure validity in observational studies.[44,45]

Other problems encountered in this type of study include incomplete documentation especially in terms of consumables used or outcomes which might be deemed minor and are therefore not routinely measured or documented. This is often overcome by use of ‘assumptions’ in order to cater for these omissions. In such scenarios assumptions have to be clearly defined and should have a basis, whether scientific or other reasoning.

1.4.6.2 Clinical trials

Randomised controlled trials provide the highest level of evidence of all types of research and are often referred to as the gold standard. The ability to control for the most important variables and measure all outcomes accurately makes randomised clinical trials the preferred option in health economics. The economic evaluation benefits from elements of the experimental study that reduce bias in the treatment comparisons, including randomisation and blinding and the fact that processes are already in place to collect clinical data also makes it easy to collect patient level data for the economic outcomes, an approach often referred to as the 'Piggyback evaluation'.[46]

The main disadvantage of collecting economic data alongside clinical trials though is that data collected through an artificial scenario may not necessarily reflect what will be obtained in a more natural setting because participants and variables are very controlled whereas in clinical settings the situation may be different. Because study participants are often very carefully selected to minimise variability, participants will not be representative of the target populations hence outcomes may not be generalisable to everyday situations.[46] In addition, clinical trials often have a lot of ethical considerations to consider, are more costly and tend to be more time consuming which makes them not always practical for economic evaluations especially in more resource limited settings.

1.4.7 Composite scores

Composite outcomes are outcome measures in which a number of individual outcomes are combined to produce a single outcome measure. The composite outcome has to be associated with the primary objective of the study, be biologically plausible and be meaningful to clinicians and patients. They are particularly useful when comparing important negative outcomes (such as maternal mortality or neonatal mortality) which are very rare. Composite scores are frequently used as primary outcomes in obstetric trials. Complications have been used to come up with composite outcomes in obstetric studies as a way of replacing neonatal or maternal mortality as outcome measures. Individual components of composite scores can be weighted or have equal weights. Weights are usually determined by a panel of clinicians. Problems with composite scores include difficulty to use and interpret, errors in sample size estimation, difficulty with interpretation of results, and variations across a number of dimensions are unclear as they are concealed within an aggregate measure.[47,48] The process of coming up with an appropriate composite score to use with a particular study often involves a group of individuals sitting down and agreeing on

appropriate weights to give each individual outcome by common consensus, sometimes referred to as a Delphi panel.[49]

1.4.7.1 Composite measures in health economics

Natural units or composite measures are commonly used as outcome measures in cost effectiveness analysis. In situations were important single outcomes are rare because of advances in medicine or other reasons, composite scores have been used in order to come up with a single measurable outcome. Outcome measures such as QALYs, DALYs, episode free days, complications averted, symptom free days have often been used to describe the effectiveness component of a cost-effectiveness analysis. Composite outcomes become useful for cost effectiveness studies when interventions being studied have got multiple outcomes which all have significance on the decision of whether to adopt one intervention over the other needs to be made, the alternative with the better composite outcome being the preferred one. The effectiveness measure must be appropriate for the research question, be easy to interpret and be convertible into a cost effectiveness ratio.[48]

1.5 COST EFFECTIVENESS OF SPINAL ANAESTHESIA

Few studies exist on the cost-effectiveness of use of spinal anaesthesia for c/section especially in low income settings. Recommendations for the use of regional anaesthesia for c/section are based mainly on the risk of failed intubation and aspiration of gastric contents in pregnant women associated with general anaesthesia.[50] Based on studies performed in higher income settings there is a general tendency for spinal anaesthesia being less expensive to perform than epidural or general anaesthesia for most surgical procedures. Based on these studies, it is usually postulated that spinal anaesthesia should be cheaper to perform than general anaesthesia in all settings. The extent to which the two differ depends on the anaesthetic agents used and the conversion rate from spinal to general anaesthesia for failed spinal.

In other surgical disciplines there is evidence that spinal anaesthesia is the less expensive alternative. In orthopaedics, in a study performed by Gonano et al in 2006, spinal anaesthesia for total hip or knee surgery was found to be less expensive than general anaesthesia (€46.4 vs €89.6, $p<0.01$), the difference being attributed to the use of newer and more expensive anaesthetic agents and the long operating hours which necessitated longer use of vapours.[51] In another study performed in the United Kingdom in 2010, the same conclusion was arrived at when repair of fracture neck of femur was performed using the two anaesthetic techniques, with spinal anaesthesia being less expensive than general anaesthesia (£193.81 versus £270.58, $p<0.0001$).[52]

When the two techniques were compared for gynaecological laparoscopy, costs of spinal anaesthesia were also found to be lower for short duration gynaecology procedures ($62.31 versus $92.31, $p<0.001$). Anaesthetic drug costs and anaesthetic supplies were less expensive for spinal anaesthesia than desflurane based general anaesthesia.[53]

Comparisons made between spinal anaesthesia and epidural anaesthesia for c/section by Riley et al in 1995, spinal anaesthesia was also found to be the less expensive alternative and better suited for caesarean sections because of its shorter operating room times. Average per patient direct anaesthetic charges were $25.21 versus $43.62 for epidural anaesthesia. The main differences in costs between the two anaesthetic techniques were noted to be indirect costs which are as a result of the extra time taken to perform the epidural block. Indirect cost differences were mainly as a result of the extra time occupied by the anaesthetist, obstetrician, surgical assistant and the extra operating room time together with the cost of patient discomfort due to postdural puncture headaches.[54]

However, contrary to the perception that spinal is less expensive than general anaesthesia, one study conducted in Poland in 2010 showed that mean direct costs of general anaesthesia for c/section were lower than for spinal anaesthesia, mean personal costs of spinal anaesthesia were higher than general anaesthesia, costs of pharmaceuticals for general anaesthesia were lower than spinal anaesthesia and costs of medical supplies were higher for spinal anaesthesia (atropine, sodium thiopentone, nitrous oxide, oxygen, sevorane and fentanyl were used for general anaesthesia; 0.5% hyperbaric bupivacaine and 2% lignocaine were used for spinal anaesthesia). The differences were attributed to the longer duration of the spinal procedure, the higher medical staff costs for the spinal technique and avoidance of use of inhalational anaesthetics.[55]

There is no readily available literature on the cost effectiveness of spinal anaesthesia versus general anaesthesia for emergency c/section. The lack of studies comparing the costs of the two anaesthetic interventions for emergency caesarean sections limits conclusions to be postulated from a few studies of elective procedures and conclusions from other surgical disciplines which may not be very accurate or appropriate as illustrated by the findings from the study conducted in Poland. There is a need for more clinical and economic evidence to guide the decision making process and to assess the interventions which are already in place so that the most cost effective interventions are used especially in more resource limited settings.

CHAPTER 2: RATIONALE FOR THE STUDY

2.1 STUDY RATIONALE

Developing countries often lag behind in terms of use of medical technologies and interventions. Limitation in the availability of resources often compounds this problem. The use of up to date interventions which are cost effective would not only free up funds for other interventions but would also ensure that patients receive the best care currently available. Spinal anaesthesia is one of these interventions and has been in use for c/section for some time now in most countries. Despite some documented advantages of spinal anaesthesia in terms of outcomes for mother and baby, our regional hospital in Swaziland only started using spinal anaesthesia for c/section on a large scale in December 2010, having previously relied solely on intra-venous general anaesthesia for both emergency and elective c/sections.

Few studies on the cost of spinal anaesthesia for c/section in developing countries exist so studies to put into perspective the cost of use of spinal anaesthesia in regional hospitals in Swaziland need to be done to encourage more of its use. The outcomes of the study will put into perspective some of the clinical and economic benefits of using spinal anaesthesia at a regional hospital when compared to the more traditional intravenous general anaesthesia. This should help inform management and clinicians on which intervention to use for their patients.

CHAPTER 3: AIMS AND OBJECTIVES

3.1 RESEARCH QUESTION

Are there any differences in clinical outcomes and complications when spinal anaesthesia is compared to general anaesthesia for emergency c/sections? How much does it cost the healthcare provider to perform emergency c/section under spinal anaesthesia and under intra-venous general anaesthesia, which of the two methods is cheapest and has the more desirable outcomes?

3.2 STUDY OBJECTIVES

The purpose of the study was:

a) To compare the clinical outcomes and complications of spinal anaesthesia versus general anaesthesia for emergency caesarean section.

b) To determine and compare the costs of performing caesarean section under spinal anaesthesia versus general anaesthesia for emergency caesarean section.

CHAPTER 4: METHODS

4.1 STUDY DESIGN

4.1.1 Type of study

Cost and effectiveness analysis of emergency c/section using data obtained through a retrospective analytical cross sectional study.

4.1.2 Perspective

The study was performed from a health system perspective. The public health system is responsible for provision of all medical supplies and expertise in Swaziland with the patient paying a token amount for services provided, so all the costs and benefits of using spinal anaesthesia for c/section are borne mainly by the health system.

4.1.3 Treatment comparator

Spinal anaesthesia was compared to intra-venous general anaesthesia for emergency c/section.

4.2 STUDY SETTING

The study was conducted at Hlathikhulu government hospital which is a regional hospital located in the south west of Swaziland in the Shiselweni region. The hospital receives referrals from three major health centres and several clinics within the region. The hospital is a 230 bed facility and is covered by 10 medical officers amongst its staff.

The maternity wing of the hospital is 32 bed setup with 25 beds in the antenatal and postnatal care (ANC and PNC), 5 in the labour ward, an extra 2 delivery beds and a full time medical officer or specialist covering the unit. On average 2600 deliveries are conducted per year, of these 2370 are normal vaginal deliveries and approximately 230 are caesarean deliveries.

A fully staffed theatre is also within 50 metres of the maternity ward. Two fully equipped theatre rooms are available just adjacent to each other. Theatre has a complement of three nurse anaesthetists and a full complement of nurses and orderlies who do both shift work and on call duties. Laboratory services are also within a 10 metre distance from maternity.

4.3 STUDY POPULATION AND SAMPLING

4.3.1 Ethical considerations

Ethical approval was obtained from the Research Ethics Committee of the University of Pretoria and the Scientific and Ethics Committee of Swaziland.

Since data was collected retrospectively, permission to use hospital charts was obtained from the hospital management together with the ethics committee.

4.3.2 Study population

Data from maternity cases that have undergone emergency c/section at Hlathikhulu hospital were used. Complete charts meeting the inclusion criteria from the period January 2010 to December 2011 were used.

4.3.3 Inclusion criteria

Maternity cases between the ages 18 years to 45 years undergoing emergency c/section at Hlathikhulu hospital were included in the study.

4.3.4 Exclusion criteria

Maternity cases with multiple pregnancy, gestation below 32 weeks and elective c/sections were excluded from the study. Elective c/sections are rarely performed hence their exclusion from the study.

4.3.5 Sampling method

Complete charts were obtained using the hospital maternity register. Purposive sampling was used.

4.3.6 Sample size

We aimed for 200 charts because of logistical constraints, of which 100 were spinal anaesthesia and 100 were general anaesthesia. Spinal anaesthesia was only recently introduced on a large scale at Hlathikhulu hospital, considering the number of c/sections performed per year and the number of complete charts we were likely to find fitting the inclusion criteria, a sample size of 200 was deemed adequate.

4.3.7 Description of procedures

C/section is performed using mainly the Pfannenstiel incision or midline incision. Both groups of patients are routinely pre-medicated with atropine and have intravenous lines inserted whilst still in the ward. The patients are also shaved, catheterised, have either ringers lactate or normal saline put up, are draped and have theatre caps put on.

Patients undergoing general anaesthesia are induced using propofol, sodium thiopentone or ketamine together with suxamethonium given intravenously and an endotracheal tube inserted (dosage is based on weight). Anaesthesia is maintained using halothane (1% to 2%), nitrous oxide and oxygen. Pre-oxygenation is done before induction. No agents are used for reversal of anaesthesia. Either pethidine or fentanyl is given intra-operatively for analgesia as per discretion of the anaesthetist. Intravenous fluids are given throughout the procedure in the form of ringers lactate or normal saline. Oxytocin or ergometrine are also given when indicated. Standard monitoring is established and maintained throughout the procedure.

Spinal anaesthesia patients are positioned in the sitting position and cleaned and draped by the anaesthetist. Intervertebral space between L2 to L5 is located and a 22 gauge spinal needle inserted. After free flow of cerebrospinal fluid, bupivacaine 0.5% is injected into the subarachnoid space. Skin infiltration with lignocaine is not performed for any patient. Routine intra-operative monitoring is performed for all patients. If the spinal anaesthetic fails or the anaesthetist fails to locate a suitable intervertebral disc space, general anaesthesia is then used for the procedure. Intravenous fluids, oxytocin or ergometrine are given according to the anaesthetist's discretion or surgeon's request.

All patients are discharged from the theatre room to the recovery room after the procedure. The patients are later transferred back to maternity ward after stabilisation. Post operatively patients are admitted and kept in the maternity ward. Management post operatively is as per ward protocol, unless if otherwise specified in the patient charts. Documentation is routinely done by the anaesthetist, a nurse or midwife and the physician.

4.3.8 Variables

Outcome variables were divided into clinical outcomes, complications and costs. The specific outcomes, together with the demographic variables and their definitions are given below. Consideration will also be made of computing a composite score (complications averted) if significant differences are noted in clinical outcomes and complications.

4.3.8.1 Demographic variables

Age:	age in years of participant
Parity:	number of pregnancies beyond 28 weeks
Gravidity:	number of pregnancies
Estimated gestational age:	number of weeks since last normal menstruation
Type of anaesthesia:	can be spinal or intra-venous general anaesthesia
Indication:	reason for c/section

Previous c/section:	whether patient had a previous c/section or not
Birth weight:	weight of baby on delivery, in grams
HIV status:	positive or negative
Hypertension:	on treatment for hypertension
Diabetes mellitus:	on treatment for diabetes

4.3.8.2 Clinical outcomes

APGAR 1:	APGAR score at 1 minute
APGAR 2:	APGAR score at 5 minutes
Blood loss:	estimated maternal blood loss during c/section in millilitres
Length of stay:	time spent in hospital after delivery of baby, in days
Pain management:	time from completion of c/section to the first dose of pethidine
Maternal mortality:	death of mother during or post delivery
Neonatal mortality:	death of baby within first 28 days of life

4.3.8.3 Complications

Post partum haemorrhage:	bleeding in excess of 500 ml post delivery
Aspiration:	aspiration of gastric contents by mother during c/section
Hypotension:	hypotension requiring treatment
Headache:	headache requiring treatment
Nausea and vomiting:	nausea or vomiting during or after procedure
Sore throat or mouth trauma:	sore throat or trauma as a result of anaesthesia
Backache:	backache after anaesthesia
Paraplegia:	due to anaesthetic technique
ICU admission:	admission of mother into intensive care unit
Nursery admission:	admission of baby into nursery or intensive care unit
Wound bleeding:	bleeding from surgical site
Wound sepsis:	signs of infection on surgical site
Other complications:	other complications due to anaesthesia not mentioned above
Additional anaelgesia:	use of anti-inflammatory drugs within first 24 hours
Blood transfusion:	whether patient was transfused during the procedure

4.3.8.4 Costs

Direct costs were collected. Costs were divided into costs of pre-operative, intra-operative and post-operative consumables. Pre-operative costs included costs of preparing patient for caesarean section and prophylactic regimes. Intra-operative costs consisted of costs of anaesthetic drugs plus gases and surgical consumables. Post-operative costs were therapeutic drug and fluid regimes, hospital stay. Costs for failed spinal anaesthesia were excluded from the analysis.

4.3.9 Outcome measurements (clinical & costs)

4.3.9.1 Measurement tools

A questionnaire was used to collect demographic, outcome and cost data simultaneously (Appendix 1). Each questionnaire was allocated a personal identification number from 1 to 200. There was no link between questionnaire and patient chart.

4.3.9.2 Measurement methods

The details of patients who had undergone c/section during the period from January 2010 to December 2011 were obtained from the maternity registers. Charts were retrieved from the hospital records department using details obtained from maternity. Charts with complete demographic data, anaesthetic sheets, theatre sheets and post operative notes were included in the study. Charts were analysed until 100 charts of spinal and 100 intra-venous general anaesthesia charts were obtained.

4.3.9.2.i Costs

Costs were determined using case specific estimates of consumption of supplies, drugs and hospital stay. Estimates of costs were obtained from the Government Central Medical Stores (CMS) and Biomedical department through the hospital pharmacy department, price lists were as of 07 July 2011. Estimates of cost of hospital stay per day were based on the hotel component of hospital stay and were obtained from the WHO-CHOICE estimates of 2008.[56]

Costs were calculated by multiplying the price per unit by the number of units consumed. Use of gases was calculated using estimates of duration of the procedure and flow rates as indicated on the anaesthetic chart. To calculate the amount and the cost of halothane used for the procedure, the formula developed by Peter Dion was used.[57] Costs were grouped into costs of pre-operative, intra-operative and post-operative consumables. (Staff costs, capital equipment depreciation, patient supplies, costs for the infant were excluded as it was assumed that they were identical and were available to all patients). Costs were reported in South African Rands. (The South African Rand is used interchangeably with the local currency- the Emalangeni, the exchange rate conversion being 1:1)

A list of consumables considered in the analysis and other parameters measured is available in the Appendices section (Appendix 2). Because not all consumables used during the procedure are routinely measured or recorded, certain assumptions had to be made in order to come up with the cost of c/section. (Table of assumptions - Appendix 3)

4.3.9.2.ii Clinical parameters

APGAR scores for the baby (Appearance Pulse Grimace Activity Respirations) measured at 1 minute and 5 minutes after delivery and are scored from 0 to10 by the midwife receiving the baby. Each of the 5 parameters is scored from 0 to 2 and the total for all 5 given at the end. The score is given for every newborn baby irrespective of mode of delivery.

Length of hospital stay post c/section was measured in days from date of procedure to date of discharge. A day was measured from 0800hrs on the morning of the day of admission into the post caesar bay to 0800hrs the following morning.

Estimated maternal blood loss measured at the end of the procedure. Estimates are made by the anaesthetist from blood collected in the suction tube using an Askir 30 surgical aspirator, clots expelled from the uterus per vagina and collected in a kidney dish and the extent to which abdominal swabs are soaked. X-ray detectable Cutisoft abdominal swabs measuring 450 mm x 370 mm x 6ply are used during c/section and each is estimated to absorb 100 ml when completely soaked. Blood loss is normally indicated on the operating sheet in millilitres or noted as scanty or left blank if insignificant or less than 100 ml.

Pain management as documented during the first 24 hours post operatively. The time to first dose of pethidine was measured as the time from completion of the procedure to the first dose of pethidine, the first dose of pethidine is given on demand. Subsequent doses are given at 6 hour intervals for the first 24 hours. Use of supplementary anaelgesia in the form of anti-inflammatory drugs was also measured.

Post partum haemorrhage was measured based on an institutional definition of estimated maternal blood loss of greater than 500ml, whether intra-operatively or post-operatively.

Neonatal mortality was recorded if death occurred before the mother was discharged from maternity so as to exclude other potential causes of death not related to delivery process.

Maternal mortality was recorded if it occurred within the admission period.

4.3.10 Management of bias

Standard guidelines are used for measurement of parameters such as APGAR, maternal blood loss, so inter-observer bias should be minimal.

4.3.11 Data management & analysis

4.3.11.1 Data collection and entry

Data on clinical outcomes, complications and costs was collected manually using a standard questionnaire. (Appendix 1 and 2: Data collection tool)

Data on clinical outcomes and complications was entered into Microsoft excel. Quantities of consumables/cost data used for emergency c/section was also entered into Microsoft excel.

4.3.11.2 Statistical analysis

Data analyses were performed using STATA software (version 11.2: StataCorp LP, College Station, Texas).

Comparison of means for demographic data was done using the two sample T test after confirming normality using the Shapiro Wilk test (SWILK test) or Mann-Whitney rank sum for non-parametric data. The Chi Square (Chi2) test was used for frequency measures. (P value of <0.05 was regarded as statistically significant). No statistical tests were done to compare indications for c/section. Results for the SWILK test are illustrated in Appendix 4.

Clinical outcomes and the individual anaesthetic complications were compared for the two anaesthetic methods using Fisher's exact test, Chi square test, or T test as appropriate. Mean costs were compared using the Mann-Whitney rank sum for non-parametric data after confirming non-normality using SWILK test.

4.3.12 Sensitivity analysis

A univariate sensitivity analysis was performed by varying costs by 10% and 20% whilst the other costs were kept constant. The inflation rate approaches 10% in Swaziland hence the use of that figure, whilst 20% was used for a worst case scenario.

4.3.13 Discounting

Outcomes and costs were assessed for less than one year so no discounting was used for the analysis.

4.3.14 Assumptions

Because of the retrospective nature of the data collection and the fact that not all consumables are routinely measured or documented in patient charts, assumptions had to be made in order to allow for estimates of costs to be made. (Appendix 3)

CHAPTER 5: RESULTS

Logistical constraints limited the sample to 200 complete charts meeting the inclusion criteria, 100 were spinal anaesthesia and 100 were general anaesthesia patients. Five of the spinal anaesthesia cases were converted to general anaesthesia representing a conversion rate of 5%. These cases were however excluded from the analysis as only the actual costs of each procedure were being taken into consideration. Patients with gestation below 32 weeks, multiple pregnancy and elective c/sections were also excluded. Charts with missing theatre, anaesthetic sheets or routinely measured clinical information were also excluded. Elective c/sections are rarely performed hence their exclusion from the analysis. C/sections for gestations below 32 weeks are classified as hystorotomies in the institution.

The other study results are presented using the following format -

5.1 Demographic characteristics

5.2 Anaesthetic complications and clinical outcomes

5.3 Costs

5.4 Sensitivity analysis

5.1 Demographic characteristics

There were no significant differences in baseline characteristics between the two anaesthetic groups. Median age was 24.5 years vs 22 years (p=0.194) for the spinal anaesthesia group versus the general anaesthesia group. The majority of mothers in both anaesthetic groups were primigravids. There were no differences in HIV prevalence between the two groups (34% vs 32%, p=0.58).Details of demographic statistics are illustrated on Table 1.

Table 1: Baseline characteristics of women undergoing caesarean section

Characteristic	Spinal Anaesthesia (n=95)	General Anaesthesia (n=100)	P- value
Age (years) *	24.5 (21 to 29)	22 (20.3 to 28.8)	0.194
Parity †	0 (42%)	0 (54%)	0.22
Gravidity†	1 (40%)	1 (54%)	0.123
Estimated gestational age (weeks)‡	39.0 (1.7)	38.7 (1.9)	0.93
Previous caesarean section (%)	28	28	0.82
HIV positive (%)	34	32	0.58
Hypertensive (%)	7	6	0.70
Diabetes mellitus (%)	0	0	-
Birth weight (g)‡	3284 (521)	3223 (450)	0.81

‡Number () = mean value and standard deviation, †= mode (frequency), *= median value (interquartile range).

The differences in mean estimated gestational ages were also insignificant (39 weeks vs 38.7 weeks, p = 0.93), as were the differences in the prevalence of Diabetes mellitus and hypertension amongst the patients.

The most common indications for emergency c/section in both anaesthetic groups were cephalo-pelvic disproportion (CPD), foetal distress, malpresentation and previous c/section respectively. (Table 2: indications).

Table 2: Indications for caesarean section

Indications	Spinal Anaesthesia (n = 95)	General Anaesthesia n = 100
Previous c/section	10	9
Ante partum haemorrhage	2	1
Breech presentation	6	3
Cord prolapse	1	3
Cephalo-pelvic disproportion	42	43
Foetal distress	14	18
Extensive genital warts	1	1
Fibroid uterus	2	0
Mal-presentation	14	11
Previous myomectomy	0	1
Poor progress	1	3
Placenta praevia	0	2
Severe oligohydramnios	1	0
Severe hypertension	1	3
Uncooperative patient	0	2

5.2 Anaesthetic complications and clinical outcomes

There were no cases of aspiration, hypotension, paraplegia, sore throat or mouth trauma, backache, maternal mortality and ICU admissions detected from the charts analysed so the above mentioned anaesthetic complications were excluded from further statistical analysis. The results of the analysis of anaesthetic complications and clinical outcomes are illustrated in Table 3.

Table 3: Comparison of anaesthetic complications and clinical outcomes

Outcome	Spinal anaesthesia (n = 95)	General anaesthesia (n = 100)	P value
Anaesthetic complications			
Aspiration	0	0	-
Post partum haemorrhage*	7	12	0.28
Headache	1	1	0.74
Hypotension	0	0	-
Paraplegia	0	0	-
Sore throat or mouth trauma	0	0	-
Backache	0	0	-
Nausea and vomiting	1	0	0.49
Maternal mortality	0	0	-
ICU admission	0	0	-
Neonatal mortality	3	3	0.63
Neonatal ICU admission	5	5	0.59
Wound sepsis	2	3	0.52
Surgical site bleeding	0	1	0.51
Blood transfusion	0	2	0.26
Other complications	2	1	0.48
Additional analgesia	3	5	0.39
Clinical outcomes			
APGAR at 1 minute	7.9 (7.6 to 8.2)	7.5 (7.3 to 7.8)	0.97
APGAR at 5 minutes	9.6 (9.2 to 9.9)	9.7 (9.5 to 9.8)	0.28
Estimated blood loss (ml)	277.5 (243.1 to 311.9)	322.4 (271.9 to 372.9)	0.073
Length of hospital stay (days)	3.5 (3.1 to 3.9)	3.4 (3.1 to 3.6)	0.68
Time to dose of pethidine(minutes)	366.7 (322.7 to 410.7)	357.9 (311.6 to 404.3)	0.61

For anaesthetic complications- * is a Chi2 p value, all other p values are one sided Fisher's exact p values. For clinical outcomes- mean (95% Confidence interval)

The complication rates for the two anaesthetic groups were generally low with the exception of post partum haemorrhage (7 vs 12, p = 0.28). There were more blood transfusions for the general anaesthetic group, but the differences were not statistically significant (0 vs 2, p = 0.26). The differences in the use of additional anaesthesia was also insignificant (3 vs 5, p = 0.39). In both anaesthetic groups three neonatal deaths were recorded (p = 0.63), and five neonatal ICU admissions were also recorded (p = 0.59). One minute APGAR scores (7.0 vs 7.5, p = 0.97) and five minute APGAR scores (9.6 vs 9.7, p = 0.28) were also similar, as were the times to the first dose of pethidine (366.7 vs 357.9, p = 0.61).

5.3 Costs

Costs were calculated using quantities of consumables used during procedure and the price per unit. A total of R173 726.72 was used for the 200 caesarean sections performed during the study period; R90 181.27 for caesarean sections performed under general anaesthesia, R83 545.45 for those under spinal anaesthesia (including the 5 cases converted to general anaesthesia). (A complete breakdown of the consumables used for the analysis, the prices per unit and total costs is in Appendices 5 and 6).

The tables below illustrate the results of the cost analysis after cases of failed spinal anaesthesia were excluded.

Table 4: Summary of costs for spinal and general anaesthesia

Mean Costs	Spinal Anaesthesia	General Anaesthesia	P value
Pre-operative consumables	25.65 (0.02)	25.71 (1.03)	0.006
Intra-operative costs			
Anaesthetic drugs	24.01 (6.54)	75.07 (18.10)	<0.001
Other consumables	80.94 (8.28)	115.03 (303.55)	0.004
Post-operative consumables	77.00 (20.46)	75.82 (25.47)	0.019
Hospital stay (Hotel component)	629.60 (371.69)	610.77 (230.84)	0.81
Total costs	837.20 (391.86)	902.43 (392.42)	<0.001

Costs are in South African Rands with standard deviations in brackets.

Spinal anaesthesia had lower mean total costs for c/section (837.20 vs 902.43, p <0.001), representing an incremental cost of -R65.23. Differences were also noted between the mean costs of anaesthetic drugs (24.01 vs 75.07, p <0.001). Mean costs for hospital stay (hotel component) were similar for the two groups (629.60 vs 610.77, p = 0.81). The other results are illustrated in Table 4.

5.4 Sensitivity analysis

Because of some differences in the types of consumables and quantities of consumables used, a univariate sensitivity analysis was performed by varying costs by 10% and 20% with the other costs held constant. Costs were varied by 10% and 20% respectively, representing an approximation of the inflation rate and an extreme case scenario. The results of the analysis remained robust after adjustment, the results of the analysis illustrated that spinal anaesthesia had the lower costs even after the variations. The results of the analysis are illustrated in Table 5 below.

Table 5: Results of sensitivity analysis

Sensitivity analyses	Spinal Anaesthesia	General Anaesthesia	P value
Baseline mean total cost	837.20	902.43	<0.001
Cost of anaesthetic drugs increased by 10%	839.61	909.94	<0.001
Cost of anaesthetic drugs decreased by 10%	834.80	894.93	<0.001
Cost of anaesthetic drugs increased by 20%	842.01	917.45	<0.001
Cost of anaesthetic drugs decreased by 20%	832.40	887.42	<0.001
Cost of hospital stay increased by 10%	900.16	963.51	<0.001
Cost of hospital stay decreased by 10%	774.24	841.36	<0.001
Cost of hospital stay increased by 20%	963.12	1024.59	<0.001
Cost of hospital stay decreased by 20%	711.29	780.28	<0.001
Cost of ringers lactate increased by 10%	840.31	905.32	<0.001
Cost of ringers lactate decreased by 10%	834.10	899.54	<0.001
Cost of ringers lactate increased by 20%	843.58	908.21	<0.001
Cost of ringers lactate decreased by 20%	830.99	896.65	<0.001
Cost of 5% dextrose increased by 10%	838.32	903.55	<0.001
Cost of 5% dextrose decreased by 10%	836.09	901.32	<0.001
Cost of 5% dextrose increased by 20%	839.44	904.67	<0.001
Cost of 5% dextrose decreased by 20%	834.97	900.20	<0.001

Cost of normal saline increased by 10%	837.25	902.44	<0.001
Cost of normal saline decreased by 10%	837.16	902.42	<0.001
Cost of normal saline increased by 20%	837.29	902.46	<0.001
Cost of normal saline decreased by 20%	837.11	902.41	<0.001
Cost of blood increased by 10%	837.20	905.47	<0.001
Cost of blood decreased by 10%	837.20	899.40	<0.001
Cost of blood increased by 20%	837.20	908.50	<0.001
Cost of blood decreased by 20%	837.20	896.37	<0.001
Cost of spinal needles increased by 10%	837.36	902.43	<0.001
Cost of spinal needles decreased by 10%	837.04	902.43	<0.001
Cost of spinal needles increased by 20%	837.52	902.43	<0.001
Cost of spinal needle decreased by 20%	836.89	902.43	<0.001
Cost of surgical gloves increased by 10%	838.81	903.88	<0.001
Cost of surgical gloves decreased by 10%	835.60	900.99	<0.001
Cost of surgical gloves increased by 20%	840.42	905.33	<0.001
Cost of surgical gloves decreased by 20%	833.98	899.54	<0.001
Cost of betadine solution increased by 10%	838.66	903.73	<0.001
Cost of betadine solution decreased by 10%	835.75	901.14	<0.001
Cost of betadine solution increased by 20%	840.11	905.03	<0.001
Cost of betadine solution decreased by 20%	834.30	899.84	<0.001
Cost of ceftriaxone increased by 10%	839.03	904.24	<0.001
Cost of ceftriaxone decreased by 10%	835.38	900.63	<0.001
Cost of ceftriaxone increased by 20%	840.86	906.04	<0.001
Cost of ceftriaxone decreased by 20%	833.55	898.83	<0.001
Cost of metronidazole IV increased by 10%	837.24	902.46	<0.001
Cost of metronidazole IV decreased by 10%	837.17	902.40	<0.001
Cost of metronidazole IV increased by 20%	837.27	902.49	<0.001
Cost of metronidazole IV decreased by 20%	837.14	902.37	<0.001

Cost of gentamicin increased by 10%	837.31	902.49	<0.001
Cost of gentamicin decreased by 10%	837.10	902.38	<0.001
Cost of gentamicin increased by 20%	837.41	902.54	<0.001
Cost of gentamicin decreased by 20%	837.00	902.32	<0.001
Cost of cloxacillin IV increased by 10%	837.20	902.55	<0.001
Cost of cloxacillin IV decreased by 10%	837.20	902.32	<0.001
Cost of cloxacillin IV increased by 20%	837.20	902.67	<0.001
Cost of cloxacillin IV decreased by 20%	837.20	902.20	<0.001
Cost of pethidine increased by 10%	838.39	903.44	<0.001
Cost of pethidine decreased by 10%	836.02	901.43	<0.001
Cost of pethidine increased by 20%	839.58	904.45	<0.001
Cost of pethidine decreased by 20%	834.83	900.42	<0.001
Cost of diclofenac IM increased by 10%	837.21	902.44	<0.001
Cost of diclofenac IM decreased by 10%	837.20	902.43	<0.001
Cost of diclofenac IM increased by 20%	837.22	902.45	<0.001
Cost of diclofenac IM decreased by 20%	837.20	902.42	<0.001
Cost of abdominal swabs increased by 10%	838.26	903.73	<0.001
Cost of abdominal swabs decreased by 10%	836.15	901.14	<0.001
Cost of abdominal swabs increased by 20%	839.31	905.03	<0.001
Costs of abdominal swabs decreased by 20%	835.10	899.84	<0.001
Cost of ETT increased by 10%	837.20	902.99	<0.001
Cost of ETT decreased by 10%	837.20	901.87	<0.001
Cost of ETT increased by 20%	837.20	903.55	<0.001
Cost of ETT decreased by 20%	837.20	901.32	<0.001
Cost of vaginal pads increased by 10%	837.66	902.88	<0.001
Cost of vaginal pads decreased by 10%	836.75	901.98	<0.001
Cost of vaginal pads increased by 20%	838.11	903.33	<0.001
Cost of vaginal pads decreased by 20%	836.30	901.53	<0.001

Costs are in South African Rand; IV = intra-venous; IM = intra-muscular; ETT = endotracheal tube

CHAPTER 6: DISCUSSION

Both intra-venous general anaesthesia and spinal anaesthesia have been successfully used for c/section and other surgical interventions for some time now. Differences in terms of outcomes and complications between the two interventions often guide decisions on which method is the preferred one and in which setting. We compared the two techniques in terms of complications, clinical outcomes and costs in a retrospective manner.

Cases of maternal mortality and other major complications of c/section are generally rare in most settings. Of the cases we looked at in our study we did not come across any cases of maternal mortality or ICU admission for the mother. Spinal anaesthesia was comparable to intra-venous general anaesthesia in terms of clinical outcomes and complications for emergency c/section.

Post partum haemorrhage was the complication which occurred most frequently (7% for spinal vs 12% for general anaesthesia, $p = 0.28$) in our study but the differences between the two anaesthetic groups were not statistically significant. The high number of cases of post partum haemorrhage probably was attributed to the conservative definition of post partum haemorrhage used in our institution, a definition of blood loss greater than 500ml is used. There were also no differences in terms of neonatal mortality, number of neonatal ICU admissions or the use of additional analgesia post operatively. Our findings differ somewhat from other studies which showed a reduction in maternal blood loss, post partum haemorrhage, blood transfusion rates and consumption of additional analgesia when spinal anaesthesia is used.[27-33] The differences in the results are not only dependent on the type of anaesthesia used, but are also dependent on the surgical technique and expertise of the surgeons performing the procedure, hence the possible variation between different setups.

No common consensus exists on the effect of the type anaesthesia used on APGAR scores, both at one minute and at five minutes. Some studies have shown better APGAR scores with spinal anaesthesia than general anaesthesia whilst others show no difference between the two.[27,28,31,32] Findings from our analysis concurred with the group that found no difference between the two interventions in terms of one minute and five minute APGAR scores, the differences in the scores were both clinically and statistically insignificant.

Time to first dose of analgesia was found to be shorter and the amount of analgesia consumed within the first 24 hours was found to be significantly more for general anaesthesia in a prospective study conducted in 2009 in Croatia for elective c/sections.[58] The time to first dose of analgesia and the amount of analgesia consumed within the first 24 hours post-operatively was found to be similar in both intervention arms in our study group. The main differences between our study group and the Croatian study was the use of non-steroidal anti-inflammatory drugs (NSAIDs) for analgesia whereas in our study analgesia was mainly opioid based. Opioids have been found to be better suited for use post c/section than NSAIDs alone.[58]

Spinal anaesthesia had significantly lower anaesthetic drug costs than general anaesthesia. The mean cost of anaesthetic drugs (R24.01 vs R75.07, $p < 0.001$) was in keeping with other surgical disciplines like orthopaedics and gynaecology where studies also showed major differences between the two interventions with spinal anaesthesia having lower costs than general anaesthesia.[52,53] The differences in anaesthetic drug costs in our analysis were

attributed to the use of more drugs, gases and vapours for general anaesthesia as opposed to spinal anaesthesia were they are not routinely used. There were small differences noted between the mean costs of pre-operative consumables, intra-operative consumables (other consumables) and post-operative consumables with the general anaesthetic group having lower mean costs than the spinal anaesthesia group. The mean cost of hospital stay (hotel component) was similar between the two groups (R629.60 vs R610.77, p = 0.81). The mean length of hospital stay was also found to be similar between the two groups (3.5 days for spinal vs 3.4 days for general anaesthesia, p = 0.68). Overall, the mean cost of performing c/section under spinal anaesthesia was lower than under general anaesthesia (R837.20 vs R902.43, p <0.001). Capital costs, labour costs, theatre cleaning costs and costs of sterilisation of surgical equipment were excluded from the analysis because they were assumed to be similar or did not change because of the perspective we used for the analysis. The overall results are similar to findings made in other surgical disciplines which also showed that spinal anaesthesia was the less expensive option.[52,53] The findings however, differ from the Polish study which showed that general anaesthesia was the less expensive option for c/section.[55] The major difference between our study and the other studies was that the other studies were all for elective procedures whilst our study was for emergency c/section, this together with the different drugs and protocols used in the different settings could provide an explanation for the differences.

A sensitivity analysis performed by varying the costs by 10% and 20% showed that results of the cost analysis remained robust to variations in the key parameters, the differences in the average costs of the two interventions remained significant after adjustment. We did not however assess the impact of having an increased complication rate would have on the costs, especially considering that some of the most expensive inputs for c/section we noted during our study were blood and blood products. A high transfusion rate and a high number of post partum haemorrhage cases would make either of the two interventions more costly. We also did not assess what sort of impact a high rate of conversion of spinal anaesthesia to general anaesthesia would have on the overall costs of spinal anaesthesia.

Based on the results from the analysis, the similarities in terms of clinical outcomes and anaesthetic complications between the two interventions means the two interventions can be used inter-changeably in our obstetric unit. The differences in the mean costs of the two interventions would make spinal anaesthesia a more economically reasonable alternative to general anaesthesia. The fact that 5% of cases that started as spinal anaesthesia ended up being converted to general anaesthesia also means that the latter still plays an important role in our setup, but however spinal anaesthesia should be the primary option for emergency c/section as its use will free up a major theatre that would have been used for general anaesthesia. The cost offsets of freeing up a major theatre could be significant as there will be an expected reduction in use of specialised equipment such as anaesthetic machines, monitors and gases which are normally a part of major theatres. Such a scenario would possibly avail more funds from the hospital budget for other hospital activities.

Limitations

Limitations of this study include its retrospective approach and the sample size. The retrospective nature of the study meant that we were limited to using complete charts and had to use many assumptions as some costs, clinical outcomes and complications are not routinely documented in patient or theatre notes. This was more apparent when it came to calculating costs, as some costs were calculated from estimates based on average theatre use and this might not be a true reflection of the actual usage of consumables. Because of the retrospective nature of the study we were also unable to assess the patient's views or preferences for the type of anaesthesia. The small sample size and the small number of complications also meant that we could not use more powerful statistical methods to control for potential confounders and bias in the study.

Because the clinical outcomes and anaesthetic complications were similar for the two groups, we did not compute a composite anaesthetic complication score. We were also unable to calculate the incremental cost effectiveness ratio (ICER) because the clinical outcomes were similar for the two groups.

A study to take into consideration the patient's views would also be useful and would allow for a more informative decision to be made. Despite the limitations of the study, we were able to compare the two types of anaesthesia and come up with some conclusions based on the relatively short period we've used spinal anaesthesia in our setup.

Conclusions

The results of the study suggest that spinal anaesthesia and intra-venous general anaesthesia are similar in terms of anaesthetic complications and clinical outcomes for emergency caesarean sections. Mean costs of spinal anaesthesia, however, were lower for spinal anaesthesia than for intra-venous general anaesthesia for emergency caesarean section in our setting.

Recommendations

Spinal anaesthesia should be made the preferred option for emergency caesarean section.

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Appendices

Appendix 1: Clinical data collection tool

VARIABLES	PATIENT DATA	*Office use*
Patient Identification Number		PIN
Age (years)		AGE
Parity		PAR
Gravidity		GRAV
Indication		IND
Estimated Gestational Age (weeks)		EGA
Type of Anaesthesia	General = 0 Spinal = 1	ANEST
Conversion to General Anaesthesia	N/A = 0 No = 1 Yes = 2	CGA
Previous Caesarean Section	No = 0 Yes = 1	PCS
HIV Status	Negative = 0 Positive = 1	HIV
Hypertensive	No = 0 Yes= 1	HYPE
Diabetic	No = 0 Yes = 1	DIAB
Birth Weight (grams)		BWT
APGAR at 1 minute		APG1
APGAR at 5 minutes		APG2
Aspiration	No = 0 Yes= 1	ASP
Estimated Blood Loss (mls)		EBL
Post Partum Haemorrhage	No = 0 Yes = 1	PPH
Length of Hospital stay (days)		LOS
Significant Headache	No = 0 Yes = 1	HEAD
Significant Hypotension	No = 0 Yes = 1	HYPO

Paraplegia	No =0 Yes=1	PARA
Sore throat or Mouth trauma	No = 0 Yes=1	STMT
Backache	No = 0 Yes = 1	BACK
Nausea and Vomiting	No = 0 Yes = 1	NAV
Maternal Mortality	No = 0 Yes = 1	MAM
ICU Admission	No = 0 Yes= 1	ICU
Neonatal Mortality	No = 0 Yes = 1	NEOM
NICU/Nursery Admission	No = 0 Yes= 1	NICU
Wound Sepsis	No = 0 Yes = 1	WOS
Surgical Site Bleeding	No = 0 Yes = 1	SSB
Blood Transfusion	No = 0 Yes = 1	BTS
Other Complications	No = 0 Yes= 1	OCS
Time to first dose of Pethidine (hours)		PETH
Additional Analgesia	No = 0 Yes= 1	ADA

Appendix 2: Cost data collection tool

ANAESTHETIC/SURGICAL DATA COLLECTION TOOL

Identification number.

	Description	Size/Type/Time	No. units	Price/ unit	Subtotal cost
Pre-Op	Atropine				
	Cannula				
	Urinary Catheter				
	Urine bag				
	Surgical blade				
	Syringe	2ml			
	Syringe	5ml			
	Syringe	10ml			
	Syringe	20ml			
	Swabs				
	Needles				
	Water for injection	10ml			
	Fluid giving set				
	Strapping				
	Theatre cap				
	Surgical Gloves				
	Methylated spirit				
	Ringers Lactate	1L			
	Normal Saline	1L			
Total					
Intra-Op	Swabs				
	Gauze				
	Spinal Needle				
	Syringe	2ml			
	Syringe	5ml			
	Syringe	10ml			
	Syringe	20ml			
	Strapping				
	Ringers lactate	1L			
	Normal saline	1L			
	5 % dextrose	1L			
	Gelafundin				
	Blood	1 unit			
	Platelets				
	Fresh Frozen Plasma				
	Betadine				
	Bupivacaine				
	Diazepam				
	Morphine				
	Fentanyl				
	Pethidine				
	Sodium Thiopentone				
	Suxamethonium				
	Propofol				
	Oxytocin				
	Oxygen				
	Nitrous oxide				
	Halothane				

	Face mask				
	Oral airway				
	Linen saver				
	Surgical blades				
	Abdominal swabs				
	Elastoplast				
	Cord clamps				
	Suction catheter				
	Endotracheal tube				
	Surgical gloves				
	Examination gloves				
	Sutures: Nylon				
	Sutures: Vicryl				
	Sutures: Chromic				
	Sutures: -				
	Face masks				
	Theatre caps				
Total					
Post-Op	Ringers lactate	1L			
	Normal saline	1L			
	5 % dextrose	1L			
	Blood	1 unit			
	Fresh Frozen Plasma				
	Platelets				
	Gelafundin				
	Ceftriaxone (IV)				
	Metronidazole (IV)				
	Gentamicin (IV)				
	Chloramphenicol (IV)				
	Pethidine				
	Morphine				
	Fentanyl				
	Amoxicillin (po)				
	Metronidazole (po)				
	Paracetamol				
	Cloxacillin				
	Syringes	2ml			
	Syringes	5ml			
	Syringes	10ml			
	Syringes	20ml			
	Betadine				
	Gauze				
	Strapping				
	Elastoplast				
	Vaginal pads				
Total					
Others	Hospital stay per day				
Total					
Overall Cost					

Appendix 3: List of assumptions

	Assumptions made
1	No wastage or spillage of drugs or other consumables during anaesthesia.
2	Equal competence in surgical technique between surgeons/physicians.
3	Equal competence between nurse anaesthetists.
4	Appropriately sized consumables were used during anaesthesia (eg. 5 ml syringes for 4 or 5 ml doses).
5	One size of hypodermic needles was used for all purposes, size G21.
6	One size of examination gloves was used – medium/large.
7	Size of surgical gloves used for procedure was 7.5.
8	Size of spinal needle used for procedure was G22.
9	Size of surgical blade used for procedure was – size 24.
10	The number of surgical gloves or examination gloves used assumed to be standard and gloves were used appropriately and only once.
11	Intra-venous fluids were used as per protocol post operatively (unless indicated otherwise), pre-operatively if not indicated it was assumed that ringers lactate was used.
12	Use of some consumables is based on average observed theatre use as they are not routinely recorded, e.g. linen savers, betadine.
13	Use of vaginal pads assumed to be 3 per day for the first three days post caesarean section.
14	Estimates of gases used (O_2, N_2O and halothane) are based on levels used to maintain anaesthesia during the procedure (assumed that no variation during the procedure).
15	Where size of ETT not specified, assumption is that size 7.5 was used (average size for hospital patients).
16	It is assumed that 6 theatre staff (surgeon, scrub nurse, assistant and anaesthetist included) were present during the procedure as numbers are not indicated.
17	Unused contents of vials for bupivacaine, propofol, pethidine, suxamethonium, oxytocin, sodium thiopentone, fentanyl, diclofenac, ceftriaxone, etc were discarded at the end of the procedure and not used for the next patient.
18	Estimates of elastoplast, strapping, cotton swabs used were difficult to make so they were excluded from the analysis.
19	25 ml of betadine was used for wound dressing per day.
20	25 ml of betadine was used for cleaning the patient before draping for spinal anaesthesia.

Appendix 4

SWILK assessment of normality of characteristics and outcomes

	P Value
Characteristic	
Age	<0.001
Parity	<0.001
Gravidity	<0.001
Estimated gestational age	0.099
Birth weight	0.74
Clinical Outcome	
APGAR at 1 minute	<0.001
APGAR at 5 minutes	<0.001
Estimated blood loss	<0.001
Time to first dose of pethidine (minutes)	<0.001
Costs	
Cost of pre-operative consumables	<0.001
Cost of anaesthetic drugs	<0.001
Cost of other intra-operative consumables	<0.001
Cost of post operative consumables	<0.001
Cost of hospital stay	<0.001
Total costs	<0.001

Appendix 5

Total Costs and Quantities – General Anaesthesia

	Description	Size/Type/ Time	No. units	Price/ unit (Rands)	Subtotal cost
Pre-Op	Atropine	0.5mg	100	1.63	163
	Cannula	16G	21	2.34	49.14
	Cannula	18G	72	2.23	160.56
	Cannula	20G	7	2.23	15.61
	Urinary Catheter	16	100	3.65	365
	Urine bag	1 bag	100	2.10	210
	Surgical blade	size24	100	0.26	26
	Syringe	2ml	100	0.22	22
	Syringe	5ml	0	0.25	0
	Syringe	10ml	1	0.37	0.37
	Syringe	20ml	99	0.58	57.42
	Swabs	-	-	-	-
	Needles	21G	200	0.09	18
	Water for injection	10ml	200	0.56	112
	Fluid giving set	1 set	100	2.10	210
	Strapping	-	-	-	-
	Theatre cap	1 cap	100	0.15	15
	Surgical Gloves	Size 7.5	300	1.61	483
	Methylated spirit	1ml	1000	0.014	14
	Ringers Lactate	1L	100	6.45	645
	Normal Saline	1L	1	10.66	10.66
Total					**2576.76**
Intra-Op	Swabs	-	-	-	-
	Gauze	1 pack	200	0.57	114
	Spinal Needle	22G	0	1.57	0
	Syringe	2ml	149	0.22	32.78
	Syringe	5ml	9	0.25	2.25
	Syringe	10ml	1	0.37	0.37
	Syringe	20ml	198	0.58	114.84
	Strapping	-	-	-	-
	Ringers lactate	1L	148	6.45	954.6
	Normal saline	1L	0	10.66	0
	5 % dextrose	1L	0	11.17	0
	Gelafundin	-	-	-	-
	Blood	1 unit	2	1516.53	3033.06
	Platelets	1 pack	0	7936.60	0
	Fresh Frozen Plasma	1 unit	0	1095.49	0
	Betadine	1ml	10000	0.072	720
	Bupivacaine	vial	0	11.45	0
	Diazepam	2mg(vial)	0	0.90	0
	Morphine	15mg/ml	0	2.70	0
	Fentanyl	100mcg	10	4.59	45.9
	Pethidine	100mg	30	3.02	90.6
	Sodium Thiopentone	500mg	24	0.68	16.32
	Suxamethonium	100mg	58	0.09	5.22
	Propofol	20ml(amp)	75	15.10	1132.5
	Ketamine	ampoule	2	10.44	20.88
	Water for injection	10ml	50	0.56	28
	Ergometrine	0.5mg/ml	0	3.48	0

	Oxytocin	5iu	125	6.30	787.5
	Needles	21G	260	0.09	23.4
	Oxygen	Rands/litre	15125	0.06	907.5
	Nitrous oxide	Rands/litre	15155	0.16	2424.8
	Halothane		1329.57	Below table	2046.63
	Face mask	1 mask	100	7.90	790
	Oral airway	Size 4	100	2.20	220
	Linen saver	1 saver	200	0.75	150
	Surgical blades	Size 24	200	0.26	52
	Abdominal swabs	1 swab	955	1.36	1298.8
	Elastoplast	-	-	-	-
	Cord clamps	1 clamp	198	0.45	89.1
	Suction catheter	1 catheter	198	0.90	178.2
	Endotracheal tube	7.0	1	5.48	5.48
	Endotracheal tube	7.5	97	5.60	543.2
	Endotracheal tube	8.0	2	5.26	10.52
	Surgical gloves	7.5	600	1.61	966
	Examination gloves	Med/large	400	0.25	100
	Sutures: Vicryl	2	5	8.47	42.35
	Sutures: Vicryl	2/0	36	7.69	276.84
	Sutures: Vicryl	1	82	8.89	728.98
	Sutures: Vicryl	0	2	8.12	16.24
	Sutures: Chromic	2/0	53	8.00	424
	Sutures: Chromic	2	38	9.83	373.54
	Sutures: Chromic	1	12	8.76	105.12
	Sutures: Chromic	0	1	8.33	8.33
	Face masks	1	600	0.08	48
	Theatre caps	1	600	0.15	90
Total					**19017.85**
Post-Op	Ringers lactate	1L	200	6.45	1290
	Normal saline	1L	0	10.66	0
	5 % dextrose	1L	100	11.17	1117
	Blood	1 unit	0	1516.53	0
	Fresh Frozen Plasma	1 unit	0	1095.49	0
	Platelets	1 pack	0	7936.60	0
	Gelafundin	-	-	-	-
	Ceftriaxone (iv)	1g	317	5.69	1803.73
	Metronidazole (iv)	500mg	51	0.59	30.09
	Gentamicin (iv)	80mg	20	2.77	55.4
	Chloramphenicol (iv)	500mg	0	3.90	0
	Cloxacillin (iv)	500mg	20	5.90	118
	Pethidine (im/iv)	100mg	333	3.02	1005.66
	Morphine (im/iv)	15mg/ml	0	2.70	0
	Fentanyl (im/iv)	100mcg	0	4.59	0
	Diclofenac (im)	75mg	10	0.80	8
	$MgSO_4$ (im/iv)	ampoule	0	1.25	0
	Amoxicillin (po)	500mg	1500	0.17	255
	Metronidazole (po)	400mg	105	0.09	9.45
	Paracetamol (po)	1g	1530	0.08	122.4
	Cloxacillin (po)	500mg	20	0.36	7.2
	Methyldopa (po)	250mg	87	0.40	34.8
	Pen V K (po)	500mg	0	0.30	0
	Nifedipine (po)	10mg	0	0.26	0
	Erythromycin (po)	500mg	0	0.57	0
	Enalapril (po)	5mg	0	0.41	0
	Hydrallazine (po)	25mg	21	0.23	4.83

	Ciprofloxacin (po)	500mg	0	0.22	0
	Syringes	2ml	334	0.22	73.48
	Syringes	5ml	20	0.25	5
	Syringes	10ml	143	0.37	52.91
	Syringes	20ml	100	0.58	58
	Needles	21G	687	0.09	61.83
	Water for injection	10ml	337	0.56	188.72
	Betadine	1ml	8000	0.072	576
	Gauze	1pack	320	0.57	182.4
	Strapping	-	-	-	-
	Elastoplast	-	-	-	-
	Vaginal pads	1	662	0.68	450.16
					7510.06
Others	Hospital stay per day	1 day	338	180.7	61076.6
Total					**90181.27**

Costs of halothane = [concentration (%) x flow (L/min) x time (min) x molecular weight (197.4) x costs (Rands/ml)] / [molar volume of gas (2412) x density (1.87)] – formula by Peter Dion[56]

Appendix 6

Total Costs and Quantities – Spinal Anaesthesia (Includes failed spinal)

	Description	Size/Type/Time	No. units	Price/ unit	Subtotal cost
Pre-Op	Atropine	0.5mg	100	1.63	163
	Cannula	16G	5	2.34	11.7
	Cannula	18G	92	2.23	205.16
	Cannula	20G	3	2.23	6.69
	Urinary Catheter	16	100	3.65	365
	Urine bag	1 bag	100	2.10	210
	Surgical blade	size24	100	0.26	26
	Syringe	2ml	100	0.22	22
	Syringe	5ml	0	0.25	0
	Syringe	10ml	0	0.37	0
	Syringe	20ml	100	0.58	58
	Swabs	-	-	-	-
	Needles	21G	200	0.09	18
	Water for injection	10ml	200	0.56	112
	Fluid giving set	1 set	100	2.10	210
	Strapping	-	-	-	-
	Theatre cap	1 cap	100	0.15	15
	Surgical Gloves	Size 7.5	300	1.61	483
	Methylated spirit	1ml	1000	0.014	14
	Ringers Lactate	1L	100	6.45	645
	Normal Saline	1L	0	10.66	0
Total					**2564.55**
Intra-Op	Swabs	-	-	-	
	Gauze	1 pack	197	0.57	112.29
	Spinal Needle	22G	100	1.57	157
	Syringe	2ml	182	0.22	40.04
	Syringe	5ml	1	0.25	0.25
	Syringe	10ml	1	0.37	0.37
	Syringe	20ml	8	0.58	4.64
	Strapping	-	-	-	-
	Ringers lactate	1L	178	6.45	1148.1
	Normal saline	1L	4	10.66	42.64
	5 % dextrose	1L	0	11.17	0
	Gelafundin	-	-	-	-
	Blood	1 unit	0	1516.53	0
	Platelets	1 pack	0	7936.60	0
	Fresh Frozen Plasma	1 unit	0	1095.49	0
	Betadine	1ml	12500	0.072	900
	Bupivacaine	vial	100	11.45	1145
	Diazepam	2mg(vial)	0	0.90	0
	Morphine	15mg/ml	0	2.70	0
	Fentanyl	100mcg	2	4.59	9.18
	Pethidine	100mg	8	3.02	24.16
	Sodium Thiopentone	500mg	2	0.68	1.36
	Suxamethonium	100mg	4	0.09	0.36
	Propofol	20ml(amp)	3	15.10	45.3
	Ketamine	ampoule	0	10.44	0
	Water for injection	10ml	4	0.56	2.24
	Ergometrine	0.5mg/ml	2	3.48	6.96
	Oxytocin	5iu	126	6.30	793.8

	Needles	21G	188	0.09	16.92
	Oxygen	Rands/litre	6178	0.06	370.68
	Nitrous oxide	Rands/litre	720	0.16	115.20
	Halothane		78.78	Below table	121.27
	Face mask	1 mask	76	7.90	600.4
	Oral airway	Size 4	5	2.20	11
	Linen saver	1 saver	200	0.75	150
	Surgical blades	Size 24	200	0.26	52
	Abdominal swabs	1 swab	780	1.36	1060.8
	Elastoplast	-	-	-	-
	Cord clamps	1 clamp	196	0.45	88.2
	Suction catheter	1 catheter	199	0.90	179.1
	Endotracheal tube	7.0	0	5.48	0
	Endotracheal tube	7.5	3	5.60	16.8
	Endotracheal tube	8.0	1	5.26	5.26
	Surgical gloves	7.5	701	1.61	1128.61
	Examination gloves	Med/large	400	0.25	100
	Sutures: Vicryl	2	12	8.47	101.64
	Sutures: Vicryl	2/0	52	7.69	399.88
	Sutures: Vicryl	1	70	8.89	622.3
	Sutures: Vicryl	0	14	8.12	113.68
	Sutures: Chromic	2/0	32	8.00	256
	Sutures: Chromic	2	61	9.83	599.63
	Sutures: Chromic	1	8	8.76	70.08
	Sutures: Chromic	0	0	8.33	0
	Face masks	1	600	0.08	48
	Theatre caps	1	600	0.15	90
Total					**10751.14**
Post-Op	Ringers lactate	1L	203	6.45	1309.35
	Normal saline	1L	0	10.66	0
	5 % dextrose	1L	100	11.17	1117
	Blood	1 unit	0	1516.53	0
	Fresh Frozen Plasma	1 unit	0	1095.49	0
	Platelets	1 pack	0	7936.60	0
	Gelafundin	-	-	-	-
	Ceftriaxone (iv)	1g	320	5.69	1820.8
	Metronidazole (iv)	500mg	54	0.59	31.86
	Gentamicin (iv)	80mg	36	2.77	99.72
	Chloramphenicol (iv)	500mg	0	3.90	0
	Cloxacillin (iv)	500mg	0	5.90	0
	Pethidine (im/iv)	100mg	394	3.02	1189.88
	Morphine (im/iv)	15mg/ml	0	2.70	0
	Fentanyl (im/iv)	100mcg	0	4.59	0
	Diclofenac (im)	75mg	10	0.80	8
	$MgSO_4$ (im/iv)	ampoule	0	1.25	0
	Amoxicillin (po)	500mg	1470	0.17	249.9
	Metronidazole (po)	400mg	150	0.09	13.5
	Paracetamol (po)	1g	1515	0.08	121.2
	Cloxacillin (po)	500mg	20	0.36	7.2
	Methyldopa (po)	250mg	42	0.40	16.8
	Pen V K (po)	500mg	80	0.30	24
	Nifedipine (po)	10mg	6	0.26	1.56
	Erythromycin (po)	500mg	0	0.57	0
	Enalapril (po)	5mg	0	0.41	0
	Hydrallazine (po)	25mg	0	0.23	0
	Ciprofloxacin (po)	500mg	10	0.22	2.2

	Syringes	2ml	395	0.22	86.9
	Syringes	5ml	28	0.25	7
	Syringes	10ml	320	0.37	118.4
	Syringes	20ml	100	0.58	58
	Needles	21G	746	0.09	67.14
	Water for injection	10ml	320	0.56	179.2
	Betadine	1ml	7675	0.072	552.6
	Gauze	1pack	315	0.57	179.55
	Strapping	-	-	-	-
	Elastoplast	-	-	-	-
	Vaginal pads	1	660	0.68	448.8
					7707.56
Others	Hospital stay per day	1 day	346	180.7	62522.2
Total					**83545.45**

Costs of halothane = [concentration (%) x flow (L/min) x time (min) x molecular weight (197.4) x costs (Rands/ml)] / [molar volume of gas (2412) x density (1.87)] – formula by Peter Dion[56]

The Research Ethics Committee, Faculty Health Sciences, University of Pretoria complies with ICH-GCP guidelines and has US Federal wide Assurance.

* **FWA** 00002567, Approved dd 22 May 2002 and Expires 20 Oct 2016.
* **IRB** 0000 2235 IORG0001762 Approved dd 13/04/2011 and Expires 13/04/2014.

UNIVERSITEIT VAN PRETORIA
UNIVERSITY OF PRETORIA
YUNIBESITHI YA PRETORIA

Faculty of Health Sciences Research Ethics Committee
Fakulteit Gesondheidswetenskappe Navorsingsetiekkomitee

DATE: 2/02/2012

NUMBER	**13/2012**
TITLE OF THE PROTOCOL	Clinical outcomes and costs: a comparison between spinal anaesthesia and intra-venous general anaesthesia for emergency caesarean sections at a regional hospital in Swaziland.
PRINCIPAL INVESTIGATOR	**Student Name & Surname:** Dr Edgar T Majirija **Dept:** Clinical Epidemiology, School of Health Systems and Public Health ;University of Pretoria. **Cell:**00268 76629576 **E-Mail:** docmajirija@yahoo.co.uk
SUB INVESTIGATOR	Not Applicable
STUDY COORDINATOR	Edgar T Majirija
SUPERVISOR (ONLY STUDENTS)	Prof Paul Rheeder **E-Mail:** prheeder@medic.up.ac.za
STUDY DEGREE	MSc Clinical Epidemiology
SPONSOR COMPANY	Not applicable
MEETING DATE	January at 1/02/2012

The Protocol was approved on 01 / 02 /2012 by a properly constituted meeting of the Ethics Committee subject to the following conditions:

1. The approval is valid for 2 years period [till the end of December 2013], and
2. The approval is conditional on the receipt of 6 monthly written Progress Reports, and
3. The approval is conditional on the research being conducted as stipulated by the details of the documents submitted to and approved by the Committee. In the event that a need arises to change who the investigators are, the methods or any other aspect, such changes must be submitted as an Amendment for approval by the Committee.

Members of the Research Ethics Committee:

Prof M J Bester	(female)BSc (Chemistry and Biochemistry); BSc (Hons)(Biochemistry); MSc(Biochemistry); PhD (Medical Biochemistry)
Prof R Delport	(female)BA et Scien, B Curationis (Hons) (Intensive care Nursing), M Sc (Physiology), PhD (Medicine), M Ed Computer Assisted Education
Prof JA Ker	MBChB; MMed(Int); MD – Vice-Dean (ex officio)
Dr NK Likibi	MBB HM – Representing Gauteng Department of Health) MPH
Dr MP Mathebula	(female)Deputy CEO: Steve Biko Academic Hospital; MBCHB, PDM, HM
Prof A Nienaber	(female) BA(Hons)(Wits); LLB; LLM; LLD(UP); PhD; Dipl.Datametrics(UNISA) – Legal advisor
Mrs MC Nzeku	(female) BSc(NUL); MSc(Biochem)(UCL, UK) – Community representative
Prof L M Ntlhe	MbChB (Natal) FCS (SA)
Snr Sr J Phatoli	(female) BCur(Eet.A); BTec(Oncology Nursing Science) – Nursing representative
Dr R Reynders	MBChB (Prêt), FCPaed (CMSA) MRCPCH (Lon) Cert Med. Onc (CMSA)

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Dr T Rossouw	(female) MBChB (cum laude); M.Phil (Applied Ethics) (cum laude), MPH (Biostatistics and Epidemiology (cum laude), D.Phil
Dr L Schoeman	(female) B.Pharm, BA(Hons)(Psych), PhD – Chairperson: Subcommittee for students' research
Mr Y Sikweyiya	MPH; SARETI Fellowship in Research Ethics; SARETI ERCTP; BSc(Health Promotion)Postgraduate Dip (Health Promotion) – Community representative
Dr R Sommers	(female) MBChB; MMed(Int); MPharmMed – **Deputy Chairperson**
Prof TJP Swart	BChD, MSc (Odont), MChD (Oral Path), PGCHE – School of Dentistry representative
Prof C W van Staden	MBChB; MMed (Psych); MD; FCPsych; FTCL; UPLM - **Chairperson**

DR R SOMMERS; MBChB; MMed(Int); MPharmMed.
Deputy Chairperson of the Faculty of Health Sciences Research Ethics Committee, University of Pretoria

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ETHICS APPROVAL: SCIENTIFIC AND ETHICS COMMITTEE, SWAZILAND

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MINISTRY OF HEALTH
P.O. BOX 5
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SWAZILAND

THE KINGDOM OF SWAZILAND

FROM: The Chairman
Scientific and Ethics Committee
P. O. Box 5
Mbabane

TO Edgar Majirija
Principal Investigator
P.O Box 226
Hlathikhulu

DATE: 03rd February 2012

REF: MH/599C

RE: Clinical Outcomes and Costs: A Comparison between Spinal Anesthesia and Intra – venous general Anesthesia for emergency Caesarean sections at a Regional Hospital in Swaziland

The committee thanks you for addressing the issues raised by the committee and the clarity on responses to the protocol amendment.

In view of the responses submitted after concerns raised and the fact that the study is in accordance with ethical and scientific standards, the committee therefore grants you authority to conduct the study. You are requested to adhere to the specific topic and inform the committee through the chairperson of any changes that might occur in the duration of the study which are not in this present arrangement.

The committee wishes you the best and is eagerly awaiting findings of the study to inform proper planning and programming to use for analysis

Yours Sincerely,

DIRECTOR OF HEALTH SERVICES
MINISTRY OF HEALTH
03 FEB 2012
P O BOX 5, MBABANE
SWAZILAND

Dr.S.M.Zwane
Chairperson Scientific and Ethics Committee
cc: Sec Members