ADEQUACY OF PHARMACOLOGIC PAIN THERAPY IN ADVANCED GYNAECOLOGIC CANCER AT MOI TEACHING AND REFERRAL HOSPITAL- ELDORET, KENYA

BY:

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DECLARATION

Student Declaration

I declare that this research thesis is my original work and has not been presented in any other university or institution for the award of the degree or any academic credit.

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DEDICATION

To my family and friends for their constant support throughout my academic journey

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I would also like to thank my colleagues and staff in the Department of Reproductive Health unit, MTRH and Moi University for their invaluable contribution.

Finally, I thank my family for their immense support and prayers

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ABBREVIATIONS

BPI	Brief Pain Inventory
EFIC	European Federation of IASP Chapters
IASP	International Association for Study of Pain
MTRH	Moi Teaching and Referral Hospital
NCCS	National Cancer Control Strategy
NRS	Numerical Rating Scale
NSAIDS	Non-Steroidal Anti-inflammatory Drugs
PMI	Pain Management Index
POS	Palliative Outcome Scale
QoL	Quality of Life
SSA	Sub-Saharan Africa
VRS	Verbal Rating Scale
WHO	World Health Organization

OPERATIONAL DEFINITIONS OF TERMS

Activities of living Activities that people tend to do daily without needing assistance and are essential for survival

Adequacy Congruence of an analgesic (opioids, NSAIDs and paracetamol) to the severity of pain. Reported as either adequate or inadequate

Advanced gynecologic cancer Distant spread gynecologic cancer usually incurable but it does respond to treatment which may slow down its progression.

Analgesic Pain relief medicine including drugs such as paracetamol, NSAIDS and opioids

Cancer treatment Remedy used in management of cancer aimed at controlling cells growth and / or cancer symptoms. It includes: radiotherapy, surgery, Chemotherapy hormonal therapy, and immunotherapy and angiogenesis inhibitors

Functional interference The degree to which pain impacts various aspects of typical daily functioning

Gynecologic cancer Cancer of the female reproductive system including ovarian cancer, uterine cancer, vaginal cancer, cervical cancer, vulva cancer and choriocarcinoma

Palliative care Approach that aims at improving the quality of life for patients and their families facing the problems associated with life threatening illnesses, through the prevention and relief of suffering

Pharmacologic pain therapy	Analgesics including opioids, non-steroidal medications and paracetamol
Quality of life	Multidimensional construct that includes performance and enjoyment of social roles, physical health intellectual functioning, emotional state and life satisfaction or wellbeing

ABSTRACT

Background: Pain is an unpleasant sensory and emotional experience associated with actual or potential damage and is common with advanced cancer. Prevalence is 40-100% in those with uterine, cervical or ovarian cancers. Under treatment of pain is well acknowledged internationally. Using self- reported pain and validated Pain Management Index (PMI), we assessed adequacy of pain management in gynecological cancer patients at Moi Teaching and Referral Hospital (MTRH).

Methods: This was a descriptive cross-sectional study at MTRH, Eldoret, Kenya, where 112 women with advanced gynecologic cancer were recruited to the study. A questionnaire-based interview using Brief Pain Inventory Tool and a structured questionnaire were used to collect data. PMI was calculated to determine the adequacy of analgesics. Interference of activities of daily living was quantified using a score derived as average of the seven domains of activities of living (range 0-10).Mean and standard deviation were used to summarize interference of activities of daily living .Association between pain medication and some predictive clinical characteristics were evaluated using Fisher's exact test. Comparison between median level of functional interference with analgesics, pain rating and cancer type was evaluated using Kruskal-Wallis test.

Results: Mean age of the participants was 47 years (SD: ± 11.54), majority were over 35 years of age .Cervical cancer was predominant at 60.7% followed by ovarian cancer at 24.1%. The median duration of illness was 12 months (IQR: 8-24).Majority of the participants were on analgesics 85.0% (96), with 78.6 %(88) utilizing opioids. Moderate to severe pain was reported by 72.7% of participants. According to the PMI, 82.1% (92) of the participants received adequate pain management. There was statistically significant association between level of pain and choice of analgesic administered (p-value=0.026), no association between the level of pain and the cancer type (p-value=0.988).Participants reported mild interference with activities of daily living (mean less than 5).

Conclusion: Opioids were utilized by majority of participants, though more than 50% of patients received more potent analgesic than required for their level of pain. Pain management was adequate among majority of the participants. Participants reported mild interference with activities of daily living (mean less than 5).

Recommendations: Continued assessment and evaluation of cancer pain management at the division thus further improving care. Further study to explore patients perspective on the adequacy of advanced cancer pain management

CHAPTER ONE: INTRODUCTION

1.1 Background of the Study

Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage (International Association of Study of Pain, IASP, 1994).In other words; pain is a reaction of the body to a potentially noxious or noxious stimulus and threatens the normal homeostasis

Cancer pain is prevalent in almost 50% of all cancer patients, more common in patients with advanced or metastatic cancer with moderate to severe pain affecting 70-80% of these patients and require strong opioids for adequate relief of cancer pain (Deng et al., 2012); (Augusto Caraceni et al., 2012). Pain is also associated with cancer treatment with more than 25% of patients enduring moderate to severe pain during treatment (He, Liu, Li, Li, & Xie, 2015)

The prevalence of cancer pain is higher in low-and middle-income countries because most patients in this setting (88%-95%) are diagnosed with advanced forms of cancer (Ferlay et al., 2015); (Reville & Foxwell, 2014)

Gynecologic cancer is any cancer that originates from women's reproductive organs. This includes cervical, ovarian, uterine, vaginal and vulvar representing 1 in 5 of all cancers diagnosed in women .Cervical cancer is the fourth most frequently diagnosed cancer and fourth leading cause of cancer death in women with an estimated 604,127 new cases and 341,831 deaths worldwide in 2020 (Global Cancer Incidence Mortality and Prevalence, 2020). Cancer rates are growing in Africa faster than they are in North America. The cervical cancer incidence rate is 40.1%, and the mortality rate is 21.8% in Kenya versus North America where the incidence rate is 6.6%, and mortality rate is 2.6% (International Agency for Research on Cancer)

Over the course of the last decade, the treatment of gynecologic cancer has evolved quite rapidly. New scientific and clinical advances have modified the standard of care and led to improved patient outcomes. Despite the headway in management, disease progression and recurrence continue to afflict women suffering from gynecological cancer. In gynecologic oncology, symptom burden for patients with advanced disease is extensive and this incudes pain amongst other symptoms (Rezk, Timmins, & Smith, 2011). Pain is a very common in gynecologic cancer patients and remains undertreated. Although adequate pain relief is achievable in more than 95% of patients, 20–70% of dying patients still experience inadequately treated pain (Emanuel & Emanuel, 1998). There is very limited literature specific to pain control in gynecologic oncology patients beyond postoperative pain, which we will not address here. Pain is related to the cancer or from its treatment and bears a significant reduction in quality of life (Rannestad & Skjeldestad, 2007).

Pain syndromes commonly seen in gynecologic cancers can result from three primary etiologies. The majority of pain experienced by individuals with cancer originates directly from the tumor (Cherny, N. I., Portenoy, 2000). Pain can also occur as a result of therapy aimed at reducing the tumor, including surgery, chemotherapy, radiation therapy, and hormonal therapy. Finally, people with cancer can develop pain totally unrelated to the cancer or its treatment

Limited clinical data have been published on adequacy of pain management in advanced gynecologic malignancies. A systematic review by (Everdingen et al., 2007) reported a moderate to severe pain prevalence of 60% in this population. Other estimations range from 40% to 100% in those with uterine, cervical or ovarian cancers (Statistical Information Team, Cancer Research UK, 2011).This lack of accurate

prevalence figure is surprising given gynecological malignancies treatment strategies are strongly associated with pain.

Gynecologic oncology patients frequently have higher rates of moderate to severe pain and high opioid needs than patients diagnosed with other cancers (Rees, 1990) (Vainio & Auvinen, 1996)

As stated in the World Health Organization (WHO) guidelines on pain relief and palliative care, assessment of pain and providing appropriate treatment for the same are important aspects of pain management. At present, opioid therapy continues to be the mainstay in treatment of moderate or severe cancer related pain associated with active disease (Portenoy, 2011). Effective opioid therapy requires individualization of the drug and daily dose in an effort to identify a favorable balance between analgesia and side effects. Liberal use of opioids is always suggested for patients with advanced-stage cancer, but a conservative approach to opioid use may result in the under-treatment of cancer pain (Gaertner, Boehlke, Simone, & Hui, 2019). Patients who do not respond to opioid analgesics or cannot tolerate the side-effects, or require high daily dosages should be offered alternative strategies. The most common is the co-administration of another analgesic, either a conventional non-opioid analgesic (e.g. non-steroidal anti-inflammatory drugs [NSAIDs]) or one of the adjuvant drugs (Rigor, 2000). When effective, co-administration of another analgesic not only improves analgesia but also allows for the reduction of the opioid daily dose, which may concurrently have the additional benefit of reducing drug-related side effects.

Pain Management Index (PMI) is a well-validated and widely used method for assessing the adequacy of pain management developed by Cleeland. PMI is modeled

on the concept of the cancer pain treatment guidelines established by the World Health Organization (WHO). Per the tenets of PMI, pain management is considered adequate when there is congruence between patient's subjective self-reported pain intensity and the prescribed analgesic(s). Another indicator for evaluating pain management is pain interference [PI], defined as whether pain interferes with daily life. The Brief Pain Inventory (BPI), another popular instrument for assessing pain, assesses the intensity of pain and interference from pain in seven areas of daily life. PMI and BPI scores are often used to assess patients' pain status and the adequacy of analgesia (te Boveldt et al., 2013) The intensity of pain reflects only the pain, whereas the PI assesses the effectiveness of pain management by using measures like the PMI.

No objective measure for pain exists. It is a symptom which when present, is a subjective indicator perceptible only to the patient. The patient's self report of pain is thus the gold standard of pain assessment. There is no universally accepted tool for assessment of cancer pain. Many different assessment tools are used throughout the world.

Functional interference is the degree to which pain impacts various aspects of typical daily functioning. Peoples' ability or inability to perform activities of daily living (daily self-care activities) is used as a measure of functional status. Common activities of daily living include feeding oneself, bathing, grooming, work, homemaking, and leisure. Untreated or inadequately treated pain in advanced cancer have severe negative impact on the physical and psychological health, functional status and quality of life of cancer patients Pain negatively impacts daily activity, mobility, functioning, sleep quality, entertainment, social interaction, and the professional life of cancer patients (Ovayolu, Ovayolu, Aytaç, Serçe, & Sevinc, 2015) (Oliveira et al., 2014).

The BPI tool is a patient-reported outcome assessment tool that measures the intensity of pain (sensory dimension) and interference of pain in the patient's life (reactive dimension)

Interference of pain on functional performance has statistical significance associated with the stage of the tumor, presence of metastasis, history of treatment modality, history of pain, and pain management adequacy. Patients with an early stage cancer have better scores on functional scales indicating better physical, role and social functioning. On the contrary, patients who have an advanced-stage cancer score higher on the symptom scale, representing a high level of symptomatology and problems, eventually indicating greater difficulties. Patients without pain have better scores on all of functional scales and global QoL (Oliveira et al., 2014)

Very little is known and documented about the extent of gynecologic cancer pain assessment, management and adequacy of its management in developing countries such as Kenya. This study seeks to highlight the adequacy of cancer pain management using PMI in a tertiary oncology center.

1.2 Statement of the Problem

Cancer pain is an international public health problem that millions of cancer patients experience at some stage of their disease. Patients with gynecologic cancer have witnessed an increase in the likelihood of survival yet suffering due to pain continues. This complicates an already well-established incidence within other stages of the disease particularly the incurable phase.

Pain is a very common in gynecologic cancer patients and remains undertreated. Although adequate pain relief is achievable in more than 95% of patients, 20–70% of dying patients still experience inadequately treated pain. There is very limited literature specific to pain control in gynecologic oncology patients beyond postoperative pain.

Pain is more than just physical suffering, it can reduce a patient's ability to work, interact socially, sleep and live a normal life. Effective pain and symptom management at the end of life increases quality of life and may prolong life rather than accelerate death .There is a compelling case to be made that pain experienced by patients with cancer must be better managed, particularly now when more people are living longer with a diagnosis of cancer.

MTRH specifically gynecology oncology division does not have a standard operating procedure / pain management protocol rather follows WHO stipulated guidelines for analgesics' prescription. With very little knowledge and documentation about the extent of gynecologic cancer pain assessment, management and adequacy in developing countries such as Kenya ,the study seeks to close in on this gap

1. 3 Justification

We seek to highlight the adequacy of pharmacologic pain therapy among advanced cancer patients and functional interference among advanced gynecologic cancer patients. Pain can take several dimensions, physical, spiritual, socio-economic or behavioral, and our aim is to assess adequacy of physical pain. To the best of our knowledge, this is the first study in this region among this population.

MTRH is a tertiary institution offering cancer care in various departments. It receives referrals from different parts of the country and largely Western Kenya .Hence the results of this study would be representative of a wider population drawn from different parts of the country.

MTRH specifically gynecology oncology section does not have a standard operating procedure/protocol that guides management of pain but follows the WHO ladder for analgesics' prescribing. Initial pain screening is done by a clinician and analgesic initiated as per severity based on verbal rating of pain. Post treatment with analgesics assessment is not done. Furthermore, no audits are done for the pain management practices. Therefore the study sought to highlight the adequacy of cancer pain management as part of audit of pain management practices among advanced gynecologic cancer patients The study involved advanced cancer patients because this cohort experiences pain as a major symptom and more so moderate to severe pain, and this is in comparison to early stage disease. Therefore it would be worthwhile to explore appropriateness of the pain therapy prescribed in such patients.

Further this study will provide reliable information for formulation of Standard operating procedures /pain management protocol unique to our set-up, for managing

pain among advanced gynecologic cancer patients and this would be crucial to improve symptom management. A better management approach will not only alleviate pain symptoms but will also improve quality of life

Finally accumulating this data will also emphasize the need for better education about pain and its control among health care providers including palliative health specialists in the hospices.

1.4 Research Questions

1. What are the pharmacological pain relieving modalities in use among advanced cancer patients in the gynecology ward?
2. Do cancer patients on treatment get adequate pain management?
3. How does cancer impact various aspects of typical daily functioning?

1.5. Objective

1.5.1 Broad Objective

To assess adequacy of pharmacologic pain therapy in advanced gynecologic cancer patients seen at MTRH

1.5.2 Specific Objectives

1. To describe the pharmacologic pain therapy utilized by advanced gynecologic cancer patients at MTRH.
2. To evaluate adequacy of pharmacologic pain therapy using pain management index in advanced gynecologic cancer patients at MTRH.
3. To assess the level of interference of daily activities amongst advanced gynecologic cancer patients at MTRH.

CHAPTER TWO: LITERATURE REVIEW

2.1 Introduction

Access to pain management is a fundamental human right ("Declaration of Montréal: Declaration That Access to Pain Management Is a Fundamental Human Right," 2011).The World Health Organization (WHO), The International Association for the Study of Pain(IASP) and European Chapters Of the IASP (EFIC) on October 11 2004 declared the treatment of pain a human right in what is referred to as "The declaration of Montreal". Pain is always a personal experience and a person's report of an experience as pain should be respected.

The assessment and management of pain is one of the key indicators of quality of care. Accurate pain assessment is essential for effective management of pain in the patient with gynecological cancers. Adequate pain control should be expected, but complete pain relief may be unrealistic.

Cancer pain is an international public health problem that millions of cancer patients experience at some stage of their disease(Neufeld, Elnahal, & Alvarez, 2017) .The World Health Organization (WHO) estimates that 5.5 million people globally receive no treatment or marginal treatment for their cancer pain (Krakauer, Wenk, Buitrago, Jenkins, & Scholten, 2010). In 2011, 2.7 million people died with unrelieved moderate or severe pain from cancer and HIV, and people in developing countries made up more than 99% of those deaths (American Cancer Society, 2015). The inadequate pain control or undertreated pain in cancer patients remains a global issue.

The prevalence of cancer pain is higher in low and middle-income countries because most patients there (88%-95%) are diagnosed with advanced forms of cancer (Ferlay et al., 2015) (Reville & Foxwell, 2014).

Over the course of the last decade, the treatment of gynaecologic cancer has evolved quite rapidly. New scientific and clinical advances have modified the standard of care and led to improved patient outcomes. Despite the headway in management, disease progression and recurrence continue to afflict women suffering from gynaecological cancer.

In gynaecologic oncology, symptom burden for patients with advanced disease is extensive and this incudes pain amongst other symptoms (Rezk et al., 2011). Pain is a very common in gynaecologic cancer patients and remains undertreated. Although adequate pain relief is achievable in more than 95% of patients, 20–70% of dying patients still experience inadequately treated pain (Emanuel & Emanuel, 1998) .

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of accurate prevalence figure is surprising given gynecological malignancies treatment strategies are strongly associated with pain.

Gynecologic oncology patients frequently have higher rates of moderate to severe pain and high opioid needs than patients diagnosed with other cancers (Rees, 1990) (Vainio & Auvinen, 1996)

Untreated or inadequately treated pain can have a severe negative impact on the physical and psychological health, functional status, and quality of life (QoL) of cancer patients (Deng et al., 2012) (Y. S. Kim et al., 2016) . Pain negatively impacts daily activity, mobility, functioning, sleep quality, entertainment, social interaction and the professional life of cancer patients. The duration and intensity of pain affect QoL and in turn, poor QoL exacerbates the severity of the pain (Rau et al., 2015)

2.1.1 Types of Gynecologic Cancer Pain

Devita, Hellman and Rosenberg, (2008) described three types of cancer pain based on the pathophysiology. The first being the somatic pain involving deep or cutaneous tissues e.g. metastatic bone pain. The second is visceral pain which involves the hollow organs due to infiltration, compression, extension or stretching; it is poorly localized and is usually associated with nausea, and vomiting. The third is neuropathic pain resulting from injury to the nerve tissue. These pains may be caused by tumor itself, treatment modalities or non-cancer related factors. One patient may experience more than one type of pain.

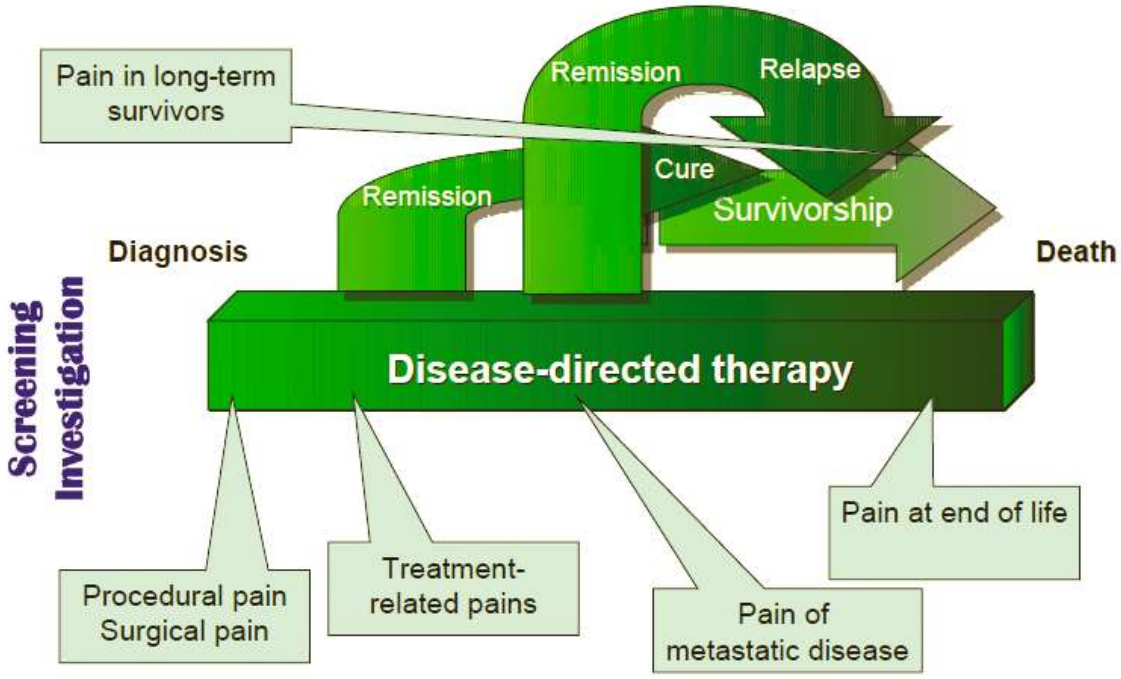

Figure 1: Model of Cancer Disease and Pain (British pain society, 2013)

Somatic pain is due to stimulation of nociceptors in the integument and supporting structures, namely, striated muscles, joints, periosteum, bones, and nerve trunks by direct extension through fascial planes and their lymphatic supply.

In 60% of patients with malignant disease of soft tissues, nerve trunk, and sacral invasion from carcinoma of the cervix, uterus, vagina, they have neuropathic pain. The infiltration of the perineal nerves results in lumbosacral plexopathies and complete destruction of the nerve, including perineural lymphatic invasions producing symptomatic sensory loss, causalgia, and de-afferentation.

Visceral pain is the result of spasms of smooth muscles of hollow viscus; distortion of capsule of solid organs; inflammation; chemical irritation; traction or twisting of mesentery; and ischemia, or necrosis, and encroachment of pelvis and pre-sacral tumors.

Pain of these types is managed by different modalities depending on the age of the patient, the expected life expectancy, availability of invasive and noninvasive pain control modalities, and the resources of the patient, community, and health care agencies. Patients with pelvic cancer can live with less pain due to better pain-control modalities that are available.

2.2 Pharmacologic interventions

2.2.1 WHO Pain Treatment Model /Ladder

The main stay of cancer pain therapy is pharmacological interventions, but radiation, anesthetic neurosurgical, psychological, physiotherapy; spiritual and social interventions also play an essential role in adequate cancer pain management. The symptom burden of pain in gynecologic oncology patients remains high. There is limited literature specific to gynecologic oncology outside of post-operative pain management. However evidence based guidelines addressing cancer pain also apply to gynecologic cancer patients

The WHO recommends a three-level ladder approach to pain management, which includes the use of opioids. This approach has been widely adopted and has led to satisfactory relief in the significant proportion of patients (D. F. Zech, Grond, Lynch, Hertel, & Lehmann, 1995). However, despite the existence of clinically proven guidelines, the prevalence of undertreated cancer pain is relatively high in Asia, that is, 59% compared with 40% in Europe and 39% in USA (Javier et al., 2016)

The purpose of the ladder was to make pain relief available readily to patients with advanced cancer by using effective and inexpensive drugs administered regularly, orally, and on an individual basis while also focusing on safety. Additionally, the WHO guidelines were to facilitate and legitimize the use of “strong” opioids

(morphine and its derivatives) in regions of the world where the use of these medications was unacceptable or illegal

The WHO guidelines though not as specific in direction, encompass a clear and simple approach that has an educational value and is easily remembered and disseminated. Regardless of the age of the WHO guidelines, they still are the cornerstone for cancer pain treatment worldwide

Several guidelines for cancer pain management have been published. In the updated European Association for Palliative Care guidelines, there is no preference among oral morphine, oxycodone, or hydro-morphine as first choice step 3 opioids for moderate to severe pain. WHO guidelines do promote better analgesia though strictly following the ladder may inappropriately delay adequate pain control.

Several retrospective studies have concluded that patients with gynecologic malignancies have higher rates of moderate to severe pain and higher rates of opioid use than patients with other solid tumors (Rees, 1990) (Vainio & Auvinen, 1996). The former study also noted that opioid requirements decrease with increasing age in a regular pattern from early adulthood life. One study looking at opioid needs of terminally ill patients with gynecologic malignancies found that opioid requirements were highest in patients with pelvic metastases (compared with other sites of disease) and that average opioid use was highest among patient with cervical cancer (Lefkowits & Duska, 2017a)

Pain control in ovarian cancer also represents a unique challenge in that the disease may take a relapsing and remitting course spread out over the course of years, making distinctions sometimes used in opioid regulations, such as “active cancer” even more

imprecise. Furthermore, the ability to take oral opiates may be limited by bowel symptoms, and bowel symptoms may confound the utility of oral opiates in treating ovarian cancer pain.

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According to Ripamonti (Ripamonti et al., 2012) an effective pain relieving therapy should consider the following:

1) Enlighten the patients about pain and its management and involve them actively in their pain management.
2) Prophylactic use of analgesics, considering their pharmacokinetic and pharmaco-dynamics to ensure zero pain onset; prescribe analgesics for chronic pain regularly rather than as when necessary.
3) The therapy prescribed should be easy to administer and manage by both patient and the family members with oral route being of first choice if well tolerated.
4) An emergence/rescue analgesic dose should be prescribed for instant relief of breakthrough pain in additional to the regular analgesics which may be similar or different depending on its bioavailability, tolerability and efficacy.
5) The analgesic prescribed should be individualized in terms of dosage, and route of drug administration.
6) Contemplate substitute route of opioid administration in oral intolerance, severe cognitive impairment, or poor pain control.
7) Prevent and manage the possible opioid related adverse effects.

The care of patients with cancer pain requires a multidisciplinary approach to ensure holistic care. This may combine psychological support, socio-cultural support, spiritual support, rehabilitation, and general pain management. This enhances performance of activities of daily living and consequently quality of life or of dying.

Physiotherapists and Occupational therapist play an essential role in the cancer pain management since they possess special skills which empower them to be patient focused and holistic. These therapist aim at enhancing patient functioning and quality of life though not on evidenced based way (Hester et al., 2010)

In addition to these therapies radiotherapy, chemotherapy, hormonal therapy, bisphosphonates and surgery are modalities mostly used in treatment and palliation. Combination of these pharmacological and non-pharmacological pain control techniques maximizes on the pain relief despite notable limitations.

According to W.H.O., 1996, there are 5 approaches to cancer pain management. These are: 1. Psychological approach which includes understanding, companionship and cognitive behavioral therapy, 2. Modification of pathological process approach which include radiotherapy, chemotherapy, hormonal therapy and surgery, 3. Drugs approach which includes analgesics, antidepressants, anticonvulsants, anxiolytics and neuroleptics. 4. Interruption of pain pathways including local anesthesia, neuroleptic agents, and neurosurgery, and 5. Immobilization, rest, cervical collar or corset, plastic splints or slings, and orthopedic surgery.

The WHO has identified cancer pain as one of the global health concern and in 1986 came up with analgesic ladder designed to guide healthcare providers in the prescription of analgesic drugs. Generally it recommends a rational approach for managing pain in different situations including the cancer pain. It advocates for a

stepped approach to the use of analgesics from different classes of analgesic such as; NSAIDS, weak opioids, strong opioid and adjuvants. Adjuvants are not originally analgesics but have been found to be effective especially to neuropathic pain e.g. anticonvulsants.

The ladder comprises of three steps and it suggests that at every step the non-opioid analgesic form the basis of pain management. This means that paracetamol and other NSAIDS should be combined with strong or weak opioid forming steps 2 and 3. This maximizes on efficacy as it keeps the adverse effects low.

The figure below illustrates the W.H.O. analgesic ladder.

Figure 2: WHO Pain Relief ladder

The three step ladder depends on severity of the pain i.e.

- Step 1 mild pain : non-opioid, +/- adjuvants
- Step 2 moderate pain: weak opioid, +/- non-opioids, +/- Adjuvants
- Step 3 severe pain :strong opioid, +/- non-opioid, +/- Adjuvants

The W.H.O. strategy relies mainly on the opioids especially morphine however the role of the adjuvants is unclearly explained. It is effective from 45% to 100% of cases worldwide. Study done on relationship between patient satisfaction and pain control indicate that patient satisfaction does not depend on the pain intensity experienced rather depend on such factors as patients perception of effort to relief pain by health workers among others(Article, Binti, Yusoff, Alrasheedy, & Othman, 2013).

WHO analgesic ladder has clear principle of regular "by the clock" i.e. taking oral medications 3-6 hourly rather than on demand. This has assisted cancer patients throughout the world, cost effectively(Hester et al., 2010).Liberal use of opioids is always suggested for patients with advanced-stage cancer, but a conservative approach to opioid use may result in the under-treatment of cancer pain.

A 10 year prospective study found that the WHO cancer pain guidelines achieved pain control in 88% of cancer patients(D. F. Zech, Grond, Lynch, Hertel, & Lehmann, 1995). Ventafridda and other authors (VentafriddaTamburini, Caraceni, De Conno, & Naldi, 1987) found that the WHO analgesic ladder was efficacious in 71% of cancer pain patients. Another study reported adequate pain control in 70-90% of patients with cancer pain, using the WHO analgesic ladder (Mercadante & Fulfaro, 2005).

Affordability and accessibility are important factors in the choice of analgesics. First step in determining drug use is if it is on the essential medicines list and if not the cost to patients.

A key component of safety and efficacy is to ensure that patients and their caregivers understand the use of the medicines they are taking and that those medicines are reviewed regularly.

In many African countries there are few affordable Step 2 analgesics and in this case a low dose of Step 3 analgesics maybe used. There should be at least one analgesic for each step of the ladder on the Essential Medicines List for each country.

Moderate pain can be treated with a combination of acetaminophen with an opiate, such as hydrocodone or oxycodone. A non-opiate alternative for moderate pain may include tramadol.

Treatment of severe pain begins with long acting opiate agonists such as morphine, hydro-morphine, oxycodone, or methadone. Morphine, oxycodone, and fentanyl are all available in extended-release form as well as short-acting. A patient taking 60 mg of oral morphine daily is a good candidate to convert to using transdermal fentanyl, equivalent to a 25 μg patch every 72 h. Transdermal fentanyl may require24–48 h to achieve pharmacologic steady state, so patients should continue using short-acting opiates while awaiting the full analgesic effect. Most pain can be fairly well managed with a combination of a long-acting opioid and a short-acting opioid for breakthrough pain (Comprehensive & Network, 2014). Dosing of the long-acting opioid should be based on the 24 h needs. In general, the breakthrough dose should be 5–15% of the 24 hour opioid dose every 3–4 h (Portenoy & Ahmed, 2018).

Most long-acting opioids can be dose-adjusted every 2–4 days based on the prior days' need for breakthrough pain medication.

There is no maximal allowable or effective dose for full opioid agonists; the dose should be increased to what is necessary to relieve pain with tolerance. Increasing pain medication needs is usually reflective of worsening of the underlying condition causing the pain. If rotating opioids, a less than fully equi-analgesic dose is usually given to allow for incomplete cross-tolerance (Portenoy& Ahmed, 2018) .

Note that a bowel regimen towards possible constipation should always be considered when prescribing opiate pain medications (Augusto Caraceni et al., 2012).While most pain medications are administered orally, trans-buccal, trans-dermal and trans-rectal options are also available.

On assessment of patient with moderate and severe pain in advanced cancer a long acting opioid is introduced peak effect is usually achieved after 60minutes with use of oral formulations and 15 minutes with intravenous formulations. Pain is reassessed again if pain is unchanged the dose is increased by 50-100%,if the score is 4-6 on pain scales the same dose is repeated and if score is 0-3 the medication is continued at current effective disease.

Pain is reevaluated at each contact and as needed to meet patient specific goals for comfort and function. Assess patient during each outpatient contact or at least each day for inpatients depending on patient's condition and institutional standards.

The majority of patients can have their pain controlled in the homecare / outpatient setting using the WHO analgesic ladder as guide; only in very severe cases may they need to be in-patient. In contrast, patients around the world suffer from the global inequality of pain relief. In 2006, developed nations consumed most of the world's opioid supply. The global mean of morphine consumption was 5.98mg per person per year, while the regional mean for Africa was only 0.33 mg(Harding, Powell, Kiyange, Downing, & Mwangi-Powell, 2010). In 2008, 20 Sub-Saharan African (SSA) countries reported no morphine use at all(Narcotics & Board, 2009)

Though the WHO ladder has been applauded for its simplicity and practicality, it has recently come under criticism due to some noted gaps. It needs revision as new

approaches to pain control such as neuro-modulation, nerve blocks, intrathecal drug administrations ,and non-pharmacological protocols also have been developed(pain is not just physical). It has also been noted to be inadequate in daily practice, especially when dealing with diverse nature and etiology of various pain conditions (Leung, 2012)

There is scarcity of rigorous research on pain management in Sub Saharan Africa, especially research that can be translated into clinical practice(Harding et al., 2010).

Pain assessment and treatment are essential parts of caring for patients, but in SSA there are many barriers to adequate pain control. Assessment goals include determination of etiology, determination if cause of the pain is treatable, impact of pain on patient's life and the best measures to control the pain. Barriers include a deficiency of culturally acceptable and validated pain assessment tools; lack of pain management education for clinicians; unavailability of opioids due to national drug policies an unreliable supply chains; under-prescribing of pain medication; and difficulty in accessing health care (Namukwaya, Leng, Downing, & Katabira, 2011) (Harding et al., 2010)

These factors contribute to a high burden of pain in SSA. In cancer patients receiving inpatient or outpatient care in South Africa, 35.7% reported cancer-related pain. Cancer had a pain prevalence of 87.5% in spite of their participation in palliative care services(Harding et al., 2011). Insufficient training in opioid prescribing may represent a barrier to optimal use of opioids by gynecologic oncologists. Surveys of Gynecologic Oncology trainees confirm that less than 20% reported being taught how to rotate opioids and only about a third were taught how to assess and treat neuropathic pain (Eskander et al., 2014)

2.3 Principles of Cancer Pain Management

The under-treatment of cancer pain is a well-known fact internationally, despite the existence of numerous guidelines for cancer pain management and wide-ranging consensus among health care professionals that 90% of patients with cancer can attain adequate pain relief with analgesics. In a systematic review published in 2008, the prevalence of negative PMI scores among patients with cancer was reported as 43% worldwide, and higher in Asia (Deandrea, Montanari, Moja, & Apolone, (2008)

A more recent report published in 2014 showed slight improvement in the prevalence of negative PMI scores being 31.8% (Greco et al., 2014). However, according to conventional criteria, this means that approximately one third of patients still do not receive pain medication that is proportional to their pain intensity

Effective pain and symptom management at the end of life increases quality of life and may prolong life rather than accelerate death (Sutradhar et al., 2014). Inadequate pain relief may depressingly impact a patient's life. presence and severity of pain has important clinical implications for pain as a variable contributing to health related quality of life provides prognostic information for survival (Efficace et al., 2006)

The WHO developed guidelines for the treatment of cancer pain in 1986 (revised in 1996) aimed at decreasing the prevalence of inadequate analgesia. The WHO method remains of paramount importance and should continue to be encouraged when approaching advanced cancer patients with pain, for the high chances of success, ranging between 70 and 90%. Evidence-based guidelines addressing cancer pain also apply to gynecologic cancer patients

As stated in the World Health Organization (WHO) guidelines on pain relief and palliative care, assessment of pain and providing appropriate treatment for it are important aspects of pain management. Systematic evaluation is indispensable for ensuring appropriate pain management, although it has been found to be effective in treating cancer pain in a majority of patients ,there is an ongoing debate whether these guidelines remain the optimal way of treating cancer pain in all patients (Vardy & Agar, 2014)

Evidence supports the use of anti-inflammatory drugs such as acetaminophen/paracetamol and non-steroidal anti-inflammatory drugs (NSAIDs) for mild cancer pain. Adding an NSAID to an opioid for stronger cancer pain is efficacious, but the risk of long-term adverse effects has not been quantified. There is limited evidence to support using acetaminophen with stronger opioids. newer evidence indicates that patients with moderate pain secondary to cancer are more likely to respond to low dose morphine than they are to codeine ,calling into question whether it's necessary to try weak step 2 opioids before initiating morphine for the control of moderate pain ,especially because there were no differences in adverse effects between the 2 groups (Bandieri et al., 2016)

Management of pain extends beyond pain relief and encompasses the patients' quality of life and the ability to work productively to enjoy recreation and to function normally in the family and society

Despite optimism generated from clinical trial data, uncontrolled pain in cancer patients remains unacceptably high, and this implies that the available effective therapies are not being utilized to the fullest extent.

Cancer pain management has three components 1. Pain assessment 2.Pain measurement 3.Pain treatment

2.3.1 Pain assessment

The assessment of cancer pain is the foundation of its management at all stages of the disease. Inadequate pain assessment is believed to be the leading barrier to adequate pain management (Herr K et al 2004). The accurate and consistent self-reporting assessment of pain is the initial and most important step for an effective and customized pain treatment.

An individual's perception of pain may be influenced by many issues including psychological, social, cultural and spiritual factors. King and colleagues(King & Care, 2008) explored the cultural earnings of pain in White British and Black Caribbean. They found that the Black Caribbean had a higher prevalence of pain and reported more refractory pain than the White British. Specific to the Black Caribbean population in this study was the belief that pain was a test of faith and a punishment. Therefore, patients may be able to accommodate distress depending on what meaning is held about the pain.

Unrelieved pain is associated with unnecessary suffering, functional impairment affects sleep and appetite, leads to pain which may impact one's survival (IASP 2009)

The tools frequently used as Self-pain reporting rate is affected by level of education of the patient with lower rates reported among those with lower education levels compared with those with above pre-university level. This is mainly attributed to poor communication skills among this population with the healthcare providers(Simone, Vapiwala, Hampshire, & Metz, 2012).

Knowledge of mechanism and ability to identify the type of cancer the pain is the base of best practice in pain management. Comprehensive and significant assessment

and reassessment of pain is critical and enhances pain relief. History, examination, psychosocial assessment, and proper record keeping should be routine, in addition to appropriate use of pain measurement tools Data collection and interviews should be conducted in relaxed, comfortable atmosphere. Medical information and previous pain management history is collected. All factors that exacerbate and alleviate pain are carefully determined.

The Palliative/Precipitative, Quality of Pain, Region/Radiation, Severity, Timing (**PQRST)** tool offers valuable guidelines for questions to help assess and measure pain viz precipitating and relieving factors, quality of pain, radiation of pain, site and severity of pain, and timing

Pain assessment may also involve relevant investigations such as x-rays but these should be used sparingly after taking a careful history from the patient and their family.

Comprehensive and significant assessment and reassessment of pain is critical and enhances pain relief. History, examination, psychosocial assessment, and proper record keeping should be routine, in addition to appropriate use of pain measurement tools.

2.3.2 Pain Measurement

Pain measurement is complicated and requires knowledge on the correct use of the measurement tool, understanding of the scoring process and the ability to correctly interpret a score. Obtaining a baseline score is vitally important for comparison with other scores after intervention and to determine treatment efficacy. All patients must be screened for pain at each contact. Pain intensity must be quantified and quality must be characterized by the patient. Comprehensive pain assessment is done with new pain and regularly performed for persisting pain.

Assessment of patient's pain is essential with rating scale but also includes patient reporting qualities of pain, breakthrough pain, treatments used and their impact on pain, patient reporting of adequate comfort and satisfaction with pain relief.

Many pain measurement tools are available but few are tested and validated for use in Africa. There are no tools designed specifically for use in end-of-life pain measurement.

European Association of Palliative Care recommends use of standardized pain assessment tools in research and clinical practice (A Caraceni et al., 2002).These include uni-dimensional scales; visual analogue scales (VAS), numerical rating scales (NRS), and verbal rating scales (VRS) especially in the cognitively impaired, very elderly or patients in the dying phase. They measure one dimension of the pain experience, for example, intensity. They are accurate, simple, and easy to use and understand. They are commonly used for acute pain assessment like post-operative pain assessment.

The multidimensional pain assessment tools provide information about the qualitative and quantitative aspects of pain. They are more useful in chronic and neuropathic pain. They require the patient to have good verbal skills and sustained concentration as they take longer to complete.

These include Brief pain inventory, McGill pain questionnaire, multi-dimensional pain inventory (Clark, Yang, Tsui, Ng, & Bennett Clark, 2002) ,pain disability index, Memorial pain assessment scale and Abbey Pain Scale for assessing pain in non-verbal or cognitively impairment patients such as in dementia

2.4 Suggested Tools for Pain Measurement in Adults

2.4.1 Numerical rating scale

The health worker asks the patient to rate their pain intensity on a numerical scale that usually ranges from 0 (indicating 'No pain') to10 (indicating the 'Worst pain imaginable'). (It is easier from 0-5)

A variation of this scale is a verbal-descriptor scale, which includes descriptors of pain such as 'Mild pain', 'Mild-to-Moderate pain', 'Moderate pain' etc.

The NRS has been found to have high sensitivity and ease of administration compared to similar but non-numerical scales such as the Verbal Rating Scale and the Visual Analogue Scale (Ferreira-valente, Pais-ribeiro, & Jensen, 2011).Other studies have demonstrated that single-item pain scales like the NRS are easily implemented, well-accepted by patients, and useful to clinicians (Wiliams, 2016)

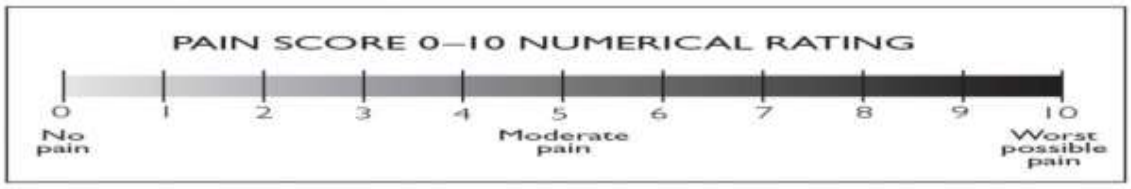

Figure 3: Pain Score numerical rating scale

2.4.2 The hand scale

The hand scale ranges from a clenched hand (which represents 'No hurt') to five extended digits (which represents 'Hurts worst'), with each extended digit indicating increasing levels of pain. **Note:** it's important to explain this to the patient as a closed fist could be interpreted as worst possible pain in some cultures.

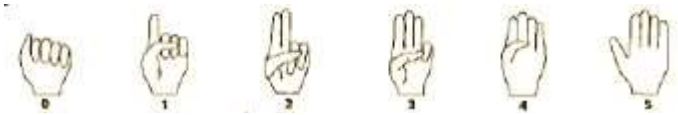

Figure 4: Pain Score hand scale

2.4.3 Verbal rating scale

Acute pain can be reliably assessed, both at rest (important for comfort) and during movement (important for function and risk of postoperative complications), with one-dimensional tools such as numeric rating scales or visual analogue scales. Both these are more powerful in detecting changes in pain intensity than a verbal categorical rating scale

Pain score	Severity of pain
None	No pain
Mild	Pain reported in response to questioning only, without any behavior signs
Moderate	Pain reported in response to questioning and accompanied by a behavioral signs, or pain reported spontaneously without questioning
Severe	Strong verbal response accompanied by facial grimacing, withdrawal of the hand, or tears

Several gaps have been identified with use of the subjective pain scoring tools and they include inability in using them to assess critically ill patients or non-verbal patients, blind or demented patients, inability to perform impeccable pain assessment (only physical pain assessment).They also lack capacity to assess other distressing symptoms (Mutinda, Mutisya, & Oluchina, n.d.)

2.4.4 The APCA African Palliative Outcome Scale (POS)

The APCA African POS (Appendix 3) is a simple and brief multi-dimensional outcome measure, designed specifically for palliative care that uses a range of patient-level indicators including pain. APCA African POS is a validated outcome scale for use in Africa (Harding et al, 2009).

It can be used in multiple settings and by a variety of different stakeholders. Its questions are short and easy to administer, which is important within the palliative care setting. The tool can help determine whether a method of treatment or a particular intervention package is working. It can also be used to clarify which

interventions or packages of care work best for patients with particular sets of problems associated with palliative care.

The question on pain asks the patient to rate their pain (from 0 = no pain to 5=worst/overwhelming pain) during the last three days.

The APCA African POS was developed and validated in English. However, it was acknowledged right from its development that often health care workers will be translating it as they administer it. In the original pilot study for the development of the tool, it was translated verbally into 14languages, including Afrikaans, Swahili, Luganda, Somali and Zulu.

The validation studies have provided rigorous evidence that the APCA African POS has sound psychometric properties and it also appears to have high levels of acceptability and utility in the African clinical setting (Harding et al, 2010).

Several factors are more important to consider when developing a comprehensive strategy to pain control such as depression, presence of other co morbidities, enhancement of adequate social support particularly to those unresponsive to analgesic, and closer monitoring of pain(Ã, Kroenke, Theobald, Wu, & Tu, 2010)

Reassessment of pain intensity must be performed at specified intervals to ensure that the analgesic therapy selected is having the maximum benefit with as few adverse effects as possible

2.4.5 Guidelines for a correct assessment of patient with pain.

(Ripamonti et al., 2012)

1. Assess and reassess the pain
   a) Cause, onset, type, duration, intensity, relief and temporal patterns of pain.
   b) Trigger factors and signs and symptoms associated with the pain.
   c) Use of analgesics and their efficacy and tolerability.
2. Assess and reassess the patient.
   a) The clinical situation by means of a complete / specific physical examination and the specific radiological and / or biochemical investigations
   b) The presence of interference of pain with the patient's daily activities, work, social life, sleep pattern, appetite, sexual functioning, and mood.
   c) The impact of disease and the therapy on the physical, psychological and social conditions.
   d) The presence of a caregiver, the psychological status, the degree of awareness of disease, anxiety, depression and suicidal ideation, his/her social environment, quality of life, and spiritual concerns or needs.

   The presence and intensity of signs, physical and/or emotional symptoms associated with cancer syndromes.
   e) Functional status.
   f) Presence of opiophobia.
3. Assess and reassess your ability to inform and communicate with the patient and the family.

Take time to spend with the patient and the family members to understand their needs.

2.4.6 Brief Pain Inventory (BPI) (Cleeland C, 1991)

This is tool which was developed with aim of evaluating cancer pain that would capture the severity and its impact on activities of living. It also measures the effects of analgesics practice and other pain treatments. It has been tested and retested

extensively for reliability. It is a self-reporting questionnaire that measures the sensory i.e. severity and reactive dimension of pain i.e. interference with daily function and affect.

The BPI is sensitive to the effect of interventions, easy to use for both patients and investigators and is suitable for study of pain across cultures. Additionally, it is highly reliable and valid. It has four items to describe the variability of pain over time i.e. pain at its worst, least, average and current and the rating is based on NRS. Since pain due to cancer can be quite variable over a day. The BPI asks patients to rate their pain at the time of responding to the questionnaire. The 'pain worst' rating can be chosen to be the primary response variable, with the other items serving as a check on variability or, alternatively, these ratings can be combined to give a composite index of pain severity. Pain is further categorized as 0(no pain), 1 (1-3 mild pain), 2 (4-7 moderate pain), or 3 (8-10 severe pain). Since pain can vary to a considerable measure over a day, the BPI asks the patients to rate their pain at the time of responding to the questionnaire. In addition, the questionnaire also asks the respondent to specify the pain at its worst, least and average over the previous 24 hours. Generally takes five minutes to finish for the short form and 10 minutes for the long form. For reactive dimension, the degree of interference is rated using percentage. An effective intervention for cancer pain control should demonstrate its effectiveness on more than a reduction in pain intensity alone. The mean of scores of interference are used as a pain interference score.

To determine the pain management adequacy Cleeland constructed pain management index(PMI) based on the worst pain on the BPI categories, then the pain levels is subtracted from the most potent level of analgesic drug therapy as prescribed scored as 0(no analgesic drugs), 1 (non-opioid), 2 (weak opioid),or 3 (a strong opioid). The

index can range from -3 (a patient with severe pain receiving no analgesic) to +3 (a patient with severe pain receiving strong opioid and reporting pain). Negative score indicate inadequate orders for analgesic drugs and score 0 and higher are considered indicators of acceptable treatment. Benefit of the PMI is to identify patients in severe or even moderate pain who are not receiving appropriate analgesic medications.

Operationally, patient's worst pain intensity is related to the pain medication as prescribed by the physician. Ward's (Ward et al., 1993) and Zelman's (Portenoy, 2011) PMIs use Cleeland's structure with slight modifications: in Ward's version, the worst pain intensity is related to the pain medication as used by the patient; Zelman's version compares current, worst and average pain intensity to the medication used . Some authors have subsequently modified Cleeland's index to improve its validity and sensitivity: Ward et al proposed a more complex index (PMI-Revised) in order to take into account the patient's least pain scores as well. De Wit et al proposed a further revision (Amsterdam PMI) in order to incorporate other dimensions of pain experience: current and average pain intensity, individual threshold of tolerability of pain, noncompliance to the therapy prescribed and the whole pain medication (including all opioids and non-opioids) actually taken by the patient.

With proper use of the WHO analgesic ladder, approximately 88% of patients reportedly obtain reasonable pain relief. Adequacy of pain management can be assessed by the Pain Management Index and the morphine consumption data. Both are based on WHO guidelines for cancer pain management The Pain Management Index (PMI) developed by Cleeland et al (Deandrea et al., 2008) is a validated method of determining congruence between a patient's reported pain intensity and strength of analgesic prescribed. In a systematic review published in 2008, the prevalence of

negative PMI scores among patients with cancer was reported as 43% worldwide, and higher in Asia (Deandrea et al., 2008). A more recent report, published in 2014, showed slight improvement, the prevalence of negative PMI scores being 31.8%. However, according to conventional criteria, this means that approximately one third of patients still do not receive pain medication that is proportional to their pain intensity (Greco et al., 2014).

A study in UK assessing pain management in gynecological malignancy in an outpatient set up, a negative PMI signifying under-treatment was seen in 63% of patients with pain. The conclusion from this study was that patients with gynecological malignancies in the outpatient setting commonly experience pain which is chronic and undertreated.

A study in Ethiopia (Tegegn & Gebreyohannes, 2017), Fifty-four (65%) patients were receiving inadequate cancer pain treatment with negative PMI which is higher than those reported by other authors (Mercadante & Fulfaro, 2005)(Deandrea et al., 2008). However, a review article by Greco et al. reported that inadequate cancer pain treatment can range from 8% to 82% (Greco et al., 2014).

On the other hand, percentage of inadequate cancer pain treatment can be influenced by the study setting. Two studies reported lower rates of inadequate management of cancer pain in the outpatient setting, 33% (Lu & Rosenthal, 2013) and 52.3% (Wu, Natavio, Davis, & Yarandi, 2012). However, a study comparing inadequacy of cancer pain management between outpatient and inpatient settings is needed

A study in South Africa by Beck and Falkson (Beck & Falkson, 2001) reported that only 21% of patients with cancer had achieved 100% pain relief. Thirty percent of patients scored negatively on the PMI. Of this group, 58.1% were experiencing severe peak pain

A Canadian study (Vuong et al., 2015) reported that 33.3% of patients reported inadequate pain management, and 106 of 354 patients reported severe pain despite taking strong opioids. In contrast a study in Ghana reported majority of patients (56%) were over-managed for their pain (had PMI score >=0) though only 26.4% had optimal cancer pain management(Abruquah, Biney, Osei-bonsu, Boamah, & Woode, 2017)

A study of the prevalence and clinical correlates of pain conducted at the MTRH from March to July2011 noted that 66% of inpatients had undertreated pain, with the highest pain scores noted in older adults as well as patients with HIV and cancer(Huang et al., 2013)

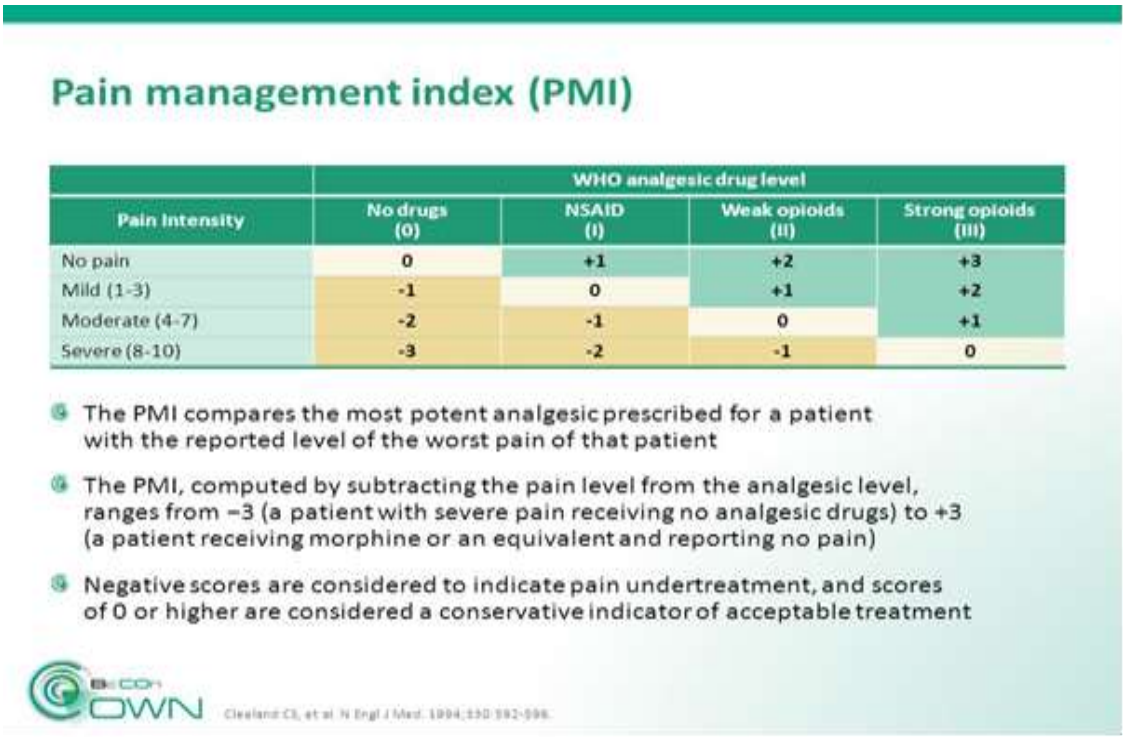

Figure 5: Pain management index

2. 5 Effects of Pain on Performance of Activities of Daily Living

Gynecologic cancer has a significant effect on patients as its diagnosis and treatment are difficult and intensive. The disease leads to a change in the patient's lifestyle. Understanding the nature of cancer and the development of new diagnostic and treatment facilities for the extension of patient survival has drawn attention to improving the quality of life (Akkuzu, Talas, & Ortac, 2014). Studies have revealed the effects of surgery, radiation and chemotherapy on the quality of life in gynecologic cancer (Akkuzu et al., 2014); (Gogoi, Urban, Sun, & Goff, 2012). There are only a few studies in the literature examining effects of pain on performance of Activities of Daily living in patients with gynecologic cancers compared to cancer in general globally

WHO defined quality of life as "individual's perception of their position in the context of culture and value system where they live and in relation to their goals, expectations, standard and concerns". The six components of quality of life include: person's physical health; psychological state; level of independence; social relationships; personal beliefs/spirituality and relationships to relevant features of environment (WHO health promotion glossary (HPG) 1998). Activities of daily living (routine life processes) collectively describe fundamental skills that are required to independently care for one self. These self-care activities involve skills that require one to manage own physical basic needs including personal hygiene or grooming, dressing, toileting, transferring or ambulating, and eating. It is an indicator of person's functional status. Inability to accomplish essential activities of daily living may lead to poor quality of life.

Untreated or inadequately treated pain can have a severe negative impact on the physical and psychological health functional status, and quality of life (QoL) (Deng et al., 2012) of cancer patients. Pain negatively impacts daily activity, mobility, functioning, sleep quality, entertainment, social interaction, and the professional life of cancer patients. The duration and intensity of pain affect QoL (Serlin, Mendoza, Nakamura, Edwards, & Cleeland, 1995) (Y. S. Kim et al., 2016) and in turn, poor QoL exacerbates the severity of the pain. At its worst, severe pain may also lead to an unwillingness to take medications and a desire for death (O'Mahony et al., 2005) .

As pain severity increases to moderate intensity, pain passes a threshold beyond which it is hard for the patient to ignore. At this point, it becomes disruptive to many aspects of the patients life. When the pain is severe, it becomes a primary focus of attention and prohibits most activities. Pain severity and degree to which patient's function is impaired are clearly highly associated. Functional interference is the degree to which pain impacts various aspects of typical daily functioning.

Improvement in QoL is one of the most integral aspects and goals of cancer care, especially for end-stage cancer (Liang, Ding, Wu, Liu, & Lin, 2015), where the focus is on symptom control and delaying disease progression. QoL is an important indicator of symptom relief and can be used as an assessment of the adequacy of pain management in cancer patients.

The BPI tool is a patient reported outcome assessment tool that measures intensity of pain (sensory dimension) and interference of pain in the patient's life (reactive dimension). The reactive aspect of pain also known as functional interference is measured by 7 items (general activity, mood, walking ability, normal work, relations with other people, sleep and enjoyment of life) on the BPI using an 11-point NRS

ranging from 0 which represents "does not interfere" to 10 which indicates "completely interferes Pain interference score is calculated by adding the scores for questions 8.1, 8.2, 8.3, 8.4, 8.5, 8.6, and 8.7 and then dividing by 7. This gives an interference score out of 10. Depending on the intensity of pain, both pain severity and pain interference were classified, using BPI-short form, into four groups: no pain (0), mild pain (1 to 3), moderate pain (4 to 7), and severe pain (8 to 10). General activities entail simple tasks like getting out bed, brushing one's teeth, showering.

This tool adequately reflects severity and impact of cancer pain, is sensitive to the effect of interventions, it is easy to use for both patients and investigators and is suitable for study of pain across cultures.

A longitudinal study in Taiwan demonstrated that cancer patients are affected in many dimensions of their lives by cancer pain. This study was conducted using four instruments to assess performance status, levels of hope and higher levels of total mood status that cancer patients experienced(Lin, Lai, & Ward, 2003)

(Roper, Tierney, Roper, Logan, & Livingstone, 2001) identified 14 activities of living as: Maintaining a safe environment, Communication, Breathing, Eating and drinking, Elimination, Washing and dressing, Controlling, temperature, Mobilization, Working and playing, Expressing sexuality, Sleeping, and Death and dying. Study done in Malaysia concluded that activities of living which also weigh in on the quality of life are affected by pain in almost all cancer patients(Hester et al., 2010). Pain occurs in both ambulatory patients as well as hospitalized patients and mainly affects daily functioning.

Study done in Beijing on quality of life in cancer patients in 2012 concluded that cancer patients with pain have poor QoL which is improved by adequate pain control(Yang, Sun, Pang, & Ding, 2012). This is one of the main outcomes which determine the effectiveness of cancer treatment. Ping further identified pain management satisfaction score, family personal monthly income, those current on chemotherapy, and cancer stage as predictors of pain controlled outcomes. Those with average family income were found to have better pain control while those on chemotherapy and in late stages of cancer had under-treatment. In addition to this a study done in Germany showed that patients with malignancies experience less pain postoperatively compared to those without(Maier et al., 2010). Te Boveldt and co-authors reported interference of pain with daily activities increased with increased intensity, yet even 10%-33% of patients suffering mild pain reported high interference with daily activities. High current pain intensity and high interference with general daily activities predicted moderate to severe pain (te Boveldt et al., 2013)

Study done in Mainland China showed that patients' appetite, mood, sleep, fatigue daily activity, side effect, pain intensity, general appearance and family support was significantly correlated to pain score while social support, attitude to cancer and its treatment is not (Deng et al., 2012).

Inadequate pain management also has a negative impact on care-givers. They are important stakeholders and play a critical role in pain relief strategies for patients (Yang et al., 2012) (Ovayolu et al., 2015) .Caregivers are closest to patients to patients and perform difficult ,disruptive and time-consuming tasks when providing care for patients. When patients have to endure cancer pain, both patients and caregivers experience deterioration in QoL.

CHAPTER THREE: METHODOLOGY

3.1 Study Site

The study was conducted at the Reproductive Health oncology division in the gynecology ward (Faraja ward) at Moi Teaching and Referral Hospital (MTRH). MTRH is situated in Eldoret Municipality in Uasin-Gishu County in Kenya. It is the second largest teaching and referral hospital in Kenya. Being the main referral hospital in Western Kenya, it serves a population of approximately 24 Million from Western Kenya, parts of Eastern Uganda and Southern Sudan. Additionally, it is the teaching hospital for the College of Health Sciences, Moi University.

Faraja ward has two divisions namely: general gynecology and oncology divisions for admission of general gynecology and gynecologic oncology patients respectively. The oncology section is run by 4 consultants (Gynecologic-oncology specialists), 5 fellows sub specializing in gyne-oncology and nursing staff. Other supporting staff includes dieticians and psychological counselors. The gyne-oncology division manages pain using WHO guidelines; no specific protocol has been developed to guide pain management for advanced cancer patients. Other than symptom management, the patients are offered psychosocial support. Post treatment re-assessment is not routinely done.

3.2 Study Design

This is a cross- sectional study, because the design is suitable when studying one or more variables with a given population at one point in time. It is also suitable for establishing associations between study variables (Mann, 2003). The study was conducted in the oncology division of the gynecology ward among advanced gynecology cancer patients from May 2019 to May 2020.

3.3 Study Population

The study population was females with gynecological cancers admitted in the oncology division in the gynecology ward who met the eligibility criteria

3.4 Target Population

The target population was 159 (MTRH records 2018) female patients admitted in gynecology ward oncology section with gynecologic cancer

3.5 Study Procedure

Research assistants (2) were recruited and trained by the principal researcher on the objectives of our study, administration of structured questionnaire and the Brief Pain Inventory tool, how to obtain informed consent from participants and how to handle and complete questionnaires and consent forms.

Study participants were recruited from the ward. All patients admitted in the oncology division were identified from the register. Those with advanced gynecologic cancer(stage 3 and 4) were identified from clinical records as per reviews made by the gynecologic oncology team(gynecologic oncology fellows and gynecologic oncology consultants).The cancer stage was corroborated by myself and all the patients' staging was concordant. Those who met the eligibility criteria were approached and participants who consented were recruited into the study. Consecutive sampling was carried out till sample size achieved. Participants exited the study after data collection was completed.

Prior to data collection, both tools were first translated to Swahili by a trained translator and then back translated to English by a different trained translator to verify accuracy. This was finally translated again into Swahili and eventually retained its originality

We collected demographic data including; age, marital status, income- generating activities, health financier, level of education. Clinical information on diagnosis and clinical stage of the cancer and the analgesia prescribed were obtained from the patient's file.

A validated and reliable multi-dimensional pain assessment tool (BPI) was used to collect information on pain severity and impact of the same on daily function or activities of daily living. The questionnaire-based data collection has an 8-item questionnaire which was applied to assess the impact and severity of pain on the daily functioning of the patient. This tool has four pain severity items and seven pain interference items rated on 0–10 scales with a 24-hour recall period. The BPI assesses pain at its "worst," "least," "average," and "now" (current pain). . The 'pain worst' rating can be chosen to be the primary response variable, with the other items serving as a check on variability or, alternatively, these ratings can be combined to give a composite index of pain severity. For this study the "worst" pain rating is used as the primary response variable.

Using BPI-SF, severity and interference pain was classified into 4 groups: no pain (0), mild (1 up to 3), moderate (4 up to 7), and severe (8 up to 10) According to the type of analgesic medication(s) patient uses, scores were given as follows: 0 (no analgesic drug), 1 (non-opioid analgesic), 2 (weak opioid), and 3 (strong opioid), and then PMI was determined. Four levels of analgesic medications were estimated by the potency: (0) no order for analgesic drug, (1) non opioid (non-steroidal anti-inflammatory drugs), (2) weak opioid (codeine), and (3) strong opioid (morphine), and then potency of drugs was compared with "worst pain." No pain was scored as "0," mild pain "1," moderate pain "2" and severe pain "3.". The information obtained using the BPI was

used to compute a pain management index which is used to gauge the adequacy of pain control .This is done using "worst" pain rating as per the BPI entry

To calculate PMI, pain level is subtracted from the most potent level of analgesic drug therapy as prescribed. A score of "0" or more indicates adequate pain management

A score of less than "0" indicates inadequate pain management

The interference items are presented with 0–10 scales, with 0=no interference and 10=interferes completely. This mean can be used if more than 50% or four of seven, of the total items have been completed on a given administration.

3.6 Sample Size Calculation

The primary outcome of the study was adequacy of pain management among patients with advanced gynecological cancers at Moi Teaching and Referral Hospital as measured using pain management index. Literature shows that 23% of patients who were being managed by physicians for pain due to advanced malignancies, which were not specified by site/organ of origin among hospitalized patients in oncology department of Singh medical college in India, had attained adequate pain management. However, there were no studies that looked into the adequacy of pain management purely for patients who were being managed for gynecological cancer in an inpatient setting. Hence, it was assumed that 50% of patients being managed for gynecological malignancies attained adequate pain management. In order to be 95% sure in determining the proportion of patients being managed for advanced gynaecological malignancies with adequate pain management at MTRH, the sample size was determined using the Fischer's formula (1998).

$$n = \left(\frac{Z_{1-\alpha/2}}{d}\right)^2 \times P \times (1-P)$$

$$= \left(\frac{1.96}{0.05}\right)^2 \times 0.5 \times (1-0.5)$$

$$\alpha = 385$$

Where Z is the standard normal distribution = 1.96, αis the type I error = .05, P is the proportion of patients reported to have adequate pain management = 0.5 d is the margin of error= 0.05..A further formula for infinite population will be used as suggested by Fisher (1998) to determine the desired sample size when the population is less than 10,000. The formula is as presented below: nf = n/ (1 +n/N) Where; nf = The desired sample size, when the population is less than 10,000. n = the desired sample when population is more than 10,000. N = the estimated population size of adult female cancer patients admitted in the gynecology ward. Therefore; nf = 385/ (1 + 385/159) which is equivalent to 112 respondents.

3.7 Sampling Technique

Consecutive sampling was used to select participants in that everyone who meets the inclusion criteria was enrolled until the desired sample size of 112 was reached. This technique was chosen as it focused on particular characteristics from the target population which will be best able to answer my research questions. The sample frame was obtained from MTRH health information and statistics department. According to the statistic of the year 2018, an average of 159 patients was admitted in the oncology division of the gynecology ward where patients with gynecologic cancer are admitted.

3. 8 Eligibility Criteria

3. 8.1 Inclusion Criteria

1. Patients with a diagnosis of advanced gynecologic cancer
2. Age ≥ 18 years

3. 8.2 Exclusion Criteria

1. Patients with speech and hearing difficulties.
2. Patients with memory impairment (assessed using mini mental state examination).

3. 9 Data analysis and Presentation

The data collected was entered into MS Access database. During entry the patient identifying information was stripped off. Data verification and cleaning was done once data entry was completed. The cleaned data was encrypted with password to ensure patient confidentiality is maintained. The password was made available to the principal investigator only. Backup of the database was done using external data drive and kept in separate safe locations to cushion against data loss. After data entry was completed the questionnaire were retained by the principal investigator.

Descriptive statistics such as the mean and the corresponding standard deviation or the median and the corresponding inter quartile range were used to summarize continuous variables such as age, level of income, duration of illness, and level of interference. Frequencies and the corresponding percentages were used to summarize categorical variables such as stage of the cancer, type of cancer, marital status, education level, pain scores, and health financier.

The proportion of patients receiving each type of pharmacologic pain therapy was reported.

Adequacy of pharmacologic pain management was derived using the PMI. The score ranged from -3 to -3. The proportion of patients with a score of zero, 1, 2 or 3 was said to have attained good pain management level.

Interference of the activities of daily living was quantified using a score derived as the average of seven Likert scale variables assessing activities of daily living. This gave a score in the range of 0 - 10. The mean and the corresponding standard deviation were used to summarize interference of activities of daily living.

Association between some predictive variables (duration of illness, level of pain, cancer types and pain medication) and outcome of interests (pain management adequacy and pain interference on functioning) using binary logistic regression and Fisher's exact test was done to identify determinants of outcome of interest. Kruskal Wallis test was used to compare median level of interference (ordinal variable) with pain medication, cancer type and pain severity. The tests of significance were considered statistically significant if the p-value was less than 0.05. Data analysis was done using SPSS version 24.

3. 10 Ethical Clearance

1. Institutional research and ethics committee (IREC) approval was obtained before commencement of the study. (Appendix 6)
2. Approval from MTRH was also obtained to conduct the research in the institution (Appendix 7)
3. Written informed consent was obtained from each study participant prior to enrollment into the study. (Appendix 3)
4. Privacy and confidentiality was ensured by consenting and interviewing study participants in private, storing data collection forms under lock and key and databases were password protected.

3.11 Data Dissemination

The abstract has also been submitted to various reputable journals for consideration for publication.

The research findings will also be presented in various conferences and seminars. A copy of this thesis document will be availed to the MTRH management to help inform protocol formulation to improve palliative services and also be used as a baseline for further research in palliative care.

CHAPTER FOUR: RESULTS

4.1 Socio demographic characteristics

A total of 112 participants were recruited into the study, of which 112 completed the study. The mean age of the women was 47 years (SD: ±11.54).Majority of the women were married 80.4 % (90) while 22 (19.6%) were either single or separated. In terms of education, majority 66.1% (74) had below secondary level of education with only 10(8.9%) having post-secondary education. Majority of the interviewed participants 68(60.7 %) were unemployed and 68 (60.7%) had national health insurance.

Table 1: Socio-demographic characteristics of the participants

Variable	N=112
Age in years	
<=20	4 (3.6%)
21-35	11 (9.8%)
>=35	97 (86.6%)
Education level	
Primary	74 (66.1%)
Secondary	28 (25.0%)
University/Tertiary	10 (8.9%)
Marital status	
Single	20 (17.9%)
Married	90 (80.4%)
Separated/	2 (1.8%)
Occupation	
Unemployed	68 (60.7%)
Formal Employment	9 (8.0%)
Business	35 (31.2%)
Health Financier	
Self	44 (39.3%)
Insurance	68 (60.7%)

4.2 Clinical Characteristics

4.2.1 Cancer Type

Cervical cancer was the most predominant cancer at 60.7% followed by ovarian cancer at 24.1%. Only 2 (1.8%) participants had endometrial cancer as shown in

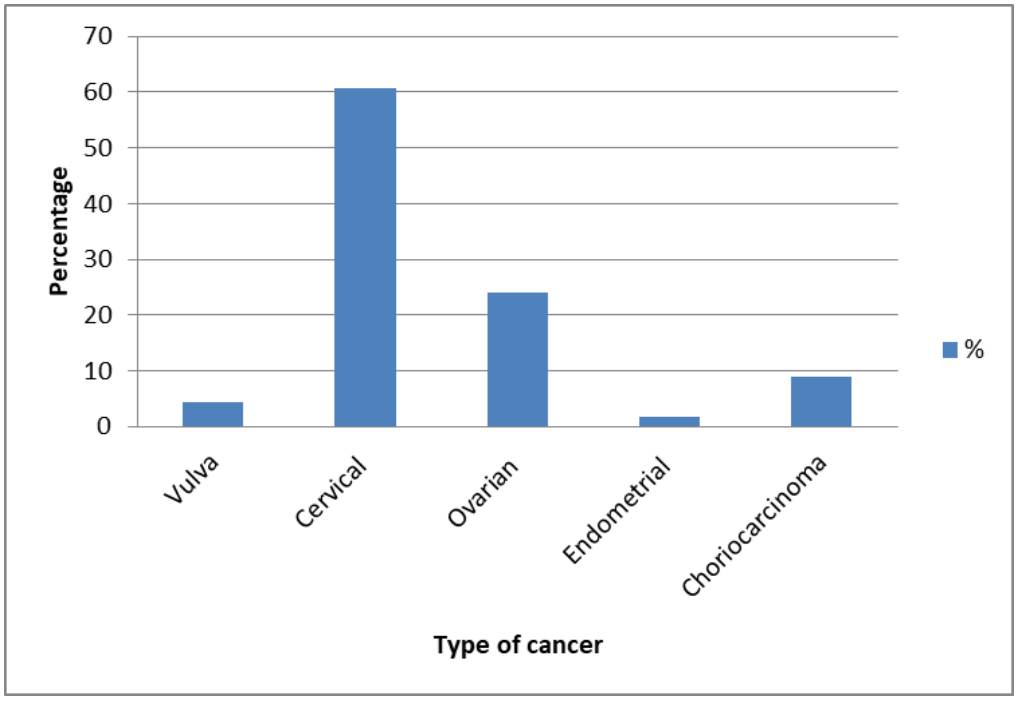

Figure 6: Cancer type

4.2.2 Duration of illness

The median duration of illness was 12 months (IQR: 8-24). Majority of the study participants 61(54.5%) reported to have had a cancer diagnosis for a period of less than 12 months and only 10 (8.9 %) had had the diagnosis for over 24 months.

Table 2: Duration of illness

Variable (N=112)	Frequency (n)	Percent (%)
Illness Duration		
< =12 Months	61	54.5
13-24 Months	41	36.6
>24 Months	10	8.9

4.3 Pharmacologic Pain Therapy

Majority of participants, 85.7 %(96) reported to be on pain medications. Strong opioids like morphine were utilized by 63.4% (71), followed by weak opioids (tramadol) utilized by 15.2 % (17). 7.2 % of participants were on other analgesics other than opioids. The data on analgesics was derived from the records as prescribed and given for the last 24 hours of interviewing the participants. Some participants were on combined analgesics so the displayed results are based on the most potent of the combination analgesic prescribed.

Table 3: Pain management

Variables	Overall (N=112)
On pain killers	
No	16 (14.3%)
Yes	96 (85.7%)
Pain therapy	
None	16 (14.3%)
NSAIDS	4 (3.6%)
Strong Opioids	71(63.4%)
Paracetamol	4(3.6%)
Weak opioids	17(15.2%)

4. 4 Adequacy/Inadequacy of pharmacologic pain therapy

4.4.1 Pain intensity/severity in the participants

Majority of the participants, 52.7 %(59) rated their pain as moderate (pain rating of 4-7), 20% (22) of them reported severe pain (pain rating of 8 or greater), 25.5 %(29) reporting mild pain (1-3). Only two participants reported having no pain (1.8%). The pain ratings given were as "worst" pain as experienced over the last 24 hours within interviewing the participants.

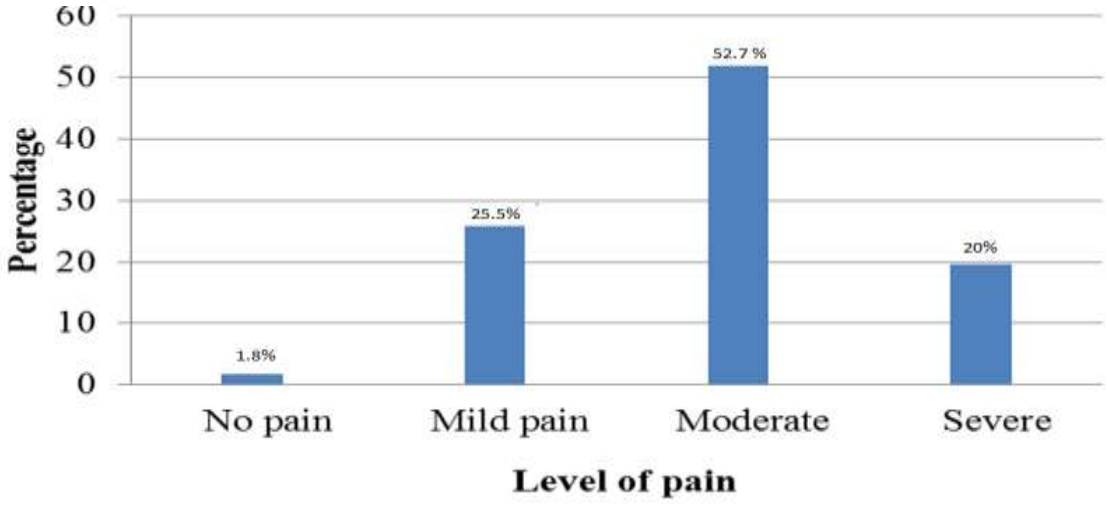

Figure 7: Proportion of Pain rating among the participants

4.4.2 Association between pain medication ,cancer type and level of pain

We assessed the association between the pain medication, cancer type and the level of pain. We observed that there was a statistically significant association between the choice of medication administered and the level of pain (p-value=0.026), however there was no association between the level of pain and the cancer type afflicting the participants (p-value=0.988)

Table 4a: Association between level of pain , cancer types and pain medication

Variable	Pain rating				Fishers' exact p value
	No pain	Mild pain	Moderate	Severe	
	Freq (Row%)	Freq (Row%)	Freq (Row%)	Freq (Row%)	
Pain medication					0.026[1]
None	2 (12.5%)	5 (31.2%)	7 (43.8%)	2 (12.5%)	
Non Opiods	0 (0.0%)	6 (54.5%)	4 (36.4%)	1 (9.1%)	
Opiods	0 (0.0%)	18 (21.2%)	48 (56.5%)	19 (22.4%)	
Cancer type					0.988[1]
Vulva Cancer	0 (0.0%)	1 (3.4%)	3 (5.1%)	1 (4.5%)	
Cervical cancer	2 (100.0%)	19 (65.5%)	32 (54.2%)	15 (68.2%)	
Ovarian cancer	0 (0.0%)	6 (20.7%)	16 (27.1%)	5 (22.7%)	
Endometrial cancer	0 (0.0%)	0 (0.0%)	2 (3.4%)	0 (0.0%)	
Choriocarcinoma	0 (0.0%)	3 (10.3%)	6 (10.2%)	1 (4.5%)	

[1] Fisher's Exact Test

4.4.3 Adequacy using PMI

Most of participants, that is, 92 (82.1%) had an acceptable treatment based on the PMI scores, (a score of 0 and above). The proportion of patients with negative PMI was 20(17.9%) , this indicated under-treatment of pain in at least 1 in 8 patients and meaning less than adequate analgesics based on WHO guidelines prescribed for this proportion of patients.

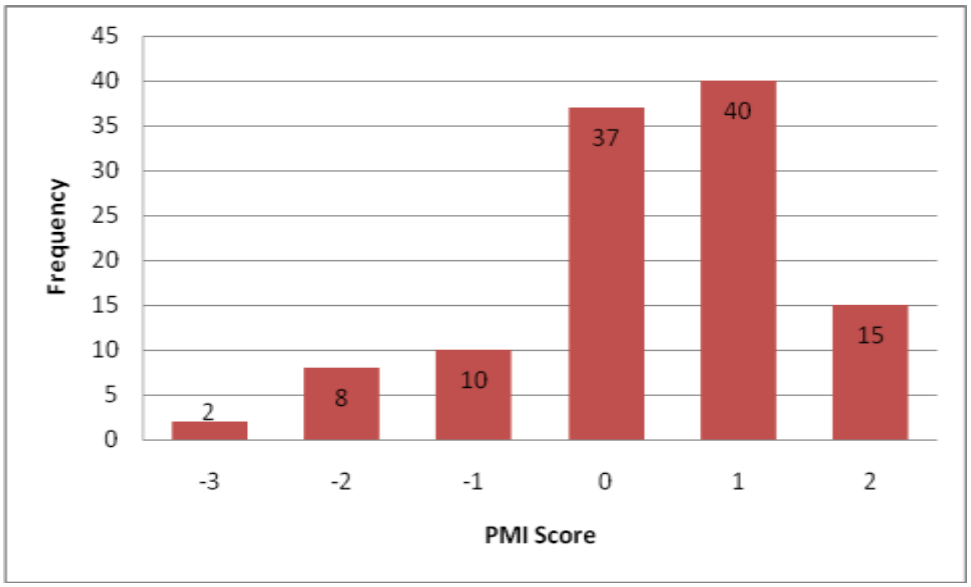

Figure 8: Proportion of PMI score

4.4.4. Relationship between adequacy of pain management and type of cancer

We observed that adequacy of pain management among women with cancer did not statistically differ by the type of cancer afflicting them (p-value=0.595)

Table 4b : Adequacy of pain management by type of cancer.

Type of cancer	Adequate (N=92)	Inadequate (N=20)	Total (N=112)	p value
				0.595[1]
Vulva Cancer	4 (4.3%)	1 (5.0%)	5 (4.5%)	
Cervical cancer	58 (63.0%)	10 (50.0%)	68 (60.7%)	
Ovarian cancer	21 (22.8%)	6 (30.0%)	27 (24.1%)	
Endometrial cancer	2 (2.2%)	0 (0.0%)	2 (1.8%)	
Choriocarcinoma	7 (7.6%)	3 (15.0%)	10 (8.9%)	

[1]Fisher's Exact Test

4.5 Interference with activities of daily living/level of functional interference

We observed that the mean level of interference in all the domains was less than 5 with the highest being interference in general activities. We observed that the scores were highly dispersed with outliers in mood, sleep and walking ability, however the median were also below 5 indicating that majority of the participants pain didn't interfere with activities (Figure 9).

We combined the scores in the 7 domain and the mean scores for the overall interference in daily activities was 25.26 (SD: ±11.54).The overall median was 19(IQR: 12-37.25) (figure 10).

Table 5: Interference of daily activities

Activity	Mean (sd)
General activity	4.321 (2.755)
Mood	3.670 (2.628)
Walking	3.589 (2.849)
Normal work	3.571 (3.086)
Relations	3.116 (2.992)
Sleep	3.241 (3.186)
Enjoyment	3.750 (3.311)

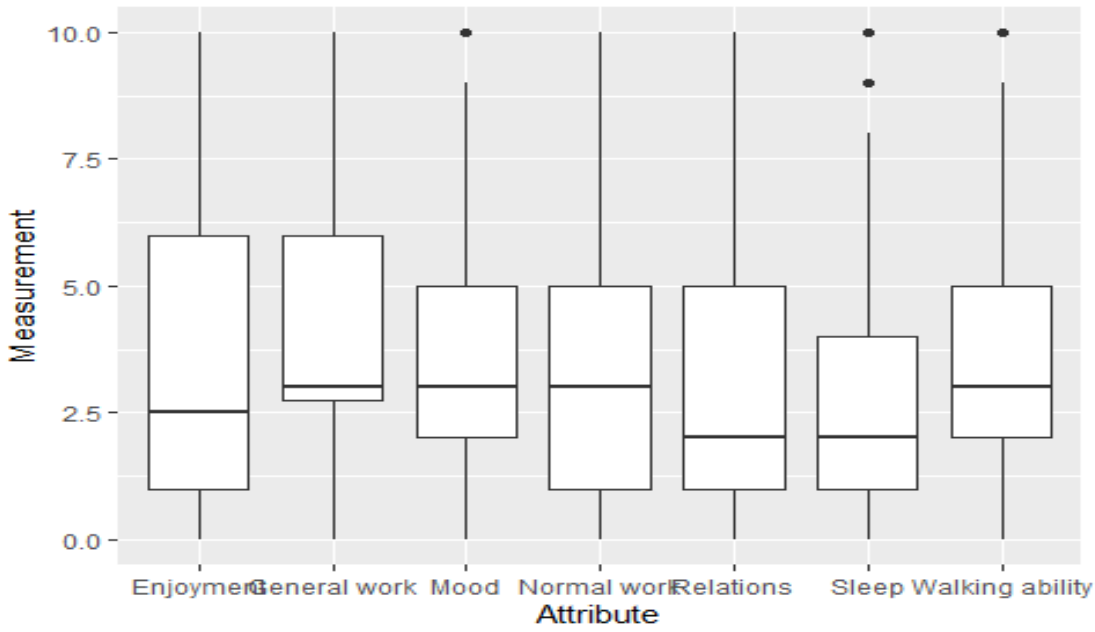

Figure 9: Box plots of the scores of interference among the participants by activity

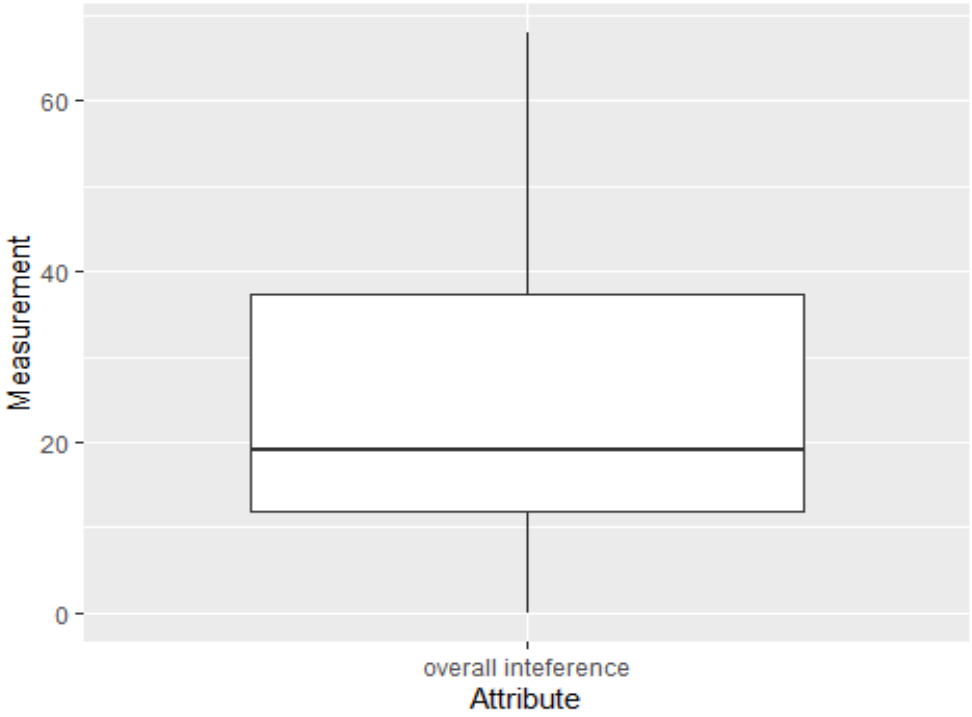

Figure 10: Box plots of the scores of interference among the participants

4.5 .1 Comparison of level of interference with pain severity, medication and type of cancer

We observed that there was a statistically significant association between interference and pain rating with those who reported to have severe pain recording a high level of interference (median=50.5) compared to those without severe pain (p-value<0.001). There was no statistically significant association between the type of cancer, pain medication and level of interference (p-value>0.05).

Table 6: Level of interference by: Pain medication, cancer types and pain severity

Variable	Median	LQ, UQ	Kruskal Wallis P-value
Pain severity			< 0.001
Mild pain	11	7.0, 15.0	
Moderate	19	14.0, 28.5	
No pain	0	0.0, 0.0	
Severe	50.5	38.25, 61.5	
Cancer Type			0.374
Vulva Cancer	18	14.0, 33.0	
Cervical cancer	16.5	11.0, 38.25	
Ovarian cancer	19	15.0, 27.5	
Endometrial cancer	59	58.5, 59.5	
Choriocarcinoma	16.5	15.25, 28.25	
Pain medication			0.126
None	14.5	2.0, 23.25	
Non Opioids	21	9.0, 37.5	
Opioids	19	13.0, 38.0	

CHAPTER FIVE: DISCUSSION

Pain is one of the most frequent and distressing symptoms experienced by cancer patients, and it affects their quality of life Okuyama et al, (2004). However, evidence from clinical practice indicates that pain of cancer patients may be treated in up to 90% cases with the current analgesics (D. F. Zech et al., 1995) (Mercadante & Fulfaro, 2005)

There are limited reports in adequacy of pain management in Kenya and specifically in advanced gynecologic cancers. To the best of our knowledge, there is no similar study conducted at MTRH. It is our fervent belief that this study will underscore the importance of cancer pain management and provoke a region-wide research to investigate the true state of gynecologic cancer pain management in sub-Saharan Africa.

5.1 Pharmacological pain therapy utilized

The symptom burden of pain in gynecologic oncology patients remains high. There is limited literature specific to gynecologic oncology outside of post-operative pain management. However, evidence-based guidelines addressing cancer pain also apply to gynecologic cancer patients. There exists several practice guidelines designed to facilitate and standardize pharmacologic cancer pain management and advise physicians worldwide on how to achieve optimum cancer pain control. In the updated European Association for Palliative Care guidelines, there is no preference among oral morphine, oxycodone, or hydro-morphine as first choice step 3 opioids for moderate to severe pain. WHO guidelines do promote better analgesia though strictly following the ladder may inappropriately delay adequate pain control.

The WHO recommends a three-level ladder approach to pain management, which includes the use of opioids. This ladder algorithm allows selection of analgesics as well as adjuvants based on the pain intensity This approach has been widely adopted and has led to satisfactory relief in the significant proportion of patients (D. F. Zech et al., 1995). More recently this model has been revisited, such that non-opioids, adjuvants, education and psychosocial support should be considered at each step along the way.

Though the WHO ladder has been applauded for its simplicity and practicality, it has recently come under criticism due to some noted gaps. It needs revision as new approaches to pain control such as neuro-modulation, nerve blocks, intrathecal drug administrations ,and non-pharmacological protocols also have been developed(pain is not just physical). It has also been noted to be inadequate in daily practice, especially when dealing with diverse nature and etiology of various pain conditions (Leung, 2012)

In this study, strong opioids (e.g. morphine) were frequently used in the management of moderate cancer pain in 71 participants (63.4%).

This compares to a study by Vuong and co-authors in Canada with 55.4% of their participants utilizing strong opioids (Vuong et al., 2015). This study looked into prevalence of undertreated pain in an outpatient radiotherapy clinic where it was noted that patients were not adequately prescribed for opioids in an outpatient setting despite experiencing severe pain.

Although strong opioids represent the first-line treatment of choice for the management of moderate-to-severe cancer pain, many countries record low or even no use of opioid analgesics relative to the estimated need for opioid analgesics

The results of this study are different from the results of a study looking into adequacy of pain management in advanced cancer (regardless of site) where weak opioids and NSAIDS were commonly used for the management of moderate and severe cancer pain (HARMINDER SINGHPain et al., 2018). The disparity in terms of prescription may be due to differences in terms of access to health care and prescription drugs, irregular supply of opioids, and reluctance of physicians to prescribe opioids. Access to opioids is significantly impaired in several Asian countries because of limited opioid formularies or excessively restrictive opioid policies (Cleary, Radbruch, Torode, & Cherny, 2013). Moreover, many physicians and patients are reluctant to use opioids because they have inadequate knowledge about their use (Y. C. Kim et al., 2015). As a result, many patients with moderate or severe pain do not receive adequate treatment to relieve their suffering.

For patients with cancer pain, it is important to select the most appropriate management of moderate to severe cancer pain regardless of their disease stage to have a positive effect on the quality of life. Opioids are the mainstay of treatment for cancer pain at the second and third steps according to the 3-step analgesic ladder of the World Health Organization. Awareness of the safe and effective use of opioids in the oncology setting is essential to the provision of adequate pain relief. As adverse effects often occur, the oncology team must be skilled in preventing and managing constipation, nausea, sedation and neuro-toxicities. Safe and effective opioid use in patients with cancer requires balance and skill. These skills include comprehensive assessment, understanding the pharmacokinetics and dynamics of these agents, and knowledge of dosing, titration and rotation. Balance speaks to the awareness that opioids might be misused (Bruera & Paice, 2015)

Most cancer patients who are prescribed opioid analgesics will derive safe and effective pain relief from these products. Thus, it is neither scientifically valid nor medically compassionate to withdraw opioid analgesics from the cancer patients who may need them. On the other hand, it is important to appreciate that inappropriate opioid use, abuse and addiction, are possible among cancer patients and steps must be taken to safeguard them. A subset of cancer patients may even be at elevated risk for opioid abuse (Pergolizzi et al., 2016)

5.2 Adequacy of pain management

Gauging the adequacy of pain management in cancer research is distinctly different from merely assessing pain intensity or pain relief because inadequacy is a predictor of functional impairment. The assessment and management of pain is one of the key indicators of quality of care. Accurate pain assessment is essential for effective management of pain in the patient with gynecological cancers. Adequate pain control should be expected, but complete pain relief may be unrealistic.

With proper use of the WHO analgesic ladder, approximately 88% of patients reportedly obtain reasonable pain relief. Adequacy of pain management can be assessed by the Pain Management Index and the morphine consumption data. Both are based on WHO guidelines for cancer pain management The Pain Management Index (PMI) developed by Cleeland et al (Deandrea et al., 2008) is a validated method of determining congruence between a patient's reported pain intensity and strength of analgesic prescribed.

In this study, a total of 112 with advanced gynecologic cancer patients participated. We found that 98.2 % of our participants had pain viz 20% (severe pain), 52.7% (moderate pain) and 25.5% (mild pain) of them had cancer-related pain. These

findings are not unusual as gynecologic oncology patients frequently have higher rates of moderate to severe pain and high opioid needs than patients diagnosed with other cancers (Vainio & Auvinen, 1996) .

This is comparable with the study result from Canada which reported 96.6% of cancer patients experience cancer related pain (Vuong et al., 2015) but much higher as compared to the study result from United Kingdom which reported only 38% of patients had cancer related pain(Yen, Gubbay, Kandikattu, Chapman, & Williams, 2012). The difference in the results between our report and this last study is could be due to the fact that the proportion of participants experiencing pain was lower, in addition to utilizing pharmacological pain therapy they were also on alternative therapies such as massage and acupuncture.

Caraceni and colleagues in 2012 reported that 70-80% of patients with advanced/metastatic cancer experience moderate to severe pain requiring strong opioids for management (Augusto Caraceni et al., 2012).

There exist several guidelines designed to facilitate and standardize cancer pain management and advice physicians on how to achieve optimum cancer pain control. Selection of an analgesic should be individualized and based on pain intensity. In this study strong opioids were frequently used (Morphine) in management of mild to moderate pain which is contrary to WHO analgesic ladder stipulation on pain intensity that reserves use of opioids for moderate to severe pain.

We observed that there was a statistically significant association between the medication and the level of pain (p-value=0.026), however there was no association between the level of pain and the cancer type (p-value=0.988). Similarly several retrospective studies have concluded that patients with gynecologic malignancies

have higher rates of moderate to severe pain and higher rates of opioid use than patients with other solid tumors(Rees, 1990) (Vainio & Auvinen, 1996).

In contrast, a study by Lefkowits et al assessing opioid needs in advanced gynecologic malignancies found that opioid requirements were highest in patients with pelvic metastases(compared with other sites of disease) and that average opioid use was highest among patients with cervical cancer (Lefkowits & Duska, 2017)

Although the PMI is the best available and most widely used instrument to measure pain treatment adequacy, it remains only a gross indicator of pain treatment adequacy because it focuses on opioid analgesic prescribing categories and does not reflect the dosing of opioids or use of non-opioid pain interventions.

Greco et al updated a systematic review initially done by Dendrea et al by encompassing PMI articles published from 2008-2013. They found a decrease in the incidence of under treatment in cancer specific centers from 58.2% to 28.7 % (Greco et al., 2014)

We found that the proportion of patients with negative PMI was 17.9% which indicated under treatment of pain. This is comparable to a study by Abruquah and co-authors (Abruquah et al., 2017) . The proportion of patients with negative PMI was 16%, which indicated under treatment of pain and less-than-adequate analgesics based on the WHO guidelines

In this study 82.1 % (92) had positive PMI indicating acceptable /adequate treatment based on the PMI scores of “0” and above .Similar findings noted by Abruquah (Abruquah et al., 2017) in a Ghanaian study who reported a positive PMI of 84%.

This contrasts a study in UK looking at similar outcomes in an outpatient set-up that reported inadequate treatment at a frequency/proportion of 63%. The conclusion from

this study was that patients with gynecological malignancies in the outpatient setting commonly experience pain which is chronic and undertreated. Other contrasting findings are by Harminder (HARMINDER SINGHPain et al., 2018) and Tegegn and colleagues (Tegegn & Gebreyohannes, 2017) who reported negative PMIs of 77% and 65% respectively.

In this study, strong opioids (e.g. morphine) were frequently used in the management of mild to moderate cancer pain therefore it is not surprising that majority of the participants in this study had adequate management for their pain, that is, PMI more than or equal to 0. This practice can lead to opioid related tolerance, dependence (physical and psychological) as well as abuse. Additionally, because patients are more frequently assessed in hospices and oncology wards compared to outpatient clinics ,there may be more pain management occurring in these settings (Greco et al., 2014). This could explain our finding of high proportion of adequately treated participants and a reduction of negative PMI (representing under-treatment). The PMI score of more than equal to 0 is a conservative measure of adequacy

5.3 Quality of life/interference with activities of daily living

Improvement in QoL is one of the most vital aspects and goals of cancer care, especially for end-stage cancer, where the focus is on symptom control and delaying disease progression (Liang et al., 2015). Quality of Life is an important indicator of symptom relief and can be used as an assessment of the adequacy of pain management in cancer patients. When cancer symptoms are not optimally managed, they can have a negative impact on all aspects of a patient's quality of life (Deng et al., 2012)

As pain severity increases to moderate intensity, pain passes a threshold beyond which it is hard for the patient to ignore .At this point, it becomes disruptive to many aspects of patient's life .When the pain is severe, it becomes a primary focus of attention and prohibits most activities. That said pain severity and degree to which patient's function is impaired are clearly highly associated.

We report pain interference in all the activities assessed. However, the level of interference was mild (based on a score on the Likert scale). The highest area of interference was noted to in “general activities” (mean interference score 4.321), “mood” (mean interference score 3.670), “walking” (mean interference score 3.589)

These results compares to findings by Harminder (HARMINDER SINGHPain et al., 2018) and Beck (Beck & Falkson, 2001). However, contrasts findings by an Ethiopian author and colleagues (Tegegn & Gebreyohannes, 2017) and another study in Ghana (Abruquah et al., 2017) who reported moderate to complete interference with daily activities (>7) with highest score of interference noted in sleep.

This study found statistically significant correlation between pain severity index and functional interference index with those who reported to have severe pain recording a high level of interference (median=50.5) compared to those without severe pain (p-value<0.001). Similarly findings in a Ghanaian study (Abruquah, et al, 2016) noted that patients with high pain intensity were more likely to have it affect their daily activity (P<0.0001). This is in contrast to results of an Ethiopian study, where the level of functional interference was high in those who perceived moderate pain (p<0.001) (Tuem, Gebremeskel, Hiluf, Arko, & Hailu, 2020).

In a study by Hwang et al, the worst pain severity independently predicted the pain interference and then the pain and in turn the pain interference score independently

predicted the global Visual Analogue Scale Global Quality of Life score (Hwang, Chang, & Kasimis, 2002)

There was no statistically significant association noted between the type of cancer, pain medication and level of interference (p-value>0.05).

5.4 Strengths and Limitations

To the best of our knowledge this is the first study describing pain experience in advanced gynecologic cancer in Western Kenya using an internationally accepted tool to assess pain severity and pain interference thus providing a foundation for future studies.

Limitations to this study include small sample size that might not be geographically representative of advanced gynecologic cancer patients and additionally it was limited to an in -patient setting.

CHAPTER SIX

6.0 CONCLUSION AND RECOMMENDATION

6.1 Conclusion

1. Opioids were utilized by majority of the participants, with more than 50% of them receiving more potent analgesic than required for their level of pain.
2. The adequacy of pain management as per the findings was acceptable which was computed using the Pain Management Index.
3. Overall , pain among the participants caused mild interference of activities of living, with the participants experiencing severe pain having significant level of interference in all the domains of activities

6.2 Recommendations

1. Continued assessment and evaluation of cancer pain management at the division thus further improving care
2. Further study to explore patients perspective on the adequacy of advanced cancer pain management

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APPENDICES

Appendix 1: Budget

Item	No.of units	Cost per unit Kshs	Sub-total cost	Total cost
Research proposal cost				
Printing charges	10	400.00	**5,000.00**	
Questionnaire photocopy	250	30.00	**7,500.00**	
Photocopy consent	250	10.00	**1,500.00**	
Binding charges	10	50.00	**500.00**	
Pens	10	20.00	**200.00**	
Biostatistician consult	1	20,000.00	**15,000.00**	
Total proposal cost				**29,700.00**
Thesis Expenses:				
Printing charges (report)	10	1,000.00	**7,000.00**	
Report binding charges	10	200.00	**2,000.00**	
Research assistant fee	2	10,000.00	**20,000.00**	
Biostatistician consult fee	1	25,000.00	**30,000.00**	
Total Final Report Cost				**59,000.00**
Publishing expenses				
Estimate Publishing Cost			**50,000.00**	**50,000.00**
GRAND TOTAL				**138,700.00**

Appendix 2: Time Frame

ACTIVITY	April	May	June	July	August	September	May	July	August	September	October	January	February	June
	2018						2019					2021		
Submission to IREC														
IREC approval														
Piloting of data tools														
Design of data base														
Data collection														
Data entry and analysis														
Report writing														
Thesis submission														
Thesis mock defense														
Thesis defense and presentation														

Appendix 3: Consent Form

Researcher's statement

Dear participant,

My name is **Caroline Mwanamisi Mruttu** Masters of Medicine in Reproductive Health student from the Moi University I am inviting you to participate in a study I intend to carry out on **"assessment of adequacy of pharmacologic pain therapy in advanced gynecologic cancer in MTRH"**as part of my course requirement.

Your participation in this study is on voluntary basis i.e. it is your choice to participate and you may opt out from the study at any stage which will not lead to any form of penalty. However, your participation in this study will help us obtain important information on the satisfactoriness of pain management practices. You will be required to sign consent before the beginning of the study.

To obtain the required information, you will be interviewed for about 15 minutes by me, the researcher, assisted by two research assistants.

This information will be kept confidential and anonymous. Identification will be by numbers only no names or any other personal particulars will be written on the questionnaire.

Please note, your opinion will be respected and considered. All the participants will be treated equally.

You will benefit from this study by being referred to the relevant personnel for assistance if need be. In additional, the study findings will be used to develop strategies on how to improve assessment and management of the cancer pain by policy makers and improve quality of cancer care.

The study may have minimal risk to you, mainly psychological as you meditate on the ailment. No invasive procedure such as pricking or collection of blood will be done. Iwill be available to answer any question that may arise in the course of the study and/ or afterwards i.e. you are free to ask any question or express any concern at any time. In case of any question or concerns you may contact the me on cell. Phone. No. 0721-889616 or contact IREC using the address below:

The Chairman IREC,

Moi Teaching and Referral Hospital,

P. O. Box 3, Eldoret.

Tel: 0787723677

You participation is highly appreciated.

Thank you.

Caroline MwanamisiMruttu

(Researcher)

Participant's statement

I have fully read / was read to me the consent explanation and understood its content. I have been given an opportunity to discuss all my concerns with the researcher. I do therefore agree voluntarily to participate in the study on**"assessment of adequacy of pharmacologic pain therapy in advanced gynecologic cancer at MTRH"**I also understand that all the information I give will be for the purpose of this study only.

Participant's Signature _____Date_____

Serial number _____

Witness'Signature_____Date _____

(Researcher /research assistant)

MAELEZO YA RIDHAA

Kwamshirikimpenzi,

Jinalanguni Caroline MwanamisiMruttumwanafunzikatikachuokikuu cha MOI ambaponinanuiakuhitimunashahadayajuuyaudaktari.

Ninafanyautafitikuhusunjiazinazotumiwakukingamaumivuitokanayonaugonjwawasaratanina ,utoshelevu wa mbinu hizi, na vile zinachangiauwezowakufanyashughulizakilasikubainayawanawakewanaoguasaratanikatikahospitaliyaRufaaya MOI. Umealikwakwaheshimakushirikikatikazoezihili la utafiti.

Kushirikikatikazoezihilinikwahiariyakomwenyewenahakunaadhabuyoyoteitakayotolewakwakutoshiriki. Walakini, kushirikikwakoniwaumuhimusanamaanaitatupatiahabariambazozitasaidiakuimarishahudumayaafyakwawagonjwawasaratani.

Ilitupatehabarimuhimukutokakwakoutahitajikaujibumaswaliutakayoulizwanamtafitiakisaidiwanawatafitiwawili.

Ili ushirikikatikautafitihuuunahitajikauwekesahihikwahiariyakokwanafasiiliyoachwahapochini.

Ni vizurikuelewayakwamba:

jinalakoamanambariyakitambulishochakohazitaandikwakwenyeilefomuyamajibulakiniutapewanambariyakushiriki,

habariutakapotoazitashughulikiwakwanjiayasiriinavyoruhusiwakisheria,

maoniyakilamshirikiniyamaanasanakwetu,

washirikiwotewatashughulikiwakwanjiasawayaanibilaubaguzi,

mshirikianauhuruwakujiondoakwautafitihuuwakatiwowotebilaadhabuyoyote.Utafitihuutakuwanamadharakidogosanayakimawazojuuyaugonjwa.

Unawezaulizaswaliamajambololotekuhusuutafitihuukwamtafitinambariyasimuyarunu nu 0721-889616 amatume la kitaifa la utafitinamaadilikutumiaanwaniifauatayo .

MwanachamaIREC,

Chuo cha rufaanamafunzo MOI

,Sandukulaposta 3,mji waEldoret.

SimuyaRununu: 0787723677

Asante

Mwanamisi(mtafiti)

Ridhaayakushirikiutafiti

Mimi nimesoma/

nimesomewanakuelezewavizurikuhusuutafitiunaofanywananinakubalikwahiariyangukushiriki. Pianinaelewayakwambahabarinitakazozitoanizamatumiziyautafitihuupekee.

Sahihiyamshiriki_____tarehe_____nambariyafomu_____

Sahihiyashahidi (mtafiti) _____tarehe_____

Appendix 4: Questionnaire

STUDY TITLE: To assess adequacy of pharmacologic pain therapy in advanced gynecologic cancer in MTRH.

SECTION 1.0 SOCIO-DEMOGRAPHIC DATA

1.1 How old are you?

1.2 What is your education level?

1. None ☐
2. Primary ☐
3. Secondary ☐
4. Others ☐ please specify……
……

1.3 What is your marital status?

1. Single ☐
2. Married ☐
3. Divorced ☐
4. Separated ☐
5. Widowed ☐

1.4 What income-generating activities do you engage in?

1. Formal employment ☐
2. Self employment ☐
3. Unemployed ☐
4. Student ☐
5. Others ☐ please specify……
……

1.5 Who is paying for your hospital bills?

1. Self ☐
2. Employer ☐
3. Insurance ☐
4. Others ☐ please specify

……
……

SECTION 2.0 DISEASEHISTORIES (INTERVIEW AND REVIEW OF MEDICAL RECORDS)

2.1 What type of cancer are you suffering from?

1. Vulva cancer ☐
2. Cervical cancer ☐
3. Ovarian cancer ☐
4. Endometrial cancer ☐
5. Choriocarcinoma ☐

2.2 How long have you have you been suffering from this disease?

…….

2.3 Are you taking any painkillers?

yes

no

if yes ,drug…….dose

frequency……

Kiambatisho cha nne: HOJAJI

KICHWA CHA KUJIFUNZA:

Kuchunguzakutoshakwatibayadawayamaumivukatikasaratanіyauzaziwa kike yajuukatikahospitalliyarufaayaMoi

SEHEMU 1.0 DATA YA KIJAMII NA IDADI YA WATU

Je,unaumrigani?

Je, nikiwangogani cha elimuulichonacho?

hakuna

msingi

sekondari

inginetajatafadhali……..

Je, nininihaliyakoyandoa?

sinamwanandoa

ndoa

nimetalakiwa

nimetengwanamwanandoa

mjane

Je, imaniyakoyakidininigani?

Kiislamu

Kikristo

Zinginezotafadhalitaja ……

Je, nishughuliganiunazojishughulishanazozinazozalishamapato?

kazirasmi

ajirayakibinafsi

hamnakazi

mwanafunzi

zinginezotafadhalitaja…….

Je,ninaniambayeanakulipiabiliyahospitali?

binafsi

muajiri

bima

SEHEMU 2.0 HISTORIA YA MAGONJWA(MAHOJIANO NA MAPITIO YA KUMBUKUMBU ZA MATIBABU)

2.1 Je, nisarataniyaainaganiunayougua?

1. sarataniyakuma

2. sarataniyamdomowakifuko cha uzazi

3. sarataniyamayaiyauzazi

4. sarataniyakifuko cha uzazi

5. choriocarcinoma

2.2 Je, umekuwaukiuguakwamudagani?

2.3 Je, unatumia dawa zozote kupunguza maumivu kwa sasa?

ndio

la

dawa…….kiwango…….mara ngapi kwa siku…….

Appendix 5: Brief Pain Inventory

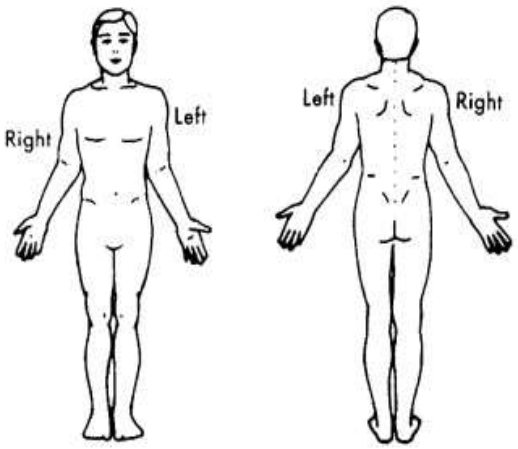
FORM 3.2 **Brief Pain Inventory**

Date____ / ____ / ____ Time:_____

Name: _____ _____ _____
Last First Middle Initial

1) Throughout our lives, most of us have had pain from time to time (such as minor headaches, sprains, and toothaches). Have you had pain other than these everyday kinds of pain today?
1. Yes 2. No

2) On the diagram shade in the areas where you feel pain. Put an X on the area that hurts the most.



3) Please rate your pain by circling the one number that best describes your pain at its **worst** in the past 24 hours.

0 1 2 3 4 5 6 7 8 9 10
No pain — pain as bad as you can imagine

4) Please rate your pain by circling the one number that best describes your pain at its **least** in the past 24 hours.

0 1 2 3 4 5 6 7 8 9 10
No pain — pain as bad as you can imagine

5) Please rate your pain by circling the one number that best describes your pain on the **average**

0 1 2 3 4 5 6 7 8 9 10
No pain — pain as bad as you can imagine

6) Please rate your pain by circling the one number that tells how much pain you have **right now**.

0 1 2 3 4 5 6 7 8 9 10
No pain — pain as bad as you can imagine

7) What treatments or medications are you receiving for your pain?

_____

_____

8) In the Past 24 hours, how much **relief** have pain treatments or medications provided? Please circle the one percentage that most shows how much releif you have received

0% 10 20 30 40 50 60 70 80 90 100%
No relief — Complete relief

9) Circle the one number that describes how, during the past 24 hours, pain has **interfered** with your:
A. General activity

0 1 2 3 4 5 6 7 8 9 10
Does not interfere — Completely interferes

B. Mood

0 1 2 3 4 5 6 7 8 9 10
Does not interfere — Completely interferes

C. Walking ability

0 1 2 3 4 5 6 7 8 9 10
Does not interfere — Completely interferes

D. Normal work (includes both work outside the home and housework

0 1 2 3 4 5 6 7 8 9 10
Does not interfere — Completely interferes

E. Relations with other people

0 1 2 3 4 5 6 7 8 9 10
Does not interfere — Completely interferes

F. Sleep

0 1 2 3 4 5 6 7 8 9 10
Does not interfere — Completely interferes

G. Enjoyment of life

0 1 2 3 4 5 6 7 8 9 10
Does not interfere — Completely interferes

Form 32: Brief pain inventory

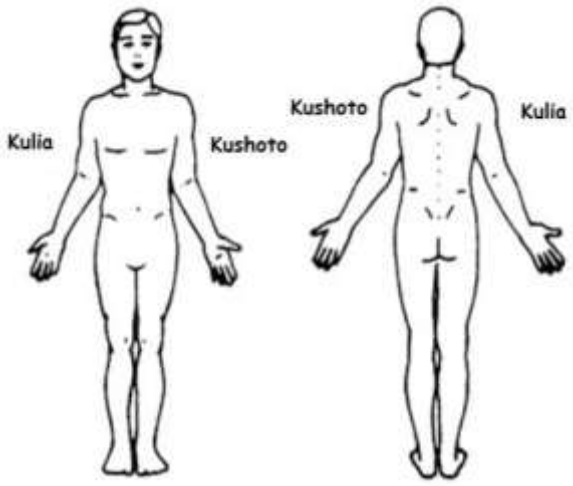
Tarehe ___/___ / ___ Saa: _____

Jina

_____ _____ _____

La mwisho La Kwanza Herufi ya kwanza ya jina la kati

1. Katika maisha yetu, wengi wetu tumekuwa na uchungu/maumivu mara kwa mara (kama vile maumivu madogo ya kichwa, sprain, na maumivu ya meno). Je, leo umekuwa na maumivu mengine zaidi ya aina hii ya maumivu ya kila siku?
   1. Ndiyo 2. Hapana
2. Kwenye mchoro, onyesha maeneo ambayo unahisi maumivu. Weka alama ya X kwenye eneo ambalo lina maumivu zaidi.



3. Tafadhali onyesha kiwango cha maumivu yako kwa kuweka mviringo kwa nambari moja ambayo inaelezea vyema kabisa maumivu yako yakiwa **mabaya sana** katika masaa 24 yaliyopita.

0 1 2 3 4 5 6 7 8 9 10

Hakuna maumivu

Maumivu mabaya sana kama unavyoweza kudhania

4. Tafadhali onyesha kiwango cha maumivu yako kwa kuweka mviringo kwa nambari moja ambayo inaelezea vyema kabisa maumivu yako yakiwa **machache** katika masaa 24 yaliyopita.

0 1 2 3 4 5 6 7 8 9 10

Hakuna maumivu

Maumivu mabaya sana kama unavyoweza kudhania

5. Tafadhali onyesha kiwango cha maumivu yako kwa kuweka mviringo kwa nambari moja ambayo inaelezea vyema kabisa maumivu yako kwa **wastani.**

0 1 2 3 4 5 6 7 8 9 10

Hakuna maumivu

Maumivu mabaya sana kama unavyoweza kudhania

kama unavyoweza kudhania

6. Tafadhali onyesha kiwango cha maumivu yako kwa kuweka mviringo kwa nambari moja ambayo inaonyesha ni kiasi gani cha maumivu ambayo uko nayo kwa **hivi sasa**.

0 1 2 3 4 5 6 7 8 9 10

Hakuna — Maumivu mabaya sana kama unavyoweza kudhania

7. Je, ni matibabu gani au ni dawa gani unazopokea kwa ajili ya maumivu yako?

_____

8. Katika masaa 24 yaliyopita, ni kiasi gani cha **nafuu** ulichopata kutoka kwa matibabu au dawa?

0% 10 20 30 40 50 60 70 80 90 100%

Hakuna nafuu — Nafuu kamili

9. Weka mviringo kwenye nambari moja ambayo inaelezea jinsi, wakati wa masaa 24 yaliyopita, maumivu **yametatiza:**

A. Shughuli zako za jumla

0 1 2 3 4 5 6 7 8 9 10

Hayatatizi — Yanatatiza kabisa

B. Hali ya akili/hisia

0 1 2 3 4 5 6 7 8 9 10

Hayatatizi — Yanatatiza kabisa

C. Uwezo wa kutembea

0 1 2 3 4 5 6 7 8 9 10

Hayatatizi — Yanatatiza kabisa

D. Kazi za kawaida (inajumuisha kazi zote za nje ya nyumba na kazi za nyumbani)

0 1 2 3 4 5 6 7 8 9 10

Hayatatizi — Yanatatiza kabisa

E. Uhusiano na watu wengine

0 1 2 3 4 5 6 7 8 9 10

Hayatatizi — Yanatatiza kabisa

F. Kulala

0 1 2 3 4 5 6 7 8 9 10

Hayatatizi — Yanatatiza kabisa

G. Starehe ya maisha/Kufurahia maisha

0 1 2 3 4 5 6 7 8 9 10

Hayatatizi — Yanatatiza kabisa

Appendix 6: IREC Approval

INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE (IREC)

MOI TEACHING AND REFERRAL HOSPITAL
P.O. BOX 3
ELDORET
Tel: 33471//2/3

MOI UNIVERSITY
COLLEGE OF HEALTH SCIENCES
P.O. BOX 4606
ELDORET
Tel: 33471/2/3

Reference IREC/2018/62
Approval Number: 0003085

10th May, 2019

Dr. Caroline Mwanamisi Mruttu
Moi University,
School of Medicine,
P.O. Box 4606-30100,
ELDORET-KENYA.

INSTITUTIONAL RESEARCH & ETHICS COMMITTEE
10 MAY 2019
APPROVED
P. O. Box 4606-30100 ELDORET

Dear Dr. Mruttu,

RE: APPROVAL OF AMENDMENT

The Institutional Research and Ethics Committee has reviewed the amendment made to your proposal titled:-

"Assessment of Adequacy of Pharmacologic Pain Therapy in Advanced Gynaecologic Cancer in Moi Teaching and Referral Hospital".

We note that you are seeking to make amendments as follows:-

1. To omit the out-patients cohort and only study in-patients.
2. Change the study design from prospective to cross-sectional.
3. Adjust the sample size from 385 to 112.

The amendments have been approved on 10th May, 2019 according to SOP's of IREC. You are therefore permitted to continue with your research.

You are required to submit progress(s) regularly as dictated by your proposal. Furthermore, you must notify the Committee of any proposal change(s) or amendment(s), serious or unexpected outcomes related to the conduct of the study, or study termination for any reason. The Committee expects to receive a final report at the end of the study.

Sincerely,

DR. S. NYABERA
DEPUTY-CHAIRMAN
INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE

cc: CEO - MTRH Dean - SPH Dean - SOM
Principal - CHS Dean - SOD Dean - SON

MU/MTRH-INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE (IREC)

MOI TEACHING AND REFERRAL HOSPITAL
P.O. BOX 3
ELDORET
Tel: 33471//2/3

MOI UNIVERSITY
COLLEGE OF HEALTH SCIENCES
P.O. BOX 4606
ELDORET

Reference: IREC/2018/62
Approval Number: 0003085

6th September, 2018

Dr. Caroline Mwanamisi Mruttu,
Moi University,
School of Medicine,
P.O. Box 4606-30100,
ELDORET-KENYA.

Dear Dr. Mruttu,

RE: FORMAL APPROVAL

The MU/MTRH- Institutional Research and Ethics Committee has reviewed your research proposal titled: -

"Assessment of Adequacy of Pharmacologic Pain Therapy in Advanced Gynaecologic Cancer in Moi Teaching and Referral Hospital".

Your proposal has been granted a Formal Approval Number: ***FAN: IREC 3085*** on 6th September, 2018. You are therefore permitted to begin your investigations.

Note that this approval is for 1 year; hence will expire on 5th September, 2019. If it is necessary to continue with this research beyond the expiry date, a request for continuation should be made in writing to IREC Secretariat two months prior to the expiry date. You will be required to submit progress report(s) on application for continuation, at the end of the study and any other times as may be recommended by the Committee.

Furthermore, you must notify the Committee of any proposal change (s) or amendment (s), serious or unexpected outcomes related to the conduct of the study, or study termination for any reason. You will also be required to seek further clearance from any other regulatory body/authority that may be appropriate and applicable to the conduct of this study.

Sincerely,

DR. S. NYABERA
DEPUTY-CHAIRMAN
INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE

cc	CEO	-	MTRH	Dean	-	SOP	Dean	-	SOM
	Principal	-	CHS	Dean	-	SON	Dean	-	SOD

Appendix 7: Hospital Approval (MTRH)

An ISO 9001:2015 Certified Hospital

MOI TEACHING AND REFERRAL HOSPITAL

Telephone :(+254)053-2033471/2/3/4
Mobile: 722-201277/0722-209795/0734-600461/0734-683361
Fax: 053-2061749
Email: ceo@mtrh.go.ke/directorsofficemtrh@gmail.com

Nandi Road
P.O. Box 3 – 30100
ELDORET, KENYA

Ref: ELD/MTRH/R&P/10/2/V.2/2010

25th September, 2018

Dr. Caroline Mwanamisi Mruttu,
Moi University,
School of Medicine,
P.O. Box 4606-30100,
ELDORET-KENYA.

APPROVAL TO CONDUCT RESEARCH AT MTRH

Upon obtaining approval from the Institutional Research and Ethics Committee (IREC) to conduct your research proposal titled:-

"Assessment of Adequacy of Pharmacologic Pain Therapy in Advanced Gynaecologic Cancer in Moi Teaching and Referral Hospital".

You are hereby permitted to commence your investigation at Moi Teaching and Referral Hospital.

MOI TEACHING AND REFERRAL HOSPITAL
CEO
APPROVED
25 SEP 2018
SIGN..... P.O. BOX 30100, ELDORET

25/09/2018

DR. WILSON K. ARUASA, *MBS*
CHIEF EXECUTIVE OFFICER
MOI TEACHING AND REFERRAL HOSPITAL

cc - DCEO, (CS)
- Director of Nursing Services (DNS)
- HOD, HRISM