Adherence to post-operative pain medication after discharge following day case orthopaedic surgery at a South African private hospital

V Booysen
orcid.org / 0000-0002-0399-3242

Dissertation submitted in fulfilment of the requirements for the degree Master of Pharmacy in Advanced Clinical Pharmacy at the North West University

Supervisor: Prof JR Bruger
Co-supervisor: Dr JM du Plessis

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Student number: 23956925
PREFACE

This mini-dissertation was presented in article format. Chapter 3 will showcase the findings of the study in the form of a manuscript ready for publishing in the following journal:

- *International journal of orthopaedic and trauma nursing*

The instructions to authors given by the journal required that the reference list be cited accordingly. The reference list at the end of the mini-dissertation has been completed according to the reference style of the North-West University.

The chapters in this dissertation are stipulated as follows:

- Chapter 1 consists of a short introduction, subsequently followed by the research methodology used to conduct this study.

- Chapter 2 presents a literature review of pain, orthopaedic day case surgery and post-operative pain management (analgesics and conceptualisation of adherence).

- Chapter 3 provides the results and discussions in manuscript format.

- Chapter 4 is the conclusion, strengths, limitations and recommendations drawn from the study.

The annexures and references follow at the end.

The supervisor and co-supervisors during the study are referred to as co-authors in the manuscript and gave permission that it may be used as part of the dissertation.
ACKNOWLEDGEMENTS

To my baby Leo and future children to come, you are the extension of our hearts and complete our world. You are the essence to life itself.

To my husband, Hannes Booysen, through all the intense deep conversations about how I wanted to quit, you kept me going. Thank you for not allowing me to give up. I love you.

To my parents, because I am your daughter, I can do anything. Your strength and power lives within me. I love you.

To my sister Ananda, when I count my blessings, I count you twice. I love you.

To my friends and family, I am so grateful that you are part of this beautiful, twisty road I call my life.

To my EXCO, I’m so blessed to be part of this team. You just ‘get me’. Thank you for always having my back and supporting me through this process.

To my Pharmacy team, you are my energy. I appreciate every single one of you. My success is measured by you.

To my fantastic supervisor, Prof Johanita Burger and co-supervisor, Dr Jesslee du Plessis, I am so proud of this mini-dissertation. Thank you for your guidance, fanatic attention to detail and never giving up on me. You are two of my favourite people.

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To Mrs Engela Oosthuizen, thank you for the formatting of this huge mini-dissertation and always being friendly and helpful.
ABSTRACT

Background: Adherence to post-operative pain medication remains a concern as low adherence rates result in suboptimal clinical outcomes, and burdens the global healthcare environment. The primary treatment goals of medications prescribed after surgery are to achieve sufficient pain control with minimal side effects to ensure optimisation of post-operative recovery. A limited number of studies have been conducted on adherence to post-operative pain medication, in orthopaedic day case surgery in South Africa. This study could contribute to the knowledge of factors affecting adherence to pain medication after surgery.

Objective: The purpose of this study was to investigate whether patients were adherent to post-operative discharge analgesics after orthopaedic day case surgery in a South African private hospital. Furthermore, demographical variables, smoking, pain, side effects and normal adherence behaviour were studied as possible factors that may affect adherence.

Method: The study followed an observational, prospective, cross-sectional design using a structured questionnaire as data-collection tool, conducted through a telephonic interview on the fourth day after surgery. The inclusion criteria of the study included 120 participants, 18 years of age and older, undergoing day case orthopaedic surgery. Participants were excluded if they could not be reached on the fourth day after surgery, after two attempts to contact them. The data collection was conducted between June 2016 and June 2017. The participants conducted a pill count, which was used to determine overall adherence. Self-reported adherence behaviour and normal adherence behaviour was established from the questionnaire. The association between participant demographics, smoking status, type and intensity of side effects, pain severity involving sleep and mobility, and adherence was determined from the structured questionnaire.

Results: A total of 120 participants were included in the study. Among them, 69 were females and 51 males. The overall adherence rate determined from the pill count was 56.7% (n = 68). No association was found between gender (p = 0.140), age (p = 0.822), smoking status (p = 1.000) and adherence to post-operative discharge pain medication. Although more than 80% of participants experienced moderate to severe pain during movement; it had no impact on participants’ adherence to prescribed analgesia (pain when repositioning in bed p = 0.237; pain when walking, standing, sitting p = 0.509). The disruption of sleep by moderate to severe pain affected adherence to post-operative discharge pain medication negatively (pain interfering with falling asleep p = 0.001; pain causing awakening from sleep p = 0.035). Adherence status was independent of the type and number of side effects experienced from the multimodal analgesic
regimens (nausea 30.0%, $p = 0.809$; drowsiness 55.9%, $p = 0.701$; gastritis 12.5%, $p = 0.403$; constipation 59.2%, $p = 0.300$; dizziness 26.7%, $p = 0.956$). Self-reporting of adherence to the current prescribed post-operative discharge medication was shown to be dependent on overall adherence found from the pill count ($p < 0.001$, Cramér's $V = 0.5$).

**Conclusions and recommendations:** The study attempted to reveal actual adherence as well as possible factors affecting adherence to prescribed post-operative discharge medication. Adherence was poor at 56.7% and interventions to increase the adherence should be considered. Pain interrupting sleep showed a dependent relationship to non-adherence. Participant education on timing of doses should be considered to optimise the drug level in the body over the sleeping period. As moderate to severe pain was experienced during movement post discharge, it could be suggested that surgeons increase intra-operative pain management techniques, e.g. intra-articular injections of analgesics.

**Keywords:** Adherence, compliance, post-operative pain medication, discharge, orthopaedic surgery.
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<td>5-HT3</td>
<td>Serotonin</td>
</tr>
<tr>
<td>ABCB1</td>
<td>ATP binding cassette subfamily B member 1</td>
</tr>
<tr>
<td>AIDS</td>
<td>Acquired immune deficiency syndrome</td>
</tr>
<tr>
<td>APS</td>
<td>American Pain Society</td>
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<tr>
<td>APS-POQ</td>
<td>American Pain Society Patient Outcome Questionnaire</td>
</tr>
<tr>
<td>APS-POQ-R</td>
<td>Revised, American Pain Society Patient Outcome Questionnaire</td>
</tr>
<tr>
<td>BMI</td>
<td>Body mass index</td>
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<tr>
<td>CNS</td>
<td>Central nervous system</td>
</tr>
<tr>
<td>COX-1</td>
<td>Cyclo-oxygenase-1</td>
</tr>
<tr>
<td>COX-2</td>
<td>Cyclo-oxygenase-2</td>
</tr>
<tr>
<td>CYP2E1</td>
<td>Cytochrome P450 2E1 enzyme</td>
</tr>
<tr>
<td>CYP2D6</td>
<td>Cytochrome 2D6 enzyme</td>
</tr>
<tr>
<td>EXCO</td>
<td>Executive committee</td>
</tr>
<tr>
<td>FACE</td>
<td>Facial expressions rating scale</td>
</tr>
<tr>
<td>GIT</td>
<td>Gastrointestinal tract</td>
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<tr>
<td>HbA1c</td>
<td>Glycated hemoglobin</td>
</tr>
<tr>
<td>HREC</td>
<td>Health Research Ethics Committee</td>
</tr>
<tr>
<td>IBM SPSS®25</td>
<td>IBM Statistical Package for the Social Sciences</td>
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<tr>
<td>IASP</td>
<td>International Association of Pain</td>
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<td>IEM</td>
<td>Ingestion event marker</td>
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<tr>
<td>Acronym</td>
<td>Full Form</td>
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<tr>
<td>IV</td>
<td>Intravenous</td>
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<tr>
<td>IM</td>
<td>Intramuscular</td>
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<tr>
<td>HIV</td>
<td>Human immunodeficiency virus</td>
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<tr>
<td>LPC</td>
<td>Locus of pain control</td>
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<tr>
<td>MAOI</td>
<td>Monoamine oxidase inhibitor</td>
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<tr>
<td>MEMS®</td>
<td>Medication Event Monitoring System</td>
</tr>
<tr>
<td>MARS</td>
<td>Medication Adherence Rating Scale</td>
</tr>
<tr>
<td>MUSA</td>
<td>Medicine Usage in South Africa</td>
</tr>
<tr>
<td>NAPQ1</td>
<td>N-acetyl-p-benzoquinone imine</td>
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<tr>
<td>NHS</td>
<td>National Health Service</td>
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<tr>
<td>NHS QIS</td>
<td>National Health Service Quality Improvement Scotland</td>
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<tr>
<td>NICE</td>
<td>National Institute for Health and Care Excellence</td>
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<td>NSAIDs</td>
<td>Non-steroidal anti-inflammatory drugs</td>
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<td>NWU</td>
<td>North-West University</td>
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<tr>
<td>PCA</td>
<td>Patient control analgesia</td>
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<tr>
<td>PGE2</td>
<td>Prostaglandin E2</td>
</tr>
<tr>
<td>PO</td>
<td>Per os (orally)</td>
</tr>
<tr>
<td>PRN</td>
<td>As required</td>
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<tr>
<td>SASA</td>
<td>South African Society of Anaesthesiologists</td>
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<tr>
<td>SAMF</td>
<td>South African Medicines Formulary</td>
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<tr>
<td>SC</td>
<td>Subcutaneous</td>
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<tr>
<td>SSRI</td>
<td>Selective serotonin reuptake inhibitor</td>
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<tr>
<td>Abbreviation</td>
<td>Description</td>
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<tr>
<td>UGT2B7</td>
<td>UDP-Glucuronosyltransferase-2B7 isoenzyme</td>
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<tr>
<td>VAS</td>
<td>Visual analogue scale</td>
</tr>
<tr>
<td>VNRS</td>
<td>Visual numeric rating scale</td>
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<tr>
<td>WHO</td>
<td>World Health Organization</td>
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**LIST OF DEFINITIONS**

<table>
<thead>
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<th>Term</th>
<th>Definition</th>
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<tr>
<td>Adherence</td>
<td>Defined as “implementation of an agreed medical treatment, its initiation and execution as prescribed.” Brotdkorb <em>et al.</em> (2016:3). It therefore entails the patient’s active participation in the therapeutic plan and their own decision to keep to the medication treatment (Ho <em>et al.</em>, 2009:3028), furthermore, to what extent the therapeutic plan was followed as agreed upon (Ettinger &amp; Baker, 2009:S60).</td>
</tr>
<tr>
<td>Arthroplasty</td>
<td>Involves the reconstruction of a diseased joint to reduce pain and to maintain or improve movement (Oxford Concise Medical Dictionary, 2010:54).</td>
</tr>
<tr>
<td>Arthroscope</td>
<td>“Is a rigid telescope fitted with a lens and illumination to create a magnified picture of a joint cavity on a television monitor” (Oxford Concise Medical Dictionary, 2010:54).</td>
</tr>
<tr>
<td>Arthroscopy</td>
<td>Is performed to inspect a joint cavity or for percutaneous surgery, e.g. meniscectomy by using an arthroscope (Oxford Concise Medical Dictionary, 2010:54).</td>
</tr>
<tr>
<td>Bimodal</td>
<td>For this study, it describes a medication regimen made up of two different drugs (McDonald <em>et al.</em>, 2016:607).</td>
</tr>
<tr>
<td>Bioavailability</td>
<td>Defined as the amount (fraction/percentage) of drug that reaches the systemic circulation (Katzung <em>et al.</em>, 2012).</td>
</tr>
<tr>
<td>Cardiotoxicity</td>
<td>Pertains to something that can damage the heart muscle (Katzung <em>et al.</em>, 2012).</td>
</tr>
<tr>
<td>Epidural infusions</td>
<td>Used for pain relief where anaesthetics and/or opioids are infused through a fine catheter into the epidural space of the sacral region (Oxford Concise Medical Dictionary, 2010:251).</td>
</tr>
<tr>
<td>First-pass metabolism</td>
<td>This occurs when an oral drug is metabolised by the liver. The amount (fraction/percentage) of drug that remains is available to have the desired effect (Katzung <em>et al.</em>, 2012).</td>
</tr>
<tr>
<td>Term</td>
<td>Definition</td>
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<tr>
<td>Ganglion cyst removal</td>
<td>Involves the surgical removal of a nerve bundle cyst that forms in tendon sheaths, most commonly the wrist (Oxford Concise Medical Dictionary, 2010:296).</td>
</tr>
<tr>
<td>Half-life</td>
<td>“The time required for the amount of drug in the body or blood to fall by 50%. Units: time” (Katzung et al., 2012).</td>
</tr>
<tr>
<td>Hallux valgus</td>
<td>“The most common foot deformity, mostly affecting females. The big toe is displaced towards the other toes and is associated with a bunion” (Oxford Concise Medical Dictionary, 2010:328).</td>
</tr>
<tr>
<td>Hepatic biotransformation</td>
<td>The process where the body transforms a potentially harmful substance to an inactive, nontoxic substance so that it can be excreted (Katzung et al., 2012).</td>
</tr>
<tr>
<td>Hyperalgesia</td>
<td>“Hyperalgesia is an abnormal state of intensified sensitivity to painful stimuli” (Oxford Concise Medical Dictionary, 2010:354).</td>
</tr>
<tr>
<td>Intrathecal injections</td>
<td>Defined as injections into the meninges of the spinal cord (Oxford Concise Medical Dictionary, 2010:385).</td>
</tr>
<tr>
<td>Lipophilic drugs</td>
<td>Refers to drugs that dissolve in fat and diffuse readily across cell membranes (Katzung et al., 2012).</td>
</tr>
<tr>
<td>Multimodal</td>
<td>In this study, it refers to the combination of various medications to make up a multimodal medication regimen (McDonald et al., 2016:607).</td>
</tr>
<tr>
<td>Neurotoxicity</td>
<td>“Is the poisonous or harmful effect on nerve cells” (Oxford Concise Medical Dictionary, 2010:500).</td>
</tr>
<tr>
<td>Nociceptive pain</td>
<td>Pain experienced from injury by burning (heat or cold), ripping of flesh (stretching), crushing (pressure) and ischaemia (Carr, 2009:2).</td>
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</table>
Non-adherence Can be described as intentional or unintentional drug forgetfulness (Brodtkorb et al., 2016:3) and causes global upset as non-adherence can be linked to increased healthcare costs and suboptimal quality of life (Ho et al., 2009:3028). In the context of this study, non-adherence (revealed from the pill count) will be considered when:

- More or less doses of the prescribed regimen were taken.
- Other analgesics were added to the prescribed regimen to aid with pain control.

Normal adherence In this study, normal adherence refers to general adherence behaviour to any prescribed acute medication.

Osteotomy “Is a surgical operation to cut bone into two parts, followed by the realignment of the ends to allow healing” (Oxford Concise Medical Dictionary, 2010:529).

Peak levels Used to measure the maximum (peak) drug level in the blood stream, usually taken 30 minutes after administration of drug (Katzung et al., 2012).

Prodrug “Drug that requires metabolism to become activated, usually by the liver” (Oxford Concise Medical Dictionary, 2010:529).

Psychotomimetic effects Adverse effects of certain drugs where the patient experiences hallucinations/delirium (Katzung et al., 2012).

Rotator cuff Is made up of four muscles (supraspinatus, infraspinatus, teres minor and subscapularis) and their tendons (Gibbs et al., 2018:165).

Rotator cuff tendon repairs Involves the surgical repair of one of the tendons forming part of the rotator cuff to relieve pain as well as to improve range of movement (Gibbs et al., 2018:165).

Somatosensory pathways Defined as sensation, e.g. touch or pressure information is carried from sense organs to reflex centers in the brain
Stroke Described as the abrupt onset of weakness normally involving one side of the body as a result of blood flow interruption to the brain (Oxford Concise Medical Dictionary, 2010:702).


Trough level Used to measure the minimum (trough) drug level in the bloodstream, usually taken just before the administration of the following dose (Katzung et al., 2012).

Unimodal In this study, it is defined as a medication regimen that is made up of only one drug (McDonald et al., 2016:607).

Volume of distribution “A proportionality factor relating to the amount of drug in the body to the concentration in the plasma” (Katzung et al., 2012).
CHAPTER 1: INTRODUCTION AND SCOPE OF THE STUDY

1.1 Background

Ambulatory surgeries, also known as day case surgery, are scheduled surgeries where the patients return home on the same day of the procedure (Hall et al., 2017:1). More than 60% of surgeries are performed in ambulatory settings as day cases in the United States (Shang & Gang, 2012:856). This number is reported to be higher in the United Kingdom, where it is estimated that up to 75% of elective surgeries are performed as day cases (Ng & Mercer-Jones, 2014:73). Improvements in surgical techniques and anaesthesia have created the potential for ambulatory surgery to improve patient outcomes and minimise cost by delivering proficient surgical services (Lemos et al., 2006:13). Early mobilisation, as well as decreased risk of post-operative infections, further benefits patients in day case surgery. The advantages for organisations include: (1) more available inpatient beds; (2) lower costs from reduced patient stays; and (3) re-aligning the roles of nursing and auxiliary staff (Anderson et al., 2016:86). Pain monitoring and treatment after surgery, however, becomes more difficult as it is left to the patient or family members of the patient. Even with analgesia and state of the art novel drug delivery systems, more than 80% of patients find post-operative pain levels ranging from moderate to severe (Shang & Gan, 2012:855).

Successful management of post-operative pain includes a multimodal approach, using several medications with differing mechanisms of action (Shang & Gan, 2012:862). A combination of paracetamol, non-steroidal anti-inflammatory drugs (NSAIDs) and opioids as frontline regimens, with the possibility of adding analgesic adjuvants like gabapentin, are regarded as current best practice for post-operative pain control (Tharakan & Faber, 2015:181). Despite their well-known side effects, opioid analgesics are prescribed habitually for post-operative pain on discharge after orthopaedic surgery (Devin & McGirt, 2015:931). Opioids act directly on the central nervous system receptors, providing a moderate to potent analgesic effect (Devin & McGirt, 2015:931). The pharmacological effects of opioid agonists are comparable to that of morphine (Finnerup et al., 2015:170; Shang & Gan, 2012:863). However, there has recently been unease because of the mistreatment of immediate-release oxycodone formulation (Kopecky et al., 2017:509; Nalamachu & Shah, 2018). To add to the unease, harmful properties such as respiratory depression, euphoria, drowsiness, constipation, nausea, vomiting and ultimately tolerance and addiction (Manchikanti et al., 2012:ES29). The tablet is formulated with a non-digestible matrix, filled with a large amount of oxycodone that is gradually freed in time by diffusion out of the matrix and undergoes extensive first-pass metabolism, hence it can take up to thirty minutes for the analgesic effect to set in (Looi & Audisio, 2007:2225). Crushing and
ingesting the matrix instantaneously releases the entire medication confined in the preparation, causing a euphoric state. There have also been reported deaths from accidental overdosing with opioids (Shang & Gan, 2012:860). Because of its high potential for abuse, caution should be exercised when prescribing this medication (Finnerup et al., 2015:171; Shang & Gan, 2012:860).

Paracetamol and NSAIDs are successful as post-operative analgesia, with insignificant side effects throughout short-term treatment (Kehlet & Dahl, 2003:1923). The analgesic effect of paracetamol is weaker (20-30%) compared to NSAIDs, opioids and cyclo-oxygenase-2 (COX-2) inhibitors. However, it has virtually no side effects at recommended doses (Kehlet & Dahl, 2003:1923; Ozmete et al., 2016:56). On the other hand, the possible side effects of normal NSAIDs (gastrointestinal- and surgical-site bleeding as well as renal failure) may limit their effectiveness in patients classified as ‘high-risk’ because of pre-existing gastric ulceration or renal dysfunction (Kehlet & Dahl, 2003:1923). The COX-2 inhibitors appear to have comparable analgesic effectiveness but superior safety profiles compared to NSAIDs (Devin & McGirt, 2015:934).

Following surgery, medications will minimise surgical stress experienced and essentially improve pain severity and frequency, physical and emotional functioning, quality of life, frequency of unfavourable effects of pain or pain treatment and deliver individual comfort (Goldsmith et al., 2016:64; Gordon et al., 2010:1173). Pain relief assists in dulling autonomic and somatic reflexes and therefore, organ function will re-establish to permit mobilisation and the intake of food. These changes could thus facilitate an improvement in post-operative outcome (Kehlet & Dahl, 2003:1922).

The human body counters surgical injury with drastic changes in neural, endocrine and metabolic systems, including changes in organ functions (Kehlet, 1997:606). These specific changes are characterised by an increase in the secretion of catabolic hormones, a decrease in anabolic hormone secretion, sleep disturbances, pain and gastrointestinal side effects with nausea and painful obstruction of the intestine (Kehlet, 1997:606; Stubbs et al., 2016:64). The body experiences different types of pain depending on the kind of injury; the most common are nociceptive, inflammatory and neuropathic pain (Kehlet et al., 2006:1618; Chung et al., 2016:1123).

Nociceptive pain is pain experienced after powerful mechanical, chemical or thermal noxious stimuli, as it causes the activation of high threshold peripheral sensory (nociceptor) neurons (van Helmond et al., 2016). The pain from a scalpel blade injuring the skin indicates the presence, site, force and time interval of a noxious stimulus, and diminishes once the pressure
is stopped (Kehlet et al., 2006:1618). Following surgery, nerve damage and inflammatory pain may induce hyperalgesia (increased sensitivity to pain) and may result in persistent post-operative pain (Devin & McGirt, 2015:932; van Helmond et al., 2016). Light touch of the surgical site, any movement including breathing, coughing and gastrointestinal motility will have the ability to induce flashes of pain (Looi & Audisio, 2007:2223).

Healthcare is adversely affected by post-operative pain morbidity and analgesic dependence (Desai & Cheung, 2012:441). Healthcare consumers, payers and professionals, all increasingly seek to measure, relate and enhance the value of pain management (Gordon et al., 2010:1173). If discharge pain medication is taken as prescribed, anxiety and discomfort experienced by patient can be minimised (Kehlet & Dahl, 2003:1922).

Medication adherence, defined as the degree to which an individual takes medication at the correct dose and dosage intervals, as discussed and agreed upon with the prescriber (O’Rourke & O’ Brien, 2017:160), is a key factor in the success of all treatment as poor adherence minimises optimum clinical benefit. According to the World Health Organization (WHO, 2003), optimal adherence increases the efficacy of developments designed at promoting healthy lifestyles, such as dietary changes, smoking cessation, increased physical activity and safe sexual behaviour. Optimising the success of adherence interventions may well have a greater influence on the health of the population compared to enhancement in specific medical treatments and thus, it would offer a meaningful positive return on investment through firstly prevention (of risk factors) and secondly avoidance of adverse health outcomes (Yap et al., 2016:64).

Patient adherence to prescribed medication is influenced by individual factors, such as patient attitude, specific illness, previous medication experiences, expectation of medication and costs (Remien et al., 2003:70; Zeber et al., 2013:891). Additional factors described to affect adherence to medication regimens include depression, smoking, movement disruption, sleep interruption, healthcare system perceptions by the patient, lack of knowledge of treatment, side effects of medication and complexity of regimen (Gordon et al., 2010:1172; Morisky et al., 2008:4). It seems then that adherence may not be static in a patient’s lifespan of treatment (Remien et al., 2003:70). Remien et al. (2003:62) furthermore stated that the issue of poor adherence to medication is seen throughout health conditions, age, gender, ethnic groups, treatment modalities and socioeconomic groups. Patient factors causing non-adherence have largely been disregarded by health stakeholders, and as a result, have received little direct systematic intervention (WHO, 2003). High self-efficacy is another factor that can predict whether a patient will adhere more to their prescribed treatment compared to individuals with low self-efficacy (Wu et al., 2015:277). Self-efficacy is the trust or self-confidence that a person
has in his or her own abilities to carry out certain behaviours to create a desired outcome (Liang et al., 2008:1101). This theory proposes that individuals’ perceptions of their abilities guide their level of motivation, emotional reactions, behaviour, thought patterns and the amount of stress experienced. Beliefs with regard to prescribed medication may additionally affect patients’ self-efficacy with medication adherence (Liang et al., 2008:1101).

A study conducted in Brazil, showed that the way patients cope with their health problems and treatment has a direct influence on medication adherence after orthopaedic procedures (Mendes Porto et al., 2014:991). According to Mendes Porto et al. (2014:991), patients can either have an external or internal locus of pain control (LPC). The results of their study showed that patients having external LPC are significantly more adherent to prescribed medication by the physician compared to those with internal LPC. The reasons provided being that patients with external LPC believed that the cure is more dependent on external factors, such as prescribed medications, and not dependant on themselves, such as luck, fate or other people (Jokic-Begic et al., 2009:114). The availability of a health professional and strict adherence to medication are crucial to factors affecting patients’ pain management (Mendes Porto et al., 2014:991). This hypothesis was earlier proved by Torres et al. (2009:138), showing that internal LPC patients have lower medication adherence because they deemed that the improvement of their health status was dependent only on themselves; therefore, patients assessed the circumstances and decided to halt medication therapy without the assistance of a health professional.

The assessment of pain care is very difficult because of the multifaceted subjective understanding as well as limited knowledge when it comes to pain management (Gordon et al., 2010:1173). The American Pain Society Patient Outcome Questionnaire (APS-POQ) was developed by the American Pain Society and first published in 1991 (Gordon et al., 2010:1172) as part of a quality assurance standard to assist healthcare organisations in the treatment of acute pain and cancer pain. In 1995, it was revised to include measures such as pain relief, pain severity, side effects, pain interference scale for physical and emotional function, and use of non-pharmacological interventions. This revised questionnaire was named the “Revised, American Pain Society Patient Outcome Questionnaire” (APS-POQ-R) (Gordon et al., 2010:1173). The updated APS-POQ-R has been established to have sufficient psychometrics for quality improvement and to measure five key features of the patients’ encounter with their pain; also a sixth feature of non-pharmacological therapies. The six aspects include: (1) pain intensity and alleviation; (2) how activity, sleep and negative emotions are affected by pain; (3) side effects of treatment; (4) role of information on pain treatment; (5) ability to participate in pain treatment plans; and (6) use of non-pharmacological approaches (Gordon et al.,
The revised questionnaire is easy to use and explain, and has understandable components with a simple scoring system (Gordon et al., 2010:1172).

The APS-POQ-R was found to be feasible in an Icelandic hospital after administering the questionnaire to 143 patients in various wards to gauge the quality of their pain management (Zoëga et al., 2014:143). The APS-POQ-R was given to 50 patients undergoing colorectal cancer surgery to rate their pain after two days; they found that a quarter of the patients experienced their worst pain while at rest, showing the need to assess pain at rest in the early post-operative period at this facility (Brown et al., 2013:191).

Adherence measurement in the outpatient setting using indirect methods include self-report, electronic adherence monitoring (e.g. device that records when a tablet container was opened), refill rates from pharmacies and pill counts. Direct methods to measure adherence include laboratory testing of blood or biological fluid to monitor the presence of drug or biological marker. Direct observation of a patient’s medication intake is a direct method to measure adherence but not really practical in the outpatient setting as patients are not always available to observe directly (Bruce et al., 2010:113; Farmer, 1999:1076; Morisky et al., 2008:4). Furthermore, Thompson and colleagues developed a medication adherence scale (i.e. the Medication Adherence Rating Scale, or MARS), which they used as a tool to identify psychiatric patients with low adherence (Thompson et al., 2000:242). This test is applied in a questionnaire format and consists of a ten-item measure of self-reported medication adherence, where the questions are worded to avoid the 'yes-saying' bias by reversing the wording, as patients tend to give positive answers to health professionals (Thompson et al., 2000:242). Despite having been validated for psychiatric patients, the MARS has additionally been used in assessment for treatment patterns, medication adherence experience and satisfaction with medications, prescribed medications and over-the-counter medications (Cohen et al., 2009:327; Mahler et al., 2010:576; Menckeberg et al., 2008:49).

Poor adherence results in less than ideal management and control of an illness, and is the main reason for suboptimal clinical benefit. It results in medical and psychosocial complications of disease, diminishes patients’ quality of life and devastates healthcare resources. Altogether, these direct consequences harm the ability of the healthcare systems around the world to accomplish population health goals (WHO, 2003).

Orthopaedic surgeries, extending from debridement to arthroplasties, have a substantial influence on functional capability post-operatively (Desai & Cheung, 2012:441). In addition, pain suffered post-operatively further upsets patient functionality, rehabilitation and longstanding functional effects (Desai & Cheung, 2012:441). Adherence to pain medication after surgery is
essential to improve morbidity necessitating the measurement of adherence in this group of patients. Based on the foregoing discussion, three main research questions were formulated for this study, viz.:

- Are participants adherent to pain medication received at discharge after orthopaedic surgery?
- Do the side effects from the prescribed medication for pain control after orthopaedic surgery result in non-adherence of these pain medications?
- Is there a difference in normal adherence (adherence to other acute prescribed medications, e.g. antibiotics) compared to adherence to post-operative pain medication?

1.2 Research aims and objectives

The aim of this study was to determine whether participants are adherent to post-operative pain control medication following day case orthopaedic surgery after discharge from a South African private hospital, and to determine whether their experience of side effects influenced their adherence.

1.2.1 Specific research objectives

The study consisted of a literature review, followed by an empirical investigation.

The specific objectives for the literature review pertained the following:

- Describing the mechanism of pain in orthopaedic surgery.
- Understanding what role each pain control medication plays in the management of post-operative pain as part of discharge medication plans.
- Understanding factors influencing participant adherence after orthopaedic surgery.

The specific objectives for the empirical investigation phase of the study included:

- Establishing the adherence status regarding discharge pain medication after orthopaedic surgery.
- Determining the association between participant’s demographic and behavioural-related variables (age, gender and smoking status) and adherence to post-operative discharge pain medication.
- Determining the association between movement (turning, sitting up, repositioning in bed) and adherence to discharge pain medication after orthopaedic surgery.

- Determining the association between sleep disturbances (falling and staying asleep) and adherence with regard to post-operative discharge pain medication.

- Determining the association between the type and number of side effects experienced from discharge pain medication after orthopaedic surgery and adherence.

- Determining the association between normal adherence patterns and adherence patterns relating to post-operative pain discharge medication.

1.3 Research methodology

The literature study made use of evidence-based research. Evidence-based research is research driven by the application of the scientific method, i.e. it seeks thorough, clear and thoughtful identification, assessment and use of the finest evidence currently available, in order to optimise decision-making about the care of each individual patient by combining the best accessible research discoveries with patient history and laboratory test results (Chiappelli et al., 2006:3).

The literature review based on books, journal articles, government publications, websites, theses and dissertations, aimed to identify what is known about medication adherence and the factors that may affect it amongst post-operative participants.

The following databases from the Library Services at the North-West University (NWU) were consulted: Academic Search Premier EBSCOhost™, A-Z journal list, Google Scholar™, MEDLINE®, PubMed and ScienceDirect®. Search terms that were used as single entities and in combinations, included “Medication adherence”, “compliance”, “postoperative or post-operative pain”, “pain” and “adherence”, “treatment guidelines” and “orthopaedic surgery”, “opioid analgesics” and “anti-inflammatory drugs”.

The empirical investigation is discussed in subsequent paragraphs.

1.3.1 Study setting

The research took place at a 363-bed private hospital in the central suburbs of Johannesburg, running at approximately 70% occupancy, servicing a racially diverse population as well as foreign patients. The target population for this research study consisted of all adult patients (≥18 years) undergoing day case orthopaedic surgery at the private hospital during the study period.
The study population comprised of all those patients meeting inclusion criteria for the study after application of exclusion criteria.

1.3.1.1 Inclusion criteria

The criteria for inclusion were:

- Adult participants (aged 18 years and older), undergoing day case orthopaedic surgery between 1 June 2016 and 31 June 2017, and receiving pain medication after discharge from the specified private hospital in Johannesburg.

- Participants willing to participate in the study, who signed the informed consent form.

- Participants who supplied a phone number on their signed informed consent form.

- Participants that were available on the fourth day after surgery, who provided re-consent to partake in the study.

1.3.1.2 Exclusion criteria

Exclusion criteria were:

- Participants that could not be reached on the fourth day after surgery, after two attempts to contact the participant to conduct the survey.

- Participants who did not want to continue with the study at the start of the telephonic survey on the fourth day after surgery.

1.3.2 Study design

The study followed an observational, prospective, cross-sectional design using a structured questionnaire as the quantitative data-collection tool, completed through a telephonic survey.

In a prospective study, the researcher decides on a population and monitors it over time to establish outcomes (Brink et al., 2010:106). A cross-sectional study is the study of a selected population to observe the association between an exposure and an outcome (Brink et al., 2010:105). Quantitative research is the use of sampling methods, where outcomes may be stated numerically and are open to mathematical manipulation, permitting the researcher to predict future events, e.g. questionnaires (Brink et al., 2010:117).
1.3.3 Sampling

A potential sample size for the study was decided by conducting a priori power analysis using the G*Power software package (Faul et al., 2007:180). A sample size of 120 was deemed adequate to detect an effect of 0.25, with a power of 0.8 and an alpha of 0.05.

1.4 Data-collection tool

A telephonic survey using questions from a structured questionnaire was used to obtain the data. The questionnaire included questions giving the following information:

- Demographic information (age, gender).
- Smoking status.
- Pain at rest and during movement.
- Side effects of the prescribed medication were experienced.
- Normal behaviour with regard to adherence to medicine treatment.
- Adherence of participants to the post-operative medication prescribed.

1.4.1 Development of the data-collection tool

The questionnaire was developed using the MARS (Thompson et al., 2000) as well as selected questions from the APS-POQ-R (Gordon et al., 2010).

The MARS was originally created to estimate medication adherence in psychiatric patients and the authors found it to be a valid and reliable tool with high internal consistency (Thompson et al., 2000:244). The MARS has regularly been used as a treatment adherence-screening tool; for example, a live MARS survey conducted by Mahler et al. (2010:575) in Germany, to ascertain whether there was an association between MARS scores and the adherence found from chronic refill records when using the tool in a self-reporting manner. It was found that the MARS has acceptable reliability and validity, and that it was a quick, simple method for the assessment of medication adherence in patients with chronic diseases and patients with risk factors of cardiovascular disease (Mahler et al., 2010:575). A study in United States inner-city clinics was conducted by Cohen et al. (2009:326), where the MARS was used in a face-to-face interview to assess whether patients were adherent to their inhaled corticosteroids; as before, the authors found that the MARS had satisfactory validity and reliability. Furthermore, it has been found that the MARS showed adequate reliability when compared to the gold-standard Morisky adherence
scale and correlates moderately with the standard and more objective measures of pill counts when reporting on intentional (stopping pain medication when feeling better or worse) and unintentional (forgetfulness/carelessness) adherence to analgesics in cancer pain (Meghani & Bruner, 2013; Unni & Farris, 2015).

The APS-POQ-R was chosen as it is designed for quality improvement activities in the management of pain in hospitals for adults (Gordon et al., 2010:1172). Furthermore, this revised version of the APS-POQ underwent an in-depth, holistic revision, testing and the psychometric properties were examined by an interdisciplinary Task Force of the American Pain Society (Gordon et al., 2010:1172). The outcomes showed clinical feasibility, construct validity and internal consistency of the instrument subscales (Gordon et al., 2010:1172). Six aspects of quality are measured, namely: (1) the severity of pain and relief thereof; (2) effect of pain on movement, sleep and negative emotions; (3) treatment side effects; (4) effectiveness of pain treatment information; (5) opportunity to contribute in decision-making of pain treatment; and (6) using non-pharmacological methods (Gordon et al., 2010:1172). Another study proved that the APS-POQ-R was a valid measure for post-operative pain experienced in Danish and Australian patients (Botti et al., 2015:735). Table 1-1 depicts the compilation of the questionnaire.

Table 1-1: Compilation of the research questionnaire

<table>
<thead>
<tr>
<th>Questions from the APS-POQ-R</th>
<th>Adaptation</th>
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<tbody>
<tr>
<td>&quot;The following questions are about pain you experienced during the first 24 hours in the hospital or after your operation: 1) &quot;Please indicate the least pain you had in the first 24 hours on a scale from 0 to 10, where 0 = no pain and 10 = worst pain possible.&quot;</td>
<td>Omitted</td>
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<tr>
<td>2) &quot;Please indicate the worst pain you had in the first 24 hour on a scale from 0 to 10, where 0 = no pain and 10 = worst pain possible.&quot;</td>
<td>Omitted</td>
</tr>
<tr>
<td>3) &quot;How often were you in severe pain in the first 24 hours? Please circle the best estimate of the percentage of time you experienced severe pain on a scale from 0% to 100%, where 0% = never in severe pain and 100% = always in severe pain.&quot;</td>
<td>Omitted</td>
</tr>
<tr>
<td>4) &quot;On a scale from 0 to 10, where 0 = no pain to 10 = worst pain possible, mark the one number below that best describes how much pain interfered or prevented you</td>
<td>Adapted to &quot;In the four days after surgery, please choose a number from zero to five (where zero is pain free and five is excruciating pain) that best&quot;</td>
</tr>
<tr>
<td>Questionnaires</td>
<td>Adaptation</td>
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<tr>
<td>from:</td>
<td>describes how much pain interfered or prevented you from:</td>
</tr>
<tr>
<td>a) Doing activities in bed such as turning, sitting up, repositioning.</td>
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</tr>
<tr>
<td>b) Doing activities out of bed such as walking, sitting in a chair, standing at the sink.</td>
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<tr>
<td>c) Falling asleep</td>
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<tr>
<td>d) Staying asleep.&quot;</td>
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<tr>
<td>5) “On a scale from 0 to 10, where 0 = not affected at all to 10 = extremely affected, indicate how the pain affected your mood and emotions:</td>
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<tr>
<td>a) Anxious</td>
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<tr>
<td>b) Depressed</td>
<td></td>
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<tr>
<td>c) Frightened</td>
<td></td>
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<tr>
<td>d) Helpless.&quot;</td>
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<tr>
<td>6) “On a scale from 0 to 10, where 0 = none and 10 = severe, indicate the severity of side-effect experienced:</td>
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<tr>
<td>a) Nausea</td>
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<tr>
<td>b) Drowsiness</td>
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<tr>
<td>c) Itching</td>
<td></td>
</tr>
<tr>
<td>d) Dizziness.&quot;</td>
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<tr>
<td>7) “How much pain relief did you receive in the first 24 hours? Please circle the best estimate of the percentage of pain relief you experienced on a scale from 0% to 100%, where 0% = no relief and 100% = complete relief.”</td>
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<tr>
<td>8) “Were you allowed to participate in pain treatment decisions? Please circle from 0 to 10, where 0 = Not at all and 10 = very much so.”</td>
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<tr>
<td>9) “How satisfied were you with the overall treatment of your pain while in hospital? Please circle from 0 to 10, where 0 = extremely dissatisfied and 10 = extremely satisfied.”</td>
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<td>10) “Were you given any information on your pain treatment options? Please answer Yes or No and then from 0 – 10 please circle how helpful this information was, where 0 =</td>
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<tr>
<td>Questionnaires</td>
<td>Adaptation</td>
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<tr>
<td>not helpful at all and 10 = extremely helpful.</td>
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<tr>
<td>11) “Did you use any non-medicinal methods to relieve your pain? Please answer Yes or No and if you have answered yes please check all that applies below.</td>
<td>Omitted</td>
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<tr>
<td>• Cold pack</td>
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<tr>
<td>• Meditation</td>
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<td>• Deep breathing</td>
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<tr>
<td>• Listening to music</td>
<td></td>
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<tr>
<td>• Distraction (e.g. watching TV or reading)</td>
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<tr>
<td>• Prayer</td>
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<tr>
<td>• Heat</td>
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<tr>
<td>• Relaxation</td>
<td></td>
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<tr>
<td>• Imagery or visualisation</td>
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<tr>
<td>• Walking</td>
<td></td>
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<tr>
<td>• Massage</td>
<td></td>
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<tr>
<td>• Other (please describe)</td>
<td></td>
</tr>
<tr>
<td>12) “How often did the doctor or nurse encourage you to use non-medicine methods? Please mark either one of the following: never, sometimes or often.”</td>
<td>Omitted</td>
</tr>
</tbody>
</table>

The following questions show normal adherence behaviours:

1) “Please answer as yes or no. Do you ever forget to take your medication?” Adapted to “Please answer as yes or no, do you sometimes forget to take the medicine?”

2) “Please answer as yes or no. Are you careless at times about taking your medication?” Adapted to “Please answer as yes or no, when you travel or leave home, do you sometimes forget to bring along your medication?”

3) “Please answer as yes or no. When you feel better, do you sometimes stop taking your medicine?” Adapted to “Please answer as yes or no, when you feel that your pain is under control, do you sometimes stop taking your medicine?”

4) “Please answer as yes or no. Sometimes if you feel worse when you take your medicine, do you stop taking it?” Adapted to “Please answer as yes or no, have you ever cut back or stopped taking your medication without telling your doctor because it made you feel bad?”

5) “Please answer as yes or no. I take my medication when I am sick.” Omitted

6) “Please answer as yes or no. It is unnatural for my mind and body to be controlled by medication.” Omitted
<table>
<thead>
<tr>
<th>Questionnaires</th>
<th>Adaptation</th>
</tr>
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<tbody>
<tr>
<td>7) “Please answer as yes or no. My thoughts are clearer on medication.”</td>
<td>Omitted</td>
</tr>
<tr>
<td>8) “Please answer as yes or no. By staying on medication I can prevent getting sick.”</td>
<td>Adapted to “Please answer as yes or no. Do you ever feel hassled about sticking to your treatment plan?”</td>
</tr>
<tr>
<td>9) “Please answer as yes or no. I feel weird, like a ‘zombie’, on medication.”</td>
<td>Adapted to “Did any of the side effects cause you to skip a dose or completely stop taking your pain relief medications?”</td>
</tr>
<tr>
<td>10) “Please answer as yes or no. Medication makes me feel tired and sluggish.”</td>
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</tbody>
</table>

**Other questions added**

1) Date of birth  
2) Gender  
3) Smoking status  
4) Was there a time that you felt the need to take different painkillers to relieve your pain?  
5) Was there a time that you felt the need to increase the dose of the prescribed medication for sufficient pain control?

The validity and reliability of the data-collection tool and how it was used to ensure the credibility of a study is described in subsequent paragraphs. Measurement errors and its effect on precision, as well as other aspects influencing the quality data collection are discussed.

### 1.4.1.1 Reliability

A data source will be reliable if successive studies yield similar results and the data being sourced will reflect the information, which it is assumed to measure (Maree, 2007:147). Neuman (2009:190) proposes the following methods of improving reliability: (1) conceptualise constructs; (2) use precise measurement; (3) use multiple indicators; and (4) use pilot tests. The questionnaire will be quantifying one concept per measure by using clear, unambiguous questions to obtain precise information (Thompson et al., 2000:244; Unni & Farris, 2015). Questions requiring factual information from a specific and limited time period result in more accurate answers (Sue & Ritter, 2007:41), the questionnaire requires information from a specific time period and should thus give accurate answers (Thompson et al., 2000:244).

In the development of the questionnaire for the study, five options were given to increase the precision and improve the reliability of questions necessitating a rating. Because reliability can be improved by replication (Tan et al., 2014:4; Thompson et al., 2000:245), the basis for the questionnaire was adapted from the APS-POQ-R (Gordon et al., 2010:1172). The reliability and validity of the APS-POQ was shown in a Norwegian study managing post-operative pain for 102 participants during the first 5 days’ post-surgery (Dihle et al., 2006:273). The Chinese version of
the APS-POQ-R was found to have internal consistency and reliability when used to predict pain management satisfaction after surgery as well as to determine patient outcomes (Wang et al., 2017:118).

The additional questions were validated with input from orthopaedic surgeons from the hospital as well as by senior researchers at the North-West University.

Bot et al. (2013:1383) conducted an assessment to ascertain whether there is a variance in result between telephone administration and paper of certain questionnaires. The questionnaires tested being: (1) arm, shoulder and hand score — short version; (2) health anxiety inventory questionnaire — 5-question short version; (3) pain catastrophising scale — 4-question version; (4) patient health questionnaire-2; and (5) a pain-rating scale (Bot et al., 2013:1383). The outcomes of the study by Bot and colleagues (2013:1385) showed that telephonic administration of questionnaires measuring disability and psychological factors can be used as substitute for paper administration in studies not requiring in-person, physical examination. Furthermore, according to Adogwa (2015:253S), there is an extremely high correlation between patient reported outcome measures captured from telephonic surveys and surveys completed on hard copies by patients themselves. Telephonically administered questionnaires thus provide a cost-effective alternative to in-person surveys (Adogwa, 2015:254S).

1.4.1.2 Validity

Validity is when a measure or instrument quantifies what it true to measure (Maree, 2007:147) Validity can largely be organised as measurement validity and non-measurement validity. This signifies how successful the conceptual and operational definitions fit together. The different types of measureable validities are face validity, content validity and construct validity (Neuman, 2009:192; Pietersen & Maree, 2007:216).

Face validity is the extent to which a tool measures what it is supposed to measure (Pietersen & Maree, 2007:217). In the present study face validity was assured through the involvement of other healthcare professionals being the orthopaedic surgeons and pharmacists, during the development of the questionnaire and by conducting protocol face evaluation by trialling it with a pharmacist telephonically.

Construct validity pertains to whether the questionnaire measures the theoretical construct that it is supposed to measure (Burns & Grove, 2009:693); in this case, adherence (Thompson et al., 2000:244). Content validity is the extent to which the measuring tool measures the entire meaning of the subject matter (Polit & Beck, 2008:458). Additional measures were taken to
ensure content validity of the composite questionnaire by sending it to health professionals for validation. The questionnaire was sent to senior researchers for further validation. The orthopaedic surgeons as well as senior researchers were asked to review the questionnaire for clarity and meaning.

1.5 Data collection process

Figure 1-1 illustrates the process and steps taken during the implementation of the data collection tool. A brief discussion of each step follows in subsequent paragraphs.

Figure 1-1: Data collection process

1.5.1 Permission

Ethical approval was obtained from the Health Research Ethics Committee (HREC) of the North-West University (NWU-0052-15-S1) (Annexure A). Goodwill permission to conduct the study at the hospital was further obtained from the General Manager of the hospital and the seven orthopaedic surgeons working in the hospital (Annexure B).
1.5.2 Recruitment of participants

Recruitment started after ethical approval was obtained. During this step of the study, a meeting was held with each individual surgeon and their receptionists to explain the aims and benefits of the study as well as to request their support regarding the study and to explain the essential role that they can play. Full colour size A0 advertisements were placed in each reception area. Permission was granted by the surgeons as recruitment took place in their offices.

The researcher collaborated with the receptionist of the surgeon and held a training session after the initial meeting. The sessions were scheduled to accommodate receptionists’ schedules.

Because of the dependent relationship between surgeons and patients, certain steps were followed to assure that no surgeons would have knowledge of which patients participated in the study:

- The receptionists identified the participants that met the inclusion criteria.
- The receptionists explained the aim of the study and the role that the participant can play.
- The receptionists explained the role of the researcher.
- Participants interested in partaking in the study were given a participant contact detail leaflet and asked to provide a telephone number and email addresses or fax numbers for the researcher so that the participant can be contacted with regard to the study.
- Sealed boxes were placed in the reception area where potential participants could drop their completed patient contact detail leaflets.
- The researcher checked the boxes on the last day of every week for the duration of the study period to collect the completed patient contact detail leaflets.

1.5.3 Process of obtaining informed consent

The researcher contacted potential participants who completed the leaflet (Annexure C). Participants established their preferred method of contact. The informed consent form (Annexure D), the questionnaire (Annexure E), as well data booklet (Annexure F) were emailed or faxed to the participant for their convenience. Offering to deliver the informed consent forms by courier accommodated potential participants without email/fax facilities.
Participants were asked to either fax/email the signed consent forms back to the researcher or to bring it along on the day of surgery if more convenient. The participants recorded the contact telephone numbers as well as convenient times on the informed consent forms. Forms were reprinted and signed when the researcher visited the potential participant to answer any queries that participants may have in a case where they forgot to email/fax or bring along the forms on the day of surgery.

The researcher received the scheduled operating day for the participant from the secretary. The theatre list was circulated by the hospital, a day in advance, via internal email communication. The researcher thus knew the day and time of the participants’ surgery. Participants arrived before 7:00 AM on the day of their surgery for procedures scheduled for the morning time-slot, and before 10:00 AM for the afternoon time-slot.

At the time of admission, the researcher was available to potential participants to answer questions regarding the study or to clarify any uncertainties about the questionnaire and explain the data booklet (Annexure F) in person. The participants used this booklet to monitor medication doses, and make notes with regard to the medicine and side effects experienced from discharge until the telephonic survey. The pill count that was required was also explained.

The researcher copied the participants’ phone numbers and preferred times of contact from the informed consent forms onto an itinerary spreadsheet (see paragraph 1.7.2.3).

1.5.4 Collecting data using the data-collection tool

The researcher phoned the participant four days after surgery to conduct a telephonic survey using the itinerary spreadsheet and the questions from the questionnaire. This survey took approximately 15 minutes to complete.

The survey started with the researcher asking the participant whether it was a convenient time for the survey. If participant agreed, the researcher reaffirmed consent, documented the date and time of the survey and proceeded with asking the questions. Participants were informed that they could withdraw at any given time. If the participant decided not to continue, the interview was ceased and a note was made on the consent form in order to keep track.

The participants were informed from first communication with the researcher that they would be expected to count their tablets at the time of the telephone call; it was also indicated in the consent forms that were emailed/faxed or couriered to them after recruitment. Participants were also shown where to complete this information in their data booklet when the researcher visited them at time of admission. If the participant did not have his/her medication with them, the rest
of the questionnaire could still be completed, but the researcher had to discuss a suitable time to contact the participant for a second time, making sure that it occurred on the same day. If this occurred, the next suitable time would be documented. Participants who could not be reached on the fourth day after surgery were excluded from the study.

The data collection period continued from ethical approval until 120-study participant’s data were collected.

On completion of the telephonic survey, the researcher first recorded the email addresses of the participants who requested feedback and then placed the completed questionnaire in a sealed box and so preserved participant anonymity. The questionnaires were kept separately from the informed consent forms. Data were captured electronically using Microsoft Excel® (2010). Questionnaires were numbered after each survey until 120 was reached. This number was captured and used as unique participant identifier (i.e. no participant name or telephone number was captured electronically).

1.6 Data analysis

The variables included in the study, the descriptive statistics and inferential statistics used to outline the objectives for the empirical study will be discussed in subsequent paragraphs.

1.6.1 Study variables

The variables used in the analysis of data is described in Table 1-2.

<table>
<thead>
<tr>
<th>Table 1-2: Study variables and description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Variable</strong></td>
</tr>
<tr>
<td>Age</td>
</tr>
<tr>
<td>Gender</td>
</tr>
<tr>
<td>Smoking status</td>
</tr>
<tr>
<td>Medicine prescribed</td>
</tr>
<tr>
<td>Medicine quantity prescribed</td>
</tr>
<tr>
<td>Theoretic pill quantity</td>
</tr>
<tr>
<td>Pain severity rating</td>
</tr>
<tr>
<td>Variable</td>
</tr>
<tr>
<td>-----------------------------------------------</td>
</tr>
</tbody>
</table>
| Variable, Description                        | experienced, was determined for the following data fields:  
• Performing activities in bed such as turning, sitting up, repositioning.  
• Performing activities out of bed such as walking, sitting in a chair, standing at the sink.  
• Trying to fall asleep.  
• Awoken from sleep.”  
Adverse effect rating scale                   | Adverse effect rating scale from zero to five where zero means no side effect was experienced from the prescribed post-operative analgesics and five is where the side effect experienced was severe, was determined for the following side-effects:  
• Nausea  
• Drowsiness  
• Gastritis  
• Constipation  
• Dizziness  
Other side effects                             | Type of other side effect experienced was recorded.                                                                                                                                                         |
<p>| Post-operative prescribed medication adherence – medication cessation | Medication cessation was used to indicate whether the participant completely stopped taking the prescribed medication at any time due to side effects experienced. Categorised as yes or no. |
| Post-operative prescribed medication adherence – Intermittent dosing | Medication intermittent dosing was indicated if the participant skipped any doses of medication. Categorised as yes or no.                                                                                   |
| Post-operative prescribed medication adherence – Perception of pain control | Medication perception was shown by whether the participant, at any time, experienced that the medication for the post-operative pain control was not working. Categorised as yes or no.                        |
| Post-operative prescribed medication adherence – Additional analgesic requirement | Additional analgesic needs were revealed if the participant took any other pain medication for pain relief. Categorised as type and dosage of other pain medication.                                               |
| Post-operative prescribed medication adherence – Increased dosing | Increased dosing was shown if the participant took extra doses of the prescribed medication. Categorised as yes or no.                                                                                     |
| Normal prescribed medication adherence – Forget | When given prescribed acute medication in general, do the participants sometimes forget to take their medication – categorised as yes or no.                                                               |</p>
<table>
<thead>
<tr>
<th>Variable</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>to take medication</td>
<td>When given prescribed acute medication in general, do the participants ever cut back or stop taking their medication without telling the prescriber because it made them feel bad – categorised as yes or no.</td>
</tr>
<tr>
<td>Normal prescribed medication adherence – Cessation of medication</td>
<td>When given prescribed acute medication in general, do the participants &quot;sometimes forget to take their medication along when they travel or leave home&quot; – categorised as yes or no.</td>
</tr>
<tr>
<td>Normal prescribed medication adherence – Forget to take medication</td>
<td>When given prescribed acute medication in general, do the participants &quot;sometimes stop taking their pain medication when they feel that their pain is under control&quot; – categorised as yes or no.</td>
</tr>
<tr>
<td>Overall treatment plan perception</td>
<td>Do the participants ever “feel hassled about sticking to their treatment plan” – categorised as yes or no.</td>
</tr>
<tr>
<td>Self-reported post-operative adherence behaviour (POAB)</td>
<td>The participants answered questions about adherence to the prescribed post-operative treatment, which were categorised as yes or no. No = 0 and Yes = 1. The cumulative score of relevant questions were further categorised into high, medium and low adherence, e.g. Cumulative score of 0 = high adherence, 1 – 2 = medium adherence and 3 – 5 = low adherence (Questions on post-operative prescribed medication adherence as above).</td>
</tr>
<tr>
<td>Normal medicine adherence behaviour (NMAB)</td>
<td>The participants answered questions about adherence to prescribed treatment normally; which were categorised as yes or no. No = 0 and Yes = 1. The cumulative score of relevant questions were further categorised into high, medium and low adherence, e.g. Cumulative score of 0 = high adherence, 1 – 2 = medium adherence and 3 – 5 = low adherence. (Questions on normal prescribed medication adherence as above).</td>
</tr>
</tbody>
</table>

### 1.6.2 Statistical analysis

The Statistical Package for the Social Sciences (IBM SPSS® 25) was used to conduct the analysis of data (IBM Corp., 2017).

Data analysis was done using descriptive, inferential statistics and effect sizes as depicted in Table 1-3.
1.6.3 Descriptive statistics

Descriptive statistics were used to define the study population regarding the demographic information. This was done by calculating the mean and standard deviation for continuous data (e.g. age), and frequencies/percentages for nominal and dichotomous data (refer to Table 1-3).

1.6.4 Inferential statistics

The inferential statistics were calculated by using the student t-test for numerical data and for categorical data, the Pearson's chi-squared test/Fisher's exact test was used (refer to Table 1-3).

When two groups are being compared, the null hypothesis is a mathematical statement that the groups are the same. Statistical significance is presented by the calculated p-value, showing the probability that the result seen in the sample was due to chance. In a two-sample test, the p-value is the probability that the variance seen between the two groups was due to chance. A p-value of 0.05 indicates a 5% likelihood that the variances seen between the two groups was owing to chance. A result of a p-value less than or equal to 0.05 is deemed to be statistically significant and hence, rejects the null hypothesis (Hickman & Disler, 2016:137). It is vital to verify the clinical relevance of the actual study results after statistical significance is shown. Statistically significant outcomes are shown in many studies, but the results are not clinically relevant (Waning & Montagne, 2001).

1.6.5 Effect sizes

Effect sizes show practical significance — which is the degree to which a difference is large enough to have an effect in practice (Steyn, 2009). Practical significance of the outcomes of the student t-test were evaluated by calculating Cohen's $d$-value, and that of the chi-squared/Fisher's exact test was determined by means of Cramér's $V$.

Cohen's effect sizes, or $d$-values, was interpreted as follows: values range of 0.2 represents a small effect size where 0.5 is a medium effect size and 0.8 is a practically significant effect (Cohen, 1988:24). Cramér's $V$ was interpreted as follows: values range of 0.1 represents a small strength of association where 0.3 is a medium strength of association and 0.5 is a practically significant strength of association (Kearney, 2017).
Table 1-3: Data analysis plan

<table>
<thead>
<tr>
<th>Objective</th>
<th>Measurement</th>
<th>Variables</th>
<th>Statistics</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Independent</td>
<td>Dependent</td>
</tr>
<tr>
<td>Demographic characteristics of the study population</td>
<td></td>
<td>Number of participants</td>
<td>Gender</td>
</tr>
<tr>
<td>Objective</td>
<td>Measurement</td>
<td>Variables</td>
<td>Statistics</td>
</tr>
<tr>
<td>-----------</td>
<td>-------------</td>
<td>-----------</td>
<td>------------</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Independent</td>
<td>Dependent</td>
</tr>
<tr>
<td></td>
<td></td>
<td>walking, sitting in a chair, standing at the sink. Falling asleep Staying asleep)</td>
<td></td>
</tr>
<tr>
<td>Establishing the adherence status regarding discharge pain medication after orthopaedic surgery.</td>
<td>Determine self-reported post-operative pain medication adherence and pill count</td>
<td>Self-reported adherence status categories (low, medium, high) Pill count (low, medium, high)</td>
<td></td>
</tr>
<tr>
<td>Determining the association between participant’s demographic and behavioural-related variables (age, gender and smoking status) and adherence to post-operative discharge pain medication.</td>
<td>Association between pill count adherence and age group, gender and smoking status</td>
<td>Pill count<em>age group Pill count</em>gender Pill count*smoking status</td>
<td></td>
</tr>
<tr>
<td>Determining the association</td>
<td>Association between pill count</td>
<td>Pill count*pain when turning,</td>
<td>Counts</td>
</tr>
<tr>
<td>Objective</td>
<td>Measurement</td>
<td>Variables</td>
<td>Statistics</td>
</tr>
<tr>
<td>---------------------------------------------------------------------------</td>
<td>----------------------------------------------------------------------------------------------------------------------------------------------</td>
<td>---------------------------------------------------------------------------------------------</td>
<td>-------------------------------------------------</td>
</tr>
</tbody>
</table>
| between movement (turning, sitting up, repositioning in bed and walking, sitting, standing) and adherence to discharge pain medication after orthopaedic surgery. | adherence and pain experienced when turning, sitting up, repositioning in bed and walking, sitting, standing.                                 | sitting up and repositioning in bed.  
Pill count*pain when walking, sitting, standing. | Descriptive  
Counts  
Chi-squared test/Fisher’s exact  
Cramér’s V |
| Determining the association between sleep disturbances (falling and staying asleep) and adherence with regard to post-operative discharge pain medication. | Association between pill count adherence and pain experienced when falling asleep and being awoken by pain.                                    | Pill count*pain when falling asleep.  
Pill count*awoken by pain.                         | Counts  
Chi-squared test/Fisher’s exact  
Cramér’s V |
| Determining the association between the type and number of side effects experienced | Association between pill count and nausea, drowsiness, gastritis, constipation and dizziness.                                              | Pill count*nausea  
Pill count*drowsiness  
Pill count*gastritis  
Pill count*constipation | Counts  
Chi-squared test/Fisher’s exact  
Cramér’s V |
<table>
<thead>
<tr>
<th>Objective</th>
<th>Measurement</th>
<th>Variables</th>
<th>Statistics</th>
</tr>
</thead>
</table>
| from discharge pain medication after orthopaedic surgery and adherence. | Association between pill count and self-reported post-operative pain discharge medication  
Association between pill count and self-reported normal adherence behaviour  
Association between self-reported adherence to post-operative pain discharge medication and self-reported normal adherence behaviour | Pill count* dizziness                                                            | Descriptive                        |
| Determining the association between normal adherence patterns and adherence patterns relating to post-operative pain discharge medication. | Association between pill count and self-reported post-operative pain discharge medication  
Association between pill count and self-reported normal adherence behaviour  
Association between self-reported adherence to post-operative pain discharge medication and self-reported normal adherence behaviour | Pill count* self-reported post-operative pain discharge medication  
Pill count* self-reported normal adherence behaviour  
High/medium/low self-reported post-operative pain adherence category*  
High/medium/low self-reported normal adherence behaviour category | Counts  
Chi-squared test/Fisher's exact  
Cramér's V |

**Objective**: Determining the association between normal adherence patterns and adherence patterns relating to post-operative pain discharge medication.

**Variables**: Pill count* dizziness

**Statistics**: Counts  
Chi-squared test/Fisher’s exact  
Cramér’s V
1.7 Ethical considerations

1.7.1 Permission and informed consent

Ethical approval was obtained from the Health Research Ethics Committee (HREC) of the North-West University (NWU-0052-15-S1) (Annexure A). Goodwill permission to conduct the study at the hospital was further obtained from the General Manager of the hospital and the seven orthopaedic surgeons working in the hospital (Annexure B). Informed consent was obtained from the study participants (Annexure D).

1.7.2 Anonymity and confidentiality

1.7.2.1 Privacy and confidentiality of participants during the recruitment process

Potential participants interested in the study could contact the researcher directly or inquire about the study at the reception desks of surgeons willing to participate in the study (contact information of the researcher was available on the advertisements). Potential participants were given a leaflet (Annexure C), asking those willing to participate to provide their contact information (e.g. telephone number and fax or email address) for the researcher to contact them with regard to the study. Sealed boxes were placed in the reception areas where potential participants could drop their forms. Only the researcher checked the boxes for the duration of the study for feedback (in this step, sealed boxes were replaced by new ones). Participants were recruited prospectively from the time the study was approved by HREC and study site, until the required sample size was reached.

Sealed boxes were opened on a weekly basis in the privacy of the researcher’s personal office to remove the leaflets. Participants were then contacted according to their preferred method. After a potential participant was contacted, his/her leaflet was stored in a sealed box, in a locked cupboard, in the researcher’s office for the duration of the study. Only the researcher had access to the leaflets. After completion of the study, the forms were stored in a locked cupboard at the offices of MUSA, where they will remain for a period of five years. After this period, the forms will be destroyed appropriately.

1.7.2.2 Privacy and confidentiality of participants during the consent process

Upon receipt of a signed consent form, the researcher copied the phone number, date of surgery and preferred time of call of the participant on a numbered itinerary spreadsheet. Hereafter, the informed consent forms were stored in a sealed box in a locked cupboard, in the office of the researcher until the study was completed. Only the researcher had access to this
cupboard. When the number of participants for the study was reached (N = 120), the researcher informed the receptionists to stop recruitment of participants.

1.7.2.3 Privacy and confidentiality of participants during the data collection process:

The researcher used the telephone number and preferred time of call as recorded on the numbered itinerary spreadsheet to contact participants. No person other than the researcher had access to this document. When not in use, the researcher locked this document in a cupboard in the office of the researcher. The itinerary spreadsheet was shredded once the data collection had been completed. The telephonic survey was conducted in the privacy of the researcher’s personal office at work, which is not shared with any other person.

Consent was reaffirmed at the start of every call. No voice recordings were made.

After the survey was conducted; the researcher placed the questionnaire in a separate box to preserve participant anonymity, as the questionnaire was separated from the consent forms. Using Microsoft Excel® (2010), the researcher captured data electronically. Only the questionnaire number was captured and used as unique participant identifier (i.e. no participant name or telephone number was captured electronically). Only the researcher, study supervisors and statistician had access to the data.

1.7.2.4 Privacy and confidentiality of participants during the data dissemination process

No data of any particular participant was shared with any surgeon or other healthcare professional. Results of the data analysis were written down in the format of a manuscript. The name of the study site will not be mentioned anywhere in the researcher’s manuscript, the mini-dissertation or any conference proceeding abstract/presentation. A short summary of the results was sent to surgeons and to the participants who requested feedback.

Anonymity was maintained by adding a statement in the informed consent form stating that all participants’ information and responses written in the questionnaire would be kept private and the outcomes would be presented in an anonymous manner in order to protect the identities of the participants (Maree, 2007:307).

Steps to safeguard the privacy of participants, hospital policies and procedures were applied, e.g. the hospital complies with the Protection of Personal Information Act (4 of 2013).

All data were handled with strict confidentiality. During the study, all hard copies of the initial leaflet with participants’ contact information, the informed consent forms and questionnaires were kept in separate sealed boxes in locked cupboards in the researcher’s office. All electronic
data were stored on the password-protected personal computer of the researcher in a locked office. The study supervisor, for assistance in data analysis, kept a copy of the dataset. Only the study supervisors, researcher and statistician had access to the data.

On completion of the study, all locally held files of the data were deleted from all personal computers. All hard copies of the data will be stored for five years in locked cupboards in the office of MUSA, after which it will be discarded appropriately.

1.8 Chapter summary

This chapter included the background to the study, the problem statement, research aims and objectives, a summary of the research methodology applied, a description of the data source and analysis as well as the criteria for the study population and finally, the ethical considerations that were taken into account. It was shown that good adherence is key to successful pain treatment outcomes and individual participant factors may negatively affect medication adherence. The subsequent chapter entails a comprehensive literature review aimed at creating understanding of available treatments used in post-operative orthopaedic cases and what influences participants to be non-adherent.
CHAPTER 2: LITERATURE REVIEW

2.1 Introduction

Rene Descartes, a French mathematician, philosopher and writer in the 1600’s, was one of the first in detailing and describing somatosensory pathways, i.e. a link between the brain and peripheral sensation (Moayedi & Davis, 2013:5). Descartes’ publication; “Treatise of man” (Descartes & Hall, 1972), explained that sensations felt by the body were directed straight to the brain, where they are then perceived. Although this seems to be simplistic thinking, Descartes was a visionary in his comprehension of sensory perception as a function of the brain (Rodriguez, 2015:339). Descartes’ understanding of the pain process is the foundation that enables the more efficient management of pain today (Rodriguez, 2015:339). Descartes’ theory ties up with the current definition of nociceptive pain being the pain that results from real or potential damage to tissue (non-neural), and arises as a result of the activation of nociceptors occurring during surgery (International Association of Pain [IASP], 2014).

2.2 Definition and taxonomy of pain

In 1986, the IASP defined pain as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or both” (IASP, 2014). “The word ‘pain’ comes from the Latin word ‘peona’ meaning ‘penalty’ or ‘punishment’ (Guindon et al., 2007:2121)”. The Oxford Concise Medical Dictionary (2010:535) further explains that pain is an answer to messages received from the peripheral nerves in injured tissue, which sends information to spinal cord nerves, where they go through a gate control. This gate transforms the next route of impulses in accordance with messages received from the brain, i.e. this could be inhibitory, where the pain perceived is minimised or vice versa.

Physical examination and accurate history taking is crucial, as pain can be categorised based on pain physiology, intensity, time course, affected tissue and syndrome (Kishner, 2014:2; Thienhaus & Cole, 2002:28):

- “Pain physiology (nociceptive, neuropathic, inflammatory).
- Intensity (mild-moderate-severe; 0-10 numeric pain rating scale).
- Time course (acute, chronic).
- Type of tissue involved (skin, muscles, viscera, joints, tendons, bones).
• Syndromes (cancer, fibromyalgia, migraine, others).

• Special considerations (psychological state, age, gender, culture)."

Pain after orthopaedic surgery is mainly the result of significant muscle and skeletal tissue reconstruction, or repair by cutting into tissue, muscles and nerves (Kishner, 2014:2; Pasero & McCaffery, 2007:160; Rodriguez, 2015:339). A secondary inflammatory response may also occur, augmenting the patient's pain level (McDonald et al., 2016:606). The types of pain are thus characterised as acute nociceptive pain, inflammatory and possibly neuropathic pain when nerves are affected (Carr, 2009:2; Kishner, 2014:2; Pasero & McCaffery, 2007:160; Thienhaus & Cole, 2002:28). These types of pain are briefly described in subsequent paragraphs.

2.2.1 Acute pain

Acute pain is an unlikable occurrence with a short duration (generally categorised as pain lasting up to six months) subsequent to tissue damage, such as orthopaedic surgery (Rodriguez, 2015:339). Subacute pain occurs when a patient does not feel fully restored or comfortable, approximately 100 days after surgery. Recurrent acute pain suggests acute episodes returning over time, e.g. gastrointestinal motility disorders (Kishner, 2014:2; Thienhaus & Cole, 2002:28). Pain, unrelieved and continuous for more than six months after surgery, is often linked to negative psychological effects such as anxiety, fear, sleep disturbances and may further lead to chronic pain syndromes (Sinatra, 2002:S18).

2.2.2 Nociceptive pain

The IASP (2014) defines nociception as the neural process of encoding noxious stimuli. This type of pain occurs due to injury or disease of non-neural tissues (i.e. tissues or organs) (Perl, 2011:34). Nociceptive pain includes injury incurred by crushing (pressure), ripping of flesh (stretching) and burning (heat or cold), or infection mediators and ischaemia (Carr, 2009:2).

2.2.3 Neuropathic pain

Neuropathic pain is defined as “pain caused by a lesion or disease of the somatosensory nervous system” and can be acute or chronic in nature (IASP, 2014). Any injury or damage to a neural structure results in nerve (neuropathic) pain (Perl, 2011:34). Nerve damage could occur from surgical or traumatic injuries to peripheral nerves or diseases affecting the central nervous system, e.g. a stroke (transient ischaemic attack of the brain) (Raja & Wallace, 2015:1).
2.2.4 Inflammatory pain

Inflammatory pain is pain that results from tissue damage (Kehlet et al., 2006:1618). When pain remains unrelieved, normal sensory inputs can produce painful sensations and is termed hyperalgesia (Kehlet et al., 2006:1618).

Hyperalgesia can be classified as primary or secondary and should become an important consideration when pain remains uncontrolled (Sinatra, 2002:S20). Primary hyperalgesia is experienced when peripheral sensitisation occurs and patients experience exaggerated responses to painful stimuli (Sinatra, 2002:S20). Secondary hyperalgesia occurs after continual pain causes central sensitisation, where nearby uninjured tissues are perceived as being painful (Sinatra, 2002:S20).

2.3 Pain mechanism after orthopaedic surgery

Acute pain activates protective reflexes preventing further injury, e.g. instinctive withdrawal from harmful stimulus and minimising muscle movement (Rodriguez, 2015:339). The sympathetic nervous system is stimulated by pain, which in turn can cause extra pressure on the heart by increasing the heart rate and blood pressure (McDonald et al., 2016:606). The stress response created by pain can lower the immune system; elevate blood sugar levels and possibly result in higher infection rates (Ibrahim & Atallah, 2016:505; McDonald et al., 2016:606). Cognitive (mental process of perception), emotional and sensory features may also be present, resolving with healing of tissue damage (Rodriguez, 2015:339).

The biology of pain is not easily explained as it has evolved over the years; however, there are a few key points that have to be understood:

- Pain is produced by the brain.
- Pain is not an indication of the tissue state.
- Pain can be sparked by elements not related to physical harm (Moseley, 2010).

The Central Nervous System (CNS) can change the awareness level of pain. Pain is created by the brain, meaning that the brain needs to interpret the stimulus. The brain interprets it by drawing on past memories as well as future intentions and then decides whether pain would be helpful in some way. It is only then that the brain creates a signal that encourages action in order to minimise further damage (Hargrove, 2010).
The tissue state and pain can be totally unrelated. For example, a soldier on the battlefield who suffered an incredible injury like losing a limb may only feel the pain after the threat is over. Chronic pain is experienced long after tissue healing has taken place (Hargrove, 2010). Another example is phantom limb pain; this is when patients still feel pain even though the limb has been amputated (Moseley, 2010).

The gate control theory of pain theorised in 1965 intended to show that the triggering of nerves not transmitting pain signals (non-nociceptive fibers) can disrupt signals from pain producing nerves (nociceptive fibers) (Moseley, 2010). This theory was superior to previous pain theories as it describes psychological and physical aspects of pain perception (Moayedi & Davis, 2013:10). Figure 2-1 (adapted from Melzack & Wall, 1965:971) shows the gate control theory and various medications that treat the different steps in nociception.

Nociception (i.e., the pain awareness process) takes place in four phases, namely transduction, transmission, perception and modulation (Rodriguez, 2015:339). These can be described as follows:

- **Transduction phase:** thermal, mechanical, polymodal and silent nociceptors located in the skin convert a stimulus, e.g. scalpel incision into an electrical neuronal activity (Meeks et al., 2015:534). This electrical stimulus starts when injured cells release histamine, bradykinins, prostaglandins and substance P; these are evidently mediators that initiate the inflammatory process (Rodriguez, 2015:340; Sinatra, 2002:S18).

- **Transmission phase:** this electrical stimulus is conducted from the nerve fibres of the dorsal root ganglion in the spinal cord to the dorsal horn at the brain. This signalling system from the site of injury to the brain takes place in microseconds (Rodriguez, 2015:340).

- **Perception phase:** the awareness and sensation of pain occurs as a result of the activation of multiple structures in the brain (Meeks et al., 2015:537). The awareness of discomfort is further interpreted into more specific sensations such as burning, pressure or sharp senses (Rodriguez, 2015:340).

- **Modulation phase:** described as the down-regulation of pain perception. It becomes inadequate in cases where extreme trauma and tissue damage is suffered; therefore, managing this type of pain requires the administration of medications such as opioids that work centrally (Rodriguez, 2015:340).
2.4 Orthopaedic day case surgery

Orthopaedics is defined as the science or procedure of fixing deformities as a result of a disease of, or injury to the bones or joints of the skeleton. This specific division of surgery may encompass operation, manipulation or traction (Oxford Concise Medical Dictionary, 2010:524).

The following orthopaedic surgeries are typically classified as day case surgeries, since the patients return home on the same day if no complications occur: arthroscopies, small joint arthroplasties, ganglion cyst removal, carpal tunnel release, hallux valgus correction, osteotomy and rotator cuff tendon repairs. A brief description of these surgeries will be given in the following paragraphs.

2.4.1 Arthroscopies and arthroplasties

Knee or shoulder arthroscopies are conducted mostly for diagnostic purposes to inspect a joint cavity through a telescope fitted with a camera. These procedures are thus minimally invasive and are considered to be the most common day case procedures (Rudkin & Rudkin, 2005:43).
Arthroplasty is the reconstruction of a diseased joint through surgery or joint replacement (Oxford Concise Medical Dictionary, 2010:65). Hand arthroplasty of the metacarpophalangeal finger joint is an extremely successful surgical procedure, where silicone-based implants are used to replace previously arthritic tissue to stabilise the joint (Trail, 2006:129).

### 2.4.2 Ganglion cyst removal and carpal tunnel release

Ganglion cysts are cystic lesions filled with hyaluronic acid that appear on tendons and close to synovial joints, usually on the dorsal side of the carpal joints (Otawara et al., 2018:40). The pain caused by ganglion cysts is due to nerve compression and therefore, the mass is surgically removed (Kim et al., 2018:200).

Carpal tunnel syndrome is known as the most frequently identified nerve entrapment syndrome (Petrover & Richette, 2018:545). Decompression of the nerves has to be done surgically to relieve the pain (Petrover & Richette, 2018:546).

### 2.4.3 Hallux valgus (bunion) correction and osteotomy

Hallux valgus (‘bunion’) is a commonly seen deformity in the foot, associated with pain and functional disability (Qasim et al., 2018:128). Osteotomy, the surgical cutting of bone, is a surgical procedure performed to correct the hallux valgus (Qasim et al., 2018:128).

### 2.4.4 Rotator cuff tendon tear repairs

Four muscles, namely subscapularis, teres minor, infraspinatus and supraspinatus, including their tendons, make up the rotator cuff. The muscles form a cuff that keep the head of the humerus in the glenohumeral joint (Gibbs et al., 2018:165). Surgery is recommended when the tendon tear is not too severe, in the case where the patient is affected by decreased range of movement or severe pain is experienced (Gibbs et al., 2018:165).

### 2.5 Epidemiology of pain

Cognitive, sensory, affective and behavioural dimensions make up the patient’s perception of pain (McQuay et al., 1997:1531). Pain is subjective, as it is influenced by past experiences, the setting, effect of pain, gender, intellectual and cultural factors (Meeks et al., 2015:534).

Population-based studies have indicated that the occurrence of widespread musculoskeletal pain intensifies with age, reaching the highest point in the seventh and eighth decade (Leveille et al., 2005:333). Tighe et al. (2015:7) showed that older patients initially had lower postoperative pain scores but resolution of this pain occurred at a slower rate than in younger
participants. In the older population, the site and intensity of pain are important elements of experienced disability and furthermore, this population tend to have pain at more than one site, further complicating matters (Leveille et al., 2005:333).

Men and women in general do not experience pain equally, as women display a lower threshold and lower tolerance, thus experiencing painful stimuli as more intense (Melchior et al., 2016:13).

Pain management in less developed countries is given low priority as the management of other diseases e.g. human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) takes priority; as noted by the United Nations Development Programme (Vijayan, 2011:3).

Approximately 80% of post-operative patients report that they have moderate to severe pain following surgery and persistent post-surgical pain occurs in 10-50% of patients (Sinatra, 2002:S18; Tighe et al., 2015:2). This is an indication that the control of acute post-operative pain management remains a focus area (Sinatra, 2002:S18; Tighe et al., 2015:2); this will be discussed in the next section.

2.6 Post-operative pain management

The main objective of post-operative pain control is to minimise pain perception and to better the post-operative experience and recuperation for patients (Malan et al., 2003:955). The perception of pain is individualistic and thus the response to pain will be a subjective phenomenon with varying analgesic needs (Rasmussen, 2007:125). Acute post-operative pain, however, is classified as moderate to severe in the majority of post-operative patients and has to be treated effectively to prevent persistent post-surgical pain (Tighe et al., 2015:2).

Healthcare providers usually align their focus on diagnosis and treatment of causative elements before focussing on symptomatic treatment, e.g. pain (Anderson et al., 2016:88; Morrison et al., 2009:8). As supporting data connecting untreated pain to adverse clinical outcomes is absent, it is believed that acute pain will resolve as healing occurs (Anderson et al., 2016:89; Morrison et al., 2009:8). Untreated pain can lead to post-operative complications, e.g. pain can restrict a person from taking deep breaths and coughing, which could lead to pneumonia (McDonald et al., 2016:606). Patients may also experience decreased mobility, sleep disturbances, anxiety and lastly, slower recovery (McDonald et al., 2016:606).

Sufficient pain control post-operatively is a necessity for effective rehabilitation of patients as it permits prompt mobilisation and faster commencement of physiotherapy and healing (Fischer & Simansky, 2005:1189). The treatment modalities that will be discussed are non-pharmacological therapies, regional anaesthesia and pharmacological therapies.
2.6.1 Non-pharmacological therapies

Non-pharmacological techniques are combined with pharmacological pain control methods to result in additive or synergistic effects in pain control (Schug et al., 2015:259). Therefore, it is important for the clinician to firstly conduct a patient evaluation pre-operatively in order to ascertain the possible psychological needs (Chou et al., 2016:134). Non-pharmacological interventions include the provision of information, stress and tension reduction, transcutaneous electric nerve stimulation, acupuncture, extreme temperature therapy and magnetic therapy (Schug et al., 2015:259). These are briefly addressed in subsequent paragraphs.

2.6.1.1 Provision of information

Information given to the patient about the procedure as well as what type of pain they may experience after surgery has been shown to reduce the experience of pain and anxiety post-operatively (South African Society of Anaesthesiologists [SASA], 2016:S88). Caution is advised when providing excessive information or expecting the patient to make too many decisions as anxiety can ensue (SASA, 2016:S88).

2.6.1.2 Stress and tension reduction

Relaxation training involves breathing techniques, altering muscle tension, distraction and listening to music (SASA, 2016:S88). Listening to music results in a slight decrease in post-operative pain and opioid needs but hypnosis does not show similar effects (Schug et al., 2015:260). Evidence of beneficial effects of relaxation methods is weak and inconsistent for the management of acute pain (SASA, 2016:S89).

2.6.1.3 Transcutaneous electric nerve stimulation

Transcutaneous electrical nerve stimulation does not show any benefit to treat post-operative pain, the possible reason being that the maximum bearable stimulation must be given to be helpful, which can be painful in itself (Breit & van der Wall, 2004:45).

2.6.1.4 Acupuncture and acupressure

Acupuncture entails the positioning of needles into specific acupuncture points in the body and acupressure is when physical pressure is applied to these specific points (Chou et al., 2016:137).
Acupuncture minimises pain post-operatively; it decreases opioid needs thus decreasing adverse effects from opioids in ambulatory knee surgery, knee arthroplasty and back surgery (Schug et al., 2015:266).

2.6.1.5 Heat and cold therapy

The two main cryotherapy methods are cold pack cryotherapy and continuous flow device cryotherapy. The continuous device cryotherapy is believed to be superior, as it does not lose its cold temperature effectiveness over time as ice packs do. Further to this, steady compression as well as continuous circulating cold flow takes place over the affected area, minimising the possibility of cold burns and tissue damage, which can happen during cold pack cryotherapy (Chughtai et al., 2017:3831).

The beneficial effects of heat and cold therapy for post-operative pain management are, however, limited. For example, Cina-Tschumi (2007:259) has shown that cryotherapy given at a temperature of 4 degrees Celsius and higher (considered comfortable for patients), showed no beneficial effects on drainage or swelling after orthopaedic surgery.

2.6.1.6 Magnetic therapy or stimulation

There are conflicting findings in the literature about the effectiveness of magnetic therapy or stimulation in orthopaedic surgery. For example, according to Schug et al. (2015:271), there is no data supporting the use of magnetic therapy for post-operative pain. Adravanti et al. (2014:401), however, conducted a study using pulsed electromagnetic fields for post-operative pain relief after total knee arthroplasty and found that knee swelling and functional scoring were significantly better in the group which received pulsed electromagnetic field treatment one month after surgery compared to the control group who underwent the standard rehabilitation protocol.

2.6.2 Regional anaesthesia

Regional anaesthesia is defined as the numbing of a specific body part to perform surgical procedures and an important addition to the multimodal approach for optimal post-surgical pain relief. This is considered another route of administration that can be used to administer medications with the intent to minimise opioid side effects like nausea and hypomotility of the gastrointestinal tract post-operatively (Garimella & Cellini, 2013:191).

Regional anaesthesia includes the following procedures, local infiltration or wound infusions, intra-articular analgesics, neuraxial blocks, peripheral nerve blocks and patient controlled analgesia. A brief description of these is provided in the paragraphs that follow.
2.6.2.1 Local infiltration and continuous wound infusions

Local infiltration analgesia is described as the infiltration of large volumes of local anaesthetics with analgesics at a proximal nerve root or into the wound (Rudkin & Rudkin, 2005:42). Continuous infusions of local anaesthetic into the wound leads to a decrease in pain experienced at rest and during movement, decreases side effects experienced and shortens the length of stay in hospital (SASA, 2016:S77).

Cardiotoxicity and neurotoxicity is a concern with local anaesthetics when administering at toxic levels (Raff, 2016:41).

2.6.2.2 Intra-articular analgesics

Intra-articular medication administration is easy and effective in achieving analgesia for diagnostic and operative purposes in knee and shoulder surgery (Rawal, 2007:144). Intra-articular local anaesthetics e.g. bupivacaine and lignocaine slightly reduce post-operative pain, but when combined with steroids or opioids, analgesic consumption is decreased and pain is reduced (Schug et al., 2015:90).

Morphine administered alone, given intra-articularly after knee arthroscopy, does not show improvement in pain control compared to placebo (Rosseland, 2005:96). However, intra-articular fentanyl given after knee surgery showed to improve analgesia compared to placebo. The fentanyl-only patients did not require additional pain management therapy in 24 hours as they rated their pain as zero on the visual analogue score (Rosseland, 2005:96).

2.6.2.3 Neuraxial block

Neuraxial block is an anaesthetic technique where local anaesthetics are placed around nerves of the spine (Chou et al., 2016:143). Epidural infusions (continuous administration via a catheter) or intrathecal injections (single) of local anaesthetics e.g. bupivacaine or ropivacaine with or without opioids, is linked to lower pain scores post-operatively and is a safe alternative in patients at risk for cardiac or pulmonary complications (Chou et al., 2016:143). In a meta-analysis conducted by Mauermann et al. (2006:1023), comparing general anaesthesia with a neuraxial block in elective total hip replacements, the authors showed reductions in time of operation, blood loss intra-operatively, incidence of deep venous thrombosis and pulmonary embolisms.
2.6.2.4 Peripheral nerve block

A peripheral nerve block ensues when local anaesthetics, i.e. lignocaine and analgesics, e.g. fentanyl is injected near a specific peripheral nerve that in turn temporarily numbs the area assisting with post-operative pain (Kapila, 2017). A peripheral nerve block can be carried out either with an indwelling catheter or as a single injection, and is effective for post-operative pain treatment as part of multimodal analgesia (Rawal, 2007:144). When administered intra-operatively as a single-dose, large volume local anaesthetic, it has shown to reduce hospital stay and short-term pain after total knee replacement (SASA, 2016:S65).

2.6.2.5 Patient-controlled analgesia

Patient-controlled analgesia (PCA) is a pain control method where a patient has the ability to self-administer an analgesic agent in small doses by using a programmable infusion pump, usually an opioid (Salamonson & Everett, 2005:22). Patients feel independent and prefer using PCA, compared to receiving painful intramuscular injections (Salamonson & Everett, 2005:22). Patient-controlled analgesia is mostly regarded as safe but programming errors and faulty equipment can ensue; thus training and monitoring tools are essential for patients and staff alike (Chou et al., 2016:140).

2.6.3 Pharmacological therapy

Post-operative pain can be treated with unimodal (one medication), bimodal (two medications) or multimodal (three or more medications) regimens, administered enterally, parenterally or intra-articularly. The unimodal regimen for surgical patients usually includes the use of opioids in high doses to achieve pain relief. As a result, however, the adverse effects experienced are amplified causing this method of treating pain to become less popular in recent years (McDonald et al., 2016:607). Bimodal regimens are superior to unimodal regimens but less effective when compared to multimodal treatment plans (McDonald et al., 2016:607). It is essential that central sensitisation of pain does not occur as this complicates the treatment regimen needed for optimal pain control; operationally this can be measured as the analgesic effect of pain medication outliving its clinical duration of action by 5.5 half-lives (Joshi et al., 2014:192). The half-life of a drug is the “time required for the amount of drug in the body or blood to fall by 50%. For drugs by first-order kinetics, this number is a constant, regardless of the concentration. Units:time” (Katzung et al., 2012).

Drugs that display analgesic effects or that aid with analgesia for post-operative pain treatment are discussed in subsequent paragraphs under subheadings of unimodal, bimodal and multimodal regimens. The side effects of these agents are shown in Table 2-1.
2.6.3.1 Unimodal regimens

2.6.3.1.1 Paracetamol

Paracetamol (acetaminophen) has more than one mechanism of action for its antipyretic and analgesic effects. Firstly, it centrally activates serotonergic descending pathways; secondly it inhibits prostaglandin synthesis and forms active metabolites that centrally influence cannabinoid receptors and finally, peripherally it has nonselective inhibitory COX actions (Allegaert & van den Anker, 2017:308). The availability of an easily administered IV paracetamol has rekindled its use with its quick onset, efficacy and predictable plasma concentration (Taylor & Stanbury, 2009:189).

Paracetamol's peak plasma concentration is approximately <15 minutes for intravenous (IV) formulations, 30 minutes for liquid preparations, 45 minutes for tablets and 1-2 hours for extended release formulations. The concurrent ingestion of opioids, anticholinergics and food may delay the peak plasma concentration. Paracetamol has a 60% to 98% oral bioavailability and a distribution volume of 1 L/kg. The total protein binding is 10% to 30% and remains as such after an overdose (Lachiewicz, 2013:17).

Paracetamol undergoes approximately 90% hepatic conjugation with 40% to 67% glucuronide via UDP-glucuronosyltransferase 1-6 (UGT1A6) and 20% to 46% sulphate via Sulphotransferase 1A1 (SULT1A1) forming inactive metabolites that are excreted in the urine. A tiny amount of unchanged drug is excreted in the urine and the other fraction (5%) in therapeutic dose is oxidised mostly by Cytochrome P450 2E1 (CYP2E1), forming N-acetyl-p-benzoquinoneimine (NAPQI). N-acetyl-p-benzoquinoneimine is joined by glutathione and these complexes become cysteine or mercaptate, which are nontoxic conjugates and thus undergo urinary excretion. Paracetamol's elimination half-life is roughly 2 to 3 hours in normal therapeutic doses but may be extended when hepatotoxicity occurs (Hayward et al., 2015:211).

Paracetamol in extreme dosages may cause irreversible liver failure. Dosage adjustments are therefore required in patients with alcohol-related liver disease, acute liver disease and glucose-6-phosphate dehydrogenase deficiency (refer to Table 2-1) (Raff et al., 2014:34).
Non-steroidal anti-inflammatory drugs and cyclooxygenase-2 selective inhibitors

Non-steroidal anti-inflammatory drugs inhibit cyclooxygenase-1 (COX-1) non-selectively and cyclooxygenase-2 (COX-2) selectively inhibits COX-1 and COX-2 (Langford, 2006:95). As with any surgery, tissue damage occurs resulting in a rise in cyclo-oxygenase, which in turn increases the prostaglandin E2 (PGE2) production (Langford, 2006:95). The increase in PGE2 has a dual action where it firstly causes the primary peripheral sensory neurons to exaggerate to painful stimuli responses, i.e. hyperalgesia and secondly, it functions as a protective agent in the gastrointestinal tract (GIT) by preventing dyspepsia and at worst gastric erosions, which could cause gastric bleeds. Non-steroidal anti-inflammatory drugs and selective COX-2 inhibitors provide analgesic effects by reducing the possibility of peripheral and central sensitisation essentially by preventing prostaglandin from being synthesised (Lee et al., 2015:40).

Non-steroidal anti-inflammatory drugs and COX-2 selective inhibitors are mostly organic acids and extensively bound (95-99%) to plasma proteins (usually albumin) with a small (0.1 L/kg to 0.2 L/kg) volume of distribution. The oral bioavailability is high (>80%) and takes approximately 2–3 hours to reach peak plasma concentrations (Honey et al., 2012:77).

Non-steroidal anti-inflammatory drugs accumulate in specific areas e.g. diclofenac reaches high concentrations in synovial fluid and most NSAIDs attain adequate concentrations in the central nervous system (CNS) for an analgesic effect centrally. Celecoxib is transported freely into the CNS and accumulates in fat, as it is highly lipophilic. Diclofenac displays topical activity and is used in dermal preparations and ophthalmologic solutions (Grosser et al., 2017:741).

The elimination half-lives with therapeutic doses for diclofenac and celecoxib are 1–2 hours and 6–12 hours, respectively; but within the class it varies widely, e.g. piroxicam at 50–60 hours. Most NSAIDs undergo hepatic biotransformation and renal excretion as the principle routes of elimination, where elimination pathways frequently involve oxidation or hydroxylation (Grosser et al., 2017:741).

Non-steroidal anti-inflammatory drugs show equal efficacy in all routes of administration. Intravenous and rectal routes result in similar adverse effects to the oral route (Schug et al., 2015:184). Non-steroidal anti-inflammatory drugs, when administered repeatedly post-operatively could, however, be linked to reducing prostaglandin synthesis causing a decrease in renal function, especially in the elderly population (Alexander et al., 2002:188). It may also cause a change in the platelet functioning, increase the risk of bleeding, gastric and duodenal
ulceration, and possible bronchospasm in asthmatics that are vulnerable to NSAIDs and aspirin (refer to Table 2-1) (Taylor & Stanbury, 2009:189).

Diclofenac inhibits the cyclooxygenase pathways in a time-dependent manner and thus, when being used post-operatively in orthopaedic surgery, it does not provide the desired effects (Fredman et al., 2000:535; Kaplan et al., 2018:4). It is essential that it be administered well in advance of first incision to provide maximal pain relief as well as other drug-sparing effects as proved by a study conducted in Israel (Fredman et al., 2000:535). Parecoxib sodium is a COX-2 selective inhibitor used parenterally in the management of pain; it is a prodrug, which becomes hydrolysed and transforms into the active form valdecoxib. Valdecoxib is roughly 28000-times more selective to COX-2 than COX-1 (Malan et al., 2003:950). In Europe, parecoxib has been approved at a dose of 40 mg given intramuscularly or IV for immediate post-operative pain management (Malan et al., 2003:951).

Cyclooxygenase-2 selective inhibitors were created with the aim of minimising the gastrointestinal adverse effects that occur when blocking PGE2 production (Guindon et al., 2007:2124). Concerns have been raised about the COX-2 selective inhibitor’s safety profile, with the subsequent withdrawal of rofecoxib because of cardiovascular concerns, and valdecoxib because of serious cutaneous adverse effects (Guindon et al., 2007:2124). Presently, there is insufficient evidence showing any clinically significant negative result on bone healing by cyclooxygenase-2 inhibitors anti-inflammatory drugs (coxibs) (Schug et al., 2015:101).

2.6.3.1.3 Opioids

Opioid medications act as agonists on the central and peripheral opioid receptors (Iwaszkiewicz et al., 2013:1; Raff et al., 2014:81). They mirror the actions of natural morphine-like ligands and therefore inhibit ascending pain pathways, altering the perception of pain (Raff et al., 2014:81). They are either classified as strong or weak and in South Africa, they are available as immediate release or long acting formulations (Raff et al., 2014:81). Molecules included in this class are morphine, pethidine, tramadol, papavertum and oxycodone. The most common side effects experienced on initiation of therapy are constipation, nausea, somnolence, itching and dizziness (refer to Table 2-1) (Garimella & Cellini, 2013:192).

Morphine extensively undergoes first-pass metabolism (liver), thus the effects of an oral dose is far less than after parenteral administration. Morphine is metabolised into morphine-3-glucuronide as well as morphine-6-glucuronide, but to a lesser extent. Morphine-6-glucuronide
is the active metabolite and has μ-agonist effects in the CNS. Morphine is renally excreted by
glomerular filtration, predominantly as morphine-3-glucuronide (Nielsen et al., 2017:338).

A small fraction of codeine is metabolically activated by O-demethylation to morphine, which
results in its analgesic effect. Codeine, as opposed to morphine, is approximately 60% as
effective orally as parenterally for analgesia (Nielsen et al., 2017:338). Cytochrome P450 2D6
(CYP2D6) catalyses the conversion of codeine to morphine and patients lacking CYP2D6
function cannot attain analgesia from codeine (Racoosin et al., 2013:2155). The opposite end of
the spectrum is ultra-rapid CYP2D6 metabolisers, converting codeine into excessive amounts of
morphine, resulting in life-threatening opioid toxicity (Racoosin et al., 2013:2155). Oxycodone is
a codeine analogue and has superior oral efficacy compared to codeine, as first-pass
metabolism occurs to a lesser extent (Kapur et al., 2014:1179).

As there is a possibility of genetic variation between patients, healthcare workers must
recognise that medication doses of opioids may need to be titrated from the hospitals’ pain
treatment protocols (Klepstad, 2007:150).

Controlled release oxycodone provides continuous pain relief with a relatively steady opioid
release, less side effects and thus ideal for post-operative pain management (Stessel et al.,
2014:124). The controlled release formulation should be taken at fixed times and the quick
release formulation should be taken for breakthrough pain and also for weaning off the
extended release opioid (Schug et al., 2015:183).

Tramadol is a morphine-derivative prodrug dependent on genetic polymorphism for activation
but then also causing the medication to be unpredictable (Beaussier et al., 2016:S122). It is
known to have more side effects than morphine when attaining similar analgesic effects and its
actions can be inhibited by ondansetron; limiting its use in an ambulatory setting (Beaussier et
al., 2016:S122).

2.6.3.1.4 Glucocorticoids

The only natural glucocorticoid is cortisol, whereas methylprednisolone, hydrocortisone,
prednisolone, betamethasone and dexamethasone are all synthetic (Chu et al., 2014:49).

Corticosteroids decrease the release of arachidonic acid from cell membranes by inhibiting the
phospholipase A2 enzyme and in doing so, the production of cyclooxygenase and lipoxygenase
is decreased (Ghosh et al., 2017:712.E3). This decreased production minimises the levels of
hyperalgesic mediators, namely thromboxanes, prostaglandins and leukotrienes (Ghosh et al.,
Corticosteroids are orally effective, administered intravenously, absorbed systemically after local administration into synovial spaces and used topically (Chu et al., 2014:49). After absorption, more than 90% of cortisol in plasma is protein bound and only the free fraction is active and can enter cells. Albumin and corticosteroid-binding globulin account for the majority of steroid binding. Synthetic steroids require enzymatic activation before they are biologically active and great care should be taken in severe hepatic failure (Hammond, 2016:R14). Metabolism by conjugation involves additions of O or H atoms to form water-soluble derivatives that are excreted in the urine (Hammond, 2016:R15).

In addition to glucocorticoids treating a variety of inflammatory conditions, Waldron et al. (2013:197) found that when dexamethasone was administered pre-operatively, it reduced the prevalence of nausea and vomiting, the necessity of morphine-based agents, as well as the quantity needed for pain relief. Furthermore, dexamethasone decreased the length of hospital stay after surgery and accelerated functional recovery without having a negative impact on wound healing (Waldron et al., 2013:198).

Perioperative administration of corticosteroids may cause mild hyperglycaemia (refer to Table 2-1) (Schug et al., 2015:xxxiv).

2.6.3.1.5 Pregabalin

Pregabalin is mostly used in the treatment of chronic pain but has recently been included in the multimodal regimen of treating post-operative pain (Eskandar & Ebeid, 2013:364). Pregabalin is a gamma-aminobutyric acid (GABA) analogue, which binds to a subunit of voltage-gated calcium channels in the CNS; the mechanism of action is alleged to reduce calcium inflow at the nerve terminals, preventing neurotransmitters like norepinephrine, substance P and glutamate from being released, hence reducing postsynaptic excitability (refer to Table 2-1) (Dauri et al., 2009:716).

Pregabalin’s oral absorption is more than 90% and takes 1–2 hours to reach its peak concentration in plasma. It does not undergo metabolisation, nor is it bound to plasma proteins, but is absorbed by the L-amino acid transport system, which can become saturated. The half-life of Pregabalin is 4.5–7 hours, with 98% being excreted unchanged in the urine (Porter & Rogawski, 2018).

The administration of antineuropathic medications such as pregabalin or gabapentin pre-operatively, has also shown improvements in early post-operative analgesia and post-operative opioid requirements compared to placebo, with no differences noted in post-operative nausea and vomiting (Dauri et al., 2009:716; Lee et al., 2015:40). Pregabalin’s side effects include

2.6.3.1.6 Ketamine

Ketamine blocks the N-methyl-D-aspartate receptor and modulates acute pain by preventing central sensitisation (Schug et al., 2015:116).

Ketamine is highly lipid soluble, thus having a rapid onset of action and metabolism occurs by N-demethylation in the liver. Protein binding is low and has a half-life of 2–4 hours (Zanos et al., 2018:632).

This class of medication does not depress haemodynamic parameters or respiration at sub-anaesthetic doses, making ketamine ideal to combine with opioids (Schug, 2015:25). Furthermore, Ketamine has been shown to be beneficial in not only acute pain but also neuropathic pain and opioid-resistant pain (Himmelseher & Durieux, 2005:216).

Common side effects experienced in acute use include nausea, psychotomimetic effects and feelings of intoxication (refer to Table 2-1) (Radvanski et al., 2015). These side effects disappear within sixty minutes of administration, as the duration of action is only 5–10 minutes and can be minimised by concurrent administration of midazolam (Radvanski et al., 2015).

Table 2-1 provides a summary of the side effects of analgesics (compiled from Rossiter, 2014).
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<th>Drug</th>
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<th>Frequency not defined</th>
<th>Post-marketing</th>
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<tbody>
<tr>
<td>Paracetamol</td>
<td>Nausea, Vomiting</td>
<td>Headache, Insomnia</td>
<td>Oedema, Hypervolemia, Fatigue, Hypokalaemia, Hypophosphatemia, Hypomagnesemia, Hypoalbuminemia, Increased transaminase levels, Anaemia, Infusion site pain</td>
<td>Pleural effusion, Pulmonary oedema, Stridor, Wheezing</td>
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<td>NSAIDs</td>
<td>Abdominal distention and flatulence, Dyspepsia, Diarrhoea, Asthma, Peptic ulcer/GI bleed, Abdominal pain or cramps, Constipation, Dizziness, Oedema, Nausea, Rash</td>
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<td>Acute hepatitis</td>
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<td>Cholestasis</td>
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<td>Nephrotoxicity</td>
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<td>Agranulocytosis</td>
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<tr>
<td>COX-2 inhibitors e.g. Celecoxib</td>
<td>Headache</td>
<td>Hypertension</td>
<td>Fever</td>
<td>Anaemia</td>
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<td>Dyspepsia</td>
<td>Erythema</td>
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<td>URTI</td>
<td>multiforme</td>
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<td></td>
<td>Arthralgia</td>
<td>Steven-Johnson</td>
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<td></td>
<td>Cough</td>
<td>syndrome</td>
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<td></td>
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<td></td>
<td>Vomiting</td>
<td>Exfoliative</td>
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<td></td>
<td>Diarrhoea</td>
<td>dermatitis</td>
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<td></td>
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<td></td>
<td>Gastroesophageal reflux</td>
<td>Hepatitis</td>
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<td></td>
<td>Sinusitis</td>
<td>Toxic epidermal</td>
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<td></td>
<td>Abdominal pain</td>
<td>necrolysis</td>
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<td></td>
<td>Nausea</td>
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<td>Back pain</td>
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<td></td>
<td>Insomnia</td>
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<td>Flatulence</td>
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<td>Rash</td>
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<td>Dizziness</td>
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<td></td>
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<td></td>
<td>Peripheral oedema</td>
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<tr>
<td>Drug</td>
<td>Side-effect occurrence</td>
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<tr>
<td>Opioid e.g. Morphine</td>
<td>Pruritus, Urinary retention, Vomiting, Constipation, Headache, Somnolence, Abdominal pain, Asthenia, Backache, Depression, Respiratory depression, Diarrhoea, Loss of appetite, Dyspnoea, Insomnia, Nausea, Fever, Rash, Orthostatic hypotension, Xerostomia, Sweating, Dizziness, Anaphylaxis (rare), Cardiac arrest, Light-headedness, Malaise, Miosis, Myoclonus, Shock, Vertigo</td>
<td></td>
<td></td>
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<tr>
<td>Drug</td>
<td>Side-effect occurrence</td>
<td>Frequency not defined</td>
<td>Post-marketing</td>
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<tr>
<td><strong>Glucocorticoids</strong></td>
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<td></td>
<td>&gt;10%</td>
<td>1-10%</td>
<td>&lt;1%</td>
<td>Arthralgia</td>
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<td></td>
<td>Insomnia</td>
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<td>Fluid/electrolyte disturbances</td>
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<td>Headache</td>
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<td>Oedema</td>
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<td>Dizziness</td>
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<td>Erythema</td>
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<td>Seizures</td>
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<td></td>
<td>Adrenal suppression</td>
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<td></td>
<td>Psychosis</td>
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<td></td>
<td>Vertigo</td>
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<td></td>
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<td></td>
<td></td>
<td>Delayed wound healing</td>
</tr>
<tr>
<td></td>
<td>e.g. Betamethasone</td>
<td>Increased appetite</td>
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<td></td>
<td></td>
<td>Blurred vision</td>
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<tr>
<td></td>
<td></td>
<td>Nervousness</td>
<td></td>
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<td></td>
<td></td>
<td>Indigestion</td>
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<td></td>
<td></td>
<td>Itching</td>
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<tr>
<td><strong>Pregabalin</strong></td>
<td>Asthenia</td>
<td>Addiction</td>
<td>Angioedema</td>
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<tr>
<td></td>
<td>Oedema</td>
<td>Anaemia</td>
<td>Suicidal behaviour</td>
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</tr>
<tr>
<td></td>
<td>Facial oedema</td>
<td>Diarrhoea</td>
<td>Decreased platelet count</td>
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<tr>
<td></td>
<td>Hypotension</td>
<td>Gynaecomastia</td>
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<td></td>
<td>Neuropathy</td>
<td>Oesophagitis</td>
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<tr>
<td></td>
<td>Pain</td>
<td>Dysmenorrhoea</td>
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<td></td>
<td>Disorientation</td>
<td>Heart failure</td>
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<td></td>
<td>Constipation</td>
<td>Hirsutism</td>
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<td></td>
<td><strong>Ketamine</strong></td>
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<tr>
<td></td>
<td>Hypotension</td>
<td>Anaphylaxis</td>
<td>Genitourinary:</td>
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<tr>
<td></td>
<td>Emergence</td>
<td>Bradycardia</td>
<td>Dysuria</td>
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<td></td>
<td></td>
<td>Cardiac arrhythmia</td>
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</tr>
<tr>
<td>Drug</td>
<td>Side-effect occurrence</td>
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<td>&gt;10%</td>
<td>1-10%</td>
<td>&lt;1%</td>
<td>Frequency not defined</td>
</tr>
<tr>
<td></td>
<td>reactions</td>
<td>Diplopia</td>
<td>Depressed cough reflex</td>
<td>Increased urinary frequency</td>
</tr>
<tr>
<td></td>
<td>Increased intracranial pressure</td>
<td>Injection-site pain</td>
<td>Fasciculations</td>
<td>Haematuria</td>
</tr>
<tr>
<td></td>
<td>Tachycardia</td>
<td>Increased intraocular pressure</td>
<td>Hypersalivation</td>
<td>Cystitis</td>
</tr>
<tr>
<td></td>
<td>Visual hallucinations</td>
<td>Nystagmus</td>
<td>Increased metabolic rate</td>
<td>Hydronephrosis</td>
</tr>
<tr>
<td></td>
<td>Increased cardiac output</td>
<td>Tonic-clonic movements</td>
<td>Respiratory depression</td>
<td>Reduced bladder capacity</td>
</tr>
</tbody>
</table>
2.6.3.2 Bi- and multimodal analgesic regimens

The concept of multimodal analgesia is to deliver superior dynamic pain relief by using different classes of analgesics with different pain relief mechanisms and thus minimising the adverse effects (Malan et al., 2003:955). Enhanced functional recovery following any surgical procedure can be achieved using multimodal medication therapy, thereby shortening the hospital stay (Joshi et al., 2014:192). Multimodal pain control regimens, including various medicines as well as different routes of administration have shown superior efficacy with decreased side effects (McDonald et al., 2016:607). The South African Society of Anaesthesiologists (SASA, 2016:S26) supplies information that a clinician should consider when combining an analgesic for a multimodal approach of oral analgesics as depicted in Table 2-2.

Table 2-2: SASA’s important information when combining analgesics

<table>
<thead>
<tr>
<th>Oral analgesic for combination</th>
<th>Important information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paracetamol</td>
<td>Lower dosages are seen when used in a combination. Care should be taken when paracetamol is duplicated with the rectal or IV route, to avoid overdosing from occurring.</td>
</tr>
<tr>
<td>Caffeine hydrate</td>
<td>Good for migraines as it has a vasodilatory effect.</td>
</tr>
<tr>
<td>Codeine phosphate</td>
<td>Analgesic effect is mild Has to be metabolised to morphine Some patients are extremely sensitive to sedatory effects and should be taken into account.</td>
</tr>
<tr>
<td>Aspirin</td>
<td>Patient history is essential to rule out previous incidences of indigestion or bleeding tendencies.</td>
</tr>
<tr>
<td>Propoxyphene napsylate</td>
<td>Weak analgesic effect and some sedation Discontinued in SA.</td>
</tr>
<tr>
<td>NSAIDs</td>
<td>Should be used with care in patients with previous dyspepsia incidents, renal impairment and bleeding disorders.</td>
</tr>
<tr>
<td>Meprobamate</td>
<td>Weak analgesic Potential physical and mental addiction after ten continuous days of use.</td>
</tr>
<tr>
<td>Doxylamine succinate</td>
<td>Uncertain of inclusion in analgesic combinations.</td>
</tr>
<tr>
<td>Promethazine</td>
<td>Anti-emetic and sedatory effect Possible increase in QT interval (Black box warning in U.S.A.).</td>
</tr>
<tr>
<td>Orphenadrine</td>
<td>Antimuscarinic effect.</td>
</tr>
<tr>
<td>Diphenhydramine</td>
<td>Antihistamine with sedatory effect Black box warning in USA.</td>
</tr>
</tbody>
</table>
The aim of multimodal analgesia regimens that include opioids, is to decrease the dose of opioid by adding analgesics with differing mechanisms of action in order to prevent opioid-induced hyperalgesia tolerance. Opioid induced tolerance – not explained by disease progression and hyperalgesia (contradictory increase in pain unrelated to original stimulus) – is a concern, as increased doses of opioids are required to maintain effective pain control (DuPen et al., 2007:116). For example, NSAIDS and COX-2 inhibitors used post-operatively to treat moderate pain or as an adjunct to multimodal regimens allows decreases in opioid requirements, thus minimising opioid-type side effects (Langford, 2006:95). Opioid-type side effects are minimised as the overall intravenous opioid requirement is reduced (Lohsiriwat, 2016:546). Alexander et al. (2002:187) showed this by administering one dose of diclofenac or ketorolac before surgery and compared the morphine usage between these two groups as well as a morphine-only treatment group; the morphine usage in the two NSAIDs groups was significantly less compared to the morphine-only group. The decrease in need for opioids results in an improved quality of recovery because fewer side effects are experienced (White et al., 2011:324).

Paracetamol combined with a NSAID creates synergistic action, and based on a systematic review, the concurrent use of NSAIDs and paracetamol showed higher efficacy than paracetamol only in 85% of reviewed studies, and 64% higher effectiveness in studies where a NSAID was used alone (Guindon et al., 2007:2125; Ong et al., 2010:1176).

2.6.4 Clinical guidelines

Clinical guidelines assist providers of healthcare and patients in making suitable assessments of clinical challenges (Hewitt-Taylor, 2004:46). Clinical guidelines are built on the best existing evidence of care or procedures (Hewitt-Taylor, 2004:46). Clinical guideline development involves using existing literature in post-operative pain management and should consist of four dimensions, namely: (1) information and education for the patient and family; (2) effective teamwork among health professionals; (3) assessing and monitoring by hospital including departmental leadership; and (4) evidence-based contemporary recommendations of post-operative pain management (Aziato & Adejumo, 2015:32). These four dimensions will be addressed in subsequent paragraphs.

Patient education about specific medication and their side effects increases the healthcare team’s ability to create or amend an analgesic regimen, and so lead to a higher degree of patient satisfaction through individualistic treatment (Rasmussen, 2007:125). According to Chou et al. (2016:133), educational classes on the management of pain is advisable as it has shown to minimise pre-operative anxiety, reduce length of hospital stay and provide better
understanding of post-operative prescribed analgesics. Additionally, patients who were counselled on discharge medication were more likely to adhere to their analgesic regimen in contrast to those not receiving any information (Zeber et al., 2013:897).

The appropriate training and education of medical, nursing and other healthcare staff is critical for the safe and effective management of acute pain. Interdisciplinary teams should be set up to create a pain management team that in turn can advise, consult and guide on training (SASA, 2016:S16).

The American Pain Society (Chou et al., 2016:143) recommends that organisational structures be put in place to set-up and improve policies and processes for effective pain control after surgery. Standardised clinical observation charts, and successful training of staff and patients on these charts (displaying pain and sedation scores), is important to provide effective analgesia (Schug et al., 2015:478).

To ensure evidence-based contemporary recommendations for post-operative pain management, research should include the latest trends and developments in this area and continual improvements in quality processes for pain outcomes should be conducted. Measurement-driven models should be initiated to guide continual quality improvements to standardise and use valid and reliable measures (Chou et al., 2016:143). Local treatment guidelines and some international treatment guidelines created for post-operative pain management will be discussed next.

2.6.4.1 Comparison of treatment guidelines

Treatment guidelines are developed from evidence-based studies, input from other experts and expert bodies to suggest the most beneficial treatment modalities in specific clinical circumstances. These treatment guidelines are used for assistance in clinical decision-making and to optimise patient care (Madera Anaya et al., 2018:47).

Table 2-3 displays the guidelines used for orthopaedic surgery as implemented and used in a New York hospital, USA, and is formulated based on data from ten other pain management protocols in other U.S. facilities (McDonald et al., 2016:608).
Table 2-3: New York pain management protocol

<table>
<thead>
<tr>
<th>What</th>
<th>When</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-operative</td>
<td>2 weeks prior to surgery</td>
<td>Attend total joint class</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Interview with nursing and anaesthesia personnel</td>
</tr>
<tr>
<td>Immediate preoperative period</td>
<td></td>
<td>Pregabalin 150 mg (1 dose p.o.)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Celecoxib 200 mg (1 dose p.o.)</td>
</tr>
<tr>
<td>Surgery</td>
<td>During surgery</td>
<td>Spinal morphine sulphate injection</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Intra-articular injection (total knee arthroscopy only)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ropivacaine 0.5% 50 ml</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Epinephrine 0.5 ml 1:1000</td>
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<tr>
<td></td>
<td></td>
<td>Ketorolac 30 mg</td>
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<tr>
<td></td>
<td></td>
<td>Normal saline 48.5 ml</td>
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<tr>
<td></td>
<td>30 minutes before end</td>
<td>Ondansetron 4 mg IV</td>
</tr>
<tr>
<td></td>
<td>surgery</td>
<td>Acetaminophen 1 g IV</td>
</tr>
<tr>
<td>Post-operative</td>
<td>Immediate post-operative period</td>
<td>Continuous cold therapy (total knee arthroscopy only)</td>
</tr>
<tr>
<td>After surgery</td>
<td></td>
<td>Acetaminophen 1 g IV (6 hourly x 3 doses)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ondansetron 4 mg IV (6 hourly x 3 doses)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pregabalin 50 mg p.o. (12 hourly for 5 days)</td>
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<td></td>
<td></td>
<td>Celecoxib 200 mg p.o. (10 post incision x 1 dose)</td>
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<tr>
<td>&gt;24 hours after surgery</td>
<td></td>
<td>Acetaminophen 650 mg (4 hourly p.r.n.)</td>
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<tr>
<td></td>
<td></td>
<td>Ondansetron 4 mg IV (6 hourly p.r.n.)</td>
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<tr>
<td></td>
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<td>If normal renal function:</td>
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<tr>
<td></td>
<td></td>
<td>Oxycodone 5-10 mg (4 hourly p.r.n.)</td>
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<td></td>
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<td>Morphine 2-8 mg (2 hourly p.r.n.)</td>
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<tr>
<td></td>
<td></td>
<td>OR:</td>
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<tr>
<td></td>
<td></td>
<td>If renal insufficiency or allergy to morphine:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>hydromorphone 2-4 mg (3 hourly p.r.n.)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>hydromorphone 0.4-1.2 mg (2 hourly p.r.n.)</td>
</tr>
<tr>
<td>Rehabilitation</td>
<td>Before physical therapy</td>
<td>Coordinate medication dosing to occur 30 – 60 minutes prior to physical therapy</td>
</tr>
</tbody>
</table>

p.o. – orally; IV – intravenous; p.r.n. – when necessary according to circumstances

An interdisciplinary expert panel appointed by The American Pain Society with involvement from the American Society of Anaesthesiologists developed a clinical practice guideline of management strategies for pre-intra- and post-operative evidence-based interventions (Chou et al., 2016:132). The authors have produced the following interventions in eleven categories as
depicted in Table 2-4 and classified them by popularity and available evidence (Chou et al., 2016:132). The eleven categories include: (1) “Pre-operative education and perioperative pain management planning; (2) Methods of assessment; (3) General principles regarding the use of multimodal therapies; (4) Use of physical modalities; (5) Use of cognitive-behavioural modalities; (6) Use of systemic pharmacological therapies; (7) Use of Local and/or topical pharmacological therapies; (8) Use of peripheral regional anaesthesia; (9) Use of neuraxial therapies; (10) Organisational structure, policies and procedures; and (11) Transitioning to outpatient care.”
Table 2-4: APS strategies for pre- intra- and post-operative evidence-based interventions

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Recommendation/Evidence</th>
<th>Reasons</th>
</tr>
</thead>
<tbody>
<tr>
<td>“Pre-operative education and perioperative pain management planning”</td>
<td>Strong recommendation, low quality evidence</td>
<td>Healthcare providers supply uniquely tailored information to patients or caregivers comprising of info on treatment choices for post-operative pain and goals that should be achieved. Information should include discontinuation of aspirin before surgery to prevent haemorrhage and continuing medication e.g. benzodiazepines to prevent a withdrawal syndrome. Education should further correct any misperceptions about analgesics prescribed for post-operative pain, e.g. Opioid use always leads to addiction. Parents or children-caregivers undergoing surgery are given education on pain assessment methods and correct analgesic administration. Clinicians should conduct a detailed history taken pre-operatively to determine medical (bleeding disorders) or psychiatric comorbidities (anxiety, depression), current medications, chronic pain history (dependence or tolerance to opioids), substance abuse (asked in a non-judgemental manner) and previous responses to post-operative medications. The healthcare team should modify and adapt the pain management plan according to the individual patients needs on an on-going basis.</td>
</tr>
<tr>
<td>“Methods of assessment”</td>
<td>Strong recommendation, low quality evidence</td>
<td>“Validated pain assessment tool to track responses to post-operative pain treatments and adjust treatment plans accordingly” as pain is inherently subjective; individual self-reporting is critical for optimal pain management. “Validated pain assessment tools include Numeric Rating Scales (NRS), Verbal rating Scales (VRS), Visual Analogue Scales (VAS), Pain thermometer and Faces Rating Scales.”</td>
</tr>
<tr>
<td>“General principles regarding the use of multimodal therapies”</td>
<td>Strong recommendation, high quality evidence</td>
<td>Multimodal analgesics should be prescribed, or multimodal analgesics and varying non-pharmacological techniques combined post-operatively for pain relief in adults and children. Multimodal analgesics work additively or synergistically to relieve pain and minimise side effects and non-pharmacological techniques may assist with additional pain relief.</td>
</tr>
<tr>
<td>Strategy</td>
<td>Recommendation/Evidence</td>
<td>Reasons</td>
</tr>
<tr>
<td>----------------------------------------------</td>
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<td>------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td><strong>“Use of physical modalities”</strong></td>
<td>Weak recommendation, moderate quality evidence</td>
<td>The panel suggests that healthcare providers contemplate “transcutaneous electrical nerve stimulation (TENS)” use as a review of over twenty randomised trials showing that 25% less post-operative analgesics were used in patients receiving TENS. TENS is thought to reduce pain by decreasing central excitability, by activating endogenous descending inhibitory pathways.</td>
</tr>
<tr>
<td></td>
<td>Insufficient evidence</td>
<td>Acupuncture, massage or cold therapy as aids to post-operative treatment can neither be endorsed nor rejected by the panel as the evidence does not clearly demonstrate any valuable effects.</td>
</tr>
<tr>
<td><strong>“Use of cognitive-behavioural modalities”</strong></td>
<td>Weak recommendation, moderate quality evidence</td>
<td>Relaxation methods, hypnosis, intra-operative positive suggestions and music have shown inconsistent results about whether there were any benefits on post-operative pain outcomes.</td>
</tr>
<tr>
<td><strong>“Use of systemic pharmacological therapies”</strong></td>
<td>Strong recommendation, moderate quality evidence</td>
<td>The intravenous (IV) route of opioids does not show superior post-operative pain control compared to the oral route, therefore oral administration should be preferred. Opioids given pre-operatively are not recommended and patients already on opioids should continue their regular use; clinicians should take this into account when prescribing post-operative analgesics as increased dosages may be necessary.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>The intramuscular route should be avoided as it can cause severe pain; it is linked to undependable absorption and has no obvious advantage over other administration routes.</td>
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<tr>
<td></td>
<td></td>
<td>If the parenteral administration is required, the panel recommends the use of an intravenous patient controlled analgesia (PCA) if pain control is required for a few hours; patients understand the device and that they are conscious enough to use the device.</td>
</tr>
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<td></td>
<td></td>
<td>Basal infusions of opioids are not recommended, as evidence shows no superior analgesic effects, and the risk of vomiting, nausea and possibly respiratory depression may be increased.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Clinicians should consider administering celecoxib in a single dose 30-60 minutes pre-operatively as this is connected to reducing post-operative opioid requirements and pain scores.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Gabapentin or pregabalin should be considered as part of the multimodal regimen as both show evidence of decreasing post-operative opioid needs.</td>
</tr>
<tr>
<td>Strategy</td>
<td>Recommendation/Evidence</td>
<td>Reasons</td>
</tr>
<tr>
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</tr>
<tr>
<td>Ketamine should be considered as part of the multimodal regimen as this has shown a decrease in overall post-operative pain medication use.</td>
<td><strong>Strong recommendation, low quality evidence</strong></td>
<td>Observations of respiratory status, sedation and other adverse events in patients receiving opioids should occur initially after surgery and with any dosage adjustments.</td>
</tr>
<tr>
<td>Acetaminophen and/or NSAIDs should be part of the multimodal treatment plan post-operatively, as they work synergistically and when combined with opioids, bring about an opioid-sparing effect barring no contra-indications. There is no viable evidence proving that NSAID use results in bone non-union after orthopaedic surgeries.</td>
<td><strong>Strong recommendation, high quality evidence</strong></td>
<td>Site-specific local anaesthetic (long acting) infiltration can be added as an adjuvant of the multimodal treatment plan in orthopaedic procedures, as available data has mixed outcomes and convenience of other methods, but routine use is not recommended and use should be limited to knowledgeable clinicians with evidence of benefit per specific procedure.</td>
</tr>
<tr>
<td>Use of local and/or topical pharmacological therapies”</td>
<td><strong>Weak recommendation, moderate quality evidence</strong></td>
<td>Site-specific peripheral regional anaesthetic techniques, using ultrasound guidance, more so in patients undergoing upper and lower extremity techniques has appeared to be successful as part of the multimodal analgesic regimen.</td>
</tr>
<tr>
<td>Use of peripheral general anaesthesia&quot;</td>
<td><strong>Strong recommendation, high quality evidence</strong></td>
<td>Peripheral regional analgesic techniques using local anaesthetics needs to be done continuously instead of a single-injection in patients having multiple or prolonged surgeries where post-operative pain might be extended.</td>
</tr>
<tr>
<td>Clonidine prolongs the duration of the peripheral neural blockade by two hours, thus prolonging analgesia, but there is a higher risk of hypotension, syncope and sedation.</td>
<td><strong>Weak recommendation, moderate quality evidence</strong></td>
<td>Epidural analgesia with local anaesthetics (possible inclusion of opioids) or spinal analgesia (intrathecal opioid) has shown to drop post-operative pain scores and lessen the use of rescue analgesics; furthermore, this technique is safer for cardiac and pulmonary patients.</td>
</tr>
<tr>
<td>The safety of magnesium, benzodiazepine, tramadol, neostigmine and ketamine administered via the neuraxial route has not been established and the panel does not recommend it.</td>
<td><strong>Strong recommendation, moderate quality evidence</strong></td>
<td>Appropriate monitoring of patients receiving neuraxial interventions are important as it can mask compartment syndrome symptoms.</td>
</tr>
<tr>
<td>Facilities that perform surgeries should have an organisational structure ready to create and</td>
<td><strong>Strong recommendation, low quality evidence</strong></td>
<td><strong>Organisational&quot;</strong></td>
</tr>
<tr>
<td>Strategy</td>
<td>Recommendation/Evidence</td>
<td>Reasons</td>
</tr>
<tr>
<td>--------------------------------</td>
<td>---------------------------------</td>
<td>---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>structure, policies and procedures&quot;</td>
<td>quality evidence</td>
<td>improve policies and procedures for effective and safe post-operative pain control.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Facilities should have access to a pain specialist to advise clinicians on high-risk patients with inadequately controlled post-operative pain because of substance abuse or tolerance to opioids, for example.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Facilities have a standard operating procedure on what training is required for clinicians to administer neuraxial blocks and enforcing that only trained individuals are to perform the procedures.</td>
</tr>
<tr>
<td>“Transitioning to outpatient care”</td>
<td>Strong recommendation, low quality evidence</td>
<td>Healthcare providers should supply education to all patients or caregivers on the pain treatment plan after surgery, which incorporates reducing of pain medication after discharge from the facility.</td>
</tr>
</tbody>
</table>

IV: intravenous; NSAIDs: Non-steroidal anti-inflammatory drugs; PCA: patient controlled analgesia; TENS: transcutaneous electrical nerve stimulation
In 2004, the organisation “NHS Quality Improvement Scotland (NHS QIS)” released a best-practice statement on post-operative pain management consistent with newer developments. Table 2-5 (NHS QIS, 2004).

**Table 2-5: NHS Quality improvement Scotland best-practice statement on post-operative pain management**

<table>
<thead>
<tr>
<th>Objective</th>
<th>Key points</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Key principles of post-operative pain management</td>
<td>Patient’s needs and expectations of safe and effective pain management should be met. All healthcare staff should receive education in post-operative pain management. A consulted anaesthetist should be available and responsible for acute pain management at facilities where acute pain services are not available.</td>
</tr>
<tr>
<td>2. Patient information</td>
<td>Written information should be supplied to patients, as it is an important resource. Post-operative anxiety and pain can be minimised with written and verbal education of post-operative expectations. Written information issued to patients should be easy to read and clearly understandable.</td>
</tr>
<tr>
<td>3. Post-operative pain assessment</td>
<td>Assessment of post-operative pain to be recorded and treated with input from the patient as far as possible. Measurement of pain to be recorded alongside recording of other vital signs. Pain assessments to be done at rest and assessed during activity. Healthcare staff to understand the subjective nature of patient’s pain.</td>
</tr>
<tr>
<td>4. Subcutaneous opioid analgesia</td>
<td>Many patients fear injections and prefer SC injections. SC and IM routes of administration display similar absorption. The use of dedicated plastic cannulas for opioid-only analgesia is strongly recommended and decreases the incidence of IM needle stick injuries. An opioid algorithm has proved to be more effective compared to analgesia ‘when necessary’. Additional analgesics may be beneficial. SC opioid analgesia is not suitable for all patients.</td>
</tr>
<tr>
<td>5. Patient-controlled analgesia</td>
<td>Patient-controlled analgesia (PCA) entails the infusion of an opioid +/- an anti-emetic from a mechanical or electronic device and is controlled by the patient. The administration of the drug is via the IV route. Mostly used in patients where the opioid requirements are expected to be high or where IV analgesia will be required for more than 24 hours. All staff involved with PCA’s should receive sufficient training on</td>
</tr>
<tr>
<td>Objective</td>
<td>Key points</td>
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<tr>
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</tr>
<tr>
<td>all its aspects.</td>
<td>Opioids may be linked to nausea, confusion and respiratory depression. Opioid-sparing effect may be seen with the addition of additional analgesics.</td>
</tr>
<tr>
<td>6. Post-operative epidural analgesia</td>
<td>Local anaesthetics in combination with opioids may relieve post-operative pain to a greater extent than using either medication alone. Pain control may be superior compared to PCA in major abdominal surgery. Staff involved in the care of patients receiving epidural analgesia should be trained in all its aspects. It may be associated with adverse effects and adjuvant medications might be beneficial.</td>
</tr>
<tr>
<td>7. Regional methods of pain relief using local anaesthesia</td>
<td>Local anaesthetics produce reversible analgesia. Local anaesthetics are used in the following nerve blocks: local infiltration, plexus block, nerve block, regional block, wound infiltration and catheter neural blockade. Staff involved with caring for patients receiving continuous regional anaesthesia should be sufficiently trained.</td>
</tr>
<tr>
<td>8. Post-operative nausea and vomiting</td>
<td>Post-operative nausea and vomiting is debilitating for patients. It is extremely unpredictable if a patient may experience it. It may lead to delayed discharge, wound rupture, oesophageal tear, aspiration, dehydration and increased pain.</td>
</tr>
<tr>
<td>9. Patients with previous opioid exposure</td>
<td>Increased tolerance to opioids’ analgesic effects may be seen in patients with long-term exposure. Higher doses of analgesics may be required to manage pain. This type of patient should be referred to an acute pain service. Multimodal analgesics regimens are beneficial for such patients.</td>
</tr>
<tr>
<td>10. Step-down analgesia and discharge medication</td>
<td>Patients often complain about inadequate pain control after discharge. Patients undergoing day case surgeries should receive adequate analgesia before discharge. Inadequate pain control results in patient distress with possible delayed discharge, unplanned hospitalisation after discharge or increased workload for General Practitioners and community services.</td>
</tr>
</tbody>
</table>

SC: sub-cutaneously; IM: Intra-muscular; PCA: Patient-controlled analgesia

In the first edition of “Acute pain management” (Schug et al., 2015), scientific evidence was published by the Australian and New Zealand College of Anaesthetists and Faculty of Pain Medicines in 1999, the multi-disciplinary committee undertook to update the guidelines every five years and the fourth edition was released in 2015 (Schug et al., 2015). This last edition
entails the best evidence available for acute pain management. Table 2-6 summarises the key messages.
Table 2-6: Australian and New Zealand College of Anaesthetists and Faculty of Pain Medicine’s acute pain management guidelines

<table>
<thead>
<tr>
<th>Key points</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. “Physiology and psychology of acute pain”</td>
<td></td>
</tr>
<tr>
<td>“Psychological aspects of acute pain”</td>
<td>Pain is a personal, multifaceted incident guided by culture, prior incidents of pain, beliefs, attitude and capability to handle pain.</td>
</tr>
<tr>
<td>“Placebo and nocebo effects in acute pain”</td>
<td>Placebo effects take place in normal care even when no placebo was given. Treatment outcome is a result of both treatment and the placebo effect combined.</td>
</tr>
<tr>
<td></td>
<td>Nocebo effects happen in clinical practice and are observed when there is a heightened response to a painful stimulus or change in adverse effects differing from initial stimulus.</td>
</tr>
<tr>
<td></td>
<td>Ethical controlling of placebo and decreasing the nocebo effects will improve responses to clinical interventions.</td>
</tr>
<tr>
<td>“Progression of acute to chronic pain”</td>
<td>Although pregabalin and gabapentin may assist with preventing chronic post-operative pain, evidence is not strong as there are inconsistent data of a small number of studies with high variability.</td>
</tr>
<tr>
<td>“Pre-emptive and preventive analgesia”</td>
<td>A pre-incisional single analgesic intervention, e.g. epidural analgesia, has a major effect on post-operative pain support.</td>
</tr>
<tr>
<td></td>
<td>Certain analgesic interventions decrease overall analgesic consumption post-operatively by increasing the probable duration of action of analgesics and is termed preventive analgesia.</td>
</tr>
<tr>
<td></td>
<td>Ketamine and local anaesthetic administration show preventive analgesic effects.</td>
</tr>
<tr>
<td>“Adverse physiological and psychological effects of acute pain”</td>
<td>If acute pain remains untreated; the injury response will become exaggerated and be detrimental to overall outcome.</td>
</tr>
<tr>
<td>“Genetics and acute pain”</td>
<td>Genetic polymorphism affects the level of certain drugs in the plasma, e.g. codeine, oxycodone and tramadol in specific patient groups.</td>
</tr>
<tr>
<td>2. “Assessment and measurement of pain and pain”</td>
<td>Self-reporting should be done as far as possible, as pain is unique to every person.</td>
</tr>
<tr>
<td>“Assessment and measurement”</td>
<td>“The pain measurement tool should be appropriate to the individual patient – developmental, cognitive, emotional, language and cultural factors should be considered.”</td>
</tr>
<tr>
<td>Key points</td>
<td>Definition</td>
</tr>
<tr>
<td>-------------------------------------------</td>
<td>-------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>treatment</td>
<td>Post-operative pain rating should include static and dynamic pain scores. Reassessment and investigation should be done when unexpected or unexpected pain is reported.</td>
</tr>
<tr>
<td>“Outcome measures”</td>
<td>Various outcome-based measures are necessary to fully comprehend the intricacy of pain and the management thereof.</td>
</tr>
<tr>
<td>3. “Provision of safe and effective acute pain management”</td>
<td></td>
</tr>
<tr>
<td>“Education”</td>
<td>Effective managing of acute pain necessitates close relationships between all parties involved in patient care. Applicable education and staff dedicated for the management of pain will result in more effective acute pain rather than the analgesics by themselves.</td>
</tr>
<tr>
<td>“Organisational requirements”</td>
<td>Successful institutional backing and commitment is essential for carrying out an acute pain service. Analgesic protocols per procedure can assist in optimising analgesics for individual patients while decreasing unwanted effects.</td>
</tr>
<tr>
<td>“Economic considerations”</td>
<td>Well-controlled pain is highly valued by patients. The development of acute to chronic pain can have long-term economic consequences. PCA error costs can be significant, these result from staff communication fault and operator fault.</td>
</tr>
<tr>
<td>4. “Analgesic medicines.”</td>
<td></td>
</tr>
<tr>
<td>Opioids</td>
<td>Dextropropoxyphene analgesic efficacy is low. High doses of opioids, especially remifentany, can induce hyperalgesia and/or acute tolerance. The prevalence of nausea and vomiting of opioids is dose-related. Pregabalin, gabapentin, non-selective NSAIDs, ketamine and systemic lignocaine are opioid-sparing and thus decrease opioid-related unwanted effects. In the treatment of acute pain, all opioids are equal, although certain ones may be preferred by some patients. Opioid-induced ventilator impairment occurs from excessive use and involves central</td>
</tr>
<tr>
<td>Systemic</td>
<td></td>
</tr>
</tbody>
</table>
Key points | Definition
--- | ---
Respiratory depression and upper airway obstruction from depressed consciousness. Pethidine and dextropropoxyphene should be used as a last resort if deciding on an opioid.
Intrathecal | Fentanyl and morphine given intrathecally prolongs spinal local anaesthetic blocks and fentanyl shows less adverse effects.
Intrathecal morphine doses of 300mcg and above heighten the chance of respiratory depression.
Epidural | Neurotoxicity has not been reported when standard clinical intrathecal doses of fentanyl, sufentanil and morphine are given.
Neuraxial administration of opioids in bolus doses may cause belated sedation and respiratory depression in comparison to lipophilic opioids.
Peripheral | Morphine alone, injected intra-articularly, does not better analgesia after knee arthroscopy.
Topical administration of opioids have not been shown to be clinically relevant.
Morphine given as intermittent subcutaneous injections have equal efficacy to intramuscular injections and are better endured by patients.
Paracetamol | Paracetamol is effective in acute pain management; adverse effects are similar to placebo.
Paracetamol given IV and intra-operatively reduces post-operative nausea and vomiting by improving analgesia, not decreasing opioid requirements.
Hepatotoxicity with therapeutic doses is rare and not associated with alcohol consumption.
Nonselective NSAIDs and coxibs | Nonselective NSAIDs and coxibs have comparable efficacy for acute post-operative pain.
Nonselective NSAIDs added to paracetamol result in a synergistic effect, especially when ibuprofen is combined with paracetamol.
Coxibs are preferred as discharge medication after orthopaedic surgery compared to nonselective NSAIDs.
Coxibs given as an add-on to PCA opioids decrease opioid consumption and post total knee arthroplasty decrease opioid-related unwanted effects.
<table>
<thead>
<tr>
<th>Key points</th>
<th>Definition</th>
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<tbody>
<tr>
<td><strong>Nonselective NSAIDs, not coxibs, could possibly cause bronchospasm in sensitive patients.</strong></td>
<td>Nonselective NSAIDs given perioperatively may increase the chance of bleeding after surgery in comparison to placebo. Coxibs do not damage platelet function, blood loss perioperatively and better than nonselective NSAIDs. Short-term use of coxibs (5-7 days) leads to gastric ulceration rates comparable to placebo and less than nonselective NSAIDs. Nonselective NSAIDs have major adverse effects, which may restrict their use. NSAIDs’ effects on bone healing remain unclear.</td>
</tr>
<tr>
<td><strong>Intra-articular administration of nonselective NSAIDs can deliver more successful analgesia compared to IV administration.</strong></td>
<td>Intra-articular administration of nonselective NSAIDs can deliver more successful analgesia compared to IV administration.</td>
</tr>
<tr>
<td>Local anaesthetics and other membrane stabilisers</td>
<td>Systemic Peri-operative IV lignocaine has a protective analgesic effect (extending beyond 5.5 half-lives of lignocaine – more than 8 hours after dose) in a wide range of surgeries. In acute neuropathic pain, the use of membrane stabilisers like lignocaine is warranted. Regional local anaesthetics Intrathecal lignocaine is more prone to trigger transient neurological effects, compared to bupivacaine and procaine. Local anaesthetic use in epidural analgesia is enhanced with the add-on of opioids Ultrasound guidance lowers the possibility of vascular puncture while performing regional blocks There are no reliable differences between bupivacaine, ropivacaine and levobupivacaine in the quality of analgesia when used for epidural and peripheral nerve block. Inhaled agents Nitrous oxide is valuable in acute pain situations as an analgesic. Methoxyflurane, in low doses, is a helpful analgesic with quick onset and useful safety data for an assortment of procedures in-hospital. Systemic Peri-operative ketamine decreases time to first analgesic, overall opioid consumption, and</td>
</tr>
<tr>
<td>Key points</td>
<td>Definition</td>
</tr>
<tr>
<td>------------</td>
<td>------------</td>
</tr>
<tr>
<td>Ketamine</td>
<td>Decreases nausea and vomiting post-operatively. Ketamine added to morphine matched outcomes of morphine-only given in higher doses and improves analgesia, lessens sedation as well as nausea and vomiting post-operatively. Ketamine reduces post-operative pain in opioid-tolerant patients.</td>
</tr>
<tr>
<td>IV magnesium</td>
<td>When added to lignocaine, reduces subsequent post-operative pain. Ketamine toxicity causes mental confusion, and abuse thereof causes chronic organ toxicity (liver and bladder).</td>
</tr>
<tr>
<td>Regional</td>
<td>Ketamine reduces post-operative pain in opioid-tolerant patients.</td>
</tr>
<tr>
<td>Anticonvulsant medicines</td>
<td>Gabapentin and pregabalin lessen pain post-operatively and overall opioid needs, and decrease the frequency of pruritus, urinary retention but heightens the possibility of sedation.</td>
</tr>
<tr>
<td>Alpha-2 agonists</td>
<td>Ketamine reduces post-operative pain in opioid-tolerant patients.</td>
</tr>
<tr>
<td>Systemic</td>
<td>The perioperative use of clonidine minimizes the intensity of post-operative pain, opioid need and nausea, but side effects like bradycardia and hypotension may limit their use.</td>
</tr>
<tr>
<td>Regional</td>
<td>Intrathecal clonidine increases the analgesic and anaesthetic duration when added to local anaesthetics.</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>Dexamethasone reduces fatigue, nausea and vomiting; it increases recovery quality and slightly lessens post-operative pain and opioid needs. Preoperative administration appears more effective compared to intra- or post-operative administration. Mild hyperglycaemia could occur with perioperative administration of corticosteroids.</td>
</tr>
<tr>
<td>Systemic</td>
<td>Subacromial injections are better, compared to oral NSAIDs in rotator cuff tendonitis. Addition of corticosteroid to lignocaine in regional anaesthesia enhances analgesia for approximately 24 hours.</td>
</tr>
<tr>
<td>Regional</td>
<td>After arthroscopy of the knee, steroids added to either local anaesthetics or opioids given intra-articularly decreases pain, analgesic usage and immobilisation.</td>
</tr>
<tr>
<td>Key points</td>
<td>Definition</td>
</tr>
<tr>
<td>------------</td>
<td>------------</td>
</tr>
<tr>
<td>5. “Patient-controlled analgesia.”</td>
<td>Patient-controlled analgesia IV opioid PCA has better effects compared to standard parenteral opioid regimens&lt;br&gt;PCA opioid administration by IV leads to higher opioid consumption, increases the possibility of pruritus but not of other adverse effects or any other differences in length of stay&lt;br&gt;Patient satisfaction with PCA is higher in comparison to standard regimens&lt;br&gt;Transdermal fentanyl PCA has inferior efficacy to IV morphine PCA&lt;br&gt;PCA opioids all produce similar efficacies but interpatient variability towards better tolerated opioids should be taken into account&lt;br&gt;Adequate analgesia has to be attained before start of PCA. Individualised PCA prescriptions should be given&lt;br&gt;Anti-emetic additions are not suggested – there is no evidence that this method is superior compared to selective administration&lt;br&gt;Medication concentrations, prescriptions and feedback forms should be standard measure to improve patient safety.</td>
</tr>
</tbody>
</table>

The South African Society of Anaesthesiologists (SASA) developed the South African Acute Pain Guidelines and released a second edition in 2015 (SASA, 2016). The primary reference of these guidelines was “Acute pain management; Scientific evidence 2015, published by the Australian and New Zealand College of Anaesthetists and Faculty of Pain Medicines.” Table 2-7 displays the recommended tools, assessments and strategies.

Table 2-7: South African acute pain guidelines

<table>
<thead>
<tr>
<th>Tools</th>
<th>Assessment</th>
<th>Strategy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Choose an appropriate pain rating scale: VAS VNRS Verbal rating scale or verbal descriptor scale Wong-Baker FACES</td>
<td>Pain intensity &lt; 5/10</td>
<td>Monitor pain at 15-minute intervals and modify the analgesic treatment as necessary up to when the patient is pain-free during rest and movement.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pain to be observed hourly, at rest and during movement for 6 hours.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Assessments to continue every 4 hours.</td>
</tr>
<tr>
<td></td>
<td>Pain intensity &gt; 5/10</td>
<td>Contact the relevant physician.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Modify the pain treatment.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Monitor pain at 15-minute and then hourly intervals.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Look for possible complications for increased pain:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Deep vein thrombosis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Infection</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Compartment syndrome.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Observe for medication adverse effects:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Nausea and vomiting</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Respiratory depression</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Excessive sedation</td>
</tr>
</tbody>
</table>

Adjusting analgesics as per the treatment ladder:

<table>
<thead>
<tr>
<th>Pain scale</th>
<th>Classification</th>
<th>Recommended treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-2/10</td>
<td>No Pain</td>
<td>“No treatment, or NSAIDs or paracetamol.”</td>
</tr>
<tr>
<td>3-5/10</td>
<td>Mild pain</td>
<td>“Paracetamol and ‘weak opioids’ like codeine and tramadol.”</td>
</tr>
<tr>
<td>6-8/10</td>
<td>Moderate pain</td>
<td>“Codeine, paracetamol, NSAIDs, morphine, tramadol and an oxycodone/naloxone combination.”</td>
</tr>
<tr>
<td>9-10/10</td>
<td>Severe pain</td>
<td>“PCA epidural and nerve blocks, morphine, paracetamol, NSAIDs and an oxycodone/naloxone combination.”</td>
</tr>
</tbody>
</table>

VAS: visual analogue scale; VNRS: visual numeric rating scale; FACES: facial expressions rating scale; PCA: patient-controlled analgesia; NSAIDs: Non-steroidal anti-inflammatory drugs.
According to SASA (2016:S16), there should be a ‘pain team’ available and able to provide the following: Patient information and pre-operative counselling; efficient and safe information on multimodal pain management at all times; provide training, formal lectures and printed communications to all healthcare staff providing care to post-operative patients; assist with connections to chronic and palliative care services; monitor patient outcomes and record results per institution for quality improvements. If there is no pain team available, a consultant anaesthetist devoted to acute pain management should be available 24 hours a day (SASA, 2016:S16).

Table 2-8 displays the medication listings and general information of drugs used for acute pain based on the SASA guidelines (SASA, 2016).

The South African guidelines are based on the Australian and New Zealand College of anaesthetists and Faculty of Pain Medicine guideline; hence they are similar in nature (Schug et al., 2015). The American Pain Society (APS) guideline (Chou et al., 2016:132) focuses a lot more on pre-operative counselling, consulting with patients about previous post-operative experiences and creating individual treatment plans. In all the discussed guidelines, continual monitoring of pain post-operatively should occur and dosages should be adjusted accordingly. The validated pain assessment scales and the pharmacological recommendations of SASA correlate to those of the American Pain Society. The APS suggests avoiding the intramuscular route for drug delivery, but as SASA indicated, it’s still the most common route of drug delivery in South Africa (SASA, 2016:S60).
Table 2-8: SASA guideline drug listing for treatment of acute pain

<table>
<thead>
<tr>
<th>Medication</th>
<th>Type</th>
<th>Relevant information</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Opioids – Mainly for severe pain</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Opioid agonists: Morphine p.o., IM, IV, PCA, neuraxial</td>
<td></td>
<td>IV opioid PCAs provide better analgesia than established parenteral regimens.</td>
</tr>
<tr>
<td>Pethidine IM, PCA</td>
<td></td>
<td>Opioids that are injected neuraxially should be preservative free.</td>
</tr>
<tr>
<td>Papaveratum IM</td>
<td></td>
<td>Neuraxial morphine respiratory depression occurs 8-12 hours after administration.</td>
</tr>
<tr>
<td>Dihydrocodeine tartrate p.o., IM</td>
<td></td>
<td>Neuraxial dose of opioids should be decreased in the elderly as respiratory depression is more prevalent.</td>
</tr>
<tr>
<td>Codeine p.o.</td>
<td></td>
<td>Elderly patients have 15% higher plasma levels of oxycodone and dosage adjustments are required.</td>
</tr>
<tr>
<td>Oxycodone p.o.</td>
<td></td>
<td>Oxycodone dosages need to be decreased in patients with renal failure.</td>
</tr>
<tr>
<td><strong>Opioid dualist:</strong> Tilidine p.o.</td>
<td>For moderate to severe pain.</td>
<td></td>
</tr>
<tr>
<td>Pentazocine IM, IV, SC</td>
<td>Pentazocine – increases peripheral vascular resistance – caution in the elderly.</td>
<td></td>
</tr>
<tr>
<td><strong>Opioid antagonist:</strong> Naloxone IV</td>
<td>If total calculated dose is rapidly administered, pulmonary oedema may occur.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Reverses all opioid effects.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Half-life is 15-60 minutes, thus re-administration may be necessary.</td>
<td></td>
</tr>
<tr>
<td><strong>Atypical opioids:</strong> Tramadol p.o., RECTAL, IV, IM</td>
<td>Over 12 years only.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Avoid concomitant use with 5-HT3 anti-emetics to prevent serotonin syndrome.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Avoid concomitant use with SSRI anti-depressants to prevent serotonin syndrome.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Avoid excessive doses and rapid IV administration as this increases incidence of nausea</td>
<td></td>
</tr>
<tr>
<td>Medication</td>
<td>Type</td>
<td>Relevant information</td>
</tr>
<tr>
<td>-----------------------------</td>
<td>-------------------------------</td>
<td>---------------------------------------------------------------</td>
</tr>
<tr>
<td></td>
<td></td>
<td>and vomiting.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>10% of Caucasian population have reduced active metabolite reduction resulting in large dose variations.</td>
</tr>
<tr>
<td>Paracetamol</td>
<td>Paracetamol p.o., RECTAL, IV</td>
<td>High dosages could result in permanent liver failure.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Caution should be exercised and dosages decreased in patients with:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Acute liver disease</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Glucose-6-phosphate dehydrogenase deficiency</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Alcohol-related liver disease</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Parenteral route only registered for 24-48 hours.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Beware of combination analgesics containing paracetamol, to prevent excessive dosing.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Accidental overdose should be treated with N-acetylcysteine.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Possible exacerbation of asthma in certain patients.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Diclofenac – IM injections need to be deep and could result in irreversible neural damage.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Indomethacin – CNS disturbances may occur.</td>
</tr>
<tr>
<td>Selective COX-2 inhibitors</td>
<td>COX-1 inhibition occurs from excessive doses.</td>
<td></td>
</tr>
<tr>
<td>Medication</td>
<td>Type</td>
<td>Relevant information</td>
</tr>
<tr>
<td>------------</td>
<td>------</td>
<td>----------------------</td>
</tr>
<tr>
<td>Meloxicam PO</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Specific COX-2 inhibitors</td>
<td></td>
<td>Similar renal effects, no antiplatelet effects and less gastrointestinal effects are experienced.</td>
</tr>
<tr>
<td>Celecoxib PO</td>
<td></td>
<td>Contra-indicated in sulphonamide allergy.</td>
</tr>
<tr>
<td>Parecoxib IM, IV</td>
<td></td>
<td>Caution in cardio- and peripheral vascular disease.</td>
</tr>
<tr>
<td>Etoricoxib PO</td>
<td></td>
<td>Possible increase in blood pressure.</td>
</tr>
<tr>
<td>Ketamine PO, PCA</td>
<td></td>
<td>Synergism with opioids.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>May give pre-emptive analgesia.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No decrease in opioid side effects.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hallucinations and excessive sweating are some of the adverse effects.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Possible improvement in patients suffering with opioid tolerance.</td>
</tr>
<tr>
<td>Magnesium p.o.</td>
<td></td>
<td>Concern for possible muscle relaxation.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Decreased blood pressure experienced.</td>
</tr>
<tr>
<td>Nitrous oxide p.o.</td>
<td></td>
<td>Prolonged use causes bone marrow depression.</td>
</tr>
<tr>
<td>Dextromethorphan p.o.</td>
<td></td>
<td>Use preventatively, pre-operatively in patients undergoing tonsillectomy as it decreases analgesic use.</td>
</tr>
<tr>
<td>Clonidine p.o., IV, EPIDURAL</td>
<td></td>
<td>Given as pre-emptive analgesia as post-operative pain intensity is less.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Side effects: hyper- and hypotension and bradycardia.</td>
</tr>
<tr>
<td>Lignocaine 2% IV</td>
<td></td>
<td>“Toxic dose: 5 mg/kg</td>
</tr>
<tr>
<td></td>
<td></td>
<td>With adrenaline: 7 mg/kg</td>
</tr>
<tr>
<td></td>
<td></td>
<td>For mucous membranes: 9 mg/kg.”</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Neurotoxicity happens ahead of cardiotoxicity.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Not for intrathecal use.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Continuous perineural infusions are not advised and longer acting molecules should be</td>
</tr>
<tr>
<td>Medication</td>
<td>Type</td>
<td>Relevant information</td>
</tr>
<tr>
<td>----------------------------------</td>
<td>------------</td>
<td>---------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td><strong>Local anaesthetics – long acting</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bupivacaine IV</td>
<td></td>
<td>“Toxic dose: 2 mg/kg.”</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cardiotoxicity happens ahead of neurotoxicity.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>In cardiotoxicity, use intralipid at 1-1.5 ml/kg IV.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Side-effects may be more pronounced with bupivacaine in high doses.</td>
</tr>
<tr>
<td>L-bupivacaine IV</td>
<td></td>
<td>Toxic dose: 2 mg/kg.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>The long-acting formulations all have similar effects if given in low doses for analgesia or motor blockade.</td>
</tr>
<tr>
<td>Ropivacaine IV</td>
<td></td>
<td>Toxic dose: 2 mg/kg.</td>
</tr>
<tr>
<td><strong>Anti-emetics</strong></td>
<td></td>
<td>All effective for the avoidance of post-operative nausea and vomiting.</td>
</tr>
<tr>
<td>Metoclopramide</td>
<td></td>
<td>They lessen the negative effects of opioids and minimise the possibility of aspiration.</td>
</tr>
<tr>
<td>Ondansetron</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dexamethasone</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Granisetron</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cyclizine</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

COX: cyclo-oxygenase; CNS: central nervous system; IM: intramuscular; IV: intravenous; MAOI: monoamine oxidase inhibitors; NSAIDs: Non-steroidal anti-inflammatory drugs; PCA: patient-controlled analgesia; p.r.n.: when necessary; p.o.: orally; SSRI: selective serotonin reuptake inhibitors; 5-HT3: serotonin
2.7 Adherence

Medication adherence is explained as the degree to which a patient takes prescribed medication at the right dose and dosage intervals as deliberated and agreed upon with the prescriber (O’ Rourke & O’ Brien, 2017:160). According to the WHO (2003:XIII), a superior impact on patient health will be seen if adherence interventions are more successful; it may even have a greater influence in patient care, in comparison to any advance in any medical treatment. Non-adherence to prescribed pain medication after surgery results in pharmacotherapeutic failure and is associated to an increase in morbidity and mortality of these patients (Vrijens et al., 2012:691). Adherence to prescribed medicine is fundamental in attainment of clinical goals and thus, intelligence about the level of adherence to a treatment protocol is vital to both clinicians and researchers (Lam & Fresco, 2015).

Adherence to post-operative analgesics is categorised as initial adherence. Accurately establishing initial adherence is difficult as there is presently no validated systemic means to quantify, as the actions that occur in the prescriber’s office is difficult to connect to the patient’s actions outside of the office (Jorge et al., 2011:21; Zeber et al., 2013:891). Medication adherence can be determined over a certain amount of time and stated as percentage (Cramer et al., 2008:46).

Adherence is understood to consist of three constructs: initiation or acceptance, compliance and persistence (Urquhart, 2001:473-474). Guénette et al. (2013:251) describes initiation as primary adherence, where the patient accepts the prescribed treatment in agreement with the prescriber. Compliance in this regard can be explained as implementation, where the patient takes the correct dosage, timing and frequency of medication. The time frame between initiation of therapy and discontinuation is termed persistence (Guénette et al., 2013:251; Urquhart, 2001:473; Vrijens et al., 2012:696). Collectively, these three constructs of adherence are key factors that can assist to establish the success of any therapy (Cramer et al., 2008:46; van Boven et al., 2016:836; Zeber et al., 2013:891).

Figure 2-2 (adapted from Carmer et al., 2008:46; Guénette et al., 2013:252; Urquhart, 2001:473 and Vrijens et al., 2012:696) depicts the three constructs of adherence and how they relate to each other.
Compliance, adherence and concordance are related but it is important to note that the differences are seen by the extent of patient involvement (Bokhour et al., 2008:377).

Adherence and compliance are often used interchangeably but the differentiating factor is that compliance deduces no involvement of a patient in the treatment plan as a collaborative effort with the prescriber (Mäkelä et al., 2013:1483; Osterberg & Blaschke, 2005:487). Adherence should further be defined as being non-judgemental, where no blame is placed on patient, prescriber or treatment (Haynes et al., 2008).

Concordance is said to replace adherence and compliance as it focuses on the counselling procedure where the patient and the prescriber concur on therapeutic decisions by incorporating their individual views from prescribing communication to support in medicine taking (Bokhour et al., 2008:377).
2.7.1 Factors influencing adherence

McHorney (2009:223) concluded that the three main reasons for non-adherence are: (1) perceived medication benefits versus harms, (2) the necessity of the medicine and (3) pharmacy costs that won’t be covered by health insurance plans.

Based on a study conducted by Beardon et al. (1993:847) in the U.K., time and again, patients were unsuccessful in filling prescriptions for dermatological conditions, obstetric medications and oral contraceptives, but were more successful in adhering to prescribed cardiovascular treatment (Shah et al., 2009:4).

There are various factors that may influence adherence, which range from something as simple as cost to more complicated and unique patient belief systems (McHorney, 2009:223).

2.7.1.1 Medication costs

Medication non-adherence has been appraised to escalate healthcare costs by over $170 billion per annum in the U.S. (Fischer et al., 2010:284).

Research has frequently documented associations between medication costs, financial burden and non-adherence (Goldsmith et al., 2017:51). The greatest issue resulting from medication cost non-adherence are the costs incurred either from loss of productivity or re-admissions to hospital; this may result in funders limiting admissions and readmissions (Ryan et al., 2014:2000).

2.7.1.2 Age

Adherence is seen to decrease when children reach adolescence as they strive to become more independent and parental supervision is decreased. Regarding the elderly, age-related decline and external factors play a big role in adherence, e.g. reduced social support, polypharmacy, added isolation and cognitive function loss (Costello et al., 2016:813). A study done by Arria et al. (2011:4) showed that when acute pain medication was prescribed to young adults aged 21-26 years, 42% of them used the medication differently than what was agreed upon by the physician.

2.7.1.3 High body mass index

A study done by Stessel et al. (2014:123) showed that patients with the higher body mass index (BMI) had a significantly higher chance of having pain at rest compared to normal weight patients undergoing the same type of surgery. Another possibility for increased pain could be
that these patients have larger volume and weight, thus the amount of intra-operative opioids administered by the anaesthetists is not sufficient.

2.7.1.4 Type of medication

Extensive research has led to the design of medications with recognised efficacy and favourable benefit-to-risk profiles (Brown & Bussel, 2011:304). Fischer et al. (2010:286) analysed adherence to various medications using 195 930 electronic prescriptions and showed that pain medications, compared to any other class of medication, had a noticeably higher initial non-adherence rate. Non-adherence can occur in two ways: (1) under-use, i.e. skipping of doses, and (2) over-use i.e. taking more than what was prescribed (Arria et al., 2011:2).

Stessel et al. (2014:124) performed a randomised controlled trial using multimodal analgesic regimens and showed that adherence was unrelated to the type of pain medication (e.g. opioids or/and NSAIDs) but was related to the patient’s level of perceived pain. The non-compliant patients claimed to not have pain and hence did not take their post-operative pain medication. It must be noted that when patients do not experience any pain, they may become non-adherent to their analgesic regimens. This was true for a prospective Spanish study (N = 233) where the absence of pain accounted for 29.4% non-adherence, side-effects accounted for 15.7% and forgetting to take their treatment accounted for 12.2% of non-adherence to their analgesic regimens (Lanas et al., 2012:712).

2.7.1.5 Complex regimens

Dosing regimens have an impact on medication adherence and studies have revealed higher adherence rates for medication taken once daily in comparison to multiple dosing medications (Jorge et al., 2011:21).

2.7.1.6 Medication information for patients

Enhancing the patient’s knowledge about their medications may increase the patient’s skills in managing it (Conn et al., 2016:280). Tolerability to medication side effects occur and indirectly adherence may be improved, e.g. if the patient is given the knowledge that the medication may make them drowsy and should be taken at night, the patient will be less likely to take it during the day and suffer the unwanted side effect (Conn et al., 2016:280).
2.7.1.7 Physician characteristics

Physician characteristics also played a role in lower initial adherence patterns. Patients were less adherent to medications prescribed by a younger physician, trainee or less informed physician (Fischer et al., 2010:286).

Complex dosing schedules, further complicated by physicians failing to explain adequately, is another barrier in patient adherence (Osterberg & Blaschke, 2005:490).

2.7.1.8 Self-efficacy

The self-efficacy theory of Bandura implies that the degree to which people can control their own motivation can effectively change their behaviour from knowledge to action (Bandura, 1990:9). The outcome being that when a patient has low self-efficacy they do not cope with situations in an effective way even though they have the skillset and know what to do (Polsook et al., 2016:68). In the Alexander technique lessons or acupuncture sessions (ATLAS), study conducted in chronic neck pain patients found that the greater self-efficacy displayed by the participants, the more adherent they were to techniques taught to assist with minimising their pain (Woodman et al., 2018:67).

The National Institute for Health and Care Excellence (NICE) guideline on medicines adherence states that non-adherence is a direct result of healthcare not fulfilling its duty, with either the initial agreement of treatment or the lack of support after treatment has been started. Further to this, non-adherence is not the patient’s responsibility to resolve (NICE, 2009).

2.7.2 Methods to monitor adherence

Adherence is not a single action, but instead a multifaceted series of behavioural support comprising of initiation, implementation and discontinuation (Zullig et al., 2017:1410).

The increase in methods to monitor adherence in recent years signifies the dire need for identifying difficulties to medication-taking and formulating interventions to address these (Pednekar et al., 2018).

There are direct and indirect methods to monitor adherence with direct being more accurate but costly and indirect being less costly but the patient has to take more responsibility in truthfully reporting information (Osterberg & Blaschke, 2005:489).
2.7.2.1 Direct methods for monitoring adherence

Direct methods for monitoring adherence is used in a clinical setting where patients are directly observed consuming medication or measuring adherence through blood level monitoring of medications or metabolites (Pednekar et al., 2018). These monitoring interventions are accurate and objective and little manipulation from the patient can take place. Manipulation could occur when the patient hides the tablet in their mouth to discard at a later stage when directly observing a patient consuming the medication. Blood level monitoring is extremely costly and can result in a false sense of adherence as patients know that they are being monitored and could only take medication before an upcoming test; this is termed as white coat adherence (Osterberg & Blaschke, 2005:489).

2.7.2.2 Indirect methods for monitoring adherence

Indirect methods for monitoring adherence are the most widely used as they are usually more cost-effective than blood level monitoring and easy to perform in an out-patient setting. Unfortunately, these methods are more open to manipulation as patients are inclined to underreport non-adherence to prevent their healthcare providers from being disappointed (Lam & Fresco, 2015).

2.7.2.2.1 Self-report measures

Self-report measures include surveys, questionnaires, interviews and patient diaries (Osterberg & Blaschke, 2005:489).

Self-report measures are believed to be the least reliable method because of the subjectivity element. Nevertheless, their low costs, ease of use and real-time responses have added to the popularity of this method. Further to this, they are extremely valuable in identifying individual patient feedback to subsequently modify future interventions (Lam & Fresco, 2015).

Interviewing patients using questionnaires, scales or surveys provides a standardised measurement to minimise the subjectivity of self-reporting (Osterberg & Blaschke, 2005:489).

The MARS is classified as a popular medication adherence rating scales as it has proven to be comparable to the Morisky adherence scale and has improved questions to better understand barriers with regard to adherence behaviours (Unni & Farris, 2015). Unintentional (e.g. absentmindedness) and intentional (not taking medication due to side-effects) behaviours of medication use are identified (Thompson et al., 2000:245). The MARS has been validated in various settings from acute to chronic care and is a widely accepted self-report measure for adherence to medication (Cohen et al., 2009:329; Mahler et al., 2010:578; Unni & Farris, 2015).
Zongo et al. (2016:61) compared three different self-report adherence tools and concluded that the measurement of normal adherence behaviour followed by an adherence rating scale may be more valuable compared to a self-report pill count done by study participants.

2.7.2.2.2 Pill count and electronic medication monitors

The pill count is an objective measure, which calculates the number of dosage units taken from the initial amount dispensed between two specified dates, e.g. scheduled appointments or visits with the patient. The costs are minimal and the method is easy to perform, however, several drawbacks have been identified (Lam & Fresco, 2015). Surplus medications are not taken into account; the incorrect number of dosage units can be removed and thus this method cannot generate an adherence pattern to identify causes for non-adherence (Lam & Fresco, 2015).

The pill count method has mostly been replaced by electronic dose monitoring systems (Siracusa et al., 2015:622). The Medication Event Monitoring System (MEMS®; AARDEX Ltd. Zug, Switzerland) monitors adherence objectively by tracking the date and time that the bottle was opened, subsequently creating time/frequency plots (Siracusa et al., 2015:622). The Sensemedic medication dispenser (Evalan, Amsterdam, the Netherlands) goes a step further by notifying patients through text message reminders sent to their mobile devices if the bottle is not opened to aid in adherence (van Vlerken et al., 2016:624). The disadvantages are the inability to determine the removal of multiple doses when the bottle is opened and accidental actuation of the container (Waldorp-Valverde et al., 2013:199). These methods are extremely expensive, the container is bulky and thus not a viable option for large population studies (Lam & Fresco, 2015).

Electronic dose monitoring is more successful when it has to do with asthma inhalers, as dose actuation is used to monitor adherence, and multiple doses cannot be taken without it affecting the count (Mäkelä et al., 2013:1483).

2.7.2.2.3 Digitising pills

The Ingestion Event Marker (IEM), Proteus Health, may be the future of adherence monitoring, as the sensor (as big as a grain of sand) can be formulated into any ingestible medication. A disposable patch is worn and it relays information from the sensor such as the time that medication was taken, type of medication as well as physiological responses, e.g. heart rate, activity and temperature; all this information is then displayed on a mobile device which is carried by the patient (Pullen, 2012:1).
2.7.2.2.4 Prescription refill records

Databases can be used to review and quantify prescription-refilling patterns to assess adherence. A centralised computer system; hand in hand with uniformity among prescribers and dispensers, create a collective dataset over a specified period (Lam & Fresco, 2015). This method works well for large population groups to assess adherence to multiple drugs and to identify patients in danger of treatment failure. It does not take into account whether the patients actually consumed the medication in the specified time period (Lam & Fresco, 2015).

Choosing a suitable medication adherence measure should focus on being easy to use, easy to carry out, cost-effective, highly reputable, practical and flexible. Unfortunately, no single measure can satisfy all of the suggested requirements. The advantages and disadvantages of known and accepted methods (summarised from Osterberg & Blaschke, 2005:489) are shown in Table 2-9.

Table 2-9: Methods to measure drug adherence

<table>
<thead>
<tr>
<th>Methods</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Direct</td>
<td>“Directly observed therapy”</td>
<td>Pills can be concealed in patient’s mouths and discarded later; unrealistic in normal practice.</td>
</tr>
<tr>
<td>“Measurement of the level of medicine or metabolite in blood”</td>
<td>Objective</td>
<td>Differences in metabolism between patients. “White coat adherence can give a false impression of adherence.” Excessive costs.</td>
</tr>
<tr>
<td>“Measurement of the biological marker in blood”</td>
<td>Objective, can be utilised to monitor placebo</td>
<td>Necessitates costly quantitative assays and sampling of body fluids.</td>
</tr>
<tr>
<td>Indirect methods</td>
<td>“Patient questionnaires, patient self-reports”</td>
<td>Uncomplicated, economical, the most widely-used and accepted method in clinical setting</td>
</tr>
<tr>
<td>“Pill counts”</td>
<td>Unbiased, easily quantified and user-friendly</td>
<td>Patients can tamper with the tablets</td>
</tr>
<tr>
<td>“Rates of prescription refills”</td>
<td>Unbiased, data obtained easily</td>
<td>Actual ingestion of medication is unknown</td>
</tr>
<tr>
<td>“Assessment of the patient’s clinical response”</td>
<td>Uncomplicated, usually easily performed</td>
<td>Clinical response may be affected by factors other than medication adherence.</td>
</tr>
</tbody>
</table>
**Methods** | **Advantages** | **Disadvantages**
---|---|---
"Electronic medication monitors" | Precise, results easily quantifiable, medication taking patterns are tracked | Costly, requires follow-up visits and downloading data from medication vials
"Measurement of physiological markers (e.g., heart rate of patients taking beta-blockers)" | Frequently easily performed | Absence of markers is a possibility (e.g., poor absorption, increased metabolism)
"Patient diaries" | “Help to correct for poor recall” | Patient manipulation a concern

### 2.8 Chapter summary

Chapter 2 provided an overview of the concept of adherence to post-operative medication after orthopaedic day case surgery. Objectives addressed were the definitions: pain, orthopaedic day case surgery, post-operative pain management and clinical guidelines. Patient adherence and factors that may possibly affect adherence and methods to monitor adherence were also outlined. The literature review’s specific objectives have herewith been reported. In the subsequent chapter, the empirical investigation results will be deliberated.
CHAPTER 3: RESULTS AND DISCUSSION

3.1 Introduction

This chapter contains the general findings and discussion of the empirical investigation with the following objectives:

- To establish the adherence status regarding discharge pain medication after orthopaedic surgery.

- To determine the association between participant’s demographic and behavioural-related variables (age, gender and smoking status), and adherence to post-operative discharge pain medication.

- To determine the association between movement (turning, sitting up, repositioning in bed) and adherence to discharge pain medication after orthopaedic surgery.

- To determine the association between sleep disturbances (falling and staying asleep) and adherence with regard to post-operative discharge pain medication.

- To determine the association between the type and number of side effects experienced from discharge pain medication after orthopaedic surgery and adherence.

- To determine the association between normal adherence patterns and adherence patterns relating to post-operative pain discharge medication.

The results and discussion are represented in the form of a manuscript, entitled “Factors influencing adherence to postoperative pain medication after day case orthopaedic surgery: A prospective, cross-sectional study”. This manuscript was submitted to the “International Journal of Orthopaedic and trauma nursing”. Instructions to the author can be found at: https://www.orthopaedictraumanursing.com/content/authorinfo (also refer to Annexure G). Proof of submission of the manuscript can be found in Annexure H.

The role of each author in the manuscript is represented in Table 3-1.
Table 3-1:  Author’s contributions

<table>
<thead>
<tr>
<th>Author</th>
<th>Role in the study</th>
</tr>
</thead>
</table>
| Mrs V Booysen (Researcher) | Design of the study  
Acquisition of data  
Interpretation of data  
Drafting the manuscript  
Preparing the final version for submission |
| Prof JR Burger (Supervisor) | Conception and design of the study  
Data analysis and supervision of data interpretation  
Guidance on writing of manuscript  
Revising the article critically for important intellectual content |
| Dr JM du Plessis (Co-supervisor) | Guidance on writing of manuscript  
Revising the article critically for important intellectual content |
| Mrs M Cockeran (Statistician) | Data analyses  
Verified interpretation of data |

The following statement provided by the co-authors confirms their roles in the study and authorises the inclusion of the manuscript in the mini-dissertation.

I declare that I have approved the above-mentioned manuscript and that my role in this study, as indicated above, is a representation of my actual contribution, and I hereby give my consent that it may be published as part of the Master of Pharmacy in Advanced Clinical Pharmacy study of Mrs V Booysen.

Prof JR Burger  
Dr JM du Plessis  
Mrs M Cockeran
3.2 Manuscript

Factors influencing adherence to postoperative pain medication after day case orthopaedic surgery: A prospective, cross-sectional study

Abstract

Background and aim

Patients struggle to adhere to prescribed pain medication after surgery because of, inter alia, side effects, sleep disturbances and pain severity. This study aimed to determine the influence of factors affecting adherence, and the extent of adherence to prescribed post-operative pain medication (POPM) following day case orthopaedic surgery at a private South African hospital.

Methods

This prospective, quantitative cross-sectional study involving 120 participants (51 males, 69 females), used a structured questionnaire completed through a telephonic survey, 4 days after surgery. Assessed parameters included the influence of pain involving sleep and mobility, side effects, post-operative adherence behaviour (POAB), normal medicine adherence behaviour (NMAB) and adherence to POPM measured by participant-reported pill count (PRPC).

Results

POPM adherence was 56.7% (n = 68), and significantly associated with severe pain affecting falling sleep (p = .001) and pain causing awakening from sleep (p = .035). POPM adherence was independent from gender (p = .140), age (p = .822), smoking status (p = 1.000), and type and severity of side effects (p > .300). POAB was significantly associated with POPM adherence (p < .001, Cramér’s $V = 0.5$).

Conclusion

The degree to which pain interferes with sleep is an important factor to consider in adherence to POPM.

Key words: adherence; post-operative pain medication; questionnaire; day case orthopaedic surgery; South Africa
INTRODUCTION

Adherence to prescribed post-operative pharmacologic therapy is of vital importance to reach therapeutic goals and enhance patient outcomes (Almazrou, Aljohani, Aljabreen et al., 2016). Patient adherence to prescribed medication is affected by individual factors such as patient attitude, previous medication experiences, specific illnesses, expectation of medication and costs (Remien, Hirky, Johnson et al., 2003; Zeber, Manias, Williams et al., 2013). Additional factors that could affect adherence include smoking, medication side effects, movement disruption, sleep interruption, patient healthcare system perceptions, lack of treatment knowledge and complexity of the regimen (Gordon, Polomano, Pellino et al., 2010; Morisky, Ang, Krousel-Wood et al., 2008).

Successful management of post-operative pain is achieved through a multimodal approach of a combination of several analgesic compounds with differing mechanisms of action. The ultimate objective of effective pain management remains to achieve the state of morbidity improvement, evidenced by reduction in post-surgical stress, both physically and emotionally, and improvement in quality of life to achieve patient comfort (Goldsmith, Curtis, McClooughen, 2016; Gordon, Polomano, Pellino et al., 2010). The reliance on the patient as well as family members of the patient, to ensure monitoring and compliance of pain treatment after surgery adds to the complexity of effective pain management. Post-operatively, more than 80% of patients experience pain levels ranging from moderate to severe (Shang & Gan, 2012).

BACKGROUND

Day case surgeries are defined as an admission and discharge on the same day. The following orthopaedic surgeries can be managed as day case surgeries: arthroscopies, meniscectomies, small joint arthroplasties, ganglion cyst removals, hallux valgus corrections and rotator cuff tendon repairs (Ng & Mercer-Jones, 2014).

Continual improvements in less invasive surgical techniques and integrated post-operative pain management guidelines have made day case surgery an acceptable option (Ng & Mercer-Jones, 2014; Shang & Gan, 2012). Roughly 60% of all elective surgeries in the United States are done as day cases (Shang & Gan, 2012), compared to 75% in the United Kingdom (Ng & Mercer-Jones, 2014).

After orthopaedic surgery, pain is caused by significant muscle and skeletal tissue reconstruction or repair and will be regarded as moderate to severe pain, which should completely resolve within six months (Kishner, 2014, Pasero & McCaffery, 2007; Thienhaus & Cole, 2002). A secondary inflammatory response ensues and neuropathic pain can result if
nerves are affected (Carr, 2009; McDonald, Corbiere, De Lisle et al., 2016). Untreated pain can lead to post-operative complications, e.g. pain can restrict a person from taking deep breaths and coughing, which could lead to pneumonia (McDonald, Corbiere, De Lisle et al., 2016). Patients may also experience decreased mobility, sleep disturbances, anxiety and slower recovery (McDonald, Corbiere, De Lisle et al., 2016). Sufficient pain control post-operatively is therefore a necessity for effective rehabilitation of patients as it permits prompt mobilisation and faster commencement of physiotherapy and healing (Fischer & Simansky, 2005).

Post-operative pain medications lessen the surgical stress experienced, thereby improving pain severity and frequency, physical and emotional functioning and quality of life (Goldsmith, Curtis, McCloughen, 2016; Gordon, Polomano, Pellino et al., 2010). Unimodal (one medication-), bimodal (two medications-) or multimodal (three or more medications) regimens involving several medications with differing mechanisms of action (Shang & Gan, 2012) can be prescribed as post-operative pain treatment. Bimodal regimens are superior to unimodal regimens but less effective when compared to multimodal treatment plans (McDonald, Corbiere, De Lisle et al., 2016). In day case surgeries, pain monitoring and treatment becomes more challenging as it is left to the patients or their family members (Shang & Gan, 2012:855).

The South African Society of Anaesthesiologists (SASA) guidelines for acute pain advocate the use of a treatment algorithm by using pain severity, medications available and patient factors (SASA, 2016). Recommended management of moderate to severe post-operative pain includes: firstly, an appropriate pain rating scale or verbal descriptor scale should be used to determine the severity of pain. Pain should be monitored at 15-minute intervals and adjustment to the analgesic treatment should be done up until the patient is pain free during rest and movement. Patients are discharged only if their pain is under control otherwise the patient's length of stay will be extended. The analgesic regimens for moderate pain and severe pain include: codeine, paracetamol, non-steroidal anti-inflammatory drugs, morphine, tramadol and an oxycodone/naloxone combination (SASA, 2016).

Non-adherence to medication involves the underuse- or overuse of prescribed medication or the addition of non-prescribed medication (Timmerman, Stronks, Groeneweg et al., 2016). Medication non-adherence is influenced by various factors, which can be organised into five interrelating domains namely (1) patient-related factors, (2) socioeconomic factors, (3) therapy-related factors (4) condition-related factors and lastly, (5) healthcare system factors (Emilsson, Berndtsson, Lötvall et al., 2011). The patient's belief in medication is a therapy-related factor that has a major impact on non-adherence of medications (Nicklas, Dunbar & Wild, 2010). It has been found that the majority of non-adherent individuals do not believe that
the positive effects of the medication outweigh the possible negative effects of the medication and thus do not see the need in taking the medication (Unni & Farris, 2011). Patient education initiatives are, therefore, imperative to ensure that patients are equipped with the knowledge of what to expect from their medication after discharge from the hospital (SASA, 2016).

Methods to monitor adherence can either be direct (directly observed therapy or blood level monitoring) or indirect (pill counts, questionnaires, prescription refill rates or electronic medication monitors). Direct methods are more accurate but costly, whereas indirect methods are less costly but the information is reported by the patient, which may be subjective (Osterberg & Blaschke, 2005). A pill count is classified as an indirect measuring tool to monitor adherence. It is an objective standardised measure used globally (Meghani & Bruner, 2013). Self-report measures allow ease of use, real-time feedback and low costs. Furthermore, it provides valuable information in identifying future interventions for improvements (Lam & Fresco, 2015). To minimise the subjectivity of self-reporting, interviews using questionnaires, scales or surveys can be done additionally to provide a more standardised measurement (Osterberg & Blaschke, 2005). The 10-item Medication Adherence Rating Scale (MARS) is a valid and reliable questionnaire used globally as it allows for the quick and easy assessment of medication adherence (Fialko, Garety, Kuipers et al., 2008; Thompson, Kulkarni, Sergejew, 2000; Unni & Farris, 2011).

The Revised American Pain Society Patient Outcome Questionnaire (APS-POQ-R) that was developed to assist health care organisations to explore patient experiences and outcomes, has internal consistency, construct validity and clinical feasibility (Gordon, Polomano, Pellino et al., 2010).

METHODS

Aim

The aim of this study was to establish the influence of various factors on, and extent of adherence to, prescribed post-operative pain medication (POPM) following day case orthopaedic surgery at a private South African hospital. To achieve this purpose, POPM adherence was determined from a pill count performed by the participants (PRPC). The relationship between post-operative adherence behaviour (POAB) and normal medicine adherence behaviour (NMAB) was assessed. Additionally, the study evaluated the relationship between POPM and demographic characteristics (i.e. age, gender, smoking status), side effects experienced and the effect of pain on mobility and sleep interruption. Participants were also given the opportunity to say why they deviated from prescribed medicine regimens.
Study design

The study followed an observational, prospective, cross-sectional design using a structured questionnaire as data-collection tool, completed through a telephonic interview four days after surgery.

Setting

The research was conducted in a 363-bed private hospital in the central suburbs of Johannesburg, South Africa. The hospital runs at approximately 70% occupancy, servicing a racially diverse population as well as foreign patients. The hospital has a surgical bed capacity of 64, and a 12-theatre complex with a dedicated theatre to support orthopaedic surgery. Approximately 140 orthopaedic surgical procedures are conducted per month.

Sample size and recruitment of participants

A possible sample size for the study was determined with an a priori power analysis, which was conducted using the software package G*Power (Faul, Erdfelder, Lang et al., 2007). A sample size of 120 was considered sufficient to detect an effect of 0.25, with a power of 0.8 and an alpha of 0.05 from day case orthopaedic surgeries performed annually at the institution.

Orthopaedic surgeons’ receptionists recruited participants who met the inclusion criteria at the hospital. The receptionists explained the purpose of the study as well as the role of the researcher to the patients. If they were willing to partake their contact information was obtained. Individuals willing to partake were contacted by the researcher and sent written information about the aims of the study. An independent person obtained written consent was received from the participant on the day of surgery. A telephonic survey using the questionnaire as a data collection tool was conducted four days after surgery. Participation was optional; there were no unfavourable consequences for regretting or retracting from partaking. Participants received no incentive for their involvement and each volunteer completed a single telephonic questionnaire of approximately 15 minutes. Consent was reaffirmed at the start of the telephonic interview. Participants were excluded if they could not be reached after two telephonic attempts on day four after surgery, or wanted to withdraw from the study voluntarily. Recruitment continued until the targeted 120 participants were interviewed. The study population, therefore, included 120 participants 18 years of age and older, who underwent day case orthopaedic surgery between 1 June 2016 and 31 June 2017 at the hospital.
A structured questionnaire was used as the data collection tool (Appendix A). The questionnaire consisted of four parts:

1. Demographic information (age, gender) and smoking status of participants.
2. Type of surgery and pain severity experienced by the participants during movement and sleep. Questions on pain severity were adapted from the APS-POQ-R (Gordon, Poloman, Pellino et al., 2010). This aimed to investigate firstly, how much pain was experienced when turning, repositioning and sitting up in bed and secondly, pain during normal movement like sitting, standing and walking. Pain was rated from 0 – 5, where zero is pain free and five is excruciating pain.
3. Prescribed medicine, type of side effects and severity of side effects experienced.
   The information on prescribed medicine was accessed from the discharge prescriptions written by the anaesthetists assisting the orthopaedic surgeons.
   Questions on pain experience were adapted from the APS-POQ-R (Gordon, Poloman, Pellino et al., 2010). This investigated the severity of nausea, drowsiness, gastritis, constipation and dizziness experienced from the prescribed post-operative pain medication. Side effects were rated from 0 – 5, where zero is none experienced and five is unbearable effects.
4. Adherence was assessed from self-reported adherence and the pill count:
   - Self-reported post-operative adherence behaviour (POAB) was established from questions adapted from the MARS (Thompson, Kulkarni, Sergejew, 2000). Questions evaluated whether participants totally stopped or skipped any doses of medication because of side effects experienced. Furthermore, the need for additional pain control from either increasing the prescribed dose or taking a different analgesic was assessed.
   - Self-reported normal medicine adherence behaviour (NMAB) was established from questions adapted from the MARS. Questions evaluated whether participants sometimes forget to take their medication, forget to take their medication along when travelling, stop taking their medication when it makes them feel bad, stop taking their medication when they feel better, e.g. pain medication, and if they feel hassled to follow their treatment plan.
   - Both POAB and NMAB were categorised as high, medium or low adherence. Adherence was scored high if the cumulative score to relevant was zero, medium if it was between one and two, and low if it ranged between three and five.
• PRPC on remaining medication, where adherence was established from initial dispensed quantity, dosage and frequency of prescribed medication – calculating what should be left after four days and what the participant said was the physical remaining quantity of the medication. Medications that were prescribed as "when necessary for pain" were not taken into consideration in the assessment of non-adherence. Non-adherence from the pill count was classified as the following:
  • Taking more doses of prescribed post-operative discharge pain medication.
  • Taking less doses of prescribed post-operative discharge pain medication.
  • Taking none of the doses.
  • Taking different pain medications than what was prescribed and dispensed upon discharge.

Statistical analysis

The SPSS® Version 25 statistic software package was used to statistically analyse the data. Statistical significance was determined at a two-sided level of an alpha of 0.05. Demographic as well as clinical data were presented as means, standard deviation (SD), percentages (%) and frequencies (n).

The independent t-test was used to compare mean values, with Cohen’s effect sizes, or $d$-values, used to measure the size of the difference in mean values. Cohen’s $d$ was interpreted as follows: values range of 0.2 represents a small effect size where 0.5 is a medium effect size and 0.8 is a practically significant effect (Cohen, 1988).

Pearson’s chi-squared/Fisher’s exact test was used to assess association between participant-related factors and adherence status. Cramér’s $V$ was used as a measure of the strength of the associations. Cramér’s $V$ was interpreted as follows: values range of 0.1 represents a small relationship, 0.3 is a medium strength relationship and 0.5 is a practically significant relationship (Kearney, 2017).

RESULTS

Demographic and clinical characteristics of participants

Table 1 shows the demographic and clinical characteristics of the participants who met the inclusion criteria. The majority of participants in the study population were female (57.5%) and non-smokers (80.0%). There was no significant difference in the mean age of males and females ($p = .705$, Cohen’s $d = 0.06$).
The type of orthopaedic day surgery the participants underwent included hand and arm (31.6%), knee (28.3%), foot (18.3%), shoulder (14.2%), injections into the spine (4.2%) and minor procedures on hip and leg (3.3%). Severe pain was reported by 64 (53.3%) participants when repositioning in bed and 46 participants (38.3%) when standing, walking or sitting. Severe pain affected the ability of 34 (28.3%) participants to fall asleep and 49 (40.8%) participants were awoken by severe pain (Table 1).

Most participants (92.5%) received multimodal medication regimens. The active ingredients given in combination for post-operative pain control were paracetamol, non-steroidal anti-inflammatory agents and an opioid (Table 2). Most participants received paracetamol, codeine and meprobamate in combination with celecoxib (38.3%) or diclofenac (17.5%).

The side effects experienced in the four days’ post-surgery were: constipation (59.2%), drowsiness (55.9%), nausea (30.0%), dizziness (26.7%) and gastritis (12.5%) (Table 1). A breakdown of the prevalence of side effects experienced by the study population during the four days following surgery is depicted in Fig. 1. Side effects subsided over the four days after surgery, with more side effects experienced on the first two days after surgery.

Measurement of adherence

Table 3 depicts the self-reported POPM and NMAB adherence, as well as adherence from the PRPC. Based on the questions asked in terms of the adapted MARS questionnaire, 59 (49.2%) participants classified themselves as being highly adherent to their POPM, compared to only 8.3% who indicated a high adherence to NMAB. The majority of the participants (75.8%) rated themselves as being medium adherent to NMAB. The low adherence percentage was similar for the two adherence types tested (POPM = 11.7% vs. NMAB = 15.8%) (Table 3).

Based on the PRPC, 56.7% (n = 68) were adherent to their post-operative discharge pain medication. There was no significant association between NMAB and adherence to POPM (p = .601). Participants’ self-reported adherence to POPM, however, was significantly associated with their pill count ($\chi^2 = 26.268$, p = <.001, Cramér’s V = 0.5). There was no association between the treatment regimen (i.e. unimodal vs. bimodal or multimodal) and adherence to POPM (p = .511).

Table 4 depicts the association between adherence status from PRPC and participant characteristics. Although the proportion of adherent males (64.7%, N = 51) was higher than that for females (50.7%, N = 69), there was no association between PRPC and gender (p = .140). Adherence was also independent of age (p = .822), smoking status (p = .340) and
type of side effects experienced (p > .300). Table 4, however, shows that PRPC was
dependent on sleep disruption (pain affecting falling sleep, p = .001, and awakening from
sleep, p = .035). A further breakdown of the effect of pain (i.e. none, moderate or severe) on
sleep disturbance and adherence status, shows that of the 34 participants who reported
severe pain when trying to fall asleep (Table 4), 24 (70.6%) were not adherent to their post-
operative pain medication. In addition, of the 49 participants who were awoken by pain at
night, 28 (57.1%) were not adherent to their post-operative pain medication (data not shown
in tables). The reasons for non-adherence when severe pain affected sleep are shown in Table
5. Based on Table 5, the majority of participants needed to take additional pain medication to
be able to fall asleep and to prevent being awoken from sleep due to pain. Overall, problems
with sleep were experienced by 59.1% of non-adherent participants compared to 37.0% of
adherent participants. Non-adherent participants furthermore reported lower side effects
compared to adherent participants (Table 4).

DISCUSSION

Non-adherence creates challenges in the management and control of an illness and hence, is
the main reason for suboptimal clinical benefit (Yap, Thirumoorthy & Kwan, 2016).
Additionally, non-adherence causes psychosocial and medical disease difficulties, diminishes
participants’ quality of life and devastates healthcare resources. These direct effects harm the
capability of global healthcare systems in accomplishing population health goals (WHO,
2003). Surgical stress, which occurs after surgery, can be minimised by analgesic medications
and deliver individual comfort by improving pain severity and frequency as well as physical
and emotional functioning (Goldsmith, Curtis & McCloughen, 2016; Gordon, Polomano,
Pelliino et al., 2010). Several factors influence adherence to prescribed medication; *inter alia*,
age, gender, type of illness, side effects from pain medication, interference with sleep,
immortality and smoking (Gordon, Polomano, Pellino et al., 2010; Liang, Yates, Edwards et al.,
2008; Morisky, Ang, Krousel-Woods et al., 2008; Remien, Hirky, Johnson et al., 2003; Zeber,
Manias, Williams et al., 2013). In this context, the main purpose of this research was to
determine whether participants are adherent to post-operative pain control medication
following discharge after day case orthopaedic surgery, as well as to determine if any factors
influenced their adherence.

The results revealed an overall adherence rate of 56.7% to prescribed post-operative
discharge pain medication as discovered from pill count (n = 68), which is comparable to the
stated adherence rates in the Cochrane review of interventions for enhancing medication
adherence. Low adherence to prescribed treatments is common, with expected adherence
rates at around 50% (Haynes, Ackloo, Sahota, et al., 2008; WHO, 2003). Patients undergoing
hip and knee arthroplasties self-reported their own management of pain as being low when severe post-operative pain was experienced 48 hours’ post-surgery (Zhu, Xu, Lei, et al., 2017).

In contrast, Stessel, Theunissen, Marcus, et al. (2017) reported that patients scheduled for elective day surgery (N = 1248) were found to be >78.4% adherent to prescribed analgesic medications four days after surgery. It should be noted, however, that the authors used self-reporting by participants to assess post-operative pain medication use as one of the following; “yes-”, or “yes, I sometimes took the medication as they were prescribed,” or “no, I didn’t take the medications as they were prescribed”. The use of this measure could have resulted in the underestimation of non-adherence in their population.

Self-reported adherence questions based on the MARS was significant for POPM adherence seen from the pill counts. This is in line with other studies showing that it is a valid and reliable self-reporting tool (Fialko, Garety, Kuipers et al., 2008; Unni & Farris, 2011). As there was a strong association between self-reported adherence and the pill count it can be speculated that either method of reported adherence may be useful for future studies.

Although there was no association between side effects and non-adherence based on pill counts, more than half of the participants were affected by drowsiness and constipation during the first two days after surgery. This was probably due to the majority of participants receiving multimodal therapy, containing an opioid. Opioids are known to cause constipation, nausea, somnolence, itching and dizziness (Garimella & Cellini, 2013).

Pain at movement in the first four days after surgery ranged from moderate to severe in more than 80% of participants but no significant association to adherence was found from the pill count. Similar results were observed by Stessel, Theunissen, Fiddelers, et al. (2014), comparing controlled-release oxycodone with naproxen as discharge medication after ambulatory surgery, and a study exploring the incidence of pain 24-hours post-operatively, using the visual analogue scale in South Africa (Murray & Retief, 2016). Our results revealed a dependent relationship between adherence from the pill count and pain interfering with falling asleep (p = .001) as well as where pain awakened participants from sleep (p = .035). This is similar to findings reported by Sjoveian and Leegaard (2017), where the majority of post-surgery orthopaedic patients complained of sleeping problems and pain at night.

To ensure adherence to medication, patients need to believe that the benefit of taking the medications outweigh the concerns of negative effects that may be experienced (Unni & Farris, 2011). In our study, the less adherent participants reported much lower side effects experienced in addition to problems with sleep. This could possibly be due to patients taking sub-therapeutic dosages. Possible interventions could include educating participants on the
need to take medications and preparing them for the possible side effects they may experience and how to manage these negative effects.

This study found that participant-reported pill count adherence was independent of age and gender, although male participants (mean age of 47.26 years) were 64.7% adherent as compared to females (mean age 48.32 years), who were 50.7% adherent. Similar results were reported in a study conducted in China by Zhu, Xu, Lei, et al. (2017). The authors ascribed these differences to women reporting higher pain intensities than men and lower self-management behaviour scores when having to manage post-operative pain after orthopaedic surgery.

Smokers often experience higher levels of pain and suffer more frequently from severe pain — these patients are, therefore, more likely to overuse pain treatment (Broekmans, Dobbels, Milisen et al., 2010; Chiang, Chia, Lin et al., 2016; Reach, Pellan, Crine, et al., 2018; Rogers, LaRowe, Ditre, et al., 2019). In contrast to these studies, results of our study showed that adherence to prescribed post-operative pain medication was independent of smoking status. A possible reason for our findings could be that our sample size was too small to really detect an effect.

**LIMITATIONS**

Response bias may have occurred as the participants were aware that a questionnaire and pill count would be conducted four days after surgery and could have caused them to be more adherent to their prescribed post-operative discharge pain medication. The pill counts were conducted by the participants themselves and given as a numerical quantity telephonically, creating the possibility for them to be dishonest. There was, however, a strong association between self-reported prescribed post-operative adherence and participant-reported pill count, which may indicate that the results of the pill count adherence could be considered truthful. Another limitation is that we did not measure pain levels *per se* but rather how pain impacted movement and sleep.

**CONCLUSION**

To our knowledge, this study could be one of the first to make use of various measurements of adherence, interference of functioning (movement and sleep) from pain, side effects and analgesic regimens to provide baseline data for post-operative orthopaedic pain management in a private hospital in South Africa. Severe pain is experienced by participants at home after discharge and when severe pain affects sleep; non-adherence to post-operative discharge pain medication results, highlighting the need for additional interventions involving patient
education initiatives in keeping with the best evidence to improve adherence to post-operative discharge pain medication.

REFERENCES


Diabetes and Metabolism 44 (6): 500-507


Table 1: Demographic and clinical characteristics of study population (N = 120)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Number of participants, n (%)</strong></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>51 (42.5)</td>
</tr>
<tr>
<td>Mean age (SD) (years)</td>
<td>47.3 (15.6)</td>
</tr>
<tr>
<td>Female</td>
<td>69 (57.5)</td>
</tr>
<tr>
<td>Mean age (SD) (years)</td>
<td>48.3 (14.8)</td>
</tr>
<tr>
<td><strong>Smoking status, n (%)</strong></td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td>24 (20.0)</td>
</tr>
<tr>
<td>Non-smoking</td>
<td>96 (80.0)</td>
</tr>
<tr>
<td><strong>Type of surgery, n (%)</strong></td>
<td></td>
</tr>
<tr>
<td>Hand and arm</td>
<td>38 (31.6)</td>
</tr>
<tr>
<td>Knee</td>
<td>34 (28.3)</td>
</tr>
<tr>
<td>Foot</td>
<td>22 (18.3)</td>
</tr>
<tr>
<td>Shoulder</td>
<td>17 (14.2)</td>
</tr>
<tr>
<td>Spine</td>
<td>5 (4.2)</td>
</tr>
<tr>
<td>Hip and leg</td>
<td>4 (3.3)</td>
</tr>
<tr>
<td><strong>Pain experienced when turning or repositioning in bed, n (%)</strong></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>17 (14.2)</td>
</tr>
<tr>
<td>Moderate</td>
<td>39 (32.5)</td>
</tr>
<tr>
<td>Severe</td>
<td>64 (53.3)</td>
</tr>
<tr>
<td><strong>Pain experienced when standing, walking or sitting n (%)</strong></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>23 (19.2)</td>
</tr>
<tr>
<td>Moderate</td>
<td>51 (42.5)</td>
</tr>
<tr>
<td>Severe</td>
<td>46 (38.3)</td>
</tr>
<tr>
<td><strong>Pain interfered with falling asleep n (%)</strong></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>65 (54.2)</td>
</tr>
<tr>
<td>Category</td>
<td>Count</td>
</tr>
<tr>
<td>----------------------------------------------------</td>
<td>-------</td>
</tr>
<tr>
<td>Moderate</td>
<td>21</td>
</tr>
<tr>
<td>Severe</td>
<td>34</td>
</tr>
<tr>
<td>Pain caused awakening from sleep n (%)</td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>64</td>
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<tr>
<td>Moderate</td>
<td>7</td>
</tr>
<tr>
<td>Severe</td>
<td>49</td>
</tr>
<tr>
<td>Prescribed postoperative pain medication, n (%)</td>
<td></td>
</tr>
<tr>
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<tr>
<td>Multimodal</td>
<td>111</td>
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<tr>
<td>Side effects experienced, n (%)</td>
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<tr>
<td>Nausea</td>
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<tr>
<td>Drowsiness</td>
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<tr>
<td>Gastritis</td>
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<tr>
<td>Constipation</td>
<td>71</td>
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<tr>
<td>Dizziness</td>
<td>32</td>
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### Table 2: Multimodal regimens

<table>
<thead>
<tr>
<th>Active ingredients in combination</th>
<th>Total, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paracetamol, codeine, meprobamate, celecoxib</td>
<td>46 (38.3)</td>
</tr>
<tr>
<td>Paracetamol, codeine, meprobamate, diclofenac</td>
<td>21 (17.5)</td>
</tr>
<tr>
<td>Paracetamol, codeine, meprobamate</td>
<td>15 (12.5)</td>
</tr>
<tr>
<td>Paracetamol, codeine, ibuprofen</td>
<td>8  (6.7)</td>
</tr>
<tr>
<td>Paracetamol, codeine, meprobamate, lornoxicam</td>
<td>7  (5.8)</td>
</tr>
<tr>
<td>Paracetamol, codeine, meprobamate, etoricoxib</td>
<td>4  (3.3)</td>
</tr>
<tr>
<td>Paracetamol, codeine, meprobamate, ibuprofen</td>
<td>3  (2.5)</td>
</tr>
<tr>
<td>Other combinations&lt;sup&gt;a&lt;/sup&gt;</td>
<td>7  (5.8)</td>
</tr>
</tbody>
</table>

<sup>a</sup> 'Other combinations' included the combinations received by only one participant.
<table>
<thead>
<tr>
<th>Measures of adherence</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Self-reported adherence to prescribed postoperative pain medication (POPM)</strong></td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>59 (49.2)</td>
</tr>
<tr>
<td>Medium</td>
<td>47 (39.2)</td>
</tr>
<tr>
<td>Low</td>
<td>14 (11.7)</td>
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<tr>
<td><strong>Self-reported normal adherence behaviour with acute medications (NMAB)</strong></td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>10 (8.3)</td>
</tr>
<tr>
<td>Medium</td>
<td>91 (75.8)</td>
</tr>
<tr>
<td>Low</td>
<td>19 (15.8)</td>
</tr>
<tr>
<td><strong>Self-reported pill count (PRPC)</strong></td>
<td></td>
</tr>
<tr>
<td>Adherent</td>
<td>68 (56.7)</td>
</tr>
<tr>
<td>Non-adherent</td>
<td>52 (43.3)</td>
</tr>
</tbody>
</table>
Table 4: Association between adherence and participant demographic and clinical characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Adherent n (%)</th>
<th>Non-adherent n (%)</th>
<th>Test value</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male (N = 51)</td>
<td>33 (64.7)</td>
<td>18 (35.3)</td>
<td>0.915&lt;sup&gt;a&lt;/sup&gt;</td>
<td>.822</td>
</tr>
<tr>
<td>Female (N = 69)</td>
<td>35 (50.7)</td>
<td>34 (49.3)</td>
<td>2.334&lt;sup&gt;b&lt;/sup&gt;</td>
<td>.140</td>
</tr>
<tr>
<td><strong>Smoking status</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoking (n = 24)</td>
<td>14 (58.3)</td>
<td>10 (41.7)</td>
<td>0.340&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1.000</td>
</tr>
<tr>
<td>Non-smoking (n = 96)</td>
<td>54 (56.3)</td>
<td>42 (43.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Side-effects</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nausea (n = 36)</td>
<td>21 (58.3)</td>
<td>15 (41.7)</td>
<td>0.580&lt;sup&gt;b&lt;/sup&gt;</td>
<td>.809</td>
</tr>
<tr>
<td>Drowsiness (n = 67)</td>
<td>39 (58.2)</td>
<td>28 (41.8)</td>
<td>0.147&lt;sup&gt;b&lt;/sup&gt;</td>
<td>.701</td>
</tr>
<tr>
<td>Gastritis (n = 15)</td>
<td>7 (46.7)</td>
<td>8 (53.3)</td>
<td>0.696&lt;sup&gt;b&lt;/sup&gt;</td>
<td>.403</td>
</tr>
<tr>
<td>Constipation (n = 71)</td>
<td>43 (60.6)</td>
<td>28 (39.4)</td>
<td>1.075&lt;sup&gt;b&lt;/sup&gt;</td>
<td>.300</td>
</tr>
<tr>
<td>Dizziness (N = 32)</td>
<td>18 (56.2)</td>
<td>14 (43.8)</td>
<td>0.003&lt;sup&gt;b&lt;/sup&gt;</td>
<td>.956</td>
</tr>
<tr>
<td><strong>Pain</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain experienced when turning or repositioning in bed (n = 64)</td>
<td>32 (50.0)</td>
<td>32 (50)</td>
<td>2.877&lt;sup&gt;b&lt;/sup&gt;</td>
<td>.237</td>
</tr>
<tr>
<td>Pain experienced when standing, walking or sitting (n = 46)</td>
<td>23 (50.0)</td>
<td>23 (50)</td>
<td>1.350&lt;sup&gt;b&lt;/sup&gt;</td>
<td>.509</td>
</tr>
<tr>
<td>Pain interfered with falling asleep (n = 34)</td>
<td>10 (29.4)</td>
<td>24 (70.6)</td>
<td>14.531&lt;sup&gt;b&lt;/sup&gt;</td>
<td>.001</td>
</tr>
<tr>
<td>Pain caused awakening from sleep (n = 49)</td>
<td>21 (48.8)</td>
<td>28 (51.2)</td>
<td>6.691&lt;sup&gt;b&lt;/sup&gt;</td>
<td>.035</td>
</tr>
</tbody>
</table>

<sup>a</sup> Student t-Test

<sup>b</sup> Pearson's chi square test
<table>
<thead>
<tr>
<th>Reasons for non-adherence, n (%)</th>
<th>Pain interfered with falling asleep (N = 24)</th>
<th>Pain awoken from sleep (N = 28)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adherent to prescribed postoperative pain medication but took additional pain medication</td>
<td>10 (41.7)</td>
<td>11 (39.3)</td>
</tr>
<tr>
<td>Took more doses of prescribed anti-inflammatory and additional pain medication</td>
<td>6 (25.0)</td>
<td>6 (21.4)</td>
</tr>
<tr>
<td>Took less doses of prescribed anti-inflammatory and additional pain medication</td>
<td>2 (8.3)</td>
<td>2 (7.1)</td>
</tr>
<tr>
<td>Did not take any prescribed postoperative medication but took other pain medication</td>
<td>1 (4.2)</td>
<td>1 (3.6)</td>
</tr>
<tr>
<td>Took more doses of prescribed anti-inflammatory</td>
<td>3 (12.5)</td>
<td>5 (17.9)</td>
</tr>
<tr>
<td>Took less doses of prescribed anti-inflammatory</td>
<td>2 (8.3)</td>
<td>2 (7.1)</td>
</tr>
<tr>
<td>Took none of the prescribed anti-inflammatory</td>
<td>-</td>
<td>1 (3.6)</td>
</tr>
</tbody>
</table>
Figure 1: Side effects experienced four days after surgery
THE POST-OPERATIVE PAIN MEDICATION ADHERENCE QUESTIONNAIRE

Thank you for taking this questionnaire!

This questionnaire focuses on adherence and possible matters that may influence adherence. These aspects are imperative to identify gaps and prospects for improvement. Please indicate your answer to the researcher either as yes or no, or as a number. The researcher will ask if clarification or more information is necessary at a specific question. Your opinion is very valuable so please be as honest as possible. Your replies are strictly confidential. The telephonic interview will take approximately 15 minutes to complete.

Your participation is completely voluntary. If a specific question makes you to uncomfortable, you may skip it and ask to proceed to the next question. Alternatively, you may also withdraw from the study without any penalties. The findings of the research will be shared with you if you are interested. You are welcome to contact Mrs V Booysen regarding this matter at Vanessa.booysen@...s.

Thank you for your time. Your participation is greatly appreciated and will greatly benefit to the success of the research project.
THE POST-OPERATIVE PAIN MEDICATION ADHERENCE QUESTIONNAIRE

<table>
<thead>
<tr>
<th>Date of surgery:</th>
<th>d</th>
<th>d</th>
<th>m</th>
<th>m</th>
<th>y</th>
<th>y</th>
<th>y</th>
<th>y</th>
<th>Questionnaire nr.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date of interview:</td>
<td>d</td>
<td>d</td>
<td>m</td>
<td>m</td>
<td>y</td>
<td>y</td>
<td>y</td>
<td>y</td>
<td>Time:</td>
</tr>
<tr>
<td>Is the participant still willing to partake in the study</td>
<td>YES</td>
<td>NO</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

DEMOGRAPHIC INFORMATION:

1. What is your date of birth? ________________
2. Gender:  
   Male  
   Female

3. Do you smoke?  
   Yes  
   No

TYPE OF SURGERY AND PAIN SEVERITY:

4. Type of surgery: ____________________________
5. In the four days after surgery, please choose a number from zero to five that best describes how much pain interfered or prevented you from where zero is pain free and five is excruciating pain:

<table>
<thead>
<tr>
<th></th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain free</td>
<td>Very mild – barely noticeable</td>
<td>Pain is noticeable – can get used to it</td>
<td>Moderate pain – it can be ignored but is distracting</td>
<td>Moderately strong pain interfering with normal daily activities. Difficulty concentrating</td>
<td>Severe pain that is disabling; unable to perform daily living activities</td>
<td></td>
</tr>
</tbody>
</table>

| Doing activities in bed such as turning, sitting up, repositioning | 0 | 1 | 2 | 3 | 4 | 5 |
| Doing activities out of bed like walking, sitting in a chair, standing at the sink | 0 | 1 | 2 | 3 | 4 | 5 |
| Falling asleep | 0 | 1 | 2 | 3 | 4 | 5 |
| Staying asleep | 0 | 1 | 2 | 3 | 4 | 5 |

**PREScribed MEDICINE AND SIDE EFFECTS:**

6. Medication name, strength and directions for use:

<table>
<thead>
<tr>
<th>First Drug</th>
<th>First Dose</th>
<th>QTY Left</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
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</tbody>
</table>
7. Did you experience any of the following side effects? Zero – no side effects experienced and five unbearable side effects experienced on day one to day 4. Please indicate the day and the severity of the side effect:

<table>
<thead>
<tr>
<th></th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>No side effect experienced</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Very mild – barely noticeable</strong></td>
<td></td>
<td></td>
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<td></td>
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</tr>
<tr>
<td><strong>Side effect is noticeable – can get used to it.</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td><strong>Mild side effects – it can be ignored but is distracting</strong></td>
<td></td>
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</tr>
<tr>
<td><strong>Moderate side effect – very distracting and unable to concentrate but will take medicine now and then</strong></td>
<td></td>
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<tr>
<td><strong>Unbearable effects experienced and unable to continue with medicine</strong></td>
<td></td>
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</table>

### Nausea

<table>
<thead>
<tr>
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<th>1</th>
<th>2</th>
<th>3</th>
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</thead>
<tbody>
<tr>
<td>Day 1</td>
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<tr>
<td>Day 2</td>
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<td>Day 3</td>
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<tr>
<td>Day 4</td>
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</tr>
</tbody>
</table>

### Drowsiness

<table>
<thead>
<tr>
<th></th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td></td>
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<tr>
<td>Day 2</td>
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<td>Day 3</td>
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<tr>
<td>Day 4</td>
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</tbody>
</table>

### Burning of the stomach

<table>
<thead>
<tr>
<th></th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
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<tbody>
<tr>
<td>Day 1</td>
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<td>Day 2</td>
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<td>Day 3</td>
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<td>Day 4</td>
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</tr>
<tr>
<td>Constipation</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
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<td>Day 1</td>
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<td>Day 2</td>
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<td>Day 3</td>
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<tr>
<td>Day 4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dizziness</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Day 1</td>
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<td>Day 2</td>
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<tr>
<td>Day 4</td>
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</tr>
</tbody>
</table>

8. Did you experience any other side-effect that you would like to make the researcher aware of? If yes, please specify:

_________________________________________________________________
_________________________________________________________________
_________________________________________________________________
_________________________________________________________________
ADHERENCE MEASURES:

9. Did any of the side effects cause you to completely stop taking your pain relief medication at any stage in the previous four days?

Yes ☐
No ☐

10. Did the side effects result in skipping of a dose of any of your pain relief medication in the previous four days?

Yes ☐
No ☐

11. Was there a time that you experienced that the medication you were given for pain did not help?

Yes ☐
No ☐

12. Was there a time that you felt the need to take different painkillers to relieve your pain?

Yes ☐
No ☐

If so, what was your painkiller/s of choice? ____________________________
13. Was there a time that you felt the need to increase the dose of the prescribed medication for sufficient pain control?

Yes
No

If yes, which drug and how many times?


14. In general, when the doctor usually prescribes medication –

a. Do you sometimes forget to take the medicine?*

Yes
No

b. Have you ever cut back or stopped taking your medication without telling your doctor because it made you feel bad?*

Yes
No

c. When you travel or leave home, do you sometimes forget to bring along your medication?**

Yes
No
d. When you feel that your pain is under control, do you sometimes stop taking your medicine?*

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
</table>

e. Do you ever feel hassled about sticking to your treatment plan?*

<table>
<thead>
<tr>
<th>Yes</th>
<th>1</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>2</td>
</tr>
</tbody>
</table>

15. How many of each tablet/capsule/suppository do you have left?

<table>
<thead>
<tr>
<th>Medication</th>
<th>Number of tablets/capsules/suppository left</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* This question was adapted from the Revised American Pain Society Patient Outcome Questionnaire (APS-FOQ-R) (Gordon, Polomano, Pellino et al., 2010)

* This question was adapted from the Medication Adherence Rating Scale (MARS) (Thompson, Kukarni; Sergejew, 2000)
3.3 Chapter summary

This chapter is presented in the form of a manuscript where the discussion and findings from the empirical investigation took place. The following chapter concludes this dissertation with the final conclusions based on the specific objectives, it describes the limitations and strengths of the study, and suggest recommendations for future research.
CHAPTER 4: CONCLUSIONS, RECOMMENDATIONS AND LIMITATIONS

4.1 Introduction

The dissertation consisted of four chapters. Chapter 1 offered a general overview of the study, reviewing the background, problem statement, the aim of the study as well as specific research objectives and the research methodology used in the study. Chapter 2 focused on pain including post-operative pain and pain management used post-operatively, globally and in South Africa. Adherence, factors affecting adherence and methods to monitor adherence were explored from the literature. Chapter 3 denoted the findings and discussion of the study in manuscript form, submitted to the International journal of Orthopaedic and trauma nursing. The emphasis of this final chapter is to draw conclusions from the specified objectives outlined in Chapter 1. The limitations and strengths of this study will be listed, closing off with a conclusion and recommendations for future studies.

4.2 Conclusions from the literature study

The specific objectives of the literature review were to describe the mechanism of pain in orthopaedic surgery, to understand the role each pain control medication plays in the management of post-operative pain as part of discharge medication plans, and to understand factors influencing participant adherence after orthopaedic surgery. These objectives have been achieved in Chapter 2 of this dissertation. The following paragraphs discuss the conclusions drawn from the findings.

4.2.1 Pain mechanism in orthopaedic surgery

Pain as a result from orthopaedic surgery is classified as acute nociceptive pain, as it involves cutting into tissue and muscles to reconstruct or repair (Kishner, 2014:2; Pasero & McCaffery, 2007:160; Thienhaus & Cole, 2002:28). Neurological pain can result if nerves are affected during this process (Carr, 2009:2). A secondary inflammatory response then occurs, augmenting the patient’s pain level (McDonald et al., 2016:606) (see paragraph 2.3).

The perception of pain is subjective and complex, as it is influenced by previous experiences, gender, cultural beliefs and intellect (Leveille et al., 2005:333). Globally, studies have shown that women show a lower threshold and tolerance to pain, and furthermore, musculoskeletal pain intensifies with increasing age (Leveille et al., 2005:333; Melchior et al., 2016:13). Moderate to severe pain is being experienced by about 80% of patients following surgery,
indicating the need for advancements in pain control (Sinatra, 2002:S18; Tighe et al., 2015:2) (see paragraph 2.5).

4.2.2 Post-operative pain management

Sufficient post-operative pain management is vital as it is an important risk factor for the development of chronic postoperative pain (Stessel et al., 2018:195). Effective post-operative pain management will reduce surgical stress and allow patients to gain individual comfort. Pain severity will be decreased as well as the frequency of pain experienced, thus allowing earlier mobilisation (Goldsmith et al., 2016:64; Gordon et al., 2010:1173).

Multimodal medication regimens for pain control are regarded best practice, as differing mechanisms of action of various medications allows superior results with minimal side effects in the successful management of post-operative pain (Shang & Gan, 2012:862). By combining the various medications, lower doses can be given compared to using any of these items alone; and this results in the side effect burden being decreased (Tharakan & Faber, 2015:181). Adherence to multimodal regimens show enhanced recovery after surgery and henceforth, decreases patient stay and possible post-operative complications (Schug et al., 2015:259) (see paragraph 2.6.3).

Post-operative pain management usually includes the combination of pharmacological therapies, non-pharmacological therapies as well as the additions of various intra-operative medications (Schug et al., 2015:259).

The most common non-pharmacological interventions are provision of information, relaxation training, transcutaneous electric nerve stimulation, acupuncture, heat and cold therapy and lastly, magnetic therapy. However, the one intervention with proven outcomes is the provision of information to the patient about what the orthopaedic procedure will entail and hence what type of pain they could expect afterwards (SASA, 2016:S88) (see paragraph 2.6.1).

Regional anaesthesia entails the numbing of a certain body part, either to perform surgery or to be used as an additive measure for post-operative pain relief (Garimella & Cellini, 2013:191). Analgesic agents are added to the local anaesthetics used for regional anaesthesia to optimise post-operative pain relief (SASA, 2016:S63). Intra-articular administration of local anaesthetics, combined with analgesics during surgery, display a reduction in post-operative pain as well as a reduction in post-operative opioid and analgesic requirements (Schug et al., 2015:90) (see paragraph 2.6.2).
### 4.2.3 Factors influencing adherence and methods to monitor adherence

Medication adherence, described as the extent to which a person takes medication at the right dose and dosage intervals as mutually decided upon with the prescriber (O’ Rourke & O’ Brien, 2017:160). Medication non-adherence poses risks such as suboptimal disease control and increases the burden on healthcare (Goldsmith et al., 2017:51). Adherence to prescribed medication is affected by various personal factors, like patient attitude, previous medication use, specific illness, expectation of medication and costs (Remien et al., 2003:70; Zeber et al., 2013:891). Therefore, it is imperative to be aware of the fact that adherence may not be static in a patient’s lifespan of treatment (Remien et al., 2003:70) (see paragraph 2.7.1).

There are various methods to monitor adherence, which are classified as either direct or indirect. Both categories have their advantages and disadvantages (Osterberg & Blaschke, 2005:489). Indirect methods to monitor adherence to medications, e.g. self-report measures and pill counts, are the most widely used as they are offer ease of use, low costs and real-time feedback but subjectivity should be taken into account (Lam & Fresco, 2015). Direct adherence monitoring methods, e.g. blood level monitoring of drugs/metabolites or directly observing patients, produces more accurate results but is costly (Osterberg & Blaschke, 2005:489) (see paragraph 2.7.2).

### 4.3 Conclusions from the empirical investigation

The specific objectives from the empirical study were to establish the adherence to discharge pain medication after orthopaedic surgery from a pill count. The relationship of adherence to post-operative discharge pain medication and the participant’s demographic factors and smoking status had to be uncovered. Parameters measured were pain severity involving sleep and movement; found from APS-POQ-R type questions asking participants to use a rating scale to express the severity of pain experienced when repositioning in bed, moving around, trying to fall asleep and lastly, pain severity if awoken by pain (paragraph 1.4.1). The type and severity of side effects were similarly measured with a rating scale for each day after surgery. Adherence was assessed using self-report measures from adapted MARS questions to ascertain categories of adherence for prescribed post-operative discharge pain medication and normal prescribed medication behaviour. Lastly, overall adherence was established from a self-reported pill count. These objectives have been achieved in the manuscript.

The study followed a prospective, quantitative cross-sectional design. A structured questionnaire was completed through a telephonic survey 4 days after surgery. The study population was 120 adult participants (mean age of 48 years ± 14.80), with more than half of
these participants being female (57.5%). The treatment regimens mostly involved multimodal regimens (92.5%).

4.3.1 Adherence to post-operative discharge pain medication and association with participant characteristics

Suboptimal clinical benefit results from non-adherence as it creates challenges in the control and management of an illness (Yap et al., 2016:64). Adherence rates to prescribed treatment is said to be around 50% globally and this rate is similarly seen in developing countries (Haynes et al., 2008:2; WHO, 2003). During this study, the researcher conducted the telephonic interview at ~96 hours (four days) post-surgery, possibly resulting in the participants being able to reflect back on the previous days with more accuracy. Self-reporting of pill count by participants may provide inaccurate results, as it was done telephonically. The overall adherence to analgesics prescribed post-operatively was 56.7%, as found from the pill count.

Overall adherence was independent of age ($p = 0.822$), gender ($p = 0.140$) and smoking status ($p = 0.340$). This concludes that non-adherence to post-operative pain medication is fairly low and that participant outcomes can be enhanced through additional interventions to improve adherence out of hospital.

4.3.2 Association between adherence and movement, sleep interruption and side effects experienced

Various factors, including movement disruption, sleep interruption, healthcare system perceptions by the patient, lack of knowledge of treatment, side effects of medication and complexity of regimen affect a patient’s adherence to medication (Gordon et al., 2010:1172; Morisky et al., 2008:4; Thompson et al., 2000:242).

The side effects measured were nausea ($n = 36; 30\%$); drowsiness ($n = 67; 55.9\%$); gastritis ($n = 15; 12.5\%$); constipation ($n = 71; 59.2\%$) and dizziness ($n = 32; 26.7\%$). The factors tested in the study were the severity of pain on disruptions in movement and sleep as well as severity and type of side effects experienced. The impact on immobility was high as more than 80% participants experienced moderate to severe pain at movement when turning, sitting up and repositioning in bed but had no significance to adherence (pain when repositioning in bed ($p = 0.237$); pain when walking, standing, sitting ($p = 0.509$). Severe pain affecting sleep was found as a factor linked to non-adherence, i.e. pain interfering with falling asleep ($p = 0.001$) and pain causing awakening from sleep ($p = 0.035$). Side effects analysed through type and severity showed no association with non-adherence (nausea, $p = 0.809$; drowsiness, $p = 0.701$; gastritis, $p = 0.403$; constipation, $p = 0.300$ and dizziness, $p = 0.956$).
Possible reasons for this could be that participants expect a certain number of side effects from pain medication and as it is possible that some of the participants experienced severe pain, hence warranting surgery, they may have been exposed to these analgesics before (Schug et al., 2015:259). Furthermore, participants should have received counselling from the pharmacist at discharge on what side effects to expect and lastly, all participants received the questionnaire beforehand so they were aware of the side effects as listed on the questionnaire; nausea, drowsiness, gastritis, constipation and dizziness. Drowsiness and constipation would be expected to be the most experienced side effects as codeine forms part of the multimodal regimens.

4.3.3 Association between adherence patterns to post-operative discharge medication and normal adherence patterns

The study set out to discover whether participants’ self-report on how they adhere to medications normally compared to their self-reported adherence to prescribed post-operative medications. From the various questions asked, the participants were categorised as high, medium or low adherent. No association was found between normal adherence behaviour and adherence to prescribed post-operative pain medication \( (p = 0.601) \). What was interesting is that a dependent relationship was found between self-reported adherence to prescribed post-operative medication and actual adherence found from the pill count, meaning that the practical significance might imply that self-reporting by the participants was truthful although self-reporting bias has to be kept in mind \( (p < 0.001, \text{Cramér's } V = 0.5) \).

4.4 Strengths

There are limited studies on adherence and factors affecting adherence in South Africa, and this study adds to the literature. This study contributes to the knowledge about post-operative adherence and what factors may possibly affect this adherence for the South African health sector. Furthermore, it provides information on possible improvement areas for adherence to prescribed post-operative discharge pain medication.

4.5 Limitations of the research

In this study, a telephonic survey was used to obtain information. Telephone surveys have some limits because of the increase in telemarketing (Braunsberger et al., 2007:758). However, in this study, participants willingly and knowingly supplied their details and therefore, expected to be contacted by the researcher. The researcher conducted the survey in a private office thereby ensuring anonymity and if hesitation to any question was noted; the participant was re-assured that their results would be kept strictly confidential. The hesitance in response to
sensitive medication questions had to be taken into account when conducting the telephonic survey (Szolnoki & Hoffman, 2013:59).

Interviewer bias or effect occurs when different answers are received from respondents, depending on which interviewer conducts the survey (Braunsberger et al., 2007:759). According to Szolnoki and Hoffman (2013:59), collection of survey data with the use of telephones has become the dominant mode of data collection all over the world during the past 60 years. Lesser costs, in comparison to face-to-face surveys, add to the benefits of telephone surveys (Szolnoki & Hoffman, 2013:58). A study was conducted where nurses contacted patients telephonically post-operatively at 12, 24 and 72 hours after knee arthroscopies. It was found that patients go through various emotions after surgery, from experiencing euphoria at 12 hours (pain still being under control) to anxiety and distress at 24 hours as the pain seemed unmanageable or 'sudden', and lastly, shifting to reflection and healing at 72 hours (Flanagan, 2009:47).

Self-reported pill counts were used to assess overall adherence to prescribed medication. Pill counts are not the most ideal indicators of adherence as the participants’ answers could be inaccurate and biased (WHO, 2003). Participants could furthermore provide socially desirable answers (Bolman et al., 2011:72). The participants may not actually have taken the pills and could have sold them, shared them, or have destroyed them, making it difficult to know if the participants’ treatment adherence was as high as reported (San Lio et al., 2008:1614). However, it was shown that other information of treatment adherence in conjunction with a pill count eliminates the manifestation of measurement bias of pill counts and supports the opinions that further variables add to the development of good treatment adherence (Bolman et al., 2011:72; San Lio et al., 2008:1615).

Another limitation may be that the sample was obtained in a private facility servicing patients who have medical insurance or patients who are able to pay for their own medical services, and would thus not be a true reflection of a more general population.

4.6 Recommendations

Future research should focus on the following aspects:

This study focused on one hospital in the private healthcare sector in the central suburbs of Johannesburg, Gauteng. It is recommended that future research projects should be implemented in more hospitals in the private as well as the public healthcare sector to reflect a greater population.
It is recommended that research on post-operative discharge pain medication adherence and factors that could possibly influence adherence should be done in the South African context; as very little data is available. Continued effort should be made to further improve post-operative pain management in ambulatory patients (Cai et al., 2017:103; Steinberg et al., 2017:311). Possible recommendations involve educating participants on the dosing of medication so as to ensure proper pain control during sleep and furthermore, adjusting multimodal regimens by the addition of longer-acting pain medications to prevent the awakening from pain experienced.

4.7 Chapter summary

This final chapter concluded the study by discussing the conclusions derived from the specific objectives outlined from the literature review and the empirical investigation. The study limitations and strengths were described and further recommendations for future research were made.


Date of access: 29 Oct. 2018.


with initial medication adherence & persistence special interest group. *Value in health*, 16(1):891-900.


ANNEXURE A: ETHICS APPROVAL CERTIFICATE

ETHICS APPROVAL CERTIFICATE OF PROJECT

Based on approval by Health Research Ethics Committee (HREC), the North West University Institutional Research Ethics Regulatory Committee (NWU-IERC) hereby approves your project as indicated below. This implies that the NWU-IERC grants its permission that, provided the special conditions specified below are met and pending any other authorisation that may be necessary, the project may be initiated, using the ethics number below.

**Project Title:** Adherence to post-operative pain medication following day case orthopaedic surgery at a South African private hospital

**Project Leader:** Dr JR Burger

**Ethics number:** NWU-IERC-2016-033

**Approval date:** 2010-02-17  **Expiry date:** 2017-02-10  **Risk:** Minimal

**Special conditions of the approval (if any):**
- Translation of the informed consent document to the languages applicable to the study participants should be submitted to the HREC (if applicable).
- Any research at governmental or private institutions, permission must still be obtained from relevant authorities and provided to the HREC.
- Ethics approval is required BEFORE approval can be obtained from these authorities.
- Any further information and any report templates is obtainable from Giselle van Zyl at Giselle.Vanzyl@nwu.ac.za.

**General conditions:**
- While the ethics approval is subject to all declarations, undertakings and agreements incorporated and signed in the application form, please note the following:
- The project leader (principal investigator) must report in the prescribed format to the NWU-IERC and HREC:
  - annually (or as otherwise requested) on the progress of the project, and upon completion of the project.
  - without any delay in case of any adverse event (or any matter that impacts sound ethical principles) during the course of the project.
- Any number of projects may be randomly selected for an external audit.
- The approval applies strictly to the protocol as stipulated in the application form. Would any changes to the protocol be deemed necessary during the course of the project, the project leader must apply for approval of these changes at the HREC and NWU-IERC. Would such changes be deemed to be in the protocol submitted without the necessary approval, such changes, the ethics approval is immediately and automatically withdrawn.
- The date of approval indicates the first date that the project may be started. Would the project have to continue after the expiry date, a new application must be made to the NWU-IERC and new approval received before or on the expiry date.
- In the interest of ethical responsibility the NWU-IERC and HREC retains the right to:
  - require access to any information or data at any time during the course of the study or after completion of the project;
  - ask further questions, seek additional information, require further modification or monitor the conduct of your research or the informed consent process;
  - withdraw or postpone approval if any unethical principles or practices of the project are revealed or suspected.
- It becomes apparent that any relevant information was withheld from the NWU-IERC or that information has been false or misrepresented.
- The IEREC would like to remain at your service as scientific and researcher, and wishes you well with your project. Please do not hesitate to contact the IEREC for any further enquiries or questions for assistance.

Yours sincerely,

Prof LA Du Plessis

Prof Linda du Plessis
Chair NWU Institutional Research Ethics Regulatory Committee (IERC)
ANNEXURE B: PERMISSION LETTERS

RESEARCH OPERATIONS COMMITTEE FINAL APPROVAL OF RESEARCH
Approval number: UNIV-2016-0011

Ms V Booyse
E-mail: vanessa.booyse@...

Dear Ms Booyse

RE: ADHERENCE TO POST-OPERATIVE PAIN MEDICATION FOLLOWING DAY-CASE ORTHOPAEDIC SURGERY AT A SOUTH AFRICAN PRIVATE HOSPITAL

The above-mentioned research was reviewed by the Research Operations Committee’s delegated members and it is with pleasure that we inform you that your application to conduct this research at [REDACTED] has been approved, subject to the following:

i) Research may now commence with this FINAL APPROVAL from the [REDACTED] Research Operations Committee.

ii) All information regarding [REDACTED] will be treated as legally privileged and confidential.

iii) [REDACTED] name will not be mentioned without written consent from the Netcare Research Operations Committee.

iv) All legal requirements regarding patient / participant’s rights and confidentiality will be complied with.

v) The research will be conducted in compliance with the GUIDELINES FOR GOOD PRACTICE IN THE CONDUCT OF CLINICAL TRIALS IN HUMAN PARTICIPANTS IN SOUTH AFRICA (2006)

vi) [REDACTED] must be furnished with a STATUS REPORT on the progress of the study at least annually on 30th September irrespective of the date of approval from the [REDACTED] Research Operations Committee as well as a FINAL REPORT with reference to intention to publish and probable journals for publication, on completion of the study.
A copy of the research report will be provided to the Research Operations Committee once it is finally approved by the relevant primary party or tertiary institution, or once complete or if discontinued for any reason whatsoever prior to the expected completion date.

[Redacted] has the right to implement any recommendations from the research.

[Redacted] reserves the right to withdraw the approval for research at any time during the process, should the research prove to be detrimental to the subjects or should the researcher not comply with the conditions of approval.

APPROVAL IS VALID FOR A PERIOD OF 36 MONTHS FROM DATE OF THIS LETTER OR COMPLETION OR DISCONTINUATION OF THE TRIAL, WHICHEVER IS THE FIRST.

We wish you success in your research.

Your

[Sign]

[Redacted]

Full member of Research Operations Committee & Medical Practitioner evaluating research applications as per Management and Governance Policy.

[Redacted]

Date: 7/3/2016

[Redacted]

Research Operations Committee

[Redacted] Ltd

Date: 9/3/2016
To whom it may concern:

I hereby give Vanessa Bocuaseri permission to conduct her research on 'ADHERENCE TO POST-OPERATIVE PAIN MEDICATION FOLLOWING DAY CASE ORTHOPAEDIC SURGERY AT A SOUTH-AFRICAN PRIVATE HOSPITAL' at my private practice with the assistance of my staff for recruitment.

Name

Signature
To whom it may concern:

I hereby give Vanessa Booyser permission to conduct her research on
'ADHERENCE TO POST-OPERATIVE PAIN MEDICATION FOLLOWING DAY
CASE ORTHOPAEDIC SURGERY AT A SOUTH-AFRICAN PRIVATE HOSPITAL'
at my private practice with the assistance of my staff for recruitment.

Signature
To whom it may concern:

I hereby give Vanessa Booyseri permission to conduct her research on ‘ADHERENCE TO POST-OPERATIVE PAIN MEDICATION FOLLOWING DAY CASE ORTHOPAEDIC SURGERY AT A SOUTH-AFRICAN PRIVATE HOSPITAL’ at my private practice with the assistance of my staff for recruitment.

[Signature]

Name

[Signature]
To whom it may concern:

I hereby give Vanessa Bocysen permission to conduct her research on 'ADHERENCE TO POST-OPERATIVE PAIN MEDICATION FOLLOWING DAY CASE ORTHOPAEDIC SURGERY AT A SOUTH-AFRICAN PRIVATE HOSPITAL' at my private practice with the assistance of my staff for recruitment.

[Signature]

[Name]
To whom it may concern:

I hereby give Vanessa Booyseri permission to conduct her research on ‘ADHERENCE TO POST-OPERATIVE PAIN MEDICATION FOLLOWING DAY CASE ORTHOPAEDIC SURGERY AT A SOUTH-AFRICAN PRIVATE HOSPITAL’ at my private practice with the assistance of my staff for recruitment.

[Signatures]

Name

Signature
To whom it may concern:

I hereby give Vanessa Booyseri permission to conduct her research on 'ADHERENCE TO POST-OPERATIVE PAIN MEDICATION FOLLOWING DAY CASE ORTHOPAEDIC SURGERY AT A SOUTH-AFRICAN PRIVATE HOSPITAL' at my private practice with the assistance of my staff for recruitment.

[Signature]

[Name]
To whom it may concern:

I hereby give Vanessa Boysen permission to conduct her research on
‘ADHERENCE TO POST-OPERATIVE PAIN MEDICATION FOLLOWING DAY
CASE ORTHOPAEDIC SURGERY AT A SOUTH-AFRICAN PRIVATE HOSPITAL’
at my private practice with the assistance of my staff for recruitment.

[Signature]

Name
Dear patient

You are being asked to participate in a study as you are over 18 years of age and will be undergoing day case orthopaedic surgery.

You will have the opportunity to share your opinions and medication experiences after discharge. This will improve our understanding of pain medication prescribed after surgery.

If you are interested please complete your full name, contact telephone number and email/fax address.

Full name: ........................................
Contact number: ....................................
Suitable time to be contacted: ....................
Email address: .................................. or Fax number........................................

Medication:

__________________________________ First dose: ________________________

__________________________________ First dose: ________________________

__________________________________ First dose: ________________________
First dose: ________________

Thank you and we are looking forward to including your valuable opinions in our research.

Regards

Vanessa Booysen

Researcher

011 [redacted]

Vanessa.booysen@[redacted]
PARTICIPANT INFORMATION LEAFLET AND CONSENT FORM

TITLE OF THE RESEARCH PROJECT:
Adherence to post-operative pain medication following day case orthopaedic surgery at a South African private hospital

REFERENCE NUMBER: ............
PRINCIPAL INVESTIGATOR: 
V. Booyse
ADDRESS:

CONTACT NUMBER:
011-

You are being invited to take part in a very important research project. Please take some time to read the information presented here, which will explain the details of this project.
this research entails and how you could be involved. Also, your participation is entirely voluntary and you are free to decline further participation. If you say no, this will not affect you negatively in any way whatsoever. You are also free to withdraw from the study at any point prior to submitting the questionnaire, even if you do agree to take part.

This study has been approved by the Health Research Ethics Committees, Faculty of Health Sciences, North-West University and will be conducted according to the ethical guidelines and principles of the International Declaration of Helsinki, South African Guidelines for Good Clinical Practice and the Medical Research Council (MRC) Ethical Guidelines for Research. It might be necessary for the research ethics committee members to inspect the research records.

Which criteria must I meet to participate in this study?
• You must be 18 years old or older
• You must be undergoing orthopaedic surgery and receiving pain medication after discharge from the specified private hospital in Johannesburg.

What is this research study all about?
• This study will be conducted at [hospital name] and will require you to complete a telephone survey four days after surgery. The interview will be performed by the researcher.
• The objectives of this research are to investigate adherence to pain control medication after discharge from the hospital after orthopaedic surgery.
• Adherence to pain control medication after surgery and discharge from the hospital is essential to minimise stress and consequently assist with the healing process.

Why have you been invited to participate?
• You are being asked to participate in this study because you are older than 18 and have undergone orthopaedic surgery.

What will your responsibilities be?
• If you agree to partake in this study you will be interviewed by the researcher in a telephone survey four days after surgery performed by the researcher, during which time you will be expected to share your opinions and experiences. The survey should take approximately 15 minutes.
• You will have to supply two contact numbers and a suitable time for the researcher to contact you on the fourth day after discharge from the hospital, to complete the survey.
• You may withdraw from the study after starting the telephone survey and at any stage during the telephone call.

What are the researchers’ responsibilities?
• The researcher is responsible for ensuring the research is conducted in accordance to the research protocol, that your data remains anonymous and confidential, and finally to give you feedback on the results of the study should you ask for it.
Will you benefit from taking part in this research?
• The direct benefits for you as a participant will be the opportunity to share your opinions and experiences. This will improve our understanding of pain medication prescribed after surgery. Thus the community will benefit from this study through the implementation of recommendations to doctors on various pain control therapies.

Are there risks involved in your taking part in this research?
• The risk to you as a participant is minimal in this study. No patient related information will be given to the doctors and only a summary of the main findings will be shared with them. Answering the questions over the phone may cause you some emotional distress, however, you may rest assured that your answers are completely confidential. No personal information will be asked and only the researcher will see your answers. Only anonymous results will be made available. Furthermore, should you be uncomfortable with answering any question, you may choose to skip it.

Who will have access to the data?
• The only people who will have access to the information you share will be the study leaders, a biostatistician and myself. Consequently, the doctors will not have access to individual participants' responses. All raw data is the property of NWU. The doctors will only receive a summary of the main findings.
• No individual participants can be identified from the data he/she supplied. The signed consent forms will be kept in a sealed box, separate from the box for the completed questionnaires. As a result, participation is completely anonymous and no participant can be identified in any publication of the results.
• All data will be handled with strict confidentiality. During the study, all hard copies of the questionnaires will be kept in locked cupboards in the researcher's office and all electronic data will be stored on the password protected computer of the researcher in a locked office. On completion of this study, all locally held files by the researcher would be deleted from personal computers. All hard copies of the data will be stored for five years in locked cupboards and all electronic data will be kept on a backup system in a locked cabinet in the office of the principal investigator at the NWU.

Who may inspect the research records?
• The Research Ethics Committee may inspect the research records.

Who are the members of the research team and what are their qualifications?
• Project leader: Dr. J.R. Burger (BPharm, MPharm, and PhD)
• Researcher/ Post-graduate student: Mrs. V Booyzen (BPharm) (BSc Hons. Pharmacology)
• Co-supervisor: Dr. J.M. du Plessis (MPharm and MBChB)
• Co-supervisor: Mrs. C.S. Mostert (BPharm)

What will happen in the unlikely event of some form of discomfort occurring as a direct result of your taking part in this research study?
• If a specific question makes you to uncomfortable, you may skip it and ask to proceed to the next question. Alternatively you may also withdraw from the study without any penalties.
Will you be paid to take part in this study and are there any costs involved?
• No, you will not be paid to participate in this study and there will be no cost to you as a result of participation in this study.

Is there anything else that you should know or do?
• If you encounter any problems or have any questions regarding your consent or the survey, you are welcome to contact the project leader, Dr. J.R. Burger at Johanita.burger@nwu.ac.za or 018 299 2254.
• You are also welcome to contact the Health Research Ethics Committee of the Faculty of Health Sciences via Ms Carolien van Zyl at +27 18 299 2094 or Carolien.VanZyl@nwu.ac.za if you have any concerns or complaints that have not been adequately addressed by the researcher.
• You will receive a copy of this information and consent form for your own records.
• The findings of the research will be shared with you if you are interested. You are welcome to contact Mrs V. Booyse regarding this matter at Vanessa.booyse@nwu.ac.za or 011 204 3255.
Declaration by participant

By signing below, I agree to take part in a research study entitled: Adherence to post-operative pain medication following day case orthopaedic surgery at a South African private hospital

I declare that:

- I have read this information and consent form and it is written in a language with which I am fluent and comfortable.
- I have had a chance to ask questions and all my questions have been adequately answered.
- I understand that taking part in this study is voluntary and I have not been pressurised to take part.
- I may choose to leave the study at any time before submitting the questionnaire and will not be penalised or prejudiced in any way.

Signed at (place) ______________________________ on (date) ______________________________ 2017.

----------------------------------------------------------
SIGNATURE OF PARTICIPANT                      SIGNATURE OF WITNESS

Please supply two contact numbers and a suitable time for the researcher to contact you on the fourth day after discharge from the hospital:

Contact number 1

Contact number 2

Suitable time: ______________

Date of surgery: ______________
Declaration by person obtaining consent

I, (name).................................................., declare that:

- I explained the information in this document to (name)..................................................
- I encouraged him/her to ask questions and took adequate time to answer them.
- I am satisfied that he/she adequately understands all aspects of the research, as discussed above
- I did/did not use an interpreter.

Signed at (place) .................................................. on (date) ........................................2017.

................................................................. .................................................................
SIGNATURE OF PERSON OBTAINING CONSENT SIGNATURE OF WITNESS

Declaration by researcher

I, V Booyse, declare that:

- I explained the information in this document to (name)..................................................
- I encouraged him/her to ask questions and took adequate time to answer them
- I am satisfied that he/she adequately understands all aspects of the research, as discussed above
- I did not use an interpreter

Signed at (place) .................................................. on (date) ........................................2017.

................................................................. .................................................................
SIGNATURE OF RESEARCHER SIGNATURE OF WITNESS
ANNEXURE E: QUESTIONNAIRE

THE POST-OPERATIVE PAIN MEDICATION ADHERENCE QUESTIONNAIRE

Thank you for taking this questionnaire!

This questionnaire focuses on adherence and possible matters that may influence adherence. These aspects are imperative to identify gaps and prospects for improvement. Please indicate your answer to the researcher either as yes or no, or as a number. The researcher will ask if clarification or more information is necessary at a specific question. Your opinion is very valuable so please be as honest as possible. Your replies are strictly confidential. The telephonic interview will take approximately 15 minutes to complete.

Your participation is completely voluntary. If a specific question makes you to uncomfortable, you may skip it and ask to proceed to the next question. Alternatively, you may also withdraw from the study without any penalties. The findings of the research will be shared with you if you are interested. You are welcome to contact Mrs V Booysen regarding this matter at Vanessa.booysen@... [REDACTED]

Thank you for your time. Your participation is greatly appreciated and will greatly benefit to the success of the research project.
THE POST-OPERATIVE PAIN MEDICATION ADHERENCE QUESTIONNAIRE

<table>
<thead>
<tr>
<th>Date of surgery:</th>
<th>d</th>
<th>d</th>
<th>m</th>
<th>m</th>
<th>y</th>
<th>y</th>
<th>y</th>
<th>y</th>
<th>y</th>
<th>y</th>
<th>Questionnaire nr.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date of interview:</td>
<td>d</td>
<td>d</td>
<td>m</td>
<td>m</td>
<td>y</td>
<td>y</td>
<td>y</td>
<td>y</td>
<td>y</td>
<td>y</td>
<td>Time:</td>
</tr>
</tbody>
</table>

Is the participant still willing to partake in the study | YES | NO |

DEMOGRAPHIC INFORMATION:

1. What is your date of birth? ________________
2. Gender:
   - Male
   - Female

3. Do you smoke?
   - Yes
   - No

TYPE OF SURGERY AND PAIN SEVERITY:

4. Type of surgery: ____________________________
5. In the four days after surgery, please choose a number from zero to five that best describes how much pain interfered or prevented you from where zero is pain free and five is excruciating pain:

<table>
<thead>
<tr>
<th></th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain free</td>
<td>Pain free</td>
<td>Very mild – barely noticeable</td>
<td>Pain is noticeable – can get used to it</td>
<td>Moderate pain – it can be ignored but is distracting</td>
<td>Moderately strong pain interfering with normal daily activities. Difficulty concentrating</td>
<td>Severe pain that is disabling; unable to perform daily living activities</td>
</tr>
</tbody>
</table>

| Doing activities in bed such as turning, sitting up, repositioning | 0 | 1 | 2 | 3 | 4 | 5 |
| Doing activities out of bed like walking, sitting in a chair, standing at the sink | 0 | 1 | 2 | 3 | 4 | 5 |
| Falling asleep | 0 | 1 | 2 | 3 | 4 | 5 |
| Staying asleep | 0 | 1 | 2 | 3 | 4 | 5 |

**PREScribed Medicine AND Side Effects:**

6. Medication name, strength and directions for use:

```
_________________________________________ FIRST DOSE: _________ QTY LEFT: _______
_________________________________________ FIRST DOSE: _________ QTY LEFT: _______
_________________________________________ FIRST DOSE: _________ QTY LEFT: _______
_________________________________________ FIRST DOSE: _________ QTY LEFT: _______
```


7. Did you experience any of the following side effects? Zero – no side effects experienced and five unbearable side effects experienced on day one to day 4. Please indicate the day and the severity of the side effect:

<table>
<thead>
<tr>
<th></th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>No side effect experienced</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Very mild – barely noticeable</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Side effect is noticeable – can get used to it.</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Mild side effects – it can be ignored but is distracting</strong></td>
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<td><strong>Moderate side effect – very distracting and unable to concentrate but will take medicine now and then</strong></td>
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<td><strong>Unbearable effects experienced and unable to continue with medicine</strong></td>
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8. Did you experience any other side-effect that you would like to make the researcher aware of? If yes, please specify:

   ______________________________________
   ______________________________________
   ______________________________________
   ______________________________________
ADHERENCE MEASURES:

9. Did any of the side effects cause you to completely stop taking your pain relief medication at any stage in the previous four days?

Yes    No

10. Did the side effects result in skipping of a dose of any of your pain relief medication in the previous four days?

Yes    No

11. Was there a time that you experienced that the medication you were given for pain did not help?

Yes    No

12. Was there a time that you felt the need to take different painkillers to relieve your pain?

Yes    No

If so, what was your painkiller/s of choice? ____________________________
13. Was there a time that you felt the need to increase the dose of the prescribed medication for sufficient pain control?

Yes
No

If yes, which drug and how many times?

______________________________

______________________________

14. In general, when the doctor usually prescribes medication –

a. Do you sometimes forget to take the medicine?*

Yes
No

b. Have you ever cut back or stopped taking your medication without telling your doctor because it made you feel bad?*

Yes
No

c. When you travel or leave home, do you sometimes forget to bring along your medication?*

Yes
d. When you feel that your pain is under control, do you sometimes stop taking your medicine?*

<table>
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<th>Yes</th>
<th>No</th>
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e. Do you ever feel hassled about sticking to your treatment plan?*

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<th>Yes</th>
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<td>No</td>
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15. How many of each tablet/capsule/suppository do you have left?

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<tr>
<th>Medication</th>
<th>Number of tablets/capsules/suppository left</th>
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* This question was adapted from the Revised American Pain Society Patient Outcome Questionnaire (APS-POQ-R) (Gordon, Fotomano, Pellino et al., 2010)

* This question was adapted from the Medication Adherence Rating Scale (MARS) (Thompson, Kukarmi; Sergejew, 2000)
Any questions?

Would you like to receive feedback?
Email:
Please follow these easy steps to assist in completing the booklet. It will benefit you to have a completed booklet when the researcher phones on the fourth day after your surgery.

1. Please indicate the date and time that you started taking your medicine.
2. There are small blocks to the left of the time of day. Please mark the box with an 'X' to indicate when you took the medicine specified.
3. At the time of the interview you will be asked to count the remainder of your medicine hence a space for 'pill count'.
4. Please complete the extra 'NOTE' section should you take more or less of the prescribed medicine than indicated by the Doctor or indicate if you substituted with a different pain killer.

If you have any queries or questions regarding the completion of this data booklet, please contact Vanessa Booyzen at 011 [masked] or Vanessa.booysen@[masked]

1st dose taken – date and time: ______________________
1st dose taken – date and time: ______________________
1st dose taken – date and time: ______________________
1st dose taken – date and time: ______________________
## DATA BOOKLET

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