

AWARENESS REGARDING NON-STEROIDAL ANTI- INFLAMMATORY DRUG-RELATED SIDE EFFECTS IN JOHANNESBURG, SOUTH AFRICA

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ABSTRACT

Introduction

Non-steroidal anti-inflammatory drugs (NSAIDs) are amongst the most commonly used medications globally, as they are highly effective and easily accessible. The NSAIDs are indicated for mild to moderate pain management. The increasing incidence of NSAID related side effects and hospitalisations has raised a concern about these medications' safety. The prevalence of these side effects has drastic consequences to a challenged South African public healthcare system. The implications of not treating severe, potentially preventable upper gastrointestinal complications attributed to NSAIDs' consumption continue to be a significant problem that healthcare professionals (HCP) face.

Aim

This research study aims to identify the level of awareness of side effects caused by NSAID use by adults based in Johannesburg, South Africa.

Method

A prospective cross-sectional survey was used, which utilised quantitative research methods. A representative purposive heterogeneous sample of 220 NSAID users aged ≥ 18 years was recruited from multiple pharmacies across Johannesburg from September 2019 to October 2019. A self-administered questionnaire was the primary means of data collection. Descriptive statistical analysis was performed on the demographic data, NSAID use and NSAID side effect awareness. A subgroup analysis was performed on participant unawareness compared to their

education level and whether there had been communication regarding the NSAID related side effects from their HCPs. The study is intended to highlight factors that contribute to the lack of NSAID side effect awareness and promote NSAIDs' responsible use. The results can be used to guide HCP to promote education and awareness of NSAID side effects to ensure safe NSAID use.

Results

The results obtained from a cross-sectional survey of 220 participants showed that NSAID use was significantly higher in females. Among the NSAIDs, ibuprofen is the most commonly used NSAID, followed by salicylates and diclofenac. The main reasons for NSAID use as described by participants were pain (55%), pain and inflammation (20.09%) and inflammation (6.82%). More than two-thirds of the NSAIDs were obtained over the counter (non-prescription), and physicians prescribed only 22% of NSAIDs obtained by participants. Almost 80% of participants believed that NSAID use was safe, and 68% thought it should be advertised. 56% of participants were unaware that NSAID use could cause a stomach ulcer, and 61% of participants were not aware that taking NSAIDs could lead to acid reflux or heartburn. 49.5% of participants indicated that they were not advised regarding the risks and side effects of taking NSAIDs from their HCP.

Conclusion

This research study confirms that NSAIDs are widely used in Johannesburg, South Africa. In most cases, they are used according to their approved indications. Most of the study sample was not aware of the side effects that are related to NSAID use. Another concerning finding in this study was the lack of communication regarding the risk and side effects of taking NSAIDs between patients and HCPs.

Keywords:

Pain, NSAIDs, Awareness, Risk, Side effects, Inflammation



DECLARATION

I declare that this thesis that I now submit for assessment on the programme of study leading to the degree Master of Science in Pharmacy Administration and Policy Regulation has not been submitted for the purpose of a degree at this or any other higher education institution. It is entirely my own work and has not been taken from the work of others save to the extent that such work has been cited and acknowledged within the text of this work.

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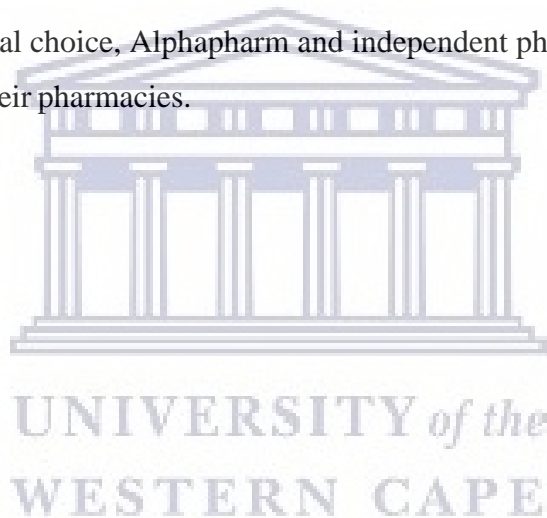
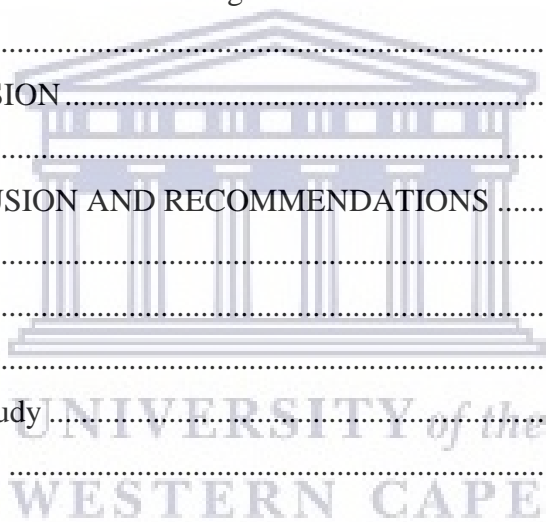


TABLE OF CONTENTS

ABSTRACT	2
Introduction	2
Aim.....	2
Method	2
Results	3
Conclusion.....	3
Keywords:	4
DECLARATION	5
ACKNOWLEDGEMENTS	6
TABLE OF CONTENTS.....	7
LIST OF ABBREVIATIONS	10
CHAPTER 1: INTRODUCTION	13
1.1 Introduction	13
1.2 Background.....	13
1.3 Problem statement	14
1.4 Aim and objectives	16
Primary Objectives.....	16
Secondary objectives.....	16
1.7 Significance of the study	16
CHAPTER 2: LITERATURE REVIEW	17
2.1 Introduction	17
2.2 Pain and analgesics	17
2.3 NSAID mechanism of action and side effects	18
2.4 Gastrointestinal side effects	18
2.5 NSAIDs in South Africa	19
2.6 Regulation of medicines in South Africa.....	20
2.7 Risk factors of NSAID- associated gastroduodenal bleeding.....	21
2.8 Factors influencing decreased awareness NSAID related side effects	21
Healthcare insurance costs	21
Gastroprotective agents	22

2.9 Conclusion.....	22
CHAPTER 3: METHODOLOGY	24
3.1 Introduction	24
3.2 Study Design.....	24
3.3 Questionnaire Design.....	24
3.3 Study sample.....	25
3.4 Data Collection	26
3.5 Data Analysis.....	26
3.6 Ethical Considerations	27
CHAPTER 4: RESULTS	28
4.1 Introduction	28
4.2 Social-demographics	28
4.3 NSAID related side effects knowledge and awareness	31
Table 2.....	44
CHAPTER 5: DISCUSSION	51
5.1 Principal findings.....	51
CHAPTER 6: CONCLUSION AND RECOMMENDATIONS	58
6.1 Introduction	58
6.2 Conclusion.....	59
6.3 Study Limitations	60
6.4 Strengths of the study.....	61
6.5 Recommendations	62
REFERENCES.....	64
APPENDICES.....	70
Appendix 1- Ethic clearance letter	71
Faculty of Community and Health Science Ethics Reference Number: BM19/6/16	72
Please remember to submit a progress report in good time for annual renewal.	72
Appendix 2- Pharmacy permission letter	73
Appendix 3- Information sheet	76



Appendix 4- Informed consent form.....	81
INFORMED CONSENT	82
Appendix 5- Questionnaire	84



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LIST OF ABBREVIATIONS

AE- Adverse Events

COX- Cyclooxygenase

DOH- Department of Health

FDA- Food Drug Administration

GI- Gastrointestinal

GPs- General Practitioners

GPA- Gastroprotective Agents

H2RAS- Histamine-2 Receptor Antagonists

HCP- Healthcare Professional

MCC- Medicines Control Council

NSAID: Non- Steroidal Anti-Inflammatory

OTC- Over the Counter

PPIs- Proton Pump Inhibitors

QOL- Quality of Life

SAEL- South African Essential Medicines List

SAHPRA- South African Health Products Regulatory Authority

SE- Side Effects

SSRIs- Selective Serotonin Reuptake Inhibitors

UGIT- Upper Gastrointestinal



LIST OF TABLES

		Page
Table 1	Socio-demographic characteristics of participants	27-29
Table 2	Sub-group analysis of the level of education of participants compared to the level of awareness regarding side effects	42



LIST OF FIGURES

Page

Figure 1	Frequency of NSAID use	30
Figure 2	Indications NSAIDs were used to treat	32
Figure 3	Places NSAIDs were obtained from	33
Figure 4	Substances that are taken in combination with NSAIDs	34
Figure 5	Time of the day that NSAIDs are taken	35
Figure 6	Participants' perception of the safety of NSAIDs	36
Figure 7	The participant's perception of whether NSAIDs can be abused or over-used	37
Figure 8	Participants views on whether NSAIDs should be advertised or not	38
Figure 9	The level of participant awareness with regards to NSAID related side effects	39
Figure 10	The level of communication between the participants and their HCPs regarding the risk and related side effects of NSAIDs	40
Figure 11	Unawareness of stomach ulcers and acid reflux/ heartburn as an NSAID related side effect and presence of communication regarding NSAID related side effects with HCP	43
Figure 12	Sub-group analysis from the participants that had received communication regarding the NSAID related side effects compared to their level of awareness regarding the related side effects	44
Figure 13	A sub-group analysis comparing the awareness of the NSAID related side effects to the participants that believed NSAID use is	45
Figure 14	A sub-group analysis comparing the awareness of the NSAID related side effects to the participants that used OTC NSAIDs	46
Figure 15	A sub-group analysis comparing the awareness of the NSAID related side effects to the participants that used prescription	47
Figure 16	A sub-group analysis comparing the awareness of the NSAID related side effects to the participants that believed NSAIDs should be advertised	48

CHAPTER 1: INTRODUCTION

1.1 Introduction

This section outlines the background, aim, rationale, problem statement and significance of this study.

1.2 Background

Non-steroidal anti-inflammatory drugs (NSAIDs) have been described as a successful group of medications as they are used by a large number of patients worldwide due to their anti-inflammatory, analgesic, and antipyretic effects (Meek, Van de Laar, Vonkeman, 2010).

It is well known that continued use of NSAIDs is related to numerous side effects. The severity of these side effects ranges from experiencing mild symptoms, such as dyspepsia or heartburn, to severe gastroduodenal ulcerations and bleeding, leading to hospitalisations and potentially even death (Russell, 2001).

In 2009, the United States Food and Drug Administration (FDA) issued an instruction to all NSAID manufacturers requesting a comprehensive warning on all NSAID packaging. The warning should include the following statement: “The product contains an NSAID, which may cause severe stomach bleeding”. The word “severe” was included to highlight the potential fatality risk due to NSAID induced bleeding (FDA, 2009).

Acetylsalicylic acid (aspirin) was discovered in the nineteenth century. Non-steroidal anti-inflammatory drugs (NSAIDs) are derivatives of aspirin. Ibuprofen was the first NSAID to be developed and was used in 1968 for its analgesic and anti-inflammatory properties (Bushra & Nousheen, 2010). Since then, multiple formulations of NSAIDs have been developed, and their use in the general population has gained popularity (Meek, Van de Laar, & Vonkeman, 2010).

The use of over the counter (OTC) NSAIDs has been estimated to be seven-fold of prescribed NSAIDs (Govender & Brand, 2018) and shown to increase with age, with approximately 40-60% of NSAID consumers being over 60 years of age (Wilcox, Shalek, & Cotsonis, 1994).

1.3 Problem statement

Non-steroidal anti-inflammatory drugs (NSAIDs) are effective anti-inflammatory and analgesic agents and are among the most commonly used classes of medications worldwide (Wongrakpanich, Wongrakpanich, Melhado, & Rangaswami, 2018). However, their use has been associated with potentially serious gastrointestinal (GIT) complications such as upper GIT bleeding. Gastrointestinal tract complications resulting from NSAID use are among the most common drug side effects in the world (Sostres, Gargallo, & Lanas, 2013). The widespread use of NSAIDs has resulted in a considerable number of affected individuals who experience GIT complications. It is estimated that one in 175 NSAID users will be hospitalised for NSAID related GIT injury in the United States. (Lazzaroni & Bianchi Porro, 2004).

The risk of upper GIT complications can occur even with short-term NSAID use, and the rate of events is linear over time with continued use (Goldstein & Cryer, 2015). There are gastroprotective therapies available. However, they are not used adequately to prevent the development of NSAID-related upper GIT complications (Goldstein & Cryer, 2015).

Goldstein and Cryer presented a report of a patient who had developed a gastric ulcer after short term NSAID use, and they further examined risk factors and prevention strategies for upper GIT mucosal injury after NSAID use. These risk factors included advanced age, previous history of GIT injury, and concurrent use of medications such as anticoagulants, aspirin, corticosteroids, and selective serotonin reuptake inhibitors (SSRIs). Strategies for the prevention of GIT injuries include anti-secretory agents, gastroprotective agents, alternative NSAID formulations, and nonpharmacologic therapies. Greater awareness of the risk factors and potential therapies for GIT complications resulting from NSAID use could help improve outcomes for patients requiring NSAID treatment (Goldstein & Cryer, 2015).

The continued use of NSAIDs has been related to numerous side effects. Despite the desired effect of NSAIDs on patients indicated for symptomatic treatment of multiple conditions, there

has been an increase in continued and overuse of these medications due to a lack of awareness of possible complications that occur consequently (Wilcox, Cryer, & Triadafilopoulos, 2005)



1.4 Aim and objectives

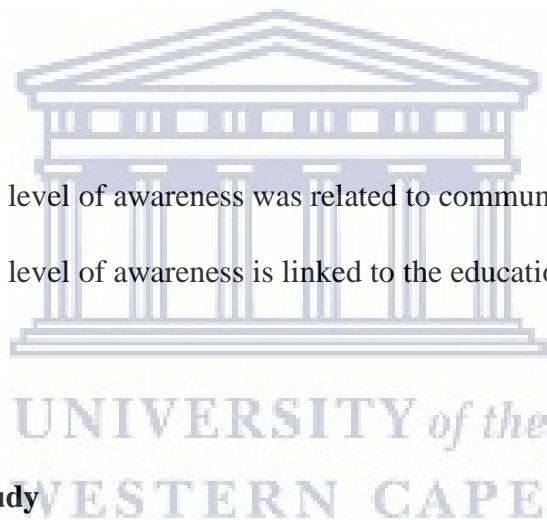
The aim is to evaluate the overall patient awareness of NSAID related side effects.

Primary Objectives

- To assess the patient's awareness of the NSAID related side effects
- To explore patient behaviour regarding NSAID use
- To explore patient's views on the safety of NSAIDs

Secondary objectives

- To determine if the level of awareness was related to communication with HCP
- To determine if the level of awareness is linked to the education level of the respondent



1.7 Significance of the study

The value of this research would be to identify factors that may contribute toward stricter enforcement of existing South African Health Products Regulatory Authority (SAHPRA) regulations and increased emphasis on consumer education. It is conceivable that this insight would provide public health role players with new avenues to decrease surgical morbidity and enhance the quality of life (QOL) for patients while simultaneously reducing government expenditure on treatment costs for preventable conditions.

CHAPTER 2: LITERATURE REVIEW

2.1 Introduction

This section is a review of the literature concerning the core ideas and concepts that are relevant to the topic.

2.2 Pain and analgesics

Pain is defined as “an unpleasant sensory or emotional experience associated with actual or potential tissue damage or described in terms of such damage” (Treede, 2008). The Global Burden of Disease is a comprehensive study comprising of regional and global research of disease burden that assesses mortality and disability from major diseases, injuries, and risk factors. Pain has been described as one of the leading factors that have contributed to the Global Burden of Disease (Moore, Derry, Simon, & Emery, 2014). Pain is characterised by its duration and by its severity. The duration of pain is either acute or chronic based on the length of time that the pain has been experienced. Pain is said to be acute if the pain is experienced for a period of fewer than six months. Pain is described as chronic if it is persistent and ongoing. The severity of pain is described as mild, moderate or severe. (Treede, 2008)

Analgesics are a common treatment used for mild to moderate pain management. This drug class consists of an ever-expanding range of non-prescription and prescription medications. Acetylsalicylic acid, ibuprofen, diclofenac, and naproxen are frequently used non-selective NSAIDs that are attainable without a prescription. At present, there are more than 20 different types of NSAIDs commercially available (Solomon *et al.*, 2017). The NSAIDs are used in the treatment of mild to moderate conditions such as headaches, dental complications, dysmenorrhoea, musculoskeletal pain and pain presented by influenza and upper respiratory tract infections. The NSAIDs, including aspirin, do not change the rate of the disease progression and are only indicated for symptomatic relief (Solomon *et al.*, 2017).

2.3 NSAID mechanism of action and side effects

The NSAIDs work to relieve pain and reduce inflammation through the inhibition of prostaglandin cyclooxygenase (COX), which prevents prostaglandin synthesis. There are two types of COX enzymes. The COX-1 enzyme is responsible for the maintenance of regular gastric function, including protective gastric functions. The COX-2 enzyme becomes regulated in zones of inflammation. Certain NSAID compounds will have an affinity for COX-1 and COX-2. The non-prescription NSAIDs are known as non-selective NSAIDs and inhibit both forms of COX. Non-selective NSAIDs are known to cause gastric injury due to local and systemic irritations (Bidaut-Russell & Gabriel, 2001).

2.4 Gastrointestinal side effects

Gastrointestinal side effects induced by NSAID usage are the most dominant category of side effects. A single dose of a non-prescription NSAID has been shown to cause a slight degree of gastric mucosa erosion (Peura & Goldkind, 2005).

Gastrointestinal side effects are classified into three categories:

- The Nuisance Symptoms-These symptoms are described by nausea, vomiting, dyspepsia, heartburn, and gastric pain.
- More Serious Side effects- These effects are identified after an endoscope is performed. The mucosal lesions will be visible at this stage.
- Serious side effects- These effects are hazardous and life-threatening. Hospitalisation is required. The symptoms include perforation and haemorrhage of the gastric lining (Peura & Goldkind, 2005).

The degree of risk of upper gastrointestinal bleeding (UGIT) among NSAID users is two to five times greater compared to non-NSAID users (Straus & Ofman, 2001). Each NSAID formulation will exhibit a different degree of risk for resultant GIT complications. Diclofenac and ibuprofen are regarded as the safest non-selective NSAIDs having the lowest degree of risk for possible UGIT bleeding and perforation. The half-life of NSAIDs that are composed of aspirin, indomethacin and naproxen is linked to an increase in the risk of UGIT injury. (Straube, Tramèr, Moore, Derry, & McQuay, 2009).

A systematic review performed by Wilcox *et al.* in 1994 showed that the potential to develop NSAID related side effects is seven times greater with the usage of a non-selective NSAID compared to a selective NSAID. Research published by (Straube, Tramèr, Moore, Derry, & McQuay, 2009) indicated that the mortality rate from non-drug GIT-related complications is 1 in 13. This rate increased to one in five patients who had prior exposure to NSAIDs (Straube, Tramèr, Moore, Derry, & McQuay, 2009). Gastrointestinal complications can happen whilst using NSAIDs, or the complications can arise up to two weeks after the last dose (Sostres, Gargallo, & Lanás, 2013).

2.5 NSAIDs in South Africa

The South African Health Products Regulatory Authority (SAHPRA) was established in 2016. SAHPRA is a statutory body established in terms of the Medicines and Related Substances Act, as amended (Act 101 of 1965) that governs the manufacture, distribution, sale, and marketing of medicines and health-care products (DOH, 2017).

Essential medicines are defined as “those that satisfy the priority health care needs of the population”, this is one of the eight elements of primary health care as outlined in the declaration of Alma-Ata’ (World Health Organization (WHO), 1978). The essential medicines programme was established in South Africa in 1996 and was revised in 2014. This programme consists of the essential medicines list and treatment guidelines for the medications of the essential list. The list comprises 14 priority medications that are intended to address the general health requirements of the population. Ibuprofen is listed in the

essential medicines list as a paracetamol alternative under first-line pain management. There is no current alternative on the essential medicines list for ibuprofen, consequently explaining the popularity of NSAIDs in South Africa (DOH, 2014). Grand-Pa™ (aspirin and paracetamol) and Disprin™ (aspirin) are the leading NSAIDs in South Africa. Grand-Pa™ and Disprin™ are easily accessible as they are available non-prescription in pharmacies or non-pharmacy locations such as grocery stores and informal stores. Grand-Pa™ has a strong marketing presence in South Africa, increasing its popularity among citizens (Govender & Brand, 2018).

2.6 Regulation of medicines in South Africa

Regulation in the pharmaceutical industry is more controlled and strictly enforced in the prescription medication industry as these preparations cannot be dispensed without a prescription from an authorised HCP. Regulation is not as strictly enforced with non-prescription formulations. Many variations of aspirin can be purchased anywhere from grocery shops and informal shops to pharmacies and are usually readily available free of charge from government clinics (Bennin & Rother, 2014).

It is a legal requirement in South Africa for all non-prescription medication packaging to contain all relevant patient information. The packaging needs to include three aspects that will need to be produced by the manufacturer and approved by the local regulatory entity SAPHRA. The patient information comes in three forms: (a) The label present on the box, which includes necessary information on the medication which will need to be present, (b) The Professional Information for medicines for human use that consists of the safety, dosage and scientific data for relevant HCP will be listed here, (c) and the patient information leaflet, which contains simplified information regarding safety and dosage instructions should be included here in layman's terms (DOH, 2017).

The mandatory requirement of providing patient information has not been strictly enforced. In many local clinics, medication is often purchased in bulk quantities. The medication is sorted and repackaged into small packets before being redistributed to the consumer. These packets

are often without all the required documentation and expiration dates, and a simple dosage instruction will be present on the box (Bennin & Rother, 2014).

2.7 Risk factors of NSAID- associated gastroduodenal bleeding

Advanced age is one of the most substantial risk factors for NSAID induced gastric complications. A systematic review performed in the United Kingdom of 18 GIT case-control and cohort studies showed a definite increase in the risk of GIT bleeding in NSAID users aged 75 years and older (Hernández-Díaz & García-Rodríguez L, 2001). South Africa's elderly (people over 60) population has increased from 2.8 million (1996) to 4.1 million (2011), with projections of 7 million people by 2030. Current socioeconomic assessments estimate that 40% of the elderly live in poverty, 38% rely on chronic medication, and 28 % have no formal education (Lehohla, 2017). Since the risk of a UGIT bleeds increases from 1.65 per 100 000 in patients older than 65 years and 12.7 per 100 000 in patients >75 years of age (Gabriel, Jaakkimainen, & Bombardier, 1991); (Hansen J, J, Lauritsen J, & Bytzer, 1996), together with social and economic deficiencies, the potential cost to South African health-care is significant.

2.8 Factors influencing decreased awareness NSAID related side effects

Level of awareness

In a survey of 4799 participants, 807 participants were identified as NSAID users (prescription or non-prescription), having taken NSAIDs twice or more in the last year, for a period of five or more consecutive days (Singh & Triadafilopoulos, Epidemiology of NSAID-induced GI complications, 1999). Approximately 75% of regular NSAID users were either unaware of or indifferent about possible gastrointestinal side effects. Moreover, just under 60 % of regular users indicated that they had expected to see warning signs before the development of NSAID induced serious side effects (Singh, Ramey, Terry, Khraishi, & G, 1997).

Healthcare insurance costs

In South Africa, medical healthcare insurance is mostly available in the private sector, and approximately 84% of the population do not have medical insurance and rely exclusively on the national healthcare system (Naidoo, 2012). The South African national healthcare system is overburdened; this often leads consumers to purchase non-prescription medicines as they are relatively inexpensive and easily accessible, without consultation, the need to consult with a healthcare professional (Mayosi & Benatar, 2014).

Gastroprotective agents

Gastroprotective agents (GPAs) are known as acid suppressants, such as histamine-2 receptor antagonists (H2RAs) and proton pump inhibitors (PPIs). These agents are effective in preventing gastrointestinal (GIT) bleeding in non-steroidal anti-inflammatory drugs (NSAIDs) users. (Kim, Kim, & Hong, 2019) Most GPAs require a general practitioner's (GPs) prescription, and the GPAs that are available non-prescription are not always available at the same vendors that sell non-prescription NSAIDs and consumers may not be aware of the necessity to use GPAs to prevent the side effects of non-prescription NSAIDs (Van Schoor, 2014). Both GPAs and selective COX-inhibitors are not included in the SA Essential Medicines List; consequently, they are not readily available and financially out of reach of the majority of South Africans (DOH, 2014).

2.9 Conclusion

In summary, due to various side effects of the NSAIDs described by the literature mentioned above, these drugs should be prescribed in the lowest effective dose possible and for the shortest duration to monitor gastrointestinal implications, especially for elderly patients who are most prone to GIT -related side effects. There are some benefits associated with the consumption of NSAIDs, such as pain and inflammation management. Patient awareness of the risk of NSAIDs can prevent the incidence of side effects from occurring and ensure that NSAIDs are used to their maximum benefit without the risks and side effects involved.

In South Africa, NSAID preparations are readily available in pharmacies, grocery stores, and a myriad of other formal and informal outlets, thus making these medicines easily accessible

to all South Africans. NSAID use is common in South Africa and most patients presenting with upper gastrointestinal tract side effects were taking non-prescription NSAIDs. These complications are potentially fatal and yet often preventable. Patients are inadequately educated on the dangerous side effects and may not adhere to dosing and administration instructions of NSAIDs. Patients who have experienced GIT side effects or those who are prone to GIT side effects often do not take adequate prevention methods such as using gastroprotective agents.



CHAPTER 3: METHODOLOGY

3.1 Introduction

This chapter presents the methodology of the study by discussing the setting, study design, population, data collection, data analysis, validation of research tools and ethical considerations. A survey refers to the process of collecting information from a sample of individuals through various methods to make an inference about the larger population (Ponto, 2015). A questionnaire is one method of obtaining information through either open or closed-ended questions or a combination of both. Questionnaires offer an objective means of collecting information about participants knowledge, beliefs and attitudes (Boynton & Greenhalgh, 2004)

3.2 Study Design

A cross-sectional design was used for this study. A cross-sectional study design is an observational type of study design, the outcomes and exposure of study participants are measured at the same time, it differs from case-control studies which select participants based on the outcome status of cohort studies by which participants are selected based on the exposure status. Cross-sectional study designs are used for population-based surveys and are used to assess the prevalence of diseases in clinic-based samples. These studies are fast and inexpensive. Another advantage of cross-sectional study design is that it allows for the comparison of multiple research variables at one point in time (Setia, 2016).

3.3 Questionnaire Design

The questionnaire comprised of three sections that covered:

- Demographic information

- A table consisting of generic and selected trade names for systemic NSAIDs
- NSAID use patterns and side effect awareness and knowledge

The demographic information section consisted of five multiple-choice tick box questions. The second section consisted of the generic and selected trade names for systemic NSAIDs. The table was used to assist participants in identifying which type of NSAIDs they were using. The third section consisted of 13 questions. The first two questions were open-ended, where the respondent could write in their feedback. The remaining 11 questions were closed-ended multiple-choice questions. The first two open-ended questions generated quantitative data where the main themes were identified by the researchers.

3.3 Study sample

In cross-sectional studies, the aim is to estimate the prevalence of an unknown parameter(s) from a target population using a random sample. Based on *Priori* calculations, a sample size of 194 participants is required to determine the level of awareness of NSAID related side effects. The study sample was increased to 220, which ensured that there were at least 194 complete questionnaires.

The study sample consisted of approximately 220 adults (over 18 years of age) in Johannesburg, South Africa. The reason for the selection of adults-only is because children are not consciously aware of their medicine consumption and the possible side effects that could occur. Children often only consume these medications from the direction of their parents under prescriptions from a doctor.

The invitation to participate aimed to include participants recruited from multiple pharmacies across Johannesburg from September 2019 to October 2019.

The pharmacies were selected using systematic sampling. A systematic sample is defined as a type of probability sampling method by which sample participants from a larger population are selected according to a random starting point but with a fixed, periodic interval (Hayes, 2019). A total of 146 pharmacies were identified in Johannesburg from the significant private pharmacy groups. A selection of 22 pharmacies was required to achieve the required

sample size. From the 146 pharmacies identified, a total of 22 were required. The pharmacies were listed in alphabetical order, and every 6th pharmacy was selected to be included in the study. Only 18 of the 22 pharmacies provided consent for questionnaires to be distributed to patients in their pharmacies. A total of 220 questionnaires were collected. The study sample did not include participants who acquired NSAIDs from a non-pharmacy source.

3.4 Data Collection

A self-administered questionnaire was the designated means of data collection. The survey was conducted using a self-completed, anonymous questionnaire. No personal data was requested or required. The questions comprised of average patient consumption, type of NSAIDs consumed, patient awareness of the risks that are involved in chronic NSAID consumption.

Once the responsible pharmacist from the selected pharmacy had provided consent for questionnaires to be distributed to the patients in the store, patients who were waiting in queues were approached and asked if they would provide consent to participate in a research project. Once consent was provided, the informed consent was signed, and the participant was given a questionnaire to complete. All participants were asked about their general demographics, including educational background, type of NSAID taken, the frequency of self-administration, the form of medicine taken, and their opinion about current NSAID availability. The questionnaire required the participants to list the NSAIDs that they consume daily and their awareness of a list of the most common NSAID related side effects. The questionnaires were distributed among pharmacies in the Johannesburg metropolitan area. The questionnaire took approximately 5-10 minutes to complete. **Please refer to Annexure 5 for the questionnaire.**

3.5 Data Analysis

The data collected were entered into a Microsoft Office Excel (2016) spreadsheet.

Descriptive statistics are defined by coefficients that summarise a given data set, which can be either a representation of the entire or a sample of a population. Descriptive statistics comprise

measures of central tendency and measures of variability (Hayes, 2021). Descriptive statistical analysis was completed on the demographic data where the mean of age was determined. The collected data were tabulated and summarised in the form of graphs, i.e. bar graphs and pie charts. Subgroup analysis is the type of analysis done by breaking down study samples into subsets of participants based on a shared characteristic (Burke J F, 2015). Subgroup analyses were performed on the overall awareness of NSAID related side effects compared to the communication received from their HCP.

3.6 Ethical Considerations

This survey was conducted without any conflicting ethical issues. Ethics approval was received before the study was conducted (**Please refer to Annexure 1 for the ethics approval**). Permission was obtained from the responsible pharmacist before any participants were recruited to the study (**Please refer to Annexure 6 for signed pharmacy permission letters**). An informed consent form was signed by the participants before the completion of the questionnaire (**Please refer to Annexure 4 for the informed consent form**). To ensure confidentiality the informed consent forms were stored in a locked cupboard and no identifying information was recorded. While anonymity could not be achieved in this study as the informed consent forms needed to be signed, all identifying information has been kept confidential. The questionnaires have been filed and are stored in a locked cupboard and will be held for five years. The data obtained has been stored on a password-protected database and will not be used for any future studies or research.

CHAPTER 4: RESULTS

4.1 Introduction

This chapter presents the findings of this study in a descriptive format in frequencies and percentages. The results cover socio-demographic characteristics and are presented according to the research questions presented.

4.2 Social-demographics

A total of 220 NSAID users completed the questionnaire. The detailed socio-demographics are summarised in Table 1.

The sample comprised of 60.45% (n=133) female participants, 39.09% (n= 86) male participants and 0.45% (n=1) non-respondents who did not answer the question.

The age range of the participants varied; most participants were between the ages of 31 and 40 years old, making that group the majority with 28% (n= 62) of the study sample. The age group of 18-30 years of age consisted of 25% (n=55) of the sample. The participants between 41-50 years of age consisted of 18% (n=40) of the study sample, followed by the 51-60 age group with 16% (35) of the sample.

The majority of the participants indicated that they have a degree (n=88, 40%), with the highest level of education reported as a post-graduate degree. 58% (n= 127) of participants possess a post-school qualification. There was a vast variation among employment, with the 'other' category falling into the majority (n=69, 31.36%) and business administration to follow with (n=44, 20%).

The most popular NSAID obtained was ibuprofen (n=95, 43.18%), followed by salicylates (n=73, 33.18%) and diclofenac (n=25, 11.36%). These three accounted for 87.72% of the overall study sample NSAID use.

Table 1: *Socio-demographic characteristics including age, gender, marital status, education, employment and type of NSAID used.*

<u>Characteristics</u>	<u>Participants Number (Percent %)</u>
Gender	
Male	86 (39.09%)
Female	133 (60.45%)
Non- respondents	1(0.45%)
Age	Mean Age: 40.9 (41-50) Standard Deviation: 15.34
18-30 years	58 (26.36%)
31-40 years	57 (25.9%)
41-50 years	46 (20.9%)
51-60 years	34 (15.45%)
Above 60	24 (10.9%)
Non- respondents	1 (0.45%)
Education	
Primary school level	1 (0.45%)
Secondary school	32 (14.54%)
National Higher Certificate	53 (24.09%)
University Diploma	18 (8.18%)
University degree	88 (40%)

Post-graduate degree	23 (10.45%)
Non-respondents	5 (2.27%)
Employment	
Not Employed	29 (13.18%)
Blue Collar Worker	9 (4.09%)
Administrative services	17 (7.7%)
Basic Administration	5 (2.7%)
Business Administration	44 (20%)
Human Resources	5 (2.7%)
Science	11 (5%)
Law/Legal	6 (2.7%)
Medical Sales Rep	2 (0.9%)
Sales Rep	8 (3.63%)
Health care professionals	14 (6.36%)
Other	69 (31.36%)
Non-respondents	1 (0.45%)
NSAID Product	
Ibuprofen	95 (43.18%)
Salicylates	73 (33.18%)
Diclofenac	25 (11.36%)

Indometacine	5 (2.27%)
Naproxen	2 (0.9%)
Nabumetone	0
Piroxicam	2 (0.9%)
Ketoprofen	0
Tiaprofenic acid	0
Tenoxicam	0
Flurbiprofen	0
Ketorolac	0
Mefenamic acid	0
Nefopam	0
Lornoxicam	3 (1.36%)
Celecoxib	6 (2.7%)
Rofecoxib	1 (0.45%)
Meloxicam	6 (2.7%)
Etoricoxib	1 (0.45%)
Non-respondents	0

4.3 NSAID related side effects knowledge and awareness

The questions that were investigated in this section include:

- Have the participant's experienced side effects from taking NSAIDs?
- For what purpose are NSAIDs taken?
- Are the NSAIDs used in combination with other substances?

- Are the NSAIDs taken before or after meals?
- Do the participants believe NSAID use is safe?
- Are the participants aware that NSAIDs can cause stomach ulcers?
- Are the participants aware that NSAIDs can cause acid reflux or heartburn?
- Have the participants been advised regarding NSAID related side effects by their HCP?

According to Figure 1, the majority of the participants, 59.54% (n=131), only take NSAIDs when necessary, 15.45% (n=34) of participants indicated that they use NSAIDs once a day, 10% (n=22) use them twice a day, 7.72% (n=17) use NSAIDs three times a day, and 7.27% (n=16) use it once a week.

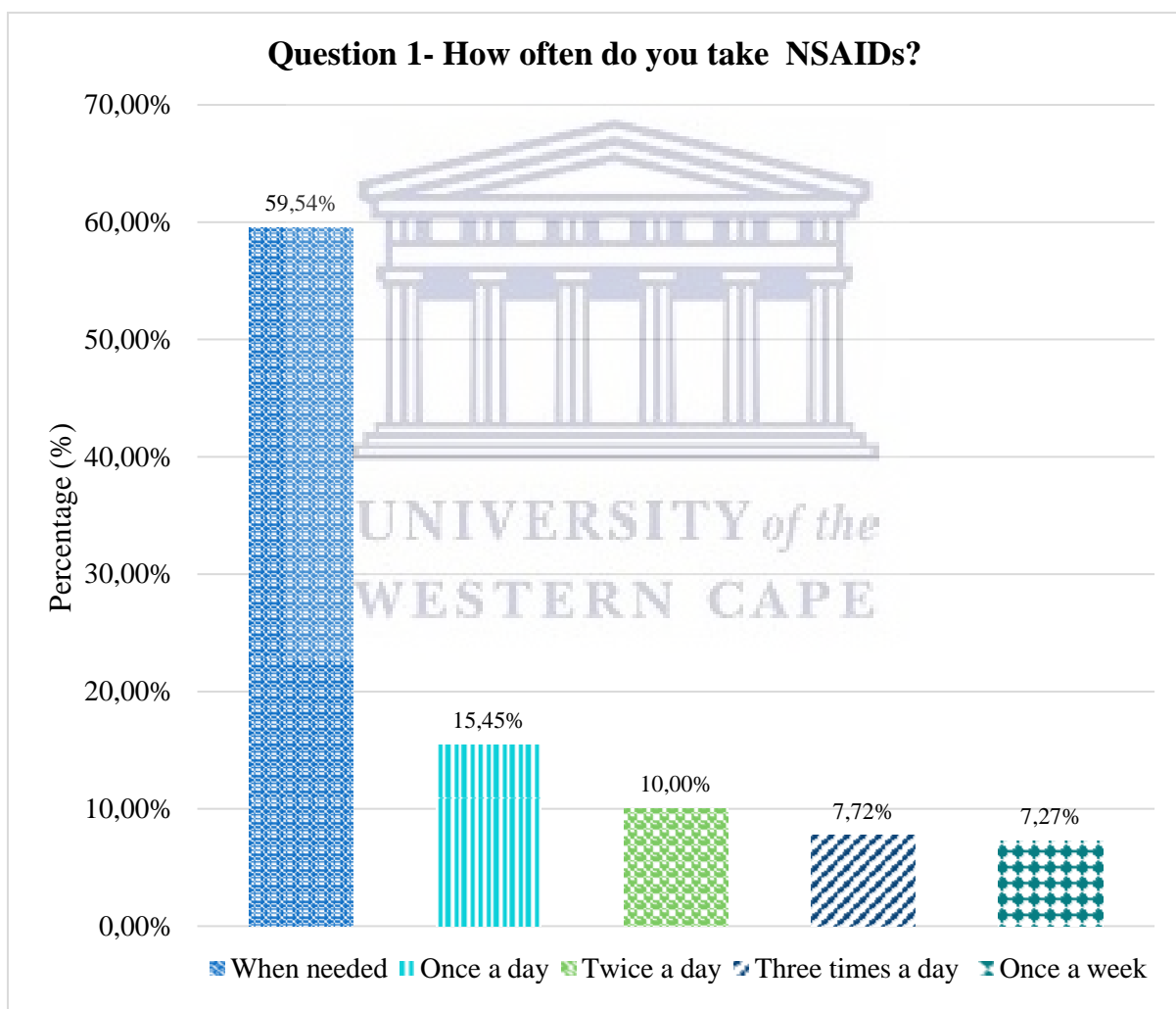


Figure 1. The frequency that NSAIDs are used.

Question 2, which asked about NSAID side effects, was not illustrated in a graph as 94.5% (n=208) of participants specified that they had not experienced a side effect related to NSAID use.

As shown in Figure 2, the NSAIDs were mainly used to treat pain, as 55% (n= 121) participants use NSAIDs for this indication, 29.09% (n=64) take NSAIDs for both pain and inflammation, 6.82% (n= 15) consume NSAIDs for inflammation only, 5.45% (n=12) use NSAIDs for common colds and influenza plus inflammation, the remaining 3.81% (n=8) identified using NSAIDs only for colds and flu, chronic disease and other reasons.



Question 3- For what purpose do you take NSAIDs?

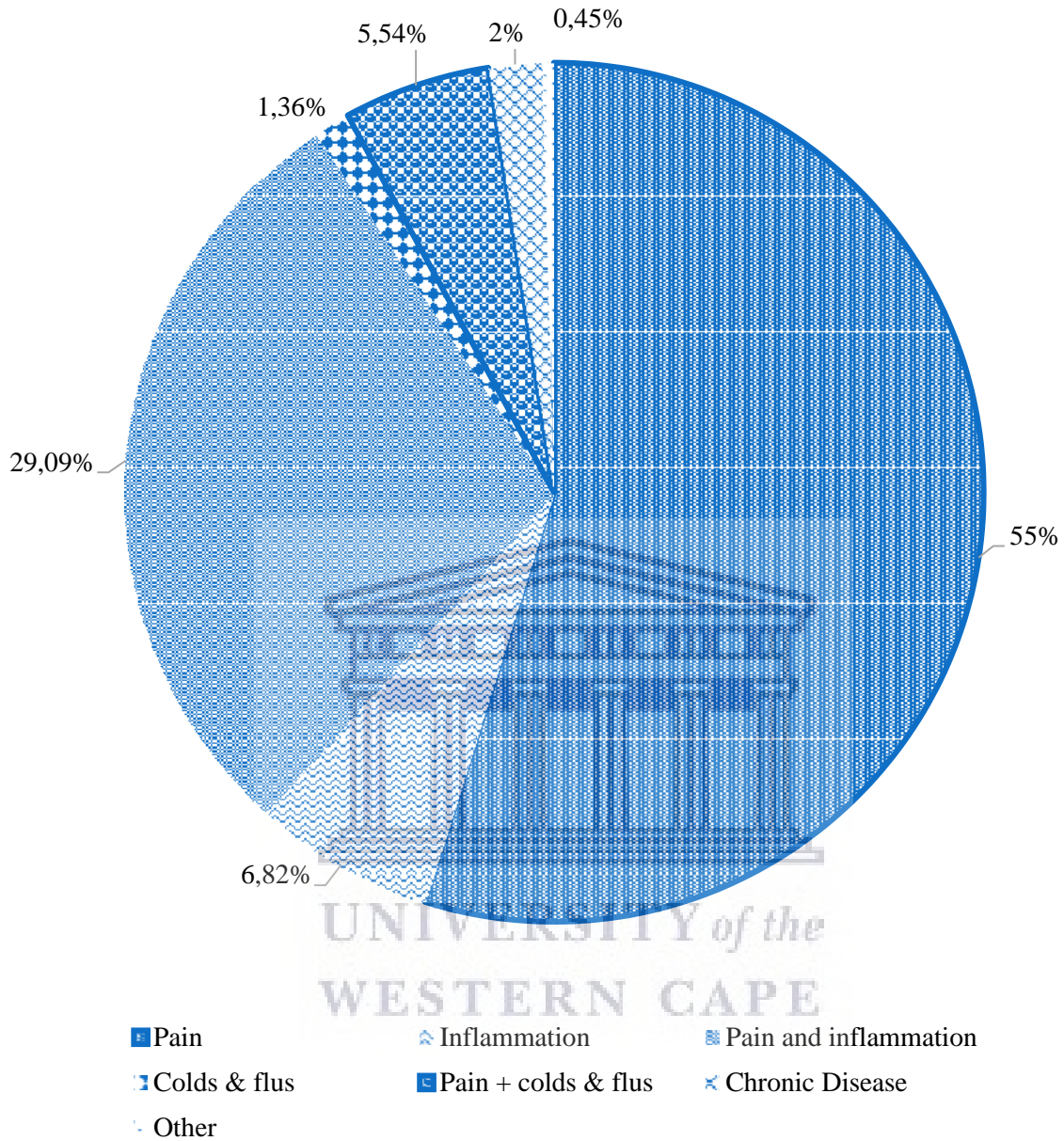


Figure 2. Percentage of different indications that NSAIDs are used to treat.

Question 4, which asked about the form of the NSAID, was not described in a graphical context as 95% (n=209) of participants indicated that their preferred form of NSAID is a pill/tablet.

Question 5 inquired about where the participants obtained their NSAIDs. Figure 3 shows the

number of NSAIDs that were obtained non-prescription compared to prescribed NSAIDs from a general practitioner. Figure 2 below shows the majority of the NSAIDs obtained by participants were non-prescription, with 77.72% (n=170) of participants indicating purchased non-prescription NSAIDs and 22.27% (n=50) of participants purchased prescription NSAIDs.

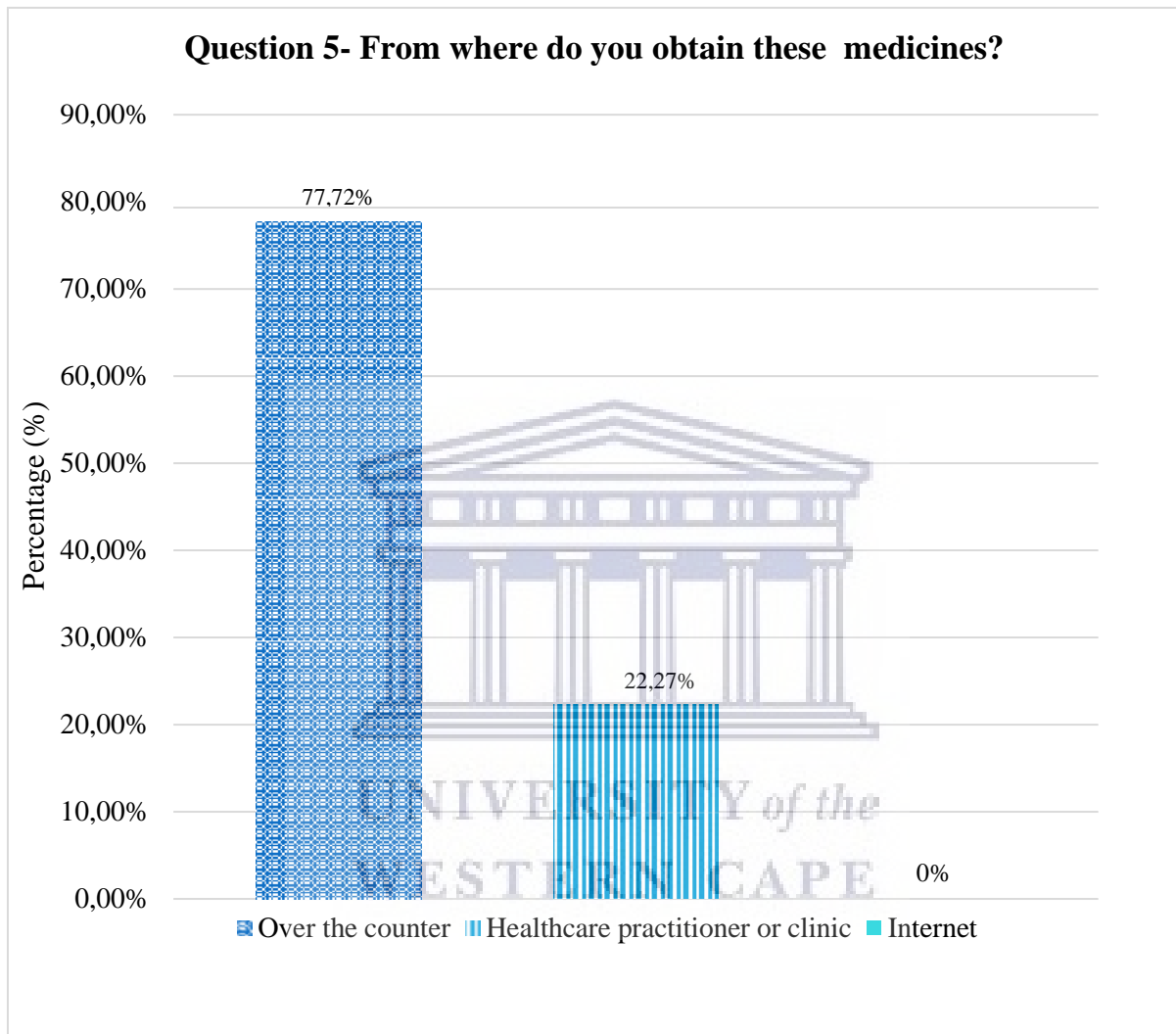


Figure 3. Locations where the NSAIDs were purchased.

Question 6 was used to assess the participant's behaviour towards NSAID use. As shown in Figure 4, most of the participants, 73.18% (n=161), do not take NSAIDs in combination with other substances, 10.45% (n=23) indicated they take NSAIDs in combination with caffeine, 8.64% (n=19) take NSAIDs with other medications, and 7.7% (n=17) have identified using NSAIDs in combination with alcohol.

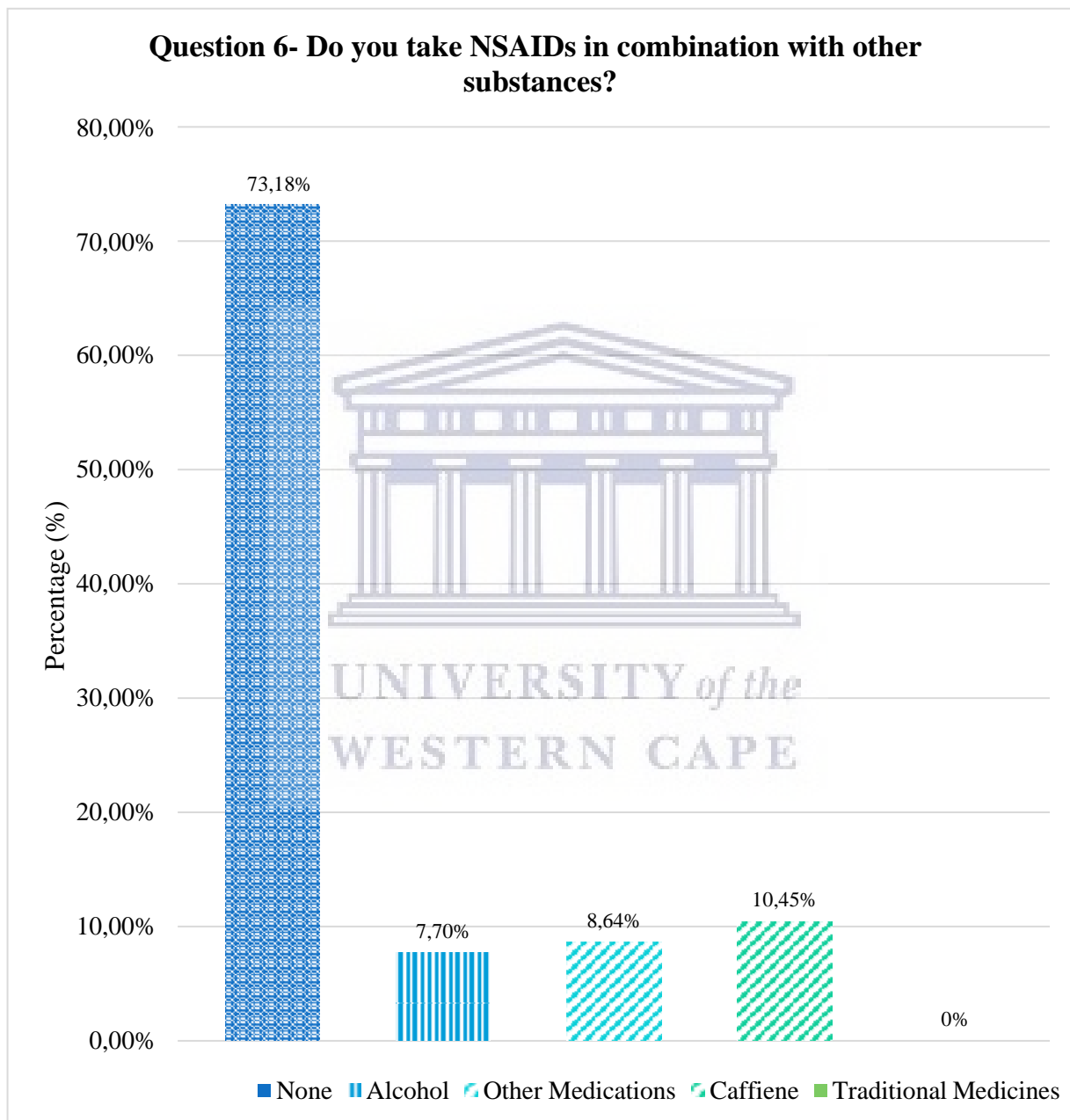


Figure 4. Substances that are taken in combination with NSAIDs.

Question 7 was intended to determine the behaviour of the participants with regards to using NSAIDS, the majority of the sample indicated they only take an NSAID after a meal or before bedtime 69.96% (n= 154), this is the recommended way of taking NSAIDS. 29.9% (n=66) of participants preferred to take NSAIDs first thing in the morning or before a meal.

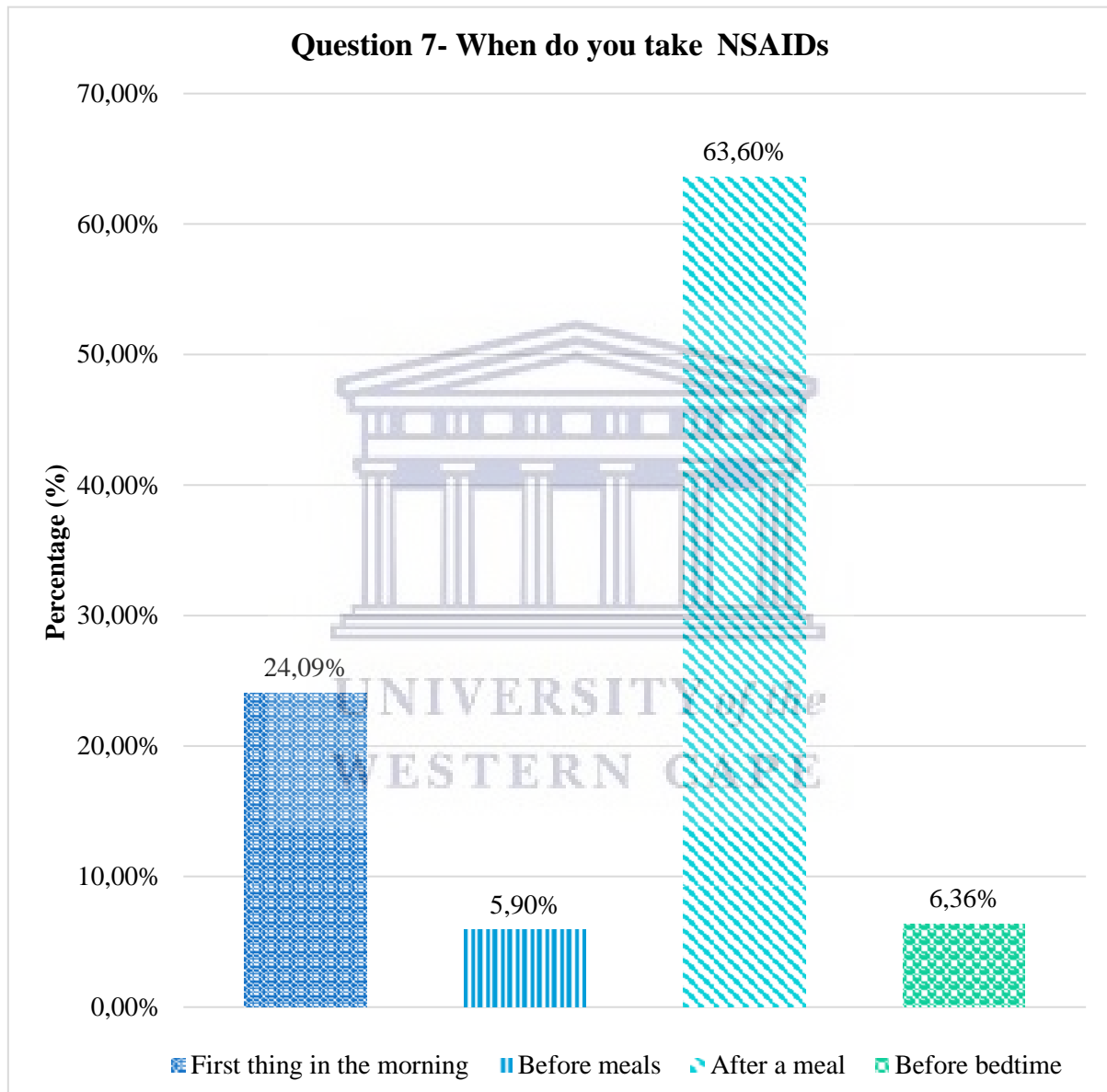


Figure 5. Preferred manner or time of day that NSAIDs are used.

Figure 6 describes the participant's perception of the safety of NSAID use. Almost 80% (n= 175) of participants perceived NSAIDs to be safe. Only 7.73% (n= 17) of the sample indicated that they think NSAIDs are unsafe, and 12.72% (n= 28) were uncertain.

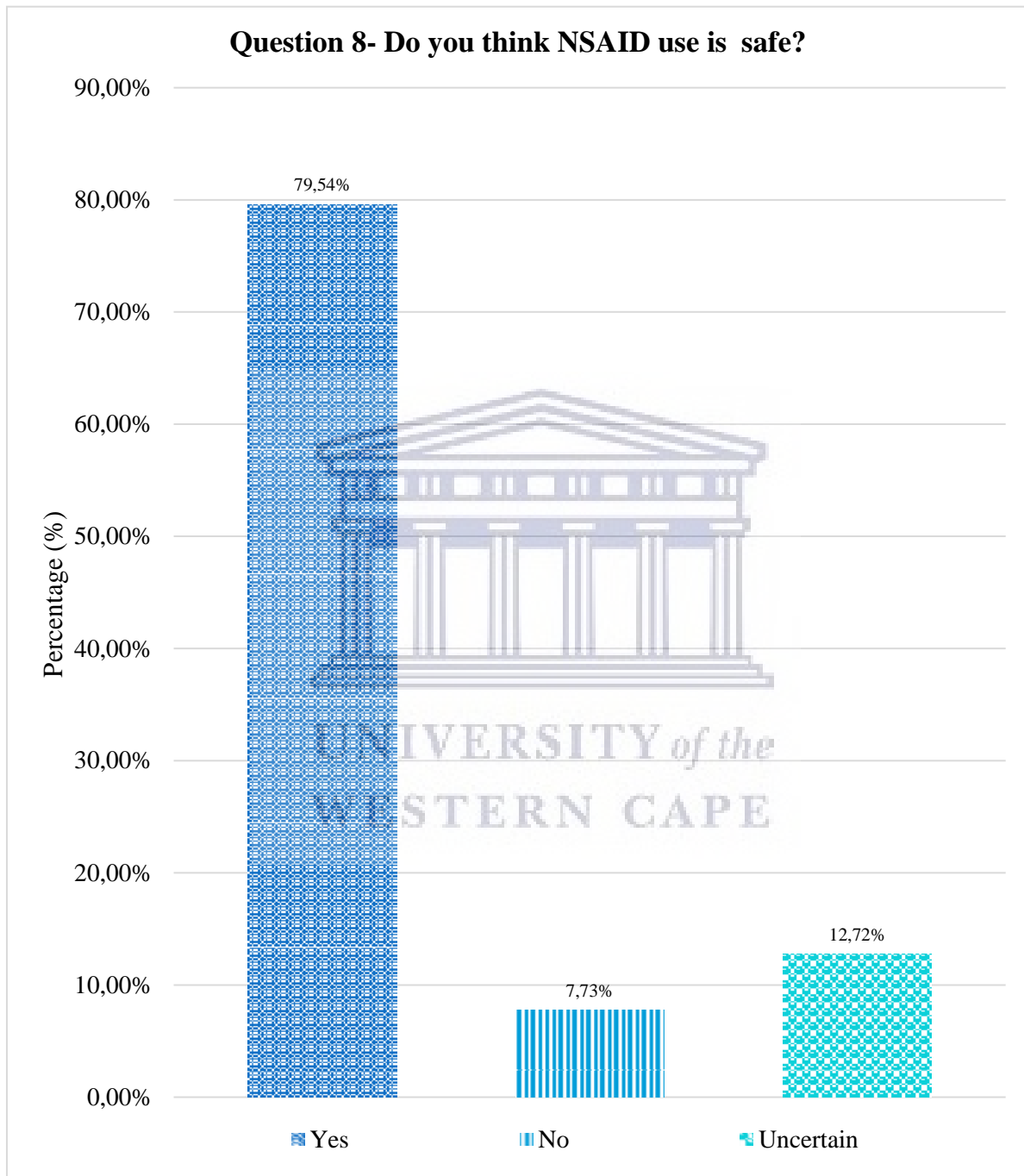


Figure 6. The participant's perception of the safety of NSAIDs.

Question 9 (Figure 7) was used to analyse whether participants were aware that NSAIDs could be abused or overused, and most of the study sample, 63.63% (n=140), identified that NSAIDs could be abused or overused. However, 25.9% (n=57) acknowledged that NSAIDs could not be abused or overused, and 10.45% (n=23) were uncertain.

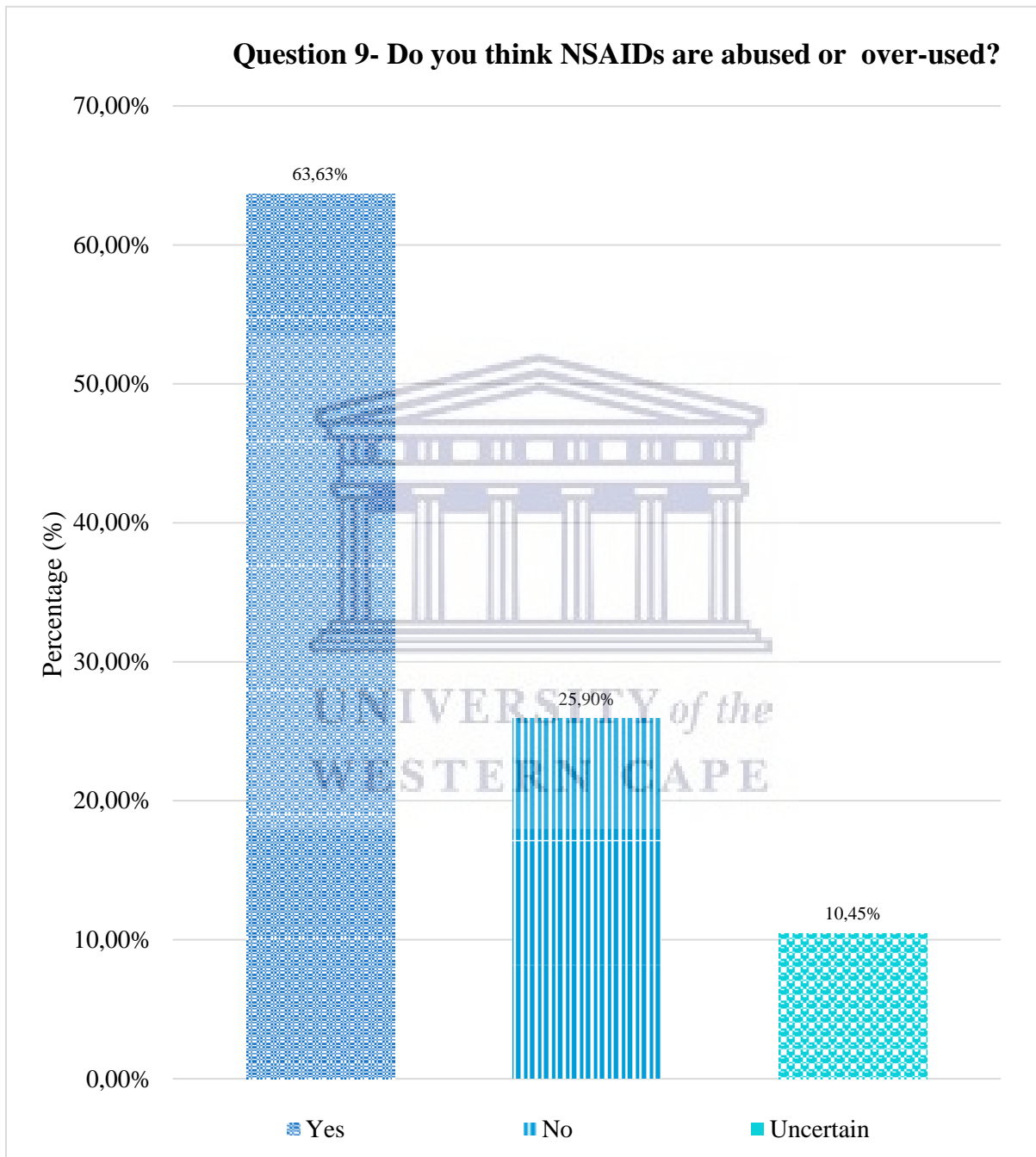


Figure 7. The patient's perception of whether NSAIDs can be abused or overused.

Question 10 assessed the participant's views on advertising NSAIDs. Figure 8 shows that 68.18% (n=150) of the sample agree with the advertising of NSAIDs and 22.27% (n=49) of the participants were uncertain.

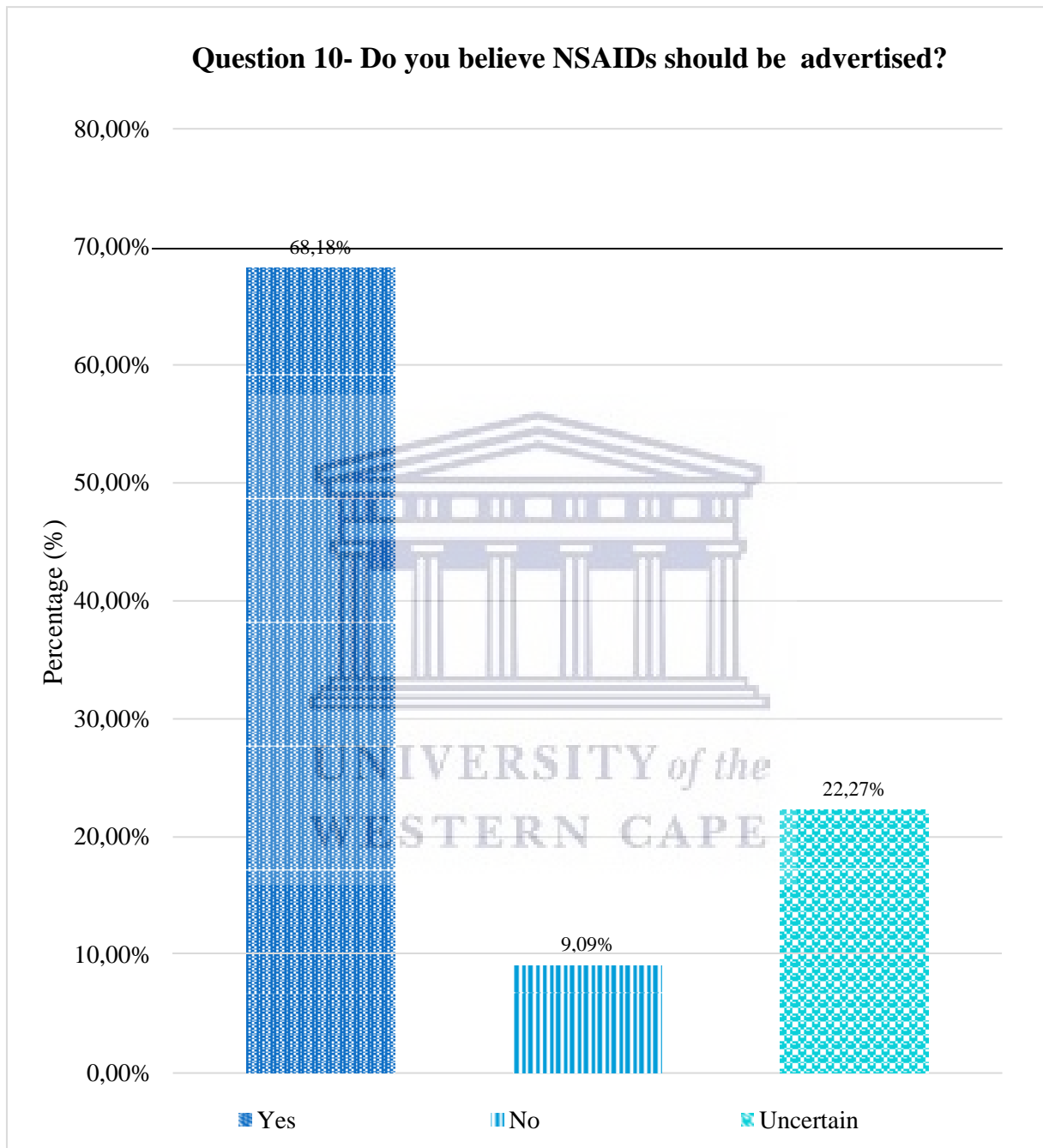


Figure 8. Participant's views on advertising NSAIDs.

Figure 9 below represents the overall awareness of GIT-related side effects related to NSAID use. With this question, unawareness is described both by answering no and by being uncertain whether NSAIDs could cause stomach ulcers and or acid reflux/heartburn. According to figure 10, 56.36% (n=124) of participants were not aware that NSAIDs could cause a stomach ulcer and 60.9% (n= 134) of the study sample were not aware that NSAID use could cause heartburn or acid reflux. Additionally, 43.63% (n=96) of the sample was aware of stomach ulcers as a related side effect, and 39.09% (n=86) of participants were aware that NSAIDs use could result in heartburn or acid reflux.

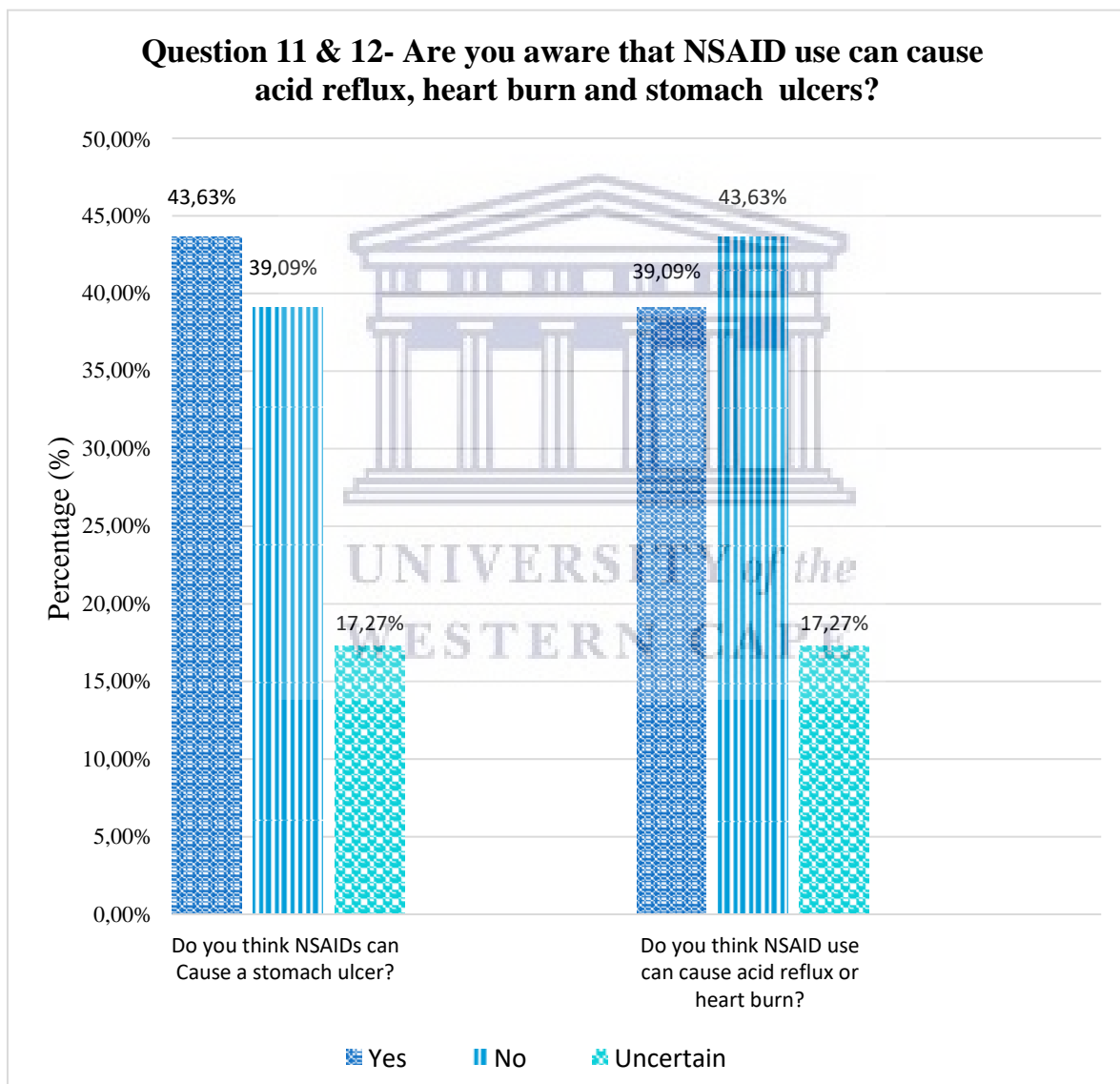


Figure 9. The level of participant awareness with regards to NSAID related side effects.

Figure 10 represents the communication between the patient and the HCP. The majority of the participants, 49.54%, n= 109, had not received communication regarding the risks and side effects related to NSAID use, and 3.2% (n=7) were uncertain if they had received the communication or not.

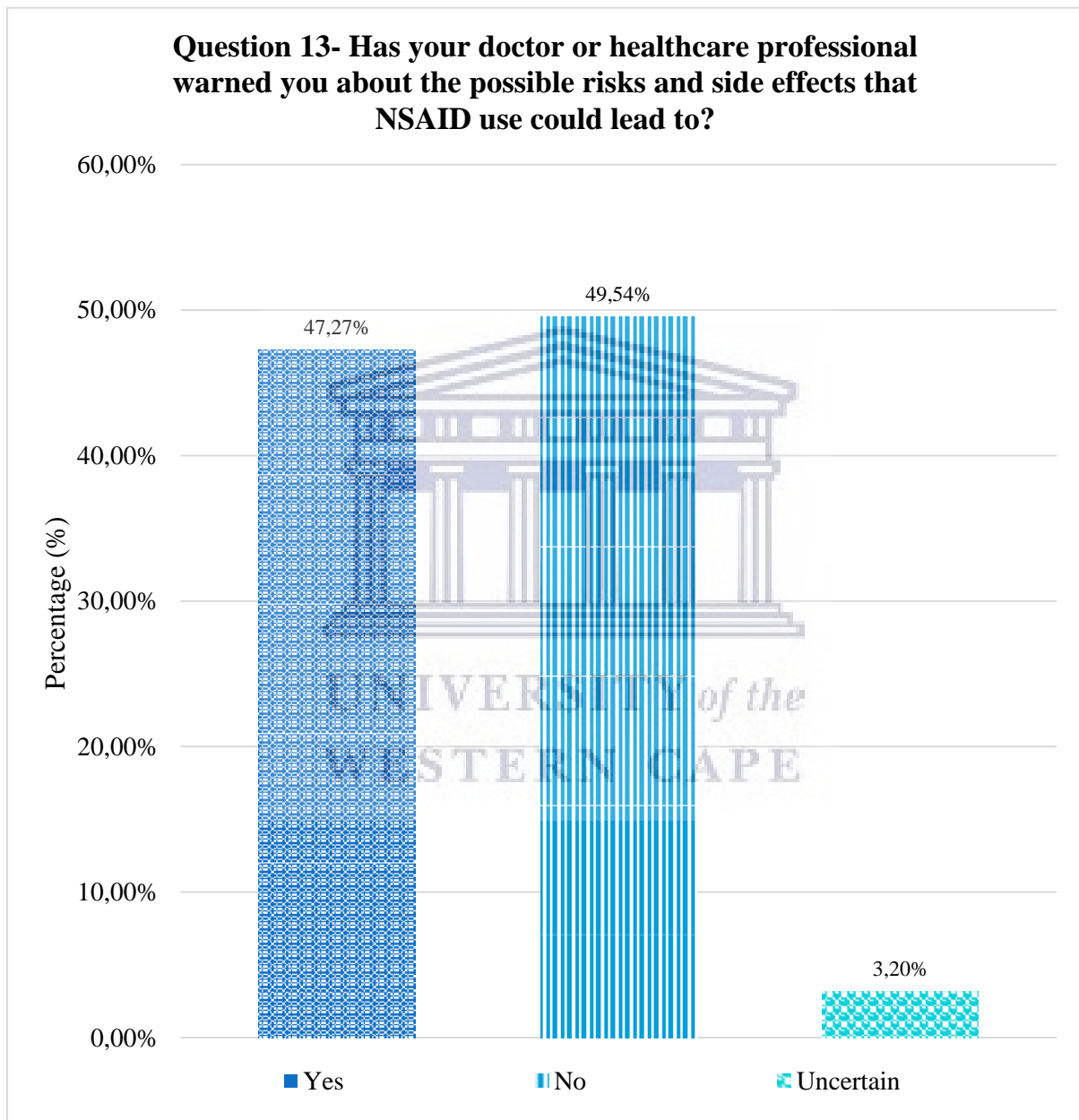


Figure 10. The level of communication between the participants and the HCPs regarding the risk and related side effects of NSAIDs.

A subgroup analysis was performed, as shown in Table 2 below. The level of education of participants was compared to the level of awareness of NSAID related side effects. The results in the table highlight that most of the education groups were not aware of the side effects associated with NSAID use. The university diploma group had the highest level of unawareness regarding NSAID related side effects, with 77.7% (n=14) of the participants that were not aware that stomach ulcers and acid reflux/heartburn are side effects associated with NSAID use.



Table 2

A sub-group analysis is describing the level of education that the participants obtained, compared to the awareness of the NSAID related side effects.

Level of education	Percentage of the sample in the study Number (%)	Participants who are aware of the NSAID related side effects Number (%)		Participants who are not aware of the NSAID related side-effects Number (%)	
		Stomach ulcer	Acid reflux/ Heartburn	Stomach ulcer	Acid reflux/ Heartburn
Primary school level	1 (0.45%)	1 (100%)	1 (100%)	0	0
Secondary school	32 (14.54%)	16 (50%)	14 (43.75%)	16 (50%)	18 (56.25%)
Higher certificate	53 (24.09%)	28(52.83%)	22 (41.51%)	25(47.17%)	31 (58.49%)
University diploma	18 (8.18%)	4(22.22%)	4 (22%)	14 (77.7%)	14 (77.7%)
University degree	88 (40%)	38(43.18%)	34 (38.63%)	50 (56.8%)	54 (61.3%)
Postgraduate degree	23 (10.45%)	9 (39%)	11 (47%)	14 (60.8%)	12 (52.2%)
No Response to the education question	5 (2.27%)	5 (100%)	5 (100%)	0	0

Figure 11 shows that 47.27% (n= 104) of the participants had received communication regarding the risks and possible side effects. This figure highlights the presence of communication between the HCPs and the participants that were not aware of the NSAID related side effects. Most of the participants that were not aware that these side effects could be caused by NSAID use had also indicated that they had not received communication from their HCP regarding the risks and potential side effects of using these medications.

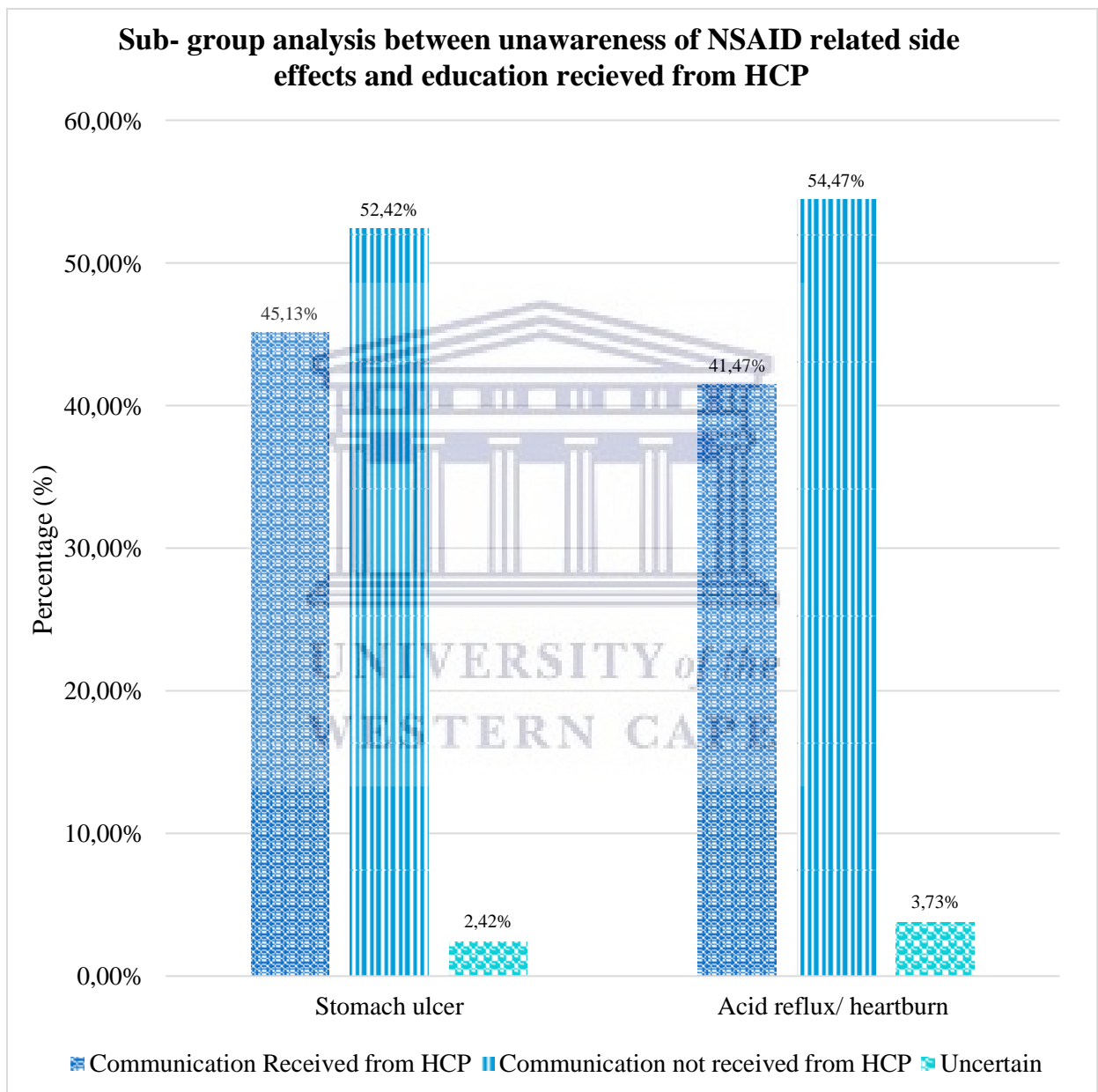


Figure 11. Unawareness of stomach ulcers and acid reflux/ heartburn as an NSAID related side effect and presence of communication regarding NSAID related side effects with HCP.

Figure 12 highlights the level of awareness of NSAID related side effects from the group of participants that have received communication regarding the related side effects of NSAIDs. This figure shows that even though participants have received informed information on the medication that they are using, they are still not aware of both the GIT-related side effects, with 53.85% (n=56) of informed participants not aware that both stomach and acid reflux could be caused by NSAID use.

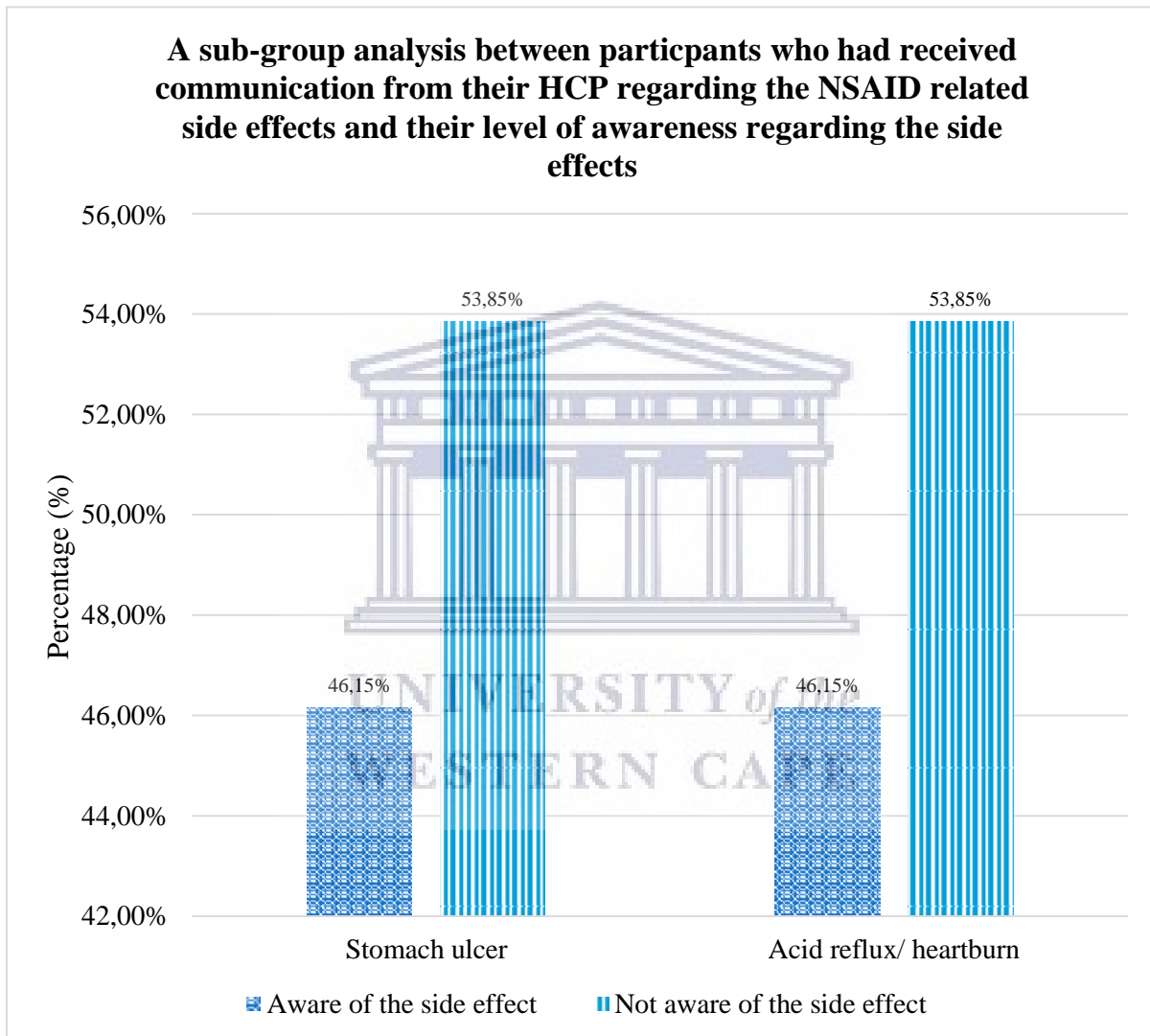


Figure 12. A sub-group analysis was performed on the participants that had received communication regarding the NSAID related side effects compared to their level of awareness regarding the related side effects.

Most of the participants in this study believed that NSAID use is safe. However, the majority of the participants in this group were not aware of the GIT side effects that are related to NSAID use. As shown in Figure 13, more participants were not aware of acid reflux and heartburn, with 67.65% (n=115) of participants not being aware of these side effects compared to stomach ulcer awareness, with 51.4% (n=106) of participants.

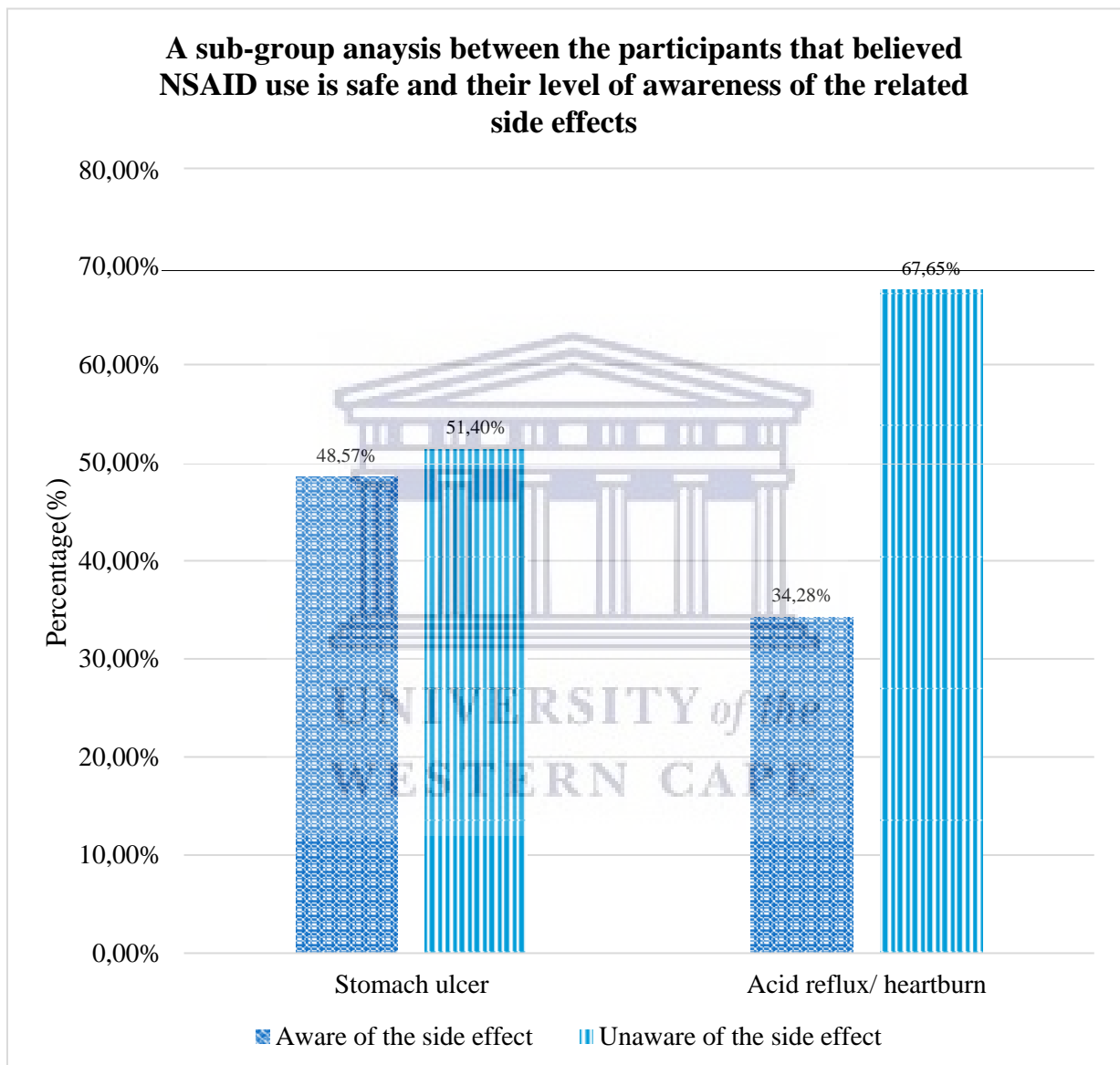


Figure 13. A sub-group analysis is comparing the awareness of the NSAID related side effects to the participants that believed NSAID use is safe.

Most of the study sample identified that they use non-prescription NSAIDs. As shown in Figure 14 most of the participants from the non-prescription group were not aware that NSAID use could cause stomach ulcers (56.14%, n=86) and acid reflux/ heartburn (66.9%, n= 103).

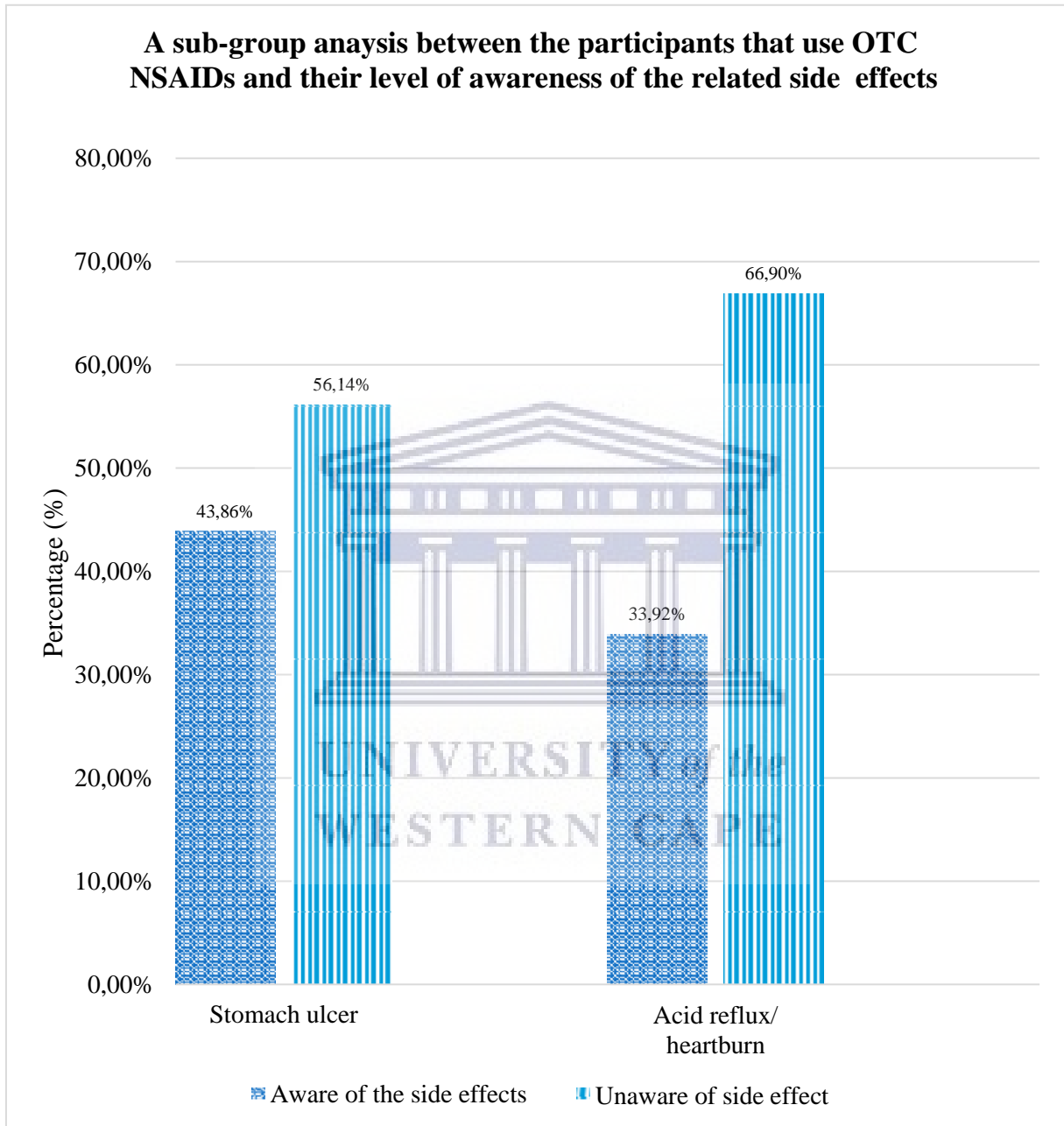


Figure 14. A sub-group analysis is comparing the awareness of the NSAID related side effects to the participants that used non-prescription NSAIDs.

The minority of the study sample indicated that they use prescription NSAIDs. However, a large group of the participants identified that they were aware NSAID use could cause acid reflux or heartburn. As shown in Figure 15, most participants were not aware that NSAIDs could cause a stomach ulcer (57.15%, n=38). Most of the participants in this group were unaware that NSAIDs could cause a stomach ulcer (57.14%, n=38).

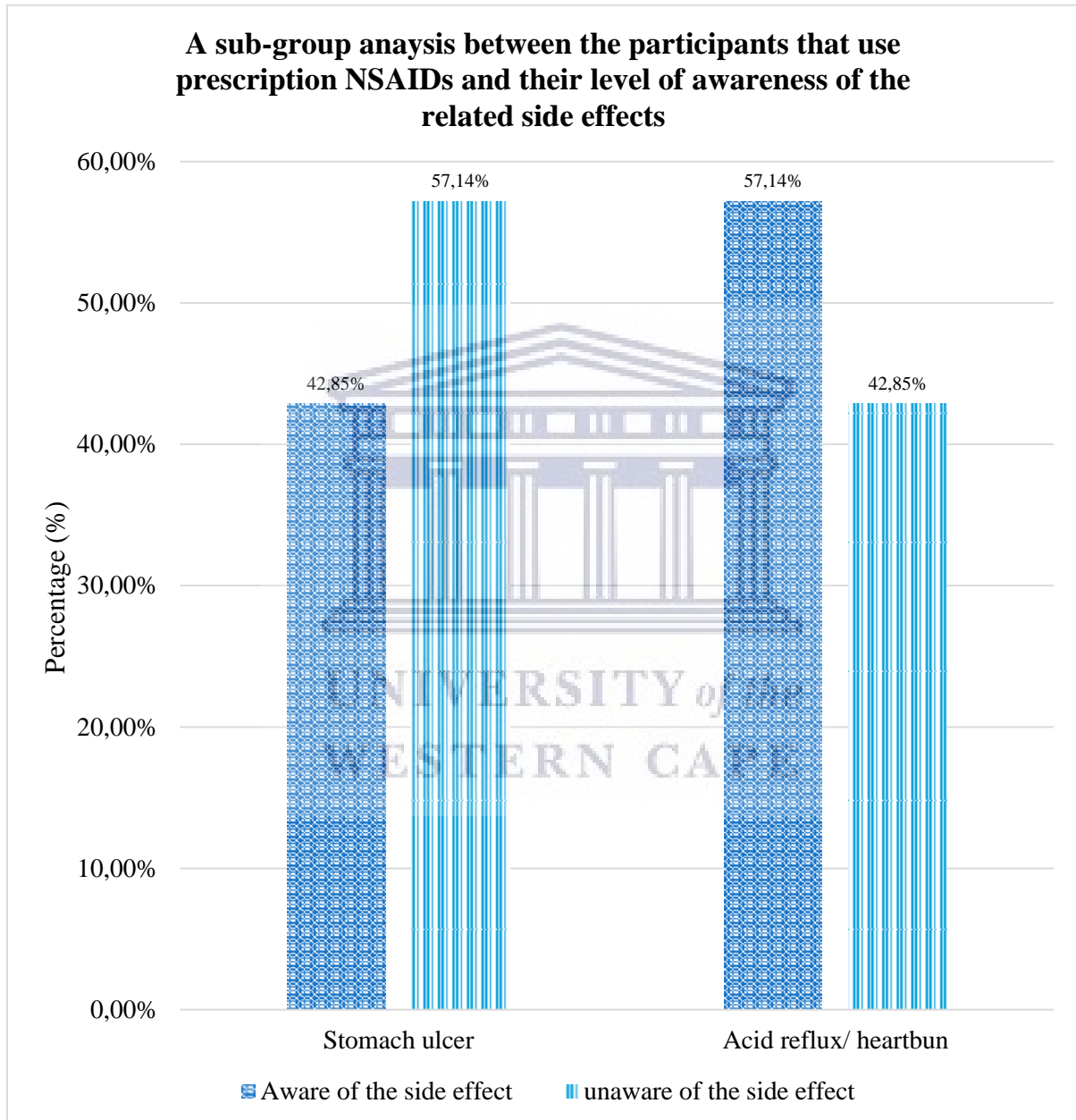


Figure 15. A sub-group analysis is comparing the awareness of the NSAID related side effects to the participants that used prescription NSAIDs.

From the 68.18% (n=150) of participants who think NSAIDs should be advertised. As illustrated in Figure 16, the majority of this proportion was unaware of the NSAID related side effects, from this group 56.6% (n=85) of participants were not aware that a stomach ulcer is an NSAID related side effect and 64.6% (n=97) of participants were not aware that acid reflux or heartburn is an NSAID related side effect.

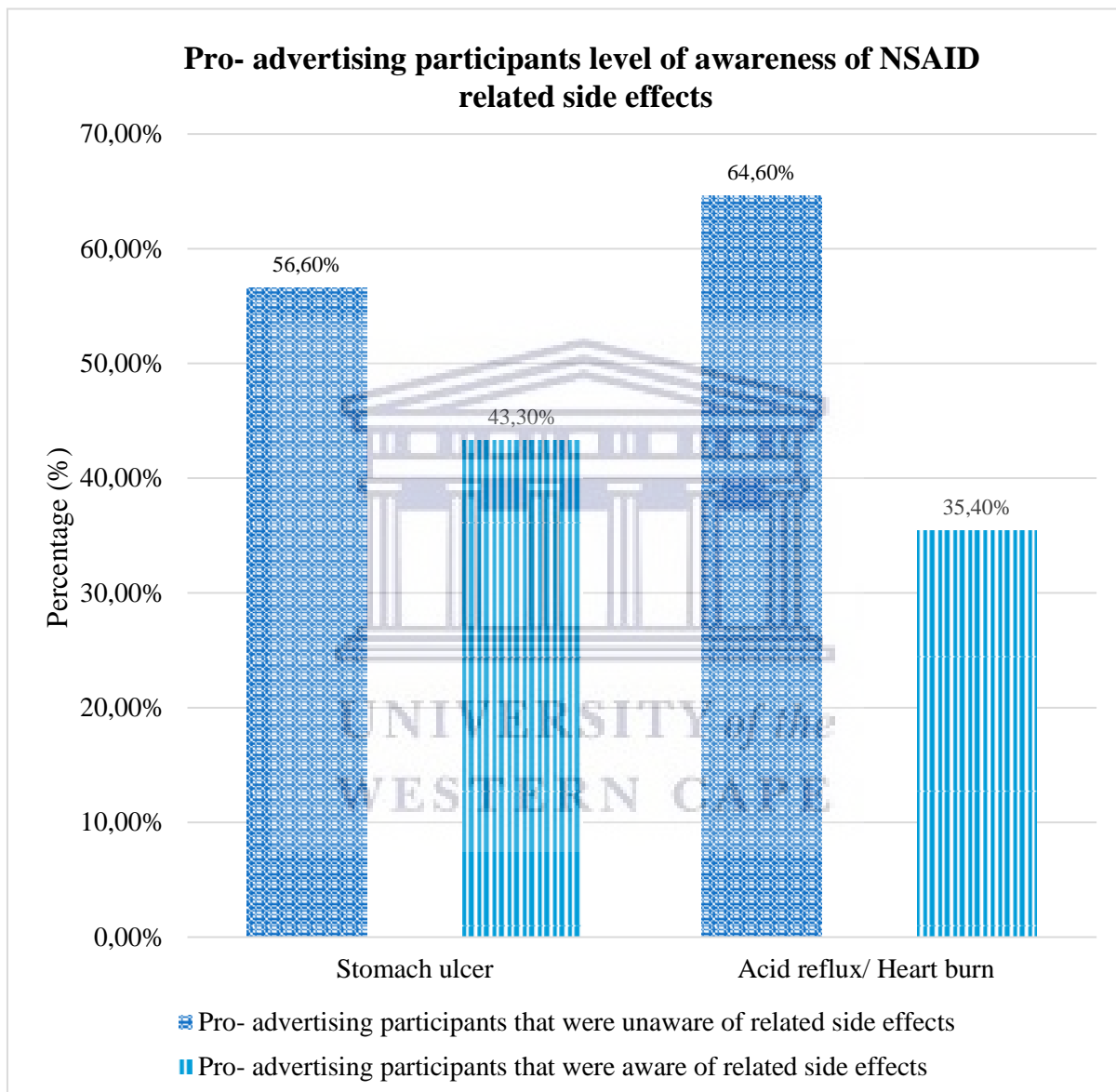


Figure 16. A sub-group analysis is comparing the awareness of the NSAID related side effects to the participants that believed NSAIDs should be advertised.

CHAPTER 5: DISCUSSION

5.1 Principal findings

Gender of the participants

The majority of the participants in this study were female (59.9%). Previous research confirms the findings that NSAIDs are mostly used or purchased by females. Research conducted by Motola *et al.* (2004) showed that the majority of the NSAID users who participated in the study were female, and these findings were also demonstrated by Roshi *et al.* (2017), in which 77% of the NSAID users were female.

Education status of the study sample

Almost half of all the participants have a university qualification, with most of the study sample identifying that they had obtained a post-school qualification.

NSAID side effect awareness in the elderly

The elderly group fell in the minority of the study sample, with only 10% of the study sample being above 60 years of age. Advanced age is a risk factor for UGIT side effects, ultimately leading to UGIT injury and bleeding Rahme, Joseph, Kong, Watson, & LeLorier, (2001). Over 54% of participants were of advanced age who were not aware of the side effects related to NSAID use, and this same percentage of advanced age participants indicated that their HCP had not informed them of the possible risks involved in NSAID use. The research performed by Popa (2011) on elderly participants over the age of 65 identified a significant difference between the participant's awareness of the side effects associated with NSAIDs and the level of communication with their healthcare providers, 75% of users indicated that their awareness of non-prescription NSAID related side effects was due to their communication with their HCP regarding the relative risks and side effects of NSAIDs. These results agree with the research findings of this study as most of the participants who were informed of the side effects by their HCP were aware of the possible side effects that were a result of NSAID use.

Employment status of the study sample

The study sample comprised of 86% participants who are currently employed, and 14% of the study group are presently unemployed. The unemployed participants still used private pharmacies to get their NSAIDs. Approximately 16% of South Africans (8 million people) have private health insurance that provides access to health care from the remaining 70% of doctors who work full-time in the private sector. Up to 25% of uninsured people pay out of pocket for private-sector care. (Mayosi & Benatar, 2014). A generic medication is often perceived as being substandard and of a lower quality than original medication (World Health Organization, (WHO), 1998); (Patel, Gauld, Norris, & Rades, 2012). This places limitations on national medicine policies and may influence consumers to rather purchase specific, preferred brands of analgesics from private establishments. Afolabi (2012) estimated that approximately 50% to 75% of health care expenses are associated with self-medication.

A generic medication is often perceived as being substandard and of a lower quality than original medication (World Health Organization, (WHO), 1998); (Patel, Gauld, Norris, & Rades, 2012).

The use of non-prescription NSAIDs

The results of this study agreed with the research conducted by Afolabi (2012), as 77.72% of participants in the study sample obtained their NSAIDs over the counter at pharmacies. Individuals who choose to use non-prescription medications need to be sure that the medicines are appropriate for their chronic or recurrent conditions and have proven records of safety, quality, and efficacy. The South African Health Products Regulatory Authority (SAHPRA) has warned the public about the risk of harmful effects when using non-steroidal anti-inflammatory drugs (NSAIDs). SAHPRA has warned consumers that non-prescription NSAIDs are to be used temporarily to reduce fever and to treat minor aches and pains such as headaches, toothaches, backaches, muscular aches, tendonitis, and strains. They have urged all consumers to read the patient information leaflet for both non-prescription and prescription medicines, as it provides important safety information (SAHPRA, 2018).

Participants NSAID usage and behaviour

The majority of the participants indicated that they only use NSAIDs when necessary. It is not recommended that an NSAID is used for a period that is longer than ten days. NSAIDs are

meant to be used for short term periods. A total of 59.5% of participants identified they only take the NSAID when needed, and 15.5% specified that they use an NSAID once a day, 10% indicated that they use the NSAIDs twice a day, 7.8% identified that they use NSAIDs three times a day. Even though the majority of the participants used the NSAIDs for short term use, the risk of upper GIT complications can occur even with short-term NSAID use (Goldstein & Cryer, 2015). The risks of NSAID use is not limited to continued use but also numerous other factors, such as advanced age and co-morbidities (Govender & Brand, 2018).

Indications that the participants used NSAIDs for

This study shows that a high number of participants identified the use of NSAIDs mostly for the management of pain (55%) followed by pain and inflammation (29.3%), inflammation (6.9%), pain and for cold and flu (5%), for chronic disease (2.3%), for colds/flu (1.4%) and other uses (0.5%). These findings are in agreement with Gutema *et al.* (2011), where NSAIDs were most frequently used for pain relief. Pain management was reported as the main reason for obtaining NSAIDs which agrees with previous research that indicates pain and painful states are associated with NSAID self-medication use (French & James, 2008).

NSAID behavioural usage

NSAID behavioural use was analysed by three questions: how often are NSAIDs taken, when are NSAIDs taken and if NSAIDs are taken in combination with other substances. More than half of the participants (59.5%) indicated that they only used NSAIDs when needed. Most of the participants indicated that they do not take NSAIDs with other substances, and 10% indicated that they consume NSAIDs with caffeine, and 7% have taken NSAIDs with alcohol. The study sample was aware of the correct way to use NSAIDs by only taking them when needed, after a meal and without caffeine or alcohol.

Types of NSAIDs used by the study sample

The study shows that the three most popular NSAIDs used were ibuprofen, salicylates, and diclofenac. Ibuprofen was the most popular NSAID among participants, with 42% of participants having identified that ibuprofen is their NSAID of choice. Ibuprofen is proposed as an alternative analgesic to paracetamol as a first-line treatment of pain management in the South African Essential Medicines list (SAEML) (DOH, 2014). At the primary care level, there

is no proposed alternative for ibuprofen, and consequently, the use of ibuprofen is common in South Africa. Salicylates were the NSAID of choice for 34% of the participants. Almost 12% of the participants identified that they use salicylates. Ibuprofen, salicylates, and diclofenac comprised 90% of the NSAIDs used by participants. The other 10% of participants identified that they were actively consuming prescription NSAIDs, indomethacin, piroxicam, lornoxicam, celecoxib, meloxicam, and etoricoxib. These results reach an agreement with (Li *et al.* (2014) research findings indicated that ibuprofen was the most commonly used NSAID. In Mozambique, NSAIDs are the most frequently used drugs, with ibuprofen being one of the most commonly used by university students (Lucas *et al.*, 2007).

Non-prescription NSAID use versus prescription NSAID use

The incidence of non-prescription NSAID usage is more remarkable compared to that of the prescription NSAIDs usage among participants, with 77.7 % of all participants currently obtaining their NSAIDs non-prescription. These findings contradicted those of Nunes, Costa, & Costa (2016), which indicated that prescription-only NSAIDs represented the majority of NSAIDs purchased. In Portugal, prescription NSAID side effect awareness was higher than non-prescription NSAID side effect awareness, with only 42.85% of participants being unaware of acid reflux/ heartburn as a side effect of NSAID use and 14% unaware of stomach ulcers, whereas the majority of non-prescription NSAID users that participated in the study were unaware. Moreover, 66.9% of the non-prescription NSAID users were not aware of acid reflux or heartburn being related to NSAID use, and 56.14% were not aware of stomach ulcers being a related side effect.

NSAID related side effects

Many of the participants indicated that they had not experienced any side effects from using NSAIDs. Moreover, 79.5% of participants indicated that they believe NSAIDs are safe. The results from this study coincide with research studies conducted by Wilcox, Cryer, & Triadafilopoulos (2005) in the United States of America which show that 56% of patients that are prescribed NSAIDs perceive them to be safe. Most of the participants that believed NSAID use is safe were not aware of the NSAID related side effects, with 51.4% of participants unaware that a stomach ulcer is a related side effect to NSAID use and 67.65% of participants unaware that NSAID use is related to acid reflux or heartburn. A cross-sectional research study was conducted in Thailand by Phueanpinit, Pongwecharak, Krska, & Jarernsiripornkul (2016)

that concluded that the overall perceived risk of NSAID consumption was low. A study in Ireland by Cullen, Kelly, & Murray (2006) revealed that NSAIDs were the most commonly prescribed medicines resulting in the perception that NSAIDs are the safest medicines and are without risk.

NSAID side effect awareness of the educated participants in the study sample

Despite the majority of the sample being well-educated with most of the participants having acquired a post-school qualification, 54% of all participants who were unaware that NSAIDs could cause stomach ulcers indicated that their HCP had not discussed the risks involved in NSAID use with them, 58% of participants who weren't aware of GIT side effects being related to NSAID consumption indicated that their HCP had not informed them of the risks involved in NSAID use. These findings are in agreement with research performed by Wynne & Long (1996), which showed that 67% of participants sampled in their study were not informed of the possible adverse effects that could occur as a result of NSAID use. These findings suggest that doctors and pharmacists are not providing the patient with adequate information regarding the risk of NSAID use.

Participants beliefs regarding advertising of NSAIDs

Most of the participants believed that NSAIDs should be advertised. However, a sub-group analysis performed on the NSAID related side effects awareness of the group that was pro-advertising showed that the majority of participants were not aware of the GIT-related side effects. Advertising of NSAIDs is known to have a direct impact on sales. 'Continental Outdoor Media' published their 2013 marketing strategy for Grand-Pa™ in Shoshanguve, an informal settlement 25km north of Pretoria. This marketing strategy demonstrated an increase in the sale of Grand-pa™ powders (Govender & Brand, 2018). Advertising of NSAIDs has been a controversial topic, but the marketing strategy in the campaign mentioned above highlights the ability of advertising to increase sales (Govender & Brand, 2018). However, an increase in sales does not lead to an increase in patient awareness and education regarding drug-related side effects.

NSAID side effect awareness in different socio-demographic groups

Even though several pharmacies from different socio-demographic areas were included in this sample, very few respondents with low educational levels participated in the study. Therefore,

this study was unable to find a correlation between lack of education, poor knowledge and awareness regarding medication-related side effects, which could be due to small population size, because previous research performed by Sulaiman (2012) in Malaysia reflected that low socioeconomic status and education level were associated with lower proportions of patients that were aware of NSAID related side effects.

HCP communication regarding NSAID side effects

Tarn and Flocke (2011) concluded that from their 117 participants, 47% could not recall how much medication to take, and 42% could not remember the potential side effects. The findings from this study agree with Tarn and Flocke (2011) as only 46% of participants indicated that their HCPs had provided them with information regarding the risk and side effects of NSAID use were aware that NSAID use could lead to GIT side effects and GIT injury. The findings above could propose that the information provided by the HCP professional to the patient was not adequate as the patient failed to understand the risk involved and failed to remember the side effects communicated to them. Kessels (2003) shows that, in general, memory to retain medical information is frequently poor and inaccurate. Patients are more focused on the diagnosis and do not register the instructions for treatment.

NSAID side effect awareness

This study shows that the majority of participants were not aware that UGIT side effects or GIT injury could be a result of NSAID use, with 60.9% of NSAID users were unaware that acid reflux or heartburn could be a side effect that is related to NSAID use whilst, 56.3% of NSAID users were unaware and uncertain that a stomach ulcer could also be a side effect from NSAID usage. The research above agrees with a research study completed by Li *et al.* (2014) that was conducted using university students as participants, which showed that a vast majority of students (78.5%) indicated that they were not aware of the side effects of taking NSAIDs. The results of this study are also in line with research conducted in India by Harlalka, Mazumdar, & Roy (2014), where 84% of their participants were unaware of the side effects that could result from ibuprofen use. Contrary to the above research performed by Hussein, Gad, & Wahdan (2015) indicated that only 26% of participants were not aware of the side effects of analgesics, with the majority having known the possible side effects. A case-control

study by Wynne and Long (1996), which sampled patients who were diagnosed with acute gastrointestinal bleeding while taking an NSAID, showed that the patients who were not aware or were uninformed of the side effects were less likely to stop using the NSAID because they were not aware that the NSAID was the potential cause of the side effect that had occurred.

Lastly, this research study was conducted in private pharmacies in Johannesburg. The population served by these pharmacies may not fully represent NSAID use behaviour and NSAID related side effects awareness in the public sector in Johannesburg. Perhaps if the public sector and the other provinces in South Africa were included, the data would have been more comprehensive and a better representation of NSAID- related side effect awareness in South Africa.



CHAPTER 6: CONCLUSION AND RECOMMENDATIONS

6.1 Introduction

The safety of patients taking NSAIDs is of critical importance. In South Africa, there should be an emphasis on patient education and awareness regarding preventable risks and side effects that are related to NSAID use. The increase in patient education and knowledge will help alleviate an already overburdened national healthcare system as there will be a decrease in preventable diseases caused by using NSAIDs.

This research study aimed to assess patient awareness regarding NSAID related side effects among participants in private pharmacies. Strategic sampling methods were used to select pharmacies in Johannesburg.

The following objectives were achieved:

- To assess the patient's awareness of the NSAID related side effects.
- To explore patient behaviour regarding NSAID use.
- To explore patient's views on the safety of NSAIDs.
- To determine if the level of awareness was related to communication with HCP
- To determine if the level of awareness is linked to the education level of the respondent.

The next section that follows will focus on the conclusion of the study, and this will include the highlights, study limitations, and recommendations for future research.

6.2 Conclusion

This study provides some insight into the awareness and knowledge of NSAID related side effects among patients in Johannesburg, South Africa. It has provided an understanding of what patients know about the risks involved in NSAID consumption and the education they have received. The study's findings show an alarming number of participants that are not aware of the side effects related to NSAIDs, and this is a significant concern as the conditions that are caused by NSAID usage are preventable.

The participants in this study were found to be aware of the correct behaviour regarding the use of NSAIDs. Most of the participants identified taking NSAIDs after a meal. Without additional substances, however, the majority of the study sample was found to be unaware of the side effects that are related to NSAID use.

NSAID use is common in South Africa, and the majority of participants in this study that were taking NSAIDs obtained them non-prescription. UGIT complications are potentially fatal and potentially preventable. The majority of participants had no education from their healthcare provider regarding the possible risks involved in NSAID use. Patients are inadequately educated on the side effects and may not always take the medication correctly.

Decreased awareness of NSAID related side effects could be due to inadequate information provided to the patient during the sale of NSAIDs. It can be speculated that the pharmacists and other HCPs assume that the patients will read the information available in package inserts, which is often not the case.

The study looked at sub-group analyses performed on education level compared to awareness and found that even though the majority of the participants were had obtained a post-school qualification were found to be unaware of the NSAID related side effects.

The large group of participants who perceived NSAIDs to be safe was also found to be unaware of the side effects related to NSAID use.

The study looked at NSAID side effect awareness in prescription users compared to non-prescription users and found that the side effect awareness was higher in prescription users and

was shockingly low for non-prescription acid reflux/heartburn awareness, which is a condition that has become quite common.

Decreased awareness was also found among the majority of participants that believed NSAIDs should be advertised, where the majority of the study sample was not aware of both side effects being related to NSAID use.

Even though the participants had indicated that they had received communication from their HCP regarding the risks and side effects of NSAID use, most of these participants have stated that they were unaware that NSAID use could cause acid reflux/heartburn or stomach ulcers.

The research was performed on HCP to patient communication regarding related side effects, and it was found that the majority of the participants were still not aware of the side effects related to NSAID use even though the participants indicated that their HCP had warned them previously of the risks and side effects related to NSAIDs.

Decreased awareness was also found among the majority of participants that believed NSAIDs should be advertised, where the majority of the study sample was not aware of both side effects being related to NSAID use.

Patient knowledge and education of the medication that they use along with the related side effects is a significant public need; the lack of awareness and education regarding NSAID related side effects in the sample is a critical problem that could lead to an increase in preventable disease and would result in unnecessary health-care costs.

6.3 Study Limitations

A questionnaire was the primary means of data collection, and there was a risk of the participant's inability to recall their previous behavioural actions with regards to NSAIDs.

As the study was conducted in private pharmacies, the study sample did not include participants who had acquired NSAIDs from a non-pharmacy source such as local shops, clinics and grocery stores.

This study only focused on the awareness of NSAID related GIT side effects. There was a possibility that there are other dangerous side effects that are associated with NSAID use that patients are not aware of.

All socio-demographic groups were not included in this research study. The exclusion of local clinics, grocery stores, and local shops limited the study sample to include the majority of individuals with formal education. This means that the research does not fully represent all socio-demographic groups in Johannesburg or South Africa as a whole.

The study sample was recruited from private pharmacies only. The public sector was not included in this study, which means that the research does not fully represent all socio-demographic groups in Johannesburg or South Africa as a whole.

6.4 Strengths of the study

This study highlighted that the communication provided to patients regarding the risks related to NSAID use was not optimal and could use improvement.

In Johannesburg, there are many areas where people do not have easy access to a computer or a data connection. Because of this, a paper-based questionnaire was a more accessible resource.

This study managed to recruit elderly participants who would not have been as easy if the survey was not paper-based. Black and white paper-based questionnaires offer a better resolution, which is preferable for people that are visually impaired and cannot view the text on a screen. Throughout this study, the elderly participants in this study often needed assistance in reading the questions.

Using strategic selection was a high strength of this method as it allowed the inclusion of various locations around Johannesburg, pharmacies in developed and impoverished regions were selected for study sites. By doing this, multiple demographics of participants were able to contribute to this study.

As the participants needed to be recruited directly by the researcher, there was face to face contact between the researcher and the participant. The participants were able to put a face behind a name and became more eager to participate in the research study. Furthermore, face to face communication helped with questions or queries that the participants had.

Another strength of this method was the benefit of time. People often do not have time to fill out a questionnaire. In a pharmacy setting, there are often many queues. The time that the patients waited in line to be seen by a pharmacist or when they were waiting for their medication was the time that they filled out the questionnaire. The waiting period made patients eager to complete the questionnaire.

Still, in this setting, the participants were approached while waiting in a queue or while waiting for their medication to be approved by their funders and to be packaged — the waiting time allowed for time for the questionnaire to be filled out.

6.5 Recommendations



The results identify the importance of further research to be conducted in other geographic areas within South Africa. Further research will help compare the research findings of this study to other regions, which will help see if there are specific trends in South Africa regarding the NSAID side effect awareness. The results also supported the need to educate the general sample about the importance of strong patient-HCP communication to help develop an understanding of the side effects related to the use of NSAIDs.

Future researchers also might want to study possible measures that the public healthcare system could take to improve the safety of non-prescription and prescription NSAID use— investigations on whether patients read the package insert to obtain further information need to be performed.

There is no standardised measure that captures and tracks NSAID non-prescription consumption. It might be advantageous to research opportunities to develop and then

implement technological systems to monitor use, a process that could help to increase the awareness of side effects and decrease the number of preventable side effects.



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APPENDICES



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Appendix 1- Ethic clearance letter



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04 September 2019

Prof N Butler
School of Pharmacy
Faculty of Community and Health Science

Ethics Reference Number: BM19/6/16

Project Title: Awareness regarding non-steroidal anti-inflammatory drug-related side effects in Johannesburg, South Africa

Approval Period: 04 September 2019 – 04 September 2020

I hereby certify that the Biomedical Science Research Ethics Committee of the University of the Western Cape approved the scientific methodology and ethics of the above-mentioned research project.

Any amendments, extensions or other modifications to the protocol must be submitted to the Ethics Committee for approval.

Please remember to submit a progress report in good time for annual renewal.

The Committee must be informed of any serious adverse event and/or termination of the study.

A handwritten signature in black ink, appearing to read 'Josias', on a white rectangular background.

*Ms Patricia Josias
Research Ethics Committee Officer
University of the Western Cape*

<http://etd.uwc.ac.za/>

BMREC REGISTRATION NUMBER -130416-050

Appendix 2- Pharmacy permission letter





REQUEST FOR PERMISSION TO CONDUCT RESEARCH IN PHARMACIES

Dear Responsible Pharmacist:

My name is Vaneshree Padayachee, and I am a master's student at the University of the Western Cape. I request to conduct research for my master's in Pharmaceutical Administration and Regulatory Affairs

My research is titled "Awareness regarding all non-steroidal anti-inflammatory drug-related side effects in Johannesburg, South Africa".

This project will be conducted under the supervision of Prof Nadine Butler.

I am hereby seeking your consent to ask several patients in your pharmacy if they take NSAIDs or not. If they have identified that they do consume NSAIDs I will proceed to present them with a questionnaire and a consent form to participate in my research study.

I have provided you with a copy of my research proposal which includes copies of the information sheet and questionnaire that will be used in the research process, as well as a copy of the approval letter which I received from the Research Ethics Committee (Human).

Upon completion of the study, I intend to provide the South African Health Products Regulatory Authority (SAHPRA) with a copy of the full research report.

If you require any further information, please do not hesitate to contact me on Vaneshree Padayachee

Tel: +273862628

Email: vaneshree.padayachee@gmail.com.

Thank you for your time and consideration in this matter. Signature of Responsible Pharmacist

Date of Responsible Pharmacist signature:

Pharmacy Location:

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Signature of researcher

I believe the participant is giving informed consent to participate in this survey

Vaneshree Padayachee

Signature of researcher Date:



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Appendix 3- Information sheet



Participant Information Sheet

My name is Vaneshree Padayachee and I am a master's student at the University of the Western Cape. As part of my studies I have to undertake a research project. I am investigating the level of awareness of non-steroidal anti-inflammatories side effects (NSAIDs).

Study Title

Awareness Regarding All Non-Steroidal Anti-Inflammatory Drug-Related Side Effects in Johannesburg, South Africa

Invitation paragraph

As part of this project, I would like to invite you to take part in completing a questionnaire. This activity will take around 8-10 minutes. You will not receive any benefits from participating in this study, and there are no disadvantages or penalties for not participating. You may withdraw at any time or not answer any questions if you do not want to. The questionnaire will be completely confidential and anonymous as I will not be asking for your name or any identifying information, the information given to me will be held securely and not disclosed to anyone else.

What is the purpose of the study?

This research project aims to identify the level of awareness of side effects caused by NSAID use by adults based in Johannesburg, South Africa

What are NSAIDs?

Non-steroidal anti-inflammatory drugs (NSAIDs) has been described as a largely successful group of medications as NSAIDs are used by large number of patients because they are effective in the treatment of pain, inflammation and fever. Although NSAIDs are generally well tolerated, side effects occur in a small but important percentage of patients.

Why have I been invited?

You have been invited to participate in this survey due as you have indicated that you are an NSAID user.

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Do I have to take part?

No. It is up to you to decide whether you would like to take part in this survey. If you decide to take part in the survey, then you can stop it at any time. A decision to withdraw from the survey at any time or a decision not to take part in the survey will not affect the standard of care you receive or your future medical care or legal rights.

How do I consent to take part in the survey?

If you complete the survey, then we will assume that you have provided your consent to take part in it.

What will the survey involve if I take part?

If you take part in the survey, you will be asked a series of questions about NSAIDs, it should take approximately 10 minutes to complete.

What are the possible disadvantages or risks of taking part in the survey?

The risk of taking part could be that you may feel inconvenienced by taking part in this survey. However, you will be free to stop the survey at any time.

What are the possible benefits of taking part in the survey?

You will not receive any direct benefits from participating in the study, and there are no disadvantages or penalties for not participating. You may withdraw at any time or not answer any questions if you do not want to. The value of the study may contribute toward harsher implementation of South African regulations and increased importance on consumer education. Attention to NSAID induced side effect awareness would provide public health leaders with new ways to enhance the quality of life for patients.

Will my taking part in the study be kept confidential?

All the information about yourself (such as your contact details and your responses to screening questions, interview questions and paper questionnaires) will be stored in one of two ways so that we can verify the information later, if necessary. All electronic data will be held on a secure database on a password-protected computer. All electronic data will be stored for 10 years and will be destroyed after this. Personally, identifiable data in



paper format (e.g. consent forms, completed questionnaires) will be stored securely in locked cabinets for 10 years. Data will be securely destroyed after this.

Will my doctor be informed?

No. We will not let your GP know that you have taken part in the survey.

What will happen to the results of the survey?

At the end of the study, we will analyse all of your information with the other participants' information. We will then publish our findings in an academic journal and at relevant conferences. We will send you a summary of these if you request this. You will not be identified in any publication arising from this survey.

What if I have questions?

This research is being conducted by Vaneshree Padayachee at the University of the Western Cape. If you have any questions about the research study itself, please contact:

Vaneshree Padayachee

Tel: +2723862628

Email: vaneshree.padayachee@gmail.com

Should you have any questions regarding this study and your rights as a research participant or if you wish to report any problems you have experienced related to the study, please contact:

Supervisor name and contact details:

Prof Nadine Butler

Tel: 012 9592472

Email: nbutler@uwc.ac.za

Director of School of Pharmacy name and contact details:

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BMREC contact details are as below:

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Appendix 4- Informed consent form



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INFORMED CONSENT

AWARENESS REGARDING ALL NON-STEROIDAL ANTI-INFLAMMATORY DRUG-RELATED SIDE EFFECTS IN JOHANNESBURG, SOUTH AFRICA CONSENT TO TAKE PART IN RESEARCH

1. I..... voluntarily agree to participate in this research survey.
2. I understand that even if I agree to participate now, I can withdraw at any time or refuse to answer any question without any consequences of any kind.
3. I understand that I can withdraw permission to use data from my questionnaire within two weeks after the questionnaire, in which case the material will be deleted.
4. I have had the purpose and nature of the survey explained to me in writing and I have had the opportunity to ask questions about the survey.
5. I understand that participation involves the completion of a questionnaire
6. I understand that I will not benefit directly from participating in this research survey.
7. I understand that all information I provide for this survey will be treated confidentially.
8. I understand that in any report on the results of this research my identity will remain anonymous.
9. I understand that disguised extracts from my questionnaire may be quoted in academic research.
10. I understand that if I inform the researcher that I or someone else is at risk of harm they may have to report this to the relevant authorities - they will discuss this with me first but may be required to report with or without my permission.
11. I understand that signed consent forms location, security arrangements and who has access to data] until [specific relevant period – for students this will be until the exam board confirms the results of their dissertation].
12. I understand that a transcript of my questionnaire in which all identifying information has been removed will be retained for one year until the student has submitted her final mini thesis

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- 13. I understand that under freedom of information legislation I am entitled to access the information I have provided at any time while it is in storage as specified above.
- 14. I understand that I am free to contact any of the people involved in the research to seek further clarification and information.

Names, degrees, affiliations and contact details of researchers (and academic supervisors when relevant).

Signature of research participant

Signature of participant Date:

Signature of researcher
I believe the participant is giving informed consent to participate in this survey



Signature of researcher Date:

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Appendix 5- Questionnaire



RESEARCH QUESTIONNAIRE

All questions contained in this questionnaire are strictly confidential and are for research purposes only.

Please tick the appropriate boxes and answer all the relevant questions

DEMOGRAPHICS

Gender: M F

Age

group:

- 18-30
- 31-40
- 41-50
- 51-60
- Above 60

Marital status: Single Partnered Married Separated Divorced Widowed

Level of education:

Primary school level Secondary School level National Higher Certificate University/ Higher Education Diploma University Degree Post Graduate degree

Type of employment:

Not employed Blue-collar worker (Cleaning, Factor workers) administrative services Basic Administration Business Administration
 HR Science Law/Legal Medical Sale Rep Sales Rep Health care Professional other
(Please specify)

Please read the explanation and list of commonly used medications in South Africa.

Non-steroidal anti-inflammatory drugs (NSAIDs) constitute one of the most widely used classes of drugs. Although NSAIDs are generally well tolerated, side effects occur in a small but important percentage of patients.

Table 1: Some generic and selected trade names for systemic NSAIDs

No	Trade Name:	Drug:	Dosage:
1	Grand-pa® Aspirin®, Disprin®	Salicylates	100mg, 300mg, 500mg
2	Arthrotec®, Dicloflam, Cataflam®, Catafast D, Flexagen®, Fortfen® capsules, Infla-ban®, Panamor®, Veltex® capsules, Voltaren®, K-fenak,	Diclofenac	25mg, 50mg, 100mg
3	Acuflex® Capsules, Aflamin® Capsules, Arthrexin® Capsules, Betacin® Capsules, Flamaret®, Indocid®, Mediflex® Capsule	Indometacine	25mg
4	Clinosyn®, Nafasol®, Naplam®, Naprosyn®, Synflex®, Aleve®, Vimovo®	Naproxen	250mg, 500mg
5	Betagesic®, Betaprofen®, Brufen®, Clinofen®, Inza®, Norflam®, Ranfen®, Bren®, Nurofen®,	Ibuprofen	200mg, 400mg
6	Relifen®, Relitone®	Nabumetone	500mg, 750mg
7	Brexecam®, Feldene® capsules, Rheugesic® Piroxicam Actor® capsules, Pixicam® capsules, Pyrocaps® capsules, Xycam® capsules	Piroxicam	20mg
8	Myproflam® capsules, Orucote®, Oruvail® capsules	Ketoprofen	200mg,



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9	Surgam®	Tiaprofenic acid	300mg
10	Tilcotil®, Tobitil®	Tenoxicam	20mg
11	Froben®	Flurbiprofen	100mg
12	Tora-Dol®	Ketorolac	10mg
13	Clinstan®, Ponstan®	Mefenamic acid	250mg, 400mg
14	Acupan®	Nefopam	30mg
15	Xefo®	Lornoxicam	4mg, 8mg
16	Celebrex® capsules, Coxleon® capsules, Exinef®	Celecoxib	50 mg, 100 mg, 200 mg and 400 mg
17	Vioxx® syrup/tablet	Rofecoxib	12.5 mg, 25 mg, or 50 mg
18	Mobic®, Adco- Meloxicam®, Arrow Meloxicam®, Coxflam®, Coxitec®, Loxiflam® Medoxicam®, Meloxixam unicorn®	Meloxicam	7.5 mg or 15 mg
19	Adco-Etoricoxib®, Arcoxia®, Exinef®	Etoricoxib	60mg,90mg,120mg

**Please note: the numbers of the corresponding medications listed above
can be used to answer the questions below:
for example: Grand-pa® will be 1.**

NSAID DRUG AWARENESS QUESTIONS

1. Do you currently use any of the medications from the list above (NSAIDs)

Name the Medicine	Strength/Dosage	Frequency Taken

2. Have you experienced any side effects from taking the medicine/s listed above

Name of Medicine	Reaction you had

3. For what Purpose are you taking NSAID Medications

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Name of medicine	Pain	Inflammation	Colds/Flu	Chronic Disease	Other (Specify)
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

4. What pharmaceutical form of these medicines are you using or have used?

Name of the medicine	Pill/tablet	Suppository	Effervescent	Injection
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

5. How do you obtain access to these medicines

Name of the medicine	Over the Counter/Pharmacies Shops	Healthcare facilities/ Clinics or General Practitioner	Internet
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

6. Do you take NSAIDs in combination with other substances?

Name of the medicine	None	Yes, with Alcohol	Yes, With other medications	Yes, with Caffeine	Yes, with Herbal/ Traditional medicines
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

7. When do you take NSAIDs?

Name of the medicine	First thing in the Morning	Before Meals	After Meals	Before Bedtime
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

8. Do you think NSAID use is safe?

Yes	No	Uncertain
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

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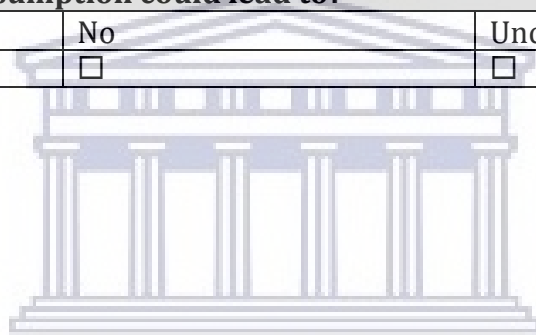


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9. Do you think that NSAIDs are abused or over-used?		
Yes	No	Uncertain
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
10. Do you believe NSAIDs should be advertised?		
Yes	No	Uncertain
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
11. Do you think that NSAIDs could cause stomach ulcers?		
Yes	No	Uncertain
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
12. Do you think that NSAIDs could cause acid reflux/heartburn)?		
Yes	No	Uncertain
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
13. Has your doctor/health care professional warned you about the possible risks and side effects that NSAID consumption could lead to?		
Yes	No	Uncertain
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>



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