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# The prescribing trends of opioid medications in geriatric patients at the Helen Joseph hospital pain management unit

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# The prescribing trends of opioid medications in geriatric patients at the Helen Joseph hospital pain management unit

By

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A research report submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, in partial fulfilment of the requirements for the degree of Master of Science in Medicine (Pharmaceutical Affairs)

Johannesburg, 2021

## DECLARATION

I, Idi Chiedza Nhiwatiwa, declare that this Research Report is my own, unaided work. It is being submitted for the Degree of MSc. Medicine Pharmaceutical Affairs at the University of the Witwatersrand, Johannesburg.

It has not been submitted before for any degree or examination at any other University.



_____

(Signature of candidate)

14th day

of August 20 22 in South Africa

## DEDICATION

To my family, thank you for reminding me of the power of an education.

# ABSTRACT

## Background

The success of pain management with opioids in geriatric patients (65 years old and older) is dependent on the mindful prescribing of opioids both prior to and during pain management by following evidenced based guidelines and acknowledging age related changes within the body. This population is vulnerable and have an increased likelihood of harm, and this includes potential, unintentional harm from prescribed medication.

## Aim

To analyse the prescribing trends of opioids and common non-opioid analgesics in the geriatric patients at Helen Joseph Pain Management Unit (HJPMU) in Johannesburg, South Africa.

## Objectives

To retrospectively review and collect data from prescriptions and patient-related information from the HJPMU geriatric patient files.

To determine if current evidence-based pain management guidelines are being followed.

To determine the probability of having opioids prescribed as a geriatric patient at HJPMU.

To analyse and present both quantitative and qualitative data respectively on the prescribing of opioids and non-opioids analgesics as well as to review the presence of co-morbidities in the patients attending HJPMU.

## Methodology

A retrospective study design was conducted to review the patient files of patients attending the HJPMU within the period of September 2020 and March 2021 within the geriatric population (> 65 years). Patient files were excluded from the review if they did not fall within the required inclusion criteria. The Regression analysis, Bivariate analysis and the 95% Confidence Interval were utilized during the study.

## Results

The median age of the patients was 70 years old with most of the patients being females (78.04%) and having at least one co-morbidity present (86.49%) which was primarily hypertension 58.78% (n=174). Most patients (45.61%) were diagnosed with both neuropathic and nociceptive pain and were prescribed opioids (76.35%). The most common opioid and non-opioid prescribed was tramadol (76.66%) and paracetamol (80.84%). There were 256 (86.49%) patients that presented with at least one underlying condition. Hypertension was the most common co-morbidity noted 58.78% (n=174) followed by joint and bone diseases 31.42% (n=93). Despite the link between neuropathic pain and diabetes, only 16.89% of the patients had diabetes as a co-morbidity. There was a significant proportion of patients with lung disease e.g., asthma or chronic obstructive pulmonary disease (15.2%) and heart disease (14.19%). The proportion of patients who presented with two comorbidities were 29.39%. While up to 21.96% of patients presented with three or more comorbidities. There is a higher probability of opioids being prescribed in males (24.78%) than the probability of being prescribed non-opioid medication (13.11%), while females presented with a higher probability of being prescribed non-opioids (86.89%) than being prescribed opioids (75.22%).

## Conclusion

This research demonstrated the prescribing trends noted of opioids and common non-opioid analgesics in the geriatric patients at HJPMU. Further studies are needed to establish the prescribing trends with the inclusion of nonsteroidal anti-inflammatory drug (NSAIDs) as non-opioids.

## ACKNOWLEDGEMENTS

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## DEFINITIONS OF TERMS

**Nociceptive pain**: Form of pain that rises from susceptible or actual damage to the non-neural tissue of the body (IASP Press,1994).

**Neuropathic pain**: Pain related to a disease or lesion of the somatosensory nervous system (IASP Press,1994).

**Chronic pain**: A pain being present for 6 months or more (Sternbach,1978)

**Analgesia**: Medication causing the absence of pain in response to that medication (IASP Press,1994).

**Geriatric population**: Population of people 65 years old and older

**Outpatients**: Patients receiving treatment from the hospital but are not hospitalized or inpatients.

**Tender**: A Pharmaceutical tender is established once a pharmaceutical company wins the bid to furnish the department of health with pharmaceutical supplies based off the Essential Medicines List (Health.gov, 2020).

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## ABBREVIATIONS

| | |
|---|---|
| HJHPMU | Helen Joseph Hospital Pain Management Unit |
| WHO | World Health Organisation |
| EML | Essential Medicines List |
| WHREC | Witwatersrand's Human and Research Ethics Committee |
| IASP | International Association for the study of pain |
| BGS | British Geriatric Society |
| AGS | American Geriatrics Society |
| EAPC | European Association of Palliative Care |
| APS | Australian Pain Society |
| DOH | Department of Health |
| SSRI | Selective serotonin reuptake inhibitor |
| SAAPG | South African Acute Pain Guidelines |
| SASA | South African Society of Anesthesiologists |
| EFNS | European Federation of Neurological Societies |
| NSAIDs | Nonsteroidal anti-inflammatory drug |
| STG | Standard Treatment Guidelines |
| TSDs | Total standardized doses |
| COT | Chronic Opioid Therapy |
| ORT | Opioid Risk Tool |
| SR | Sustained release |
| IR | Immediate release |
| CR | Controlled release |

# Chapter 1: Overview of study

## 1.1 Introduction

This chapter will provide the overview of the study such as the background of the study, the aim, objectives, methodology used in the study, ethics considerations, definitions, setting, and validity of the study.

## 1.2 Background

It is an established fact that with advancing age, the rate and occurrence of certain pain syndromes increases over time (Kaye et al.,2010). Geriatric chronic pain can be defined as an unpleasant emotional and sensory experience. The age group 65-79 is considered as pre-geriatric, while > 80 years is considered as geriatric. Chronic pain is a perception of actual or potential tissue damage for three months or longer. (Lynch, 1999). The pain is often accompanied by symptoms of suffering, demoralisation, anxiety or depression and functional impairment, with a substantial form of suffering and economic impact (Ras, 2020).

Population statistics in South Africa for the year 2020 show that 5.43 million people of the of the 59.62 million people are aged 60 years and older. (Statistics SA, 2020). Gauteng has the highest recorded percentage of geriatric population in the country with over 1.31 million of the geriatric population residing in the Gauteng province. The geriatric population is a vulnerable population that experiences the expected age-related changes in the body. The geriatric population has age-related physiological changes which impact on the pharmacodynamics and pharmacokinetics within the body. These age-related factors need to be considered by medical professionals when opioids are being prescribed (Van Heerden et al., 2016).

It has been noted that there is a shift in the age distribution around the world with people above of the age of 80, almost tripling in size while the population of 65 years and older

steadily being increased from 17.5% to 36.3 % (Liossi, 2006). The shift in this vulnerable population intensifies the need in ensuring that the prescribing of opioids and overall patient care follow the regulated guidelines to maximise on patient care (Liossi, 2006). The geriatric population is vulnerable to many medical conditions including adverse effects of prescription medications. This is due to the expected age-related decline in cytochrome P-450 function. The cytochrome P-450 decline along with the high possibility of polypharmacy further increase the likelihood of medication-related harm (Kaye et al., 2010).

External factors affect the overall patient care experienced by geriatric patients. Factors include social support, funding, polypharmacy, and hospital staff and medication availability (Liossi, 2006). As a government or state-run hospital, Helen Joseph hospital has an allocated pain management unit called the Helen Joseph Pain Management Unit (HJPMU) which solely focuses on both Chronic and Acute pain management. The HJPMU also caters to patients obtaining Chemotherapy and require pain management. As a state hospital, all medications that are made available are medications based on the allocated approved tenders as well as the approved medications present on the current Essential Medicines List (EML).

For this reason, pain management in the geriatric population needs to be effected on evidence-based guidelines. However, factors such as the age-related body changes, dependence and polypharmacy are additional factors that can influence the treatment and overall wellbeing of the most vulnerable yet largest population percentage in South Africa. For medical practitioners to ensure that they provide the best care possible to their geriatric patients, evidence-based guidelines are encouraged to be utilized.

The South African Acute Pain Guidelines (SAAPG) are guidelines which were developed following the World Federation of Societies of Anaesthesiologists (WFSA) and International Association for the study of pain (IASP) guidelines. These guidelines identified the need for improvement in the management of pain in developing countries, including South Africa (SASA, 2015).

The SAAPG guidelines provide guidance on the overall management of both chronic and acute pain and this includes pain management in the geriatric population. The guidelines

provide guidance on the recommended administration, dosing and titration of pain related medications as well as provide information on the management and prevention of potential opioid tolerance that can be experienced within patients (SASA, 2015).

The IASP recommends use of opioids, including tramadol, as both first line and second-line treatment for the management of peripheral neuropathic pain. The European Federation of Neurological Societies (EFNS) recommends the use of opioids only as second line treatment (Chetty et al., 2013). The pain management guidelines for geriatric patients, established by the British Geriatric's society, advises a low initial dose, slow dose titration and the use of long intervals to allow for an effective and positive experience for the patients (Dunham et al., 2020).

Research by Chau, (2008) showed that geriatric patients are at a higher risk of experiencing the side effects from opioid medications and therefore, adjuvant therapy with other non-opioid medications should be encouraged. Constipation, nausea and pruritus are examples of the undesirable side effects the patients could experience from using opioids.

Evidence based guidelines offer many advantages including effective pain control, assessment of risk vs benefit, improvement in quality of life, cost effectiveness, time saving and overall improvement in treatment outcome.

A review of 2017/2018 national budget showed that for the provinces with predominate urban populations, example Gauteng and Western Cape, up to 37% of allocated budget is spent on health. Helen Joseph Hospital is in the Gauteng province, which has the highest value in the healthcare bill of R41,2 billion (Financial Statistics South Africa, 2019).

## 1.3 Aim

To analyse the prescribing trends of opioids and common non-opioid analgesics in the geriatric patients at Helen Joseph Pain Management Unit (HJPMU) in Johannesburg, South Africa.

## 1.4 Objectives

To retrospectively review and collect data from prescriptions and patient-related information from the HJPMU geriatric patient files.

To determine if current evidence-based pain management guidelines are being followed.

To determine the probability of having opioids prescribed as a geriatric patient at HJPMU.

To analyse and present both quantitative and qualitative data on the prescribing of opioids and non-opioids analgesics as well as to review the presence of co-morbidities in the patients attending HJPMU.

## 1.5 Overview summary

Chapter 1 describes the brief introduction to the research as well as the aims, objectives, and overview of the research. Chapter 2 is the chapter that focuses on the literature review which covers the literature reviewed in relation to the research. Chapter 3 is illustrating the methodology used during the research while chapter 4 focuses on the results and discussion.

# Chapter 2: Literature Review

The purpose of this review is to gain a clearer understanding of the overall pain experienced within the general geriatric population, as well as the review of previous studies, articles and current guidelines.

With age, patients become more vulnerable and the ability to endure severe and persistent pain declines. This may be related to decline in endogenous opioid component as shown in the meta-analysis by Gibson (2003).

Another study, conducted by Zhang (2003), looked at the effects of aging on the spinal dynorphin expression and hyperalgesia in rats with peripheral inflammation. This study revealed that, greater hyperalgesia and up-regulation of spinal dynorphin was expressed in the aged rats than expressed in young rats. The data indicated that overall, nociception is controlled differently in geriatric patients. This should be considered when the selection of treatment plans and approaches for geriatric patients with persistent pain is reviewed.

Ingrasciotta et al (2019) conducted a study on a global scale show that geriatric patients predominantly use both weak and strong opioids. One study from South Italy on 116 486 elderly patients revealed that 13.2% of patients were using weak opioids while 8.1% were using strong opioids. The overall pain management in geriatrics has been conducted around the world and in this case in the South of Italy, the study looked at the analgesic drug use in elderly patients. Further findings reviewed the inappropriate use of NSAIDs in patients with chronic kidney disease and congestive heart failure. (Ingrasciotta et al.,2019).

Raff et al. (2014) demonstrated the use of Chronic Opioid Therapy (COT) for chronic non-cancer pain. Opioids should be prescribed for moderate and severe pain and are not appropriate for the primary choice of medication but rather as a secondary option.

According to the South African Standard Treatment Guidelines (STGs), which are guidelines followed by the government funded hospitals and facilities in South Africa, the overall aim of pain management in the government sector is to reduce the pain and

improve the overall function, sleep, and quality of life of the patients. The guidelines look at nociceptive pain, neuropathic pain, and chronic cancer pain (STG EML, 2019).

The STGs also acknowledge the relationship between pain and mental health/ illness such as anxiety, post-traumatic stress disorder and depression (STG EML, 2019).

While pain management focuses on relieving the pain experienced by patients, the ideal overall form of pain management would be a multimodal approach which is provided by medical practitioners from various medical disciplines. (IASP Press,1994).

### 2.1 Nociceptive pain

By definition, this is a type of pain that arises from threatened or actual damage to the non-neural tissue of the body. This is related to the activation or stimulation of the nociceptors within the body. Nociceptive neurons present as central or peripheral neurons of the somatosensory nervous system that have a capability of encrypting noxious stimuli (IASP Press,1994).

### 2.2 Neuropathic pain

By definition this is a form of pain related to a lesion or disease of the somatosensory nervous system. Diagnostic investigations such as biopsies or laboratory tests are used to confirm the presence of lesions of the somatosensory nervous system, ultimately to confirm any form of trauma in the nervous system. The incidence of an underlying cause of the lesion, such as a stroke or diabetes mellitus, results in the disease of the somatosensory nervous system (IASP Press,1994).

## 2.3 Chronic pain

Though persistent pain and chronic pain are commonly used interchangeably, the term persistent pain has been preferred as it is not connected with undesirable connotations related to chronic pain. The chronic pain being defined as a pain experienced for 6 months or more (Sternbach,1978). Chronic pain can progress from an acute episode of acute pain such as low back pain, post zoster pain and postoperative related pain. Risk factors can relate to the development of chronic pain from the initial acute pain. Risk factors such postoperative complications, repeated surgeries, or chemotherapy (SASA, 2015).

Walter et al., 2006 looked at the biographical pain data of patients with chronic pain. The study investigated the most common cause of the chronic pain presented in the patients. It revealed that the most common cause of the chronic pain experienced by the patients was chronic lower back pain. Of the 276 patients, it was noted that chronic lower back pain was the most common primary diagnosis presented in these patients, while chronic pain with injury related pain (e.g., Motor vehicle accidents) was noted as the least common reason for chronic pain in the patients (Walter et al., 2006).

## 2.4 Aging and decline in Cytochrome P450

Aging results in changes in the biotransformation of medications in the body. This directly affects the safety and efficacy of the medications taken. Wauthier et al., (2007) demonstrated that the geriatric population is considered as the most medicated population with geriatric patients taking approximately three times more medicines compared to younger patients. A clearer understanding of the underlying mechanisms of age-related changes on drug metabolizing enzyme activities within the body, is of vital importance to improve pharmacotherapy and the general treatment of pain using opioids in the elderly.

The cytochrome P450 enzyme (CYP450) system contains haemoproteins. These haemoproteins carry out oxidative, peroxidative and an overall reductive metabolic

transformation of a plethora of exogenous compounds. This system is found in most living organisms such as plants, animals and even forms of bacteria and yeasts (Wauthier et al., 2007). The increase in age causes both pharmacodynamics and pharmacokinetics changes in the body. A loss in the effectiveness of the heart as a pump and a noted decrease in the capacity of the kidneys in the body to remove certain substances from the circulation are examples of notable changes in the body. Changes in the body include a reduction in the capacity and elasticity of the lungs which leads to the decrease in oxygenation of the blood (Masoro, 1987).

### 2.5 Dementia and Opioid prescriptions

The assessment of pain in geriatric patients can be difficult. One of the reasons for this is the impairment of communication as seen in cases of dementia. The use of opioids is common among geriatric patients. Over 7 million people aged 65 or above have filled at least one opioid related prescription (Dublin et al., 2015). Despite the benefits of opioids in the reduction of pain, the prolonged use has potential negative risks and side effects. Researchers have shown that opioid use may result in neuropathologic problems, which may lead to a weakening in cognition. Due to this possible link, Dublin et al., (2015) surveyed the risk factors of developing dementia related to opioid use.

Overall, 2,500 patients over the age of 65 without a diagnosis of dementia were analysed. The study continued to analyse the patients over ten years to evaluate the effects of opioids and NSAIDs use in geriatric patients. The results of the study indicated that the continued use of these prescription medications could result in the development of dementia and Alzheimer's disease. The ratios for dementia were noted as 1.06 (95% CI = 0.88-1.26) for 11 to 30 total standardized doses (TSDs), 0.88 (95% CI = 0.70-1.09) for 31 to 90 TSDs, and 1.29 (95% CI = 1.02-1.62) for 91 or more TSDs, versus 0 to 10 TSDs. Therefore, older adults presented with a slightly higher risk of developing a form of cognitive impairment while on the prolonged use of opioids (Dublin et al., 2015).

## 2.6 Opioid Receptors

Opioid receptors are created by the cell body in the dorsal horn of the human spinal cord and they respond to exogenous and endogenous opiates. The opioid receptors are peripherally distributed along the nerve fibre within the body. Once these receptors are activated, there is a reduction in the release of neurotransmitters that come from the primary afferent neuron (SASA, 2015). Nerve related injuries or inflammation cause the loss of the opioid receptors.

## 2.7 Guide on prescribing opioids

The World Health Organisation (WHO) has established a guideline on the prescribing of analgesics for patients in pain, including patients on palliative care. The WHO analgesic ladder (Table 1) contains three stages which are related to various stages of pain and pain relief options (World Health Organization Analgesic Ladder, 2009). The first step advises non-opioid analgesics for mild pain such as, paracetamol or nonsteroidal anti-inflammatory drugs (NSAIDs) while the second step recommends weak opioids such as, tramadol, for moderate pain. The third and final stage advises potent opioids for severe pain such as, morphine and fentanyl (WHO Analgesic Ladder, 2009).

**Table 1: World Health Organisation analgesic ladder**

| | |
|---|---|
| Freedom from pain | |
| Step 3 | Opioid for moderate to severe pain<br>Non-opioid or adjuvant medications |
| Increase in pain | |
| Step 2 | Opioids for mild to moderate pain<br>Non-opioid or adjuvant medications |
| Increase in pain | |
| Step 1 | Non-opioids or adjuvant medications |
| Pain | |

## 2.8 Opioids in geriatrics

In terms of daily morphine equivalents, tramadol dosing should be considered to be the same for an opioid-naïve patient and patients who has taken opioids. This is due to the low binding affinity of tramadol (Bettinger et al., 2017). The benefit of taking opioids should always outweigh the potential risks. Tramadol's mechanism of action works by inhibiting the reuptake of serotonin and norepinephrine. Tramadol is known to cause constipation in geriatric patients. Less common adverse effects are; an increased risk of serotonin syndrome, increased susceptibility to prolonged bleeding and an increase in the blood pressure and heart rate (Bettinger et al., 2017).

General principles of prescribing opioids in geriatric patients include the following; slow titration with frequent monitoring and using extended-release opioids where possible (Bettinger et al., 2017).

## 2.9 Pain relief management in geriatrics

Ingrasciotta et al., (2019) demonstrated the analgesic use within the geriatric population in Southern Italy. The study reviewed the previous pain relief medication prescribed versus the current pain relief treatment the patients were taking. It was noted that majority of the patients that had previously taken NSAIDs treatment were currently taking strong opioids (51.9%) and weak opioids (43.2%).

The American Geriatrics Society (AGS), (2009) established a revised version to their guidelines and with recommendations for both opioids, non-opioids, and adjuvant drugs (Table 2). The guidelines provided the starting dose of the pain medications along with additional comments on the maximum daily dose, as well as potential side effects that may be experienced when the medications were taken for persistent pain management.

**Table 2: Opioid and non-opioid recommendations as per AGS**

| **Medication (Active ingredient)** | **Starting dose** | **Comments** |
|---|---|---|
| Non-opioids | | |
| Paracetamol | 325–500 mg every 4hr<br>or<br>500–1,000 mg<br>every 6hr | Maximum daily dose of 4 grams.<br>Reduction in maximum dose 50% to 75% in patients with hepatic deficiency. |
| Opioids | | |
| Morphine Sulphate | 2.5–10 mg every 4hr | Used for breakthrough pain. |
| Tramadol and Tramadol SR | 12.5–25 mg every 4-6 h | Potential side effects; drowsiness, constipation, and nausea.<br>Increased risk of seizures if used in high doses are used in predisposed patients. |
| Fentanyl | 12–25 µg patch every 72hr | The lowest dose of the patch recommended for patients is 60 mg or less as per 24-hour of the oral equivalents of morphine.<br>Initial dose taken takes up to 24 hours to peak. |
| Adjuvant drug | | |
| Amitriptyline | 10 mg nocte | Older persons rarely tolerate doses >75 to 100 mg daily |
| Gabapentin | 100 mg nocte | Monitor sedation, ataxia, oedema. |
| Pregabalin | 50 mg nocte | |

## 2.10 Adjuvant analgesics

Adjuvant analgesics are commonly used in geriatric patients (Hulla et al., 2012). Antidepressants are the most common form of adjuvant analgesics prescribed. It is noted that physicians prefer selective serotonin reuptake inhibitors (SSRIs) over tricyclic antidepressants (TCAs) even though geriatric patients are 73% more likely to be prescribed TCAs (Borson et al., 2002).

## 2.11 Opioid selection for non-cancer pain

The factors that are taken into consideration when selecting the most suitable opioids are; previous exposure to opioids, overall health status of the patient, allergy medical history and the severity of pain presented in the patient (Raff et al.,2014). According to the chronic pain guidelines established by Raff et al. (2014), tramadol is considered as first-line for opioid selection for mild to moderate pain while morphine is considered as second line for moderate to mild pain and first line for severe pain within the geriatric patients for non-cancer pain.

Fentanyl is considered second line for the severe pain (Raff et al., 2014). These same guidelines established by Raff et al. advise the start of the chronic opioid therapy (COT) to begin at a low dose, < or equivalent to 10 mg/day of the morphine equivalent (Table 3). These guidelines also advise on the importance of re-assessing the doses prescribed after 72 hours to review the tolerability and overall pain management within the patient. The dose may be titrated and increased over time, however, the daily maximum dose should not exceed 90 mg daily of morphine equivalent (Raff et al., 2014). The guidelines note that a maximum of 400 mg/day of tramadol is suggested for both immediate-release and slow-release form of tramadol. The maximum recommended dose for morphine is 40 mg daily (Raff et al., 2014).

**Table 3: Recommended doses for oral opioids according to SA Guidelines in COT**

| Opioid | Initial dose | Min. time interval for increase (days) | Suggested dose increase | Min. daily dose before converting IR to CR |
|---|---|---|---|---|
| **Tramadol** | 50 mg<br>4-6 hourly | - | Maximum dose 400 mg/day | N/A |
| **Tramadol SR** | 100 mg<br>12 hourly | 2 | Maximum dose 400 mg/day | N/A |
| **IR Morphine** | 5-10 mg<br>4 hourly. 40 mg/ day | 7 | 5-10 mg/day | 20-30 mg |
| **CR Morphine** | 10 - 30 mg<br>12 hourly | Minimum:2<br>Recommended: 14 | 5-10 mg/day | N/A |

**Table 4: The National Institute on Drug Abuse (NIDA) opioid risk tool**

| **Factor** | **Female** | **Male** |
|---|---|---|
| | Risk Score | |
| Substance abuse family history | | |
| Alcohol | 1 | 3 |
| Illegal Drugs | 2 | 3 |
| Prescribed drugs | 4 | 4 |
| Substance abuse history | | |
| Alcohol | 3 | 3 |
| Illegal Drugs | 4 | 4 |
| Prescribed drugs | 5 | 5 |
| Age between 16 - 45 years old | 1 | 1 |
| Sexual abuse history | 3 | 0 |
| Psychological disease | 2 | 2 |
| Depression | 1 | 1 |
| Scoring Totals | | |

## 2.12 Opioid risk tool

The National Institute on Drug Abuse (NIDA) in the United States of America, established an opioid risk tool (ORT) which is a self-reporting screening tool to assess the potential risk of opioid abuse (Table 4). This tool is encouraged to be used prior to opioids being prescribed and initiated. A risk score of 8 or >8 have been considered as high risk for experiencing opioid abuse (Webster, 2005).

## 2.13 Opioid related adverse effects

While adverse effects of opioids cannot be prevented, the management of the adverse effects is crucial to increase the potential tolerability of the medication as well as to ensure limited negative effects on the quality of life of the patients while on the opioid treatment. Raff et al., (2014) have noted management tips for common adverse effects (Table 5).

**Table 5: Management of opioid related adverse effects**

| **Common adverse effects** | **Management** |
|---|---|
| Nausea and Vomiting | Anti-emetic therapies |
| Constipation | Increase fibre and liquids; Use of laxatives or stool softeners |
| Pruritus | Antihistamine |
| Sedation | No pharmacological therapies advised |

Though the most common adverse effects are generally tolerable, intolerable adverse effects have been noted. The guidelines by Raff et al., (2014) advise that intolerable adverse effects can be managed by the reduction of opioid dosage, change in the route of administration, as well as the switch to an alternative form of pain management (Raff et al., 2014). The European Association of Palliative Care (EAPC) recommend the reduction of opioid dose, rotation amongst opioids and the use of medication to target the symptoms of the adverse effects (Chau, 2008).

## 2.14 South African Pain Guidelines

According to the South African STGs, the goal of the pain management includes; the reduction of pain, improved overall well-being and sleep. The patient's family plays a crucial role in the patient's treatment experience and therefore should be involved in the treatment process (STG, 2016). The guidelines are utilized in the overall pain management within the government funded hospitals, such as Helen Joseph Hospital, whereby the medications prescribed or available are reliant on the medications the EML established by WHO and SA DoH. The STG identifies patients > 65 years of age as high-risk patients.

The STGs advise that in geriatric patients; the dose of opioids, such as morphine, be reduced and the dosage interval increased. In addition, the guidelines strongly encourage the titration of pain relief medications more specifically, weak and strong opioids (STG, 2016). Tramadol is the most prescribed opioid within the public and government funded hospitals. It is regarded as a weak opioid agonist. Morphine sulphate is regarded as a strong opioid and is rated as the most prescribed strong opioid prescribed in the public sector with a recommended geriatric dose of 2.5 mg-5 mg/4hr. Paracetamol is the most common non-opioid prescribed within the public or government sector (STG, 2016).

The South African Society of Anaesthesiologists (SASA) have established guidelines on acute pain management. The guidelines state that paracetamol, gabapentin and pregabalin are non-opioids commonly prescribed and used for the chronic neuropathic pain (SASA, 2015). Paracetamol and opioid derivatives are commonly prescribed for outpatients receiving acute or chronic pain management and do not require to be hospitalised while obtaining treatment. Topical and transdermal analgesics are useful in decreasing the dependence on oral drug therapy i.e., fentanyl patches.

As the study is being conducted in South Africa, the guidelines provide guidance on the role of traditional healers and the potential use of herbal medications by the patients. The guidelines also provide clarity on the sensitivity to the perception of pain and the relation to weakness by those in belief of the customs. These perceptions could influence the

percentage of males actively seeking assistance in relation to pain management (SASA, 2015).

### 2.15 Australian Pain Society and United States of America pain guidelines

The Australian pain society demonstrated the preferred dosages of opioids and non-opioids in the form of pain guidelines (Australian Pain Society, 2019). The guidelines advise the starting dose of morphine at 10 mg twice daily orally while the fentanyl patch is recommended at 12 µg with the patch being changed every 72 hours (Table 6).

**Table 6: Australian Pain Society opioid dose recommendations**

| **Medication (active ingredient)** | **Starting dose** | **Considerations** |
|---|---|---|
| Morphine | 10 mg bd po | Caution/contraindicated in renal impairment<br>Bowel regimen to check for and prevent constipation |
| Fentanyl patch | 12 µg/hr every 3 days | Dosing above 25 µg/hr is not recommended without specialist input.<br>Not recommended for opioid naïve residents |

In the United States, the following recommended starting doses were established by a multiple disciplinary (Anaesthesiology and Perioperative department and Psychiatry department) team at Mayo Clinic College of Medicine and Science (Table 7). The recommendations are in line with the understanding of the importance of appropriate pain management within the vulnerable patients. These recommendations were established following the increase in concern of the opioid use within the geriatric population (Gazelka et al., 2020).

**Table 7: Recommended starting doses of opioids in the elderly**

| Opioid | Dose (mg) | Frequency |
|---|---|---|
| Tramadol | 50 | Every 4 to 6 hours |
| Morphine | 7.5 | Every 4 to 6 hours |
| Fentanyl | Transdermal | Not recommended for opioid-naïve patients |
| Opioid-naïve patients are advised to avoid the use of long-acting opioids. | | |

## 2.16 European Pain Guidelines

The AGS panel on persistent pain guidelines are followed by the Spanish geriatricians. (Schofield,2018). No official geriatric pain guidelines or recommendations of chronic pain management were noted for Belgium (Schofield,2018). Scottish Intercollegiate Guidelines Network (SIGN) advises that opioids, with the average dosages of between 24 to165 mg daily, are effective in the reduction of pain or physical disability within the geriatric population. The efficient review of opioids in the geriatric patients revealed that the older age group was associated with a lower possibility of opioid misuse.

SIGN conducted a study whereby the patients received opioids (n=15,160). The study noted that less than 1% of the patients >60 years old and 4% of those < 60 years had been identified with a form of opioid abuse (SIGN, 2013).

## 2.17 Impact of Pain and barriers identified

The quality of life in the geriatric patients is impacted by the presence of pain. Pain has been shown to also have psychological, physical, and social consequences. A level of profound psychological impact has been noted in patients with chronic pain, whereby they are four times more likely to struggle with anxiety or depression (Brennan et al., 2007).

Pain can lead to a reduction in mobility, which consequently can result in the reduction of strength. The presence of pain negatively affects the immune system of the patients (Human Rights Watch, 2009).

The BGS (2013) presented the types of physiological changes experienced along with the direct effect these changes have on the drug handling and prescribing trends related to geriatric patients (Table 8). Due to the age-related bodily changes, the prescribed dosages of opioids and non-opioids differs and are relatively lower than that of the average adult.

**Table 8: Physiological changes in older people that affect drug handling**

| Physiological | Age related changes | Clinical consequence of change |
|---|---|---|
| Function and absorption of the gastrointestinal tract | Reduction in GIT blood flow and a delay in GIT emptying. | Alteration in the drug absorption and increased risk of opioid related GIT adverse events |
| Distribution | Increase in the body fat and decrease in water. This causes a lower level of plasma proteins and increase in drugs that can link to the proteins. | Drug interaction potential rises. |
| Hepatic metabolism | Decrease in hepatic blood flow, liver mass and liver cells | An increase in half-life of the drug. |
| Renal excretion | Reduction in renal blood flow and tubular secretion | Reduction in excretion of drugs and GFR which results in the accumulation of medication. |
| Pharmacodynamics changes | Decrease in receptor density<br>Increase in receptor affinity | Increase in sensitivity to the therapeutic and side effects |

## 2.18 Limitations and Barriers identified in pain management

Despite the increase in the research being conducted in relation to geriatric pain management, data would suggest that pain in geriatrics is still broadly under recognized and undertreated despite noteworthy physical and social consequences (Coggins, 2014). Barriers have been identified in 3 categories: health care professionals, family, and the health care system.

Barriers identified in relation to health care professionals include a limitation in education received regarding pain assessment, management of the health care facilities, concern around potential regulatory related scrutiny, the fear of opioid-related side effects and the challenges in the process of assessing pain in the cognitively impaired patients (Coggins, 2014).

The success of pain management in geriatric patients is greatly dependent on the involvement of the patient's family or care givers. Fear of negative medication side effects, concerns related to potential opioid abuse and the failure to understand the overall treatment aim are among the barriers to successful pain management. Geriatric patients have noted a fear in discussing pain and treatment with their medical doctors due to the fear of being a perceived as a bad patient (Coggins, 2014). As in most state hospitals, Helen Joseph hospital services are negatively affected by limited funding, high numbers of patients and the challenge of serving a multicultural community with diverse attitudes towards opioids use.

## 2.19 NSAIDs and geriatric patients

Nonsteroidal anti-inflammatory drugs (NSAIDs) present with numerous side effects and contraindications. Side effects include and are not limited to, constipation and stomach ulcers. Due to this, cautious use is recommended in geriatric patients (Chen, 2018). Many pain-related guidelines discourage the use of NSAIDs in geriatrics. For this reason, the collection of NSAIDs prescribing trends were not included in the review in this study.

NSAIDs are advised to be prescribed with extreme caution in highly select and vulnerable individuals due to the of the high risk of negative adverse effects. Geriatric patients prescribed NSAIDs would have had to have failed other safer or more tolerable forms of pain medications. (Coggins, 2014). Though NSAIDs are often prescribed in geriatric patients they are still considered a risk to the geriatric patients. (Hulla et al., 2012). NSAIDs are known to play a role in hospitalization related to drug-to-drug interactions. NSAIDs have negative interactions with common prescribed drugs such as antihypertensives, aspirin and selective serotonin receptor inhibitors (Barkin et al., 2010).

### 2.20 Medications on Pharmaceutical Tender list with DoH

A pharmaceutical tender is established between a pharmaceutical production company and the DoH whereby companies bid to have a contract with the DoH to supply all government or public health care facilities with medication or medical devices. Based on the EML. The medications established as essential are provided to the public healthcare facilities and therefore are available as options to the prescribers when prescribing medications to the patients (Health.gov, 2020). Based off the current approved tenders, the following medications are on tender between pharmaceutical companies and the DoH (Table 9).

### 2.21 WHO Essential Medicines list

The South African STGs and the South African EML are guided by the WHO's Essential Medicines List (EML). According to the guidelines, the EML is defined as a crucial list that contains minimal medication requirements for a basic health-care system (Table 10). The aim of the list is to allow for the availability and accessibility of, cost–effective and safe medicines to cover conditions considered as priorities (WHO EML, 2021).

**Table 9: Pain medications listed on the tender list on the BID forms**

| Medication | Dose (mg) | Pack size<br>Tablets or Capsules |
|---|---|---|
| Opioids | | |
| Morphine sulphate | 10 mg | 60 |
| | 30 mg | 60 |
| | 60 mg | 60 |
| Tramadol hydrochloride | 50 mg | 100 and 20 |
| | 100 mg | 60 |
| Tramadol hydrochloride and Paracetamol | 37.5 mg / 325 mg | 60 |
| Non-opioids | | |
| Paracetamol | 500 mg | 100 and 20 |
| Amitriptyline | 10 mg | 100 and 28 |
| | 25 mg | 168, 28, 500, 56 and 84 |

**Table 10: Opioids and Non-opioids on the WHO EML**

| Medication | Doses |
|---|---|
| Paracetamol | Liquid: 120 mg/5 ml; 125 mg/5 ml<br>Suppositories: 100 mg<br>Tablets: 100-500 mg. |
| Fentanyl | Transdermal patch (µg/hr)<br>12 ;25 ;75 ;100 |
| Morphine | Granules 20 mg-200 mg<br>Injection ampoule: 10 mg/1 ml<br>Slow-release tablet: 10 mg – 200 mg<br>IR Tablet: 10 mg |
| Amitriptyline | Tablet: 10 mg; 25 mg; 75 mg. |

## 2.22 Pharmacokinetics and pharmacodynamics considerations

Due to the expected physiological changes related to age, the pharmacokinetics and pharmacodynamics should be considered upon the prescribing of the opioid medications to the geriatric patients. Paracetamol is considered one of the safer analgesic options being the less prone to adverse effects when taken within the required prescribing ranges. Narcotics, such as morphine, are considered to have a higher potential of adverse effects and therefore lower dosages are encouraged. Ouslander (1981) confirmed that the lower dosages reduce the possibility of central nervous system (CNS) and respiratory depression. Ouslander (1981) also noted that the review of pain management should be a multiple disciplinary form of management. The management of the pain acknowledges that along with the emotional and physical effects, it can take a toll on mental health and patients. Therefore, medications such as amitriptyline, which are used for analgesic and anti-depressant properties, may result in higher blood levels in geriatric patients. For this reason, regular neurological assessment is advised in geriatric patients on these drugs.

**Table 11: WHO model list of essential medicines dosage forms and definitions**

| Dosage form | Definition |
|---|---|
| Tablets | • Tablets which can be uncoated or coated. Tablets can be chewed, dissolved to form a solution or even crushed. |
| Capsules | • Capsules in oral form and can be established as a slow release or enteric coated. |
| Granules | • Oral granules and can be added to liquid to create a solution |
| Oral powder | • Dispensed in oral powder form and can be added to liquid to create a solution |

## 2.23 Formulations and dosage forms

Most patients are classified as outpatients and therefore are receiving medication in the form of either oral medication or transdermal patches. The WHO defines solid oral dosage forms as either capsules, tablets or granules that are taken orally (Table 11).

## 2.24 Prescribing abbreviations and terminology

The aim of using the medical abbreviations is to allow for safe, clear and level of consistency in the prescribing of medications (Table 12). There is an international standard of medical abbreviations which was also noted on the prescriptions used at the HJPMU. The abbreviations and terminology used are internationally recognised (safetyandquality, 2016).

## 2.25 Prescribing trends

Worldwide assessment of prescribed medications and prescriptions estimates about 50% of prescriptions are classified as inappropriate prescriptions (WHO, 2009). This impacts the effectiveness of therapy and quality of life of the patient directly (Hardon, 1991).

A study conducted by Summoro et al., (2015) in the Northwest of Ethiopia demonstrated the average number of medicines per patient obtaining medication as an outpatient. Analgesics (11%–49%) were stated to be the most prescribed medicines on the outpatient prescriptions in the three hospitals that took part in the study.

Summoro et al., (2015) also noted that tramadol was the third highest prescribed medication at 9.0% and the most prescribed analgesic at the Wolaita Sodo University Teaching and Referral Hospital. Tramadol was the most prescribed opioid prescribed at 9%. Paracetamol was the most prescribed non-opioid medication at 5.4%.

Though pain management looks at both pharmacological and non-pharmacological therapies to achieve pain management, this research report focuses on the pharmacological aspect (prescribing trends) as well as the external factors such as demographics and medical related history which can influence the success of the pain management.

**Table 12: Recommendations for Terminology, Abbreviations and Symbols**

| **Dosing and Frequency or Timing** | |
|---|---|
| **Intended meaning** | **Abbreviation** |
| At night | nocte |
| Every 4 hours | 4 hourly |
| Every 6 hours | 6 hourly |
| Every 8 hours | 8 hourly |
| Every 12 hours | 12 hourly |
| Twice daily | Bd |
| Three times daily | tds |
| Four times daily | qid |
| **Units of measure and concentration** | |
| milligram(s) | mg |
| millilitre(s) | mL |
| microgram(s) | mg |
| gram(s) | G |
| Dose forms | |
| capsule | cap |
| tablet | tab |

# CHAPTER 3: Methodology

## 3.1 Study Setting

This study was conducted at the Helen Joseph Hospital which is in Johannesburg. All patient records of patients attending the clinic are stored in the HJPMU with permission received from the Head of Department of HJPMU, Helen Joseph Hospital Management and WHREC.

## 3.2 Study design

A retrospective systematic review of medical cases in the HJPMU over a set period of time, 6 months. The data was obtained from patients' hospital records. The collection of the data was conducted in the HJPMU to ensure the confidentiality of patient information. No patient identification data was obtained to ensure patient confidentiality was maintained.

## 3.3 Sample Size

In the year 2020, the HJPMU recorded to have seen total of 2886 patients. The patient numbers were affected by the COVID-19 pandemic and country related restrictions imposed. In the first half of the year 2021, the clinic saw an average of between 221 to 250 geriatric patients per month which is an average of about 236 geriatric patients per month with an average of 11.8 geriatrics patients seen daily over a period of Monday to Friday. Therefore, based on 11.8 geriatrics patients seen over five times per week (59 geriatric patients seen per week) ,1416 geriatric patients were seen over the period of six months the clinic during the COVID-19 pandemic.

The sample size calculation involved the review of the population size. The population size of 1416 was obtained and at a 95% confidence level with a 5% margin of error (p

value =0.05 or 5%) resulted in a sample size of 303 patient files. The patient files were reviewed in an alphabetical order based off the surname of the patients.

The sample size was calculated using the following equations:

Unlimited population size: $n = \frac{z^2 \, x \, \rho \, (1-\rho)}{\varepsilon^2}$ Equation 1

Finite population: $n' = \frac{n}{1+\frac{z^2 \, x \, \rho(1-\rho)}{\varepsilon^2 \, x \, N}}$ Equation 2

z value (1.96 for 95% confidence interval)

ϵ = margin of error (0.05)

N = population size (1416)

P = population proportion (0.5)

$n = \frac{1.96^2 \, x \, 0.5 \, x \, (1-0.5)}{0.05^2}$ = 384.16

$n' = \frac{384.16}{1+\frac{1.96^2 \, x \, 0.5 \, x \, 0.5}{0.05^2 \, x \, 1416}} = 303$

### 3.4 Data collection

Data collection was conducted following the retrospective review of patient files at the Helen Joseph Pain Management Unit.

### 3.5 Inclusion and exclusion criteria

This study included male and female patients who were 65 years and older at the time the patients received the treatment at the HJPMU between September 2020 and March 2021. These patients attending Helen Joseph Pain Unit are patients obtaining treatment for cancer and non-cancer pain, neuropathic pain, nociceptive pain, surgical pain, musculoskeletal pain and overall pain management for both acute and chronic pain.

This study excluded patient files with insufficient data i.e., missing medicine prescriptions, missing identification documentation to confirm age, In-patient geriatric patients (patients admitted into the hospital).

### 3.6 Data collection

The collection of the data was being captured on the data collection sheet on Microsoft Excel (Appendix I). The following data was captured:

- Age
- Gender
- Chronic pain
- Comorbidities and allergies
- Medical and Surgical history (inclusive of prescriptions)
- Diagnosis
- Neuropathic or Nociceptive pain
- Physiotherapy
- Opioids and non-opioids prescribed
- Social support

### 3.7 Data Analysis

The overall aim was to present and display the prescribing trends of the pain related medication. The review of ages, gender, diagnosis, types of pain, medical history and surgical procedures were also reviewed to obtain information on the patient backgrounds as it has been established that successful pain management has a multifocal and broad approach. To determine whether the doses prescribed are in line with the evidence-based guidelines, the prescribed dosages were compared to the recommended initial and titration doses noted in South African and international guidelines. The categorical variables were described by the absolute frequencies and proportions. The differences in proportions were assessed using Chi-square test. A graphical presentation was used to display results for categorical variables described such as the allergies or co-morbidities of the sample.

A bivariate analysis was performed in relation to the demographics as well as the prescriptions for both opioids and non-opioids. The bivariate analysis was used to determine demographics and probability of being prescribed opioid or non-opioids for geriatric patients attending the HJPMU. Regression analysis involving the univariate and multiple logistic regression was conducted to adjust for confounding factors. The 95% confidence interval (CI) was used to approximate the ultimate precision of the odds ratio (OR). The akaike information criterion (AIC) was utilized to establish the value of the model's prediction performance. The analysis was performed using STATA statistical software. Significance was set at 5 which indicates a 5% chance of error.

### 3.8 Ethic Considerations

For this study to be conducted, the following approvals were obtained. The University of Witwatersrand's Human and Research Ethics Committee (WHREC) provided the Ethics certificate for protocol no: M210742 (Appendix III). The Head of the Anaesthesiology department of the HJPMU provided the written approval and consent for the access to the patient files (Appendix IV). The Helen Joseph Hospital Management provided approval for the study to be conducted at the hospital (Appendix V).

# Chapter 4: Results and Discussion

## Results

Based off the 95% confidence level, a sample size of 303 patient files for patients attending and receiving treatment from the Helen Joseph Pain Management Unit within the period of September 2020 to March 2021 was required. However, a final total of 296 (97.7%) of the files fulfilled the required inclusion criteria to be reviewed.

### 4.1 Demographics and Baseline characteristics

There were 296 geriatric patients whose records were reviewed for this study within the period of September 2020 to March 2021 at The Helen Joseph Hospital Pain Management Unit. The median age of the patients within the sample was 70 years with an interquartile range of 67-75 years, Figure 1.

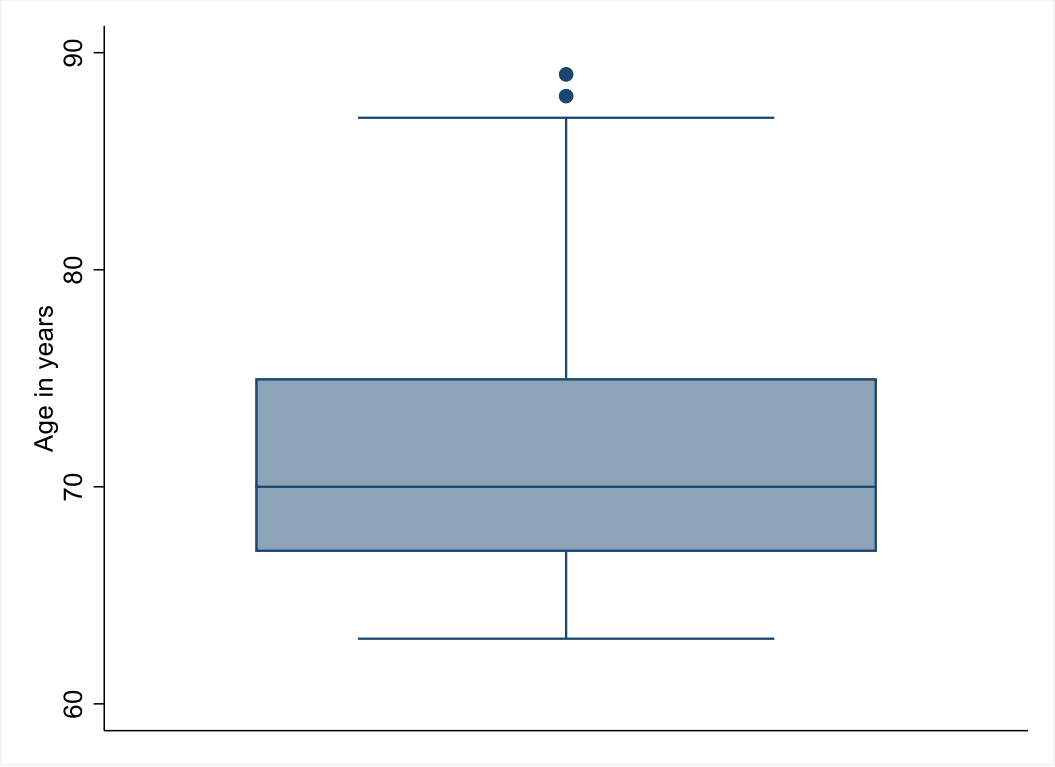



**Figure 1: Age distribution of geriatric patients**

**Table 13: Baseline characteristics & demographics of the geriatric patients at HJPMU**

| Variables | Frequencies | Percentages |
|---|---|---|
| Gender | | |
| Female | 231 | 78.04 |
| Male | 65 | 21.96 |
| Social support | | |
| No | 15 | 5.07 |
| Yes | 270 | 91.22 |
| Missing | 11 | 3.72 |
| Alcohol intake | | |
| No | 224 | 75.68 |
| Yes | 62 | 20.0 |
| Missing | 10 | 3.38 |
| Employment status | | |
| No | 21 | 7.09 |
| Retired | 247 | 83.45 |
| Yes | 23 | 7.77 |
| Missing | 5 | 1.69 |
| Ever received Chemotherapy | | |
| No | 258 | 87.16 |
| Yes | 10 | 3.38 |
| Missing | 28 | 9.46 |
| Physiotherapy | | |
| No | 142 | 47.97 |
| Yes | 145 | 48.99 |
| Missing | 9 | 3.04 |
| Surgical history | | |
| No | 28 | 9.46 |
| Yes | 265 | 89.53 |
| Missing | 3 | 1.01 |

The additional baseline characteristics or demographics of the geriatric patients are summarised in Table 13.

Most of the geriatric patients who attended the HJPMU were females (78.04%), had a form of social support (91.22%), classified as non-alcoholic drinkers (75.68%) and had retired from working and were obtaining a pension (83.45%).

Most of the patients had never received chemotherapy (87.16%), had done a form of physiotherapy (48.99%) and had a form of surgical history (89.53%). Areas where certain information or variables was not stated in the patient files was noted as ‘missing’ in the data presented.

### 4.2 Comorbidities and allergies among the geriatric patients

The presence or absence of comorbidities for the geriatric patients was also retrieved and the results are displayed in Figure 2. Overall, there were 256 (86.49%) patients that presented with at least one underlying co-morbidity. The most common co-morbidity noted was hypertension which was reported in 58.78% (n=174) patients, followed by joint and bone related disease (i.e., Osteoarthritis) reported in 31.42% (n=93) of the patients. There was a significant proportion of patients with diabetes (16.89%), lung disease (i.e., Asthma) or COPD (15.2%) and heart disease (14.19%).

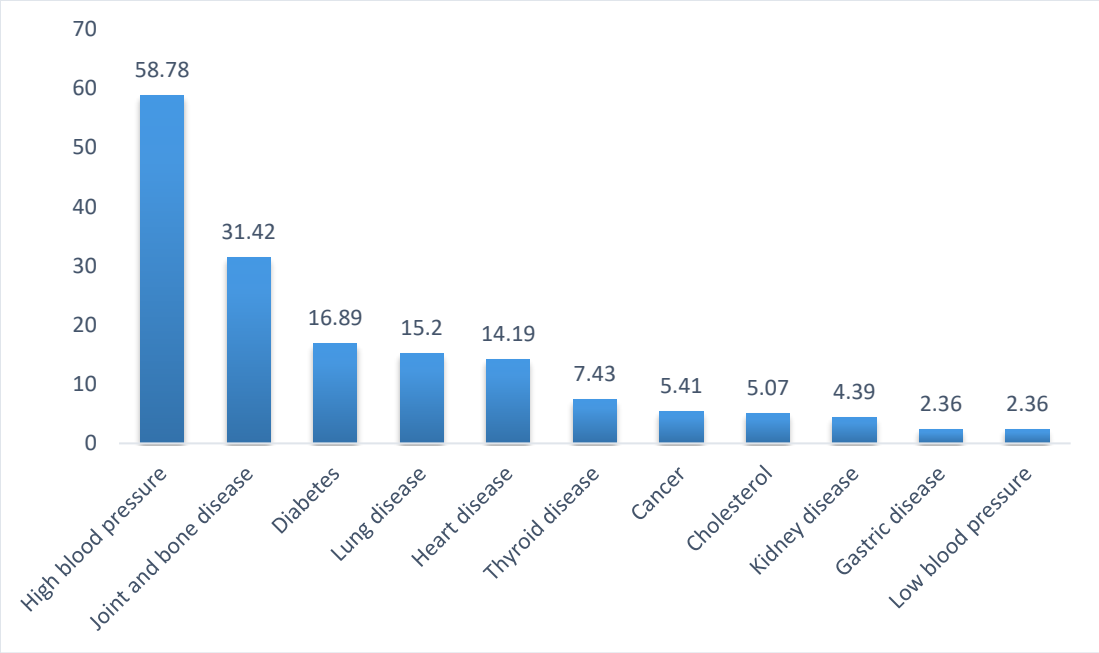



**Figure 2: Distribution of co-morbidities present amongst the geriatric patients**

The number of comorbidities was also assessed as shown in Figure 3. Generally, the increase in the number of co-morbidities present in geriatric patients is directly proportional to the increase in the number of medications taken by the patients. In the sample, 35% of the patients presented with one underlying comorbidity. There were 29.39% of patients who presented with two comorbidities and 21.96% of patients who presented with three or more comorbidities.

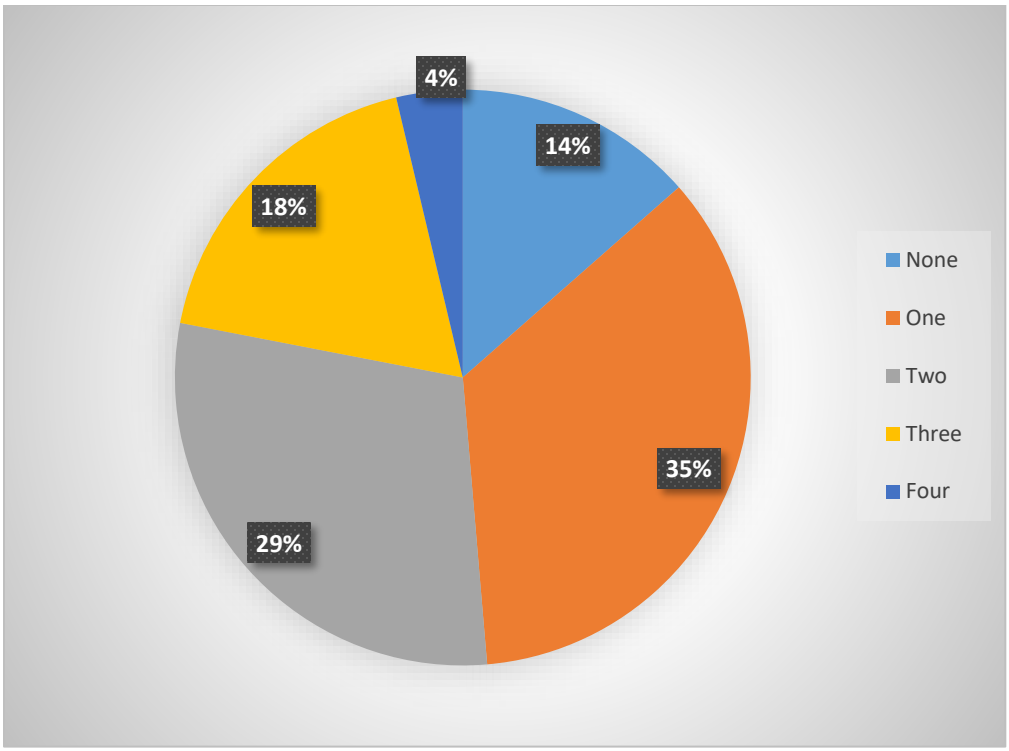



**Figure 3: Number of known comorbidities present amongst the geriatric patients**

There were 50 (16.89%) of patients who reported being allergic to a form of active ingredient or medication. Amongst the patients who were allergic to medication, most patients were allergic to Penicillin (40%), Figure 4.

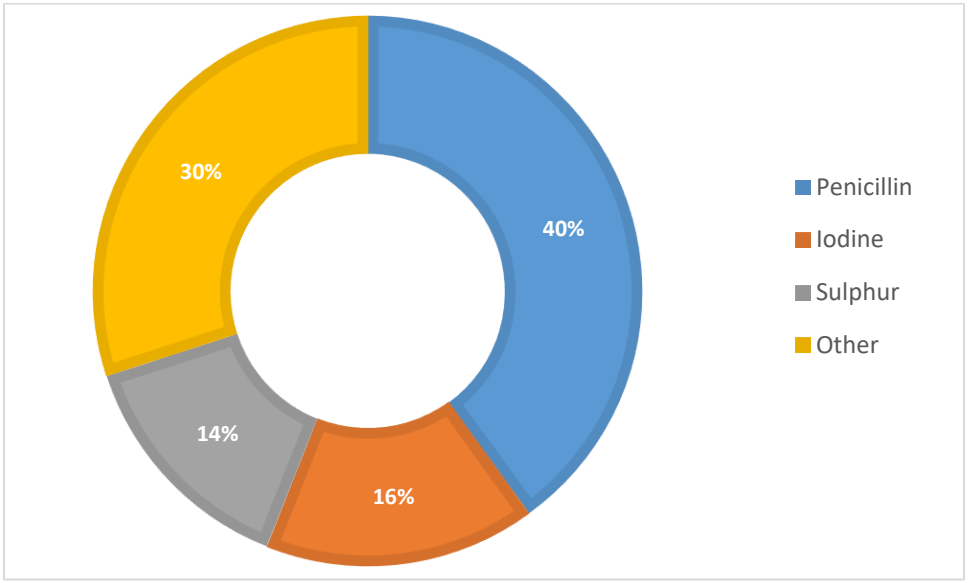



**Figure 4: Recorded allergies and active ingredients**

### 4.3 Pain medication types

Most of the patients (45.61%) were diagnosed with both neuropathic and nociceptive pain. There were 96.96% of patients who were prescribed a form of pain medication. it was noted that 45.95% of the patients were taking an average of three medications or had three pain related medications prescribed on their prescriptions. This is inclusive of the adjuvant medications (Table 14). The geriatric patients were prescribed a varietyof medication. All the patients were prescribed oral formulations except for one patient who obtained a fentanyl patch. The pain medication types are summarised in Table 15.

As expected, majority of the patients were prescribed opioids (76.35%) and 3 (1.33%) of these patients were prescribed two opioids. The proportion of patients who were prescribed opioid medication (76.35%) compared to those who were prescribed non-opioid medication (20.61%) was significantly different, p-value<0.0001. The most common opioid medication was tramadol which was prescribed in 76.66% of the patients while the most common non-opioid medication was paracetamol which was prescribed in 80.84% of the patients, Figure 5. There were 7.09% of patients who were taking the anti-coagulant, warfarin and 17.57% who were taking medication for either anxiety or depression. (Table 14).

**Table 14: Medical history and prescription trends of the geriatric sample**

| Variable | Frequency | Percentage |
|---|---|---|
| Type of pain the patient had | | |
| Neuropathic and Nociceptive | 135 | 45.61 |
| Neuropathic only | 53 | 17.91 |
| Nociceptive only | 59 | 19.93 |
| Not stated | 49 | 16.55 |
| Patient on pain medication | | |
| No | 9 | 3.05 |
| Yes | 287 | 96.96 |
| Total number of pain medications prescribed | | |
| 0 | 9 | 3.04 |
| 1 | 25 | 8.45 |
| 2 | 88 | 29.73 |
| 3 | 136 | 45.95 |
| 4 | 33 | 11.15 |
| 5 | 5 | 1.69 |
| Classification group of medication | | |
| Non-opioid medication | 61 | 20.61 |
| Opioid medication | 226 | 76.35 |
| Not on medication | 9 | 3.04 |
| Warfarin | | |
| No | 275 | 92.91 |
| Yes | 21 | 7.09 |
| Medication for anxiety or depression | | |
| No | 244 | 82.43 |
| Yes | 52 | 17.57 |

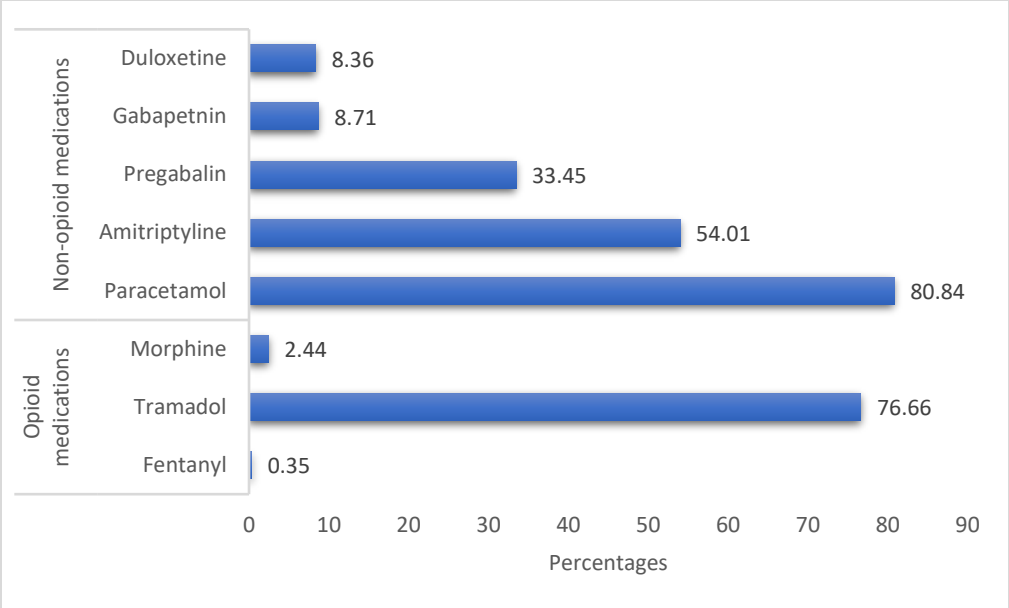



**Figure 5: Opioids, non-opioids and adjuvant medications prescribed**

Paracetamol was the most prescribed pain medication (77.38%) with the most common dose prescribed was 500 mg/8hr (44.26%). Tramadol was the most prescribed opioid (74.66%). The most common dose of tramadol prescribed was 50 mg/8hr which was present in 36.49% of the prescriptions. The adjuvant pain medications were underrepresented with gabapentin (8.45%) and duloxetine (8.44%) being the least prescribed adjuvant analgesics. Amitriptyline was the most prescribed (52.7%) adjuvant analgesic while pregabalin was present in 30.41% of the prescriptions (Table 15).

### 4.4 Bivariate analysis of patients prescribed pain medication

The bivariate analysis of the prescribed opioids stratified by baseline characteristics or demographics is shown in Table 16. There is no significant difference noted in age, pain type, having social support, had done physiotherapy, having comorbidities or being on Warfarin between patients who were prescribed opioids and those who were prescribed non-opioids. However, the bivariate analysis showed marginal significance in the gender difference between patients on opioid medication and those on non-opioids medication. More males were prescribed opioid medication (n=56, 24.78%) compared to those in the non-opioids' medication.

**Table 15: Medication dosages prescribed per active ingredient**

| Medication group | Medication types | Dosages | Frequency | Percentages |
|---|---|---|---|---|
| Non-opioid medication | Paracetamol | 500 mg/8hr | 131 | 44.26 |
| | | 500 mg/6hr | 3 | 1.01 |
| | | 1 g/8hr | 98 | 33.11 |
| | Amitriptyline | 10 mg/nocte | 32 | 10.81 |
| | | 25 mg/nocte | 100 | 33.78 |
| | | 50 mg/nocte | 20 | 6.76 |
| | | 12.5 mg/nocte | 3 | 1.01 |
| | | 150 mg/nocte | 1 | 0.34 |
| | Pregabalin | 75 mg/12hr | 41 | 13.85 |
| | | 75 mg/8hr | 1 | 0.34 |
| | | 75 mg/24hr | 22 | 7.43 |
| | | 25 mg/24hr | 14 | 4.73 |
| | | 25 mg/12hr | 6 | 2.03 |
| | | 50 mg/12hr | 4 | 1.35 |
| | | 100 mg/8hr | 1 | 0.34 |
| | | 150 mg/24hr | 1 | 0.34 |
| | Gabapentin | 200 mg/8hr | 1 | 0.34 |
| | | 600 mg/6hr | 1 | 0.34 |
| | | 300 mg/8hr | 13 | 4.38 |
| | | 600 mg/8hr | 2 | 0.68 |
| | | 300 mg/12hr | 2 | 0.68 |
| | | 300 mg/6hr | 1 | 0.34 |
| | | 100 mg/8hr | 4 | 1.35 |
| | | 100 mg/12hr | 1 | 0.34 |
| | Duloxetine | 60 mg daily | 8 | 2.7 |
| | | 30 mg daily | 17 | 5.74 |
| Opioid medication | Fentanyl patch | 25 µg | 1 | 0.35 |

**Table 15: Medication dosages prescribed per active ingredient *continued***

| | | | | |
|---|---|---|---|---|
| | Tramadol | 50 mg/8hr | 108 | 36.49 |
| | | 100 mg/8hr | 86 | 29.05 |
| | | 50 mg/12hr | 10 | 3.38 |
| | | 100 mg/12hr | 17 | 5.74 |
| | Morphine | 30 mg/12hr | 3 | 1.01 |
| | | 60 mg/12hr | 2 | 0.68 |
| | | 120 mg/12hr | 1 | 0.34 |
| | | Syrup (5ml/6hr) | 1 | 0.34 |

## 4.5 Regression analysis of pain medication

The probability of having been prescribed opioids in relation to factors which influence the probabilities of being prescribed the opioids. Factors associated with this probability among the geriatric patients was estimated using logistic regression (Table 17). There was no significant difference in age (p=0.691), gender (p=0.012), pain type (p=0.917) (p=0.512) in both genders, having social support (p=0.281), had done physiotherapy (p=0.745), having comorbidities (p=0.177) and Warfarin (p=0.569) between patients who were prescribed opioids and those who were prescribed non-opioids in both the univariate and the adjusted models. Male patients had an increased odd of 2.182 of being prescribed opioids for pain compared to female patients. This likelihood, however, was marginally significant, p-value=0.057 at the univariate level. In the adjusted model, the odds of having been prescribed opioid medication was 4.269 times among male patients compared to female patients with 95%CI of 1.371 to 13.294 and this was statistically significant holding all other variables constant, p-value=0.01

**Table 16: Bivariate analysis of demographics and probability of being prescribed opioid or non-opioids**

| Variable | Non-opioid medication n (%) | Opioid medication n (%) | p-value |
|---|---|---|---|
| Age | | | |
| Median (IQR) | 70 (67-75) | 70(67 –75) | 0.8856 |
| Gender | | | |
| Female | 53(86.89) | 170(75.22) | 0.052 |
| Male | 8(13.11) | 56(24.78) | |
| Pain type | | | |
| Neuropathic & Nociceptive | 28(58.33) | 100(52.63) | |
| Neuropathic only | 9(18.75) | 44(23.16) | 0.744 |
| Nociceptive only | 11(22.92) | 46(24.21) | |
| Social support | | | |
| No | 1(1.69) | 13(5.99) | 0.182 |
| Yes | 58(98.31) | 204(94.93) | |
| Physiotherapy | | | |
| No | 29(49.15) | 111(50.68) | 0.834 |
| Yes | 30(50.85) | 108(49.32) | |
| Patient had comorbidities | | | |
| No | 10(16.39) | 29(12.83) | 0.471 |
| Yes | 51(83.61) | 197(87.17) | |
| Warfarin | | | |
| No | 57(93.44) | 209(92.48) | 0.797 |
| Yes | 4(6.56) | 17(7.52) | |

**Table 17: Probability of geriatric patients being prescribed opioids at the HJPMU**

| **Variable** | **Univariate model** | | **Adjusted model** | |
|---|---|---|---|---|
| | **Odds Ratio (OR) (95%CI)** | **p-value** | **Adjusted odds ratio (AOR) (95%CI)** | **p-value** |
| Age | 1.003 (0.956 to 1.053) | 0.892 | 0.988 (0.932 to 1.047) | 0.691 |
| Gender | | | | |
| Female | Ref | | | |
| Male | 2.182 (0.978 to 4.868) | 0.057 | 4.269 (1.371 to 13.294) | 0.012 |
| Pain type | | | | |
| Neuropathic and Nociceptive | Ref | | Ref | |
| Neuropathic only | 1.369 (0.597 to 3.141) | 0.459 | 0.952 (0.373 to 2.425) | 0.917 |
| Nociceptive only | 1.171 (0.537 to 2.554) | 0.692 | 1.331 (0.566 to 3.126) | 0.512 |
| Social support | | | | |
| No | Ref | | Ref | |
| Yes | 0.271 (0.035 to 2.112) | 0.212 | 0.311 (0.037 to 2.592) | 0.281 |
| Physiotherapy | | | | |
| No | Ref | | Ref | |
| Yes | 0.941 (0529 to 1.672) | 0.835 | 0.889 (0.438 to 1.806) | 0.745 |

**Table 17: Probability of geriatric patients being prescribed opioids at the HJPMU *continued***

| | | | | |
|---|---|---|---|---|
| Patient had comorbidities | | | | |
| No | Ref | | Ref | |
| Yes | 1.331 (0.609 to 2.911) | 0.472 | 2.041 (0.724 to 5.749) | 0.177 |
| Warfarin | | | | |
| No | Ref | | Ref | |
| Yes | 1.159 (0.375 to 3.581) | 0.798 | 1.582 (0.326 to 7.667) | 0.569 |

## Discussion

The data analysis supports the theory that evidence based guidelines are being followed, utilized and reviewed by the medical professionals at the HJPMU. The data also demonstrates the increased likelihood of geriatric male patients being prescribed opioids in comparison to geriatric female patients. The data reveals that Tramadol is the most common opioid prescribed overall in all patients attending the HJPMU regardless of the root cause of the pain.

### 4.6 Demographics socio-economic factors

The collection of data on the age, gender, comorbidities, allergies, medical history, pain diagnosis and social support resulted in the following medical trends and findings.

The proportion of females (78.04%) that presented at HJPMU was greatly significant in comparison to that of males (21.96%) at a p-value of 0.05. The significant difference could be related to potential factors such as the comfort or ability to ask for help, the pain thresholds experienced, the social support provided as well as the presence or absence of other co-morbidities which would other increase or decrease the urgency to ask for assistance.

Opioids are known to have negative side effects. Side effects such as sedation, nausea, and vomiting. Due to this, social support from family and friends is vital to ensure that the patients receive added care and that their quality of life is not negatively altered by the adverse effects. A portion of the patients (5.07%) noted to not have any form of social support whereby they lived alone and could not identify immediate support. The risk in the lack of support in vulnerable patients taking opioids, increases the risk of falls and injuries in the patients.

The combination of alcohol (ethanol) and opioids are known to be a deadly combination in which alcohol is known to worsen or increase the risk of respiratory depression especially in geriatric patients. Due to this knowledge, it is crucial for medical practitioners to be aware of the alcohol use by patients prior to the initiation

of pharmacological pain management including the prescribing of the opioids. The ORT considers the use of alcohol as an increased risk in opioid abuse or dependence.

The legal age of retirement in South Africa is from the age of 65 years old and therefore majority of the patients (83.45%) are currently on pension and therefore not currently working. There is a proportion of geriatric patients who are not employed but are *not* currently on pension (7.09%). There was a portion of patients who are employed (7.77%) and therefore the opioids prescribed would need to be reviewed by the medical professionals acknowledging the potential adverse event of sedation which would negatively affect the patients while working.

The overall medical history of patients is reviewed when the geriatric patients are seen at the HJPMU. The HJPMU caters to both patients with a history of chemotherapy (3.38%) and those who do not (87.16%). Pain management involves a multidisciplinary team and therefore the along with use of pharmacological therapy to ensure pain management, physiotherapy is encouraged for most of the patients, however due to COVID-19, the physiotherapy also includes home exercises which were advised due the national lockdown restrictions. This would have directly affected the number of patients (48.99%) who were and are currently obtaining physiotherapy along with pharmacological therapy. Physiotherapy was noted both in patients receiving pharmacological treatment as well as those not receiving any medication for the pain management. Coggins (2014) noted that physiotherapy can be used alone or in conjunction with pharmacotherapy. A high portion of the patients currently obtaining treatment at the HJPMU have a form of surgical history (89.53%) of which some causes of the surgery were part of the treatment management of resolving the pain. Types of surgeries noted were, lower back pain surgeries, caesarean sections and even appendectomies.

With the increase in age, the increase in the presence of comorbidities increases and it noted in the patients that were seen at the HJPMU. Of the 296 patients, 256 patients (86.4%) presented with one or more comorbidities. The most common co-morbidity was hypertension which was reported in 58.78% while 31.42% of the patients have a bone or joint related disease and diabetes was the third most common comorbidity. The presence of comorbidities therefore confirm that the patients are taking other chronic medications for their comorbidities and therefore increase the risk of

polypharmacy and drug interactions within the geriatric population. 35% of the patients had only one underlying comorbidity while patients (29.39%) presented with two comorbidities and a portion of the patients (21.96%) presented with three or more comorbidities. The increase in the presence of multiple comorbidities in the elderly are directly linked to the probability of polypharmacy and increase in risk of adverse events experienced when these patients take analgesic medications (Bettinger, 2017).

The process of obtaining the patient's medical history is importance as it includes obtaining further information on potential medicine allergies that the patients may have. The reporting of allergies was fully reliant on the information provided by the patients and their families. It was noted that (16.89%) of the patients had reported medical related allergies of which 40% of those patients reported having an allergy to Penicillin. The portion of patients (30%) reported having 'other' medicine allergies such as metoclopramide, acetylsalicylic acid, metronidazole, and amitriptyline. Non-medication related allergies were also reported by the patients such as allergies to bees, pollen, and mushrooms.

### 4.7 Pain diagnosis and management

From table 16 it can be seen that most patients attending the HJPMU were diagnosed with a mixture of neuropathic pain and nociceptive pain (45.61%). Nociceptive pain diagnosis was higher (19.93%) than the diagnosis of Neuropathic pain (17.91%). There was a portion of patients who did not have the diagnosis stated on the source materials (16.55%).

As pain management involves more than pharmacotherapy, a portion of patients (3.05%) were not currently receiving medication. Most patients had initially started on medication and had progressed and were taking alternative forms of therapy such as physiotherapy to assist in the pain management.

### 4.8 Prescribed pain medications

The HJPMU prescriptions from September 2020 to March 2021 were reviewed and most of the patients were noted to have been prescribed opioids (76.35%) and that some patients were prescribed two opioids (1.33%). As majority of the patients were diagnosed with a mixture of neuropathic pain and nociceptive pain (45.61%) this could be the reasoning for the high percentage of opioids being prescribed to the geriatric population. There were a portion of patients who were prescribed non-opioid medication (20.61%). The most common opioid medication prescribed was tramadol at various dosages in 76.66% of the patients while the most common non-opioid medication prescribed was paracetamol which was prescribed in 80.84% of the patients. Both the tramadol and paracetamol are part of the EML and therefore available at the state hospital. As tramadol is a Schedule 5 drug, the additional 'Provincial Government Health TPH 172' form is required when prescribing tramadol.

Upon review of the patient files, it was noted that patients taking the anticoagulant, Warfarin (7.09%), had patient files that clearly indicated that the patient was taking the anticoagulant. Depression or anxiety are commonly experienced by patients with chronic pain. There is a link between the neurotransmitters and the nerve pathways which are related to pain as well as depression and anxiety. 17.57% of the patients reported to being on medication for either anxiety or depression.

### 4.9 Prescribing dosages of opioids and non-opioids at HJPMU

The most common dosages prescribed for the following medications used for the pain management were noted as paracetamol 500 mg/8hr (44.26%), tramadol 50 mg/8hr (36.49%), morphine 30 mg/12hr (1.01%), fentanyl patch 25 ug (0.35%), amitriptyline 10 mg/nocte (10.81%), pregabalin 75 mg/12hr (13.85%) and gabapentin 200 mg/8hr (0.34%). Patients noted as taking anticoagulant warfarin (7.52%).

### 4.10 Prescribing dosages and Guidelines

The dosages noted in the results were compared to that of the AGS guidelines established by the American Geriatrics Society. The guidelines recommend that paracetamol for the geriatric population is 325 mg-500 mg every 4hrs or 500 mg-1000 mg every 6 hours. The dosages prescribed for the geriatric population with the dosages of 500 mg/8hr (44.6%), 500 mg/6hrs (1.01%) and 1 g/8hr (33.11%) are within the required guidelines.

Amitriptyline was prescribed at 10 mg/nocte (10.81%), 25 mg/nocte (33.78%) and 50 mg/nocte (6.76%). The guidelines recommend the starting dose of the Amitriptyline to be 10 mg at night and that the dose can be increased but to a maximum daily dose below 75 mg-100 mg as geriatric patients seldom tolerate doses greater than 75 mg to 100 mg within 24 hours. At the HJPMU, tramadol (including slow release) was prescribed at 50 mg/8hr (36.49%), 100 mg/8hr (29.05%), 50 mg/12hr (3.38%) and 100 mg/12hr (5.74%). All the doses do not exceed the adult maximum dose of 400 mg per day. The recommended starting dose is 25 mg every 4 hours of which the dose can be increased at a steady rate and with consistent monitoring to prevent potential side effects such as drowsiness, constipation, and nausea.

The second most common opioid prescribed was morphine (S6 drug) and the AGS recommend a starting dose of 2.5 mg -10 mg every 4 hours. The most common doses prescribed at the HJPMU was 30 mg/12hr (1.01%), 60 mg/12hr (0.68%), 120 mg/12hr (0.34%) and one patient received the morphine syrup 5mg/6hr. Fentanyl (S6) patches contain fentanyl and have a half-life that allows for the patch to last for a period of 72 hours (3 days). The AGS recommended starting dose is between 12-25 µg every 72 hours. The patient received the 25 µg patch and therefore received the maximum daily dose of the fentanyl. The initial dose of the fentanyl peaks at between18 - 24 hours for an overall analgesic effect to occur. The use of the patches is welcomed as per Raff et al. (2014) guidelines, the change in route administration decreases the risk of dependence and experience of adverse effects.

Amitriptyline is used both for the analgesic property as well as for its sedative properties. The AGS advise the starting dose of 10 mg nocte while the elder patients seldom tolerate doses greater than 75 -100 mg per day. At the HJPMU, the dosages

prescribed fall in line of the guidelines where 10 mg/nocte (10.81%), 25 mg/nocte (33.78%) and 50 mg/nocte (6.76%).

Gabapentin had the most variety in the dosages prescribed at the HJPMU. The highest dose prescribed was 300 mg/8hr (4.38%) while the least common dosages prescribed were 200 mg/8hr, 600 mg/6hr, 300 mg/6hr and 100 mg/12hr all at 0.34% of the sample. The AGS advise that a starting dose of gabapentin 100 mg is prescribed and that while increasing the dose, the patients are required to be monitored to prevent sedation, ataxia, and oedema.

The most common dose of pregabalin prescribed was 75 mg/12hr (13.85%) while the least common dose prescribed was 75 mg/8hr (0.34%), 100 mg/8hr (0.34%) and 15 mg/24hr (0.34%). In relation to the Scottish Intercollegiate Guidelines Network, the HJPMU prescribing trends are in line with the SIGN recommendation doses which advise a maximum daily dose of between 24-165 mg/day (SIGN, 2013).

The STGs note that for patients that are classified as high risk for respiratory depression, tramadol may be used instead of morphine. This is because tramadol is less likely to cause respiratory depression than Morphine. Although the risk of respiratory depression is to a lesser extent, respiratory depression may still occur with tramadol. The STGs recommend a starting dose of Amitrityline10 mg at night and a dosage of morphine 2.5 mg-5 mg 4hrly for the geriatric population. The prescribing trends fall in line with the STGs.

The review of pain management did not include the NSAIDs as the South African STGs advise that that NSAIDs hold a high-risk patient in geriatric patients with peptic ulcer disease history, or on concomitant warfarin, aspirin, or corticosteroids (SA STG and EML, 2019).

APS established guidelines on Pain in Residential Aged Care Facilities recommend the starting dose of morphine to be 10 mg twice daily and acknowledge that it is constant pharmaceutical oversight and review of the patient is required recommended. The prescribing trends noted at the HJPMU were in line with these guidelines. The APS guidelines advise that the fentanyl in various formulations such as a transdermal patch or oral parental formulations should have had a starting dose of 12 µg/hr every 72 hours (3 days) of which the prescribing trends at the HJPMU follow.

The guideline for opioid prescribing for geriatrics with non-cancer pain was established by the SA Rheumatism and Arthritis Association, PainSA, SASA and Cape Pelvic Pain Society. The guidelines noted that a maximum of 400 mg/day of tramadol is suggested for the normal dose as well as the slow-release form of tramadol. The maximum recommended dose for morphine is 40 mg daily (Yang et al., 2021).

Based off the review of the prescribing trends at the HJPMU the most notable probability was that of the increased likeliness of opioids being prescribed in males (n=56, 24.78%) than that of the females. Based off the statistics, males are 4.269 times more likely to be prescribed an opioid for pain management in comparison to the female population. No noteworthy difference in age, diagnosis of main, comorbidity, social support, surgical or medical history between patients prescribed opioids and those prescribed non-opioids were noted.

# Chapter 5- Conclusion and Recommendations

## 5.1 Conclusion

The following trends were noted during the review of the data obtained. Up to 45.62% of the geriatric patients were diagnosed with both neuropathic and nociceptive pain. The most common opioid prescribed was tramadol (76.66%). The most common non-opioid prescribed for pain was paracetamol (80.84%). The most common co-morbidity was hypertension (58.78%). Despite the link between neuropathic pain and diabetes, only 16.89% of the patients presented with diabetes. There was significant difference noted in the prescribing trends between males and females with males being more likely to be prescribed opioids for the pain. More females (75.22%) attended the clinic in comparison to males (24.78%). The adjuvant analgesics were underrated in this data with gabapentin (8.45%) and duloxetine (8.44%) being the least prescribed of the adjuvant analgesics.

Overall, evidence-based guidelines were followed, particularly in relation to the opioid dosages prescribed for the geriatric patients. The initial and recommended doses were in line with the SAAPG, STG, and APS guidelines. The WHO analgesic ladder was followed with opioids being prescribed for moderate to severe pain. While non-opioids such as, paracetamol were often prescribed for the patients. The prescribing of strong opioids such as, morphine and fentanyl, were in line with the APS guidelines. The opioids prescribed are in line with both the WHO EML and the treatment guidelines set in South Africa.

## 5.2 Recommendations

Future studies to conduct research in relation to the prescribing trends of pain medications and potential drug-drug interactions with other chronic medications taken in a larger sample size of geriatric patients attending the HJPMU. The future studies could analyse the influence the presence of other mediations have on the dosing of opioids.

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# APPENDICES

## Appendix I - Data Collection Sheet

The prescribing trends of known opioids in the geriatric patients at the HJPMU

Data collection sheet Date:

Patient number:

Age:

☐Male or ☐Female

☐First time patient: ☐Returning patient:

☐Chronic pain ☐Acute Pain

☐Hepatic related disease ☐Renal disease

Cancer treatment: ☐Yes or ☐No

☐Depression or ☐Anxiety

Diagnosis: _____

Previous surgical procedures: ☐Yes or ☐No

If yes specify _____

Medicines (Active ingredients):

☐Paracetamol

☐Ibuprofen

☐Mefenamic acid

☐Morphine

☐Oxycodone

☐Codeine

☐Tramadol hydrochloride

☐Amitriptyline

☐Carbamazepine

Other_____

Number of opioids prescribed (per prescription)

☐0-1 ☐2-3 ☐>4

Number of chronic medications prescribed (per prescription)

☐0-1 ☐2-3 ☐>4

## Appendix II – Letter to Hospital management and HoD of HJPMU

Helen Joseph Hospital
Johannesburg
South Africa

March 2021

RE: Request to obtain permission to obtain access to patient files from the Helen Joseph hospital Pain Unit

Dear sir/madam

I am currently completing my MSc. Medicine (Pharmaceutical Affairs) through the University of Witwatersrand.

For the research, I would like to conduct my study in the reviewing of the prescribing trends of opioid medications in geriatric patients (65 years old and older) that attend the Helen Joseph Hospital Pain Unit.

This would require me to retrospectively review patient files of patients (303 prescriptions) attending the HJHPMU both as new and returning patients for the period of September 2020 to March 2021.

I plan to review the following in the patient files

- Demographic information
- Prescriptions (both acute and chronic)
- Hospital chart notes
- Medical History

Therefore, your permission to grant me access to the patient files will be greatly appreciated.

Thank you,

Kind regards,

Ms. Idi Chiedza Nhiwatiwa

## Appendix III – WHREC clearance certificate M210742

UNIVERSITY OF THE WITWATERSRAND JOHANNESBURG

R49 Ms IC Nhiwatiwa

**HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)**
**CLEARANCE CERTIFICATE NO. M210742**

| | |
|---|---|
| **NAME:** (Principal Investigator) | Ms IC Nhiwatiwa |
| **DEPARTMENT:** | School of Therapeutic Sciences<br>Department of Pharmacy and Pharmacology<br>Medical School<br>University |
| **PROJECT TITLE:** | *The prescribing trends of opioid medications in geriatric patients at the Helen Joseph Hospital Pain Management Unit* |
| **DATE CONSIDERED:** | 2021/07/30 |
| **DECISION:** | Approved unconditionally |
| **CONDITIONS:** | |
| **NOTE:** | If contact information regarding student study participants is required, please contact the Registrar's office - <Nicoleen.Potgieter@wits.ac.za> |
| **SUPERVISOR:** | Professor MP Danckwerts |
| **APPROVED BY:** | Dr CB Penny, Chairperson, HREC (Medical) |
| **DATE OF APPROVAL:** | 2021/09/14 |

**This Clearance Certificate is valid for 5 years from the date of approval. An extension may be applied for.**

**DECLARATION OF INVESTIGATORS**

To be completed in duplicate and **ONE COPY** returned to the Research Office secretariat on the 3rd floor, Phillip Tobias Building, Parktown, University of the Witwatersrand, Johannesburg.

I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated from the research protocol as approved, I/we undertake to submit details to the Committee. **I agree to submit a yearly progress report**. When a funder requires annual re-certification, the application date will be one year after the date when the study was initially reviewed. In this case, the study was initially reviewed in **July** and therefore reports and re-certification will be due in the month of **July** each year. Unreported changes to the study may invalidate the clearance given by the HREC (Medical).

Signature of Principal Investigator

14-Sep-2021
Date

## Appendix IV - Permission to conduct research letter from HJPMU Head of Department



GAUTENG PROVINCE
HEALTH
REPUBLIC OF SOUTH AFRICA

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

FACULTY OF HEALTH SCIENCES


Dr Brian Gardner
HCU, Department of Anaesthesia & Pain Management Unit
Helen Joseph Hospital
1 Perth Road
Auckland Park
2092
Tel: (011) 489-0084
Mobile: 082 575 1736
Email: Brian.Gardner@wits.ac.za


23 August 2021

Permission to conduct research for MSc: Ms. Idi Nhiwatiwa

Project Title: The prescribing trends of opioid medications in geriatric patients at the Helen Joseph Hospital Pain Management Unit

PROTOCOL NO: M210742

Permission is granted for Ms. Idi Nhiwatiwa to access patient records to conduct research toward a MSc Medicine (Pharmaceutical Affairs) degree in the Helen Joseph Hospital Pain Management Unit.

Regards,

Brian Gardner

## Appendix V - Approval letter from Management Helen Joseph Hospital

**GAUTENG PROVINCE**
HEALTH
REPUBLIC OF SOUTH AFRICA

**Gauteng Department of Health**
Helen Joseph Hospital
Enquiries: Dr. M. Mukansi
Research Committee: Chairperson
Tel :( 011) 489-0306/1087
Fax :( 011) 489 1038
E mail:Murimisi.mukansi@wits.ac.za

18 June 2021

To whom it may concern

**Subject: HELEN JOSEPH HOSPITAL RESEARCH COMMITTEE APPLICATION**

**PROTOCOL TITLE**: Request to obtain permission to obtain access to patient files from the Helen Joseph plan Clinic

**Principal Investigator:** Idi Chiedzwa Nhiwatiwa

**Ethics Clearance:** Pending

**Co- investigator:** Idi Chiedzwa Nhiwatiwa

**Department:** Helen Joseph Hospital

**Committee Recommendations**
The Committee is giving you Conditional access while awaiting the final ethical clearance certificate from the University of Witwatersrand HREC.

It is the duty of the researcher to collect the data to the relevant department after the Research Committee approved the study.

Dr. M. Mukansi
Chairperson of HJH Ethic and Research Committee